

## Meiotic drive reduces egg-to-adult viability in stalk-eyed flies

Sam Ronan Finnegan, Nathan Joseph White, Dixon Koh, M. Florencia Camus, Kevin Fowler and Andrew Pomiankowski

### Article citation details

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### Review timeline

Original submission: 17 June 2019  
Revised submission: 8 August 2019  
Final acceptance: 9 August 2019

Note: Reports are unedited and appear as submitted by the referee. The review history appears in chronological order.

## Review History

### RSPB-2019-1414.R0 (Original submission)

#### Review form: Reviewer 1 (Gerald Wilkinson)

##### Recommendation

Accept with minor revision (please list in comments)

##### Scientific importance: Is the manuscript an original and important contribution to its field?

Excellent

##### General interest: Is the paper of sufficient general interest?

Good

##### Quality of the paper: Is the overall quality of the paper suitable?

Excellent

##### Is the length of the paper justified?

Yes

**Should the paper be seen by a specialist statistical reviewer?**

No

**Do you have any concerns about statistical analyses in this paper? If so, please specify them explicitly in your report.**

No

**It is a condition of publication that authors make their supporting data, code and materials available - either as supplementary material or hosted in an external repository. Please rate, if applicable, the supporting data on the following criteria.**

**Is it accessible?**

Yes

**Is it clear?**

N/A

**Is it adequate?**

N/A

**Do you have any ethical concerns with this paper?**

No

#### **Comments to the Author**

This well written paper summarizes experiments that estimate egg-to-adult survival differences among male and female stalk-eyed flies that do or do not carry X chromosome drive. The authors have done a thorough job of reviewing the relevant literature and the experiment was conducted with care. They used a Bayesian approach to estimate selection coefficients, which provides compelling evidence for deleterious effects of the SR X chromosome on egg-to-adult survival in both sexes. I think this study provides valuable information on a relatively poorly studied drive system.

I have no substantive criticism of the paper. I offer the following comments as suggestions for the authors to consider.

p. 9, line 199: In my opinion the best published evidence for the accumulation of deleterious alleles on the SR X is the presence of fixed differences between SR and ST X -linked genes that was discovered by Reinhardt et al 2014 PLoS Genetics in their comparison of testes transcripts from these two types of males. They found 955 fixed differences in transcripts from SR and ST X chromosomes, but only 8 on autosomes. Given that 24 of the X-linked differences involving nonsynonymous changes it seems likely that at least some of these changes could have consequences.

p. 12, line 248: One potential difference between this experiment and that done by Wilkinson (2006) is that the UCL SR stock population was created by selecting flies that exhibit 100% drive, which is more extreme than what was used by Wilkinson et al. in their 2006 study. Given that recombination is reduced on the SR X, alternative SR haplotypes could carry traits with different fitness effects.

p. 16, lines 326 and p. 17, line 360: These passages are redundant. I recommend deleting the passage in the Methods and keeping the passage in the Results.

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## Review form: Reviewer 2

### **Recommendation**

Accept with minor revision (please list in comments)

**Scientific importance: Is the manuscript an original and important contribution to its field?**

Good

**General interest: Is the paper of sufficient general interest?**

Acceptable

**Quality of the paper: Is the overall quality of the paper suitable?**

Good

**Is the length of the paper justified?**

Yes

**Should the paper be seen by a specialist statistical reviewer?**

No

**Do you have any concerns about statistical analyses in this paper? If so, please specify them explicitly in your report.**

No

**It is a condition of publication that authors make their supporting data, code and materials available - either as supplementary material or hosted in an external repository. Please rate, if applicable, the supporting data on the following criteria.**

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N/A

**Is it clear?**

N/A

**Is it adequate?**

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### Comments to the Author

In the manuscript “Meiotic drive reduces egg-to-adult viability in stalk-eyed flies”, Finnegan and colleagues investigate the consequences of carrying an X chromosome meiotic driver for egg to adult viability in stalk-eyed flies. They use crosses of adults of known genotypes to create all possible offspring genotypes, and compare the observed distribution of eclosed offspring to that expected, in order to infer differences in egg-to-adult viability. They find that SR shows viability costs which are comparable in males and females, and which are additive in females.

