Discussion Draft

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We performed hypothesis testing of models from the literature and adapted here fit the main results from this study. We choose to examine three modifier models and two functional and cell physiology models (table X). It is a bit challenging to test all of these models together since they were built to describe different patterns of recombination variation. The three modifier models were built to explain variation in genome wide recombination rates between sexes (heterochiasmy), while the COM model was built to describe the interference pattern and difference in the recombination landscape between the sexes. In cases where the models can’t be extended to predicting results, we list a ‘NA’ for the prediction.

# Reversed heterochiasmy direction

Female biased heterochiasmy is the most common pattern observed, however male biased heterochiasmy is not especially rare (Brandvain and Coop 2012). Our results of male biased heterochiasmy is novel due to the shorter evolutionary distances between the examined strains.

The direction of heterochiasmy under the two locus modifier model is dependent on female specific recombination modifier suppresses or increases recombination, if the modifier is linked to the driving locus, and the meiotic stage (reduction or equatorial division) that the driver acts (see Table 1 of Brandvain and Coop (2012)).

Under the spindle based model, faster male evolution of the genome wide recombination rate, is primarily driven by a more efficient spindle assembly checkpoint (SAC) acting on chromosome structures at metaphase I alignment. The SAC prevents anueploidy by ensuring all bivalents are correctly attached to the microtubulue spindle before starting the irreversible metaphase-to-anaphase transition (cite). A stable chromosome structure, known as bi-orientation, requires, i) kinetochores attached to opposite poles of the cells and ii) at least one crossover to create tension across a proportion of sister cohesion (cite). Unstable bivalents on the meiosis I spindle, cause the SAC to delay anaphase and allow time for the bivalent to stabilize on the microtubule spindle. If they fail to attach, the SAC triggers apoptosis. Genetic variants which increase the number of unstable bivalents (such as those affecting recombination rate or cohesion), will be selected against in favor for genetic variants causing faster stabilization of bivalents on the MI spindle. Multiple lines of evidence indicate that the effectiveness of SAC in spermatogenesis is greater compared to oogenesis (LaneKauppi, Subrahman). These differences in SAC strength have been connected to conserved features of gametogenesis; centrosome spindle and cell volume (cite). This model nominates conserved differences in in the context of meiosis between males and females as the primary source of distinct evolutionary trajectories in genome wide recombination rates.

# Greater between cell variation

Our results of greater between cell variation in females are supported by empiracal results from human and mouse (Lynn et al. 2002, Gruhn et al. (2013)).

While the modifier models parameterize sexual dimorphism in the strength of selection which can shape the variance in a trait these types of models make predictions for variance between individuals but not within individuals where the genetics are constant.

In the spindle based selection model, the less efficient SAC in oocytes leads to relaxed selection on the metaphase I chromosome structure. This will result in increased variance in chromosome structure and crossover number per cell, not just across strains, but across cells within individuals. Oocytes at metaphase I, have an acentriolar spindle comprised of diffuse network of microtubules with multiple microtubule organizing centers (Schuh Ellenburg 2007). This is another way the spindle based selection model is linked to conserved sex differences in gametogenesis (cite).

# Typical landscape

Our results on the broad scale pattern of crossover placement are supported by the literature. As reviewed in (Sardell and Kirkpatrick 2020), sexual dimorphism in the broad scale recombination landscape is a highly conserved trait. The two locus modifier and SACE model predicts sexual dimorphism in the broad scale recombination landscape, for diminishing the effect of drive systems and maintaining larger chromosome blocks under linkage in males respectively.

The two mechanical models both predict sexual dimorphism in the recombination landscape for distinct reasons. The COM model, predicts the sex differences in the recombination landscape via interference is due to a combination of the length of the axis and differing strengths of chromosome movements during the pairing process (Hultén 2011, Rubin, Macaisne, and Huynh (2020)).

