CHAPTER 8

Parsimony and Bayesian phylogenetics

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8.1 Introduction

Methods of phylogeny reconstruction are often divided into statistical methods (which require an explicit model of evolution) and non-statistical methods. Among methods with an explicit statistical justification, the most widely used are the methods of maximum likelihood, resulting from Felsenstein's (1973, 1981c) work, and more recently, Bayesian phylogenetic methods based on Monte Carlo Markov chains, following Li (1996), Mau and Newton (1997), and Larget and Simon (1999).

The aim of a statistically based method is to estimate tree topologies and values of possibly relevant parameters, as well as the uncertainty inherent in those estimations. A method that could do that with reasonable accuracy would be attractive indeed. It is often claimed that it is advantageous for a method to be based on a specific evolutionary model, because that allows incorporating into the analysis the 'knowledge' of the real world embodied in the model. Bayesian methods have become very prominent among model-based methods, in part because of computational advantages, and in part because they estimate the probability that a hypothesis is true, given the observations and model assumptions. Early work on phylogenetics suggested the desirability of probabilifying the falsehood or truth of hypotheses. This includes early papers by Farris (1973, 1977, 1978), who later reconsidered the question of whether phylogeny estimation is to be viewed as a statistical problem or not, and moved to the position that phylogenetic inference is best viewed in non-statistical terms (Farris 1983). When he first approached phylogeny as a statistical problem, Farris (1973, p. 250) pointed out that the tree to be selected "should be the most probable tree on the basis of available data," and that (for tree T and data X) this probability (normally called *posterior probability*) can be calculated with Bayes' Theorem:

$$\Pr(T|X) = \frac{\Pr(X|T)\Pr(T)}{\Pr(X)}$$

where $\Pr(T)$ is the prior probability of the tree being analyzed (i.e. the probability, *a priori* of any observation, of the tree being the true one), the factor $\Pr(X|T)$ is the likelihood of the topology (i.e. the probability of the data, given the tree), and the denominator $\Pr(X)$ is the prior probability of the observed data (calculated as $\sum \Pr(X|T)\Pr(T)$ for all possible topologies). Farris (1973) noted that because the prior probability of each tree topology can be assumed to be the same (equal prior probabilities are usually called a *flat prior*), and because $\Pr(X)$ is fixed for the given observations, the choice, equivalent to parsimony, depends only on the likelihood of the tree. Farris (1973) developed a very general model, with minimal assumptions; under that model, the most likely tree is equivalent to the most-parsimonious tree. In the very same issue of *Systematic Zoology*, Felsenstein (1973) laid the basis for his subsequent developments of a very different model, with much more specific assumptions (including assumptions of Markovian evolution and Poisson substitution), conceived mostly as applicable to the evolution of DNA sequences. In the approach of Felsenstein (1981c) the values of parameters as well as branch lengths are jointly estimated

in order to maximize the likelihood function of a tree.

Bayesian approaches to phylogenetics have taken Felsenstein's methods a step further, and instead of producing point estimations of all parameters to maximize the likelihood, they have suggested integrating the likelihood across the different possible parameter values (i.e. branch lengths and substitution model parameters):

$$\Pr(X|T) = \int_{B_T} \int_{\Phi} \Pr(X|T, \beta_T, \varphi) f(\beta_T, \varphi)\, d\varphi d\beta_T$$

where B_T is the set of possible branch lengths (β_T) of topology T, Φ is the set of all possible substitution parameter values (φ) of the model, and $f(\beta_T,\varphi)$ is the prior distribution of these parameters. Both Farris (1973) and Felsenstein (1973) had considered such a type of integration desirable, but noted that a major problem with this approach is that it involves the calculus of a multidimensional integral for every possible topology, which is exceedingly complex and computationally demanding.

In order to overcome this problem, some researchers (e.g. Farris 1973; Hasegawa and Kishino 1989; Smouse and Li 1989) have attempted to compute the Bayesian posterior probability of a topology using the parameter values that maximize its likelihood factor (e.g. the maximum likelihood estimate of branch lengths). However, this approximation (as noted by Goloboff 2003, for the case of maximum likelihood) ignores an infinite number of additional hypotheses that result from alternative sets of branch lengths (or other parameter values) for that topology.

Others, instead, have suggested calculating the exact probabilities, integrating the likelihood of a topology across all possible sets of branch lengths (e.g. Rannala and Yang 1996) or other parameters (e.g. Sinsheimer *et al.* 1996). The complexity of this procedure, however, precludes its applicability to data sets of more than a few sequences, and therefore these methods were hardly ever used.

8.2 Markov chain Monte Carlo

Recently, three independent groups originally applied Markov chain Monte Carlo methods (MCMC) to approximate the posterior probabilities of trees (Li 1996; Mau 1996; Mau and Newton 1997; Yang and Rannala 1997; Larget and Simon 1999; Mau *et al.* 1999; Newton *et al.* 1999; Li *et al.* 2000).

The idea in a MCMC is to make computationally feasible the integration of the posterior probabilities across the parameters of interest (e.g. topology, branch lengths, substitution parameters). The chain uses a proposal mechanism, which consists of gradual modifications from a starting point (ideally, randomly chosen), and it alternatively changes some parameter values (e.g. topology, branch lengths, substitution parameters), stochastically and aperiodically. These proposals or transitions are accepted with a probability given by the Metropolis–Hastings algorithm (Metropolis *et al.* 1953; Hastings 1970; see Larget and Simon 1999 or Huelsenbeck *et al.* 2002 for details) and the Markov chain proceeds until it reaches a stationary state.

