

Fine-scale variation in the recombination landscape of adaptively diverging threespine stickleback fish



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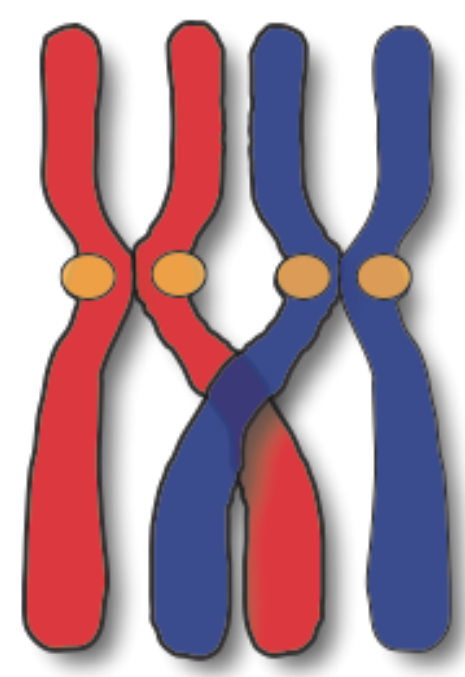
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Allelic shuffling caused by meiotic recombination is one of the major molecular mechanisms generating genetic diversity. By making and breaking new allelic combinations it can directly influence the patterns and efficacy of natural selection and adaptation. The rate and placement of recombination is shown to vary among taxa, species, individuals, sexes and across genome [1].

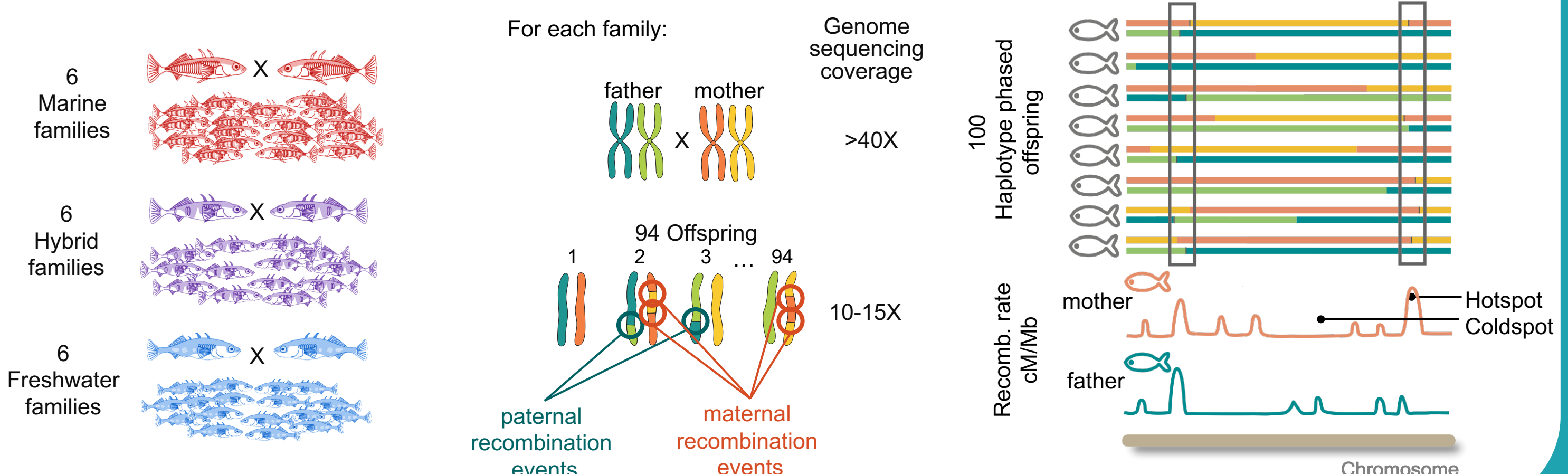
How does meiotic recombination vary across the genome and between adaptively diverging species?

We are studying recombination rate variation in adaptively diverging threespine stickleback fish using nuclear family and ChIP sequencing. We find considerable variation across the genome with both crossover hot- and coldspots, large differences in the recombination landscape between the sexes, and evidence of recombination suppression in F1 hybrids of diverging marine and freshwater ecotypes. We examine the genomic features associated with crossover and the DNA double strand break (DSB) landscape.



