

Hybrid Incompatibility Driven By Nuclear - Mitochondrial Sexual Conflicts

Manisha Munasinghe^{1*}, Andrew G. Clark¹

¹ Department of Computational Biology, Cornell University, Ithaca, NY, United States

✉ mam737@cornell.edu

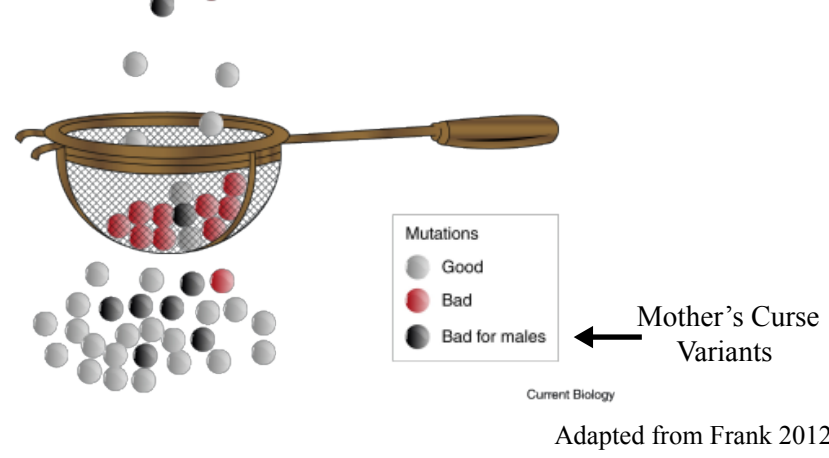
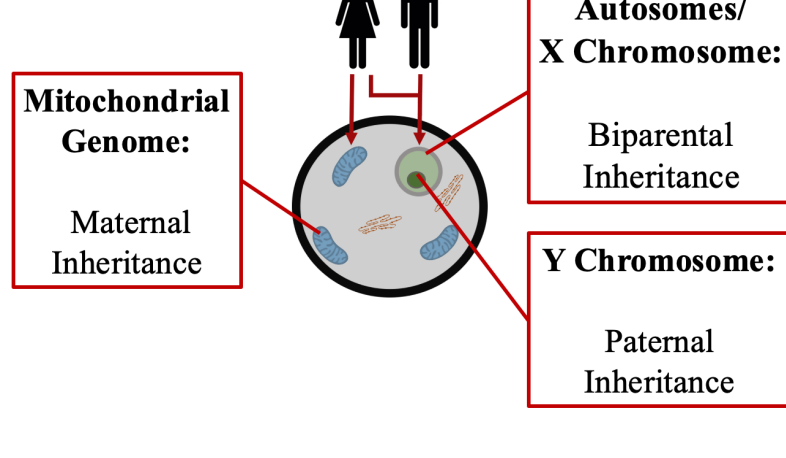
🐦 @ManishaMuna

🐱 mam737



Transmission Asymmetries Can Both Cause and Resolve Conflict

The maternal inheritance of mtDNA means that mutations that are beneficial in females can spread in a population even if they are deleterious in males, a form of sexual conflict previously described as Mother's Curse.^{1,2}



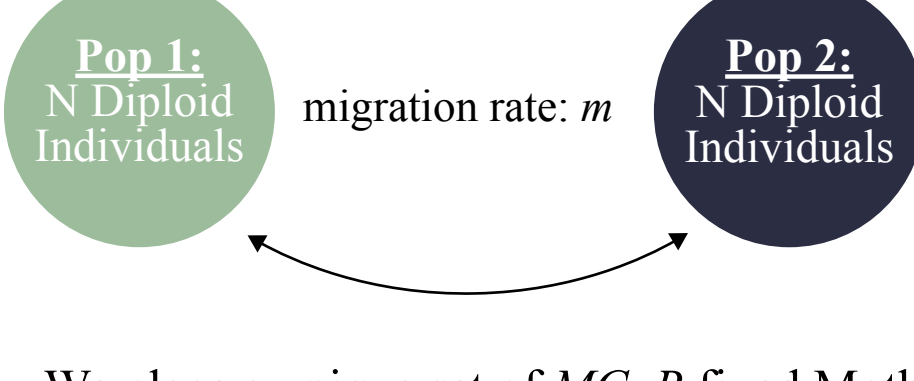
Adapted from Frank 2012

Restorers emerge in the nuclear genome to rescue male fitness and disrupting these interactions is thought to act as a form of Dobzhansky-Muller incompatibilities.

