

Evolution at multiple loci: linkage disequilibrium

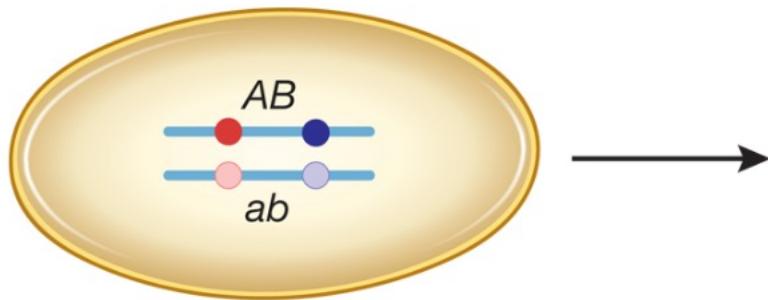
- What is linkage disequilibrium and how does it arise?
- How do we quantify linkage disequilibrium?
- How does linkage disequilibrium break down?
- How can linage disequilibrium be used to understand evolution?

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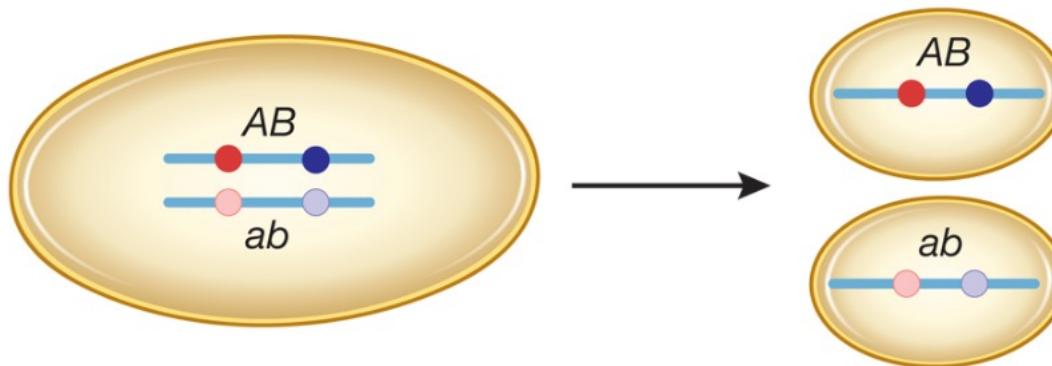
We need to think about multiple loci

Haplotypes: A set of alleles at different loci.

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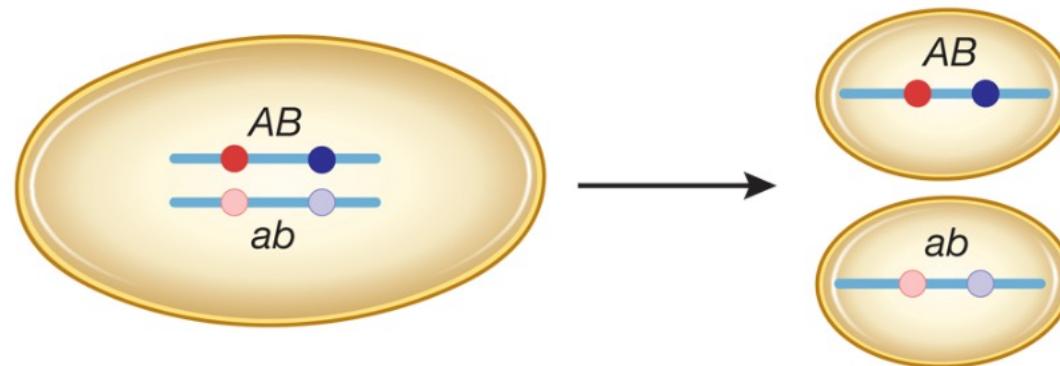


Haplotypes: A set of alleles at different loci.



What is linkage disequilibrium?

- Linkage Disequilibrium
 - Statistical associations between alleles at different loci

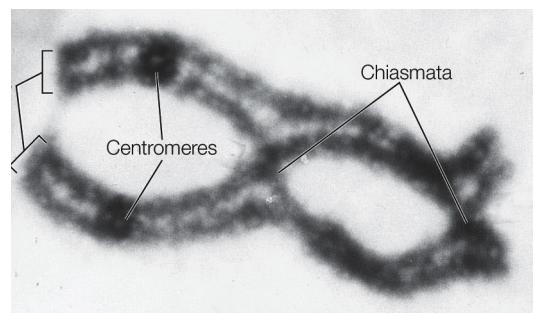
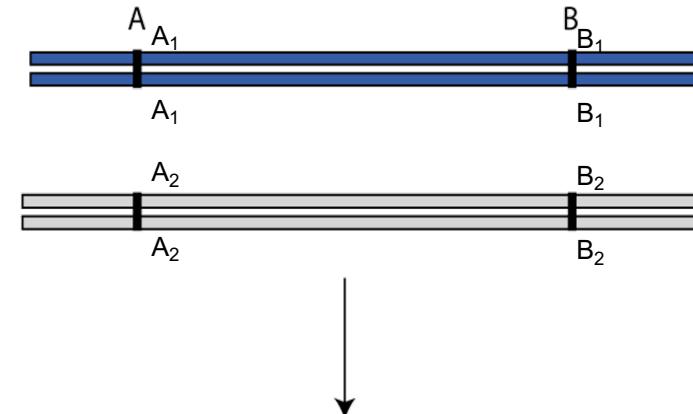


What is linkage disequilibrium?

