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Dear Editor, February 6, 2018

Please find the attached manuscript, entitled "Haploid selection, sex ratio bias, and transitions between sex-determination systems", which we submit to you for consideration for publication in *PLoS Biology*. Laurence Hurst and Nick Barton would be well qualified Academic Editors for this manuscript.

In this manuscript, we develop and thoroughly analyse models to show what conditions favour the evolution of new sex-determination systems. Evolutionary transitions between sex-determination systems are an active research focus due to the surprising diversity and lability of sex determination systems, which is becoming increasingly apparent (Bachtrog et al. 2014, *PLoS Biology*). Transitions in such a fundamental trait of large effect warrant evolutionary explanation; our results suggest several new scenarios under which new sex-determining systems are favoured, which could help to explain why the evolution of sex-determining systems is so dynamic.

Previous modelling studies, including Muralidhar and Veller (2018, *Nature Ecology and Evolution*) and van Doorn and Kirkpatrick (2007, Nature; 2010, Genetics), have shown that a new sex determining allele can spread if it is more tightly linked to a sexually-antagonistic locus. Our work finds several surprising results in light of previous results. First, when the old sex determining allele is already tightly linked to a sexually-antagonistic locus, more loosely linked sex determining factors can invade under some circumstances, offering a new potential explanation for sex chromosome turnover. Second, when we include selection in the haploid phase (among gametes or gametophytes, including meiotic drive), entirely new predictions are generated for the spread of new sex determining factors. In particular, selective differences between male and female diploids are no longer necessary; conflicts between haploid and diploid selection can instead drive the invasion of new sex chromosomes. Interestingly, new sex chromosomes can spread under conditions where they balance the sex ratio but also under conditions where they lead to more skewed sex ratios. Indeed, transitions during which sex ratio biases increase or decrease are equally likely to evolve under a wide range of conditions. We conclude that haploid selection should be considered as a pivotal factor driving transitions between sex-determining systems.

Overall, we have developed an extensive set of models that explore the forces driving transitions between sex determination systems, an important aspect of diversity. Of partic-

ular interest, we find several results (e.g., looser linkage and sex ratio biases evolving) that are surprising, given previous theory. We hope you agree that this work is of broad interest to the readership of *PLoS Biology* and we eagerly anticipate your response.

Sincerely,

Michael Scott, Matthew Osmond, Sarah Otto