Adaptive vs. relaxed selection on animal mitochondrial genes

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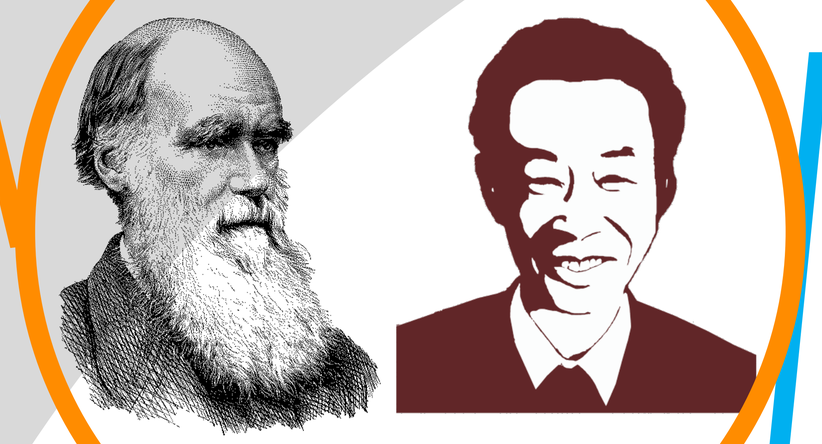
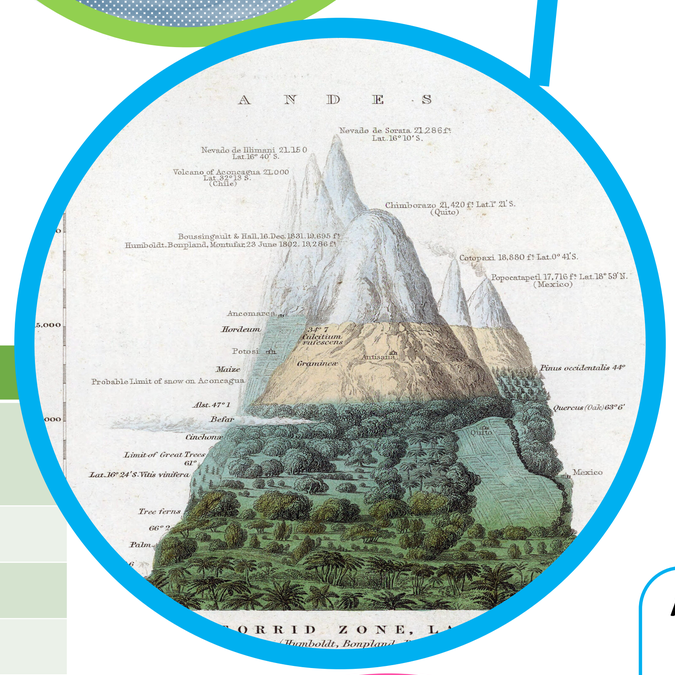
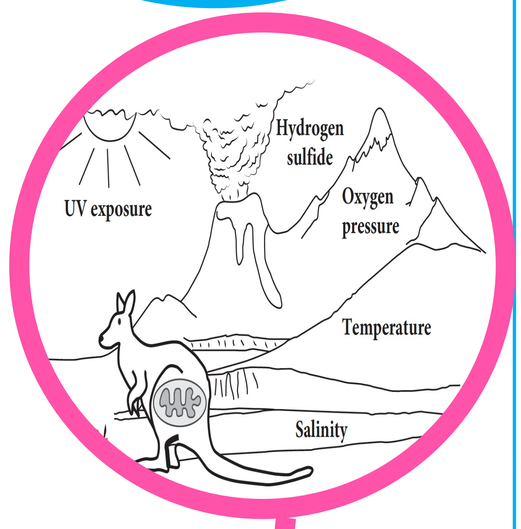
Introduction

Mitochondrial genes are highly popular targets for phylogenetic and population genetic analyses in animals. Variation in mtDNA sequences was historically assumed to be neutral due to the extreme functional constraints on oxidative phosphorylation (OXPHOS). While the idea of strict mtDNA neutrality has been systematically obliterated, the field may have overcorrected. Publicly available animal mitogenomes are abundant, and elevated d_N/d_S ratios (the ratio of nonsynonymous to synonymous substitution rates) have been interpreted as signs of positive selection in many lineages with an interesting energetic phenotype. However, relaxed purifying selection can also produce this pattern. Here, we reevaluated eight individual case studies describing elevated d_N/d_S ratios in the mtDNA of specific lineages of birds, mammals, snakes, fishes, insects, mollusks, and primates. We also explored the general hypothesis that mtDNA is under positive selection in high vs. low elevation lineages.