If the Markov chain is irreducible (i.e. it is possible for the chain to visit every possible set of parameters and tree topologies) its stationary state converges to the joint posterior probability distribution of the parameters being modified (Tierney 1994). Thus, the frequency with which a given topology is visited in the Markov chain approximates its marginal posterior probability (Mau *et al.* 1999). Thus, the results of MCMC are directly interpreted in probabilistic terms; they can estimate the probability that a particular tree is the true tree for these sequences, conditional on the stochastic model of substitution (Li *et al.* 2000). Additionally, since the posterior probability distribution is simultaneously estimated, measures of uncertainty can be derived from the Markov chain.

The outcome of the stationary state of the MCMC is a set of phylogenetic trees (with their associated parameters). In phylogenetic applications of MCMC, the relative frequency of each topology (irrespective of branch length and substitution parameter values) is interpreted as its posterior probability (given the stochastic model and data). Therefore, it seems straightforward to take the topology with the highest posterior probability as the point estimate of the true topology. This was clearly recognized by several authors (Li 1996; Rannala and Yang 1996;

Yang and Rannala 1997; Larget and Simon 1999; Mau *et al.* 1999). The estimated tree was referred to as the maximum posterior probability (MAP) tree by Rannala and Yang (1996).

However, the availability of the approximation of the posterior distribution of trees also allows the evaluation of the variability of the estimates (e.g. topology or any other parameter integrated by the MCMC). As noted by Mau *et al.* (1999), summarizing the distribution of MCMC trees indeed presents a challenge and several methods have been proposed for such purpose.

For instance, Mau *et al.* (1999) and Rannala and Yang (1996) noted that a Bayesian ''credible set'' can be obtained as the collection of topologies having the sum of their posterior probabilities constrained to be no less than a specified value (e.g. 0.95). Li (1996) also considered alternative ways to estimate the posterior probability of the true phylogeny from the MCMC results, such as the use of the tree that has the minimum topological distance to the majority (e.g. 90%) of the MCMC trees, or the use of a majority-rule consensus of the set of topologies generated by MCMC.

In the latter option, the frequency of the clades has been interpreted by most Bayesian phylogeneticists (e.g. Huelsenbeck *et al.* 2002) as the posterior probability that the clade is true, following ideas of Newton *et al.* (1999) and Larget and Simon (1999). These authors propose summing the posterior probabilities of the trees in which each clade of the MAP is present as a way to summarize uncertainty in the tree topology estimate. This approach, which sums the frequency with which a particular clade appears in the Markov chain in order to estimate its posterior probability, is certainly the most commonly used way to summarize MCMC results. This approach is implemented in available software packages (e.g. MrBayes of Huelsenbeck and Ronquist 2001; BAMBE, of Simon and Larget 1998), and is frequently reported in empirical analyses using Bayesian methods. Here we will focus on some undesirable properties found on this frequently used option to summarize MCMC results. Other alternative ways to summarize the results are less frequently used, and they differ from this one in depending much more on whether the chain has succeeded in finding the actual MAP(s). As the chain is not conceived as a search mechanism, but instead as a sampling mechanism, it is extremely unlikely that it will find the individual trees of maximum *a posteriori* probability, except in very small data sets.

8.3 Problems with estimations of monophyly by MCMC

In this section, the discussion will be within the realm of the rules and goals postulated by defenders of model-based methods. We also have other general concerns about model-based methods; these reflect a viewpoint not shared by Bayesians, and are therefore discussed in the following section. While the MCMC can be used to estimate any parameter of the evolutionary process, we are concerned here with the estimates that are relevant for phylogenetic studies: estimations of monophyly of groups. Other parameters, such as transition:transversion (ts:tv) ratios, while possibly the primary interest for other evolutionary studies, are only of secondary interest to the phylogeneticist. Part of the attraction of MCMC Bayesian methods is that the values estimated for those other parameters, such as ts:tv ratios, do not rely on estimation of a tree topology, an advantage for such studies which we do not dispute. However, the fact that our examples show that there are problems when the estimations of monophyly are carried out in a certain way suggests that establishing proper estimations from MCMC is far from automatic, and raises concerns about the validity of the inferences of those other parameters as well.

The most common approach to estimating probability of monophyly of a group X is by summing the posterior probabilities of all the trees where group X is monophyletic. This can be done for the groups present in the individual tree of highest posterior probability (as proposed in Larget and Simon 1999), or for each of the groups found in the analysis; these options make no difference for our argument.

Huelsenbeck *et al.* (2002, p. 674) claimed that, since ''Bayesian inference is based on the likelihood function, it should inherit many of the nice statistical properties of the maximum-likelihood

method.'' The ''nice statistical property'' for which likelihood has been held superior to parsimony is, quintessentially, statistical consistency. Statistical consistency has been proven for maximum likelihood, but only as a byproduct of the consistent estimation of the branch lengths between taxa (see Rogers 1997; Chang 1996; with discussion in Goloboff 2003). If the tree topologies are estimated without estimating branch lengths—integrating branch lengths for a given tree topology, as done in the Bayesian methods—then statistical consistency might be lost (as discussed in Goloboff 2003). And even if Bayesian analysis used optimal branch lengths (which would slow it down considerably), the fact that posterior probabilities of individual clades are estimated from sums of posterior probabilities of the trees having the clade still creates problems. So, the idea that Bayesian analysis should automatically ''inherit the nice statistical properties of maximum likelihood'' is no more than wishful thinking; Bayesian analysis with MCMC involves substantial modifications to maximum-likelihood.

