Crossover interference and the sex difference in recombination

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Joint work with Ken Paigen, Petko Petkov, and Jin Szatkiewicz
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Abstract

Many organisms exhibit large differences in recombination rate between the sexes. Why? The lengths of chromosomes at the key stage of meiosis can be quite different between males and females, and analysis of extremely large mouse backcrosses, with high density genotype data on a single chromosome, indicates that crossover interference (the tendency for crossovers to not occur too close together) is similar in the two sexes, but on a physical level, and by physical think μm not bp. Longer female chromosomes, with a constant level of interference, would then allow more crossovers.

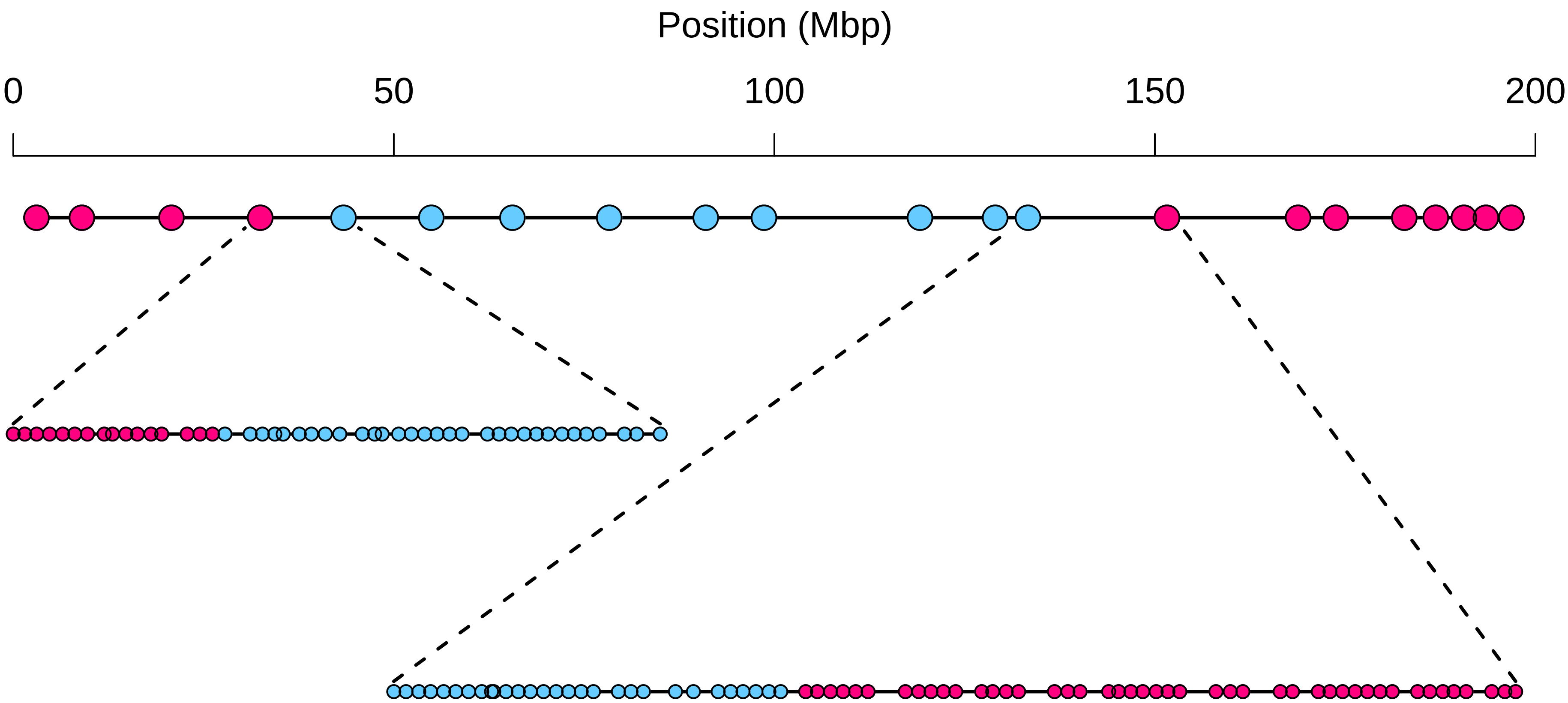
Mouse backcrosses

Cross	Sample size
(B $\times$ C) $\times$ B	1466
(C $\times$ B) $\times$ B	1528
B $\times$ (B $\times$ C)	1459
B $\times$ (C $\times$ B)	1533

