# Conserved Pattern, Heterochiasmy Results

The landscape aspects of heterochiasmy is more conserved than the genome wide rate differences. The conserved features are:

**1. Sexual dimorphism in broad scale recombination landscape**

The sexual dimorphism in broad scale crossover location (recombination landscape) is conserved in house mouse, with males having telomere bias and females having more uniform placement of crossovers along chromosomes. (Sardell Kirkpatrick 2019)

**2. Sexual dimorphism of within mouse variance for CO per cell**

We observe more between cell variance in females across all strains, beyond what is expected due to technical variance. The same pattern of sexual dimorphism for variance across crossover number per cell has been observed in humans (Lynn et al) and other inbred house mouse strains (Gruhn et al).

**2. Sexual dimorphism of chromatin configuration and interference strength**

This prediction combines the findings of chromatin compaction and interference differences which are intertwined by the transmission of interference along the chromosome axis and the inverse relationship chromatin compaction (axis length and DNA loop sizes).

Our results confirm those presented in Petkov et al 2004) …

In physical units (micro meters) (2D / SC length) the measures of interference are conserved across sexes in mouse, while the normalize measure of interfocal distances (IFD) suggest that males have stronger interference.

This is because the counting units are the BASES of DNA loops which is conserved along the 2D length of chromatin axis. When this space is transformed to account for all of the DNA base pairs which are sequestered into the DNA loops above the axis, the strength of interference will vary depending the on underlying chromatin structure.

The chromatin structure which has longer loops (and shorter axis) will have more DNA bps folded / sequestered into the DNA loops. Thus the strength of interference will be stronger because with each step (count) along the 2D axis,

more bases pairs are being skipped above the axis. (as outlined in Petkov 2004).

The conserved sexual dimorphism patterns above suggest there are distinct features of the recombination landscape in males and females (seen across many species and decoupled from the genome wide recombination rate. This in turn suggests distinct evolution trajectories for crossover counts per cell dependent on the cell being in spermatogenesis or oogenesis.

# Evolved Patterns, Predictors of Recombination rate evolution within (males)

A primary goal of this study was to identify additional meiotic traits which correlated with the faster evolution of genome wide recombination rate observed in males. We find that DSB number and interference strength were the strongest correlates to the increase in genome wide recombination rate evolution.

## A. Evolution of DSB number (moderate support for SC length evolution)

<transition/ connection of conserved sexual dimorphism relationship for DSB #/ chromatin configuration (Lynn et al (female DSB estimates, Brick?)>

1. More DSBs in the high rec strains

2. The conserved ratios of DSB : CO implies that the increase in DSB numbers are accompanied by proportional increase in crossovers. This is evidence that shifts support away from the CO:NCO decision to an earlier prophase stage such as when the chromatin compaction is set up.

3. DSB number being driven by the number of chromatin loops which is positively correlated with axis length.

4. These results supported by the moderate support of longer SC length in the high rec males.

We have results that mirror those presented in Baier et al 2014, suggesting that the variation in MLH1 counts – across house mouse spermatocytes – is due to the same mechanism, differences in chromatin configuration.

5. Reconcile the lack of stronger signal for SC length evolution in high and low rec male groups). The support is too weak due to the noise in our single bivalent data (no ability to track chromosomes across cells as in Baier et al). Even in the reduced bivalent dataset this is still a factor for our sample sizes.

## B. Evolution if interference strength, stronger inference observed in high recombining males

**I. Review results**

**1.**Evolution of stronger interference is strongly correlated (shows the strongest correlation with genome wide evolution). The positive correlation is contrary to most expectations and empirical results (but we note that those are largely across longer time scales and genome wide averages)

2.The difference in interference patterns is driven by a paucity of short IFD observations in the high rec males (the short IFD drive down the mean IFDs in low rec strains, whereas the medians are similar)

3. Chromosome size effects are unlikely to cause this pattern since the IFD distributions show less variance in the high rec strains, which would have MORE Chromosomes (for example Chm1 to Chm9) compared to the low rec strains which have fewer 2Cos (presumably limited to large chromosomes (for example Chrm1 to Chrm5).

4. These results are different from the sex differences since the inferences measures are significantly different in both the raw and normalized IFD.