I found the manuscript generally well written, and the experiments to have been conducted and analysed carefully. The scale of the experiment and the genotyping effort is impressive, and the results are consistent with viability costs of SR in males and females.

My main point is that given its somewhat unusual nature, I think the central analysis could be explained better. If I understand correctly, the response variable is a proportion of observed to expected individuals of a certain sex and genotype? Meaning at least in the raw data, viability can be greater than 1 given sampling error? Further, what (if any) was the extent of genotyping failure, and is there a possibility that failure was biased towards certain genotypes (e.g. detecting heterozygote females requires both fragments to be amplified)? Also, can you give additional data somewhere on how many cages were set up and what proportion of eggs were fertilised? I think this can be worked out from the results given, but seems like important information to give directly. Finally, it would be good to give full model results as e.g. supplementary tables.

Besides, I only have a number of minor (some of which admittedly a bit pedantic) comments on wording, typos, figures, and other suggestions that I hope the authors will find useful:

L20: meiotic drive and stalk-eyed fly are in the title and thus redundant here

L24: This sentence (and the one starting L26) implies that the same selfish genetic element is found in different species, which I think is not correct and potentially misleading.

L33f: I don't think the numbers are necessary in the abstract

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L38: “act to maintain” sounds quite certain. Better “may act to maintain”?

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L206: directly

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 L505: this final sentence seems a bit confused. Re-word?  
 L717: typo: blue lines  
 Table 1: XST/Y for cross B  
 Figure 1 could be more compact with the same information content  
 Figure 2 and 3 could be easily combined, which would also make the comparison between males and females easier

## Decision letter (RSPB-2019-1414.R0)

29-Jul-2019

Dear Professor Pomiankowski

I am pleased to inform you that your manuscript RSPB-2019-1414 entitled "Meiotic drive reduces egg-to-adult viability in stalk-eyed flies" has been accepted for publication in Proceedings B.

The referees and Associate Editor have recommended publication, but also suggest some minor revisions to your manuscript. Therefore, I invite you to respond to the referees' comments and revise your manuscript. Because the schedule for publication is very tight, it is a condition of publication that you submit the revised version of your manuscript within 7 days. If you do not think you will be able to meet this date please let us know.

To revise your manuscript, log into <https://mc.manuscriptcentral.com/prsb> and enter your Author Centre, where you will find your manuscript title listed under "Manuscripts with Decisions." Under "Actions," click on "Create a Revision." Your manuscript number has been appended to denote a revision. You will be unable to make your revisions on the originally submitted version of the manuscript. Instead, revise your manuscript and upload a new version through your Author Centre.

When submitting your revised manuscript, you will be able to respond to the comments made by the referee(s) and upload a file "Response to Referees". You can use this to document any changes you make to the original manuscript. We require a copy of the manuscript with revisions made since the previous version marked as 'tracked changes' to be included in the 'response to referees' document.

Before uploading your revised files please make sure that you have:

- 1) A text file of the manuscript (doc, txt, rtf or tex), including the references, tables (including captions) and figure captions. Please remove any tracked changes from the text before submission. PDF files are not an accepted format for the "Main Document".
- 2) A separate electronic file of each figure (tiff, EPS or print-quality PDF preferred). The format should be produced directly from original creation package, or original software format. PowerPoint files are not accepted.
- 3) Electronic supplementary material: this should be contained in a separate file and where possible, all ESM should be combined into a single file. All supplementary materials accompanying an accepted article will be treated as in their final form. They will be published alongside the paper on the journal website and posted on the online figshare repository. Files on figshare will be made available approximately one week before the accompanying article so that the supplementary material can be attributed a unique DOI.

