Evaluating genomic signatures of "the large X-effect" during complex speciation

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Abstract

The ubiquity of the "two rules of speciation"— Haldane's rule and the large X-effect— imply a general, special role for sex chromosomes in the evolution of intrinsic postzygotic reproductive isolation. The recent proliferation of genome-scale analyses has revealed two further general observations: (1) complex speciation involving some form of gene flow is not uncommon; and (2) sex chromosomes in male- and in female-heterogametic taxa tend to show elevated differentiation relative to autosomes. Together these observations are consistent with speciation histories in which population genetic differentiation at autosomal loci is reduced by gene flow while natural selection against hybrid incompatibilities renders sex chromosomes relatively refractory to gene flow. Here I summarize multi-locus population genetic and population genomic evidence for greater differentiation on the X (or Z) *versus* the autosomes and consider the possible causes. I review common population genetic circumstances involving no selection and/or no interspecific gene flow that are nevertheless expected to elevate differentiation on sex chromosomes relative to autosomes. I then review theory for why large X-effects exist for hybrid incompatibilities and, more generally, for loci mediating local adaptation. The observed levels of sex chromosome *versus* autosomal differentiation, in many cases, appear consistent with simple explanations requiring neither large X-effects nor gene flow. Discerning signatures of large X-effects during complex speciation will therefore require analyses that go beyond chromosome-scale summaries of population genetic differentiation, explicitly test for differential introgression, and/or integrate experimental genetic data.

Keywords

Intrinsic postzygotic reproductive isolation is famously characterized by "two rules of speciation"— Haldane's rule and the large X-effect (Coyne 1992; Coyne 2018; Coyne & Orr 1989; Coyne & Orr 2004). Haldane's rule refers to the preferential sterility or inviability of hybrids of the heterogametic (XY) sex relative to their homogametic (XX) siblings (Laurie 1997; Orr 1997). The large X-effect refers to the disproportionately large role of the X chromosome in reducing hybrid fitness (Coyne 1992; Coyne & Orr 1989; Presgraves 2008; Turelli & Orr 2000). These general observations hold in male-heterogametic (*XY*/*XX*) and female-heterogametic (*ZW*/*ZZ*) taxa, implying that sex chromosomes play an important role

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during speciation. A third, and possibly related, pattern has emerged from multi-locus population genetics and population genomics analyses of speciation from a wide range of taxa: X (and Z) chromosomes often show greater population or species differentiation than autosomes (see below). Putting these observations together, it is tempting to infer that sex chromosomes are less exchangeable between species, and hence more refractory to gene flow, than autosomal loci. If so, then the elevated differentiation at sex chromosomes would imply a special, important role during complex speciation— *i.e.*, speciation with some form of gene flow (Figure 1; Harrison & Larson 2014; Payseur & Rieseberg 2016; Seehausen *et al.* 2014; Sousa & Hey 2013; Wolf & Ellegren 2017).

The large X-effect might limit sex-linked gene flow between species in three ways. First, and most simply, strong natural selection ($N_e s >> 1$) against incompletely dominant "foreign" alleles that are incompatible with the local genetic background or local environment is more effective for hemizygous, sex-linked genotypes than for heterozygous autosomal ones (Lasne *et al.* 2017; Muirhead & Presgraves 2016). Second, incompatibility alleles on the X chromosome could, in principle, have larger effect sizes than those on autosomes (Coyne & Orr 1989; Turelli & Orr 1995). Third, the X chromosome can have a higher density of incompatible alleles than autosomes, reflecting a faster rate of accumulation (Coyne & Orr 1989; Masly & Presgraves 2007; Naveira 2003; Presgraves 2008). Why hybrid incompatibilities often accumulate faster on the X is unclear, but there is no shortage of hypotheses, including: faster-X evolution (Charlesworth *et al.* 2018; Charlesworth *et al.* 1987); recurrent bouts of meiotic drive (Frank 1991; Hurst & Pomiankowski 1991; Patten 2018); gene transposition (Moyle *et al.* 2010); and/or interspecific divergence in sex chromosome regulation (Campbell *et al.* 2013; Lifschytz & Lindsley 1972). Regardless of the causes, all three— hemizygous selection, larger effect sizes, and higher densities— reduce the opportunity for linked (compatible) alleles to escape their locally deleterious (incompatible) chromosomal backgrounds by recombination (Barton & Bengtsson 1986; Muirhead & Presgraves 2016). As a result, gene flow at incompatible alleles and at linked loci will tend to be more strongly reduced on sex chromosomes.