B = C57BL/6J
C = CAST/EiJ

Genotyping

Chr 1 only (for now), by brute force



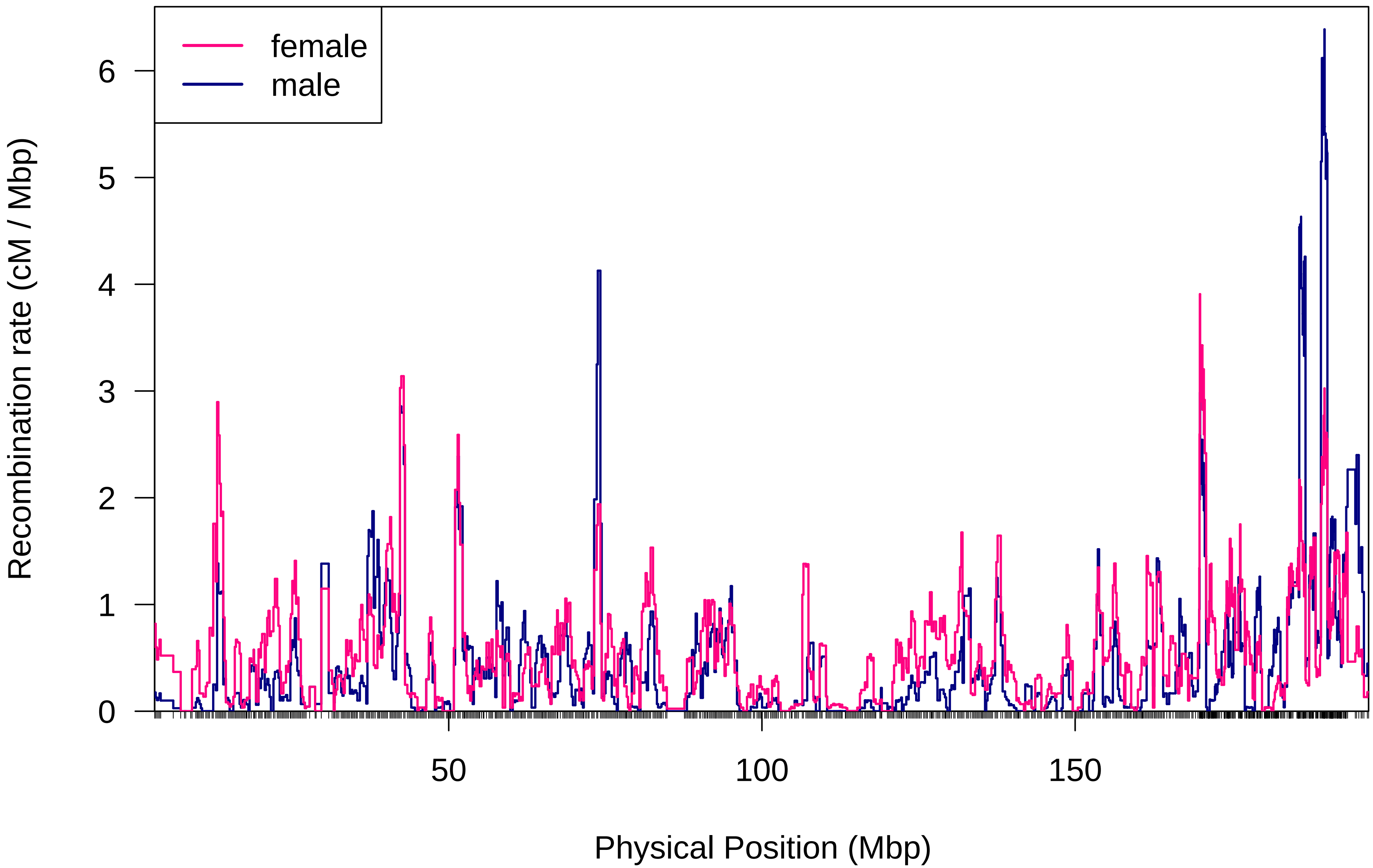
Counts

	No. crossovers					
	0	1	2	3	4	Ave.
