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Molecular Clocks and Explosive Radiations

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Abstract. Molecular data are ideal for exploring evolutionary history because of its universality, stochasticity, and abundance. These features provide a means of exploring the evolutionary history of all organisms (including those that do not tend to leave fossils), potentially within a statistical framework that allows testing of evolutionary hypotheses. However, the discrepancy between molecular and paleontological dates for three key "explosive" radiations inferred from the fossil record—the Cambrian explosion of animal phyla and the post-KT radiations of modern orders of mammals and birds—have led to a reexamination of the assumptions on which molecular dates are based. Could variation in the rate of molecular evolution, perhaps associated with "explosive" radiations, cause overestimation of diversification dates? Here I examine four hypothetical causes of fast molecular rates in explosive radiations—body size, morphological rate, speciation rate, and ecological diversification—using available empirical evidence on patterns of variation in rate of molecular evolution.

Key words: Cambrian explosion — KT — Generation time effect — Adaptive radiation — Substitution rate — Morphological evolution

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Introduction

Molecular clocks, if we can get them right, are one of the most useful tools in evolutionary biology, providing us with a way of examining the evolutionary past and processes of all extant lineages. The ability to date the origin of all biological lineages would allow us to answer important questions that are currently opaque to us. Some of these questions will have great practical implications, for example, the ability to trace the origins of emerging diseases (e.g., Korber et al. 2000). In other cases, molecular dates will shed light on long-standing controversies in evolutionary biology, such as the "explosive" origins of the animal phyla in the early Cambrian. Many of the modern animal phyla enter the fossil record more or less simultaneously half a billion years ago, prompting suggestions that the Cambrian explosion of animal body plans is too rapid to be explained by simple microevolutionary processes. However, molecular dates point to a much earlier origin of phyletic lineages, leading to the suggestion that the animal phyla have a long hidden history (e.g., Bromham et al. 1998; Runnegar 1982; Wray et al. 1996). These molecular dates could therefore have an important influence on our interpretation of the tempo and mode of evolution in deep time.

However, the molecular dates for the radiation of animal phyla have been called into question. Molecular dates for some other explosive radiations identified from the fossil record have also been the subject of controversy. Like the dates for the Cambrian explosion of animal phyla, molecular dates for the post-KT explosion of modern mammal and bird orders are also up to twice as old as the fossil evidence would

suggest (e.g., Kumar and Hedges 1998; Madsen et al. 2001). Because of this repeated pattern, it has been suggested that some aspects of explosive radiations might speed the molecular clock (Archibald 1999b; Conway Morris 1998; Lee 1999; Valentine et al. 1999; Vermeij 1996). There are many aspects of the estimation of molecular dates that could have serious effects on their accuracy and precision, such as the appropriateness of substitution models, the accuracy of calibration dates, and the use of nonindependent data points in analyses (e.g., Bromham 2003; Smith and Peterson 2002). However, this paper is concerned with specific aspects of explosive radiations that might influence the rate of molecular evolution, generating dates estimates that are consistently too old.

There are four main hypothesized links between features of adaptative radiations and the rate of molecular evolution: body size, rate of morphological change, speciation rate, and ecological diversification.

1. Rates of molecular evolution are apparently inversely associated with body size (and its covarying life history traits) for various genes in vertebrates (Bromham 2002; Bromham et al. 1996; Martin and Palumbi 1993; Mooers and Harvey 1994). This has prompted the suggestion that the presumed small size of stem lineages of major radiations could generate faster early rates, making dates too old (Bromham et al. 2000; Conway Morris 1998; Vermeij 1996).
2. A study that reported correlated rates of molecular and morphological evolution for a number of phylogenies (Omland 1997) has prompted the suggestion that elevated pace of phenotypic change in explosive radiations could increase the rate of molecular evolution (Archibald 1999b; Conway Morris 1998; Lee 1999).
3. If the observed relationship between species diversification rates and genetic distance for angiosperms (Barraclough et al. 1996; Barraclough and Savolainen 2001) is indicative of a more general relationship between speciation rate and rate of molecular evolution, an increased speciation rate in explosive radiations might result in faster rates of molecular evolution.
4. Adaptive radiations are characterized by radiation into new niches, which might increase genomic rates of change as species adapt to new lifestyles and are released from previous constraints.

