# 1.Heterochiasmy Results

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

**1. Typical landscape**

A difference in the general placement (general recombination landscape), with males having telomere bias and females having more uniform placement of crossovers along chromosomes.

**2. Short axis / longer DNA loops will have stronger interference**

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).

In physical units (micron) the counting model fits interference well to the 2D linear space of the axis these measures of interference are conserved across sexes in mouse. 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.

**3. Within mouse variance differences**

In our results we observe more between cell variance in females (across all strains). This pattern has been observed in humans (Lynn et al). (But results of reporting observations of single meiosis in both sexes).

# Models

**1.Gamete selection**

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**

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.Difference in acentromeric spindle and SAC**

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 changes the shape of the spindle). (Our hypothesis is that the tension in a centrosome spindle is stronger (or more uniform) since all MT-KT are anchored at single points across cells (the two centrosomes). This will also make prediction for the spindle assembly checkpoint (SAC), which is stronger/stricter in smaller gametes with centrosomes. (the SAC is more sensitive to achiasmate bivalents on the spindle / better at detecting a lack of tension).

Whereas in the acentrosome spindle is more diffuse (across a larger area) and the tension across bivalents are anchored by multiple MTOCs, resulting in weaker tension force or less uniform strengths across all the bivalents within the cells. The SAC in eggs seems to be weaker/leakier, that is more achiasmate bivalents are required to trigger the SAC (stop the division).

## 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**

# 2.Predictors of Recombination rate evolution within (males)

This section focuses on the largest axis of variation over a short time scale. We can’t distinguish if this is 3 independent instances of evolution in gwRR OR if the patterns are due to shared standing variation, incomplete lineage sorting, but these points are for describing the general patterns.

## A. DSB Differences and moderate support for SC length differences

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 (pachytene stage in the high rec males).

(Review Baier et al 2014)

## B. INTERFERENCE

**1. Review results**

-The rapid evolution of the genome wide rate in our high rec strains is due to more enrichment of 2CO which have distinct rec landscape from the 2COs in low rec strains.

-Caveats: chromosome size effects,

However, the IFD distributions show less variance in the high rec strains, which would have MORE Chromosomes (Chm1 to Chm7) compared to the low rec strains which have fewer 2Cos (presumably limited to large chromosomes).

-Also:

-These results are different from the sex differences because the difference is seen in both the raw and normalized IFD.

-The difference in interference patterns is driven by the difference in the rates of small IFD observations.

**2. 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?)
   2. Quantifing using the gamma distribution:
   3. Caveats, This doesn’t make since for the general recombination landscape: i) finite chromosome length and ii) limited range of crossovers per chromosomes (1 to 4).
2. Alternative interference characterization: i) the number of crossovers are held constant and ii) transform / generalize the rec landscape, (focus on how the rec landscape would change instead of the genome wide rate) iii) assume crossover assurance.

-The Goldstein model, 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 to 2 crossovers, (driven by crossover assurance).

-Examples of empirical results which show this result / pattern

-(cattle) comparison WITHIN sexes

- Preliminary results for F2 cross (Hannah’s work), (PWD vs CAST)

(maybe more once I start looking closer)

4. HYPER-Crossover experiments. (review the effects when crossover number is artificially altered)

**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.

Consequences of evolution in the number and placement of crossovers / evolution of interference strength:

1. **Spindle / SAC model**: The number and placement of crossovers changes the resulting amount of sister cohesin involved the tension signal, which affects the tetrad/chiasmata structure at MI when the homologs are pulled apart (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.

# Future steps

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