Homologous recombination

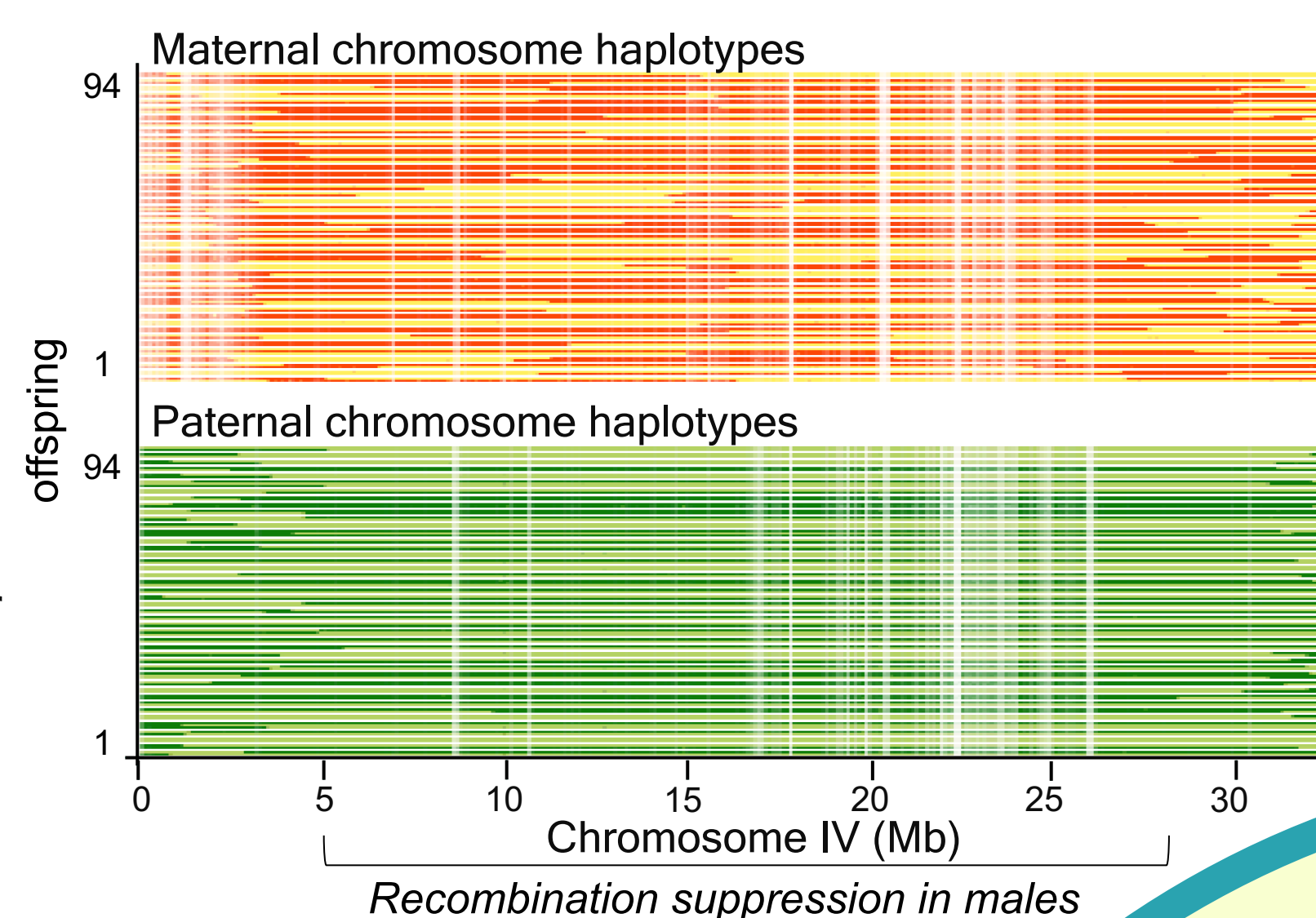
Individualized crossover map construction for 36 parents by nuclear family sequencing



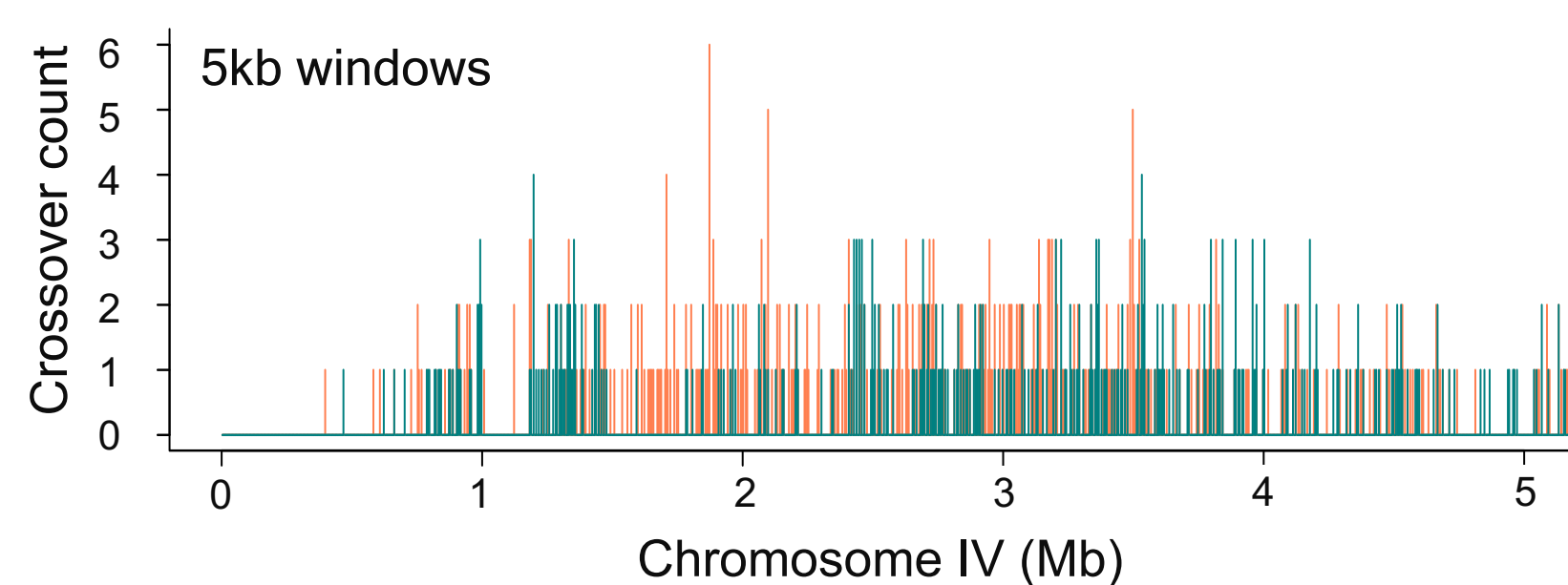
Sex differences in recombination rate and genomic location