Molecular phylogeneticists have largely ignored these hypothesized causes of fast rates in explosive radiations, but these hypotheses should be seriously explored. Rate variation is widespread and is sometimes associated with species traits, such as life history, reproduction dynamics, or population size. So if traits evolve as species evolve, then we should expect rates to evolve along trees. If explosive radiations are characterized by a consistent change in any of these species traits, or by macroecological phenomena such as increased speciation rate, then it may potentially generate concerted changes in rates of molecular evolution (where the substitution rate changes in a consistent direction in multiple independent lineages, producing a consistent, directional pattern of rates across the phylogeny). It would seem appropriate to test these hypotheses for fast rates in explosive radiations when trying to resolve the difference between molecular and paleontological dates for the KT and Cambrian radiations.

Body Size

One of the most consistently identified trends in rates of molecular evolution is the negative body size trend in vertebrates (Martin and Palumbi 1993). This has been identified for both mitochondrial and nuclear genes for mammals (Bromham et al. 1996) and reptiles (Bromham 2002) and for DNA–DNA hybridization data for mammals (Mooers and Harvey 1994). The cause of this relationship is not certain. The two most common explanations are a DNA copy error effect, driven by difference in generation time (Bromham et al. 1996; Li et al. 1996; Ohta 1993), and variation in mutation rate due to metabolic rate (Martin 1995, 1999; Martin and Palumbi 1993; Rand 1994). The generation time effect assumes that smaller animals with more rapid generation turnover will copy their germline DNA more often per unit time than their larger relatives and therefore collect more DNA replication errors. The hypothesis that DNA copy frequency influences substitution rate is supported by the observation of male-driven evolution: in mammals, the male germline has a greater number of replications than the female germline, and so genes that spend proportionally more of their time in males (comparing Y-chromosome genes to somatic to X-chromosome) have a greater rate of substitution (Chang et al. 1994; Ellegren and Fridolfsson 1997; Shimmin et al. 1993).

Generation time appears to explain the rate variation in mammal and bird genes better than variation in metabolic rate (Bromham et al. 1996; Mooers and Harvey 1994). However, generation time is not an entirely satisfactory explanation of the body size relationship, because (like the metabolic rate hypothesis) it predicts an increase in mutation rate with decrease in body size. Mutation rate is expected to be reflected predominantly in the silent (synonymous) substitution rate, yet the body size effect has been noted for both synonymous and nonsynonymous substitution rates (Bromham 2002) and total genetic distance (Martin and Palumbi 1993; Mooers and

Harvey 1994). It is possible that there is an additional factor that influences rates of molecular of evolution that also scales with body size (Bromham 2002; Bromham et al. 1996).

The negative body size effect for vertebrates demonstrates that lineage-specific rate variation can be widespread among species, rather than being the exception to the rule, and that even closely related species can vary systematically in rate. Furthermore, the body size trend implies that rates can evolve along the phylogeny as species' size and life history characters change over evolutionary time. This could be important for dating the origin of mammal lineages from molecular data. Almost every order of modern mammals increased in average body size from the first appearance in the fossil record to the present day. So if substitution rates are influenced by body size (or its correlates), then rates could have slowed down in many mammalian lineages, particularly during the early part of the radiation of modern mammals. Could the body size effect produce sufficient change in rates to bias molecular date estimates of the origins of modern mammal orders?

To illustrate the potential for concerted change in rate due to evolving body size, we can explore a very simple example. Consider three mammalian species: rat, cow, and human. Each of these species is much larger than its earliest identifiable ancestor from the fossil record (Fig. 1). Although the origins of the rodent lineage are unclear, recent discoveries have pointed to the Mixodontidae as a possible ancestral group (Meng et al. 1994). Mixodonts first appear in the latest Palaeocene (60–52 Mya), known primarily from dentition, with a jaw length of around 1.5 cm (Dasheveg and Russell 1988; Li et al. 1987). The extinct primate *Purgatorius* is considered by some to be the earliest known member of modern primates. A purported late Cretaceous specimen (based on a single tooth [Van Valen and Sloan 1965]) is disputed (e.g., Archibald 1999a; Martin 1990), but there are more informative fossils of *Purgatorius* from the early Eocene, suggesting a body size of less than 100 g. And the "rabbit-sized" *Diacodexis*, from the early Eocene (54–38 Mya), is widely considered to be basal to the radiation of modern artiodactyls (Janis et al. 1998; Rose 1996; Stucky 1998). This increase in body size is not simply an artifact of choosing large extant species: the mode of extant species is also greater than that of the putative ancestral taxa (Fig. 1).