It is important to note, however, that while Haldane's rule ranks among the strongest patterns in biology (Coyne 1992; Coyne 2018), the generality of the large X-effect is less firmly established. Direct evidence for the large X-effect comes from experimental backcross analyses in which the X chromosome has a disproportionately large phenotypic effect on hybrid fitness, given its physical size and gene content (Coyne & Orr 1989). The stronger evidence for Haldane's rule implies a stronger pattern or one easier to ascertain. After all, querying Haldane's rule requires only F_1 progeny, whereas querying the large X-effect requires genetic mapping in F_2 backcross progeny. Direct evidence for the large X-effect has, unsurprisingly, come from the usual suspects (*Drosophila*, mouse, *Caenorhabditis*; Bi *et al.* 2015; Coyne & Orr 1989; Cutter 2018; Good *et al.* 2008) and some emerging genetic models (*e.g.*, *Heliconius* butterflies, sticklebacks, *Silene*; Demuth *et al.* 2014; Kitano *et al.* 2009; Naisbit *et al.* 2002). In the absence of such direct evidence, population genetic data provide putative indirect evidence: X- and Z-linked loci tend to show more sequence divergence, more allele frequency differentiation, less phylogenetic discord, and/or steeper clines in hybrid zones (see below). For some taxa, then, direct evidence for

large X-effects predicts reduced gene flow on the X whereas, for most, indirect evidence of reduced gene flow on the X often serves as a proxy for large X-effects.

In this note, I survey the recent explosion of speciation genomics data to assess the evidence for elevated differentiation on sex chromosomes and consider its potential causes. (Due to the paucity of data from Y and W chromosomes, "sex chromosomes" refers hereafter to X or Z chromosomes only.) The results bear on the roles of sex chromosomes *and* gene flow during speciation. I first aggregate data from multi-locus and genome-scale analyses. These show consistently greater population genetic differentiation on X chromosomes *versus* autosomes. Then, before turning to why the large X-effect and related phenomena provide natural explanations for the greater differentiation of sex chromosomes during complex speciation, I consider how many common population genetic circumstances— including ones involving neither selection nor gene flow— can readily produce the same observations. While the evidence for greater population differentiation on sex chromosomes is overwhelming, the reasons why are not well established.

Greater differentiation on sex chromosomes than autosomes is general

To assess the evidence for greater differentiation on sex chromosomes, I gathered information from multi-locus population genetic and population genomic studies of divergence between populations or species. Using *ISI Web of Science* (for details, see Supplementary Table S1) and the collated references of two recent, large literature reviews (Payseur & Rieseberg 2016; Wolf & Ellegren 2017), I identified 104 studies with multi-locus or genome-scale analyses of speciation and/or divergence history. I then filtered the dataset to include only taxa that have heteromorphic sex chromosomes and that separately report sex chromosome *versus* autosomal differentiation. I eliminated redundant studies that focused on the same population or species pairs by including newer, typically larger studies in place of older, typically smaller ones. To survey as many studies as possible, I included analyses that together use a wide range of approaches, including summaries of population differentiation (*e.g.*, F_{st}; Nei 1987; Wright 1951), cline-width analyses of hybrid zones (Maroja *et al.* 2015), phylogenetic discordance (*e.g.*, Patterson's *D*; Durand *et al.* 2011; Green *et al.* 2010), and/or explicit genome scans for introgression (*e.g.*, G_{min}; Geneva *et al.* 2016). The final dataset comprised 48 studies that reported on genomic patterns of divergence and/or introgression among >126 taxon pairs (Supplementary Table S1). Most studies (89.7%) in the final dataset used genome-scale data (*e.g.*, whole genome sequencing, RNAseq, *etc.*), but some involved multi-locus population genetic surveys (10.3%; number of loci=12–51, with   4 on the X or Z chromosome; Supplementary Table S1). Most of the data (80.6%) come from female-heterogametic *ZW* taxa (birds, Lepidoptera), with the remainder (19.4%) from male-heterogametic *XY* or *XO* taxa (mammals, Diptera, Orthoptera).

As Table 1 shows, X-linked and Z-linked loci show more differentiation, steeper clines, less phylogenetic discordance, and/or less introgression than autosomal loci for 94.6% of taxon pairs. Overall, the pattern appears slightly stronger for *ZW* taxon pairs (97%) than *XY* taxon pairs (84%, Fisher's Exact *P*=0.026). The fixation index, F_{st}, is the most commonly reported summary of population genetic differentiation, with point estimates reported for 101 taxon pairs (Table S1). For 97% of these taxon pairs, mean F_{st} estimates for X- or Z-linked loci

exceed those for autosomal loci (Figure 2). Median X/autosome (or Z/autosome) ratios differ significantly among major taxonomic groups (Table 2; Kruskal-Wallis test, df=4, $P<$ 0.0007). The median X/autosome ratio of F_{st} among male-heterogametic XY taxa (F_{stX}/F_{stA}=1.40) does not however differ from the median Z/autosome ratio of F_{st} among female-heterogametic ZW taxa (F_{stZ}/F_{stA}=1.82; Table 2; Mann-Whitney test, P=0.076). Conclusions on the presence or absence of major taxonomic differences should be considered preliminary, for two reasons. First, representation of XY versus ZW taxa is unbalanced, with only ~10% of F_{st} estimates coming from XY taxa. Second, in addition to potential biological differences among major taxonomic groups, there are systematic and consequential sampling differences. For instance, the only significant difference between major taxa occurs between the two ZW groups, birds and Lepidoptera (Mann-Whitney test, Bonferroni P=0.0072). In the present dataset, however, taxon pairs in birds are less differentiated (and hence possibly younger) than those in Lepidoptera, with both F_{stZ} and F_{stA} significantly smaller in birds (Table 2; Mann-Whitney tests, P=0.022 and 0.0028, respectively). As shown below, the F_{stZ}/F_{stA} ratio is, and is expected to be, larger for less differentiated taxon pairs. With the data available, and the caveats concerning taxon sampling, there is no firm basis on which to infer differences in sex chromosome *versus* autosome differentiation among major taxonomic groups. These findings therefore confirm that the greater differentiation of sex chromosomes relative to autosomes between taxa is a strong, general pattern that holds comparably well in XY and ZW taxa.