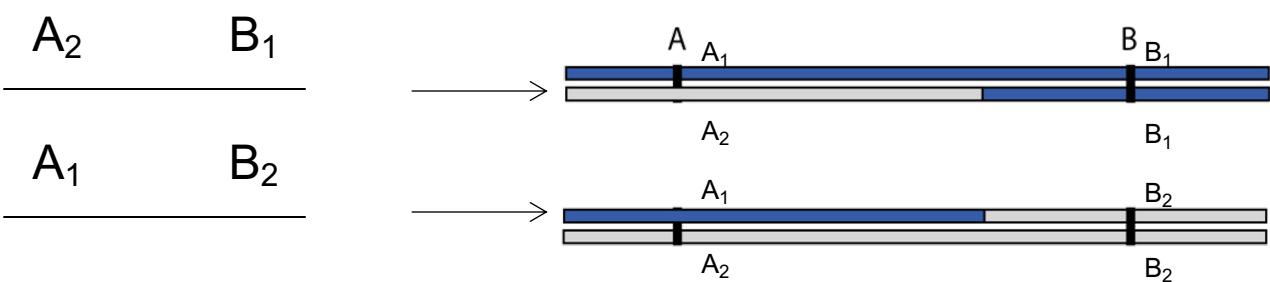
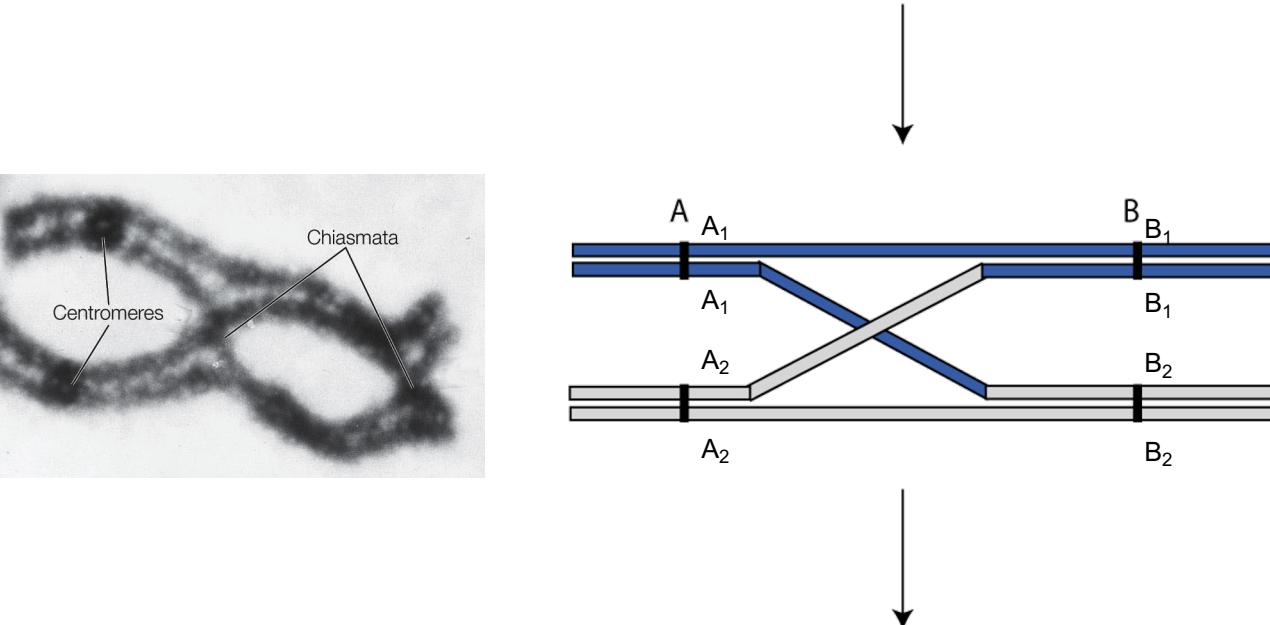
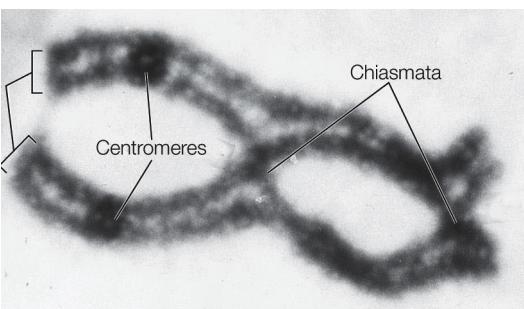
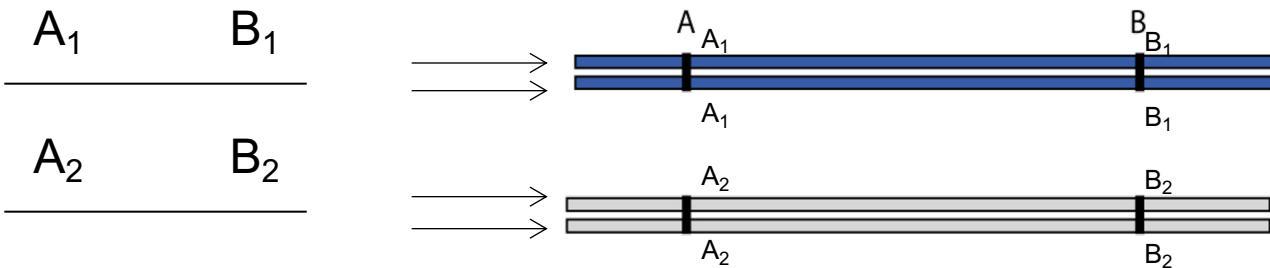
Linkage Disequilibrium