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Methods

Mt genomes (1209 in total) were used to test 8 published case studies (Table 1) and whether high elevation exerts positive selection on mtDNA (n = 154) via d_N/d_S ratios and RELAX (Fig. 1)

Table 1. Case studies evaluated

Case	Focal Taxa	Reference Taxa	Hypothesis
1	Bats	Flightless mammals	Pos. w/ flight
2	Birds	Flighted birds	Relax. w/ flight loss
3	Insects	Flighted insects	Relax. w/ flight loss
4	Snakes	Lizards	Pos. w/ snak-iness
5	Elephantfishes	Non-electric fishes	Pos. w/ electric
6	Knifefishes	Non-electric fishes	Pos. w/ electric
7	Primates	Other mammals	Brain-energy hypoth.
8	Salamanders	Frogs	Relax w/ low MR

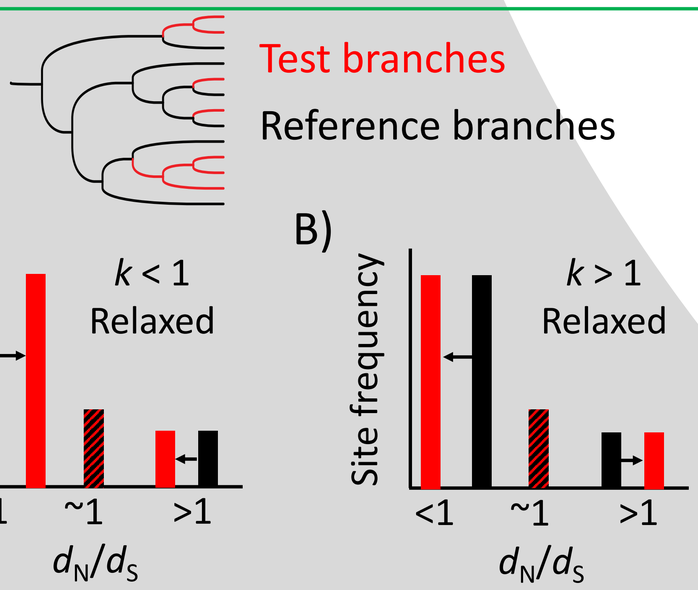

Fig. 1. Using RELAX to detect (A) relaxed and (B) intensified/positive selection on test branches in a phylogeny relative to reference branches. Under relaxed selection, d_N/d_S categories are pushed towards 1, while under intensified/positive selection they are pushed away from 1.

