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3. The Letter was written with input from the ERG Water Group.

## Mitochondrial DNA and Population Size

IN THEIR REPORT “POPULATION SIZE DOES NOT influence mitochondrial genetic diversity in animals” (28 Apr., p. 570), E. Bazin *et al.* present compelling evidence that selective sweeps occur in animal mitochondrial DNA (mtDNA) and reduce genetic diversity below the level expected at mutation-drift equilibrium in some taxa. They also assert that this evidence implies that mtDNA has limited relevance to biodiversity and conservation studies. I contest this claim on two fronts.

First, the selective sweeps that they detect occur at very deep phylogenetic levels (phyla to class), which translate into deep evolution-

ary time (hundreds of millions of years). It is rare that conservation biologists are interested in how mtDNA diversity is distributed at such a level. Rather, it is standard practice that genetic diversity is interpreted in the context of a relevant, almost always closely related, control group (1). This practice is designed to account as best as possible for the potentially confounding historical, demographic, mutational, and selective variables that influence genetic diversity.

Second, it is well established that the geographical distribution of mtDNA diversity as determined by lineage-sorting, and not just diversity per se, is informative with respect to biodiversity conservation (2–4). Use of this criterion is recognized to address the very differences in accumulation or maintenance of genetic diversity within different taxa described by Bazin *et al.*—otherwise known as the “how much divergence is enough” question (3).

Clearly, conservation biologists should not ignore selective sweeps; they do occur, and sometimes rapidly (5). However, mtDNA diversity is abundant at the population, species, and genus level of animals (2), and it is here that it can be, and is, most relevant and rou-

tinely exploited for conservation purposes. This would not be the case if selective sweeps were as dominant a force as implied by Bazin *et al.* Despite their claims, Bazin *et al.*'s results have limited relevance to most standard applications of mtDNA in conservation.

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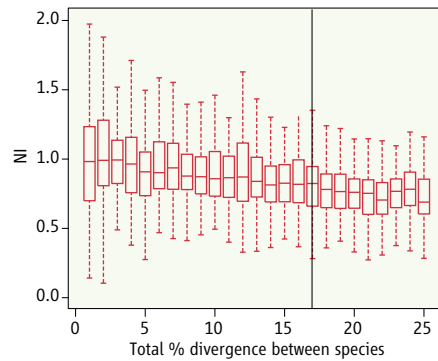
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IN A META-ANALYSIS OF GENETIC POLYMORPHISM, E. Bazin *et al.* suggest that mitochondrial DNA (mtDNA) is more profoundly affected by nonneutral evolution than nuclear loci (“Population size does not influence mitochondrial genetic diversity in animals,” Reports, 28 Apr., p. 570). This interpretation has already led some to conclude that mtDNA is of little utility in studies of evolution and conservation. It is well known

that multiple evolutionary processes must be considered in interpreting patterns of genetic diversity at any gene region (1, 2). However, dismissing mtDNA as a more biased analytical tool is neither necessary nor justified (3).

First, it is inappropriate to approximate effective population size ( $N_e$ ) from census size, as is implied by Bazin *et al.*'s "intuitive" predictions. Bottlenecks, fluctuating population size, reproductive strategies, and geographic structure, none of which can be inferred reliably from present census size, profoundly impact  $N_e$  and genetic diversity (4). Indeed, invertebrate taxa and fish generally have greater census size than tetrapods, but there is also greater diversity in life history and reproductive strategies, traits that alter patterns of sequence divergence within and among taxa.

Second, the neutrality index (NI) may be inappropriate for distantly related taxa because the high substitution rate and site heterogeneity of mtDNA often lead to mutational saturation in protein-coding genes (see figure). This saturation biases the NI toward values  $<1$  as species divergence increases. The smaller number of invertebrate mtDNA genomes currently available tends to force



more distant outgroup comparisons.