Sex chromosome differentiation without gene flow

Given the growing evidence for complex speciation with gene flow, it has proven tempting to interpret the widespread elevated differentiation of X and Z chromosomes as evidence for a large X-effect. Elevated differentiation of sex chromosomes is not however unique to large X-effects. Simpler scenarios involving neither selection nor gene flow can produce qualitatively similar patterns. The most commonly reported measure of population genetic differentiation between taxa in Table 1, F_{st}, does not by itself provide a basis to distinguish population histories with or without gene flow: F_{st} values can be interpreted in the context of migration-drift equilibrium (Slatkin 1985; Whitlock & McCauley 1999) or strict isolation (Nei 1976, 1987; Wright 1951). Assuming an ancestral population of size N that becomes subdivided t generations ago into descendant populations each also of size N with no gene subsequent flow, then for autosomal loci, $F_{st} = 1 - e^{-t/2N}$ (Nei 1976, 1987; Wright 1943). Letting the effective size of the X chromosome equal $2Nx$, where $x=N_X/N_A$, then for X-linked loci, $F_{st} = 1 - e^{-t/2Nx}$. For populations of constant size, equal sex ratios, and the usual assumption that N_X/N_A=3/4 (x=0.75), the ratio of expected F_{st} for X-linked loci to that for autosomal ones, depends on $t/2N$: F_{stX}/F_{stA} is ~4/3 for very small $t/2N$ and slowly approaches one as $t/2N$ increases (Figure 3). Among 101 taxon pairs with F_{st} estimates in Table 1, the ratio F_{stX}/F_{stA} declines with F_{stA}, as expected (Spearman r=−0.33, P=0.00066; Figure 4). However, 81% have F_{stX}/F_{stA} ratios that exceed 4/3 and may therefore require explanation (Figure 4). As previously noted, F_{st} is a relative measure of differentiation and therefore sensitive to within-population levels of diversity, a function of effective population size (Charlesworth 1998; Cruickshank & Hahn 2014; Nachman & Payseur 2012; Nei 1973; Noor & Bennett 2009; Payseur & Rieseberg 2016; Ravinet *et al.* 2017; Wolf & Ellegren

2017). The simplest explanation, then, for why observed F_{stX}/F_{stA} ratios are often higher than expected is that the ratio of sex-linked to autosomal effective sizes, N_X/N_A, is <0.75. In birds, for instance, Z/autosome ratios of nucleotide diversity imply N_Z/N_A ratios that are typically <0.75, with some as low as ~0.25 (Huang & Rabosky 2015; Irwin 2018; Mank *et al.* 2010; Wright *et al.* 2015). Under these circumstances, F_{stZ} can be as much as four-fold higher than F_{stA} during the early stages of divergence (when $t/2N$ is small; Figure 3).

It is therefore important to consider what circumstances can reduce N_X relative to N_A. With no gene flow, demography can differentially impact N_X and N_A. First, historical effective population size changes— like the bottleneck-and-recovery events that might be expected during the founding of new populations— can disproportionately cause strong, transient reductions in N_X/N_A (Pool & Nielsen 2007). Second, deviations from 1:1 breeding sex ratios can cause N_X/N_A to deviate from 3/4 (Caballero 1995; Hedrick 2007): if breeding sex ratios are biased towards an excess of the heterogametic sex (*XY* males or *ZW* females), then the expected N_X/N_A ratios are <3/4. For reasons that are unclear, however, observed adult sex ratios in nature tend to the opposite, with an excess of the homogametic sex (*XX* females and *ZZ* males; Pipoly *et al.* 2015). Third, when variance in fecundity differs systematically between the sexes, N_X/N_A can deviate from 3/4: if the variance in fecundity for the homogametic sex exceeds that of the heterogametic sex, then expected N_X/N_A ratios are <3/4 (Caballero 1995; Charlesworth 2001). Sexual selection on males in *ZW*, but not *XY*, taxa should therefore reduce N_Z/N_A (Huang & Rabosky 2015; Wright *et al.* 2015). Finally, with migration, sex-biased gene flow can elevate differentiation on sex chromosomes *versus* autosomes (Keinan & Reich 2010; Laporte & Charlesworth 2002): migration that is heterogametic sex-biased— as tends to be the case in mammals and birds (Greenwood 1980; Trochet *et al.* 2016)— will cause gene flow on autosomes to effectively exceed that on X (or Z) chromosomes (Hedrick 2007; Laporte & Charlesworth 2002).

