

A Bayesian approach for evaluating the impact of historical events on rates of diversification

Brian R. Moore^{a,1} and Michael J. Donoghue^{b,1}

^aDepartment of Integrative Biology, University of California, Berkeley, CA 94720; and ^bDepartment of Ecology and Evolutionary Biology, Yale University, New Haven, CT 06520

Contributed by Michael J. Donoghue, November 29, 2008 (sent for review June 22, 2008)

Evolutionary biologists often wish to explore the impact of a particular historical event (e.g., the origin of a novel morphological trait, an episode of biogeographic dispersal, or the onset of an ecological association) on rates of diversification (speciation minus extinction). We describe a Bayesian approach for evaluating the correlation between such events and differential rates of diversification that relies on cross-validation predictive densities. This approach exploits estimates of the marginal posterior probability for the rate of diversification (in the unaffected part of the tree) and the marginal probability for the timing of the event to generate a predictive distribution of species diversity that would be expected had the event not occurred. The realized species diversity can then be compared to this predictive diversity distribution to assess whether rates of diversification associated with the event are significantly higher or lower than expected. Although simple, this Bayesian approach provides a robust inference framework that accommodates various sources of uncertainty, including error associated with estimates of divergence times, diversification-rate parameters, and event history. Furthermore, the proposed approach is relatively flexible, allowing exploration of various types of events (including changes in discrete morphological traits, episodes of biogeographic movement, etc.) under both hypothesis-testing and data-exploration inference scenarios. Importantly, the cross-validation predictive densities approach facilitates evaluation of both replicated and unique historical events. We demonstrate this approach with empirical examples concerning the impact of morphological and biogeographic events on rates of diversification in Adoxaceae and *Lupinus*, respectively.

Adoxaceae | key innovations | *Lupinus* | speciation | extinction

Documenting the patterns and understanding the causes of variation in diversification rates is a central objective of evolutionary biology. Rates of diversification may be influenced both by the origin of intrinsic traits—“key innovations,” such as morphological, behavioral, or physiological novelties—and the incidence of extrinsic events—“key opportunities,” such as episodes of biogeographic or climatic change. Accordingly, a comprehensive understanding of the causes of differential diversification requires the ability to explore the impact of a diverse array of both intrinsic and extrinsic factors.

Several recent phylogeny-based methods have greatly enhanced our ability to test key innovation hypotheses regarding the influence of intrinsic factors, principally discrete binary traits, on rates of diversification (1–3). Despite remarkable progress in this area, we perceive the need to extend the phylogenetic study of diversification-rate correlates in 3 ways: to more fully accommodate inherent sources of uncertainty (associated with estimated divergence times, diversification-rate parameters, event histories, etc.), to address a wider range of historical events (associated with episodes of change in morphology, biogeography, and ecology), and to expand the fundamental mode of inference (to enable both hypothesis testing and data exploration).

With these considerations in mind, we describe a Bayesian approach for identifying correlates of differential diversification

rates that relies on cross-validation predictive densities, which effectively asks “How diverse would the effected lineage be if the inferred event had no impact on rates of diversification?” The cross-validation predictive densities approach provides a versatile inference framework (under both hypothesis-testing and data-exploration scenarios) for investigating the influence of diverse types of historical events (whether unique or replicated), while simultaneously accommodating various sources of uncertainty. We illustrate this approach with two empirical analyses, first exploring the impact of fruit evolution on rates of diversification in the plant group Adoxaceae and then investigating the influence of biogeographic dispersal into South America on rates of diversification in lupines.

Cross-Validation Predictive Diversity Densities Cross-validation predictive densities (4, 5) are related to the more familiar technique known as *posterior predictive densities simulation*, which has been applied to a number of problems in evolutionary biology, such as detecting positive selection on amino acid sites (6), evaluating the adequacy of nucleotide substitution models (7), and mapping mutations (8) and traits on phylogenies (9). Both are sampling-based approaches that provide a means of evaluating the adequacy of a given model. Posterior predictive simulation involves drawing model parameter values from their respective marginal posterior probability distributions (previously estimated from the original data under the candidate model) to generate a distribution of “future” (predictive) observations. If the model provides an adequate description of the original data, relevant aspects of the predictive and realized observations should be similar.

Cross-validation predictive density simulation is similar, but includes the additional step of parsing the data into two complementary subsets, referred to as the “training” and “testing” partitions (10). This entails estimating the marginal posterior densities for parameters of the model from a subset of the data (the training partition), which are then sampled to generate a posterior predictive distribution. This predictive distribution is compared to the complementary subset of the data (the testing partition), and the adequacy of the model is then assessed by its ability to predict relevant aspects of the excluded data. Importantly, by integrating over their respective marginal posterior probability densities, this approach accommodates uncertainty associated with those parameter estimates.

