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# A new approach to DNA-aided ancestral trait reconstruction in mammals

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## A recommendation of

Wu J, Yonezawa T, Kishino H. 2016. **Rates of Molecular Evolution Suggest Natural History of Life History Traits and a Post-K-Pg Nocturnal Bottleneck of Placentals.** *Current Biology* 27: 3025-3033. doi: 10.1016/j.cub.2017.08.043

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Reconstructing ancestral character states is an exciting but difficult problem. The fossil record carries a great deal of information, but it is incomplete and not always easy to connect to data from modern species. Alternatively, ancestral states can be estimated by modelling trait evolution across a phylogeny, and fitting to values observed in extant species. This approach, however, is heavily dependent on the underlying assumptions, and typically results in wide confidence intervals.

An alternative approach is to gain information on ancestral character states from DNA sequence data. This can be done directly when the trait of interest is known to be determined by a single, or a small number, of major effect genes. In some of these cases it can even be possible to investigate an ancestral trait of interest by inferring and resurrecting ancestral sequences in the laboratory. Examples where this has been successfully used to address evolutionary questions range from the nocturnality of early mammals [1], to the loss of functional uricases in primates, leading to high rates of gout, obesity and hypertension in present day humans [2]. Another possibility is to rely on correlations between species traits and the genome average substitution rate/process. For instance, it is well established that the ratio of nonsynonymous to synonymous substitution rate, dN/dS, is generally higher in large than in small species of mammals, presumably due to a reduced

effective population size in the former. By estimating ancestral dN/dS, one can therefore gain information on ancestral body mass (e.g. [3-4]).

The interesting paper by Wu *et al.* [5] further develops this second possibility of incorporating information on rate variation derived from genomic data in the estimation of ancestral traits. The authors analyse a large set of 1185 genes in 89 species of mammals, without any prior information on gene function. The substitution rate is estimated for each gene and each branch of the mammalian tree, and taken as an indicator of the selective constraint applying to a specific gene in a specific lineage – more constraint, slower evolution. Rate variation is modelled as resulting from a gene effect, a branch effect, and a gene X branch interaction effect, which captures lineage-specific peculiarities in the distribution of functional constraint across genes. The interaction term in terminal branches is regressed to observed trait values, and the relationship is used to predict ancestral traits from interaction terms in internal branches. The power and accuracy of the estimates are convincingly assessed via cross validation. Using this method, the authors were also able to use an unbiased approach to determine which genes were the main contributors to the evolution of the life-history traits they reconstructed.

The ancestors to current placental mammals are predicted to have been insectivorous - meaning that the estimated distribution of selective constraint across genes in basal branches of the tree resembles that of extant insectivorous taxa - consistent with the mainstream palaeontological hypothesis. Another interesting result is the prediction that only nocturnal lineages have passed the Cretaceous/Tertiary boundary, so that the ancestors of current orders of placentals would all have been nocturnal. This suggests that the so-called "nocturnal bottleneck hypothesis" should probably be amended. Similar reconstructions are achieved for seasonality, sociality and monogamy – with variable levels of uncertainty.

The beauty of the approach is to analyse the variance, not only the mean, of substitution rate across genes, and their methods allow for the identification of the genes contributing to trait evolution without relying on functional annotations. This paper only analyses discrete traits, but the framework can probably be extended to continuous traits as well.

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