Resetting the rules: Sex-chromosome turnover as an escape hatch for mitonuclear conflict

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Abstract

Mitochondrial and nuclear genomes must remain coadapted to sustain oxidative phosphorylation, yet their distinct inheritance often fosters conflict. Sex chromosomes are a key arena for these dynamics: by biasing co-transmission between nuclear-encoded mitochondrial (N-mt) genes and maternally inherited mtDNA, they can amplify or suppress mitonuclear incompatibilities. Existing syntheses emphasize stable XY (mammals) and ZW (birds) systems, where genomic context is conserved. In contrast, many fishes and amphibians undergo frequent shifts among XY, ZW, and polygenic or environmental sex determination, repeatedly resetting the linkage backdrop for mitonuclear interaction. I propose a comparative framework in which sex-chromosome turnover acts as an evolutionary "escape hatch" from Y- or W-linked deleterious N-mt alleles by entrapping N-mt loci into, or releasing them from, non-recombining sex-linked strata, thereby altering the sex bias and intensity of conflict through time. This hypothesis predicts cyclical pulses of hybrid dysfunction and genomic "scars'' that record historical entrapment, offering testable predictions for when turnover entrenches versus relieves mitonuclear conflict. By integrating evidence from stable and labile vertebrate systems, this article outlines how sex-chromosome dynamics shape mitonuclear coadaptation, postzygotic isolation, and ultimately lineage diversification.

Keywords

Sex-chromosome turnover, Mitonuclear conflict, Hybrid-zone dynamics, Mitochondrial sweeps, Postzygotic isolation

Introduction: Mitonuclear coadaptation, conflict and the sex-chromosome connection

Predicting when reproductive barriers arise is central to understanding the tempo of speciation. One repeatedly observed source of hybrid breakdown is mitonuclear conflict, which occurs when maternally inherited mitochondrial genomes interact in maladaptive ways with nuclear-encoded mitochondrial (N-mt) genes (Burton & Barreto 2012, Hill 2019, Rand & Mossman 2020). Sex chromosomes matter in this context because they can bias how N-mt loci are inherited together with mitochondria, potentially amplifying or alleviating these conflicts (Mank 2012, Dean et al. 2014, Hill 2019). Yet, most previous syntheses of hybrid incompatibilities have treated sex chromosomes as fixed features of the genome that modulate the strength of reproductive barriers, without explicitly considering how turnover in sex-determining systems might itself change the dynamics of mitonuclear conflict (e.g., Haldane 1922, Coyne & Orr 2004, Presgraves 2010, Hill 2019, Vicoso 2019).

Here I argue that turnover in the identity of the sex-determining chromosome itself, whether a lineage maintains a long-standing conserved XY or ZW pair (a stable system) or frequently shifts between different sex-determining loci (a labile system), can change the strength, sex-bias, and genomic location of mitonuclear conflict over evolutionary time (Kitano & Peichel 2012, Vicoso 2019). I propose an “escape-hatch” framework in which new sex-determining regions capture or release N-mt loci, generating pulses of conflict and leaving detectable genomic scars. Because turnover reshapes which N-mt loci sit on X/Z, the magnitude and even the direction of classic speciation patterns such as Haldane’s rule and the large-X/Z effect should vary with sex-chromosome age and identity (Ellegren 2009, Coyne 2018).

Sex chromosome turnover is common across vertebrates. Repeated shifts in the chromosome carrying the sex-determining region rewire inheritance, alter recombination landscapes, and change the genomic backdrop for sexual selection (Kitano & Peichel 2012, Payseur et al. 2018, Vicoso 2019, Xu et al. 2024). These changes also affect how key loci become linked to one another, influencing both rates of lineage diversification and the tempo of reproductive isolation (Palmer et al. 2019, El Taher et al. 2021).