Statistical associations between alleles at different loci

- Two homologous chromosomes in diploids (except in the gametes, which are haploid)
- Each chromosome has two (identical) *sister chromatids*
- *Recombination:*
 - Chromosomes exchange short segments
 - happens in the germline during *meiosis*.

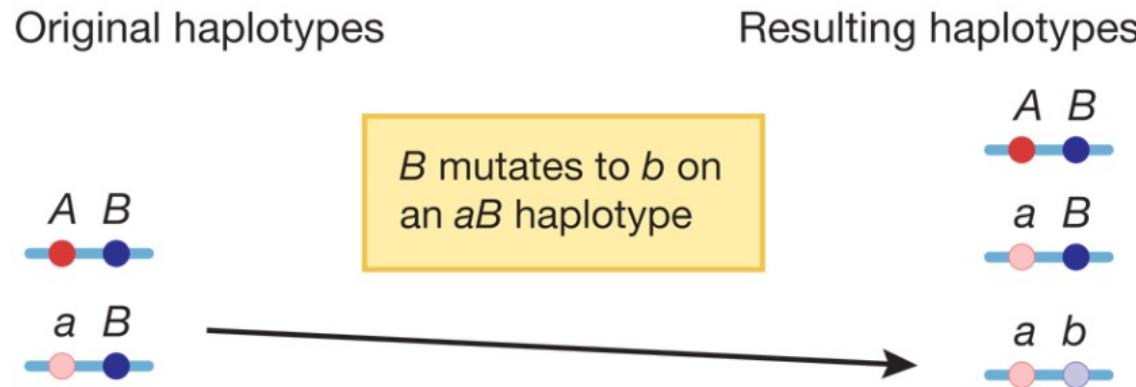


Represented as



How is LD generated?