Bazin *et al.* rightfully emphasize the necessity of adequately testing for deviation from the neutral model for mtDNA, as with all loci. Further, the meta-analytical tools developed by Bazin *et al.* and others can help assess the time scale of selective sweeps relative to demographic events commonly considered by evolutionary biologists (e.g., effects of glaciation, high variance in reproductive success, and recent/incipient speciation). All genetic data come with complications, but we argue that it is inappropriate and unnecessary to dismiss the contribution that mtDNA sequence data—still one of the most powerful universal sources of genetic variation for nonmodel

◀ Neutrality indices simulated for a single nonrecombining 1 kb coding region. For each interspecific distance class, 100 coalescent simulations were performed comparing an ingroup taxon of  $n = 10$  and expected within-species pairwise divergence of 2% to a single outgroup taxon. Simulations assume a transition:transversion ratio of 2 and a relative substitution rate of 2:1:20 for the first, second, and third codon positions, respectively. Thick horizontal bars indicate medians, and boxes include 50% of the distributions. The vertical line indicates the cutoff point used by Bazin *et al.* in their meta-analysis.

animals—can make to studies of conservation, taxonomy, and historical demography.

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## Letters to the Editor

Letters (~300 words) discuss material published in *Science* in the previous 6 months or issues of general interest. They can be submitted through the Web ([www.submit2science.org](http://www.submit2science.org)) or by regular mail (1200 New York Ave., NW, Washington, DC 20005, USA). Letters are not acknowledged upon receipt, nor are authors generally consulted before publication. Whether published in full or in part, letters are subject to editing for clarity and space.

### Response

Berry and Wares *et al.* independently comment on our conclusion that mtDNA might not be a reliable marker of species population size and diversity. They introduce four arguments: (i) age of selective sweeps, (ii) census size versus effective size, (iii) distance to outgroup, and (iv) the usefulness of mtDNA despite selective sweeps.

1) Despite the fact that our study is based on comparisons between distantly related taxa, the selective sweeps we think have contributed to decreased mtDNA diversity in large populations must be recent ones, because they have

influenced the level of polymorphism observable within species.

2) We agree that effective population size can be very different from census population size, to an extent largely variable between species. Our analysis, however, recovers a positive relationship between nuclear genetic diversity and indicators of species abundance, indicating that effective and census population sizes are correlated. The lack of relationship with mtDNA markers can therefore hardly be due to the census versus effective size problem, especially given the much larger data set analyzed.

3) It is true that very distant outgroups can bias the NI analysis because of saturation of the synonymous divergence ( $d_s$ ), as neatly demonstrated by Wares' simulations. Our data set does not show strong variation of mitochondrial  $d_s$  across taxa: the average  $d_s$  is 0.262 in invertebrates versus 0.266 in vertebrates.

4) We do not mean to argue that mtDNA markers should be abandoned; there are many practical reasons why they can be useful. We strongly caution mtDNA users, however, that within-species mtDNA variations are likely to be influenced by natural

selection, especially in invertebrate species, where adaptation might be the rule. The age of the most recent mtDNA ancestor, in particular, should not be connected to any climatic, geologic, or biotic event unless confirmation is obtained from nuclear markers.

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### TECHNICAL COMMENT ABSTRACT

#### Comment on "Population Size Does Not Influence Mitochondrial Genetic Diversity in Animals"

**Connie J. Mulligan, Andrew Kitchen, Michael M. Miyamoto**

Bazin *et al.* (Reports, 28 April 2006, p. 570) found no relationship between mitochondrial DNA (mtDNA) diversity and population size when comparing across large groups of animals. We show empirically that species with smaller populations, as represented by eutherian mammals, exhibit a positive correlation between mtDNA and allozyme variation, suggesting that mtDNA diversity may correlate with population size in these animals.

Full text at

[www.sciencemag.org/cgi/content/full/314/5804/1390a](http://www.sciencemag.org/cgi/content/full/314/5804/1390a)