A major axis of that influence arises through interactions between the mitochondrial and nuclear genomes (Burton 2022). Mitochondria are central not only to ATP production through oxidative

phosphorylation (OXPHOS) but also to diverse processes such as heat generation, apoptosis, calcium homeostasis, steroid synthesis, and production of reactive oxygen species (Rand et al. 2004, Ballard & Pichaud 2014). These functions depend on tight coordination between maternally inherited mitochondrial DNA (mtDNA) and hundreds of nuclear-encoded mitochondrial (N-mt) genes (Hill 2019). This cooperation persists despite very different inheritance routes: mtDNA is typically transmitted only through females, whereas nuclear loci recombine biparentally. The asymmetry in transmission can generate conflict whenever selection on mtDNA differs from selection on the nuclear background or when hybridization brings together incompatible mitonuclear combinations (Hill 2019, Havird et al. 2019, Rand & Mossman 2020).

Sex chromosomes intersect with these dynamics because they bias the co-transmission of nuclear loci with mtDNA. Z chromosomes spend two-thirds of their evolutionary history in males, X chromosomes spend two-thirds in females, while W and Y are confined to the heterogametic sex, with the W chromosome co-inherited with mtDNA and the Y entirely decoupled from it (Mank 2012). If an N-mt gene becomes trapped in a low-recombination, sex-linked stratum (**Fig. 1**), its inheritance pattern shifts in ways that can generate maladaptive combinations, sex-biased segregation distortion, or hybrid breakdown (Radcliffe et al. 2025). These interactions underlie classic patterns such as Haldane's rule (Haldane 1922, Orr 1997) and the large-X/Z effect, and they set the stage for turnover to change both the intensity and the sex bias of mitonuclear conflict.

Previous reviews have emphasized the forces that drive sex-chromosome turnover or stabilization, including sexually antagonistic selection, mutation load ("hot-potato" dynamics), genetic drift, recombination architecture and heterochiasmy, sex-reversal "fountain-of-youth" effects, and the long-term evolutionary pull toward conserved systems (Mank 2012, Beukeboom & Perrin 2014, Charlesworth 2017, Vicoso 2019). Here, I add a mechanistic mitonuclear dimension by highlighting how turnover can entrap N-mt loci into (or release them from) sex-linked strata, generating predictable mtDNA-conditioned barriers to gene flow.