Sticklebacks show strong female-biased heterochiasmy. Females recombine 1.76X more than males.

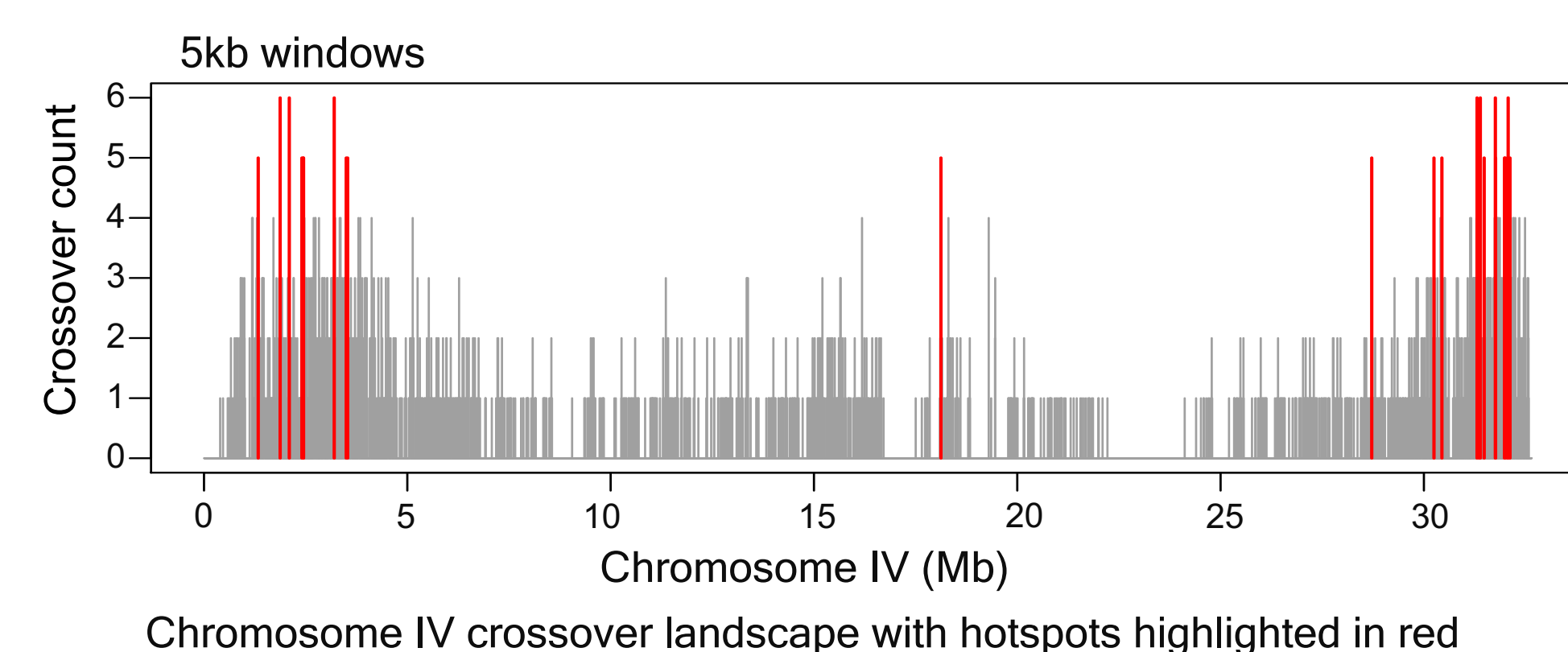
Crossovers are enriched at the chromosomal periphery. This pattern is pronounced in males where 75% of crossovers occur within first or last 15% of chromosomes. In females only 45% of crossovers occur within this range



Fine scale recombination landscape is heterogeneous and poorly correlated between sexes (spearman's ρ : 0.18)



