

Relaxed molecular clocks for dating historical plant dispersal events

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Age estimation from molecular sequences has emerged as a powerful tool for inferring when a plant lineage arrived in a particular area. Knowing the tenure of lineages within a region is key to understanding the evolution of traits, the evolution of biotic interactions, and the evolution of floras. New analytical methods model change in substitution rates along individual branches of a phylogenetic tree by combining molecular data with time constraints, usually from fossils. These 'relaxed clock' approaches can be applied to several gene regions that need not all have the same substitution rates, and they can also incorporate multiple simultaneous fossil calibrations. Since 1995, at least 100 plant biogeographic studies have used molecular-clock dating, and about a fifth has used relaxed clocks. Many of these report evidence of long-distance dispersal. Meta-analyses of studies from the same geographic region can identify directional biases because of prevailing wind or water currents and the relative position and size of landmasses.

Inferring past plant dispersal: from which data and why?

The geographic ranges of the lineages seen today are often interrupted by large expanses of inhospitable habitat, for example, an ocean. This raises questions about how and when they acquired their disjunct habitats. When lineages arrive in new habitats they will usually diverge and sometimes speciate, therefore, dating dispersal and lineage splits has broad implications for understanding rates of diversification [1], the evolution of biota [2,3] and associated faunas [4–6], and the time taken for species to adapt to novel environments [7–10]. Recent biogeographic studies that have included time estimates have revealed strikingly fast diversification rates in some floras, such as the Cape Region of South Africa, the recency of species accumulation even in ancient lineages, such as ferns [1], and the persistence of precarious mutualisms over many millions of years, such as the interactions between figs and fig wasps and between yucca and yucca moths [4,6].

The ideal materials from which to estimate the ages of lineages and their presence in particular places are abundant fossils. However, isolated fossils often provide only screenshots from which we extrapolate in time and space. Extinction followed by recolonization is particularly difficult to infer from the fossil record. It is often more parsimonious to interpret the history of taxa with extended

fossil records in a framework of continuity [11,12]. Yet, there is ample direct evidence of rapid species expansions following dispersal from the study of invasive species, phylogeographic molecular data, and natural experiments such as Krakatau, an island sterilized by a massive eruption in 1883 [13–16].

The idea of dating the divergence of lineages from the time-dependent change of their genomes, the molecular clock hypothesis, is 40 years old [17], and plant geographers have applied sequence- or protein-based dating since the 1990s [18–28]. With increasing computer power and access to readily implemented molecular evolutionary

Glossary

Chronogram: a phylogenetic tree in which branch lengths correspond to time.

Crown group: any node in a phylogeny with two or more descendent branches reaching the present.

Gene coalescence: coalescence theory examines the genealogical relationships between copies of genes in a sample. It assumes that all alleles in an extant pool must have descended from a single allele (to which they coalesce). For neutral nuclear alleles in a random mating population, the mean coalescence time is given by $4N[1 - (1/i)]$ generations, where i is the number of sampled gene copies. Chloroplast or mitochondrial genes have mean coalescence times of $N[1 - (1/i)]$, rather than $4N[1 - (1/i)]$.

Genetic distance: refers to the number of substitutions at which two sequences differ. Rather than simply taking the observed number, one calculates a more likely number by assuming an underlying nucleotide substitution model, based on what is known about the specific genome region that was sequenced.

Nucleotide substitution models: these models try to capture the probability of a nucleotide changing to another, using several variables, such as the frequency of the base, the mean mutation rate, and a modification of that mean rate, dependent upon the identity and position of the nucleotide (for example, if it is a purine or pyrimidine, or in the first, second or third position in the codons of coding genes).

Posterior rate: in Bayesian analysis of molecular data, the posterior (or posterior probability density) is the probability distribution over the parameter state space, given the data under a chosen model of evolution. In molecular clock work, the posterior rate is the parameter of the greatest interest because it allows the age of any node in the tree to be calculated.

Prior rate: in Bayesian analysis of molecular phylogenetic data, priors represent one's assumptions about the probabilities of different parameter values. The prior rate is calculated by dividing the median genetic distance from the root to the tips (terminal branches in the tree) by an assumed age of the root. This would amount to the entire analysis being circular were it not the case that prior assumptions can be greatly changed by the actual data, which comprise the nucleotide substitutions, one or multiple time constraints (from fossils), and a given topology.