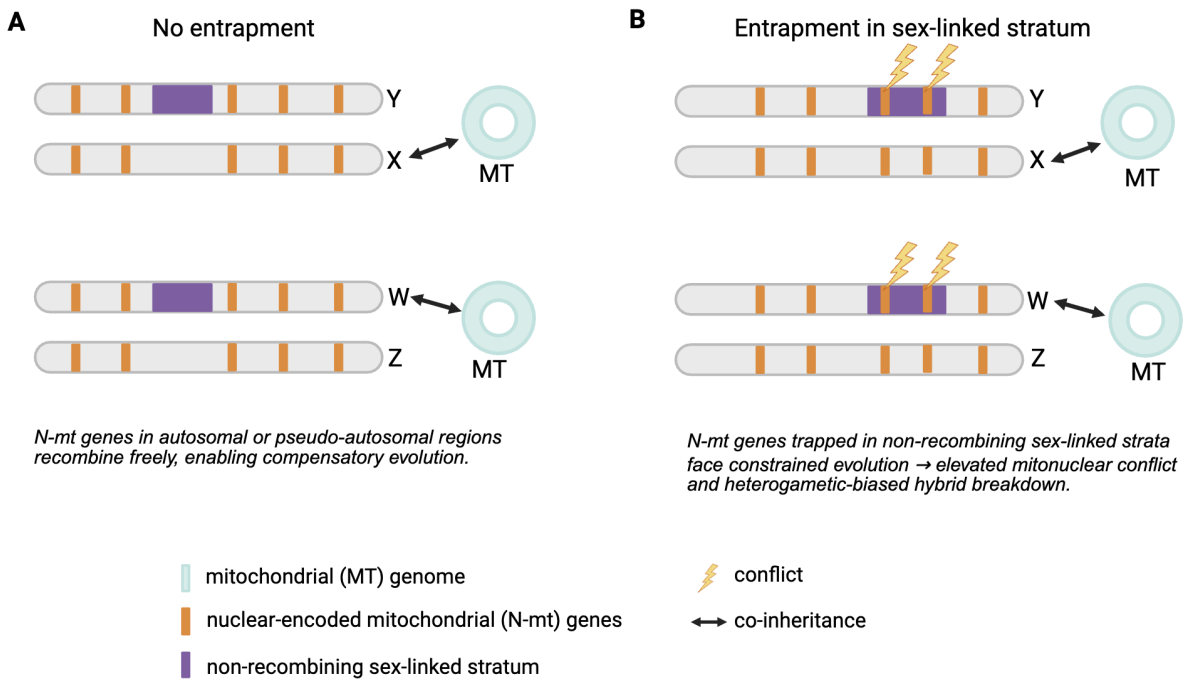

Figure 1. Entrapment, not enrichment: how sex-linked strata bias mitonuclear loci. Schematic chromosomes illustrate two genomic contexts for nuclear-encoded mitochondrial (N-mt) genes (orange). **(A)** N-mt genes within autosomal or pseudo-autosomal regions recombine freely and can track mitochondrial evolution, minimizing mitonuclear conflict. **(B)** Local capture of N-mt genes in a non-recombining sex-linked stratum (purple) constrains compensatory evolution (Princepe & de Aguiar 2024), intensifying mitonuclear conflict (lightning bolts) and often generating heterogametic-biased hybrid breakdown. MT = mitochondrial genome (light blue).

Insights from stable XY and ZW systems

Stable XY. In taxa with stable XY systems such as mammals, the X is largely recombining in females and hemizygous; the Y is gene-poor and decoupled from mtDNA. Across mammals, N-mt genes are often depleted from the X (consistent with selection to relocate conflict-prone loci to autosomes) (Drown et al. 2012, Dean et al. 2014), reducing persistent sex-linked mitonuclear conflict even as heterogametic males often bear hybrid costs (**Table 1**).

Stable ZW. In taxa with stable ZW systems such as birds, the Z spends two-thirds of its time in males, while the W is maternally co-inherited with mtDNA. The avian Z retains many functional genes, including some N-mt loci, and female-biased dysfunction is common (Ottenburghs

2022). Several avian hybrid zones show coincident clines of mtDNA and Z-linked alleles (Lopez et al. 2021, Del-Rio et al. 2022), patterns consistent with (i) mitonuclear entrapment of N-mt loci in Z-linked low-recombination strata or (ii) W-linked meiotic drive causing mitochondrial sweeps (Irwin 2025) (**Table 1**). Because female-biased hybrid breakdown could also arise from intrinsic W–Z genic incompatibilities that are unrelated to mitochondria, we treat "entrapment'' here as strictly mtDNA-conditional and recommend (e.g., fitness of F_1 females vs. F_1 males), mito-aware genomic cline analyses (e.g., local ancestry near SDR vs. genome-wide), and physiological assays of OXPHOS performance in reciprocal hybrids to help separate these mechanisms.

Recent simulations and theoretical work (Irwin 2025) indicate that W-drive can rapidly displace mitochondrial haplotypes across hybrid zones even in the absence of strong mitonuclear incompatibilities. This model predicts step-like changes in female-biased ancestry, transient sex-ratio skews during the sweep, and no localized dip in introgression at the SDR once the sweep is complete. Discriminating W-drive from entrapment therefore requires joint analysis of cline shape and symmetry, temporal sex-ratio dynamics, and genomic evidence for centromeric or kinetochore-associated W-linked drive elements.

Takeaways. Stable systems show that mitonuclear conflict can leave persistent, sex-linked signatures, but their ancient architectures limit leverage to ask how *changes in linkage* reshape conflict dynamics.

Table 1. Comparative predictions for mitonuclear conflict across sex-chromosome systems. Predictions for the strength, persistence, and sex-bias of mitonuclear conflict across stable versus labile sex-determination lineages and heterogametic systems (XY vs ZW). Rows highlight representative taxa, characteristic genomic context (e.g. age of the SDR, degree of N-mt linkage), predicted amplification vs relief phases of conflict, expected patterns of hybrid dysfunction, and genomic signatures of barriers. Conflict tends to be most entrenched in ancient, stable X/Z systems, whereas labile lineages with frequent turnover experience more episodic, lineage-specific conflict. ZW systems (purple) often show stronger maternal-haplotype asymmetries because the W chromosome co-inherits with mitochondria, while XY systems (blue) typically display male-biased breakdown during early phases when newly formed strata capture N-mt loci.