More formally, suppose that X is a set of observations $\{x_i; i = 1, 2, \dots, n\}$. The cross-validation predictive densities compose the set $\{f(x_i|X_{(i)}); i = 1, 2, \dots, n\}$, where $X_{(i)}$ denotes all elements except x_i . Conveniently, the density $f(x_i|X_{(i)})$ predicts what values of x_i are

Author contributions: B.R.M. and M.J.D. designed research; B.R.M. performed research; B.R.M. analyzed data; and B.R.M. and M.J.D. wrote the paper.

The authors declare no conflict of interest.

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¹To whom correspondence may be addressed. E-mail: brian.moore@berkeley.edu or michael.donoghue@yale.edu.

This article contains supporting information online at www.pnas.org/cgi/content/full/0807230106/DCSupplemental.

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likely when the model is fitted to all of the observations except x_i . The actual value $x_{i,obs}$ can then be compared with this predictive density in various ways to evaluate whether $x_{i,obs}$ is likely under the model (4). These cross-validation predictive densities are calculated as

$$f(x_i|X_{(i)}) = \int f(x_i|\theta, X_{(i)}) \cdot (\theta|X_{(i)}) d\theta \quad [1]$$

where the integrand is evaluated over the marginal density of the model parameters, θ .

The application of cross-validation predictive densities to the current problem is straightforward. Suppose that the history of our study group includes an event k that is inferred to occur along an internal branch v_k of the phylogeny at some time in the past t_k , which subtends a subclade comprising n_k species. We may suspect that event k is a key innovation/opportunity (hypothesis-testing scenario), or we may wish to investigate whether this event coincides with a shift in diversification rate (data-exploration scenario). Under either mode of inference, we are essentially attempting to address the same question: "If k did not influence rates of diversification, how many species would have descended from v_k ?"

Given point estimates for t_k and $\lambda_{(k)}$ (the rate of diversification in lineages not descended from v_k , for the moment assuming a Yule stochastic branching process), the expected diversity of the group associated with event k is simply

$$E(n_k|\hat{t}_k, \hat{\lambda}_{(k)}) = e^{\hat{\lambda}_{(k)}\hat{t}_k}. \quad [2]$$

(11). However, this conditional expectation assumes that the age and the diversification rate are known without error. Because these parameter values are estimates from data, they are associated with uncertainty. Accordingly, it would be more appropriate if the predictive diversity distribution $E(n_k)$ accommodated uncertainty in estimates of t_k and $\lambda_{(k)}$. This could be achieved by integrating over the marginal posterior densities for these parameters $\Pr(t_k|X)$ and $\Pr(\lambda_{(k)}|X_{(k)})$ estimated from the joint posterior probabilities of the entire data set and the training data set, respectively. This cross-validation predictive diversity density is calculated as

$$E(n_k|t_k, \lambda_{(k)}) = \int \int (e^{\lambda_{(k)} t_k}) dt_k d\lambda_{(k)}. \quad [3]$$

Although possible to solve analytically, Eq. 3 is conveniently evaluated using Monte Carlo integration. This merely involves repeatedly sampling pairs of event times and diversification-rate estimates from their respective marginal posterior densities, calculating the expected diversity, and storing each result to a list. The resulting array of expected species diversities is then summarized as the predictive diversity density, $E(n_k)$.

By comparing the predictive diversity density to the realized diversity $n_{k,obs}$ we can calculate the probability of realizing the observed species diversity under the estimated background diversification rate. This posterior predictive P -value is calculated as the proportion of predictive diversities that exceeds the realized diversity,

$$P_{n_{k,obs}} = \frac{1}{N} \sum_{i=1}^N I(n_{k_i} \geq n_{k,obs}). \quad [4]$$

(5, 12, 13), where $I(\cdot)$ is the indicator function that takes the value 1 when its argument is true and the value 0 otherwise, and n_{k_i} is the predicted species diversity based on the i th sample from the marginal probabilities of t_k and $\lambda_{(k)}$. Probabilities more extreme than a specified value (conventionally $\alpha = 0.05$) suggest that the observed species diversity $n_{k,obs}$ differs significantly from that

predicted under the background diversification rate $\lambda_{(k)}$, which therefore suggests that event k is correlated with a significantly increased rate of diversification. Of course, we can also evaluate both tails of the cross-validation predictive diversity density if the hypothesis predicts that the event may be correlated with either significant increases or decreases in diversification rate or if we are adopting an exploratory data analysis (EDA) perspective in which the direction of the effect is unspecified.