Separate from such demographic considerations, the effects of linked natural selection within allopatric populations can also differentially affect N_X and N_A. Recurrent background selection against deleterious mutations (Charlesworth 2012a; Charlesworth *et al.* 1993) and recurrent hard selective sweeps of beneficial mutations (Betancourt *et al.* 2004) can cause N_X/N_A ratios to differ from 3/4. The direction and magnitude of the deviations are, however, contingent on taxon-specific particulars of recombination regimes. In general, N_X/N_A is reduced by linked selection in taxa for which recombination occurs in both sexes (as in birds, mammals) but not in taxa with recombination restricted to the homogametic sex (as in *Drosophila*, Lepidoptera; Betancourt *et al.* 2004; Charlesworth 2012b). Details of genome organization can, through indirect effects on recombination rate, modulate the effects of linked selection on sex chromosomes *versus* autosomes. For instance, as crossover assurance mechanisms typically require one crossover per chromosome (or chromosome arm) per meiosis (Dumont 2017; Wang *et al.* 2015), small chromosomes experience higher effective rates of recombination per physical unit than large chromosomes. As a result, larger chromosomes experience more hitchhiking effects and, consequently, reduced diversity and elevated differentiation. In birds, chromosome size is a strong predictor of nucleotide diversity (Ellegren 2013; Huynh *et al.* 2010; Mugal *et al.* 2013) and F_{st} (Manthey *et al.* 2016). Notably, the Z chromosome is one of the largest in birds. The excess differentiation

of Z chromosomes *versus* autosomes in birds may therefore be attributable, in part, to its relative susceptibility to recurrent background selection and selective sweeps.

Sex chromosome differentiation with selection and gene flow

During simple, strictly allopatric speciation histories like those considered above, all loci in the genome become partitioned into two non-interbreeding descendant populations at the same divergence time in the past (*e.g.*, the Isolation Model; Wakeley & Hey 1997); Figure 1a). During complex speciation, however, the gene flow occurs concurrent with or subsequent to the initial population divergence time (Figure 1b,c). Under complex speciation, gene flow, selection, and recombination can interact to cause genomic heterogeneity in differentiation: gene flow impedes differentiation whereas selection can cause localized "genomic islands" of divergence; the physical sizes of genomic islands depend on the strength and efficacy of differential selection relative to the local chromosomal rate of recombination (reviewed in Nosil *et al.* 2009; Ravinet *et al.* 2017; Seehausen *et al.* 2014; Wolf & Ellegren 2017). The elevated differentiation of sex chromosomes may, under this scenario, represent a special case of such genomic islands of differentiation.

Many of the studies reviewed in Table 1 explicitly note the possibility that elevated differentiation and/or reduced introgression on sex chromosomes may be a by-product of the large X-effect, with the implication that selection against hybrid incompatibilities disproportionately limits gene flow on the X (or Z) chromosome. In general, there are two scenarios by which a large X-effect for hybrid incompatibilities could cause elevated sex chromosome differentiation during complex speciation. First, under a classic secondary-contact model (Figure 1b), two populations first accumulate the hybrid incompatibilities that cause the large X-effect during an extended period in allopatry and then later experience gene flow upon secondary contact. Second, under a parapatry model (Figure 1c), the origin and persistence of hybrid incompatibilities in populations connected throughout their history by gene flow occurs more readily at X-linked loci than at autosomal loci (Hollinger & Hermisson 2017). For some of the species in Table 1, direct evidence exists for intrinsic postzygotic isolation and for large X-effects— *e.g.*, in mice, *Drosophila*, *Anopheles*, and *Heliconius*, sticklebacks, and *Ficedula* (Good *et al.* 2008; Kitano *et al.* 2009; Masly & Presgraves 2007; Naisbit *et al.* 2002; Slotman *et al.* 2005; Wiley *et al.* 2009). For others, however, such direct evidence is lacking or doubtful. Indeed, some population pairs would seem to be too young to have evolved strong or appreciable numbers of hybrid incompatibilities— *e.g.*, between geographic populations of modern humans (Keinan *et al.* 2009)— and it seems unlikely that intrinsic postzygotic isolation is relevant (but see Corbett-Detig *et al.* 2013).

