

On the power to detect rare recombination events

Alison E. Wright^{a,1}, Iulia Darolti^b, Natasha I. Bloch^c, Vicencio Oostra^d, Benjamin A. Sandkam^e, Séverine D. Buechel^f, Niclas Kolm^f, Felix Breden^g, Beatriz Vicoso^h, and Judith E. Mank^{b,e}

We read with great interest the recent work in PNAS by Bergero et al. (1) 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. Bergero et al. interpret these results to suggest that our previous findings of population-level variation in the degree of sex chromosome differentiation in this species (2) are 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 indicate that crossing over between the X and Y is rare across most of the guppy sex chromosome (2), and the report by Bergero et al. (1) is entirely consistent with this. Indeed, figure 2 of ref. 1 is strikingly concordant to figure 3 of ref. 2, especially when taking into account the fact that Bergero et al. used less stringent parameters for read mapping. We have recently expanded our analysis across related species (3), and our results show similar patterns in a sister species. Importantly, our work (3) 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 can prevent divergence of the Y (4), explaining the homomorphy on the guppy sex chromosomes, despite their significant age.

Our previous work (2) suggested that this persistent X-Y recombination varies across populations; however, Bergero et al. (1) do not detect these differences

in their data. The crucial questions are about infrequent recombination events between the X and Y and why these differ between upstream and downstream populations. Bergero et al. are unable to provide this level of granularity in their recombination estimation due to low sample sizes.

To illustrate, the estimates of X-Y recombination outside the male hotspot range from 1 in 100 to 1 in 1,000 (1, 5, 6), and we used these estimates to conduct a conservative power analysis (7). On the basis of the sample sizes Bergero et al. (1) report, and using the upper bound of recombination outside the hotspots (1/100), we estimate that the authors (1) have very low power to detect even a doubling (power = 0.07, Cohen's $h = 0.08$) or a tripling (power = 0.12, Cohen's $h = 0.15$) of the recombination rate between pairs of high- and low-predation populations. In reality, we observe (2) far more subtle differences between populations in X-Y recombination, 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.

1 R. Bergero, J. Gardner, B. Bader, L. Yong, D. Charlesworth, Exaggerated heterochiasmy in a fish with sex-linked male coloration polymorphisms. *Proc. Natl. Acad. Sci. U.S.A.* **116**, 6924–6931 (2019).

2 A. E. Wright et al., Convergent recombination suppression suggests role of sexual selection in guppy sex chromosome formation. *Nat. Commun.* **8**, 14251 (2017).

^aDepartment of Animal and Plant Sciences, University of Sheffield, Sheffield S10 2TN, United Kingdom; ^bDepartment of Genetics, Evolution and Environment, University College London, London WC1E 6BT, United Kingdom; ^cDepartment of Biomedical Engineering, University of Los Andes, Bogotá 111711, Colombia; ^dResearch Centre for Ecological Change, University of Helsinki, Helsinki FI-00014, Finland; ^eDepartment of Zoology, University of British Columbia, Vancouver V6T 1Z4, Canada; ^fDepartment of Zoology, Stockholm University, Stockholm SE-106 91, Sweden; ^gDepartment of Biological Sciences, Simon Fraser University, Burnaby V5A 1S6, Canada; and ^hInstitute of Science and Technology Austria, 3400 Klosterneuburg, Austria

Author contributions: A.E.W. analyzed data; A.E.W., I.D., N.I.B., V.O., B.A.S., S.D.B., N.K., F.B., B.V., and J.E.M. wrote the paper.

The authors declare no conflict of interest.

Published under the [PNAS license](#).

¹To whom correspondence may be addressed. Email: a.e.wright@sheffield.ac.uk.

Published online June 18, 2019.

- 3 I. Darolti et al., Extreme heterogeneity in sex chromosome differentiation and dosage compensation in livebearers. <https://doi.org/10.1101/589788> (28 March 2019).
- 4 M. Stöck et al., Ever-young sex chromosomes in European tree frogs. *PLoS Biol.* **9**, e1001062 (2011).
- 5 C. Haskins, E. F. Haskins, J. McLaughlin, R. E. Hewitt, "Polymorphisms and population structure in *Lebistes reticulatus*, an ecological study" in *Vertebrate Speciation*, W. F. Blair, Ed. (University of Texas Press, Austin, TX, 1961), pp. 320–395.
- 6 A. P. Lisachov, K. S. Zadesenets, N. B. Rubtsov, P. M. Borodin, Sex chromosome synapsis and recombination in male guppies. *Zebrafish* **12**, 174–180 (2015).
- 7 J. Cohen, *Statistical Power Analysis for the Behavioral Sciences* (Routledge, 1988).