Comparative predictions for mitonuclear conflict across sex-chromosome systems				
Axis	Labile XY	Labile ZW	Stable XY	Stable ZW
Exemplars	Some fishes, amphibians	Some fishes, amphibians	Mammals	Birds, butterflies, some snakes
State / Age	Young / neo-XY; patchy suppression	Frequent XY↔ZW switches; homomorphy common	Ancient, conserved XY; long-term suppression	Ancient, conserved ZW
N-mt context	Recent capture of N-mt loci possible	Episodic capture/release of N-mt as SDR moves	X depleted of N-mt; Y decoupled from mtDNA	Z retains many genes; W co-inherited with mtDNA
Conflict expectation	Amplification soon after capture; relief after turnover/expansion	Transient female-biased conflict when W-linked strata trap N-mt	Moderate, persistent (few N-mt loci involved)	Persistent, female-biased; possible W-drive
Hybrid dysfunction	Episodic **male-biased** (heterogametic) breakdown	Lineage-specific; often short-lived	**Male-biased**; large-X effect	**Female-biased**; large-Z effect
Turnover dynamics	Frequent XY↔polygenic transitions	Frequent XY↔ZW; sex-reversal 'fountain-of-youth' recombination	Rare/absent	Rare/absent
Genomic signatures	Sharp local clines at SDR; transient barriers; limited strata	Moving SDR hotspot; test entrapment vs W-drive	Entrenched X-linked barriers; weak mito–X coupling	Mito–Z cline coincidence; entrenched Z effect

Note: Female-biased dysfunction in ZW clades can arise from Z-W genic incompatibilities independent of mitochondria. "Entrapment" specifically predicts mtDNA-conditional effects (see Comparative genomics and new opportunities *section for recommended diagnostics).*

Labile systems as natural experiments: fishes and amphibians

Teleost fishes: labile and fast. Multiple teleost lineages (cichlids, sticklebacks, salmonids, Medaka, darters) exhibit rapid and repeated sex-chromosome turnover, often accompanied by fusions and even XY↔ZW switches within <15–20 million years (Myr) (Kitano & Peichel 2012, Lubieniecki et al. 2015, Myosho et al. 2015, El Taher et al. 2021, Radcliffe et al. 2025). Cichlids are among the fastest; more than a dozen independent XY/ZW systems have been documented across at least ten linkage groups in East African radiations (<2 Myr old), including several that co-occur in compound (W + Y + B-chromosome) systems (Gammerdinger & Kocher 2018). This pattern supports a "hot-potato" model in which new sex-determining alleles repeatedly invade (often linked to sexually antagonistic variants) and later degenerate or are replaced, generating cycles of turnover and transient compound systems (Blaser et al. 2014). Sticklebacks show homologous sex chromosomes but differ widely in the tempo of recombination suppression and Y degeneration (Yoshida et al. 2014, Sardell et al. 2021); neo-sex fusions arose independently and recently in different species (Kitano et al. 2009). Darters have experienced at least two turnovers since the orangethroat–rainbow split (~22 Mya), including a second event within the orangebelly lineage, implying a faster apparent tempo than amphibian benchmarks (Radcliffe et al. 2025) (**Table 1**). These lineages demonstrate that the genomic context for mitonuclear interactions can be reshaped remarkably fast.

Anurans: labile and variable. Many frogs retain homomorphic, recombining sex chromosomes (limiting long-term entrapment), yet others (e.g., *Xenopus*; brown frog complexes) show recurrent strata formation and XY↔ZW transitions (Evans et al. 2024, Miura et al. 2024, Uno & Matsubara 2024). In *Xenopus*, Evans et al. (2024) inferred seven turnovers across ~321 Myr, implying a minimum rate of ≈0.022 events Myr^{-1} (~1 per 46 Myr); because extinct/cryptic events are missed and mt calibrations may overestimate divergence, true rates are likely higher. In Ranidae, Jeffries et al. (2018) estimated ~0.02 turnovers Myr^{-1}, or ~1 turnover every 50 Myr of lineage-specific time (so sister taxa ~25 Myr apart often differ by one turnover) (**Table 1**).