Instead, for such young species or population pairs, a kind of "large X-effect" may also exist for alleles contributing to local adaptation rather than to hybrid incompatibilities. Under a secondary contact model, and assuming adaptation from new mutations, locally adaptive alleles can accumulate faster on the X chromosome than on autosomes during the allopatric divergence phase (Charlesworth *et al.* 1987). This faster-X evolution occurs when the average dominance of newly arising beneficial mutations is sufficiently small: making the

standard assumption that the ratio of effective population sizes for the X to that for the autosomes is $N_X/N_A = 3/4$, then faster-X evolution will occur when $\bar{h} < 0.5$ (Charlesworth *et al.* 1987); if $N_X/N_A > 3/4$, however, the conditions for faster-X evolution are more permissive ($\bar{h} > 0.5$; Charlesworth *et al.* 2018; Vicoso & Charlesworth 2009). Adaptation from standing genetic variation, on the other hand, results in faster evolution at autosomal loci (Charlesworth *et al.* 2018; Connallon *et al.* 2012; Orr & Betancourt 2001). The fact that population genetic and genomic data tend to find that X-linked loci have higher substitution rates, and show more signatures of positive selection, than autosomal loci in male- and in female-heterogametic taxa (Dean *et al.* 2015; Garrigan *et al.* 2014; Meisel & Connallon 2013; Nam *et al.* 2015; Sackton *et al.* 2014) suggests that an appreciable fraction of adaptation involves new, recessive beneficial mutations (but see Wright *et al.* 2015). Under a parapatry model, and assuming strong migration-selection balance, locally adaptive alleles can show greater differentiation on sex chromosome *versus* the autosomes (Lasne *et al.* 2017). The X-autosome disparity in adaptive allele frequency differentiation is expected to be maximized— achieving as much as four-fold higher levels of differentiation on the X— when alleles are of intermediate dominance, when migration is male-biased, and when migration is strong relative to selection (Lasne *et al.* 2017). This kind of strong migration-selection equilibrium model is however unlikely to produce a chromosome-wide effect, as the opportunity for recurrent migration and recombination implies that the physical scale of genomic signatures of local adaptation will be limited (Charlesworth *et al.* 1997; Lasne *et al.* 2017).

It is worth noting that for some taxa in Tables 1 and 2, the effects of sex linkage *per se* on population differentiation relative to autosomes may be confounded with the effects of chromosomal inversions. When loci mediating hybrid incompatibility or local adaptation fall within inversions, they limit the exchangeability of the inversion— as well as the linked loci within the inversion— between populations (Kirkpatrick & Barton 2006; Noor *et al.* 2001; Rieseberg 2001). Under these circumstances, autosomal inversions with incompatible alleles can elevate differentiation at all loci within the inversion, thereby dampening the relative differentiation on the X chromosome (*e.g.*, *Drosophila mojavensis-D. arizonensis*; Lohse *et al.* 2015). Conversely, X-linked inversions can exacerbate elevated differentiation on the X chromosome (*e.g.*, *Anopheles;* Slotman *et al.* 2005). Interestingly, in birds, inversion differences appear to accumulate more readily on the Z chromosome than any autosome (Hooper & Price 2017). The further observation that inversions are enriched among sympatric bird species is suggestive of a role in mediating gene flow (Hooper & Price 2017).

Conclusions

The elevated population genetic differentiation on sex chromosomes relative to autosomes represents a strong, general pattern (Tables 1, 2). These observations are consistent with a role for the large X-effect during complex speciation with gene flow. However, drawing conclusions about gene flow or the role of sex chromosomes from chromosome-scale summaries of population genetic differentiation is incautious. In many cases, the same observations can be explained without gene flow by the incidental effects of demography and/or linked selection within populations. Distinguishing these possibilities, and establishing a role for large X-effects during complex speciation should therefore involve

formal, statistical rejection of simple speciation histories (Payseur & Rieseberg 2016). Then, assuming a complex speciation, selection against large X-effects in hybrids should most strongly affect the loci involved in hybrid incompatibility and/or local adaptation, whereas demography and recurrent background selection will in contrast tend to produce more dispersed chromosome-wide effects. These alternative histories might therefore be further distinguished by analyses that identify excess heterogeneity in differentiation among sex-linked loci (Lasne *et al.* 2017; Lewontin & Krakauer 1973; Payseur 2010). The strongest tests of a role for large X-effects during complex speciation will come from systems in which population genomic and experimental genetic data can be integrated to test the extent to which loci with validated roles in hybrid incompatibility or local adaptation have impacted the history and genomic distribution of introgression (reviewed in Ravinet *et al.* 2017).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