However, the dynamics of these restorers are greatly influenced by whether they are found on an autosome, X chromosome, or Y chromosome due, in part, to asymmetries in their transmission as well.³⁻⁵

Here, we use SLiM3⁶ to expand analytical theory to investigate the consequences of sexually antagonistic mitochondrial-nuclear interactions in a subdivided population.

Modeling Disruption of Mother's Curse Variants and Nuclear Restorers Via Migration

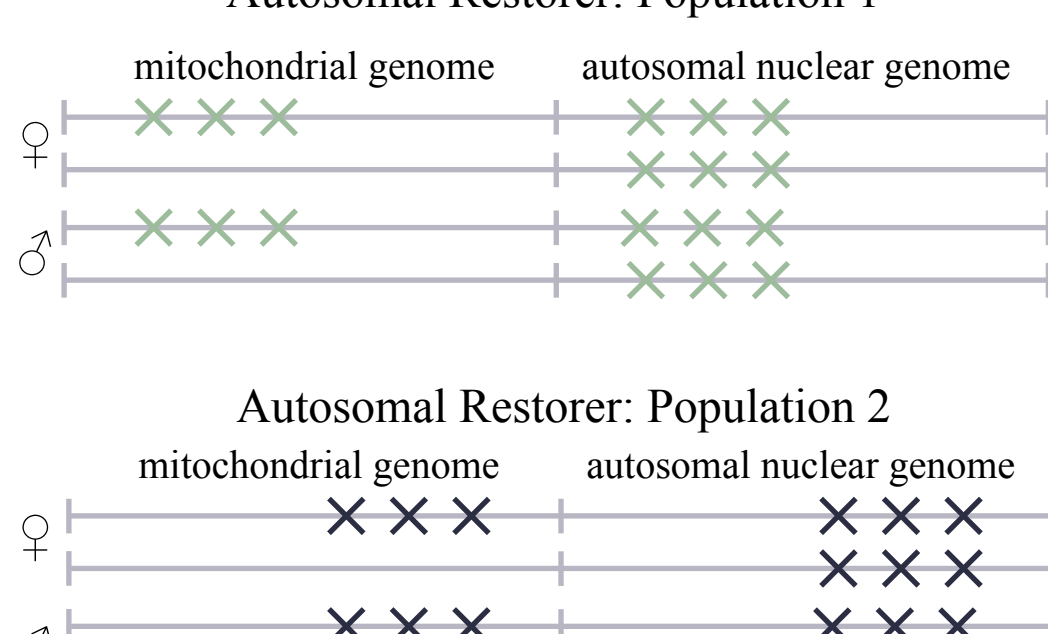


Initialize 2 diploid, dioecious populations, each of size N , with a symmetrical migration rate m between them.

We consider 2 genomic elements - a haploid mitochondrial genome and a nuclear genome that represents either an autosome, X chromosome, or Y chromosome.

We place a unique set of MC_R fixed Mother's Curse variants on the mitochondrial genome and restorers on the nuclear genome of each population as it is unknown how many of these interactions are found within the genome.

Visual Schematic of Population Initialization



We do not introduce new mutations into the genome at any point, but we do allow recombination to occur between nuclear restorers, with the exception of Y-linked restorers.

The fitness of Mother's Curse variants in females is the same across all nuclear restorer types, while the fitness in males depends on the transmission pattern and ploidy of the nuclear restorer (visualized below in Tables 1a-c). The final fitness of an organism is then the sum of these effects over all Mother's Curse loci.

Each Mother's Curse variant has the same fitness cost and all restorers share the same strength of restoration in males. For each Mother's Curse variant, there is one corresponding restorer