Fine-scale recombination landscape has discrete recombination hotspots



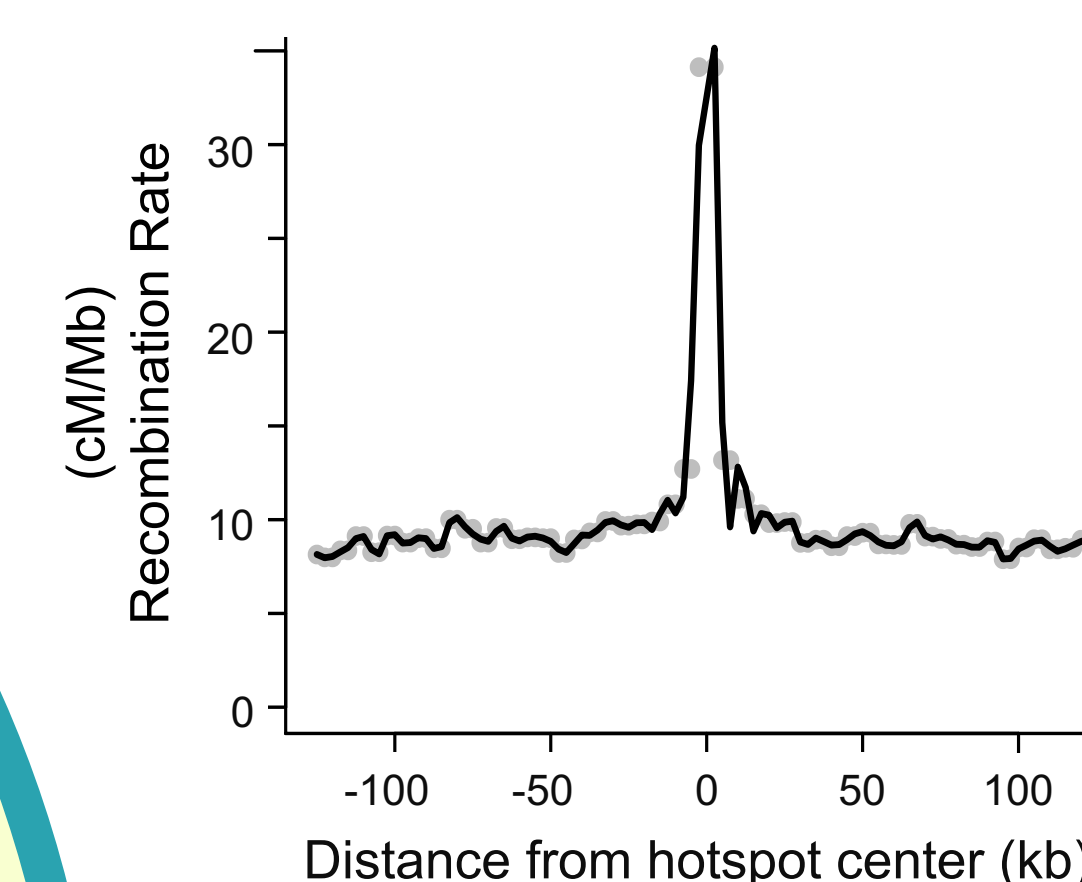
At fine scale (5kb), 432 hotspots were identified across the genome

Hotspots cluster at chromosomal periphery

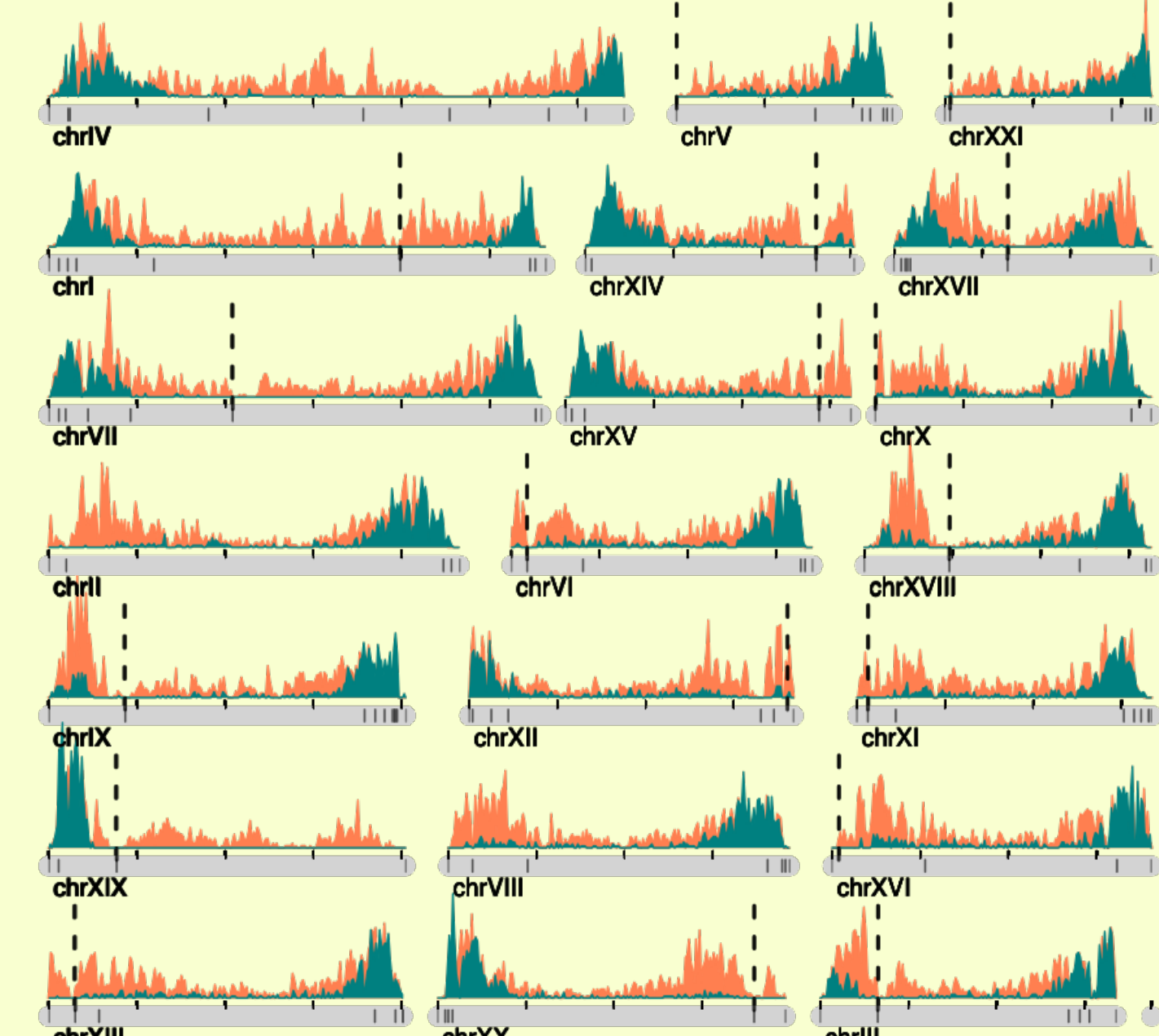
Hotspot intensity ranges from 0.15cM to 0.45cM.