Given the increase in body size, it seems fair to assume that average generation times have also increased for these lineages. Can we predict how much rates of molecular evolution would have changed, given a general generation time effect on mammalian substitution rates? The best estimate of the magnitude of the generation time effect for mammals is for synonymous substitution rates for the mitochondrial

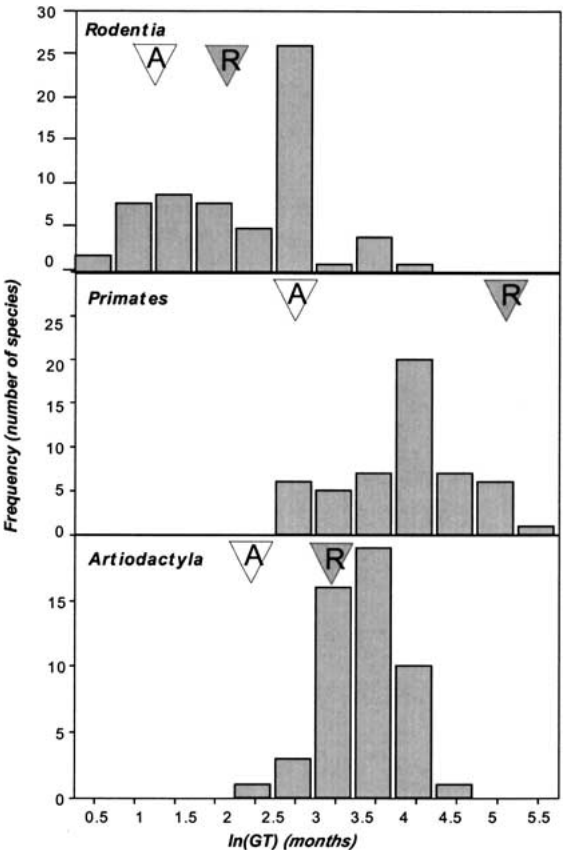

Fig. 1. Distribution of log generation length (months) for extant species of three mammalian orders. Note that an estimate of generation time was not available for all species, so the histogram represents a subset of the species in the order 63 of 171 rodent species, 53 of 136 primate species, 50 of 79 artiodactyl species. The log generation times of the representative species used in this model—*Rattus norvegicus* for Rodentia, *Homo sapiens* for Primates, and *Bos taurus* for Artiodactyla—are indicated by *gray triangles* marked "R." The predicted ancestral log generation times, based on comparison of the size of the ancestral taxon to an extant "analogue," are indicated by *white triangles* marked "A"—these estimates are expected to be conservative. The smaller species of *Mus* were used as an extant analogue of the mixodonts. The early primate *Purgatorius*, with an estimated body size of 100 g, is smaller than any extant primate, so the average generation length for three of the smallest species of prosimians was used (each with a body size of around 200 g). The only extant artiodactyl species close to the early artiodactyl *Diacodexis* in size is the Lesser mouse deer, *Tragulus jarvanicus*. Generation time data were taken from Silva and Downing (1995) and sources listed by Bromham et al. (1996).

protein-coding gene, *cytochrome b*, estimated from a relatively large number of phylogenetically independent comparisons spanning most major groups of mammals (Bromham et al. 1996). A regression through the origin allowed a rough prediction of change in rate as generation time evolves (see legend to Fig. 2). Starting with an arbitrary initial rate at the root of the rat–cow–human triplet, every lineage begins with the rate of the lineage immediately before the node. The rate then changes halfway along the lineage (Penny et al. 1998) by a factor determined by