Takeaways. Turnovers often occur on ecological- to mid-evolutionary-timescales (10^4 - 10^6 years) and are typically accompanied by local recombination suppression around newly arising sex-determining loci (Saunders 2019, Palmer et al. 2019). These “resets” repeatedly alter the linkage context for nearby N-mt genes, creating natural experiments: some turnovers generate sharp but transient mitonuclear conflicts when N-mt loci become newly sex-linked, whereas others erase conflict when recombination is restored or the sex determining region (SDR) shifts to a different chromosome. Several teleost radiations show sub-Myr to few-Myr turnovers - often with fusions and XY↔ZW switches - illustrating that genomic context can be rewritten remarkably fast.

Classic models of sex-chromosome turnover highlight a recurring set of mechanistic levers (i.e., sexually antagonistic selection, mutational load on non-recombining Y/W regions, genetic drift, heterochiasmy and recombination-landscape variation, and sex reversal) (reviewed in Vicoso 2019) that jointly influence when new SDRs arise, when recombination is suppressed, and whether existing systems become evolutionarily “trapped” or are replaced. These same factors are expected to modulate the likelihood and strength of mitonuclear entrapment, with strongest effects in young non-recombining strata and weaker effects under homomorphy or when sex-reversed recombination (“fountain-of-youth” effects) (Perrin 2009) maintains gene exchange between the sex chromosomes (see **Box 1** for a concise synthesis of how each driver affects mitonuclear entrapment or relief). Together, fishes and amphibians provide the comparative power to test how quickly sex-linked genomic architecture and the associated mitonuclear interactions can be remodeled.

Box 1. Turnover drivers and mitonuclear forecasts

- Sexually antagonistic selection near sex determining region (SDR) → favors recombination suppression → N-mt entrapment if nearby → early, strong heterogametic breakdown.
- Mutation load/hot-potato → favors replacement of the old Y/W → conflict relief if N-mt leaves SDR → decaying genomic scar.
- Heterochiasmy/low male recombination → broader non-recombining strata around the SDR → stronger/longer entrapment unless fountain-of-youth recombination intervenes.
- Sex reversal (e.g., seen in some anurans) → intermittent X-Y recombination → weak/episodic entrapment.
- Chromosomal relocation of the sex-determining gene → rapid relinking of N-mt to (or from) SDR → asymmetric clines conditioned on mt haplotype.

Turnover as an evolutionary "escape hatch"

I propose that sex-chromosome turnover functions as a genomic escape hatch. When deleterious mitonuclear interactions are amplified because an N-mt gene is entrapped in a Y- or W-linked stratum, a subsequent turnover (either restoring recombination or moving the sex-determining locus) can release that locus from persistent sex-biased inheritance (**Fig. 2**).

Predictions

1. *Amplification phase:* Nascent non-recombining strata that capture N-mt loci produce intensified, often heterogametic-biased conflict, segregation distortion, and steep genomic clines centered on the SDR (**Fig. 2**).

2. *Relief phase:* Later turnover or recombination expansion decouples the locus from tight sex linkage, lowering conflict and eroding barriers (**Fig. 2**); this leaves a genomic "scar" characterized by attenuating introgression deficit/discordant ancestry through time.

3. *XY vs. ZW asymmetries*: Because the W co-transmits with mtDNA whereas the Y does not, ZW systems should more often exhibit persistent female-biased breakdown and mt

sweeps via W-drive; XY systems may show more frequent *relief* via turnover if N-mt loci are purged from tight X-linkage (**Table 1**).