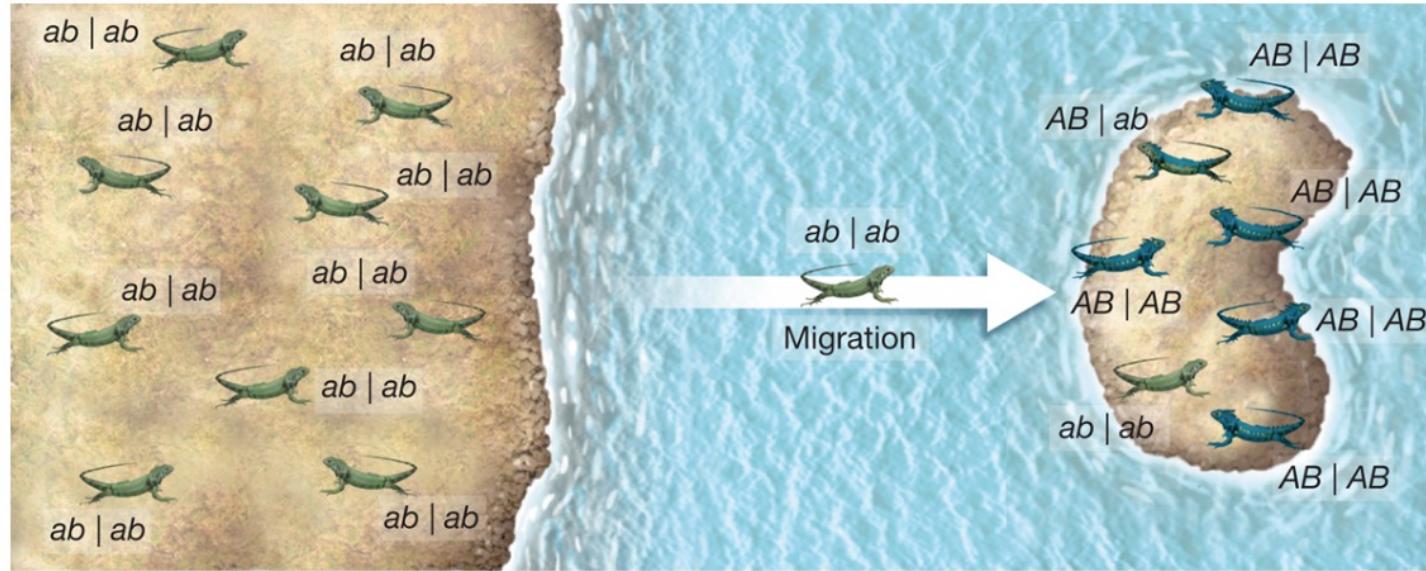
Mutation



initially perfectly associated (i.e. linked) with one allele of the other locus

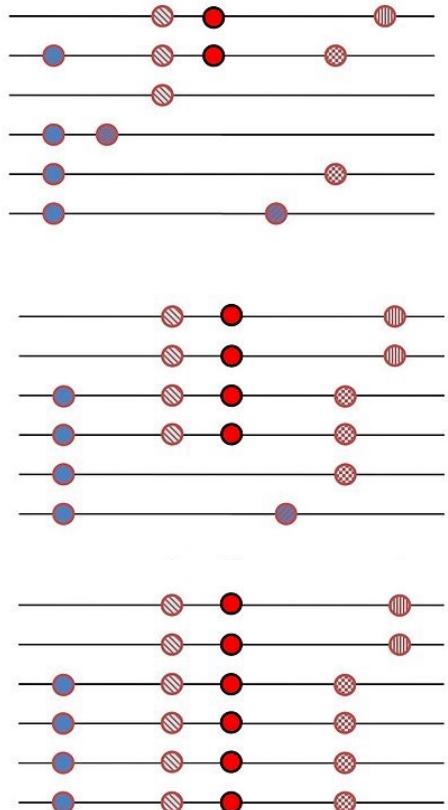
How is LD generated?

Migration/admixture



How is LD generated?