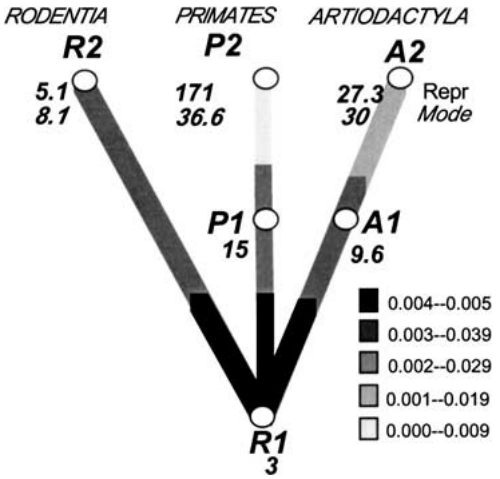

Fig. 2. Model tree for rate changes due to changing generation time for three mammalian lineages, Rodentia, Primates, and Artiodactyla. The relationships are presented as a polytomy, but the results are little different if calculated for a bifurcating triplet if the initial splits are close to the root (as expected for an explosive radiation). Because the ancestral taxon of all three lineages is not known, for simplicity the earliest rodent (R1) is considered to approximate the ancestral condition. Estimated generation times in months for the ancestral condition (R1 for rodents, P1 for primates, and A1 for artiodactyls) are given at the base of each lineage, the generation time for the representative extant species is given at the tip of each lineage (R2, P2, and A2), and the mode of extant orders is given in *italics* below it (see Fig. 1 for generation length data). A regression equation based on data of Bromham et al. (1996) allowed change in generation time to be used to estimate change in substitution rate (based on synonymous substitutions for *cytochrome b:* $\ln(A/B) = -0.5[\ln(GT_A/GT_B)]$, $R^2 = 0.32$). The changes in rate predicted by the model, with an initial rate at R1 of 0.005 sub $\cdot$ site$^{-1} \cdot t^{-1}$ and an arbitrary time scale of 90 units of time (t) from root to tip (with the primate and artiodactyl ancestors [P1 and A1] at 55t), show a deceleration in rate in each of the three test lineages.

the postulated change in generation time between the ancestor and the tip, given the relationship between generation time and synonymous substitution rate (Fig. 2). This simple model produces a ratio of relative branch lengths that is broadly similar to empirical estimates of rate variation for these three species (Yang and Nielsen 1998). It also produces faster rates early in the history of the lineages, slowing down in the later part of the phylogeny. So for this particular model, a calibration rate estimated based on one of the intraordinal dates (P1 or A1) would be slower than the rate early in the phylogeny, which could cause overestimation of the ordinal divergence by between 50% and 140%.

However, while this very simple example illustrates the potential for evolving rates, it does not necessarily imply that published molecular estimates for the mammalian radiation are incorrect. This example is based on synonymous substitution rate for a single gene and life history data for three species. Whether this pattern could account for the discrepancy between molecular and palaeontological dates of the eutherian radiation depends on several factors: (i) the degree and rate of increase in generation time/body size subsequent to ordinal divergence; (ii) whether the generation time/body size effect is genomewide or a feature of only a small number of genes; and (iii) whether the generation time/body size effect for mammals is restricted to synonymous substitution rate. A generation time effect only on synonymous substitutions might have a minimal effect on molecular dates for the mammalian radiation, which are predominantly based on nonsynonymous changes. However, the inverse body size effect observed for total genetic change for other vertebrates (Bromham 2002; Martin and Palumbi 1993; Mooers and Harvey 1994) suggests that we should not rule out the possibility of a more general life history trend in molecular evolution rate that could effect molecular dates for the mammalian radiation.

It is not clear whether a body size/life history effect on rate of molecular evolution could provide a general explanation of the surprisingly old molecular dates for other explosive radiations. The radiation of bird orders or metazoan phyla was not necessarily accompanied by increased average body size, and it is not known if the body size effect on rate of molecular evolution applies to nonvertebrate lineages. However, it does illustrate the point that if rates are correlated with species characters, and if those characters change in a concerted way over the course of an adaptive radiation, then it could produce a systematic pattern in rates that could produce a consistent bias in molecular date estimates.