1a) Autosomal Restorer

♀	
mt _A	1
mt _a	1 + s _f

1b) X-Linked Restorer

♀	
mt _A	1
mt _a	1 + s _f

1c) Y-Linked Restorer

♀	
mt _A	1
mt _a	1 + s _f

♂	AA	Aa	aa
mt _A	1	1	1
mt _a	1-s _m	1- (d*s _m)	1

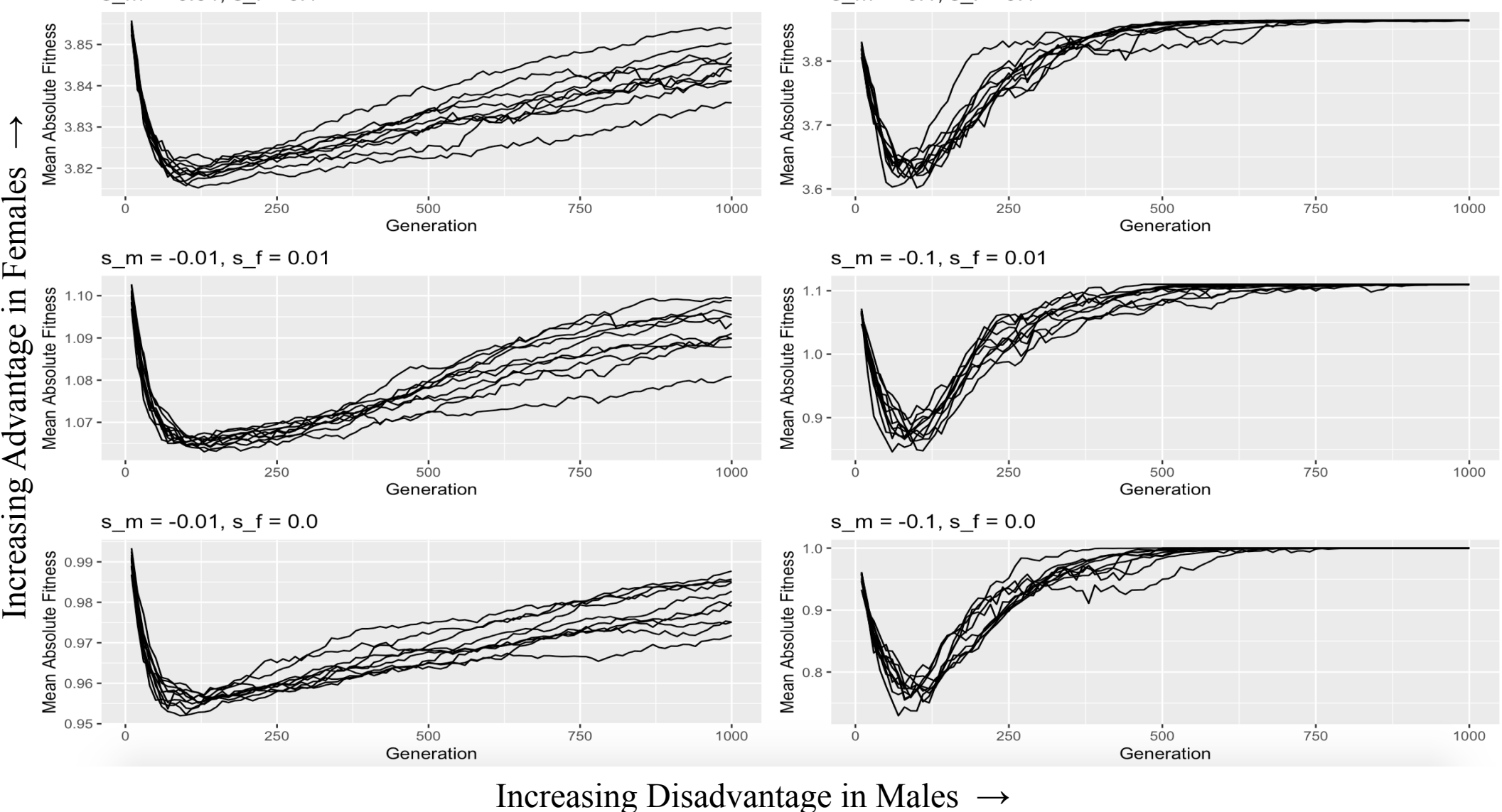
♂	XY	xY
mt _A	1	1
mt _a	1-s _m	1