Estimating the posterior probability for monophyly of a given group as the sum of posterior probabilities of the trees with that group may create serious problems, and it is easy to see why. Imagine that there is a single tree of highest likelihood[1], where group *X* is not present. Imagine that there are many trees of a likelihood only slightly inferior, where group *X* is monophyletic. The sum of the likelihoods of the trees with the group may exceed the likelihood of the one tree without the group, and then the method would conclude that the group has a relatively large probability of being monophyletic. While there are many situations under which such an asymmetry could occur, some of them are surprisingly simple. Consider the case of Fig. 8.1, a 25-taxon data set, with taxon *A* having only missing entries. The data determine a perfectly pectinate tree, except for the placement of *A*. The strict consensus for these data (analyzed with either parsimony or likelihood) is an unresolved bush, which does express the fact that the monophyly of *no* group is actually supported by the data. Note that *A* can float in the skeleton tree of the remaining taxa; each of the 45 trees with alternative placements of *A* has exactly the same likelihood (and thus, under a flat prior on tree topologies, the same posterior probability). However, of all those trees, only two (*A* sister to *B*, or *A* sister to *C*) make the group *BC* non-monophyletic; the proportion of trees with the group *BC* monophyletic is thus $43/45 = 0.955$. That is almost exactly the posterior probability for monophyly of *BC* estimated by MrBayes (see Fig. 8.1; values on the branches are values reported by MrBayes, numbers above the branches are the frequencies of the groups in the 45 most-parsimonious trees). The group *BCD*, instead, is made non-monophyletic by two additional locations of taxon *A*, so it is monophyletic in a proportion of $41/45 = 0.911$. As one moves towards the middle of the tree, the proportions of locations which make the group non-monophyletic decreases: 6/45 for group *BCDE*, 8/45 for group *BCDEF*, etc. Past the middle of the tree, the proportions start increasing again. This is reflected almost exactly in the posterior probabilities reported by MrBayes. Since this is perfectly expected, the proposal mechanism used by MrBayes seems—at least for data sets as simple as this one—to provide a sample of the tree space adequate to estimate the sums of posterior probabilities for different groups; our criticism has nothing to do with sampling problems, but simply with the quantity that is being estimated. The (estimated) sum of posterior probabilites of the trees with and without a group provides a measure with no apparent utility. Using such a measure leads to the unfounded conclusion that, even when what we know about *A* is nothing, we can still estimate with some precision its placement in the tree! That location of *A* is determined rather by the priors on trees, but that means that the priors on groups are highly unequal. That an equal prior on trees may mean an unequal prior on groups has been discussed by Pickett and Randle (2005); Pickett and Randle also note that using flat priors on some aspects of a simulation may impose non-flat priors on other aspects. While the non-flat priors on groups (which undoubtedly exist) influence the posterior

[1] Whether the likelihood is calculated as the likelihood for optimal branch lengths, or the sum of the likelihoods for all the branch lengths for the given topology, makes no difference to our argument.

```
ROOT  AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
X     AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
W     GGGGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
V     GGGGGGGGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
U     GGGGGGGGGGGGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
T     GGGGGGGGGGGGGGGGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
S     GGGGGGGGGGGGGGGGGGGGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
R     GGGGGGGGGGGGGGGGGGGGGGGGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
Q     GGGGGGGGGGGGGGGGGGGGGGGGGGGGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
P     GGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
O     GGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
N     GGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
M     GGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
L     GGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
K     GGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
J     GGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGAAAAAAAAAAAAAAAAAAAAAAAAAAAA
I     GGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGAAAAAAAAAAAAAAAAAAAAAAAA
H     GGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGAAAAAAAAAAAAAAAAAAAA
G     GGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGAAAAAAAAAAAAAAAA
F     GGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGAAAAAAAAAAAA
E     GGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGAAAAAAAA
D     GGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGAAAA
C     GGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGG
B     GGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGG
A     ????????????????????????????????????????????????????????????????????????????????????
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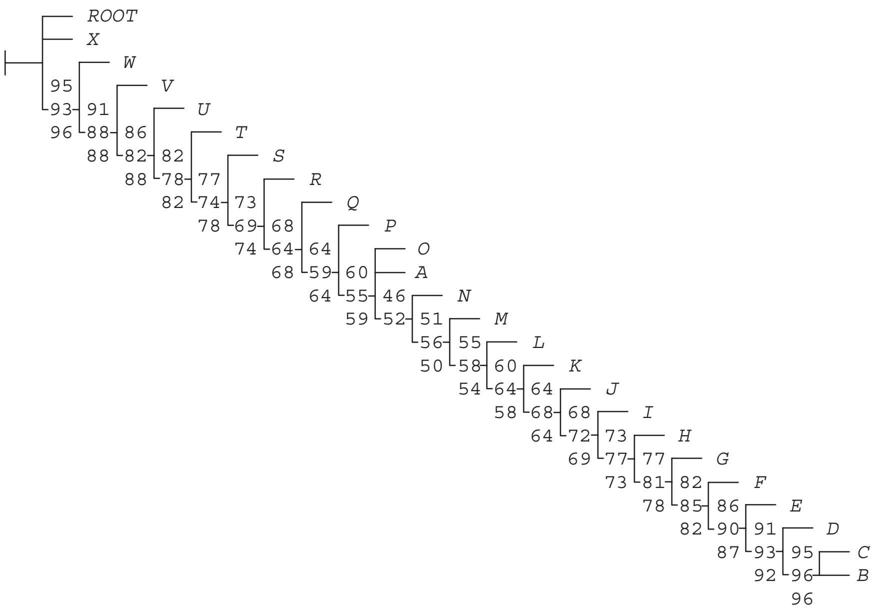

Figure 8.1 A data set with a taxon (A) scored only with missing entries. No group has any actual support, since the monophyly of any group can be violated at no cost. The numbers on the branches are the posterior probabilities of monophyly, estimated by MrBayes with 100 000 generations, using four chains, with a sampling frequency of 100, and a 'burn-in' of 250 (i.e. discarding the first 25 000 generations). The numbers above the branches indicate group frequency in the most-parsimonious (dichotomous) trees. The numbers below the branches show the bootstrap frequencies, as calculated by PAUP* (with 100 replications, analyzing each resampled data set with a branch-and-bound solution). Tree topology corresponds to the analysis with MrBayes.

probabilities reported by MrBayes, that is only part of the picture; the other aspect is the shape of the likelihood landscape, which is what our examples show.

Admittedly, the example of Fig. 8.1 is contrived in that no worker will attempt to analyze a matrix where a taxon is represented only by missing entries. But the same effects may come in much

more subtle flavors; for example, a sub-clade of a larger clade that can connect with different rootings (all with about the same likelihood) to the rest of a tree will produce, inside the clade with an undetermined root, the same effect observed for Fig. 8.1. This can also happen even for groups of a relatively large size (which non-flat priors on groups of different sizes do not easily explain), as in the example of Fig. 8.2, analyzed with MrBayes under the No Common Mechanism model (= parsimony). Under such a model, group *N–Z* is well supported by the data, and group *T–Z* is not: each of the characters that might support the monophyly of *T–Z* becomes an ambiguous synapomorphy when taxon *M* is the sister group of *N–Z* (so that there are trees of best fit that do not have *T–Z* as monophyletic). However, this happens only when *M* is the sister group of *N–Z*; for each of the other (numerous) possible locations of *M* in the rest of the tree, the group *T–Z* is required to provide the best fit to the data. The group *T–Z* is present in about 91% of the most-parsimonious trees for the data set[2]. Not surprisingly, MrBayes reports unsupported group *T–Z* as strongly supported, with a posterior probability of 0.93.