Morphological Rate

Molecular evolution has been considered to be largely independent of phenotypic evolution, based on both theoretical and lab-based studies. Although adaptations (usually) result from genetic change, the number of nucleotides affected by any given selection event will be vanishingly small compared to the total genome size. Most substitutions will occur in noncoding regions, or will not cause an appreciable change of gene function, so are expected to be effectively neutral (Kimura 1983; Ohta 1993). So if we are concerned about the effect of pace of phenotypic evolution on the validity of the molecular clock, we need to consider whether there is any general increase in genomewide molecular evolution rates associated with rapid morphological evolution, rather than the specific effect of a given adaptive event on a very small number of nucleotides.

A connection between pace of adaptation and rate of molecular change may exist at a vary broad level—for example, HIV has one of the highest known DNA substitution rates, which is at least partly

responsible for its ability to adapt rapidly to host immune response. But a number of observations speak against a more general association between phenotypic and genetic rates of change. There is no obvious relationship between amount of morphological change and molecular branch length along phylogenies. Fast-evolving "hypotelic" taxa do not have consistently longer branches than slowly evolving bradytelic taxa. "Living fossils" such as coelacanths do not have particularly slow rates of molecular change. A long-term experiment of the bacterium *Escherichia coli* over 10,000 generations found that periods of rapid adaptation were not accompanied by bursts of molecular change: instead the molecular change accumulated more or less steadily throughout the experiment (Papadopoulos et al. 1999). However, a recent study reporting an association between molecular and morphological branch lengths (Omland 1997) has been used to suggest that rapid phenotypic evolution associated with explosive radiations should be accompanied by faster molecular rates (Archibald 1999b; Conway Morris 1998; Lee 1999).

Omland (1997) found a significant correlation between morphological and molecular branch lengths for eight phylogenies, using both root-to-tip pathways for each species and rates of change along the tips of phylogenies. However, this relationship may be an artifact of the analysis, for two reasons. First, by using all root-to-tip pathways, the correlations were performed on nonindependent data points, which could generate a spurious association between variables. Second, using parsimony to estimate both molecular and morphological rates may have introduced a shared measurement bias that could cause estimates of rate to be correlated. Because parsimony does not model multiple hits, it tends to underestimate the number of substitutions on long unbroken branches. For long branches, rates estimated by parsimony are likely to be artificially low for both molecular and morphological rates, potentially generating an artificial association between the two. A subsequent analysis of morphological and molecular rates for a larger sample of data sets used three new methods designed to overcome these biases (Bromham et al. 2002). Molecular rates were estimated using maximum likelihood, which is robust to node density effect, thus breaking the shared measurement bias. Statistical independence was ensured by using only phylogenetically independent comparisons. These methods revealed no evidence of an association between morphological and molecular rates for the 13 vertebrate phylogenies tested.

Neither of these studies (Bromham et al. 2002; Omland 1997) is a particularly satisfactory way to explore the possibility of a link between phenotypic and genotypic rates of changes. The "total evidence" data sets that both studies relied upon were designed to delineate phylogenetic relationships, not to measure rates of adaptive change. Genes chosen for phylogenetics tend to be "housekeeping genes," associated with basic functions such as metabolism and gene expression. Morphological characters for these data sets are easily measurable characters chosen to delineate natural groups (for example, skull measurements predominate in vertebrate data sets). In order to explore the possibility of a link between phenotypic and molecular rates more thoroughly, it would be helpful to look at a much wider range of taxa and a broader range of datatypes, for example, measures of morphological disparity or estimates of whole-genome change (Bromham et al. 2002). Based on current evidence, there is no reason to believe that there is a general link between morphological and molecular rates of change that could influence the accuracy of molecular date estimates.