Selection



Non-random mating



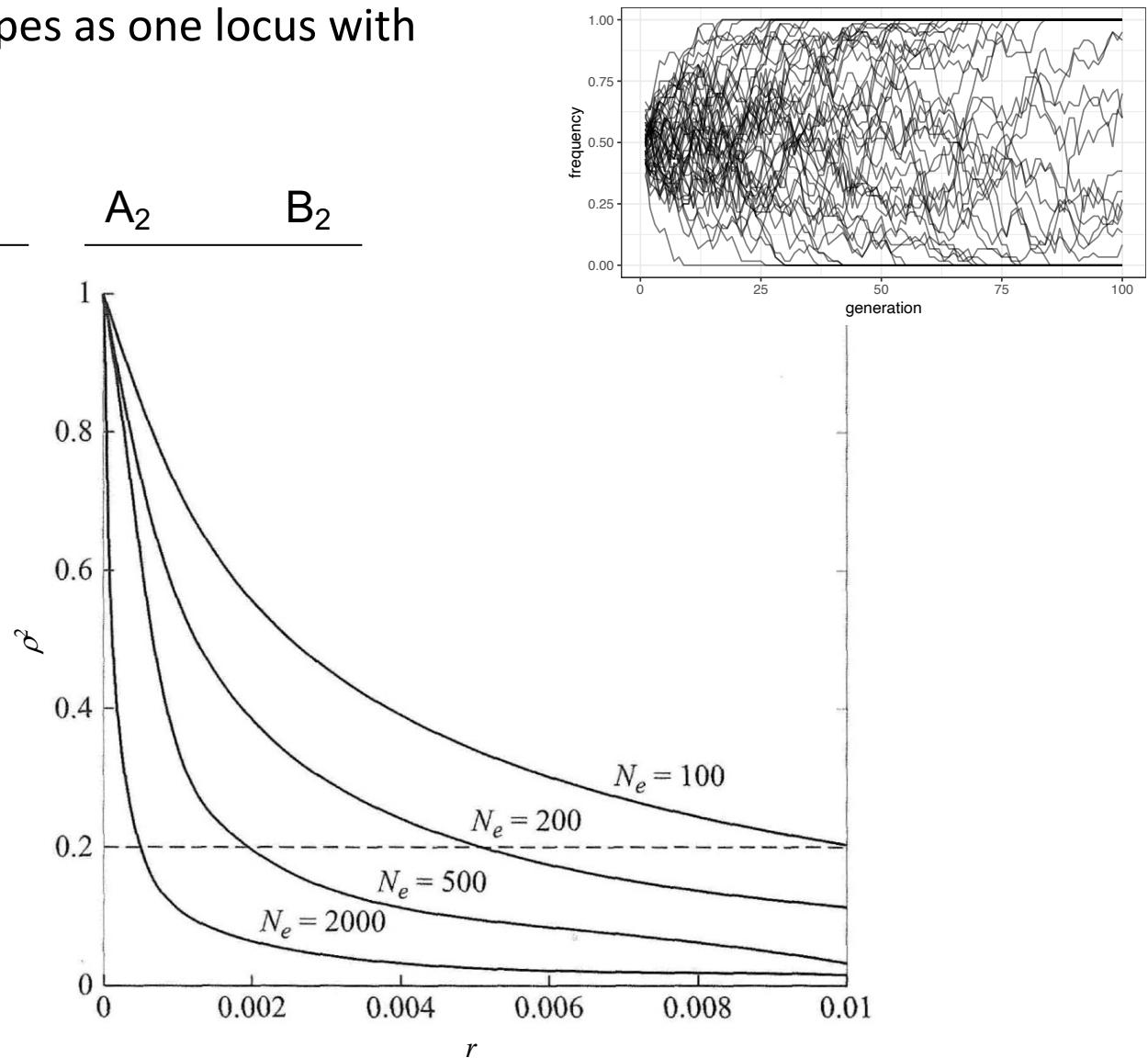
Linkage and effective population size

Sampling error in finite populations may result in deviations from independent segregation (imagine the four gamete types as one locus with four alleles)



Drift generates linkage disequilibrium

Linkage can therefore be used to estimate effective population size!



- What is linkage disequilibrium and how does it arise?
- How do we quantify linkage disequilibrium?
- How does linkage disequilibrium break down?
- How can linage disequilibrium be used to understand evolution?

How do we quantify LD?

D = coefficient of linkage disequilibrium

$$D = h_{AB} - f_A f_B$$

$$D_{AB} = h_{ab} - f_a f_b$$

How do we quantify LD?

$$D = h_{AB} - f_A f_B$$

Exercise:

$$n_{AB} = 50, n_{Ab} = 20, n_{aB} = 10, n_{ab} = 20, (n_{\text{total}} = 100)$$

Calculate haplotype frequencies:

$$h_{AB} = \underline{\hspace{2cm}}, \quad h_{Ab} = \underline{\hspace{2cm}}, \quad h_{aB} = \underline{\hspace{2cm}}, \quad h_{ab} = \underline{\hspace{2cm}}$$

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Calculate haplotype frequencies:

$$h_{AB} = \underline{\textcolor{red}{0.5}}, \quad h_{Ab} = \underline{\textcolor{red}{0.2}}, \quad h_{aB} = \underline{\textcolor{red}{0.1}}, \quad h_{ab} = \underline{\textcolor{red}{0.2}}$$

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Calculate allele frequencies:

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Calculate allele frequencies:

$$f_A = \underline{\textcolor{red}{0.7}}, \quad f_a = \underline{\textcolor{red}{0.3}}, \quad f_B = \underline{\textcolor{red}{0.6}}, \quad f_b = \underline{\textcolor{red}{0.4}}$$

How do we quantify LD?

$$D = h_{AB} - f_A f_B$$

Exercise:

$$n_{AB} = 50, n_{Ab} = 20, n_{aB} = 10, n_{ab} = 20, (n_{\text{total}} = 100)$$

Calculate haplotype frequencies:

$$h_{AB} = \underline{\textcolor{red}{0.5}}, \quad h_{Ab} = \underline{\textcolor{red}{0.2}}, \quad h_{aB} = \underline{\textcolor{red}{0.1}}, \quad h_{ab} = \underline{\textcolor{red}{0.2}}$$

Calculate allele frequencies:

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Calculate D:

$$D_{AB} = \underline{\hspace{2cm}}, \quad D_{Ab} = \underline{\hspace{2cm}}, \quad D_{aB} = \underline{\hspace{2cm}}, \quad D_{ab} = \underline{\hspace{2cm}}$$

How do we quantify LD?

$$D = h_{AB} - f_A f_B$$

Exercise:

$$n_{AB} = 50, n_{Ab} = 20, n_{aB} = 10, n_{ab} = 20, (n_{\text{total}} = 100)$$

Calculate haplotype frequencies:

$$h_{AB} = \underline{\underline{0.5}}, \quad h_{Ab} = \underline{\underline{0.2}}, \quad h_{aB} = \underline{\underline{0.1}}, \quad h_{ab} = \underline{\underline{0.2}}$$

Calculate allele frequencies:

$$f_A = \underline{\underline{0.7}}, \quad f_a = \underline{\underline{0.3}}, \quad f_B = \underline{\underline{0.6}}, \quad f_b = \underline{\underline{0.4}}$$

Calculate D:

$$D_{AB} = \underline{\underline{+0.08}}, \quad D_{Ab} = \underline{\underline{-0.08}}, \quad D_{aB} = \underline{\underline{-0.08}}, \quad D_{ab} = \underline{\underline{+0.08}}$$

How do we quantify LD?