Stem lineage: any branch in a phylogeny with two or more descendent branches. When using trees to develop evolutionary scenarios, one assumes that the various synapomorphic characters found in a group evolved somewhere along its stem lineage. The concept is extremely important when calibrating molecular clocks. This is because (the age of) a calibration fossil that has the synapomorphies of clade A should be used to constrain the node where the stem lineage of clade A diverges from its sister(s) (see also Figure 1). This is the only assignment of the fossil constraint that properly accounts for the fact that the apomorphic morphological traits of clade A evolved somewhere along its stem lineage. Not knowing exactly when that was, one lacks a criterion for assigning them to a particular place on the stem.

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models, the number of studies using genetic distances to calculate ages of dispersal events has mushroomed. Between 1992 and 1998, ~20 phylogeographic papers used a clock approach. Over the past six years (to May 2005) that number has quadrupled, with more and more studies relying on relaxed clocks.

Molecular clock-based dating of divergence events (i.e. nodes in a phylogeny) involves the following steps: (i) obtaining the genetic distance (see Glossary) between two sequences or taxa in the analysis, one of which must have a known age (or age range), usually determined from fossils; (ii) calculating the substitution rate by dividing the genetic distance by the known age; (iii) using that rate to convert genetic distances between taxa of interest into estimates of their absolute ages. These steps are dealt with in the sections below.

Genetic distances between sequences are calculated using nucleotide substitution models. The distance unit is number of substitutions per nucleotide site or of substitutions per codon. The number of nucleotide substitutions is generally correlated with time because when changes are neutral (no selection), substitution is driven by mutation and genetic drift. Under selection, substitution between different parts of the genome, gene regions and organisms varies, but can nevertheless remain stable within some genes, sets of codons, or other types of data partition and within subsets of taxa. Local datasets (combinations of taxa and gene regions) can thus exhibit roughly regular, or clock-like, accumulation of substitutions [29–31]. However, it is clear that there is no universal clock [32,33].

Studies in plants have uncovered striking heterogeneity in the rate of nucleotide substitution among lineages [32,34]. Unfortunately, assessing the rate of heterogeneity is difficult because the power of relative rate tests or likelihood ratio tests depends on the amount of signal in the data. Where sequence divergence is low or sampled sequences are short, the power of these tests is correspondingly low [33,35]. Small datasets therefore sometimes satisfy the 'clock assumption' [i.e. the accumulation of substitutions does not differ statistically between sister-groups], but large variations (uncertainty) in estimates of branch lengths (and dates) weaken any conclusions [27,30,36–38].

Problems from faulty branch-length estimation

Molecular clock dating stands or falls with the accuracy with which genetic distances can be estimated. Contradictions between molecular clock-based age estimates and fossil-based estimates, and also between different dating approaches, have spurred efforts to understand their causes [39–41]. It is clear that dating biases can result from misspecification of genetic distances (branch-lengths in the trees), either because of incorrect topology among early-diverging branches or incorrect nucleotide substitution models. The parameter values estimated to represent the true substitution process are based on observed nucleotide (or amino acid) changes, which are produced through evolution with a high degree of stochasticity. Current models accommodate many aspects of heterogeneous substitution across sites, but because