Results

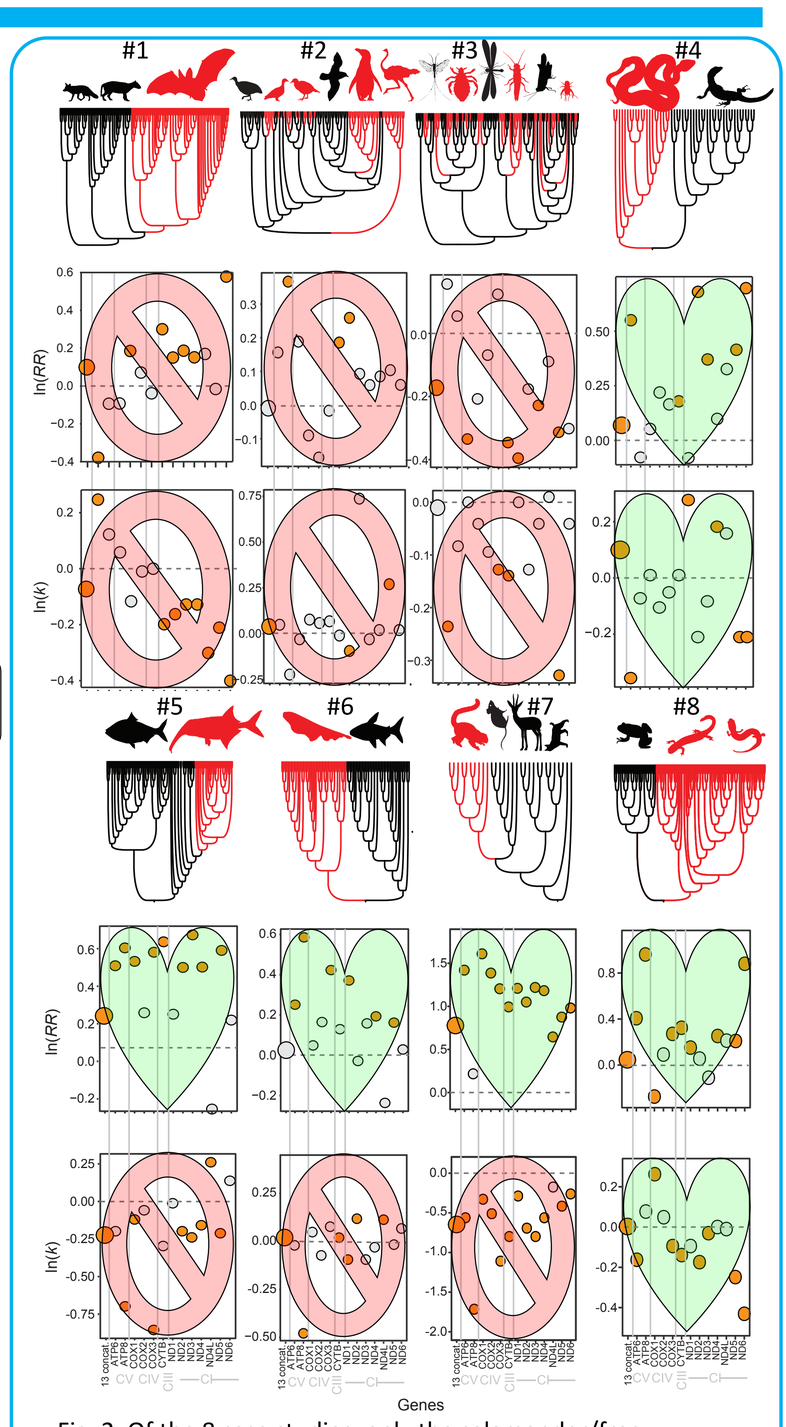

Fig. 2. Of the 8 case studies, only the salamander/frog comparison (#8) was convincingly supported. For each case study top row shows topology of test and reference branches (in red/black), middle row is ln*RR* of test vs. reference d_N/d_S, and bottom row in ln k of the RELAX test statistic.

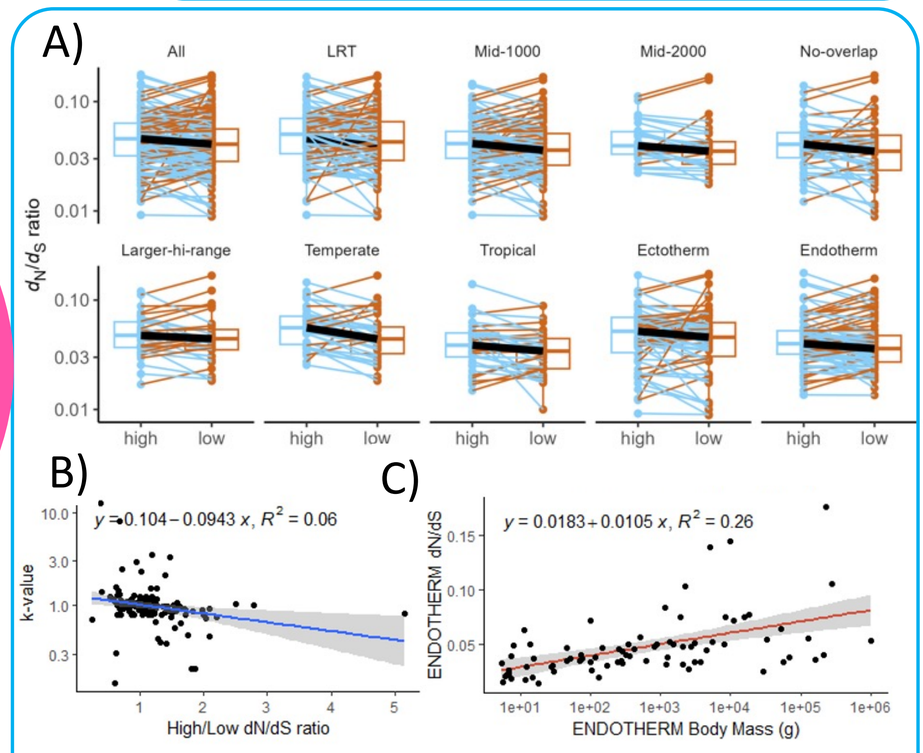

Fig. 3. Across 154 comparisons, there was a modest, but significant increase in d_N/d_S in high elevation compared to low elevation species (A). However, this may be driven by relaxed, not intensified positive selection in high elevation taxa (B), possibly due to lower effective population sizes at high elevation (C).

Conclusions

Almost none of the previous case studies held up – some were convincingly overturned (e.g., the brain-energy hypothesis in mammals). d_N/d_S ratios were elevated at high elevation, but likely not due to positive selection. d_N/d_S ratios should be explicitly evaluated considering **both** positive and relaxed selection.