♂	XY	Xy
mt _A	1	1
mt _a	1-s _m	1

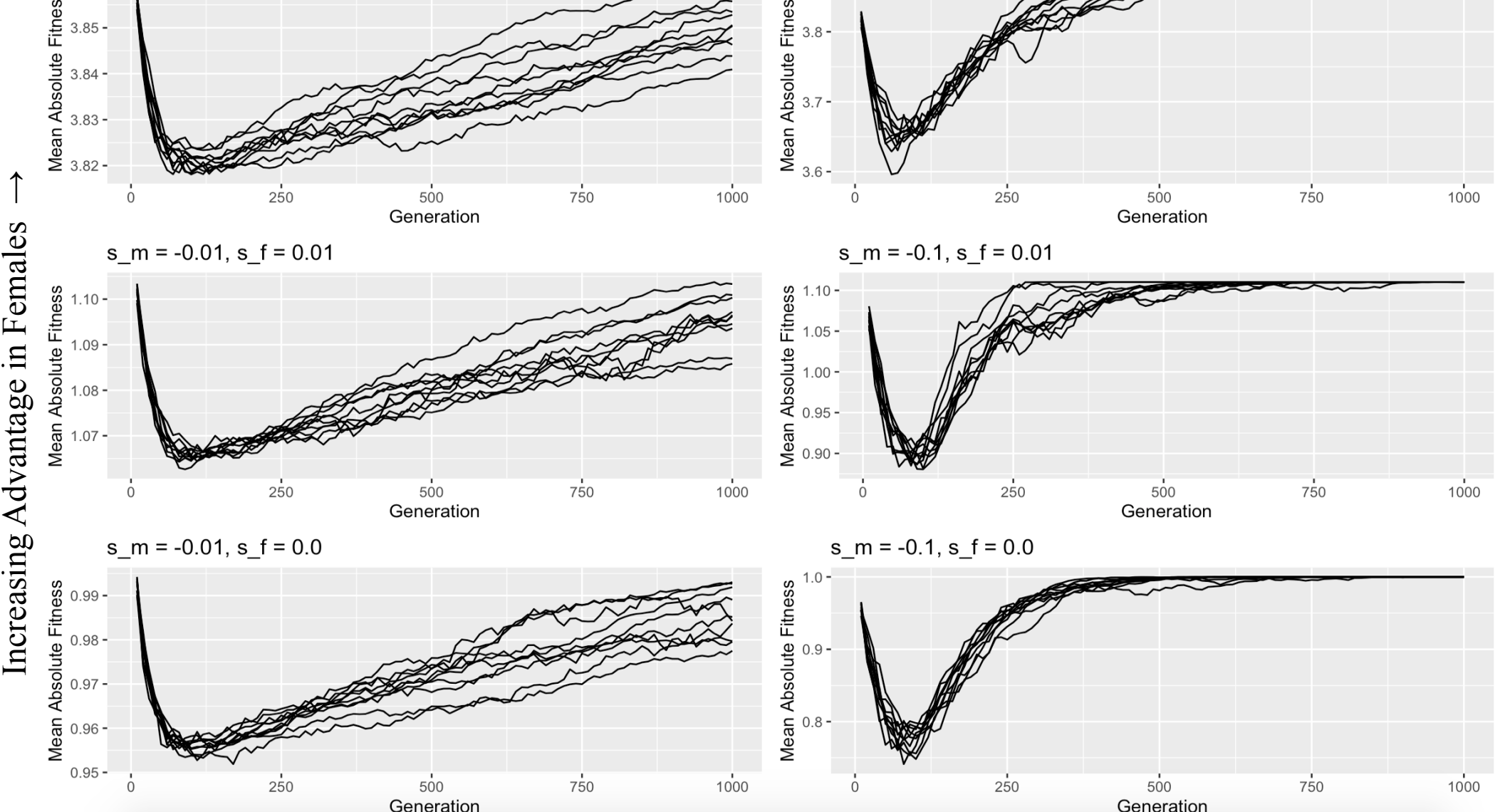
To visualize the following results, we fix the following: $N = 1000$, $m = 0.01$, $MC_R = 20$

Migration Disrupts Interactions And Reduces Fitness Until Restorers Spread Through Both Populations