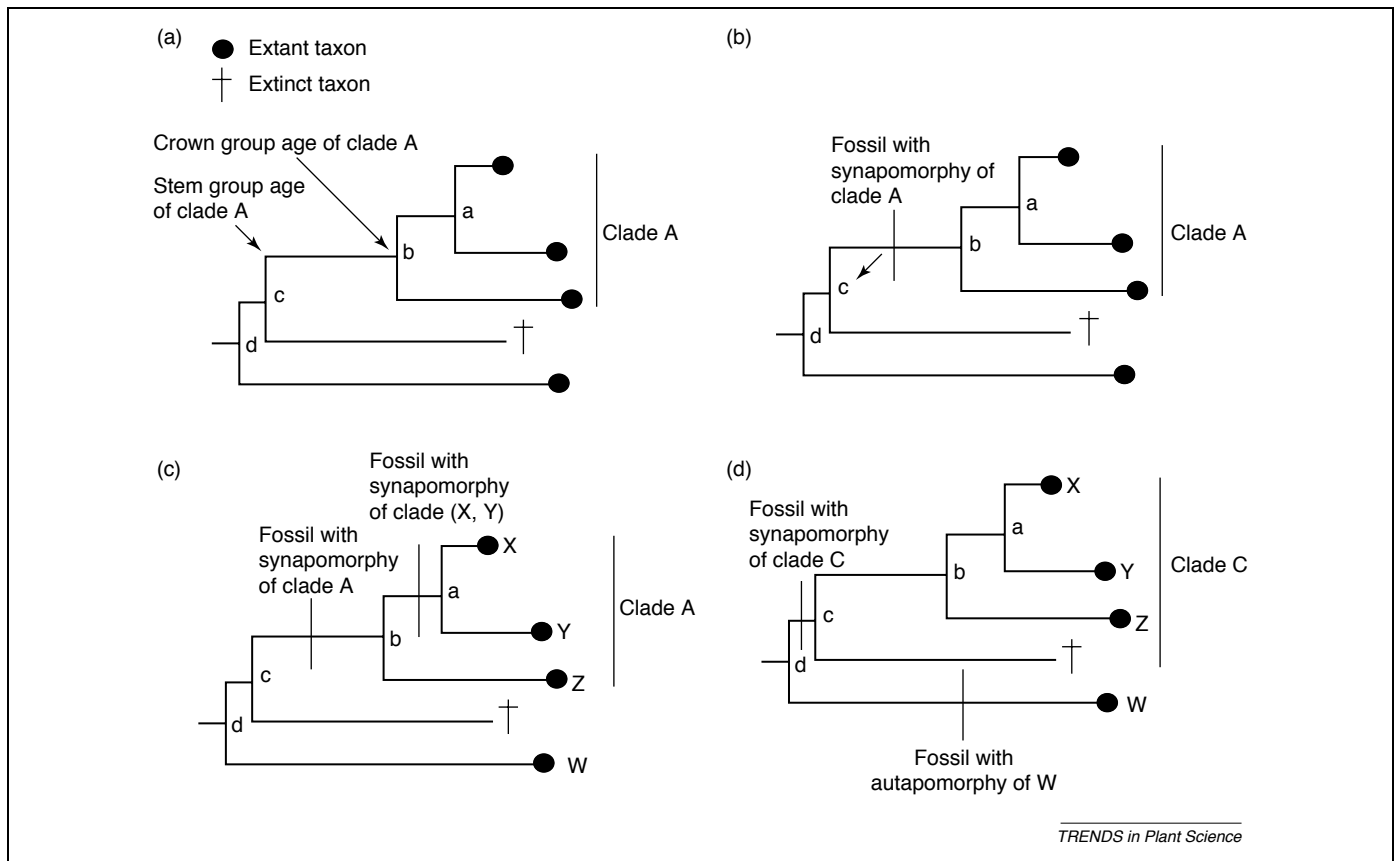
the same model or combination of models is used for all sequences in a dataset, heterogeneity among species cannot be dealt with beyond influencing average parameter values. Efforts are underway to improve models by including parameters for covariation between neighboring nucleotides and variation over time in nucleotide composition [31,42,43]. Assuming 'neighbor dependence' of nucleotides is the basis for accommodating rate heterogeneity between taxa, and therefore these models offer considerable promise for molecular age estimation.

Another problem is the choice of gene region on which to base the estimates. In theory, one can choose a level of phylogenetic resolution by sampling the gene regions that accumulate substitutions at an appropriate rate. In practice, biogeographers have little choice in the matter because of limited suitable material from rarely collected species in remote areas and because taxon sampling must be adapted to allow calibration. Direct calibration with preserved 'ancient' DNA is commonly used for emerging diseases, using frozen tissue samples [44]. In principle, this should be possible for plant tissues given that DNA can be obtained and sequenced from 17-million year (my)–20-my-old fossils [45].

