Does the speciation clock tick more slowly in the absence of heteromorphic sex chromosomes?

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Introduction

The genetic basis of postzygotic isolation – one path through which speciation proceeds – has been one of the most active areas of recent evolutionary research. Perhaps the most universal pattern thus far revealed is that genetic interactions driving speciation frequently involve sex chromosomes. However, the speciation process in the absence of sex chromosomes remains understudied, despite the many taxa without chromosomal sex-determination [1]. Though some aspects of postzygotic isolation in organisms with "alternative" sex-determination mechanisms were recently reviewed [2], many specific predictions regarding the evolution of postzygotic isolation in organisms lacking sex chromosomes remain untested. We synthesize these predictions and discuss appropriate methods for testing them, with a primary focus on the prediction that sex chromosomes influence speciation rates [3]. Our goal here is to generate discussion and motivate tests of these hypotheses, rather than to present in-depth tests of the hypotheses themselves.

Postzygotic isolation is attributable to genetic interactions

If species are groups of organisms reproductively isolated from other such groups [4], then speciation is the process whereby one such group diverges into distinct, non-interbreeding lineages. As isolated lineages diverge, accumulated genetic differences eventually cause postzygotic isolation, the sterility and/or inviability of hybrid offspring. Postzygotic isolation is most commonly attributed to Dobzhansky-Muller interactions (DMIs), where novel allelic combinations cause reduced fitness of hybrid offspring as a result of epistatic (gene × gene) interactions [5, 6]. Many DMIs are attributable to interactions between sex chromosomes and autosomes. Because the so-called "rules" of speciation (Haldane's rule, the large X-effect, and Darwin's corollary; see below) can be attributed wholly or in part to the action of sex chromosomes [7, 8], sex chromosomes are considered to play a "special" role in speciation [9]. Additionally, because sex chromosomes are apparently so prone to involvement in DMIs, it follows that they might also affect other aspects of speciation, such as the rate at which it proceeds.

These "rules" of speciation stem largely from work on *Drosophila* and a few other groups with morphologically differentiated (heteromorphic) sex chromosomes (DSCs). Although DSCs have arisen independently and repeatedly in many lineages [10], they are far from a universal characteristic of sexually reproducing eukaryotes [1].

Sex-determination mechanisms vary widely

Mechanisms determining sex in plants and animals, the two groups most commonly possessing discrete sexes, are diverse and range widely over short phylogenetic distances [1]. Sex-determination mechanisms should be viewed as an evolutionary continuum. Although the known mechanisms can be grouped into distinct categories – for instance, genetic/non-genetic, chromosomal/non-chromosomal, homogametic/heterogametic – they grade into each other, as when homogametic sex

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Abbreviations:
DMI, Dobzhansky-Muller interaction; **DSCs,** differentiated sex chromosomes; **NDI,** net diversification interval.

chromosomes "degenerate" into heterogametic sex chromosomes. Among vertebrates, heterogamety evolved independently in birds (ZW), snakes (ZW), and mammals (XY) [10], while the mechanisms of sex-determination in amphibians and in other reptilian groups are more variable, including both homomorphic sex chromosomes and environmental mechanisms [1, 11]. Invertebrates possess diverse and often poorly characterized sex determining mechanisms. Sex-determination in insects is known to be particularly variable – for instance, lepidopterans have DSCs (ZW), hymenopterans are haplodiploid, and many – but not all – flies have DSCs (XY or ZW) [1]. Most plant species are hermaphroditic or monoecious, although dioecy has evolved many times. DSCs are present in four angiosperm families, and although most of the species within these families are not heterogametic, DSCs have evolved repeatedly within two families [12]. Thus the question of whether sex chromosomes influence speciation rates involves evolutionary processes across a wide range of multicellular organisms.

The "rules" of speciation invoke conflict between sex chromosomes and autosomes

Haldane's rule

The first "rule" of speciation is that when one sex is more severely affected by hybridization (e.g. absent, numerically reduced, or less classically fit), it is usually the heterogametic sex [13]. This depends on the sex chromosomes themselves, rather than on some sex-specific phenomenon – it has been documented in cases of both male (XY) and female (ZW) heterogamety. Haldane's rule holds for both sterility and inviability [7, 13, 14] and in both plants and animals [15].

Despite the near-ubiquity of Haldane's rule, it appears to have no single cause. The leading explanation is the dominance hypothesis, which implicates recessive alleles on the X (Z) chromosome that are masked in the homozygous sex (XX/ZZ) but exposed in the hemizygous sex (XY/ZW) [16]. A second explanation with support is the faster-male hypothesis, which proposes that male sterility arises faster than female sterility in XY systems, perhaps because spermatogenesis is especially sensitive to disruption or because male fertility genes evolve more quickly [17]. However, this explanation has received support only for sterility and is only applicable in XY systems [14]. The faster-male phenomenon could conceivably be found in organisms without sex chromosomes, as discussed in a recent review [2], but it is important to distinguish this from true manifestations of Haldane's rule, which by definition require heterogamety. A third hypothesis with some support is that Haldane's rule is attributable to sex-ratio meiotic drive (biased transmission of one sex chromosome over the other) [18], a situation that may result in faster evolution in the heterogametic sex [17].

