My main question is how exactly you would do the analysis. Could you send me an email that spells out all the steps and variables you will measure? I'm looking for details here.

Chapter 3 Outline, Do cell specific effects or chromosome specific effects shape broad scale recombination patterns?

# Background

Wang et al 2019, demonstrates that there is within nucleus covariation for CO count per cell. The proposed mechanism is that within a nucleus, all chromosomes (homologs) have a positive correlation between chromosome axis length, DSBs and COs. This relationship generates an over-dispersed distribution in CO counts per cell, the tail ends of the distribution have cells with more or fewer COs than expected if CO count was purely driven by chromosome effects.

**Main question:**

Is there within nucleus co-variation in CO position / foci spacing (i.e. CO interference)?

Significance**:**

The result of within nucleus covariation for CO number (via SC length) fits with chromatin compaction regulation / DNA loop size and axis length being regulated at a ‘global’ scale within single cells. Whereas, broad scale CO positioning and crossover interference are regulated at a chromosome level (or at least is further removed from global level).

Are broad scale CO positioning patterns driven by single cell effects, like SC length and CO count, or are they driven by chromosome level effects? Answering this question would shed insight on how meiotic processes might be interconnected.

- Many biological processes are summaries or averages but these processes happen within single cells.

- A conserved feature of heterochiasmy is the telomere bias in male and uniform CO positing in female yet there are still gaps in understanding this.

# Approach:

Tests of within cell summary statistics between empirical data and simulated (randomized data).

Simulate null distribution of relative CO position, keeping the empirical observation of CO counts per cell but draw randomized relative CO positions (from a pool of all empirical positions for a mouse). The difference between empirical and simulation distributions would be tested. This would be the same sort of simulations as the Wang 2019 paper, but for CO positioning instead of CO count.

**Ideal data set:**

Within all covariation requires whole cell bivalent measures (all 20 chromosomes). Within between cell variance requires a decent sample of cells from each mouse, ~25 good cells. The total cell sample size will limit the sex and strains that are looked at. Generating the whole cell data will require adding in some hand measures for the bivalents the algorithm missed (usually 1-3 missed per cell). This is feasible for a medium dataset, hand measuring 3\*25 bivalents takes about 3 hours. Focus on PWD,MSM, KAZ and a dom strain). What is the effect of rapid evolution of the mean on the between cell variation?

**Interpretations**

1. There is within cell covariation in CO position (all data);

-Cell specific effect generate distinct CO position patterns

-SC length regulation and CO position are linked processes (Rapid Prophase Movements? CO:NCO decision)

2. Within cell covariation, but it’s variable across strains or sexes

-Different modes of selection (relaxed vs purifying) via sex specific constraints for CO positioning (spindle or checkpoints)

-Broad scale CO positioning can evolve

3. No covariation for CO positioning; (null = observed)

- CO position is conserved process across the dataset (biophysical constraint for CO:NCO decision)

- Major determinate of CO positing patterns is chromosome specific