We have so far implicitly assumed the availability of marginal posterior densities for the parameters required to generate the cross-validation predictive diversity density. Our approach leverages dedicated implementations of Bayesian MCMC methods to estimate marginal posterior densities for these parameters. A number of existing programs can be used to approximate the joint posterior probability density of phylogeny and absolute or relative divergence times (under a strict or a relaxed molecular clock) and, importantly, to allow estimation of the marginal posterior densities of the diversification-rate parameters [i.e., μ and/or λ , depending on whether a birth-death or a Yule prior is used to model the branching process, respectively (14–17)]. Similarly, estimation of event history relies on methods deemed most appropriate to the particular problem at hand. For instance, we can infer evolutionary changes in discrete morphological and molecular traits (8, 9, 18–22), the evolution of ecological associations (23, 24), and events in biogeographic history (25, 26).

The methods described above have been implemented in the freely available program, tRate. This command-line R package can be run on multiple platforms (Windows, Macintosh OSX, and Unix versions) to perform cross-validation predictive density simulation and to calculate posterior predictive P -values. tRate works in conjunction with other applications, which provide estimates of the marginal posterior probability distributions of divergence times and diversification-rate parameter and inferred event histories (e.g., using programs such as BEAST, BayesTraits, and AReA, as illustrated in the empirical examples below). The tRate distribution bundle may be obtained by contacting B.R.M.

Two Worked Examples In practice, evaluating correlates of differential diversification by means of cross-validation predictive densities entails a 4-step protocol (Fig. 1). Step 1 involves estimating the joint posterior probability density of the phylogeny and divergence times from the complete set of nucleotide sequences. In step 2, the history of the event is estimated from the resulting posterior probability distribution of trees. The training data partition is defined in step 3 by excluding the subset of species associated with the event and then subjecting the remaining data set to a second round of phylogeny/divergence-time estimation. Finally, we draw from the marginal posterior densities of t_k and $\lambda_{(k)}$ (estimated in steps 2 and 3, respectively) to generate the cross-validation predictive diversity density (using Eq. 3), which allows us to assess whether the realized species diversity correlated with the event is significantly higher or lower than predicted (using Eq. 4). Below we illustrate this procedure with two examples: the first investigates the influence of morphological events on rates of diversification under an EDA perspective, and the second case evaluates the impact of biogeographic events under a hypothesis-testing inference scenario.

Is Fruit Type Correlated with Differential Rates of Diversification in Adoxaceae? In a recent exploration of biogeographic and morphological correlates of diversification rate in the plant clade Dipsacales (27), we inferred several instances in which trait changes occurred in close proximity to significant shifts in diversification rate [independently inferred using a maximum-likelihood approach (refs. 28 and 29)]. However, a number of these apparent correlations were nonsignificant under the key-innovation test of Ree (2). One such case involved the evolution of fruits with a single seed in Adoxaceae, which we revisit using the cross-validation predictive densities approach.