Recombination rate within hotspots is about 3.7 times more than surrounding region

In general stickleback hotspots are 'semi-hot' in comparison with reported mammalian hotspots [2,3]



49,848 crossover events detected with 3.8kb median resolution

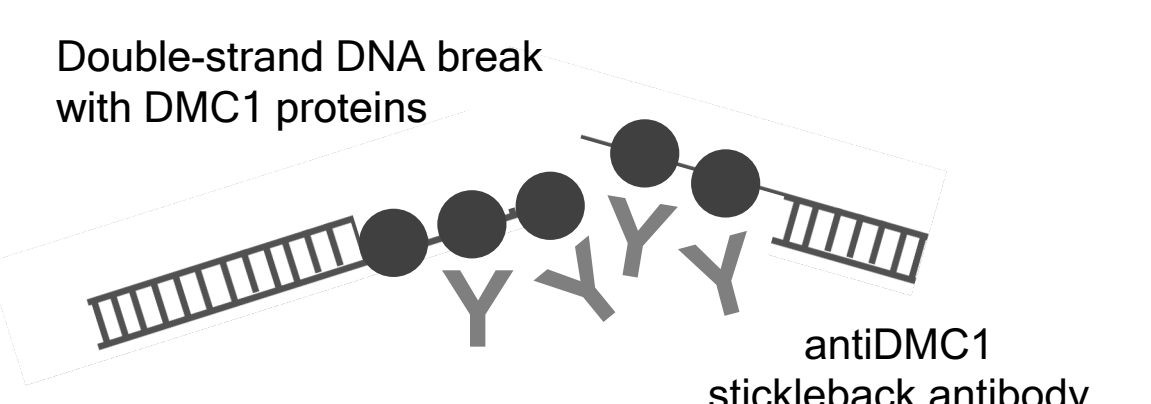


36 individual fishes, 3338 meiotic products

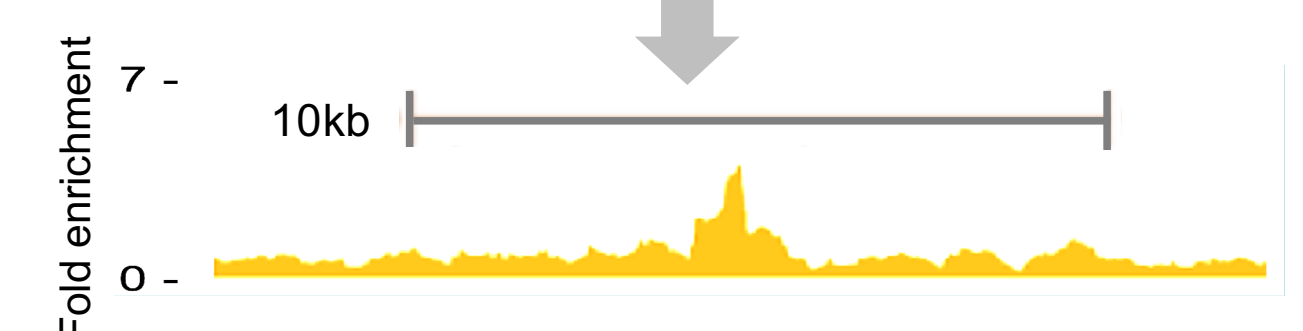
80% of crossovers occur in less than 35% of the genome

Male DSB hotspots and crossover events are associated with open chromatin marks

Male double strand break (DSB) landscape was identified by DMC1 ChIP sequencing of testes.