Calibration always involves dividing the genetic distance between two sequences by time (Figure 1). In biogeographic work, the time entered in this equation is usually the age of the oldest fossil of a close relative of the focal taxa. Where close relatives have no fossil record, biogeographic studies can require the inclusion of phylogenetically distant outgroups simply because they do have a fossil record. This can entail relying on conserved gene regions that are alignable across distant relatives and/or that are available from GenBank (when collecting certain taxa is not feasible). However, these more conserved regions might not be variable among the sister species whose divergence one wishes to date. The only way to proceed then is to analyze separate datasets and to bridge them by using one of the nodes dated in the first analysis as a calibration point in the second analysis (secondary calibration, e.g. [46,47]). Successive bridging is likely to compound the estimated error [48]. Extrapolation, and how much is acceptable, lies at the heart of all controversy surrounding the use of molecular clocks.

Converting genetic distances to absolute times – the issue of calibration

Besides erroneous branch-length estimation, another cause of discrepancies between fossil-based ages and molecule-based ages is the tenuous association between a node in a gene tree and the time point or time bracket used to convert (genetic) distance into rate. Genes evolve at different rates and, therefore, will reflect disruption of gene flow differently, with some coalescing long before and others long after the disrupting dispersal event. As long as sampling is appropriate to gene coalescence times, this presents no problem because clade divergence and gene divergence will at least have the same topology. However, many botanical molecular time estimates have relied on nuclear rDNA internal transcribed spacers (ITS), which are known to exist in paralogous copies that can persist



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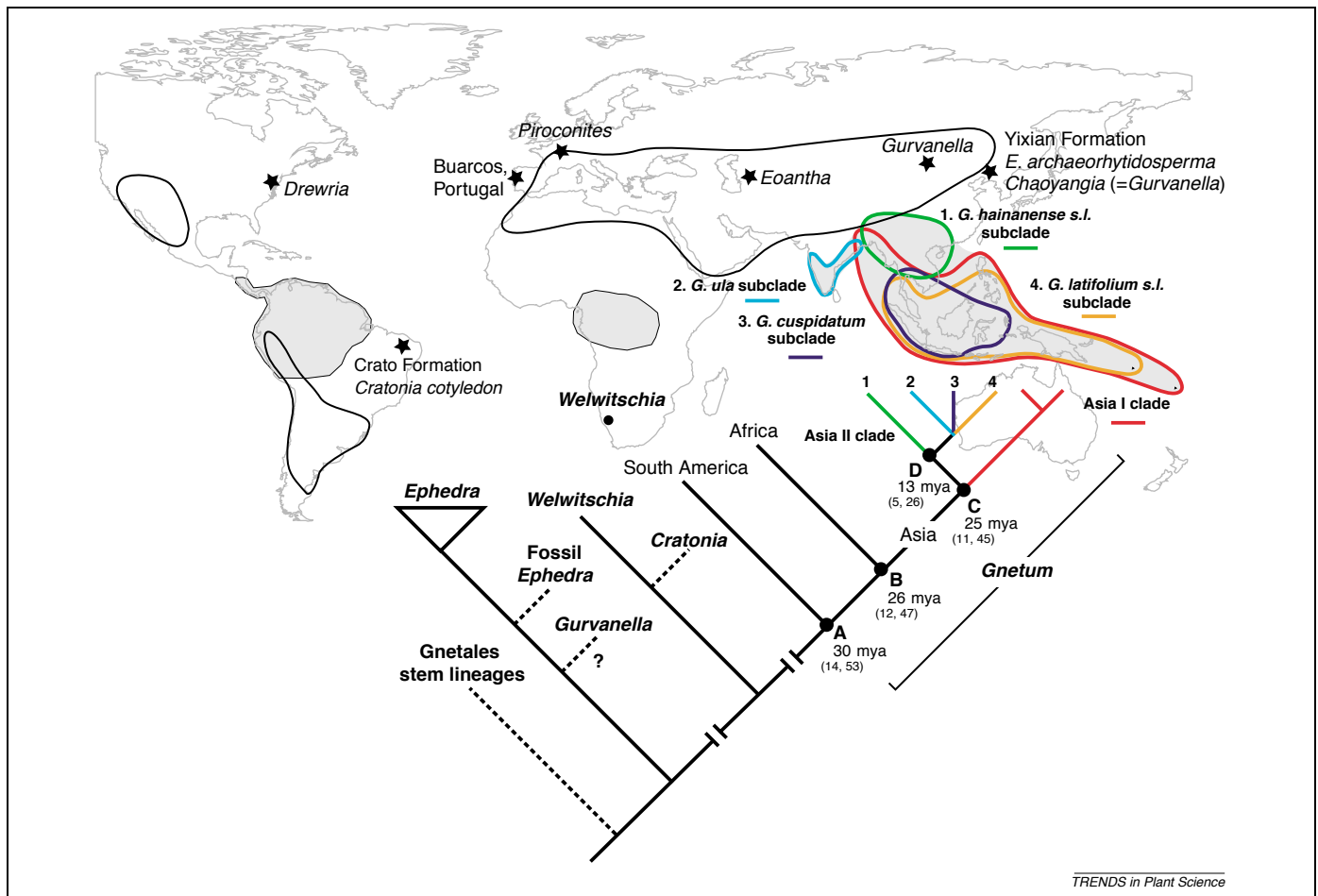
Figure 1. (a) Clade A, like every clade, has two ages, the age of its stem lineage and the age of its living 'crown' group. Molecular data concern the age of the crown group. Many seeming contradictions between molecule-based estimates and fossil-based estimates dissolve once the distinction of stem group age and crown group age is understood. Both ages are biologically relevant because each stem group (age) becomes a crown group (age) with the inclusion of phylogenetically more distant outgroups. (b) A fossil exhibiting a character that is synapomorphic for clade A could represent any point (time slice) along the stem of clade A. The only objective way to handle this problem is to take the age of the fossil as the minimum age of node c, the split between living representatives whose sequences are the dataset. (c) To constrain the crown age of clade A, a fossil with a synapomorphy of a subclade of A, such as (X,Y), is required. (d) Two fossils are available to constrain node d, with varying completeness of preservation and unequal reliability of dating. It seems best to use them sequentially and to evaluate the resulting time estimates against independent evidence, such as climate data, geological data, ages of coevolved organisms or biomes, or molecular clock-based estimates that rely exclusively on other calibration fossils, for instance, the fossil of (X,Y) used in (c).

