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MtZoa – a new mitochondrial protein replacement matrix for metaozan phylogenetics

Mitochondrial DNA is a crucial source of information in the attempt to resolve the evolutionary relationships among animals, but the answers we get can only be as good as the methods we use. MtZoa is an amino-acid replacement matrix estimated specifically to reflect the evolutionary processes that have been in operation within Metazoa over the past half-a-billion years or so (Rota-Stabelli et al. 2009). MtZoa is intended for use with metazoan-wide mitochondrial protein datasets, and as such it fills the gap between the more taxonomically restricted matrices such as MtArt for arthropods (Abascal et al. 2007), and the more general matrices such as the WAG matrix (Whelan and Goldman 2001). The authors compare the performance of MtZoa with other static matrices and with the mechanistic GTR model (which involves estimating the entire replacement matrix from scratch for each new dataset). As expected, MtZoa outperforms other static matrices on the datasets for which it is intended. Additionally, MtZoa outperforms the parameter-rich mechanistic GTR model when performance is measured by the Bayesian Information Criterion, which penalises the inclusion of extra parameters. In this respect, it will be interesting to see how taxonomically-based matrices such as MtZoa perform relative to the recently proposed matrices based on protein structure (Le et al. 2008).

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Evolutionary constraints on mitochondrial DNA depend on the locomotive demands of the host

Bird mitochondria are much more efficient than those of other mammals (Herrero and Barja 1998), and this efficiency probably evolved as a response to the high metabolic demands of flight. However, not all bird species place the same metabolic demands on their mitochondrial DNA (mtDNA), as not all birds fly. Indeed, flightlessness has evolved a number of times independently within birds (e.g. penguins, kiwis, and the kakapo).

Shen et al. (2009) hypothesised that the mitochondrial genome might experience relaxed selection in flightless birds. As a result, mutations that decrease mitochondrial efficiency (i.e. most amino-acid changing mutations) should be tolerated more often in flightless birds than in their flying relatives. This hypothesis was tested by comparing the ratio of non-synonymous to synonymous changes (dN/dS) in

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the mtDNA of flightless versus flying birds. However, the difference in *dN*/*dS* of flightless versus flying birds was small. The authors then hypothesised that selective constraint might instead depend on locomotive speed, since some flightless birds (such as emus) can run faster than other birds fly. Using this metric, the authors show that birds with lower locomotive ability tend to have less constrained mtDNA (i.e. higher *dN*/*dS*) than those with higher locomotive ability. Even more surprisingly, this effect is repeated in mammals. This study forms part of a growing number of studies that have suggested the evolution of mtDNA is measurably affected by the metabolic demands of the host. It would be interesting to know whether the nucleus-encoded mitochondrial proteins experience similar selective regimes to their mitochondrion-encoded counterparts.

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Longevity, mutation rates, and the evolution of avian mitochondrial DNA

Two recent studies focus particularly on the evolution of avian mitochondrial DNA (mtDNA). Galtier et al. (2009a) show that, as is the case for mammals, longer-lived birds tend to have slower rates of amino acid substitution. They interpret this result as support for the longevity hypothesis—the idea that mitochondrial mutation rates are to a large extent controlled by selection on longevity (for a succinct review, see Galtier et al. 2009b). If you believe the mitochondrial theory of ageing (and not everybody does; e.g. Blagosklonny et al. 2008), then one way of achieving a longer lifespan is to reduce the rate at which somatic mitochondria accrue mutations. Thus, selection for increased longevity could result in selection for a lower mitochondrial mutation rate, which in turn results in a reduced mitochondrial substitution rate.

In a second study, some of the same authors (Nabholz et al. 2009) analyse avian mtDNA in more detail. The authors look exclusively at substitutions at third codon positions, which should for the most part be selectively neutral and thus reflect the underlying mutation rate. The results of this study are illuminating in a number of respects. First, they demonstrate that birds tend to have much lower substitution rates than mammals. This observation is in agreement with the longevity hypothesis (since birds tend to live longer than mammals of a similar size), but contradicts the metabolic rate hypothesis (since birds tend to have higher mass-specific metabolic rates than mammals of a similar size). Second, they demonstrate the mtDNA mutation rate is extremely variable in birds—although the average rate of change is approximately 2% per million years, there is more than 30-fold variation about this value among different lineages. This suggests that, in most cases, the application of strict molecular clocks to bird mtDNA is inappropriate. Finally, they show that mtDNA diversity in birds tends to be driven by the underlying mutation rate, rather than the effective population size of the species (although the available data on effective population size were limited).

