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On the power to detect rare recombination events

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We read with great interest the recent work¹ describing differences in male and female recombination patterns on the guppy (*Poecilia reticulata*) sex chromosome. We fully agree that recombination in males is largely confined to the ends of the sex chromosome. The authors interpret these results to suggest that our previous findings, of population-level variation in the degree of sex chromosome differentiation in this species², is incorrect. However, we suggest that their results are entirely consistent with our previous report, and that their interpretation presents a false controversy.

Our population genomic results indicated that crossing over between the X and Y is rare across most of the guppy sex chromosome², and the report by Bergero et al.¹ is entirely consistent with this. Indeed, Fig 2 from Bergero et al.¹ is strikingly concordant to Fig 3 in our report², especially when taking into account the fact that they used less stringent parameters for read mapping. We have recently expanded our analysis across related species³, and our results show similar patterns in a sister species. Importantly, our work³ shows that the guppy sex chromosome system is in fact far older than previously assumed, implying a persistent low level of recombination between the X and Y. Even very rare recombination events between the sex chromosomes prevents divergence of the Y⁴, explaining the homomorphy on the guppy sex chromosomes despite their significant age.

Our previous work suggested that this persistent X-Y recombination varies across populations, however Bergero et al.¹ did not detect these differences in their data. The crucial question is about infrequent recombination events between the X and Y, and why these differ between upstream and downstream populations. Bergero et al.¹ are unable to provide this level of granularity in their recombination estimation due to low sample sizes.

To illustrate, estimates of X-Y recombination outside the male hotspot range from 1/100 to 1/1000^{1,5}, and we use these estimates for a conservative power analysis⁷. On the basis of the sample sizes reported¹, and using the upper bound of recombination outside the hotspots (1/100), we estimate that Bergero et al.¹ have very low power to detect even a doubling (power = 0.07, Cohen's h = 0.08) or tripling (power = 0.12, Cohen's h = 0.15) of recombination rate between pairs of high and low predation populations. In reality, we observed² far more subtle differences between populations in X-Y recombination, and so our power analysis is extremely conservative. Linkage mapping on small scales simply does not have sufficient power to detect these rare events.

Bergero et al.¹ admit that “given the rarity of such events, it will be difficult to estimate if such differences really exist”. We whole-heartedly concur that methods based on direct inference are not likely to work without vastly greater sample sizes. We respectfully argue that their lack of evidence for population level recombination rate variation may simply be due to lack of power to detect rare crossing-over events outside of hotspots. In other words, the absence of evidence is not evidence of absence.

References:

- ¹Bergero R, Garnder J, Bader B, Yong L, Charlesworth D (2019) Exaggerated heterochiasmy in a fish with sex-linked male colouration patterns. PNAS online early.
- ²Wright AE, Darolti I, Bloch NI, Oostra V, Sandkam B, Buechel SD, Kolm N, Breden F, Vicoso B, Mank JE (2017) Convergent recombination suppression suggests a role of sexual selection in guppy sex chromosome formation. Nature Communications 8: 14251
- ³Darolti I, Wright AE, Sandkam BA, Morris J, Bloch NI, Farre M, Fuller RC, Bourne GR, Larkin DM, Breden F, Mank JE. (2019) Extreme heterogeneity in sex chromosome differentiation and dosage compensation in livebearers. BiorXiv. <https://doi.org/10.1101/589788>
- ⁴Stöck M, Horn A, Grossen C, Lindtke D, Sermier R, Betto-Colliard C, Dufresnes C, Bonjour E, Dumas Z, Luquet E, Maddalena T, Sousa HC, Martinez-Solano I, Perrin N (2011) Ever-Young Sex Chromosomes in European Tree Frogs. PLoS Biology 9: e1001062.
- ⁵Haskins C, Haskins EF, McLaughlin J, Hewitt RE (1961) Polymorphisms and population structure in *Lebistes reticulatus*, an ecological study. Vertebrate Speciation, ed Blair WF (Univ of Texas Press, Austin, TX), pp 320–395.
- ⁶Lisachov AP, Zadesenets KS, Rubtsov NB, Borodin PM (2015) Sex chromosome synapsis and recombination in male guppies. Zebrafish 12:174–180
- ⁷Cohen J (1988) Statistical Power Analysis for the Behavioral Sciences. Routledge.