through speciation events, and some such estimates might turn out to be erroneous.

An important concept relevant to calibration is the distinction between stem lineage and crown group [33,41, 49,50] (Figure 1a). For a fossil to be used for calibration, it must exhibit at least one trait that is synapomorphic for a clade in the tree. Such a fossil provides a minimum age for the node just below the clade whose synapomorphy it exhibits (Figure 1b and c). Fossils must be used in this conservative way because there is no objective criterion for assigning them 'somewhere' along stems (and stems can be long). When facing a choice between several fossils (Figure 1d), one would choose the older, all else being equal, or perhaps explore their effects sequentially if they differ in reliability. Figure 1 highlights that the use of multiple fossil dates reduces errors in calibration.

Of the ~100 plant geographic studies to date that have used strict or relaxed molecular clocks, more than half have relied on average substitution rates from other studies or have calibrated substitution rates by the ages of geological events, such as the ages of islands or the origin of a mountain chain, rather than by fossils, usually because suitable fossils were lacking. However, constraining nodes in a phylogenetic tree by geological events (e.g. [51]) risks circularity in biogeographic analyses because it

already assumes that those events caused the divergence, rather than testing temporal coincidence. Geological events nevertheless provide an important validation of estimates reached by other calibrations [52–55]. This also seems the safest use of the ages of oceanic islands that have endemic taxa on them. Using island ages directly to constrain the ages of their endemic species overlooks the possibility that an insular endemic could have split from its mainland relative(s) before arriving on the island or that it might have arrived millions of years after the island originated. Only when an original colonist has diversified can the island age be used as a minimum age constraint. However, this strict criterion is not always used (e.g. [56,57]). Studies that have relied on fossil calibration points have generally found the age of island radiations to be younger than the islands they occupy [27,28,58,59]. An exception is the single Hawaiian species of Begoniaceae, *Hillebrandia sandwicensis*, which was dated to 51-my–65-my [60], older than even the sunken islands of the Hawaiian chain. However, the study relied on calibration with a fossil accepted as 55-my-old [61] but dated to 33-my by modern work. Applying the new calibration, as well as additional calibrations to an enlarged gene and taxon set [62], yields an age for the divergence of *Hillebrandia* from mainland relatives more