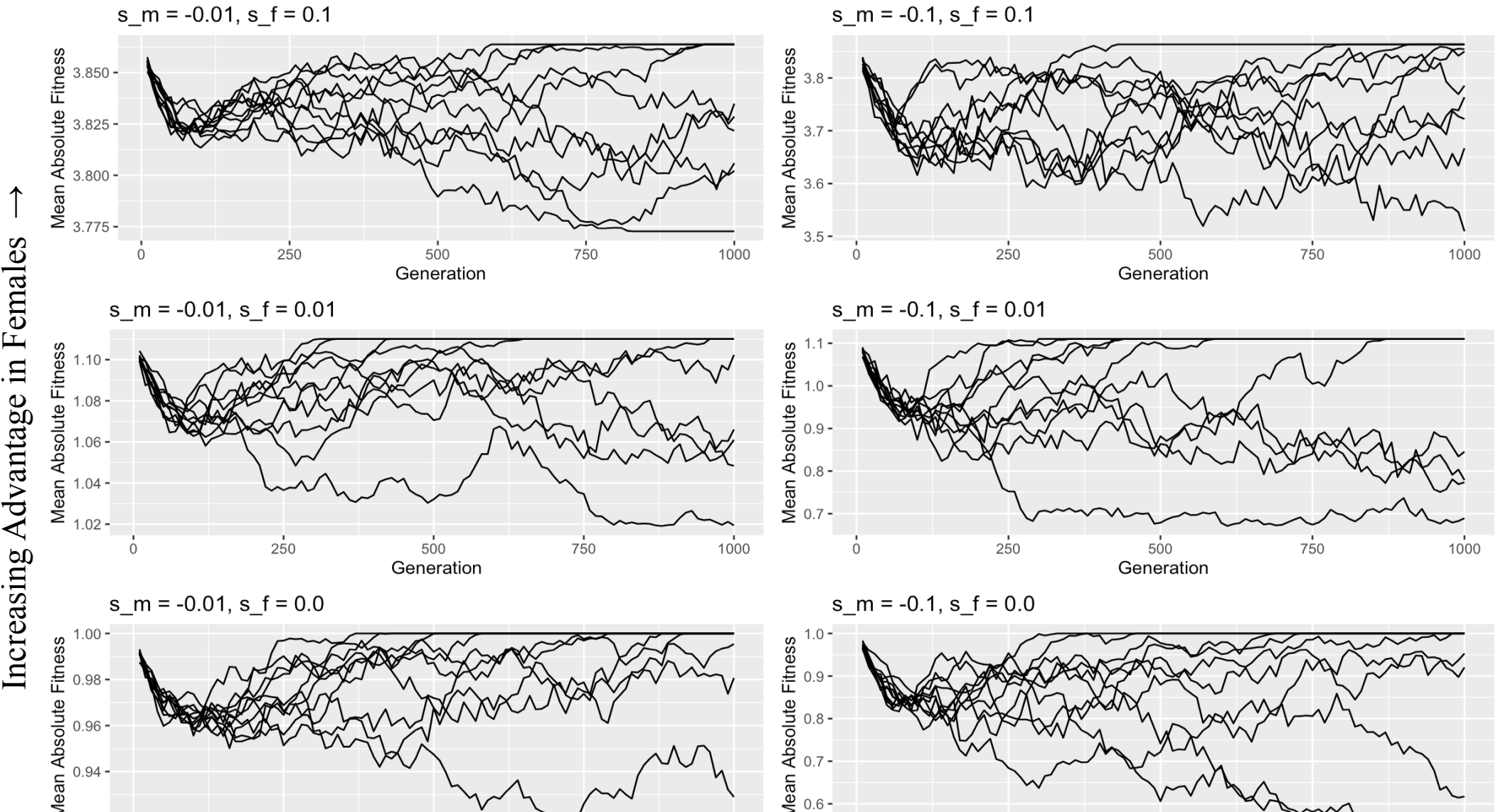
(2a) Autosomal Restorers: Mean Absolute Fitness Averaged Across Both Populations



(2b) X-Linked Restorers: Mean Absolute Fitness Averaged Across Both Populations



(2c) Y-Linked Restorers: Mean Absolute Fitness Averaged Across Both Populations



Deleterious Cost Drives Fitness Trajectories

Fitness trajectories are largely driven by the deleterious cost of these variants in males.

As the cost of these mitochondrial Mother's Curse variants in males increases, not only is the subsequent drop in fitness after migration relatively stronger but it is also recovered faster as the selective pressure for nuclear restorers is stronger