female	25	50	23	1.6	0.1%	1.01
male	32	51	16	0.2	0.0%	0.84

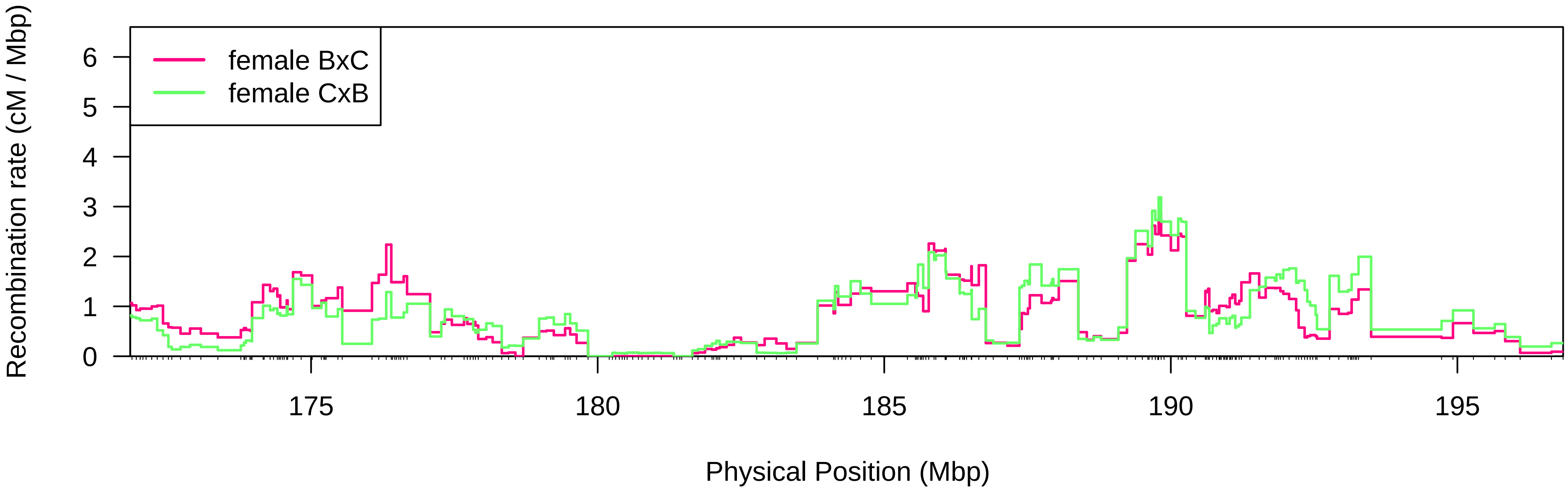
	No. chiasmata					
	0	1	2	3	4	Ave.
female	0	10	78	10	1%	2.02
male	0	33	65	1	0%	1.69