The large X-effect

The second "rule" involves the tendency of genes contributing to hybrid breakdown to localize disproportionately to the X (or Z) chromosome. The X(Z) chromosome has been shown to impact hybrid fertility and/or viability much more than individual autosomes in many crosses, even when the X is neither physically larger nor more gene-dense than the autosomes [7]. Though initially proposed to explain both hybrid sterility and hybrid inviability, it appears to hold true more often for hybrid male sterility than for hybrid female sterility or for hybrid viability in either sex [9].

The large X-effect has been more controversial than Haldane's rule, and its causes are less well understood. Hypotheses currently favored invoke faster evolution of the X chromosome relative to autosomes (faster-X), meiotic drive, and the sensitivity of spermatogenesis to the disruption of X chromosome inactivation [9].

Darwin's corollary

The third "rule" is the observation that many crosses demonstrate asymmetric fitness (hybrids with an A mother and a B father may be more severely affected than those with a B mother and an A father). This could be explained by conflicts between a number of uniparentally-inherited factors and the nuclear genome, including X-autosome interactions, nuclear-mitochondrial conflicts, and maternal effects. In plants, additional potential sources of asymmetric dysfunction exist, including nuclear-plastid conflicts, gametophyte-sporophyte interactions, and conflicts between the haploid male and diploid female contributions to triploid endosperm function [8].

Are speciation rates influenced by the presence of sex chromosomes?

In species with DSCs, the first manifestations of postzygotic isolation appear nearly always to involve sex chromosome-autosome conflicts. These interactions underlie both Haldane's rule and the large X-effect, and Darwin's corollary is also partially explained by them [7, 8]. A logical prediction of the dominance theory (Haldane's rule) is that postzygotic isolation should evolve more slowly in taxa with small X chromosomes than in those with large X chromosomes [16], which is supported by evidence from *Drosophila* [19]. An extension of this logic is that postzygotic isolation should evolve even more slowly in taxa lacking DSCs [3]. Though proposed a decade ago, this prediction remains empirically unexamined.

Proper tests of this hypothesis will involve replicated, phylogenetically grounded comparisons of speciation rates in sister clades with and without DSCs. Few, if any, datasets of the appropriate breadth and depth have been compiled, and post-hoc comparisons of the results of different studies are difficult because of the variety of methods used to calculate speciation rates.

Measurements of speciation rates rely upon a "speciation clock" – that is, the assumption that reproductive isolation accumulates at a constant (clock-like) rate [20]. The most accurate calculations, therefore, are derived from controlled crosses that quantify intertaxon reproductive isolation, which can be incorporated into measures of biological speciation intervals (BSIs).

As studies of this sort are impracticable for many groups and also for examining large numbers of taxa simultaneously, a less rigorous metric, the net diversification interval (NDI), is often calculated instead. NDIs use the number of extant taxa within a clade and its age to extrapolate a speciation rate [5]. Numerous methods of calculating NDIs have been devised that may or may not incorporate, for example, estimates of extinction rates. However, NDIs calculated with the same methodology and with comparably accurate estimates of clade age and diversity may in the future provide insight into the question of whether sex chromosomes influence speciation rates.

Data from a recent study provide limited evidence for the hypothesis that speciation occurs more rapidly in clades possessing DSCs. NDIs calculated for 28 families of reptiles and birds [21] show that, in general, lizards and snakes (squamates) – where DSCs are common – have speciated more quickly than turtles and crocodilians – where DSCs are rare and absent, respectively (Fig. 1). Furthermore, within groups, the same pattern can be seen at the family level. In snakes (range: 5.4–16.8 MY), Typhlophidae (16.8 MY) has the slowest NDI and is the only family lacking DSCs. In turtles (range: 12.7–68.3 MY), Geoemydidae (12.7 MY), the only family in which DSCs have been described, has the shortest NDI. In lizards (range: 9.7–17.5 MY), the only family examined that consistently possesses DSCs (Amphisbaenidae: 9.7 MY) has the fastest NDI, and the one family examined that consistently lacks DSCs (Agamidae: 13.3 MY) has the second-lowest NDI [11, 22]. However, this pattern is contradicted by birds, which have NDIs comparable to turtles and crocodilians but universally possess ZW sex chromosomes [1].

What genetic conflicts might play roles in postzygotic isolation when DSCs are absent?