Speciation Rate

Explosive radiations are characterized by the rapid generation of many new lineages. An investigation of rates of molecular evolution in the *rbc*L gene of flowering plants revealed an association between the species richness of a clade and molecular branch length (Barraclough et al. 1996; Barraclough and Savolainen 2001). A similar finding was reported for DNA–DNA hybridization for passerines birds (but not for nonpasserines [Barraclough et al. 1998]). Neither the generality of the relationship nor its underlying causes are known. Lineages with high rates of molecular evolution may be predisposed to speciation. Higher rates of molecular evolution might generate more genetic variation which could be selected for in incipient species, although it seems unlikely that mutation rate would be a limiting factor in the evolution of most new species. More plausibly, higher rates of molecular evolution could influence the formation of new species by speeding the evolution of hybrid incompatibility (see Wu 2001). Alternatively, faster species diversification could drive a higher substitution rate. For example, if speciation results in repeated subdivision of the population, the lowered effective population size could accelerate the rate of fixation of nearly neutral substitutions. Allele frequencies in small populations are greatly affected by random sampling, so that the frequency of alleles of small selective effect (nearly neutral mutations) will be governed by drift rather than selection. So while the fixation of advantageous alleles is faster in large populations (or populations undergoing exponential growth [Otto and Whitlock 1997]), the rate of fixation of nearly neutral mutations will be higher in small populations (Ohta 1987). If rapidly speciating lineages spend more time at a low population size, this

may drive the observed association between species richness and rate of molecular evolution. A third possibility is that molecular rate and diversification rate may both be correlated with another causal factor, for example, small body size. Any influence of speciation rate on rate of molecular evolution could have important consequences for attempts to reconstruct the molecular phylogeny of adaptive radiations and, in particular, could cause consistent errors in molecular date estimates for explosive radiations. It is imperative that this relationship is examined for more genes and a wider range of taxa.

Ecological Diversification

Explosive radiations are often characterized by lineages evolving rapidly into new niches. For example, the diversification of animal phyla in the early Cambrian is often interpreted as the creation of a complex, multilayered ecology, with the introduction of predators and the acquisition of defences by the predated. The radiation of modern mammals and birds is commonly interpreted as filling niches left vacant by the final extinction of the dinosaurs in the late Cretaceous. Adaptive radiations such as these may be associated with many evolutionary processes that could potentially effect rate of molecular evolution, such as novel adaptations as they evolve into a new niches, release from the constraints of the old niches, and genetic bottlenecks as a new species emerges from a small founding population.

To explore whether the process of rapidly diversifying into empty niche space speeds the rate of molecular evolution, it would be helpful to be able to compare rates of molecular evolution in clades undergoing rapid ecological diversification with closely related lineages that have not diversified. Island endemic radiations may provide a useful test case. Founded by a few colonists, released from the constraints of the mainland, island lineages often undergo accelerated rates of change and diversification to produce many new lineages. The degree of morphological and ecological change of island endemic radiations is illustrated by classic examples such as Darwin's finches on the Galapagos or silverswords on Hawaii. Because island radiations have long been a focus of studies on species diversification, there is a wealth of sequence data, morphological measurements and, for some islands, geological dates of origin for island endemic clades. A study of island birds species reported an increased rate of nonsynonymous change (Johnson and Seger 2001). However, a study of substitution rates in 17 separate island adaptive radiations and their mainland relatives, including Darwin's finches on the Galapagos Islands, *Drosophila* on the Hawaiian islands, and *Anolis* lizards in the Carribean, found no such association (L. Bromham, unpublished). Further investigation of adaptive diversification and rates of molecular evolution would shed more light on the hypothesis that explosive radiations speed the molecular clock.

Could Explosive Radiations Speed the Molecular Clock?

Of the four hypothesized causes of fast rates during explosive radiations—small body size, rapid morphological change, accelerated speciation rate, and ecological diversification—none has yet been shown to provide a general explanation for the discrepancy between molecular dates and the fossil record for three key explosive radiations inferred from the fossil record (Cambrian metazoans, early Tertiary mammals and birds).

Body size provides the most convincing case study. The simple model presented here illustrates that an association between substitution rate and life history could cause a molecular slowdown during the mammal radiation. Whether this is sufficient to make molecular date estimates of the mammalian radiation too old depends on the universality of the generation time effect, which has been demonstrated only for vertebrate taxa and for relatively few genes. There is currently no evidence to suggest a link between molecular evolution rates and rate of morphological evolution or ecological diversification, but clearly these hypotheses should be tested further. The speciation rate effect requires broader testing: if the relationship observed between species richness and substitution rate for angiosperms is indicative of a more general phenomenon, it could be an important source of error in molecular dates.