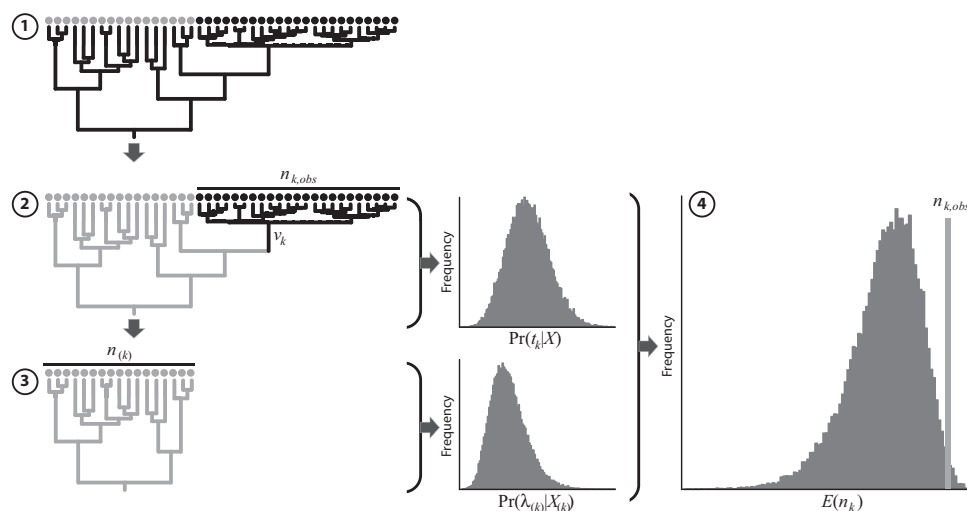


Fig. 1. Evaluating correlates of differential diversification rates using cross-validation predictive densities. Step 1 involves estimating the joint posterior probability density of the phylogeny and divergence times from the entire data set of nucleotide sequences. In step 2, the history of the event is estimated from the resulting posterior probability distribution of trees. Step 3 entails constructing the training data partition by removing the subset of species associated with the event and then subjecting this reduced data set to a second round of phylogeny/divergence-time estimation. Finally, we draw from the marginal posterior densities of t_k and λ_k (estimated in steps 2 and 3, respectively) to generate the cross-validation predictive diversity density (using Eq. 3), which permits us to assess whether the realized species diversity is significantly higher or lower than predicted (using Eq. 4).

We estimated the posterior probability density of phylogeny and divergence times for Adoxaceae using BEAST (16), assuming that substitution rates evolved under the uncorrelated-lognormal model and that the branching process conformed to a Yule prior, and the evolutionary history of fruit morphology was then inferred using a Bayesian model-averaging approach (20, 22) [see [supporting information \(SI Text, Figs. S1 and S2, Tables S1–S3, and Dataset S1, and Table S4\)](#) for details]. These findings suggest that fruits with a single seed evolved independently in the most recent common ancestor of *Viburnum* and separately in *Sinadoxa corydalifolia* (Fig. 2).

This example illustrates several features of the cross-validation predictive densities approach. Credible intervals for divergence times suggest that these estimates are associated with considerable uncertainty. As detailed above, the current approach accommodates this uncertainty by integrating estimates over the marginal posterior density of divergence times for the node associated with the event. We are also free to adopt either a punctuated model of evolution, in which trait change is assumed to occur only at speciation [as required by some methods (ref. 1)], or a more gradualist model, in which change may occur along branches [as assumed by other methods (refs. 2 and 3)]. Under the punctuated scenario, t_k corresponds only to the posterior density of divergence times for the event node (e.g., the crown node of *Viburnum*: node 2, Fig. 2). By contrast, under the gradualist scenario, t_k comprises the composite posterior density of the two nodes bracketing the branch along which the event is inferred (e.g., nodes 1 and 2 bounding the stem of *Viburnum*: Fig. 2). More generally, t_k can comprise the composite posterior density of divergence times for a series of ancestor-descendant branches over which the event is plausible, providing a flexible means for accommodating uncertainty in the inferred event history.

Results of the cross-validation predictive densities approach indicate that origin of single-seeded fruits in *Viburnum* is correlated with significantly higher species diversity than predicted under the background rate of diversification in Adoxaceae, whereas the independent origin in *S. corydalifolia* evidently had little impact on diversification rates (Fig. 3). By contrast, no overall correlation between fruit form and diversification rate is detected when these 2 events are evaluated collectively—either by using the key innovation test of Ree (2) or by explicitly combining the 2 posterior predictive P -values estimated for each event using the cross-validation predictive densities approach (see [SI Text](#) for details). Considering the 2 independent events in the same analysis fails to identify the correlation of diversification rate and single-seeded fruits in the case of *Viburnum*.

The ability to dissect the partial correlations in these data

motivates reevaluation of the problem—although both *Viburnum* and *S. corydalifolia* possess fruits with a single seed, they appear to be dispersed in different ways. The drupes of *Viburnum* are dispersed by birds, whereas the fruits of *S. corydalifolia* may be dispersed by water (30). Accordingly, we may wish to revise our original question (the influence of single-seeded fruits) to focus on the role of bird-dispersed fruits, which could subsequently be explored in other groups. This example illustrates how data exploration—and specifically the evaluation of individual events—may guide the formulation of hypotheses regarding correlates of diversification rate.

Did Dispersal to South America Promote Rates of Diversification in *Lupinus*? Hughes and Eastwood (31) recently documented the adaptive radiation of *Lupinus*, in which the movement of this North American plant clade into South America apparently promoted extremely rapid rates of diversification via geographically driven speciation across the newly forming Andean mountain range. Although this study demonstrated high absolute rates of diversification in the Andean lineage, the lack of appropriate methods precluded statistical evaluation of the predicted correlation between elevated rates of diversification and dispersal of *Lupinus* into the Andes. Because biogeographic range and morphological traits are inherited in fundamentally different ways (25, 32), existing trait-based tests are inappropriate for evaluating the impact of biogeographic history on rates of diversification. Under the cross-validation predictive densities approach, however, biogeographic dispersal is merely another type of historical event.