Online supplementary material will also carry the title and description provided during submission, so please ensure these are accurate and informative. Note that the Royal Society will not edit or typeset supplementary material and it will be hosted as provided. Please ensure that the supplementary material includes the paper details (authors, title, journal name, article DOI). Your article DOI will be 10.1098/rspb.[paper ID in form xxxx.xxxx e.g. 10.1098/rspb.2016.0049].

4) A media summary: a short non-technical summary (up to 100 words) of the key findings/importance of your manuscript.

5) Data accessibility section and data citation

It is a condition of publication that data supporting your paper are made available either in the electronic supplementary material or through an appropriate repository.

In order to ensure effective and robust dissemination and appropriate credit to authors the dataset(s) used should be fully cited. To ensure archived data are available to readers, authors should include a 'data accessibility' section immediately after the acknowledgements section. This should list the database and accession number for all data from the article that has been made publicly available, for instance:

- DNA sequences: Genbank accessions F234391-F234402
- Phylogenetic data: TreeBASE accession number S9123
- Final DNA sequence assembly uploaded as online supplemental material
- Climate data and MaxEnt input files: Dryad doi:10.5521/dryad.12311

NB. From April 1 2013, peer reviewed articles based on research funded wholly or partly by RCUK must include, if applicable, a statement on how the underlying research materials – such as data, samples or models – can be accessed. This statement should be included in the data accessibility section.

If you wish to submit your data to Dryad (<http://datadryad.org/>) and have not already done so you can submit your data via this link

[http://datadryad.org/submit?journalID=RSPB&manu=\(Document not available\)](http://datadryad.org/submit?journalID=RSPB&manu=(Document%20not%20available)) which will take you to your unique entry in the Dryad repository. If you have already submitted your data to dryad you can make any necessary revisions to your dataset by following the above link. Please see <https://royalsociety.org/journals/ethics-policies/data-sharing-mining/> for more details.

6) For more information on our Licence to Publish, Open Access, Cover images and Media summaries, please visit <https://royalsociety.org/journals/authors/author-guidelines/>.

Once again, thank you for submitting your manuscript to Proceedings B and I look forward to receiving your revision. If you have any questions at all, please do not hesitate to get in touch.

Yours sincerely,

Professor Loeske Kruuk  
Editor  
mailto: [proceedingsb@royalsociety.org](mailto:proceedingsb@royalsociety.org)

Editor (LK) comments: Please do not start the abstract with an acronym, even if it is one that is well-established within the field. I would suggest "Sex-ratio (SR) meiotic drive...", or "Sex-ratio meiotic drive (SR)..." , whichever is more appropriate.

Reviewers' Comments to Author:

Referee: 1

Comments to the Author(s)

This well written paper summarizes experiments that estimate egg-to-adult survival differences among male and female stalk-eyed flies that do or do not carry X chromosome drive. The authors have done a thorough job of reviewing the relevant literature and the experiment was conducted with care. They used a Bayesian approach to estimate selection coefficients, which provides compelling evidence for deleterious effects of the SR X chromosome on egg-to-adult survival in both sexes. I think this study provides valuable information on a relatively poorly studied drive system.

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Table 1: XST/Y for cross B

Figure 1 could be more compact with the same information content

Figure 2 and 3 could be easily combined, which would also make the comparison between males and females easier

## Author's Response to Decision Letter for (RSPB-2019-1414.R0)

See Appendix A.

## Decision letter (RSPB-2019-1414.R1)

09-Aug-2019

Dear Professor Pomiankowski

I am pleased to inform you that your manuscript entitled "Meiotic drive reduces egg-to-adult viability in stalk-eyed flies" has been accepted for publication in Proceedings B.

You can expect to receive a proof of your article from our Production office in due course, please check your spam filter if you do not receive it. PLEASE NOTE: you will be given the exact page length of your paper which may be different from the estimation from Editorial and you may be asked to reduce your paper if it goes over the 10 page limit.

If you are likely to be away from e-mail contact please let us know. Due to rapid publication and an extremely tight schedule, if comments are not received, we may publish the paper as it stands.