**II. Review the assumptions for measuring CO interference in different ways.**

1. The logical model: Crossover interference is a mechanism of suppressing crossovers, negative relationship between interference strength and gwRR. More crossovers can fit along the chromosomes and results in more crossovers overall.
   1. Examples of empirical results supporting this pattern; Otto Payseur, (Ruiz-Herrera? Bomblies?), gamma
   2. Caveats for gamma estimates, The assumptions for infinite space and (no upper and lower bounds for number of crossovers don’t fit realities of meiotic chromosomes and recombination landscape: i) finite chromosome length and ii) limited range of crossovers per chromosomes and crossover assurance.
2. Alternative interference characterization: i) the number of crossovers are held constant or prioritize crossover assurance (0 < CO# = 1 to 4) and ii) generalize the rec landscape, (focus on how the rec landscape would change instead of the genome wide rate).

-The Goldstein model (reviewed in Otto and Payseur 2019), models predicts a positive correlation with interference strength and higher recombination rate. A modifier which changes the probability of the recombination landscape having 0 crossovers or 2 crossovers, (driven by crossover assurance).

3. Examples of empirical results which show this pattern

- cattle pedigree paper, comparison WITHIN sexes (Jersey to Holstein)

- Beth’s (PWD - CAST) F2 cross (Hannah’s IFD measures),

- Peromyscus Chromosome 1 (Peterson et al 2019)

# Explanation and Model review

**1. Gamete selection (and haploid selection) (Lenormand 2003)**

The process where gametes are competing – so there is stronger selection for 1 form of gamete vs the other (stronger directional selection) (the gamete with more competition / the sex with more variance in reproductive fitness will have lower overall recombination rate.

**2.SACE (Sardell Kirkpatrick 2019)**

Extension of reduction principle. Results in large blocks of genetic areas being kept together in male meiosis.

**3.Two-locus (protect for drivers)**

Asymmetric division of egg opens them up to meiotic drivers. Recombination modifiers for sex specific female landscape will decrease the chances of driving centromeres to segregate to the egg by increasing the number of crossovers and placing them across a larger area of the genome (uniform placement).

**4. Sexual dimorphism in spindle and checkpoints**

1.A fundamental difference in meiosis (MI) for males and females is the presence of the centrosome which serves as a nucleation site for MT at each pole and influences the shape of the spindle.

My hypothesis – for this model leading to distinct evolutionary trajectories for the gwRR in sperm and egg is that the tension in a centrosome spindle is stronger (or more uniform) since all MT-KT are anchored at single points at the cell poles.

This will also makes the spindle assembly checkpoint (SAC) stricter in smaller gametes with centrosomes (sperm) and more sensitive to achiasmate bivalents on the spindle (and correcting MT-KT attachments or triggering apoptosis).

Whereas in the acentrosome spindle is more diffuse (multiple aMTOCs diffused across a larger area) resulting in less effective SAC, that is more achiasmate bivalents are required to trigger the SAC to stop division entry into anaphase (there’s a much higher rate of achiasmata / aneuploidy

These physiology differences in meiocytes results in stronger selection on the recombination landscape in males compared to females. Which can produce directional pattern in male and relaxed selection on the gwRR (and recombination landscape) in males and females respectively.

-2. Connect to stronger interference (positive correlation of interference strength

-- the faster evolution in males – driven by the rec landscape

A consequence of the stronger interference strength in the high rec males is that there is a greater amount (proportion of the chromosomes/bivalents

**5. Model prediction**

The models above which predict directional selection on the recombination landscape in males: **SACE** and **Spindle differences** are most parsimonious for the models review in this paper. The reduction principle wouldn’t predict males diverge in genome wide rates and two locus modifier doesn’t predict males gwRR would be higher than females.

1. (Hollis et al 2020, Lee et al 2019). This model predicts a difference in the meiotic spindles or division mechanism between high and low rec strains.

**ii. SACE**: For the 2CO in the high rec males, larger blocks of chromosomes are kept together in the next generation.

This model would predict greater reproductive variance for males.

## Review of modifier / popgen models

Indirect forces common assumptions themes across all the modifier models.

## Review of cell biology

Look at conserved features of gametogenesis that distinguish male and females

**Different Centrosome spindle**

**Asymmetrical division**

# Future steps

* Acknowledge that sex average measures data can obscure distinct patterns
* Rethink how interference is measured