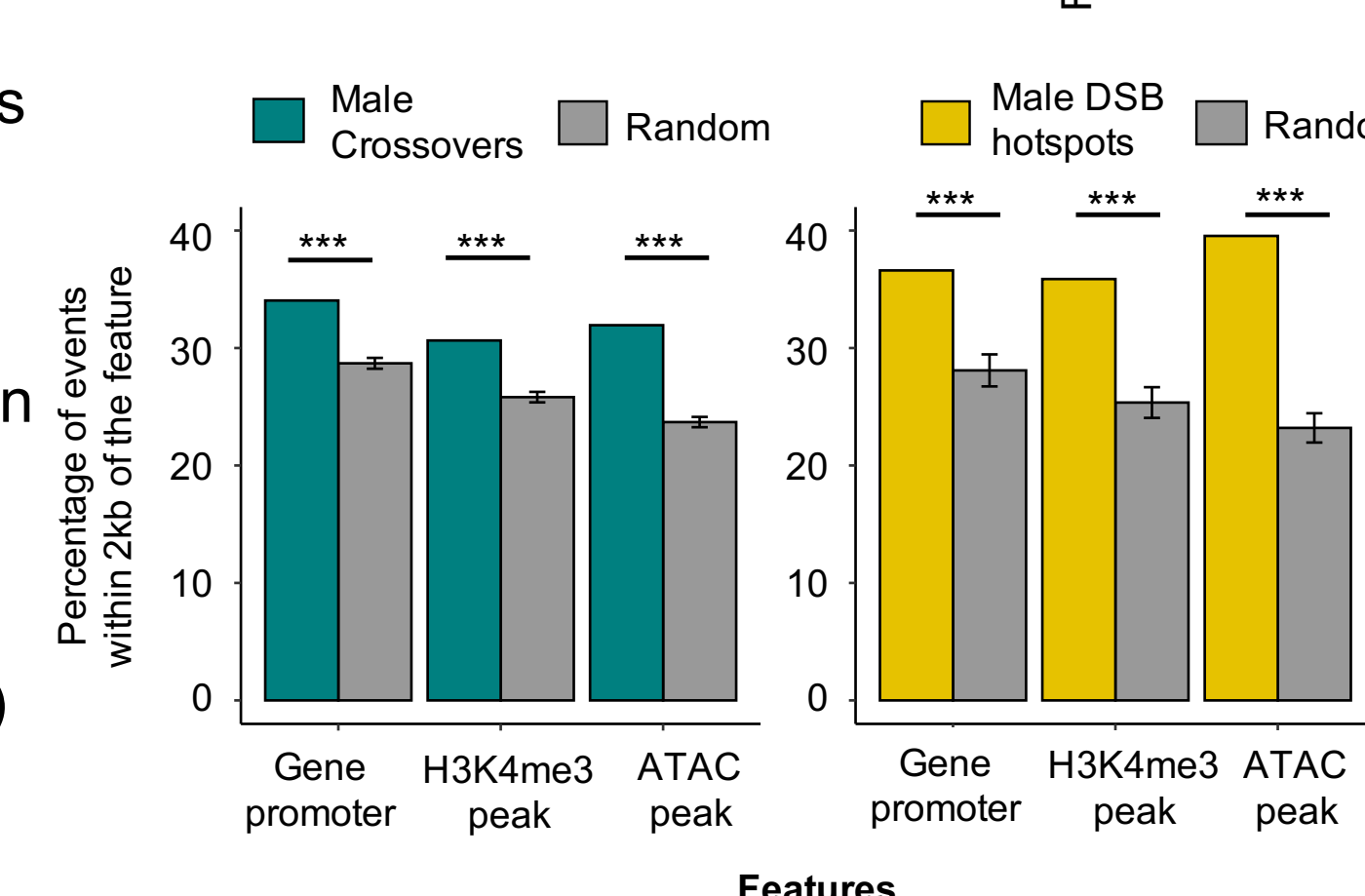


1090 DSB hotspots were identified across the genome.

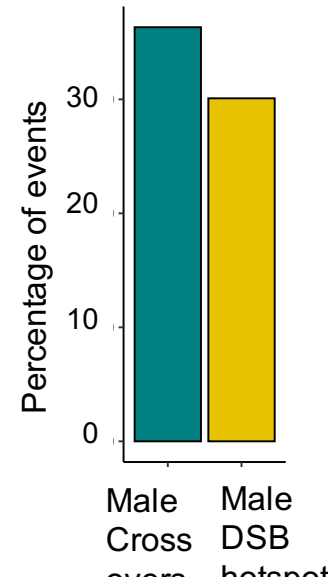


Male DSB hotspots and crossover events are significantly associated with

- gene promoters
- H3K4me3 marks in testes
- Nucleosome depleted regions (ATAC-seq peaks) in primary spermatocytes



Percentage of events more than 5kb away from any of the open chromatin mark



Male DSBs as well as crossovers are preferentially enriched at functionally active open chromatin marks. However, considerable fraction of crossovers and DSB hotspots away from open chromatin signature suggest a possibility of additional novel mechanisms of recombination regulation in sticklebacks.