Under the spindle based model we hypothesize that the sexual dimorphism in the recombination landscapes hinges on sex differences on the requirements for chromosome cohesion in late meiosis I. The irreversible process of the metaphase to anaphase transition is initiated by the protyltic decay of the sister cohesion connecting homologs (cite). The number and placement of crossovers alter the distribution of sister cohesion and the resulting chromosome structure when bivalents are aligned and bi-oriented on the metaphase plate (cite). Different timing of cell cycle between oogenesis and spermatogenesis may impose the the different selective pressures on sister cohesion. Faster spermatogenesis may select for synchronization of the separation homologs. While in oogenesis, the slower cell cycle and multiple arrest stages may require chromosome structures with greater stability on the MI spindle.

# Chromatin Structure

Our results from musculusMSM and musculusPWD show that the SC length and chromatin compaction is uncoupled from the direction of heterochiasmy. These results slightly depart from predictions which nominate chromatin organization (axis length) as the primary driver of heterochiasmy (Petkov et al. 2007). While the relationship may hold for more general heterochiasmy patterns across broad scale comparisons, these results indicate that rapid male specific evolution in gwRR, is through a different trait than chromatin compaction.

Only the COM model predicts sexual dimorphism in chromatin structure will be longer in oocytes due to greater cell volume. This prediction model might fit broader pattern such as in *Arabidopsis* where pollen is the larger cell and has longer axis length (Cahoon and Libuda 2019).

# Evolution of Interference

Examples of evolution of interference strength are rare and may be complicated by changes in the underlying karyotype structure (Segura et al 2014). The general pastern of empirical measures of interference strength is that it has a negative correlation to the genome wide recombination rate (Otto and Payseur 2019). This fits the logic of the chromosome axis acting as the ‘real estate’ for DSBs and aligns with known molecular mechanisms (cite). Two examples of the opposite direction, a positive correlation of interference strength and genome-wide recombination rate, involve descriptions of observations at the single bivalent level; the between lab-raised and wild mice of *Peromyscus leucopus* from (Peterson, Miller, and Payseur 2019) or large effects on genome wide recombination rates across a short evolutionary differences; the within-sex comparison of two breeds of cattle with different genome wide recombination rates (Ma et al. 2015). We propose that there is a difference in resolution and power between these two groups of empirical results with the positive and negative relationship between genome wide recombination rates and interference strength.

We propose that the **spindle based selection model** can explain the positive correlation and evolution of stronger interference strength via selection on the amount of sister cohesion connecting homologs (figure X, table X). The evolution of genome wide recombination rates in our study is driven by a transition of recombination landscapes from single crossovers to two crossovers. All else being equal, interference strength would be expected to be equal or even weaker. Our results show that the two crossovers are spaced further apart when SC length is controlled for and chromosome size effects are minimized, in the strain with more two crossover chromosomes. Assuming that chromatin compaction between pachtyene and metaphase is uniform along chromosomes, an outcome of this further spacing of two foci results in an increased area of sister cohesion connecting homologs (Figure X). This model gives rise to the possibility that the chromosome structure at metaphase is the target of selection which is achieved by changing the average recombination landscape across bivalents within the cell. This interpretation has potential to fit with hypotheses mentioned above for explaining other results regarding the evolution of the recombination landscape.

The **COM** model predicts that interference and the recombination landscape arises from known oscillatory movements during prophase, however it lacks evolutionary based predictions. While the **SACE** modifier model does not explicitly model evolution of interference strength we note that a logical outcome of the main prediction of maintaining larger chromosome blocks in males, would be a landscape with stronger interference strength.

We have focused on the model involving direct selection on the recombination pathway, that is the impact on the meiotic process on an individual, but we make note on models centering on indirect selection or fitness outcomes of offspring which could also explain our results. Models from Goldstein et al, reviewed in (Otto and Payseur 2019) and Veller 2017, predict that interference strength evolves whenever increased recombination rates evolve. The simulations under this model indicate that the space across multiple loci or between multiple crossovers increases in a positive manner with the genome wide recombination rate. A distinguishing feature of their model is that the number of crossovers per chromosome is kept constant. The range of crossovers per chromosome is quite small, 1-3, for the majority of chromosomes (Otto and Payseur 2019, Stapley et al. (2017)). Constraining the number of crossovers per chromosome in models may fit empirical data better than those where recombination rate across an abstracted genetic space is unconstrained.

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