$$D_{AB} = \underline{+0.08}, D_{Ab} = \underline{-0.08}, D_{aB} = \underline{-0.08}, D_{ab} = \underline{+0.08}$$

$$D_{AB} = -D_{Ab} = -D_{aB} = D_{ab}$$

$$h_{AB} = f_A f_B + D \quad \text{Coupling}$$

$$h_{Ab} = f_A f_b - D \quad \text{Repulsion}$$

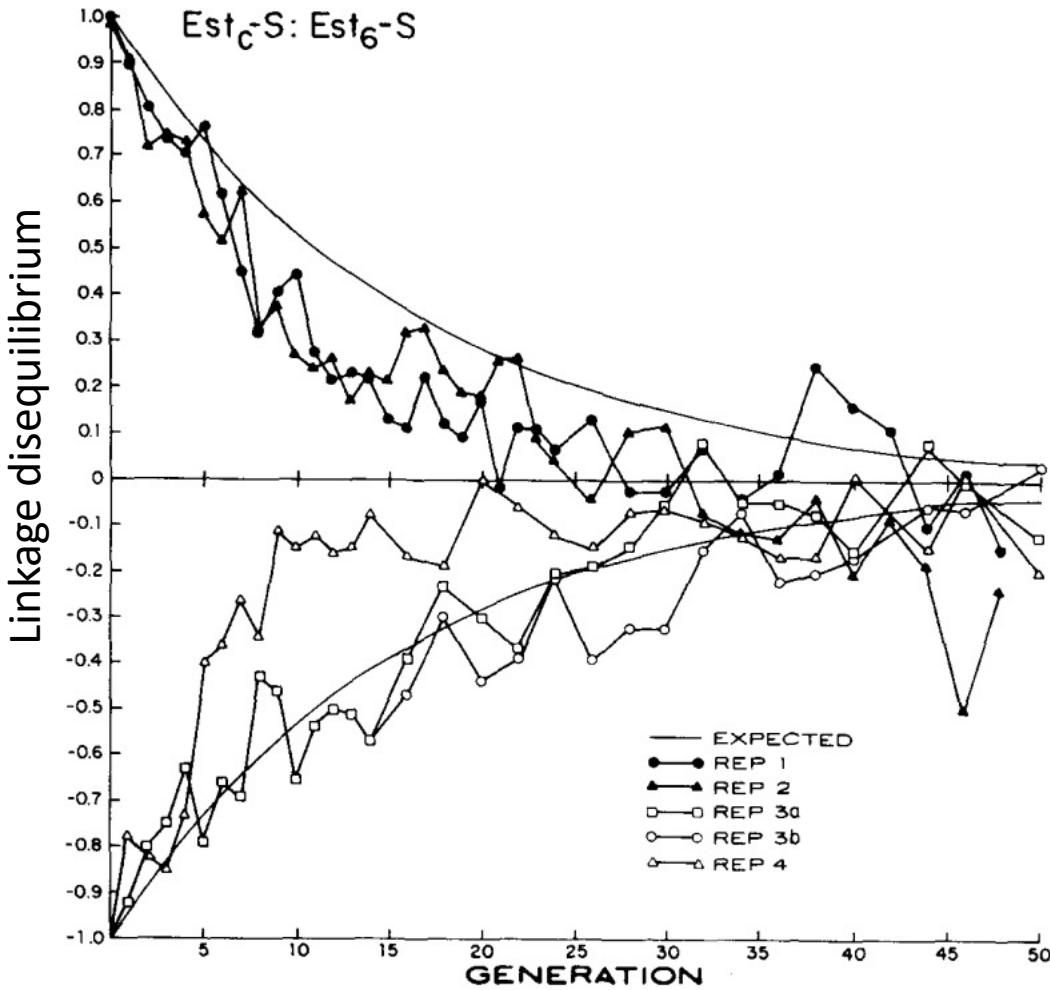
$$h_{aB} = f_a f_B - D \quad \text{Repulsion}$$

$$h_{ab} = f_a f_b + D \quad \text{Coupling}$$

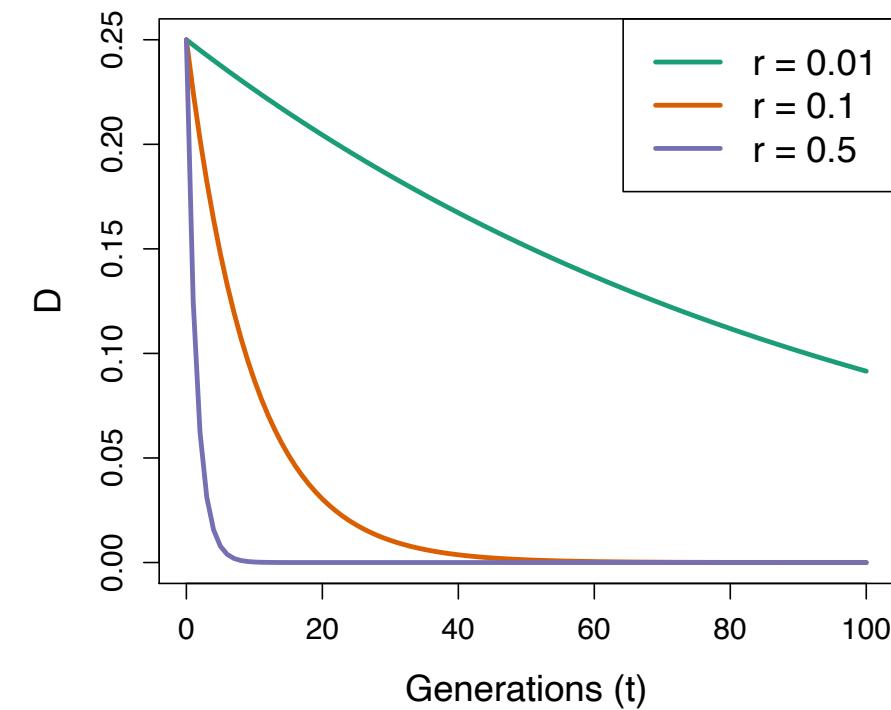
D = the excess of coupling to repulsion gametes.

