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Signature of Sexual Conflict is Actually Conflict Resolved

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There has been substantial interest of late in using population genetic methods to study sexual conflict, where an allele increases the fitness of one sex at some cost to the other (Mank 2017). Population genomic scans for sexual conflict offer an important advance given the difficulties of identifying antagonistic alleles from more traditional methods, and could greatly increase our understanding of the extent and loci of sexual conflict. This is particularly true for studies in natural populations, for which obtaining accurate fitness measurements for each sex can be challenging. In this issue of *Molecular Ecology*, Bissegger et al. (XX, XXX-XXX) present a cautionary tale about how to interpret these population genomic data.

Several recent reports have used differences in allele frequency (such as F_{ST}) between males and females to assess the extent of sexual conflict in a population. Because allele frequencies are identical between the sexes

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at conception for autosomal loci, the thinking goes that any significant sex differences observed in adults must result from discrepancies between males and females in how an allele influences viability, predation or disease (Mank 2017). Over the life cycle of a cohort, we might expect allele frequency differences to increase as sex differences in mortality accumulate (Fig. 1).

Although some assessments have found significant differentiation in a few loci (Flanagan & Jones 2017; Wright et al. 2018; Wright et al. 2019), others have identified hundreds, even thousands of loci that show major differences in allele frequency between females and males (Cheng & Kirkpatrick 2016; Dutoit et al. 2018; Lucotte et al. 2016). While the former have been argued to be evidence of sex-specific genetic architecture, and therefore conflict resolved (Wright et al. 2018), the latter findings were taken as the signature of ongoing sexual conflict manifesting across a large proportion of the genome.

However, the observation of widespread allelic differences between the sexes presents an intriguing mystery. The selection coefficients required to produce significant differences in allele frequency by sexual conflict are quite high (Kasimatis et al. in press; Kasimatis et al. 2017), and strong selection coefficients on a large number of loci across the genome would result in excessive sex-specific mortality rates (Fig. 1). If true, populations would be expected to experience unbearable mortality loads, as vanishingly few individuals would carry the correct allelic complement for their sex and would not survive to reproduce. How could any species, particularly those with low fecundity such as humans (Lucotte et al 2016; Cheng & Kirkpatrick 2016) and passerines (Dutoit et al. 2018), possibly persist in the face of these predicted mortality rates?

In this issue, Bissegger et al. (2019) present at least a partial explanation for these findings. They searched the stickleback genome for regions with allele frequency differences between males and females. Similar to other studies (Cheng & Kirkpatrick 2016; Dutoit et al. 2018; Lucotte et al. 2016), they initially found an implausibly large number of loci with substantial differences between the sexes. Further analysis revealed that these were in fact regions that had recently duplicated from the autosomes to the Y chromosome. Because the stickleback reference genome assembly was done on a female, it currently lacks a Y sequence, and so sequence reads from the Y duplications in male samples mapped back to the original autosomal location. This created perceived allelic differences between the sexes that were in fact due to male-specific mutations accumulating on the Y chromosome (Fig. 2). Subsequent copy number expansion of the Y duplications can in turn generate even higher patterns of intersexual allele frequency differences.

This explanation carries an interesting irony. Although many have concluded that intersexual allele frequency differences are the product of sexual conflict (but see Wright et al. 2018; Wright et al. 2019), the pattern found by Bissegger et al. (2019) actually represents at least the partial resolution of sexual conflict.

Duplication to the Y chromosome is a well accepted route by which sexually antagonistic variation can become male-specific, thereby resolving conflict. Fisher (1931) predicted that the Y chromosome would accumulate genetic variation beneficial to males, and recent surveys have suggested that the rate of translocation from the autosomes to the Y chromosome can be very high (e.g. Tobler et al. 2017).

Duplications to the sex-limited chromosome could account for much of the signal of allele frequency differences in other species currently attributed to ongoing conflict. This is particularly likely for observations that sex-biased genes in particular exhibit elevated allele frequency differences (Cheng & Kirkpatrick 2016; Dutoit et al. 2018), given that genes duplicated to a Y chromosome will show male-specific expression. Indeed, the loci with the most extreme allele frequency differences might actually be those for which conflict has been most effectively resolved via Y duplication and subsequent copy number expansion.