If you have any queries regarding the production of your final article or the publication date please contact [procb\\_proofs@royalsociety.org](mailto:procb_proofs@royalsociety.org)

Your article has been estimated as being 10 pages long. Our Production Office will be able to confirm the exact length at proof stage.

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#### Electronic supplementary material:

All supplementary materials accompanying an accepted article will be treated as in their final form. They will be published alongside the paper on the journal website and posted on the online figshare repository. Files on figshare will be made available approximately one week before the accompanying article so that the supplementary material can be attributed a unique DOI.

Thank you for your fine contribution. On behalf of the Editors of the Proceedings B, we look forward to your continued contributions to the Journal.

Sincerely,

Editor, Proceedings B

<mailto:proceedingsb@royalsociety.org>

## Appendix A

Dear Loeske,

We provide responses below to the editor and referees' comments, which were all extremely useful.

With thanks,

Sam Finnegan  
Andrew Pomiankowski  
(on behalf of the authors)

Editor (LK) comments: Please do not start the abstract with an acronym, even if it is one that is well-established within the field. I would suggest "Sex-ratio (SR) meiotic drive...", or "Sex-ratio meiotic drive (SR)...", whichever is more appropriate.

Done

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This is a good point. We now cite Reinhardt et al. (2014) for evidence that SR and ST X-chromosomes have diverged (lines 188-189). It's not clear whether the nonsynonymous changes are deleterious.

p. 12, line 248: One potential difference between this experiment and that done by Wilkinson (2006) is that the UCL SR stock population was created by selecting flies

that exhibit 100% drive, which is more extreme than what was used by Wilkinson et al. in their 2006 study. Given that recombination is reduced on the SR X, alternative SR haplotypes could carry traits with different fitness effects.

Thank you for this suggestion. We have incorporated more discussion of differences with Wilkinson et al. (2006) in the Discussion, lines 408-415, including the one put forward by Referee 1.

p. 16, lines 326 and p. 17, line 360: These passages are redundant. I recommend deleting the passage in the Methods and keeping the passage in the Results.

We have deleted the redundant sentence line 326

p. 20, line 427: While I realize it is too late to do this now, genotyping a sample of eggs would confirm that the expected ratios of genotypes were attained in the larvae.

This is a very useful suggestion, thank you. We will look at doing this in future work.

p. 23, line 491: citation should be Wilkinson et al. 2006, not 2003.

Changed

p. 23, line 499: While I agree that multiple factors may be involved in maintaining drive in the wild, I suspect many readers will wonder if the selection estimates you obtained for SR-carrying males and females are sufficient to stabilize the polymorphism by themselves or if selection against SR at some other stage must also be involved. Given that 100% sex-ratio distortion results in a two-fold increase in female offspring production, I suspect additional selection is needed, but undoubtedly not nearly as much as what would be required if no viability selection was present.

This sounds simple but is not. The general rule is that heterozygous fitness determines invasion and homozygous fitness (in females) determines polymorphism or extinction. But it requires an ecological model as well as a population genetic model and assumptions about the mating rate. Extrapolation from sm, sf and h requires quite a bit more work and we leave this to future work.

Referee: 2

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Thank you for this comment. First, the referee's summary of our first analysis is correct. We have added some more text make this clearer, now giving an example for how we calculated expected genotype numbers for each sex.

As is usually the case with molecular biology, there were some instances of genotyping failure (those with Genotype=NA in the raw data file). It is of course not possible to tell if those that failed were biased towards one genotype or another. We have never explicitly tested if there is bias in genotyping failure. However, when genotyping known heterozygous females, we have not observed cases where only one band has amplified. On the basis of this comment, we will endeavour to make a more explicit test of this for future work.

We have added information in the results briefly giving the number of cages set up. We have also now included a brief sentence in the discussion giving the results of a trial designed to measure Cross A and Cross B fertility, which we found are similar. The data from this trial we have put in the supplementary information along with full model results from the main analysis, as suggested.

Besides, I only have a number of minor (some of which admittedly a bit pedantic) comments on wording, typos, figures, and other suggestions that I hope the authors will find useful:

We thank the referee for their attention to detail in the following comments.