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- **How does linkage disequilibrium break down?**
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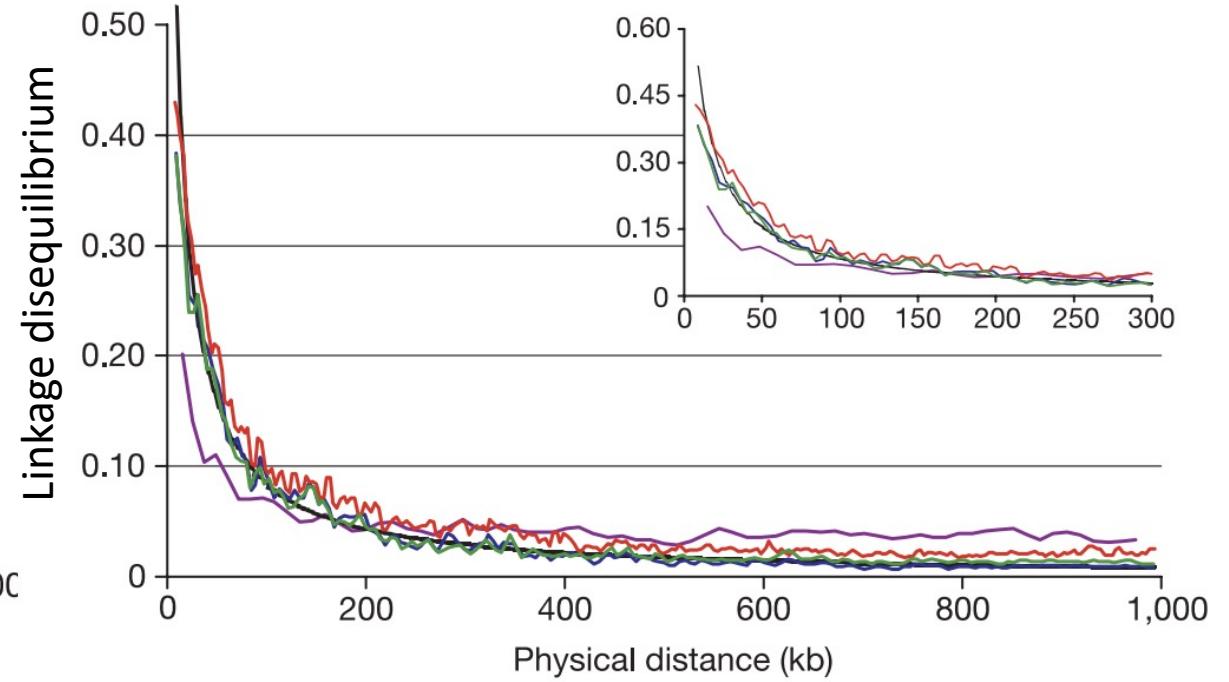
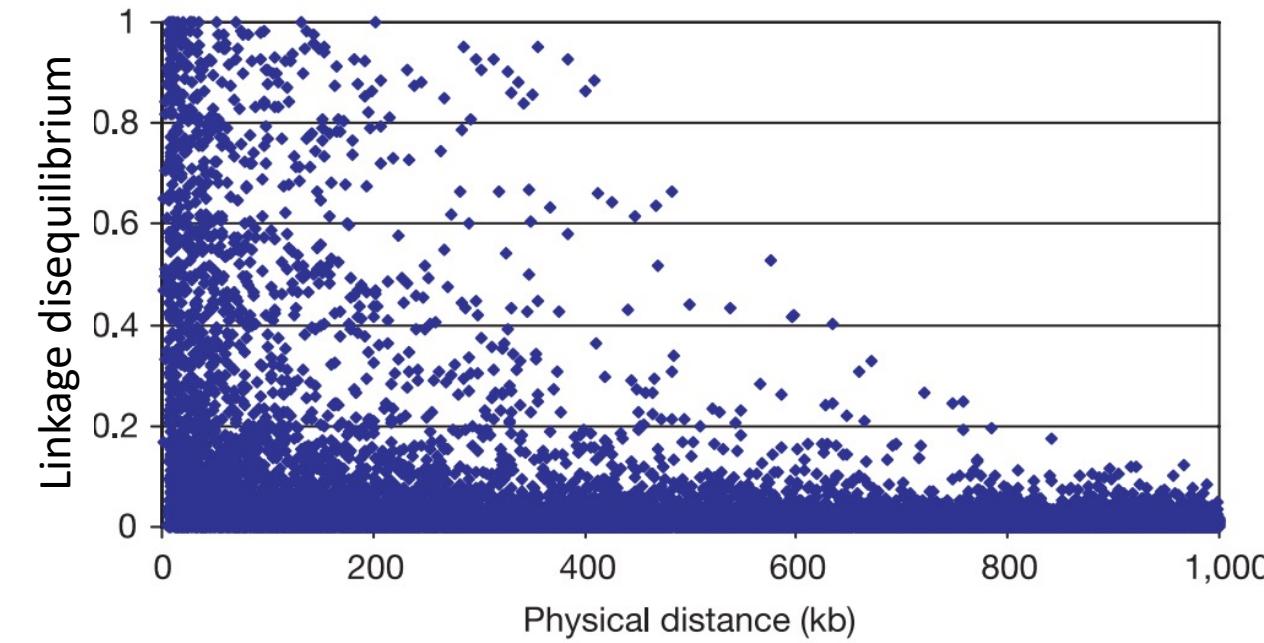
What happens to LD over time?