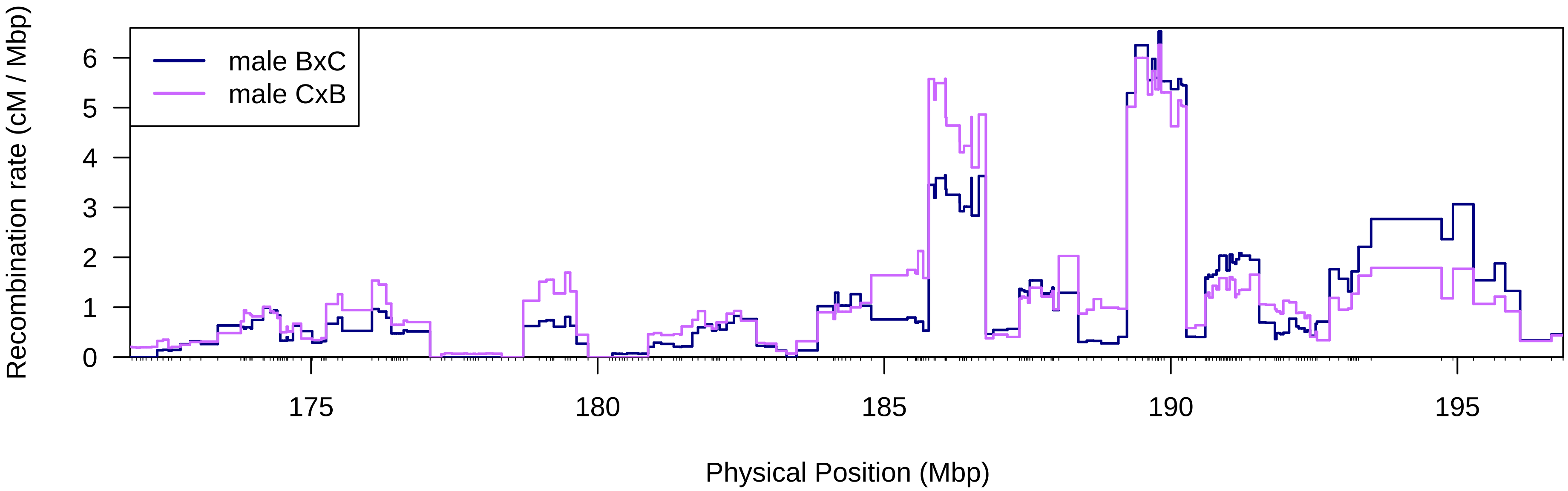
(Assuming no chromatid interference.)