Nabholz et al. (2009) also analyse the relationship between longevity and mtDNA mutation rates in birds in more detail. Although they confirm that longer-lived birds tend to have lower mutation rates (in agreement with the longevity hypothesis), further analysis indicates that longevity is a worse predictor of mutation rates than body size. This result suggests that, in contrast to mammals, bird mtDNA mutation rates are not primarily driven by selection on longevity. It is perhaps the case that because birds have such high metabolic demands, selection acts primarily on mitochondrial efficiency rather than on longevity. From this viewpoint, the exceptional lifespan of many birds could be seen primarily as a by-product of their highly efficient mitochondria, rather than a direct result of selection. It will be fascinating to unravel further the evolutionary forces and interactions that have shaped avian mtDNA and life-history.

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Population mitogenomics of extinct species

Sequencing mitogenomes from ancient specimens has traditionally been hindered by a variety of factors, including extensive DNA damage and fragmentation, elevated levels of contamination, and undesirable demands on sample materials. In the past few years, the situation has been improved by multiplex-PCR techniques and high-throughput sequencing technology. The first studies of ancient population mitogenomics were published by Gilbert et al. (2007, 2008), who obtained sequences from the hair shafts of 15 woolly mammoths.

The field of ancient population mitogenomics has been expanded in two recent studies, both of which present novel methodologies for sequence retrieval. In the first study, Briggs et al. (2009) employ a "primer-extension-capture" approach to isolate target sequences from a library of degraded DNA. In this approach, 5′-biotinylated oligonucleotide probes bind specifically to small mitogenomic fragments in the library and are then captured using magnetic streptavidin beads. Using this method, the authors are able to overcome the significant influence of contamination in the process of sequencing the mitogenomes of five Neanderthals. The authors estimate that there was less than 1.4% contamination from modern human DNA, which is an astonishing achievement given that mitochondrial DNA represents only about 0.001% of the endogenous DNA present in a typical Neanderthal bone.

Based on phylogenetic analyses of the Neanderthal mitogenomes, along with those from a representative sample of modern humans, Briggs et al. (2009) estimate that the last common ancestor of the five Neanderthals existed about 110,000 years ago. Examination of the ratio of non-synonymous to synonymous rates of substitution reveals that the species probably had a smaller effective population size than modern humans.

In the second study, Stiller et al. (2009) present a cost-efficient method for sequencing multiple mitogenomes simultaneously. The authors use multiplex PCR to amplify DNA in 31 cave bear samples, tag the products using sample-specific barcodes, and then analyse the pooled products on a high-throughput sequencing platform. After conducting only two sequencing runs, the authors achieve a remarkable 96% coverage of the 31 mitogenomes.

Stiller et al. (2009) suggest that the levels of genetic divergence among the 31 cave bears reflect the existence of three distinct species. However, this inference will need to be strengthened by evidence from nuclear loci, given that the observed patterns of mitochondrial divergence are not inconsistent with those that might be expected from a single population (Rodrigo et al. 2008).

The new methodological approaches presented by Briggs et al. (2009) and Stiller et al. (2009) are significant not only because they overcome previous limitations associated with ancient DNA analysis, but also because they have the potential to reduce substantially the cost of sequencing ancient mitogenomes. This opens the way for the large-scale generation and analysis of mitogenomic data from extinct species.

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Tracking the demographic history of seals using mitochondrial DNA

In view of the rapidity and magnitude of anthropogenic climate change, the ability of animal populations to respond to environmental change is becoming an increasingly important concern. Mark de Bruyn et al. (2009) have examined this issue using a superlative study system: Southern elephant seals (*Mirounga leonina*) in the Antarctic. The modern distribution of this highly mobile species is circumpolar, including large colonies in Argentina, South Georgia, Macquarie Island, and the Kerguelen

Islands. Throughout much of the Holocene, however, the species also occupied a favourable habitat on the Victoria Land Coast in the Ross Sea, Antarctica. Open beach habitat became available after glacial retreat about 8000 years ago, but has disappeared in the past few hundred years as a result of glacial expansion and sea-ice enclosure.

de Bruyn et al. (2009) used ancient DNA techniques to study the extinct population of the Victoria Land Coast. By radiocarbon-dating and sequencing 223 samples of ancient seals, the authors were able to produce a precise demographic reconstruction using coalescent-based methods. de Bruyn et al. (2009) concentrated on the first hypervariable region of the mitochondrial genome, thereby maximising the efficiency with which information could be gained from the degraded ancient DNA.

The analyses of the DNA sequences yielded a number of key results. There was convincing evidence that the Macquarie Island population was the ancestral source of the Victoria Land Coast population, although it appeared that some recent back-migration had occurred. The genetic reconstruction of demography was consistent with the physical evidence, showing population growth coincident with the opening of the habitat on the Victoria Land Coast. Prior to its drastic crash and eventual extinction within the past millennium, the population achieved levels of genetic diversity that were much higher than its putative source population.

In their comprehensive study, de Bruyn et al. (2009) have been able to trace the entire life of a population over a period of ~7000 years, from colonisation through expansion to extinction. By revealing the capacity of a species to exploit a newly available habitat and to achieve high levels of genetic diversity in several hundred generations, the authors have provided some insight into the potential behaviour of animal populations in response to future climatic and environmental change.

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