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Figure 2. Former and current ranges of *Ephedra*, *Gnetum* and *Welwitschia* (Gnetales), and time estimates (with 95% confidence intervals) for major divergences within *Gnetum* from a Bayesian relaxed clock calibrated with ten seed plant fossils [119]. The ten seed plant fossils were needed to estimate divergence times within *Gnetum* because *Gnetum* itself has no fossils. The geographic range of *Gnetum* is indicated by the shaded areas, the non-shaded areas indicate that of *Ephedra*. The range of *Welwitschia* is represented by the black dot. Stars indicate the localities of fossils. Broken lines in the phylogeny indicate a few particularly important extinct lineages of Gnetales.

in keeping with now submerged islands in the Hawaiian chain dating back 32-my [63]. A similar age has been estimated for the endemic Hawaiian fern *Diellia* [64], implying that the lineage jumped between islands as the Hawaiian chain evolved.

A final way to convert genetic distances into absolute time is to use the age of a habitat to which a clade is strongly adapted [27,65], but this approach can be misleading because the ages of many habitats are imprecisely known.

Given the difficulty of calibrating genetic distances to convert them into absolute times, it is clear why it is desirable to use multiple calibrations wherever possible. However, even with ancient and relatively good fossil records, such as those of Calycanthaceae, Chloranthaceae, *Ephedra*, *Nothofagus* or Nymphaeaceae, seeming contradictions between paleobotanical studies [11,12] and molecular clock studies can arise [47,66–69]. These dissolve when it is understood that the young molecular estimates for living clades in these families simply indicate that a diversification in an area is young (Figure 1a). Old lineages do not necessarily stop dispersing and diversifying. Striking examples of this are found

among aquatic plants [69–72] and among the seed plant lineage Gnetales (Figure 2).

Relaxing the clock assumption, multiple genes and simultaneous multiple calibrations

Analytical methods that relax the assumption of rate constancy among lineages became available in 1997 [73], and several more have been introduced since then [36,37,74–76,120]*. Rather than superimposing fossils on particular nodes in a phylogenetic tree, these methods use fossil dates to provide upper or lower bounds, or time brackets, on nodes. Several time brackets can be used sequentially or simultaneously, and it is helpful to have at least one constraint near the root of the tree and one nested among the tips.

Because of its straightforward use, most biogeographic studies have used the penalized likelihood (PL) approach [37,77–80]. Penalized likelihood assumes that substitution rates of ancestral and descendent lineages (about a node) are auto-correlated in time, and introduces a penalty for abrupt rate changes between them. Another

* Drummond, A.J. and Rambaut, A. (2005) BEAST v1.3, Available from <http://evolve.zoo.ox.ac.uk/beast/>.

approach to relaxing the clock assumption is to use 'local clocks' [76,81]. This method assumes that the ages of calibration nodes are known and then assigns different constant rates to different parts of the tree. It is suitable for lineages with well-understood fossil constraints [76,82,83].

Bayesian approaches to relaxing the clock are implemented in multidivtime [36,84,85], PhyBayes [75], and BEAST*. Because of the speed of the Markov chain Monte Carlo likelihood calculation, it is possible to simultaneously use branch lengths obtained from different genes (or data partitions, for example, first, second and third codon positions), each with its own fitted molecular evolutionary model. The idea is that single genes can be misleading about divergence times, but that combining multiple genes with different patterns of rate change introduces internal constraints and thus improves the extraction of information about the true organismal divergence time, which is presumed to lie somewhere in the middle. The approaches differ in that multidivtime and PhyBayes assume autocorrelated rate change, which in multidivtime is modeled as lognormally distributed, whereas in BEAST and PhyBayes the user can choose between different models of rate change, including lognormally distributed, gamma-distributed, and exponentially distributed change. BEAST version 1.3, released on 30 August 2005, does not assume autocorrelated rate change (Table 1) and is the only software that can infer phylogenies under a relaxed clock model.