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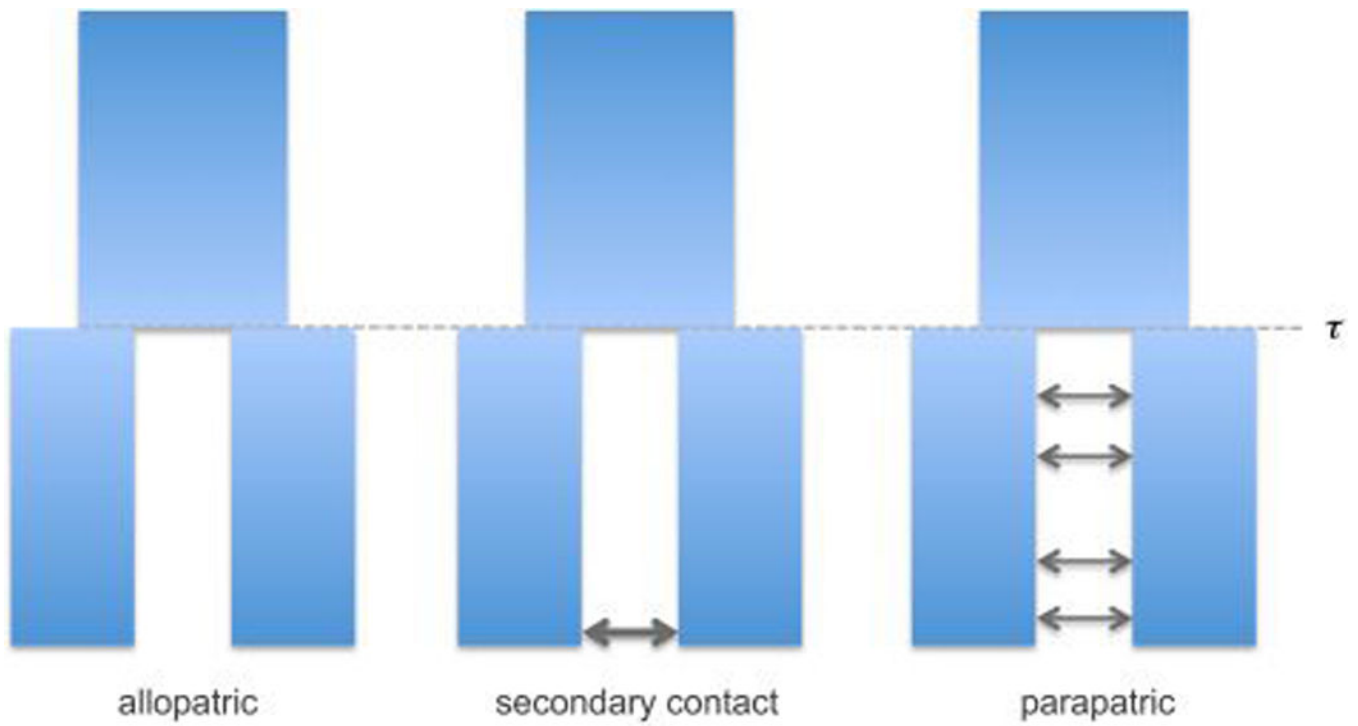
Figure 1.
Three models of speciation history: (A) simple speciation with no gene flow; (B) complex speciation with gene flow upon secondary-contact; and (C) complex speciation with recurrent gene flow.
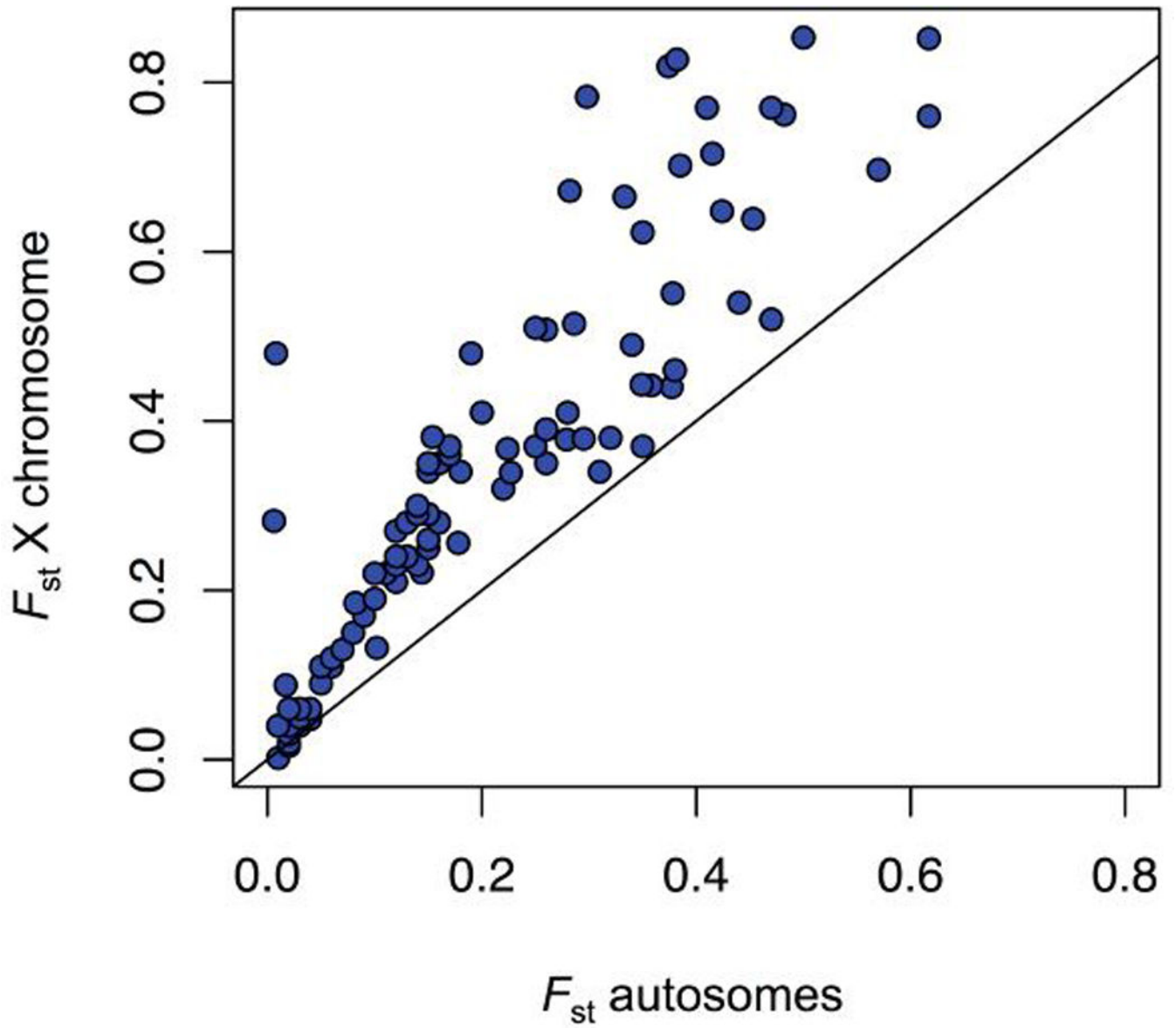
Figure 2.
Sex chromosome (X or Z) differentiation exceeds autosomal differentiation for 97% of
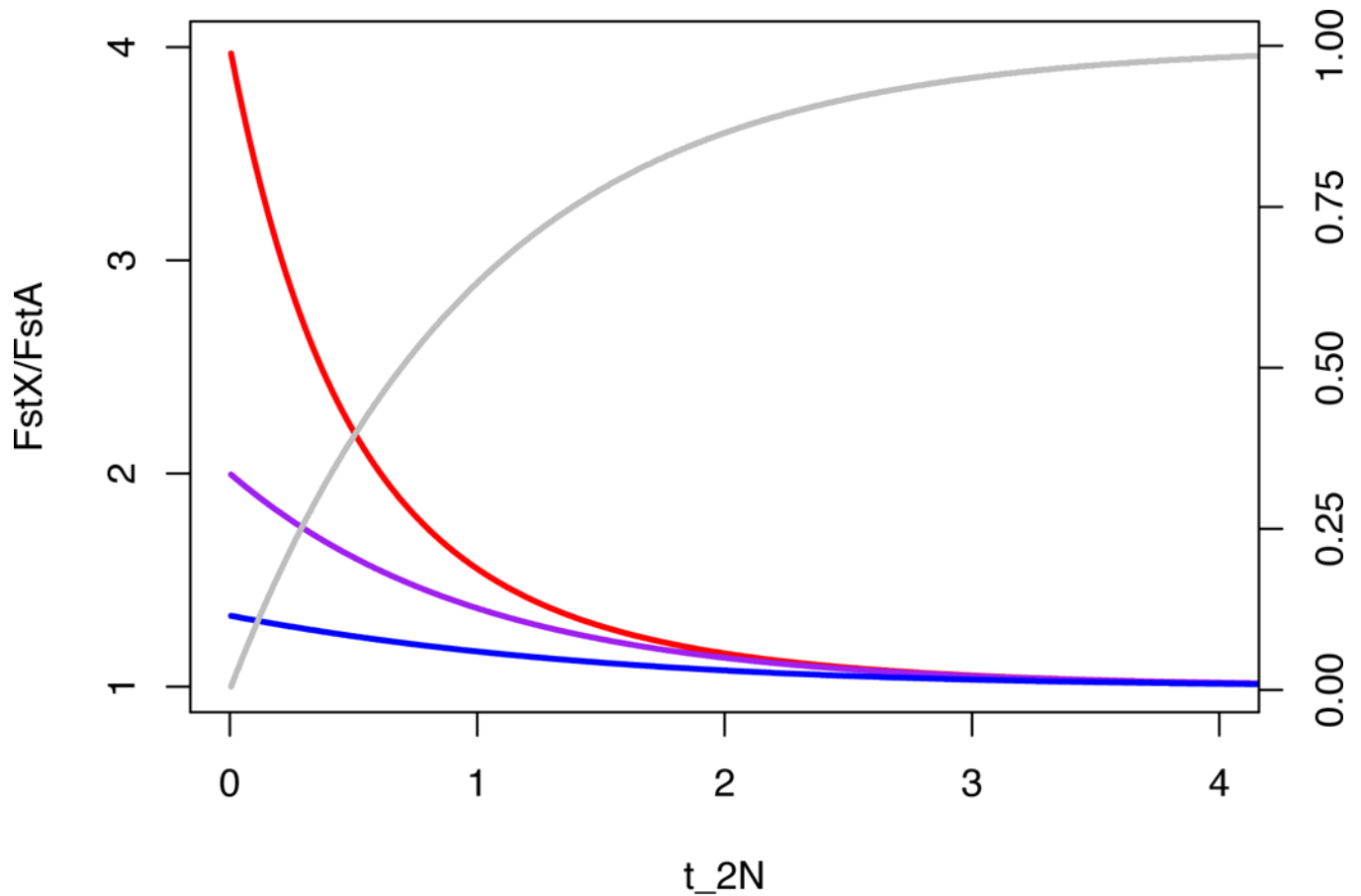n=101 taxon pairs (see Supplementary Table S1 for data).