Recombination rate



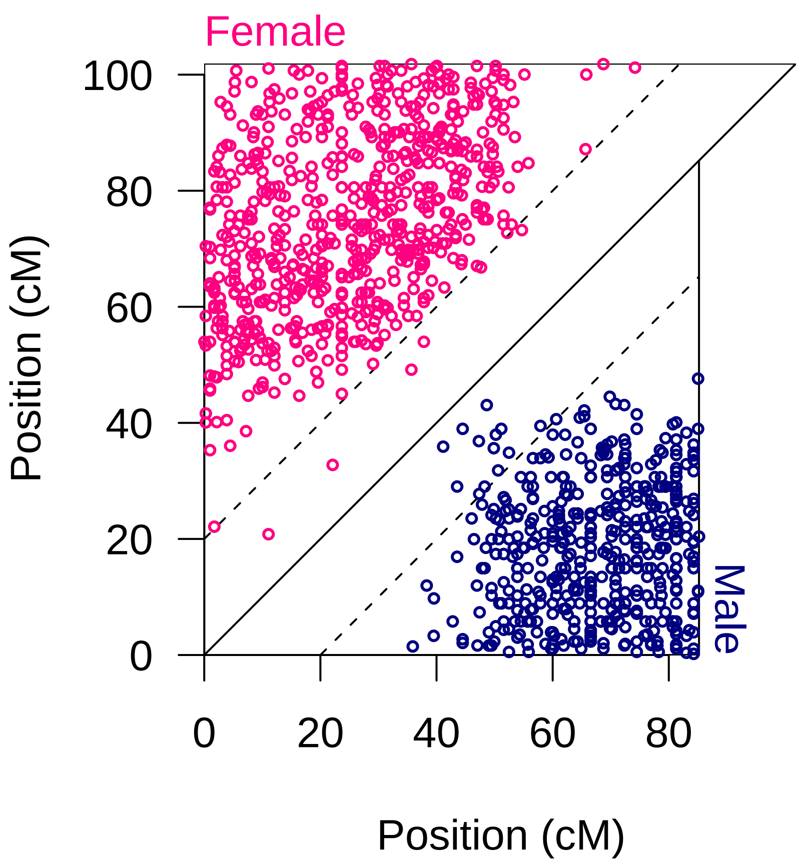
Distal 25 Mbp

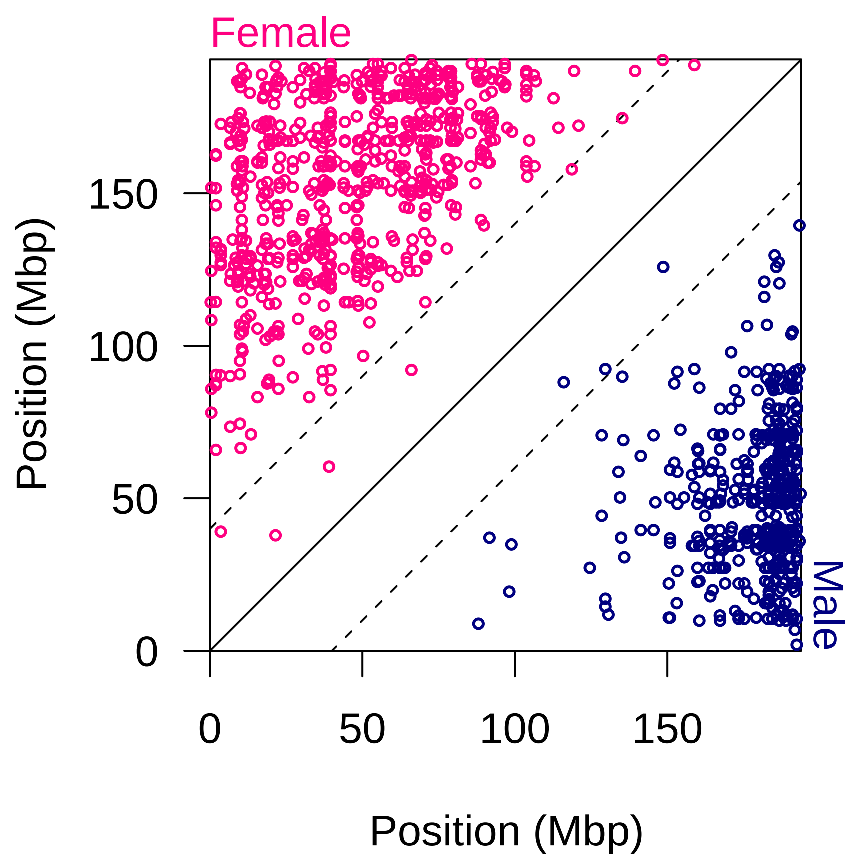




Double-XO locations

Crossover locations, for meiotic products exhibiting exactly two crossovers



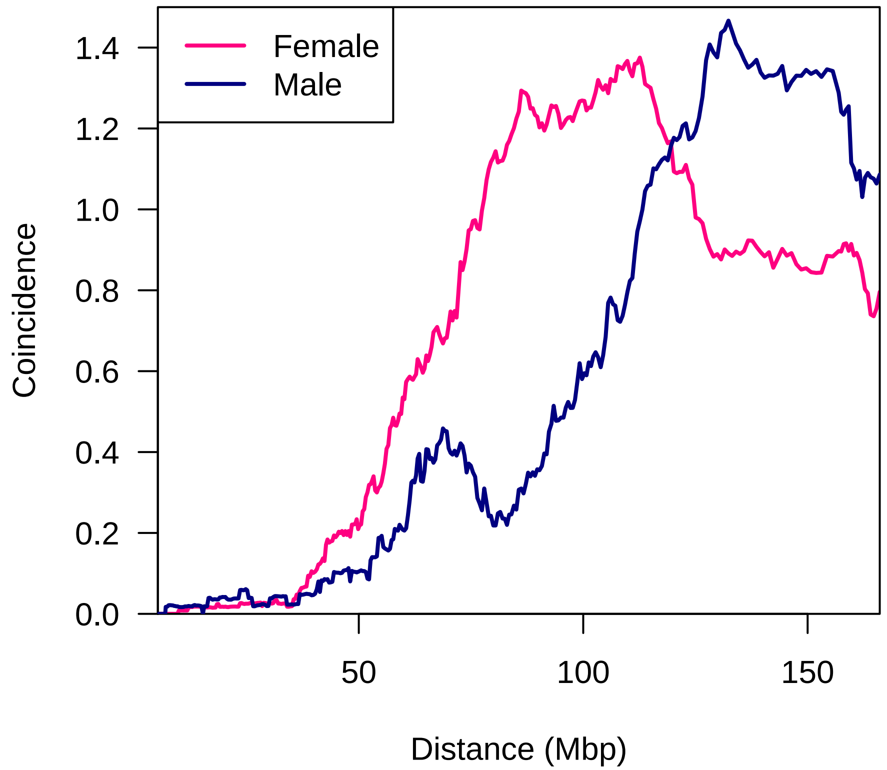


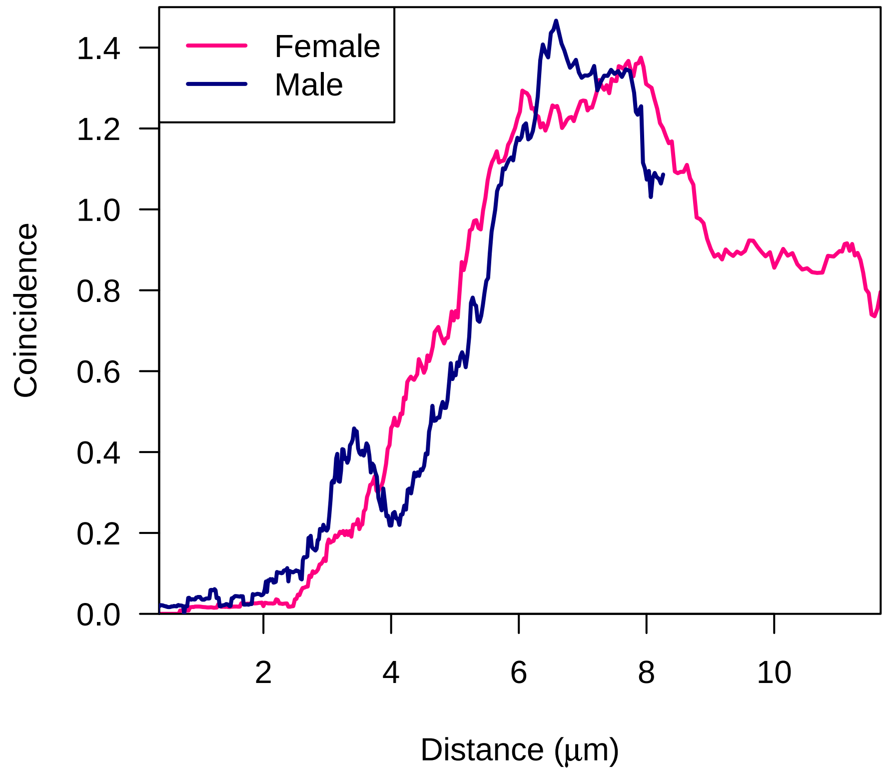
Coincidence

Consider two small intervals separated by a distance, d.

$$C(d) = \Pr(\text{XO in both}) \,/\, \{\, \Pr(\text{XO in first}) \times \Pr(\text{XO in second})\}$$

Convert from Mbp to μm assuming constant level of compaction.





Summary

- Clear sex differences in recombination rate
- Differences in compaction + constant interference
  $\longrightarrow$ difference in recombination rate?
- Nature of local differences in recombination rate?
- Imprinting effects?
- Interesting statistical problems remain
  - Characterizing differences in local recombination rate
  - Forming a good nonparametric estimate of the coincidence function
  - Fitting a model that accounts for both recombination rate variation and interference