Summary

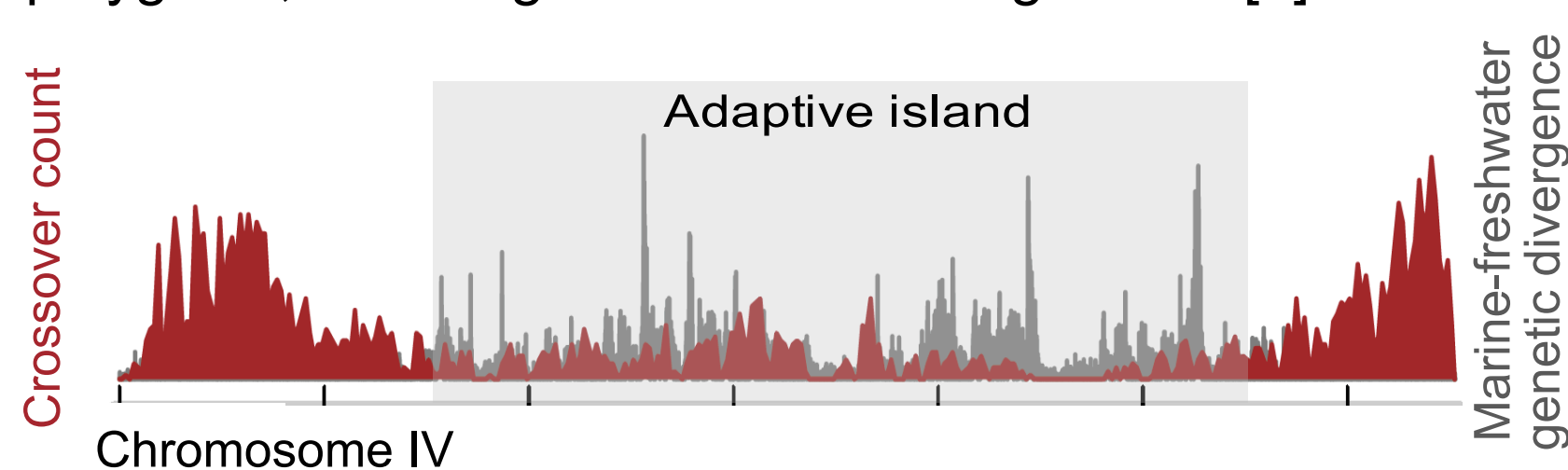
- High-resolution sex- and ecotype-specific recombination maps have been produced for 36 marine, freshwater and hybrid sticklebacks
- This powerful data set captures ~50,000 meiotic crossovers from ~3300 meiotic products
- Our dataset enables us to explore how recombination varies and evolves during adaptive divergence

- Sticklebacks show strong female-biased heterochiasmy
- Males crossovers are almost entirely located in the chromosome periphery
- Sticklebacks have fine scale hotspots that are 'semi-hot' compared to mice and other organisms
- Reduced recombination around adaptive loci enable inheritance as linked adaptive cassettes
- F1 hybrid females show lower recombination rate consistent with theoretical predictions of natural selection favoring recombination suppression in hybrid zones
- Male double strand breaks and crossovers are associated with functionally active open chromatin regions

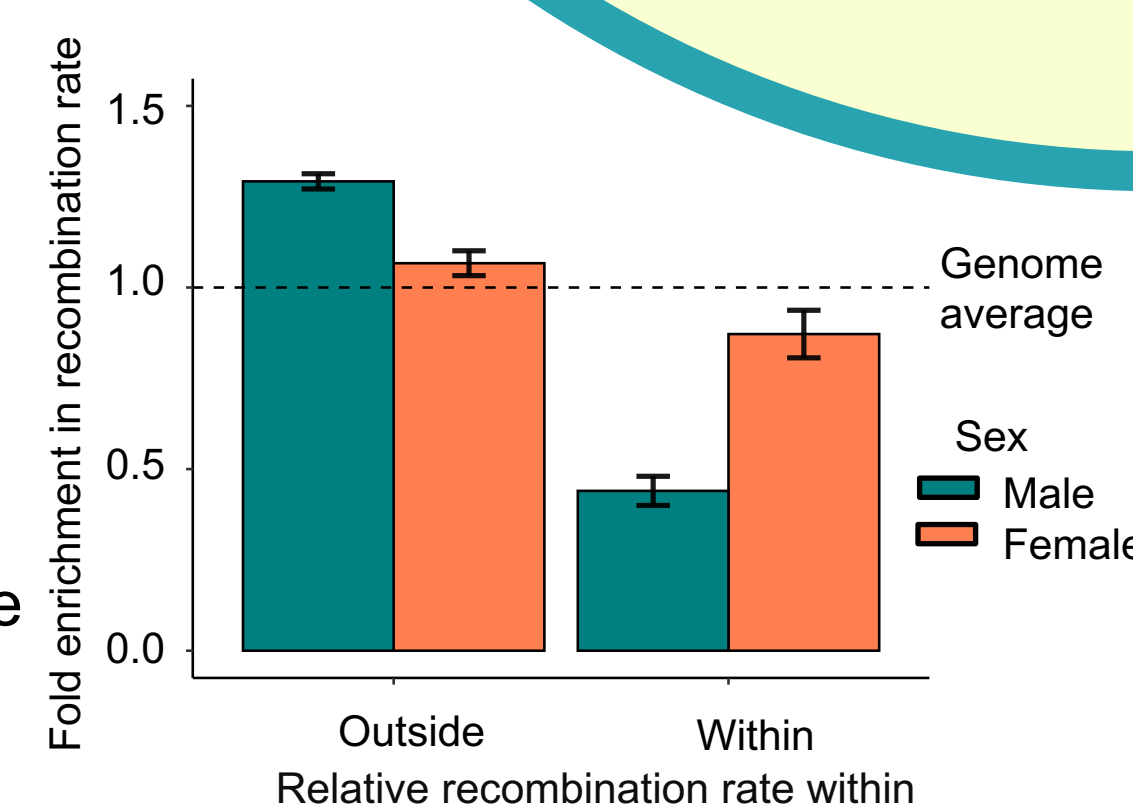
Recombination landscape shapes freshwater-marine adaptive divergence