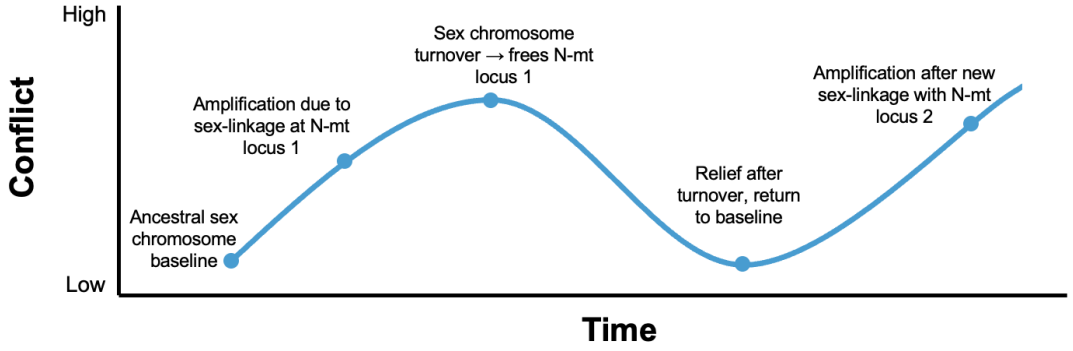

Figure 2. Turnover as an evolutionary "escape hatch." Conceptual timeline showing how cycles of sex-chromosome turnover modulate the intensity of mitonuclear conflict through time. Conflict is low under the ancestral sex-determining region (SDR). When a turnover event establishes a new SDR that captures an N-mt locus, conflict is amplified (upslope) as compensatory evolution is constrained in the non-recombining stratum. A subsequent turnover that frees that locus from the SDR relieves conflict (downslope). If a later turnover again captures a different N-mt locus, conflict rises anew. These repeated amplification-then-relief cycles predict pulses of hybrid incompatibility and leave alternating genomic "scars" of reduced introgression at formerly sex-linked regions.

Hybrid zones and speciation consequences

Hybrid zones provide natural experiments to test how sex-linked mitonuclear entrapment versus escape predicts patterns of reproductive isolation.

Stable XY (mammals): Persistent hybrid breakdown often affects the heterogametic sex (males), largely due to hemizygous exposure and incomplete dosage compensation rather than mitonuclear conflict, as most N-mt loci have relocated to autosomes (Drown et al. 2012).

Stable ZW (birds): Show persistent coincidence of mitochondrial and Z-linked clines with female-biased hybrid sterility or inviability. Entrapment versus W-drive (Irwin 2025) can be distinguished by the spatial scope of the signal (SDR-localized versus genome-wide mtDNA

sweep, **Fig. 3**), the tempo of mitochondrial haplotype replacement, transient female-biased sex ratios, and W-centric cytological features.

Turnover-prone fishes: Exhibit two-phase dynamics: sharp incompatibilities arise after new sex-linkage (amplification) and relax following subsequent turnover (relief), predicting temporal heterogeneity in barrier strength across related taxa (**Fig. 2, 3**).

Homomorphic frogs: Ongoing recombination and sex reversal limit entrapment (Dufresnes & Crochet 2022), producing only localized, ephemeral barrier peaks and weak large-sex-chromosome effects.

The tempo and mode of postzygotic isolation thus depend not only on sequence divergence but also on sex-chromosome age and turnover history. Below we outline emerging genomic and hybrid-zone approaches that make these tests feasible.

Comparative genomics and new opportunities

Recent advances in genome assembly, resequencing, and hybrid-zone methods now enable mito-aware tests layered onto standard pipelines for sex-chromosome detection.

- *Chromosome-level assemblies and dated strata:* High-quality chromosome-scale genomes let us place each nuclear-encoded mitochondrial (N-mt) gene in its precise physical context relative to the sex-determining region (SDR). When assemblies are available for multiple related taxa, we can date when each SDR arose, when nearby recombination suppression expanded, and whether N-mt genes were repeatedly captured or released during turnover (Wright et al. 2017, Palmer et al. 2019, Vicoso 2019).

- *Detection signals across degeneration levels:* Different tools work best at different ages of sex-linked strata. In young strata, look for sex-biased heterozygosity, male/female coverage shifts, and peaks in sex-differentiated F_{ST}. In older strata, where allelic diversity is purged, tests of monophyly or topology-weighting of gene trees can reveal ancient non-recombining blocks (Bachtrog 2013, Charlesworth 2017, Darolti et al. 2019).