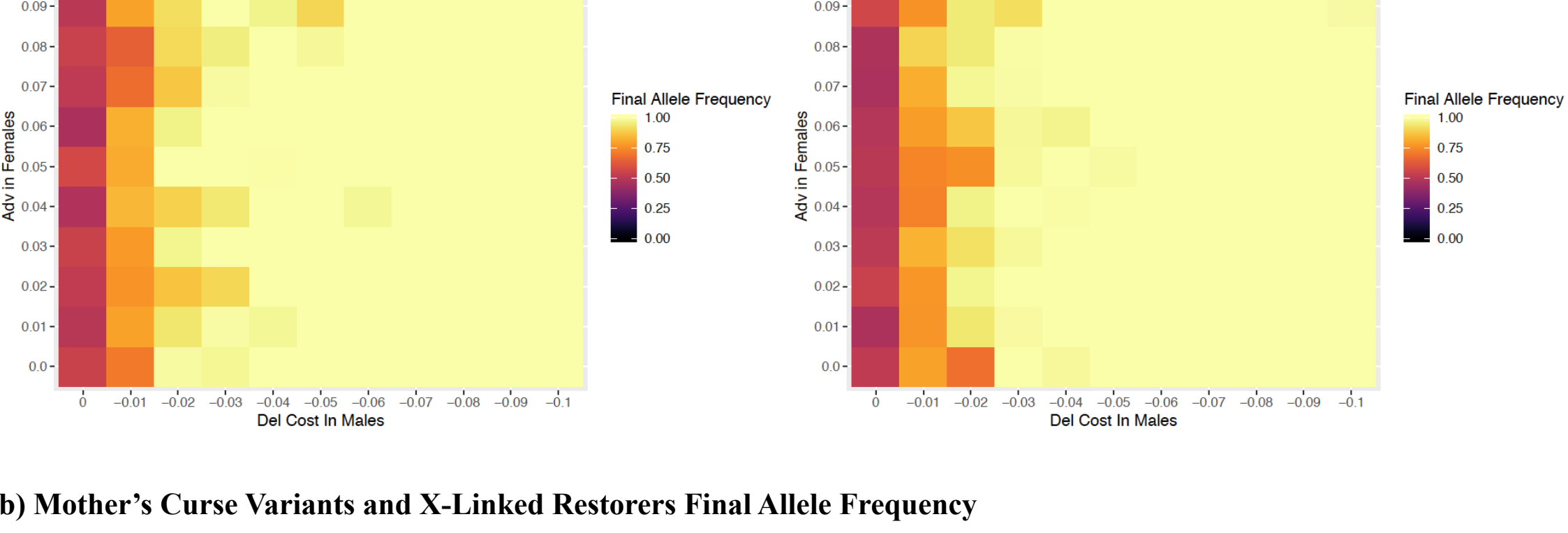
Y-Linked Restorers Show Unique Fitness Trajectories

There is very little difference between the fitness trajectories of autosomal and X-linked restorers. While the reduction in fitness and time to recover is largely dependent on the deleterious cost in males, fitness is almost always fully recovered.

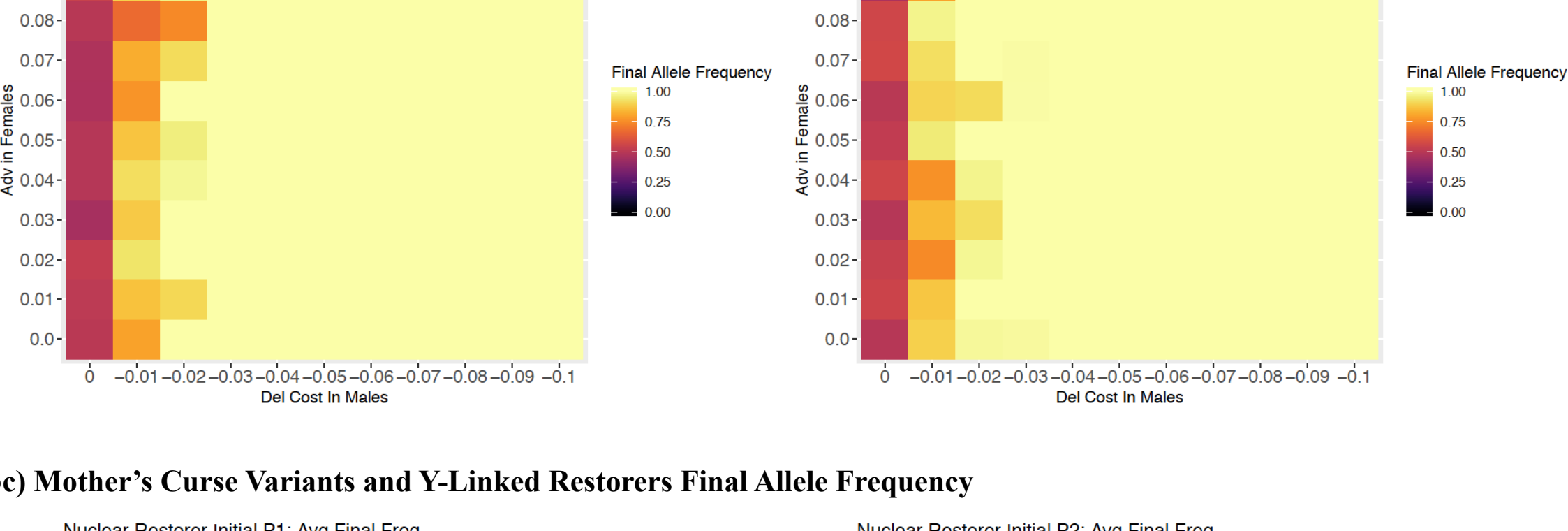
However, Y-linked restorers show a very different pattern. We still see an initial reduction in fitness, but the final fitness at the end of the simulation is much more variable with some runs showing a constant reduction in fitness.