Studies that compared PL, Bayesian approaches and local clocks, using simulated and empirical data [82,86] found that local clock models and Bayesian approaches outperform PL under certain conditions. When data are clock-like, PL overestimates the rate, suggesting that the method might have an intrinsic bias; a similar effect was observed when data were not clock-like (a possible example of PL overestimation can be found in [55]). Empirical studies that applied PL, multidivtime, and the strict clock to the same data have not identified consistent differences [54,72,87–90]; all the methods sometimes over- or underestimated ages as judged by oldest fossils. Given the nature of the fossil record, this is clearly not a valid test of inference methods. Of greater relevance is the finding that simulation studies for the Bayesian methods show that the choice of the prior rate has a considerable effect on posterior rate estimates, whereas empirical studies have found that widely different prior rates had almost no effect on estimated dates.

All current methods of relaxing the clock assumption recover reliable rates and ages only when several calibration points are accurate. In practice, uncertainties in calibrations owing to misidentified or misdated fossils [39,41,49,50], taxon sampling effects [91], and asymmetric tree shape can reduce the reliability of date estimates. Where data are approximately clock-like, assuming a strict clock can be the best way to improve the precision and perhaps accuracy of rate and date estimates [37,86]; results from relaxed clocks

should always be evaluated in relation to those from strict clocks calibrated at single nodes.

The importance of large amounts of sequence data for narrowing confidence ranges is also becoming increasingly clear [38,90]. To calculate errors on branch lengths (and ages), most studies have followed a bootstrapping procedure [27,39]. When nucleotide substitutions are approximately normally distributed, standard deviations rather than confidence intervals have also been calculated [92,93]. An advantage of Bayesian approaches is that 95% confidence intervals around age estimates are directly reported by available software. Another approach that provides confidence intervals around estimates is the mean path length method, which assumes a strict clock but allows multiple calibrations [94].

Molecular clock-based biogeography

Dispersal across the Northern temperate zone

The striking similarities between the floras of North America and Asia have long drawn the attention of plant geographers. Do floristic similarities date back to Paleocene or Eocene times when warm climates would have permitted the crossing of the North Atlantic and Beringian land bridges or are they more recent, such that one has to assume island hopping across the North Atlantic or Beringia? This question is often answered in favor of a recent (Miocene) crossing [54,95–98]. However, a few plant disjunctions have been inferred to date back to the Eocene warm-temperate forest belt that extended from California through southeastern North America, Europe and the Mediterranean to eastern Asia, following the regression of the epicontinental Turgai Sea that had formerly separated Europe and Central Asia. Today, some of these taxa are restricted to the humid tropics; the new hypotheses about their northern routes from Asia to Europe and North America, and from there to South America or Africa, are in stark contrast to earlier suppositions about southern, Gondwana connections [79,92,93,99,100].

Long-distance dispersal in the Southern temperate zone

Australasia is the part of the world where dispersal and vicariance explanations of historical biogeography have clashed most severely [101]. Molecular-clock dating for New Caledonia and New Zealand endemics, together with new fossils [102], indicates that in spite of the isolation of these islands for the past 85-my–65-my, their floras are mostly the result of Oligocene and more recent long-distance dispersal [102,103]. Striking cases include lineages of Sapotaceae ([104], although calibration of the ITS sequences used is based on extrapolation from other plant families), *Myosotis* [105], *Lepidium* [106] and *Nothofagus* [68]. *Nothofagus*, which has an 80-my-old fossil record, is one of the clearest examples of an ancient lineage with a complicated history of extinctions and new radiations, some of them following dispersal events, others probably relictual.

Dispersal across the Atlantic

Molecular clock-based divergence times for sister clades occurring on both sides of the Atlantic often implies

* Drummond, A.J. and Rambaut, A. (2005) BEAST v1.3, Available from <http://evolve.zoo.ox.ac.uk/beast/>.