In the absence of sex chromosome-autosome interactions, other genetic conflicts must necessarily play greater roles in postzygotic isolation. Cytonuclear conflicts – those between a uniparentally inherited cytoplasmic factor, such as mitochondria, and the nuclear genome – seem to play large roles in taxa with alternative mechanisms of sex-determination, such as yeast (haploid mating types), the wasp *Nasonia* (haplodiploidy), and the copepod *Tigriopus* (polygeny) [23–26]. Though also known to exist in groups possessing DSCs, cytonuclear conflicts are not among the primary incompatibilities identified in these organisms [6]. Beyond cytonuclear conflicts, other genetic conflicts that might be expected to play important roles in postzygotic isolation include autosome-autosome incompatibilities and chromosomal rearrangements. Indeed, postzygotic isolation attributable to chromosomal rearrangements (chromosomal speciation) appears to play a larger role in plants than in animals, possibly because plants often lack DSCs which would otherwise be the dominant source of incompatibility [3]. Further genetic mapping of incompatibilities in non-DSC species will provide increased understanding of the number and nature of these conflicts.

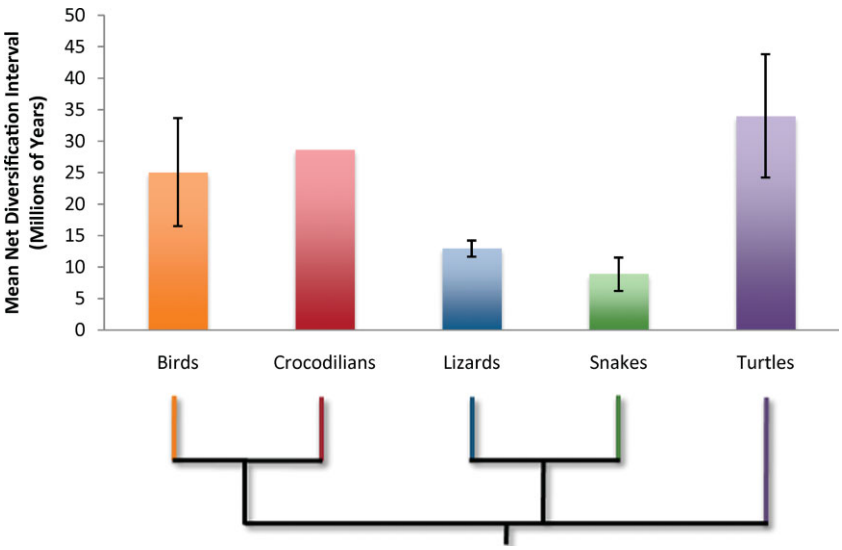

Figure 1. Net diversification intervals (NDIs) in reptiles and birds. Mean NDIs (±standard error) are mapped onto a phylogenetic tree. Heteromorphic sex chromosomes are present in birds, common in squamates (lizards and snakes), rare in turtles and absent in crocodilians. Sex-determination data are from [1, 11, 21]. Phylogeny and NDI data are from [20].

Do sterility and inviability accumulate at different rates in the absence of DSCs?

In *Drosophila* and Lepidoptera, hybrid sterility in the heterogametic sex evolves faster than hybrid sterility in the homogametic sex and also faster than hybrid inviability in either sex [14, 17, 27]. In birds, hybrid sterility arises before hybrid inviability [28]. If this pattern is driven by rapidly evolving gametogenesis genes in the heterogametic sex [17], then taxa lacking a heterogametic sex should accumulate inviability and sterility at comparable rates in both sexes. In *Tigriopus* (polygeny) males do not accumulate hybrid sterility faster than females [26]. Studies using tomatoes also support this idea, suggesting both that male and female sterility may accumulate at the same rate [29, 30] and that similar numbers of QTL underlie pollen and seed sterility in two of three crosses [30]. Additional explicit tests of this question are needed, however, in order to characterize this as a pattern in non-DSC taxa.

Conclusions and prospects

Sex chromosomes play a large role in the process of speciation as we currently understand it. The impacts of Haldane's rule and the large X-effect are both pro-

found and widespread, implying that sex chromosomes evolve incompatibilities more rapidly than do autosomes. Thus, we might expect sex chromosomes to accelerate the rate of speciation. Indeed, some of the available data supports this. However, it is difficult to comment on the universality of this pattern when data are available for so few groups.

The best evidence for an influence of sex chromosomes on speciation rates will come from comparative studies in phylogenetically well-defined groups in which DSCs have clearly been gained and lost. Squamates may be a particularly attractive group for such studies because of the repeated evolution of heterogamety (both XY and ZW), as well as an apparently large number of taxa with environmental sex-determination.

Clearly, knowledge of the genetics of speciation for taxa with alternative mechanisms of sex-determination remains woefully behind that for those with DSCs. However, this is changing rapidly with the development of species lacking DSCs as alternative models of speciation (e.g. *Mimulus, Helianthus, Solanum, Nasonia, Tigriopus*). Emerging evidence from these taxa suggests that, in comparison with DSC-possessing species, speciation in the absence of sex chromosomes may proceed very differently indeed.

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