```
ROOT    AAAAAAAAAA AAAAA
A       AAAAAAAAAA AAAAA
B       AAAAAAAAAA AAAAA
C       AAAAAAAAAA AAAAA
D       AAAAAAAAAA AAAAA
E       AAAAAAAAAA AAAAA
F       AAAAAAAAAA AAAAA
G       AAAAAAAAAA AAAAA
H       AAAAAAAAAA AAAAA
I       AAAAAAAAAA AAAAA
J       AAAAAAAAAA AAAAA
K       AAAAAAAAAA AAAAA
L       AAAAAAAAAA AAAAA
M       AAAAAAAAAA GGGGG
N       GGGGGGGGGG AAAAA
O       GGGGGGGGGG AAAAA
P       GGGGGGGGGG AAAAA
Q       GGGGGGGGGG AAAAA
R       GGGGGGGGGG AAAAA
S       GGGGGGGGGG AAAAA
T       GGGGGGGGGG GGGGG
U       GGGGGGGGGG GGGGG
V       GGGGGGGGGG GGGGG
W       GGGGGGGGGG GGGGG
X       GGGGGGGGGG GGGGG
Y       GGGGGGGGGG GGGGG
Z       GGGGGGGGGG GGGGG
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Figure 8.2 A data set with a group (T–Z) unsupported but found in many optimal trees, and thus with a high estimated posterior probability. See text for details.

The examples of Figs 8.1 and 8.2 were not derived from any model, and for this reason may perhaps be dismissed by Bayesians as being irrelevant. But the same effect can appear even in simulated data, where there are no violations of the model. The easiest way to produce the effect is to mimic the conditions of Fig. 8.1. For this, we used as the model tree a perfectly pectinate tree, as in Fig. 8.3, with taxa *A* and *B* forming a monophyletic group at the tip of the tree, and successive terminals appearing as successive sister groups. All the branches in the tree had a length of

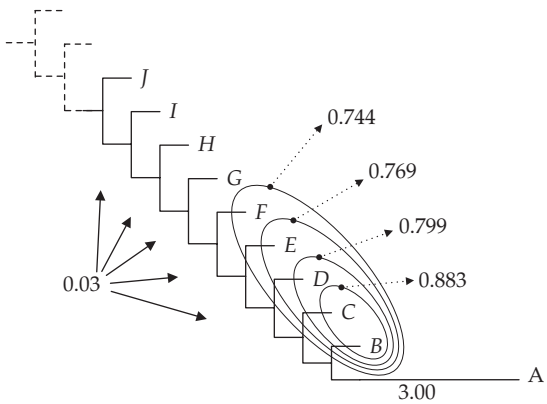

Figure 8.3 Tree shape used in the simulations (results reported in Fig. 8.4). Data were generated for trees with different numbers of taxa, using a Jukes–Cantor model. All branches were of length 0.03, except the branch leading to *A*, with a length of 3.0. The simulations generated 1 000 characters each. MrBayes analyses used 50 000 generations, with three chains, sampling every 50 generations, and a burn-in of 250 (i.e. discarding the first 12 500 generations). The posterior probabilities are shown for four incorrect groups (for 50 taxa, average posterior probability for 20 replications); note that the posterior probabilities decrease towards the middle of the tree, just as in Fig. 8.1.