Nuclear Restorers Spread And Fix, While Mother's Curse Variants Remain Segregating

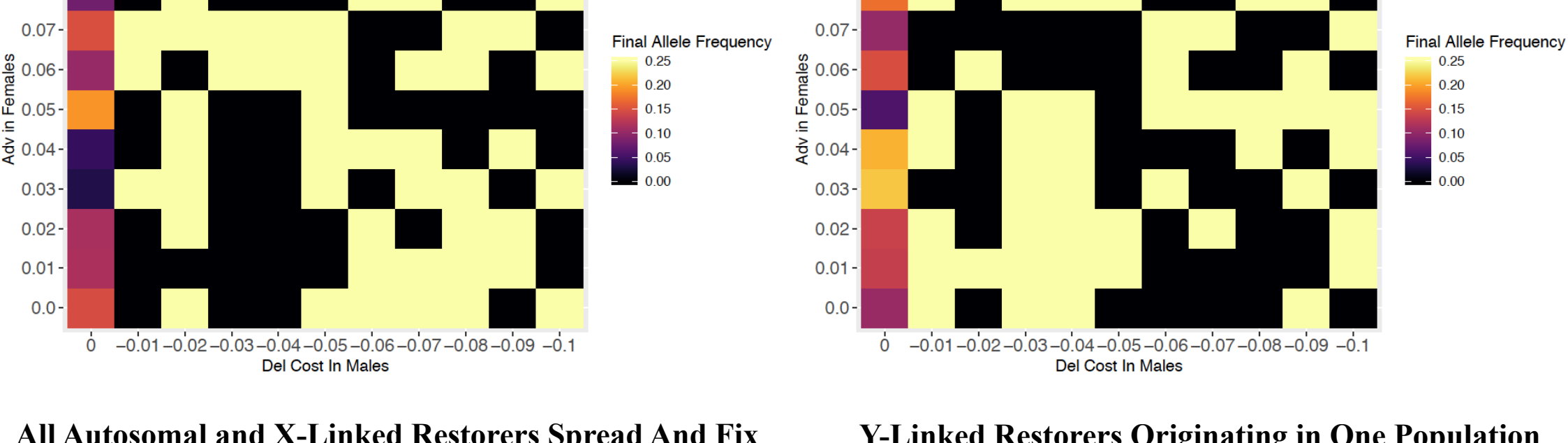
(3a) Mother's Curse Variants and Autosomal Restorers Final Allele Frequency



(3b) Mother's Curse Variants and X-Linked Restorers Final Allele Frequency



(3c) Mother's Curse Variants and Y-Linked Restorers Final Allele Frequency



All Autosomal and X-Linked Restorers Spread And Fix

All restorers ultimately spread and reach fixation in both populations

There is no relative advantage of one mitochondrial haplotype over another after both restorer sets fix. Without any selective pressure, the frequency of each mitochondrial haplotype is driven predominantly by genetic drift.

Y-Linked Restorers Originating in One Population Fix and Replace the Others

We still see fixation of Y-linked restorers, but a lack of recombination in the Y Chromosome allows only one haplotype to fix as it replaces the other.

As one Y haplotype and all linked restorers is lost, fitness cannot be recovered for any individuals carrying the associated mitochondrial haplotype potentially explaining the fitness plots of Y-linked Restorers (2c).