Figure 3.
The ratio of F_{st} for X-linked loci to F_{st} for autosomal loci under the assumptions of simple speciation in which subpopulations of size N split from an ancestral population t generations ago with no gene flow. The gray line shows how differentiation on the autosomes (F_{stA}) increases with divergence time ($t/2N$). The F_{stX}/F_{stA} ratio is shown for the cases in which the ratios of effective population sizes, N_X/N_A=0.75 (blue), 0.5 (purple), and 0.25 (red). For all 101 taxon pairs reviewed here, F_{st}<0.60 (highlighted gray box), consistent with $t/2N$ 1 in the absence of gene flow or with gene flow (Roux *et al.* 2016).
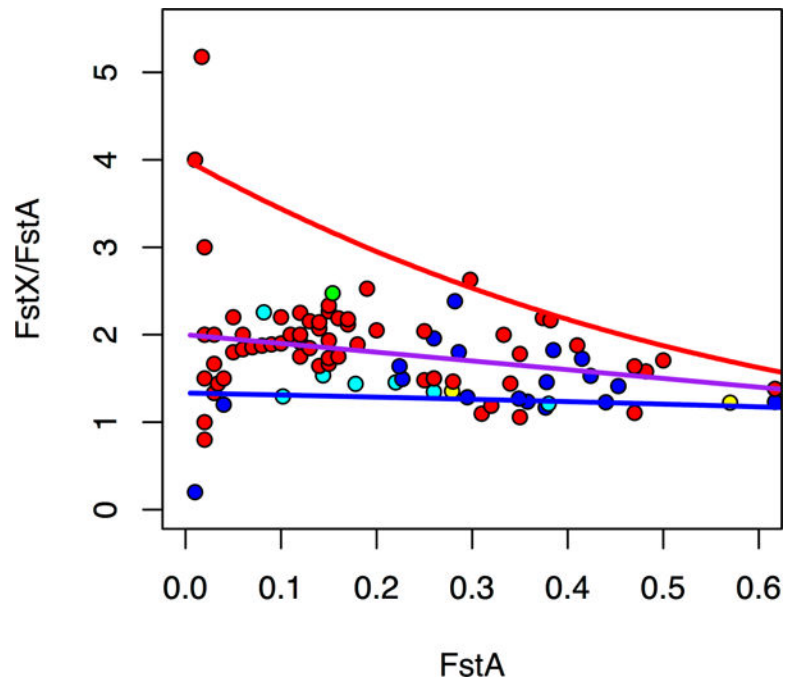
Figure 4.