[2] We calculated the frequency of group *T–Z* in most-parsimonious trees by taking a pseudo-random sample of 1 000 most-parsimonious trees. We generated each by a Wagner tree where both the insertion and addition sequences were randomized (as implemented in TNT; Goloboff *et al*. 2004), followed by tree bisection and reconnection (TBR) branch swapping. Randomizing the insertion sequence means that, for each taxon to be added to form the Wagner tree, the pre-existing locations to insert the new taxon are tried in a random order; this eliminates bias in tree shapes in the resulting Wagner trees for poorly informative data.

0.03 (thus, a probability of no change along the branch of 0.978; we used a Jukes–Cantor model), except for the branch leading to taxon *A*, which was very long (with a length of 3; that is, a probability of no change of 0.287). The model tree was used to generate simulated data sets, with 1 000 characters, for different numbers of taxa. Since *A* has a very long branch, it connects to the rest of the tree with about the same likelihood at every possible location. The effect is therefore the same as that of Fig. 8.1. In most of the simulations, MrBayes reports a high posterior probablity that the group *BC* is monophyletic, which is in fact false. The estimated probability of monophyly of the wrong group *BC* actually increases with the number of taxa, since then the alternative locations of *A* that make a significant contribution to the sum of posterior probabilities for group *BC* also increases. Because there is significant variability in different simulated data sets, we used 20 replications for each of 5, 10, 20, 30, 40 and 50 taxa. The results are shown in Fig. 8.4. While there is of course some sampling error in our measurements, the trends evident in Fig. 8.4 make it clear that the high posterior probability attributed to the wrong groups (often over 0.90) is not the effect of sampling error or lack of convergence in the chains. As the number of taxa increases, so does the apparent confidence on the false groups (the more so for the smaller groups), while the confidence on the true groups decreases (the more so for the smaller groups). Whereas the reference to smaller and larger groups makes sense in these examples, with pectinate trees, this does not mean that MCMC analysis will in general favor groups of a given size; the problem arises because of the relative differences in likelihood (= posterior probabilities, since we used a flat prior on trees) of those trees with and without each group, and this effect could potentially happen for groups of any size. These results could possibly derive as well from violations of the model, or from examining data for several genes where some of the taxa have not been sequenced for all the genes.

The examples are not intended to be realistic, but they show unequivocally that the estimations of posterior probabilities of individual groups may lead to grossly mistaken conclusions, and in real cases such an effect can easily be confounded by other factors. For the simulated examples, a taxon

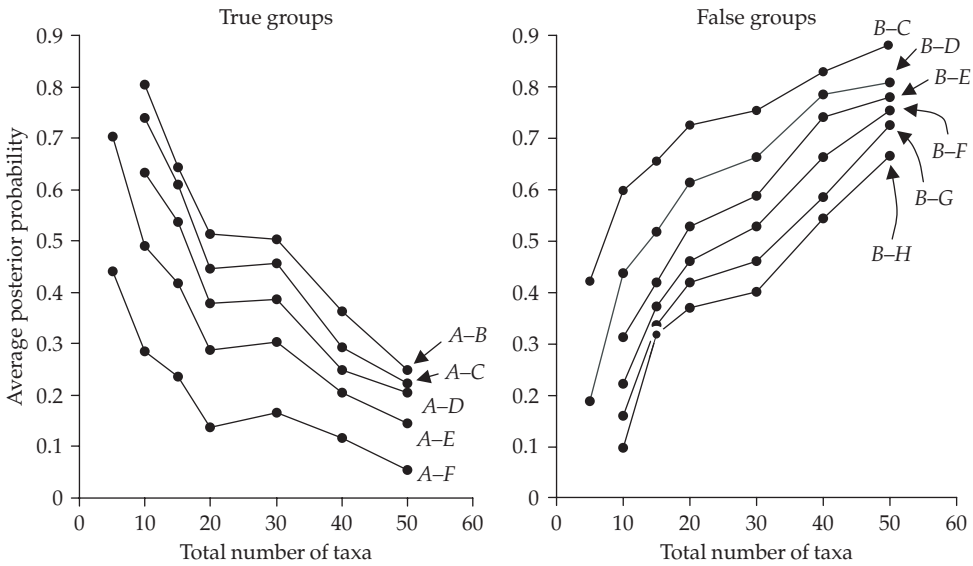

Figure 8.4 Results for the simulations, using the model tree shown in Fig. 8.3, for different numbers of taxa. As the number of taxa increases, so does the estimated posterior probability of the false groups (*BC*, *BCD*, etc.), the more so the smaller the group. All the averages reported correspond to 20 replications for each number of taxa.

with a branch as long as the branch leading to *A* cannot be confidently placed anywhere in the tree; every location will have roughly the same fit. The most serious problem faced by Bayesian analysis is not that it places *A* in some definite location (i.e. in the middle of the tree), but rather that it leads one to conclude that there is a very high probability that *A* is not placed as sister to *B*, which is the one true placement. A proper method should recognize, in cases like Fig. 8.3, that no conclusion is possible. Note that our criticism of Bayesian analysis, in this case, is not equivalent to Siddall's (1998) criticism of likelihood; Siddall (1998) criticized likelihood because in his simulations it separated long branches that were in fact sisters; Swofford *et al.* (2001) showed in their reply that, while likelihood indeed separates long sister branches (for small numbers of characters), the likelihoods of the alternative trees that place those long branches together is only slightly inferior, so that the maximum likelihood analysis actually implies that no decision is possible. That is not the case for the Bayesian results; they attribute a high probability to false groups that should at least be recognized as ambiguous.