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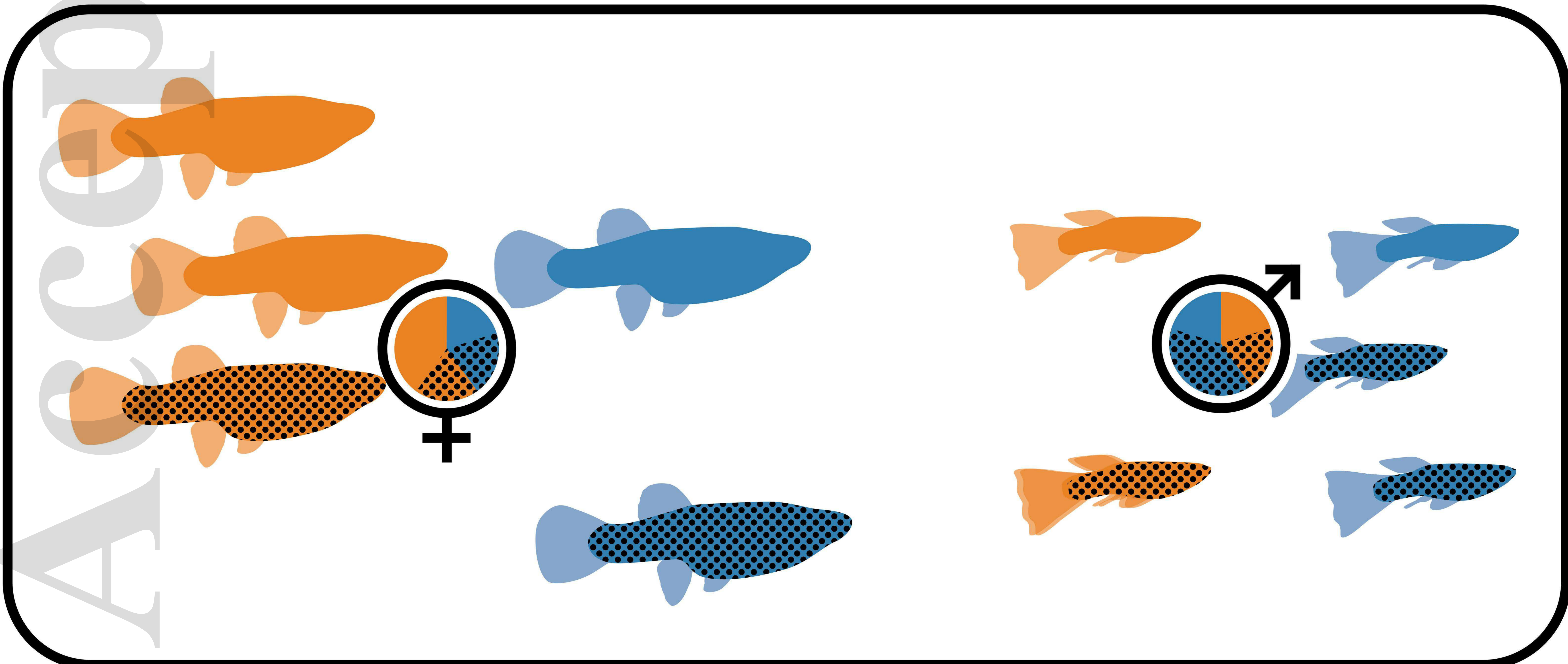
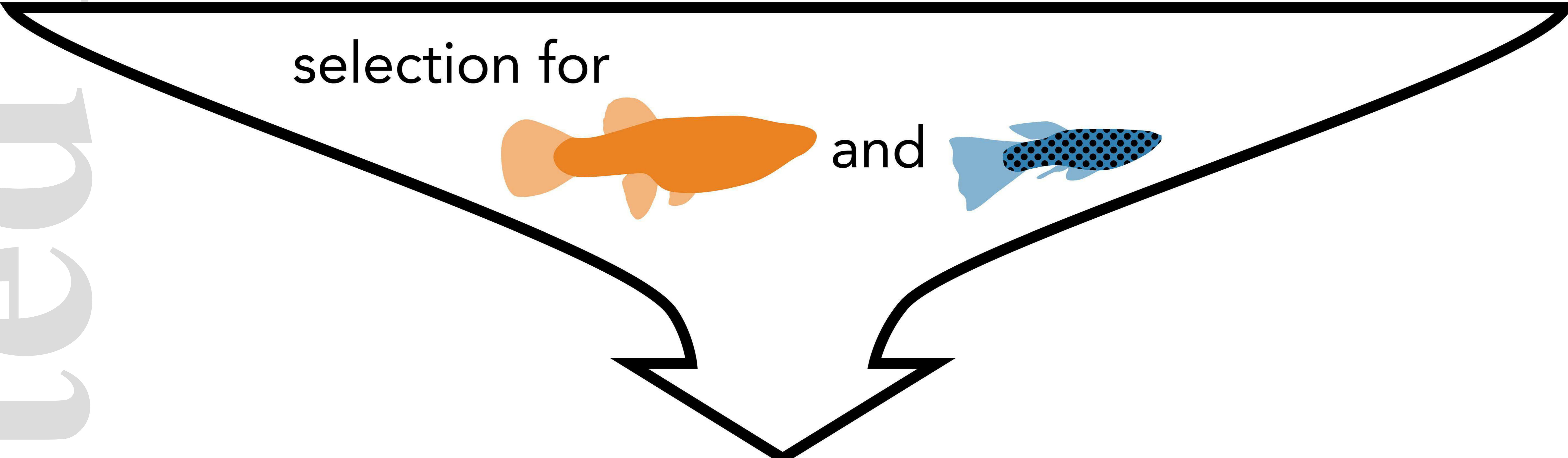
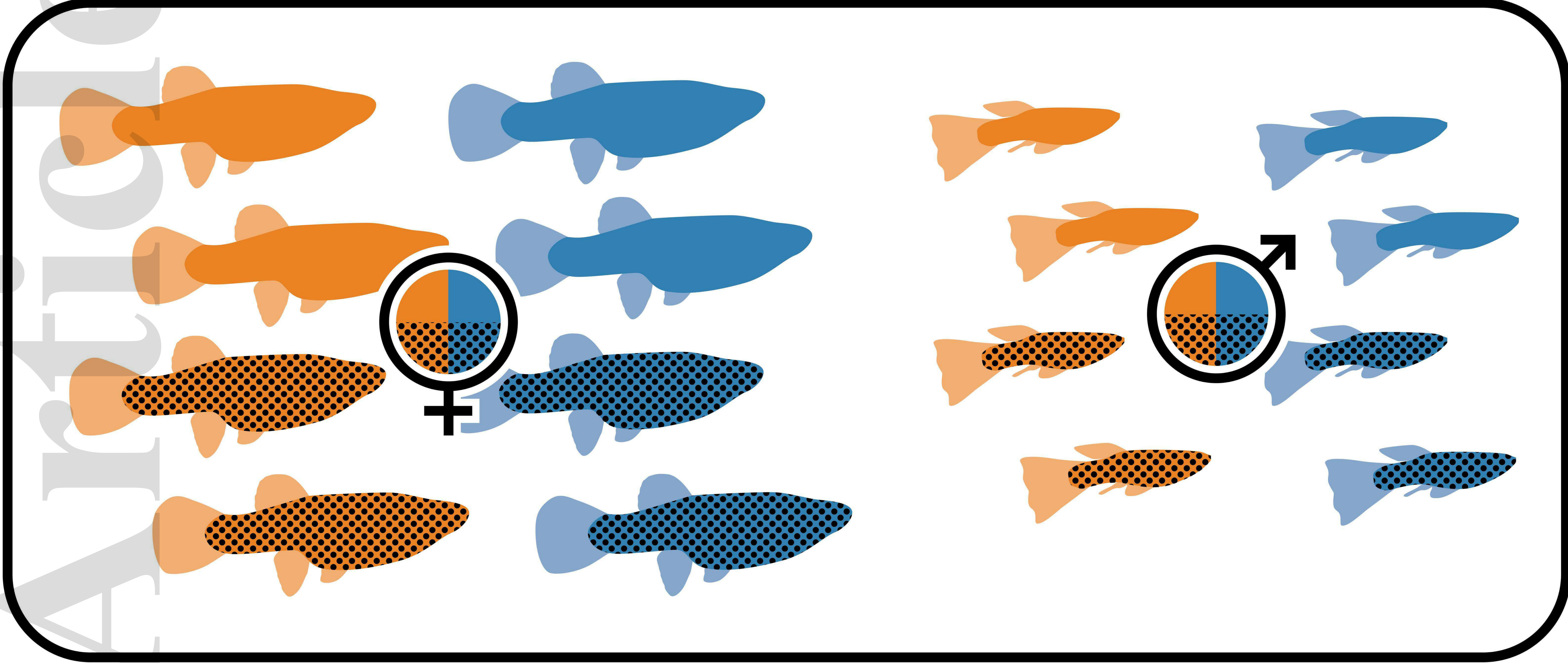
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Fig. 1. Opposing selection at multiple loci between males and females. Two loci, one encoding colour and another for pattern, are associated with different mortality rates between the sexes. Selection for optimal female phenotype (orange, plain) and male phenotype (blue, spotted) results in both significant mortality and sex-specific allele frequency differences in adults.

Fig 2. Duplication to the Y chromosome leads to perceived differences in male and female allele frequency. Duplications from autosomal loci (green) to the Y chromosome (blue) map back to the autosomal locus on the female reference genome. Y-specific mutations on duplicated regions (blue stars) lead to false inflation of allele frequency differences between the sexes.

random assortment of alleles during meiosis
= equal frequencies of phenotypes at birth



sex-specific allele frequencies
differ in adult population