- *Hybrid-zone toolkits:* Apply genomic-cline approaches (e.g. Gompert & Buerkle 2011) but treat the mtDNA ancestry as a focal covariate ("mito-aware" genomic clines) to test whether sex-linked N-mt loci show steeper, mtDNA-coincident barriers than neutral loci. For example, a locus whose ancestry cline steepens only in individuals carrying a foreign mitochondrial haplotype points to mito-aware selection. Related ancestry-distortion approaches (Li et al. 2022, Heidbreder et al. 2025) likewise reveal Dobzhansky–Muller–type loci that resist introgression. Coupled with ABBA–BABA tests and local-ancestry barrier scans, these methods map selection acting on mitonuclear combinations in hybrid zones (Radcliffe et al. 2025).

- *Expression and physiology:* Transcriptomic and physiological assays can connect genotype to phenotype: single-cell or sex-biased OXPHOS-gene expression, dosage-compensation testing, and reciprocal-hybrid measurements of mitochondrial function (e.g. respiration or ATP production) can all indicate whether incompatibilities translate into measurable fitness costs (Hill 2019, Mossman et al. 2019, Moran et al. 2025).

- *Discriminating entrapment vs. W-drive (ZW):* Distinguishing a localized mitonuclear barrier caused by entrapment from a genome-wide maternal sweep driven by a W-linked meiotic-drive allele requires integrating multiple diagnostics. Spatially, entrapment produces localized barriers near the SDR, whereas W-drive produces genome-wide displacement of the mitochondrial cline (**Fig. 3**). Temporally, a W-driven sweep is expected to leave a step-like contraction in Bayesian skyline plots of mtDNA diversity that reflects a recent selective sweep of one haplotype. Additional evidence can come from sex-ratio distortions through time, distinctive W-linked centromere features, and screens for endosymbionts that sometimes mediate female-biased transmission distortions (Irwin 2025).

Together these approaches connect genomic architecture to hybrid breakdown across radiations in diverse taxa and enable comparative tests of entrapment and escape-hatch turnover.