8.4 Potential problems of the statistical approach

Statistically justified, model-based approaches to phylogeny have come to dominate the field in the last decade, but many authors still feel that those model-based justifications miss the mark. The controversy, not surprisingly, has often involved criticism and even misrepresentation from both sides. Among the topics on which the debate has centered are the questions of statistical consistency, the complexity of the evolutionary models used, the possible empirical basis of the evolutionary models on which the inferences are to be based, and whether epistemological considerations support the use of specific models of evolution.

The issue of consistency has been discussed mostly in relation to the likelihood vs. parsimony controversy (Steel *et al.* 1993; Siddall 1998; Farris 1999; Swofford *et al.* 2001). We consider that consistency, since it is relevant, at best, only under unrealistic conditions (i.e. infinite, or at least massive amounts of data evolving under the same model[3], with a perfect fit to the model), is not a very relevant property at the time of deciding among possible methods of phylogenetic inference. Even some statistically inclined phylogeneticists hold this point of view (e.g. Kim 1996; Sanderson and Kim 2000). The focus of this chapter is on Bayesian methods: Bayesians, with their claim that Bayesian analysis, being based on likelihood methods, should inherit the ''nice statistical properties'' of likelihood (see above), have adhered (implicitly, at least) to the notion that consistency is desirable. However, as we show later, the only feasible implementation of Bayesian phylogenetic analyses is likely to suffer from inconsistency.

The complexity of the inferential models used has also appeared in the likelihood vs. parsimony controversy. Although several likelihoodists (Goldman 1990; Steel and Penny 2000; Lewis 2001) had suggested that parsimony requires estimation of many more parameters than maximum likelihood, Goloboff (2003) reconsidered the problem and concluded that, if anything, parsimony requires estimation of fewer parameters than traditional maximum likelihood methods (a similar conclusion had been reached by Farris 1986, p. 22). Bayesian phylogenetic methods could in theory integrate uncertainty in some parameters during the MCMC (thus not requiring 'estimation' of those parameters). The problem is that the parameter space to be explored then becomes more complex, so that the chain would have to be run for much longer to insure convergence and an adequate sampling.

Finally, the epistemological questions about using evolutionary models and their empirical basis are perhaps the problems that have been less openly discussed in the literature. Several authors have presented the controversy in terms of which of the two approaches can be justified under Karl

[3] Note that we say here ''under the same model.'' While it is true that current-day techniques allow sampling of very long DNA sequences, the chances of all the sites still obeying to the same model decrease as the sequences become longer and include different genes or gene regions (as pointed out by Pol and Siddall 2001). The amount of data available for a given model will always be in the order of a few kilobases.

Popper's philosophy (Popper 1968). Most notable among recent philosophical defenses of model-based approaches is perhaps the paper by de Queiroz and Poe (2003). They argue that parsimony can be justified as a Popperian approach only by reference to specific models of evolution. de Queiroz and Poe (2003) say that it is not true that characters provide falsifiers of phylogenies (which Farris 1983 had used to characterize phylogenetic hypotheses as falsifiable), because a phylogeny cannot *per se* make impossible any particular character distribution. de Queiroz and Poe (2003) argue that, having disposed of other possible justifications, the only way to falsify a phylogeny is to show that it is less probable than its rival, and that parsimony can only be justified as Popperian if coupled with specific evolutionary models that specify those probabilities. But de Queiroz and Poe (2003) have not actually disposed of other possible justifications: they present only part of Farris' arguments. Farris (1983) had made it clear that no character could provide absolute falsification, and that the relationship between falsifier and hypothesis is purely logical. That is, if a given apparent character-state homology between two taxa is truly due to common ancestry, then it follows that a phylogeny that places them apart is truly false. Contra de Queiroz and Poe (2003), a strictly logical justification of parsimony, made without reference to a specific evolutionary model, is possible. Probabilistic models are necessary only to interpret the results of a parsimony analysis probabilistically; they are unnecessary otherwise.

The question of whether some apparent homologies are more probably truly homologous than others only enters the picture when we accept statistical justification and specific models. Contrary to some defenders of parsimony (e.g. Siddall and Kluge, 1997; Kluge 1997, 2001; Kluge, Chapter 2 of this volume), we do not argue that such a type of justification is philosophically and intrinsically flawed. Our concerns have to do with common sense, more than with philosophy. If one knew with certainty that sequence evolution is driven exclusively by a reduced set of parameters, and that those parameters remain very stable over time, then model-based methods of phylogeny reconstruction would be perfectly justified. Using those model-based methods would have the advantage that they make it possible to provide measures of uncertainty with a direct interpretation.