More generally, these hypotheses illustrate the importance of considering correlates of rate variation when assessing the accuracy and precision of molecular date estimates. Comparative studies continue to reveal species traits that correlate with rate of molecular evolution, for example, with population size (e.g., eusocial animals may have faster rates than their nonsocial relatives [Schmitz and Moritz 1998]), reproductive traits (e.g., snakes with larger clutch sizes have faster rates [Bromham 2002]), or niche (e.g., mangroves have faster rates than their nonmangrove relatives [Zhong et al. 2002]). Lineage-specific rate variation is, in itself, sufficient to cause significant bias in date estimates. For example, the rate of molecular evolution in murid rodents appears to be at least twice that in hominids (Easteal and Collett 1994; Gu and Li 1992; Li et al. 1996; Wu and Li 1985; Yang and Nielsen 1998), yet this variation will not always be detected by commonly used "clock tests" (e.g., relative rates test, Tajima test, linearized

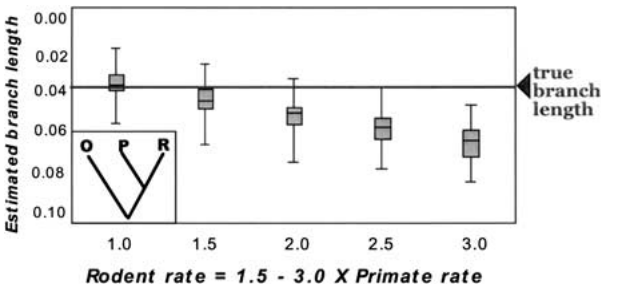

Fig. 3. Demonstration of the influence of rate variation on the accuracy of molecular date estimates, using simulated DNA based on sequence data used in a study that estimated dates of divergence of modern mammalian orders (Hedges et al. 1996). For the sequences used in this study, clock tests are expected to detect less than a fifth of the sequences for which the rodent lineage has a rate 1.5 times that of primates (see Bromham et al. 2000). Sequences of length 700 were simulated along a triplet representing rodent and primate lineages and an outgroup, where the rodent lineage had a substitution rate 1.0–3.0 times faster than the primate and outgroup rate (given that, in this simulation, all sites are equally variable, this result is expected to be applicable to much longer sequences for which only a proportion of all positions are variable). Each simulated data set was subjected to the Tajima (1993) test, and those data sets that passed the Tajima test were analyzed as if rate constant. Box plots represent mean, maximum, minimum, and quartiles of the estimates given by all data sets that passed the Tajima test at each level of rate heterogeneity. The true branch length of the primate lineage (*horizontal line*) is overestimated by increasing amounts as the degree of the undetected rate variation rises. See Bromham et al. (2000) for details of the analysis.

tree methods, parametric bootstrap [Avise 1994; Bromham et al. 2000; Rambaut and Bromham 1998; Robinson et al. 1998; Scherer 1989; Tajima 1993]). If these sequences are included in molecular clock studies which assume constant rates, the result will be consistent overestimation of the date of divergence between these taxa (Fig. 3).

But the problem becomes even more daunting: if substitution rates are influenced by species characters, then they should evolve along phylogenies as species evolve. This deterministic change in rate could produce concerted patterns in rates across different lineages, which will be much trickier to deal with than rates which vary stochastically over phylogenies. Unlike a random walk of rates over the tree, which is expected to decrease the precision of date estimates, systematic variation in rates could produce consistent and repeatable bias in date estimates. If rates ran fast during a given explosive radiation, then dates based on a calibration rate either taken from subsequent divergence events or averaged over the whole tree will tend to produce molecular dates estimates that are too old, no matter what genes, taxa, or calibration points are used (Bromham and Hendy 2000; Bromham et al. 1999, 2000). It is not clear how current variable-rate phylogenetic methods (e.g., Kishino et al. 2001; Sanderson 2002), which effectively model rate changes as a random walk of rates over the tree, will fare when faced with systematic rate variation of this kind.

The discrepancy between molecular and palaeontological dates for several major radiations has led to reexamination of the accuracy and precision of both molecular clocks and the fossil record. If nothing else, the controversy over dates for these explosive radiations has prompted exploration of the determinants of variation in rate of molecular evolution, which may (hopefully) lead not only to more reliable molecular date estimates but also to a deeper understanding of molecular evolution.

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