The posterior probability density of chronograms for *Lupinus* was estimated as in the previous example, and the biogeographic history of the group was inferred using a maximum-likelihood approach (25, 26) [see [SI Text, Fig. S1, Tables S1 and S2, Dataset S2, and Table S5](#)]. Two episodes of dispersal into South America were inferred: one lineage dispersed from eastern North America into lowland habitats of South America and the second from Central America into the Andean region (Fig. 4). Results of the cross-validation predictive densities approach suggest that movement into the Andes of South America is correlated with significantly higher species diversity in *Lupinus* [as predicted by Hughes and Eastwood (ref. 31)], whereas the dispersal into the lowland habitats apparently had little impact on diversification rate (Fig. 5).

Importantly, combination of the posterior predictive P -values for the 2 episodes of South American dispersal in *Lupinus* does not support an overall correlation between dispersal into South America and increased diversification rate (see [SI](#)). Again, the analysis combining both cases obscures the strong correlation

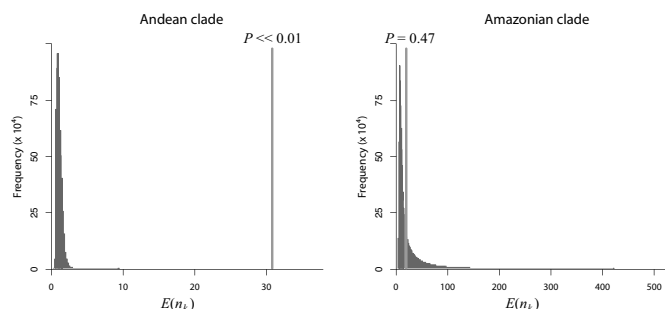


Fig. 5. Estimated correlation between biogeographic dispersal into South America and rates of diversification in *Lupinus*. Each histogram depicts the predictive distribution of South American species diversity, and the vertical line indicates the observed species diversity, with the corresponding posterior-predictive probability. These results indicate that the Andean clade experienced significantly increased rates of diversification relative to background rates of diversification in *Lupinus*, whereas the other South American lineage did not.

effects of subsequently evolved features (43). Such considerations emphasize the need for methods that can simultaneously evaluate the influence of multiple variables on rates of diversification. In theory, the cross-validation predictive density approach could be extended in this direction by comparing the predictive “influence” of various events (4).

Concluding Thoughts. Existing methods have been developed in the context of testing key innovation hypotheses, which (appropriately) evaluate the overall association between a given character state and diversification rate. Ideally, such hypotheses draw upon robust evolutionary theories of the general mechanisms that influence

probabilities of speciation and/or extinction, from which specific instances can be identified and tested. Unfortunately, theory on the factors influencing rates of diversification is currently rather thin, such that the need to approach all inference problems from a hypothesis-testing perspective is somewhat problematic. For instance, the virtually exclusive reliance on this inference mode increases the incidence of type III error (i.e., “testing” hypotheses that were initially suggested by the data) and limits the ability of empirical data to directly inform theory. Accordingly, it is often desirable (and entirely appropriate) to alternate between hypothesis testing and data exploration; it is reasonable to explore empirical data, learn something in the process, and then (re)formulate a hypothesis that can subsequently be evaluated using additional data.

Moreover, some inference problems naturally pertain to the influence of *particular* historical events on rates of diversification. That is, rather than asking “Are rates of diversification correlated with a particular morphological/biogeographic/ecological *state*?” we may instead wish to ask “Are rates of diversification correlated with a particular morphological/biogeographic/ecological *event*?” We believe that it is both useful and valid for evolutionary biologists to search for the cause(s) of individual evolutionary events, even when broader comparative tests may not be possible. Our hope is that the cross-validation predictive densities approach will facilitate the study of both unique and replicated historical events and thereby will foster the reciprocal illumination between empirical patterns and theoretical explanations that is critical to understanding of the causes of diversification.

ACKNOWLEDGMENTS. We thank Mary Moore, John Huelsenbeck, Tom Near, Stephen Smith, and David Tank for stimulating discussion. We are indebted to Paul Fine and Mark Pagel for constructive and insightful reviews. Our work on this problem has been supported by the NSF through the Phylogeography Working Group at the National Evolutionary Synthesis Center (NESCent), Cyberinfrastructure for Phylogenetic Research (CIPRES), and two Assembling the Tree of Life (ATOL) awards.

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