The alternative is considering that sequence evolution is driven by too many parameters, which may change too much over time, and that the samples (of sequences) we may expect to ever obtain are far below what could reasonably allow accurate inferences. Of course no one expects inferences that are 100% error-free; but the problem is how much is too much. Philosophical positions aside, many people who use parsimony place themselves at the 'too much' side of the scale, and tend to think that the probabilities estimated by using specific models are likely to be so far off that there is no point in trying to consider the results in terms of real probabilities. All we can expect is to simply provide the best explanation of the data, and it is best to remain silent about the probability of the resulting hypothesis being true. When de Queiroz and Poe (2003) claim that parsimony can be justified only by reference to some specific model, they mean "parsimony *as a statistical method* can be justified only by reference to some specific model," which is true in itself, but then most proponents of parsimony do not view parsimony as attempting to provide the tree with the highest posterior probability: any attempt to provide a figure representing an actual probability, in the case of a process as complex as phylogeny, is no more reliable than a guess[4]. In this sense, the number of things that model-based methods try to estimate (statistically speaking) is much greater, and then it is natural that researchers with no previous experience in the field are attracted by estimation methods which are apparently omnipotent.

To some extent, the two aims—providing the best possible rationalization of the data by means of a phylogeny, or providing the best statistical

[4] Measures of support such as the Bremer support (Bremer 1994; Goloboff and Farris 2001) or resampling (Farris *et al.* 1996; Goloboff *et al.* 2003b) are often interpreted as somehow measuring the truth content of the hypothesis, but this is not correct: all they measure is how much evidence supports the hypothesis.

estimation of the phylogeny—are both defensible in their own right. The difference is not only regarding whether a probabilistic model forms the basis for inferences or not; the difference is also about how the results are to be interpreted. Which aim a particular worker prefers and pursues may depend on many factors, actual personal interests, or even peer pressure, among others. But, fashions in science aside, the decision of whether using phylogenetic methods based either on models or pure logic depends also to a good extent on the dose of skepticism the researcher holds. Several defenders of model-based methods (e.g. Swofford *et al.* 2001) have suggested that, in different fields of science, the first approach is based on intuitive methods and that, as the field becomes mature, explicit statistical justifications replace the original intuitive ones. This claim is not strictly true (or testable, at least), and it is presented as if somehow the current use of statistically justified methods was evidence of maturity—when the alternative interpretation, namely that the use of statistical methods in phylogenetics is still premature and unjustified, may be much more reasonable to some workers. But how is one to decide whether the field is mature enough, or whether our knowledge of the mechanisms of evolution is detailed enough, to justify using those models? The answer to this need not be an all-or-none answer; there is instead a gray area between those who believe that our ignorance of evolutionary mechanisms is almost total (a view which some supporters of parsimony seem to hold), and those who believe that our knowledge is so complete as to guarantee even the most detailed inferences (as some likelihoodists and Bayesians seem to believe). At what particular point of this scale a particular worker finds himself/herself will depend on how he/she resolves a large number of subtle issues; such a decision requires reason and logic, but it cannot be accomplished with a statistical test. This, of course, is not to say that anything goes; for example, a model-based method that may produce incorrect estimations—even without violations of the model from which it is derived—is clearly to be avoided. Such is the case with estimations of posterior probabilities of monophyly by MCMC, as we have already seen.

Furthermore, whether the data can be modeled reasonably will depend on the nature of the data. While a Poisson model of substitution seems reasonable for some types of DNA sequence data, it seems unfounded to apply such a model to morphological data (although it has been attempted, by Lewis 2001). It is unfounded because there is very little ground to think that all characters of the given organisms have about the same probability of changing along a given branch of a tree, and that alternative states in morphological characters are like units turned on and off. Some vertebrates have mammary glands, and some arthropods have chelicerae, but within a given group of tetrapods, who could claim that the chances of gaining mamary glands are the same as—or even comparable to—the chances of gaining chelicerae? For genomic data, which include so many different types of transformations (insertions, deletions, translocations, inversions, etc.), postulating reasonable models is also very difficult or impossible. Therefore, for these types of data, only the parsimony aproach has been used so far (starting from Sankoff and Blanchette 1998), for no other approach seems reasonable. Even the simplest case, insertions/deletions, presents a serious challenge to modeling; although some programs (like POY; Wheeler *et al.* 2003) have implemented "maximum likelihood models" for insertions/deletions; these Poisson "models" are based simply on attributing some probability to an insertion as a function of other parameters (like branch "length"). Wheeler *et al.* (personal communication[5]) present the likelihood methods in POY as "interpretive tools, without any necessary relationships to the actual process of change in nature." They point out themselves that this has a meaning quite different from the use of Poisson models in DNA sequences: in those models, a base that is to replace another one exists outside the sequence and therefore, given a certain chance of replication error, there is a certain chance for each possible base to be inserted. Thus, Poisson

[5] Wheeler, W., Aagesen, L., Arango, C., Faivovich, J., Grant, T., D'Haese, C., Janies, D., Smith, W., Varon, A. and Giribet, G. (unpublished manuscript). *Dynamic Homology and Phylogenetic Systematics: A Unified Approach using POY.*

substitution models are based on more than just attributing arbitrary probabilities of change to events; the probabilities postulated by those models are based on some knowledge of the mechanisms that govern the process of DNA substitution, at least in the absence of selection and constraints (whether the model is factually correct, of course, is a different matter, but it is plausible and coherent in itself). Gaps, on the other hand, are not units to be incorporated into a string of DNA being synthesized. A Poisson model for gaps, while it seems natural given the widespread use of Poisson models for DNA substitutions, may be totally inadequate. Other likelihood 'models' of insertions/deletions (e.g. Thorne *et al.* 1992; Miklós *et al.* 2004; see De Laet, Chapter 6 in this volume, for comments on these) do not use Poisson models, but still are based on arbitrarily assigning probabilities to the possible events. In those models, the final probability is no more real than are the figures obtained by parsimony analysis. On the other hand, analyzing sequences of unequal length by prealigning them and then discarding positions with gaps (a practice common among likelihoodists, and Bayesians) is probably even more inadequate, so that we are again in a situation where probabilities cannot really be assigned meaningfully. Much the same can be said of other types of chromosomal rearrangement.