L20: meiotic drive and stalk-eyed fly are in the title and thus redundant here  
We have kept stalk-eyed fly as the title is stalk-eyed flies. Meiotic drive has been dropped

L24: This sentence (and the one starting L26) implies that the same selfish genetic element is found in different species, which I think is not correct and potentially misleading.  
Clarified.

L33f: I don't think the numbers are necessary in the abstract  
On balance we have decided to keep the numbers in.

L35: is the effect additive in males, too?

The male is hemizygous for the X

L38: “act to maintain” sounds quite certain. Better “may act to maintain”?

changed

L57 & 58: references here include non-SR meiotic drive (Manser, Silver), an expansion that is not explicit in the text.

these references have been removed

L67: and so TO not have a stabilizing

changed

L92: Taylor and Jaenike 2002?

Referenced added

L110: First mention of Drosophila -> Drosophila simulans, D. affinis, etc

changed

L119: Better be explicit what alternatively refers to? E.g. “Alternative to stabilizing selection on males, SR may...”

changed

L134f: There was a recent paper using this argument more generally for expectations about sex-specific fitness effects of sex chromosomes (Patten 2018, Evolution 73-1:84–91).

Thank you for this pointer. We have modified the text to be a bit more precise. In particular we now reference a different Patten paper, Rydzewski et al. (2016), as this is more pertinent to the argument here.

L136: Sufficient seems odd here. Technically, a very low frequency is already sufficient

changed

L152: Full stop after reference.

changed

L154: typo: cause

changed

L184: I’m not sure how best to address this, but this final paragraph doesn’t follow well from the previous one. Is there a way to re-arrange the previous paragraphs so what you did follows more logically from the rest of the introduction?

We disagree. This is where we set out our research.

L206: directly

changed

L223: D. pseudoobscura  
changed

L224: typo: with of all  
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L256: (XSR/XST)  
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L281: the analysis that follows -> subsequent analyses  
changed

L285ff: I find this paragraph much too detailed for the main MS. Give brief info here and outsource details into supplement.

We have created a SI for this information and reduced what is said in the main MS

L311 & 312: estimated  
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changed

L392ff: the 95% credible intervals here suggest heterozygotes are different from either homozygote class, but L374–376 says otherwise. Is that because the Bayesian analyses have higher power?

This difference arises as the two analyses are carried out on slightly different datasets. The first analysis uses cage as a level of replication, whilst the second estimates selection coefficients from raw genotypic counts. Both analyses give results that point in the same direction and are similar, but will of course be slightly different. It would not be correct to say one has more power.

L412: was largely  
changed

L448: Yet viability was quite low here (means 40-63%). Is this normal for stalk-eyed flies?

Yes. This is within the bounds of what we normally see in our developing stocks.

L449f: Food quality was manipulated but had no effect. Are you saying there was an excess of food (and nutrition) in all your treatments? Should the food manipulation have pushed further?

Following a previous pilot by Cotton (2016, PhD thesis, Chapter 3), we chose to manipulate the quality of food (% corn), rather than the quantity, by altering the relative concentrations of corn and sugar. Most of the previous studies in this group has used quantity of food, as a manipulation of food condition.

Unfortunately, the manipulation of food quality had no obvious effect on viability. So we could not consider how “low-quality” environmental conditions altered the viability loss caused by the  $X^{SR}$  chromosome. As referee 2 suggests we should have pushed the food manipulation further. This is the intention of work going on at the moment.

L467: or indeed in populations with lower frequencies, if polyandry suppresses drive. Maybe just say correlates with drive frequency?

We have rephrased here.

L505: this final sentence seems a bit confused. Re-word?

changed

L717: typo: blue lines

changed

Table 1: XST/Y for cross B

changed

Figure 1 could be more compact with the same information content

Thank you for this comment. We have reduced the overall size of this figure by reducing the length of arrows, so it is now more compact.

Figure 2 and 3 could be easily combined, which would also make the comparison between males and females easier

We have combined these two figures as suggested.