F_{stX}/F_{stA} ratios change with autosomal differentiation, F_{stA}. Blue dots are point estimates from 101 taxon pairs (see Table S1), and curves are based on theoretical expectations F_{stX} and F_{stA} in the absence of gene flow with ratios of effective population sizes, N_X/N_A=0.75 (blue), 0.5 (purple), and 0.25 (red). For plotting purposes, two extreme outlier data points (F_{stZ}/F_{stA}>20) have been excluded. Major taxa are color-coded (blue=Lepidoptera, red=birds, cyan=mammals, yellow=Diptera, green=plants).

Table 1.

Sex chromosomes are more differentiated than autosomes

Taxa	Sex chromosomes	Yes[a]	No[a]	Sub-total
Lepidoptera	*ZW*	19	2	21
Birds	*ZW*	82	1	83
Sub-total		101	3	104
		0.971	0.029	
Diptera	*XY*	10	2	12
Orthoptera	*XO*	1	0	1
Fish	*XY*	0	1	1
Mammals	*XY*	9	1	10
Plants	*XY*	1	0	1
Sub-total		21	4	25
		0.840	0.160	
Total		122	7	129
		0.946	0.054	

[a]Yes/No = X or Z chromosome is/is not more differentiated than autosomes, respectively.

Table 2.

F_{st} estimates on sex chromosomes *versus* autosomes

Taxa	Sex chromosomes	*n*		Median F_{st} autosomes	Median Ratio
Lepidoptera	*ZW*	18	0.515	0.355	1.44
Birds	*ZW*	73	0.290	0.140	1.89
Sub-total	*ZW*	91	0.340	0.160	1.82
Diptera	*XY*	2	0.540	0.425	1.29
Mammals	*XY*	7	0.256	0.178	1.44
Plants	*XY*	1	0.380	0.150	2.47
Sub-total	*XY*	10	0.335	0.199	1.40
Total		101	0.340	0.160	1.78