8.5 Discussion

Strictly speaking, our simulations do not demonstrate that the estimations of posterior probabilities of individual groups produced by MrBayes are inconsistent. That would require either running data sets with infinite numbers of characters, or an analytical treatment of the multidimensional integral across all possible trees. Neither of those is possible. Admittedly, in cases like our simulations, as the number of characters increases, the difference in likelihood between the correct and alternative placements of the long branch increases. Eventually this difference might be so great as to make the likelihood of the individual best placement of the long branch (the correct one) higher than the sum of the likelihoods of the alternative (wrong) placements. However, as the number of taxa increases, this situation becomes less and less likely, for the sum of likelihoods of the alternative placements increases as well. So, it is hard to predict what would happen for infinite numbers of characters in cases with very large numbers of taxa. However, even if there is the potential for Bayesian estimations of monophyly to provide correct topological estimations for infinite numbers of characters, there is still the problem that Bayesian analysis claims to do much more than simply producing consistent estimations: it also claims to measure the degree of support of the conclusions, in a statistical sense. Our examples show that it does not.

Several recent papers (Suzuki *et al.* 2002; Alfaro *et al.* 2003; Cummings *et al.* 2003) have compared bootstrap and clade credibility values. In terms of the problem discussed above, some of those comparisons could never have been very informative, despite large amounts of computational effort. For example, the study of Cummings *et al.* (2003) used over 15 years of CPU time, but examined only data sets with four taxa. The problems pointed out here with Bayesian analyses can arise only with larger numbers of taxa, so Cummings *et al.*'s effort could never have led to discovery of those problems. Moreover, even for larger numbers of taxa, the problem pointed out here could not have been discovered by comparing posterior probabilities with the bootstrap values produced by PAUP* (the program used in essentially all published comparisons between bootstrap and Bayesian credibilities; Swofford 2002). When bootstrapping or jacknifing, in the case of multiple trees for a resampled matrix, PAUP* weights each group found according to its frequency. This produces exactly the same results as summing posterior probabilities of monophyly: groups that are very frequent in optimal or quasi-optimal trees always appear as highly supported, regardless of their actual support. Fig. 8.1 shows, below the branches, the bootstrap values estimated by PAUP*; they are almost exactly the same as Bayesian estimates. The relative (although not universal) agreement between bootstrap and Bayesian estimations has been taken as mutual confirmation, but in fact MrBayes and PAUP*'s implementation of bootstrapping and jacknifing share similar biases. Alternative implementations of resampling

methods (such as the one in TNT; see Goloboff *et al*. 2004) avoid this problem by producing the strict consensus for each resampled matrix.

What happens with other ways to summarize the results of a MCMC? As noted above, they depend on whether the chain succeeded in finding the individual trees of highest posterior probability. For larger numbers of taxa, it is extremely unlikely that the chain will ever pass through the optimal tree(s), let alone pass through the optimal tree(s) enough times to estimate their posterior probability with any accuracy. Although tree bisection reconnection (TBR) forms the basis for both tree search and MCMC algorithms, rearrangements leading to worse trees are often accepted under MCMC, while they are normally rejected in a tree search. For equivalent numbers of rearrangements, then, a tree search (specially one combining different algorithms, like the methods in TNT; see Goloboff 1999, for details) is much more likely than a MCMC to find an optimal tree. Even if MCMC and a tree search had the same chances of finding an optimal tree for the same number of rearrangements, the numbers of rearrangements required to find optimal trees during a search cannot ever be achieved in Bayesian analyses. For example, in the case of a relatively small matrix of 84 taxa (from Goloboff 1995), TNT requires at least 5–10 million rearrangements to produce the first hit to minimum length. For Chase *et al*.'s (1993) data set (*zilla*, 500 taxa), it takes TNT an average of about 500 million rearrangements to find an optimal tree for the first time[6]; for the 854 taxa used in Goloboff (1999), it takes about 5 000 million rearrangements (about 18 min in an 800 MHz machine). Running 5 000 000 000 generations of a MCMC is impossible (in practical terms).

Suppose anyway that the chain succeeds in finding the trees of maximum *a posteriori* probability a certain number of times. The posterior probability of each individual tree will thus be negligible (the more so the more taxa are included in the analysis). In our view, such a low posterior probability is perfectly reasonable, and illustrates the fact that the statistical significance of phylogenetic conclusions cannot be meaningfully assessed in real cases. But statistically minded phylogeneticists will likely show continued interest in making probabilities more robust, i.e. in producing more 'acceptable' values. The alternative is to identify a credible set of trees. A strict consensus of the credible set of trees may contain exclusively well-supported groups, but only to the extent that the chain was run for long enough to find some trees that are relatively close to optimal trees. For the simulations carried out here (small numbers of taxa, very clean data without violations of the model, chains quickly converging), credibility sets of 90% still display, in many cases, false groups. Only running very large numbers of generations would avoid that problem, but in the case of larger data sets this will be impossible.

[6] Note that the figure of 500 million trees corresponds to analyses using sectorial searches, tree drifting, and tree fusing. Davis *et al*. (Chapter 7) report the numbers of rearrangements required to find optimal trees for *zilla* using only TBR; those numbers are much larger.

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