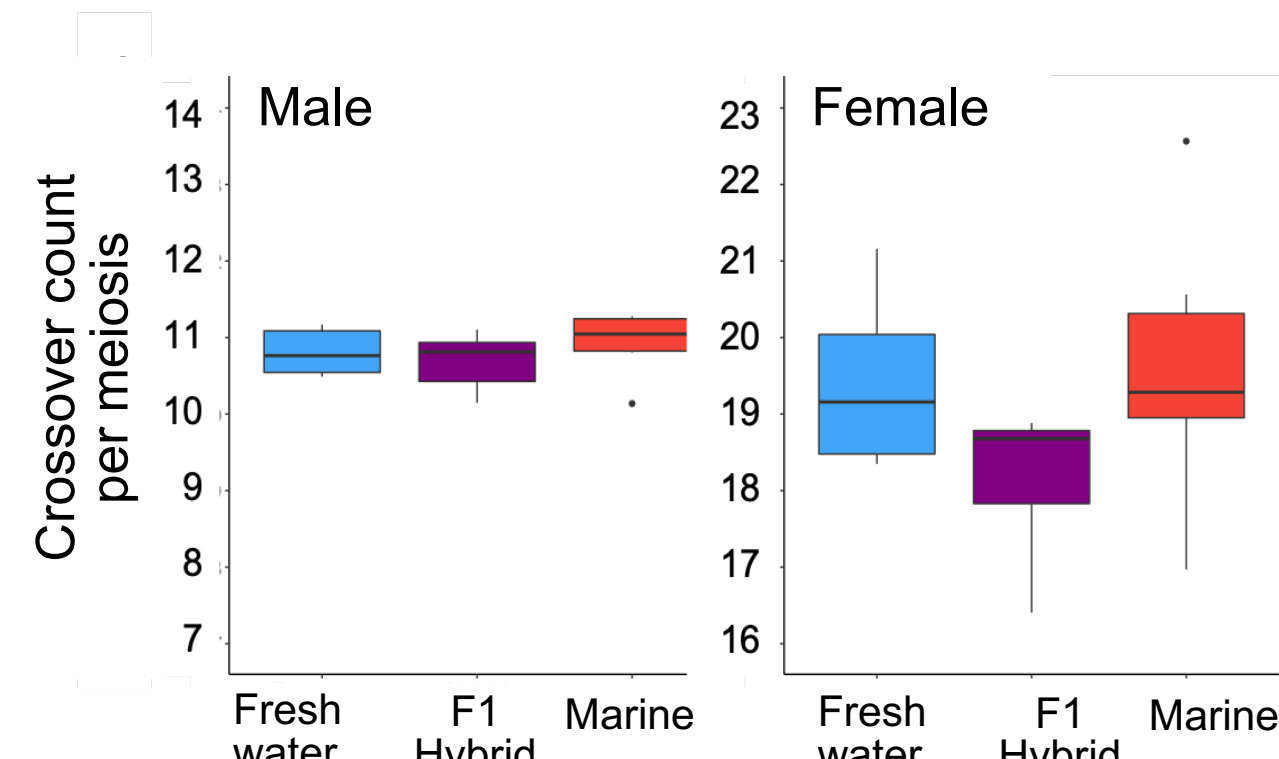
Adaptive divergence of marine and freshwater sticklebacks is polygenic, involving >242 loci across genome [4].



- Overall recombination rate between adaptive loci on the same chromosome is significantly lower – enabling adaptive alleles to be inherited as linked adaptive cassettes
- Considerable female recombination occur between adaptive loci



Reduced recombination in F1 hybrids



Theory predicts that natural selection will favor recombination modifiers that reduce deleterious recombination in hybrid zones of adaptively diverging species [5].

Our data support this — recombination is suppressed in F1 hybrids females enabling their offspring to inherit non-recombined adaptive cassettes.

Sexual dimorphism in recombination rate may have important evolutionary implications.

References

- [1] J. Stapley et al., *Philos Trans R Soc Lond B Biol Sci* 372 (2017)
- [2] K. Paigen, P. Petkov, *Nat Rev Genet* 11 (2010)
- [3] K. Paigen et al., *Plos genetics* 4 (2008)
- [4] F.C. Jones et al., *Nature* 484 (2012)
- [5] D. Charlesworth et al., *Genetics* 91 (1979)

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