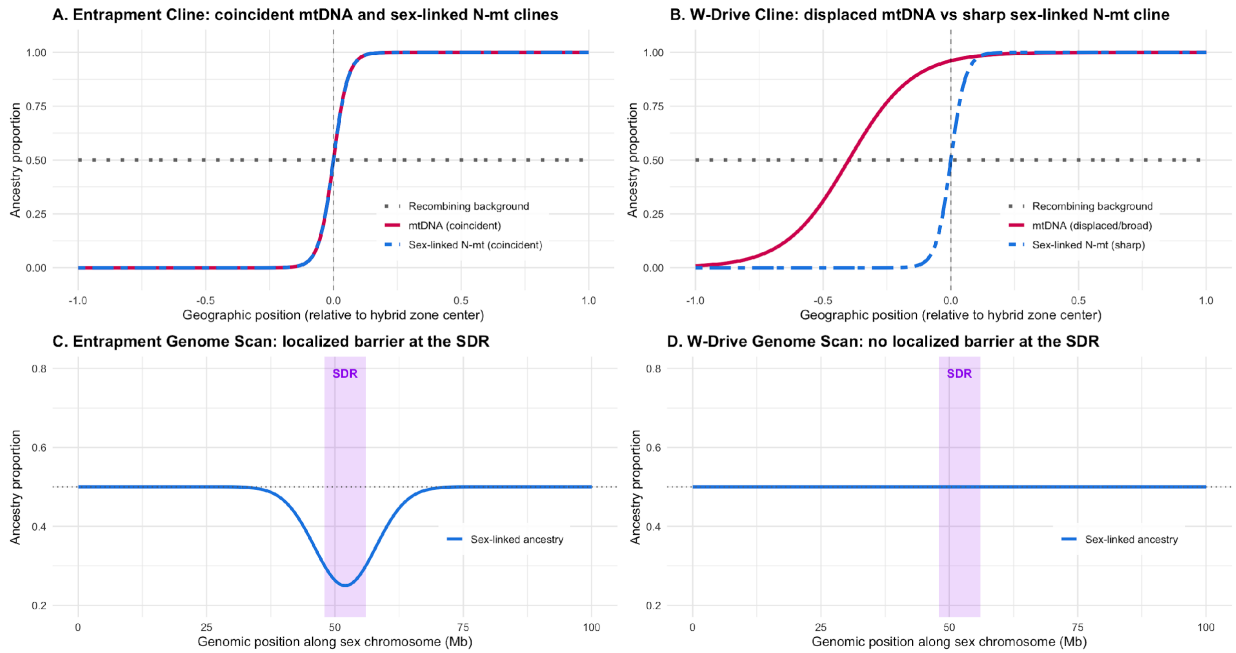

Figure 3. Hybrid-zone and genome-scan signatures distinguishing sex-linked mitonuclear entrapment from W-driven mitochondrial sweeps. (A) *Entrapment cline*: In a hybrid zone, a nuclear-encoded mitochondrial (N-mt) locus captured in a newly non-recombining sex-linked stratum shows a steep ancestry cline that coincides with the mitochondrial cline at the hybrid-zone center, reflecting mito-aware selection against mismatched combinations. Recombining background loci remain near-neutral (~0.5). **(B)** *W-drive cline*: A W-driven sweep moves the mitochondrial ancestry far across the contact zone, capturing much of the range of the other species. As a result, the mtDNA cline no longer sits at the center of the zone (x = 0); it becomes shifted (displaced) toward one side and broadened, because the sweep acts genome-wide on mitochondria, not just locally at the sex-linked stratum. The positional and width mismatch between mtDNA and the sex-linked N-mt cline are indicative of a maternal sweep rather than local entrapment. **(C)** *Entrapment genome scan*: Along the sex chromosome, introgression is near-neutral (~0.5 ancestry proportion) in recombining regions but shows a localized dip at the sex-determining region (SDR), a persistent "genomic scar" where the N-mt locus was entrapped. **(D)** *W-drive genome scan*: Introgression along the sex chromosome remains flat (~0.5) across both recombining and SDR regions because a W-linked sweep is predicted to displace mitochondrial haplotypes genome-wide rather than creating a local incompatibility. Accordingly, no localized barrier appears at the SDR.

Outlook: Implications for sexual conflict and speciation

Integrating stable and labile systems reframes sex chromosomes not as static repositories of incompatibilities but as dynamic elements that can repeatedly amplify or alleviate conflict. This perspective explains why some clades exhibit strong, persistent large-X/Z effects (Ellegren 2009, Llopart 2012) whereas others show transient or negligible sex-linked barriers. Because the rate/direction of sex-chromosome turnover shapes when and where N-mt loci become entrapped, we can forecast when mitonuclear conflict will influence lineage persistence, species diversification rates, and geographic patterns of biodiversity (**Box 1**). Key priorities include estimating the prevalence of N-mt entrapment, the half-life of conflict following turnover, how ecological stressors (e.g., hypoxia, temperature) modulate conflict severity, and how XY vs ZW asymmetries interact with recombination landscapes and the fountain-of-youth.

Concluding Remarks

Viewing mitonuclear incompatibilities through the lens of sex-chromosome turnover reframes long-standing patterns such as the large-X/Z effect (Ellegren 2009, Llopart 2012) as dynamic outcomes of local entrapment rather than immutable rules. This perspective highlights turnover as a macroevolutionary switch that can repeatedly reshape hybrid-zone barriers, lineage persistence, and diversification rates by alternately trapping and releasing conflict-prone N-mt loci. With chromosome-level assemblies, hybrid-zone genomics, and mito-aware expression assays now within reach across many vertebrate clades, the predictions laid out here, including episodic pulses of hybrid breakdown, XY vs ZW asymmetries, and decaying genomic scars, are ready for decisive testing. Mapping turnover histories alongside mito-nuclear architecture promises a more predictive understanding of how sex chromosomes influence both the origin of species and the distribution of biodiversity.

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