Table 1. Programs for molecular clock-dating that relax the clock assumption of a homogeneous substitution rate^a

Method, software	Penalized likelihood in 'r8s'	Multidivtime	PhyBase	BEAST
Refs	[37]	[36,85]	[75]	^b
Platforms	Unix (MacOSX), Linux	Unix (MacOSX), Linux, Windows	Unix (MacOSX), Linux, Windows	Unix (MacOSX), Linux, Windows, requires Java 1.4
Optimization	Smoothing (as in regression analysis)	Bayesian MCMC	Bayesian MCMC	Bayesian MCMC
Input data	Tree with branch lengths Value for the penalty parameter	Tree Sequences	Tree Sequences	Sequences Several priors
Model of rate evolution	Autocorrelation between ancestral and descendent branches	Several priors Autocorrelation, with rates drawn from a log-normal distribution	Several priors Autocorrelation, with rates drawn from six different distributions (see text)	Various models are implemented and can be fitted to the data
Allows polytomies in input topology	Yes (collapse option)	Yes	No	Not applicable
Handles multiple simultaneous calibrations	Yes	Yes	No	Yes
Handles multiple data-sets with different rates	No	Yes	No	Yes
Provides error estimates	No (separate bootstrapping is required)	Bayesian 95% credibility intervals	Credibility intervals must be calculated by the user	Bayesian 95% credibility intervals
Relative speed	Very fast	Medium	Slow	Fast

Abbreviation: Bayesian MCMC, Bayesian Markov chain Monte Carlo.

^aModified from a comparison that includes other approaches such as strict clocks, local clocks and nonparametric rate smoothing [121].

^bDrummond, A.J. and Rambaut, A. (2005) BEAST v1.3, Available from <http://evolve.zoo.ox.ac.uk/beast/>.

Oligocene and Miocene over-water dispersal [53,78,79,83,92,107–109]. The genus *Senecio* alone contains several examples of dispersal from the Mediterranean or Africa to the New World [110], and the legume family adds another 30 to 40 cases [78]. However, ~110 angiosperm genera have trans-Atlantic disjunct species, and the disjunctions analyzed to date constitute only a small sample. This might explain why a search for directional biases from South America to Africa, or vice versa, has so far been fruitless [111].

Dispersal across the Indian Ocean and the tropical Pacific

The close floristic ties between East Africa, the Seychelles, India and Southeast Asia, areas that were last physically connected in the Cretaceous, have been attributed recently to dispersal across the Indian Ocean [26,79,83,88,112,113]. The idea of a taxon rafting on India as it moved northwards is supported in the case of the Myrtales family Crypteroniaceae [89,114]. One of the most striking, and still unexplained, disjunctions in plant geography is that between *Gleditsia amorphoides*, a legume tree occurring in Argentina, Bolivia and Paraguay, and its closest living relatives in China [25,115]. This disjunction could either be due to long-distance dispersal across the Pacific, followed by range expansion and extinction, or to migration across Beringia to North America, followed by dispersal from North America to South America and extinction in North America.

Looking for common patterns

As increasing numbers of disjunctions are analyzed, biogeographers – eager as ever to identify major patterns – are beginning to ask whether the direction and timing of long-distance dispersal events exhibit regularities [103,111,116,117]. Wind and ocean surface

currents affect dispersal and, because many wind systems have been stable for geologically relevant periods [118], one expects to find biases in the predominant direction of passive dispersal in spite of lineage-specific differences in dispersal and establishment capability. By combining oceanographic and climatic data with dated phylogenies (chronograms) for many taxa, this expectation should be testable. However, the growing body of evidence suggesting that plants and animals cross dispersal barriers more readily than was previously believed [63,101] implies that only meta-analyses of large samples of studies will have a chance of discovering predominant patterns. Or it might not be that principles derived from island biogeography will be explanatory for the patterns we see today. For example, the common observation that North American clades are nested within Old World radiations might simply be because North America is a fraction of the size of Eurasia and that Eurasia is therefore more likely to serve as the source area for North American clades (M. Lavin, personal communication).

Perspectives

Controversies about the use of molecular clocks are similar to those about using gene sequences to 'barcode' the identity of organisms. Genetic clocks and barcodes have proven their value, particularly in epidemiology and in the identification of contraband endangered species. When biogeographers can estimate the timing of past events with reasonable accuracy, they will be able to test hypotheses concerning the mechanisms responsible for the distribution of organisms. For this reason, molecular age estimation is an important addition to the tools of biogeography. New data and inferences have enabled biogeographers to assess the likelihood of the antiquity of a lineage or recency in an area. A drawback of most

current approaches to clock dating is that they do not simultaneously analyze topology, branch lengths and temporal information from the fossil record. In the Bayesian framework, this should become possible, allowing us better age estimates from a combination of fossil and molecular data.

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