$$\Delta D = -rD$$

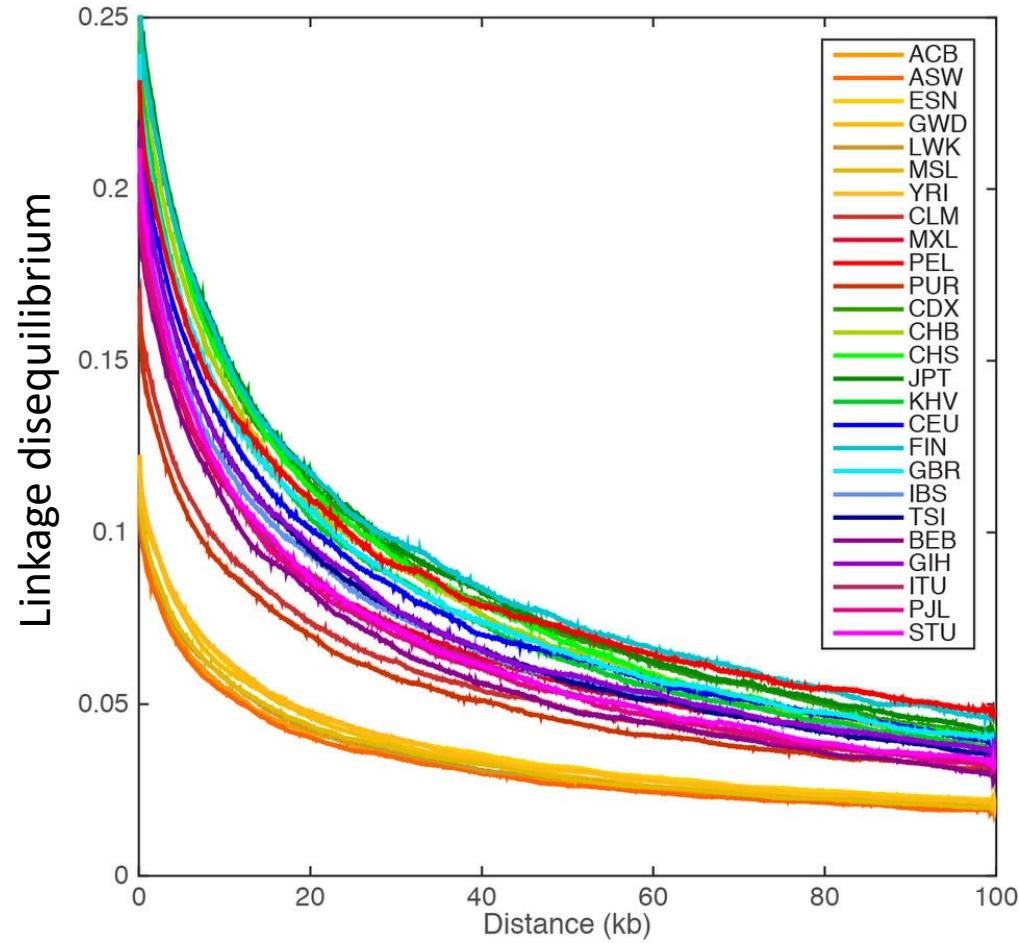


LD breaks down with physical distance



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LD is variable between populations due to drift

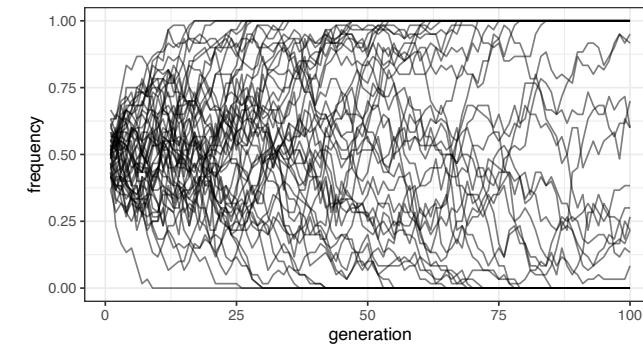


LD is high in humans

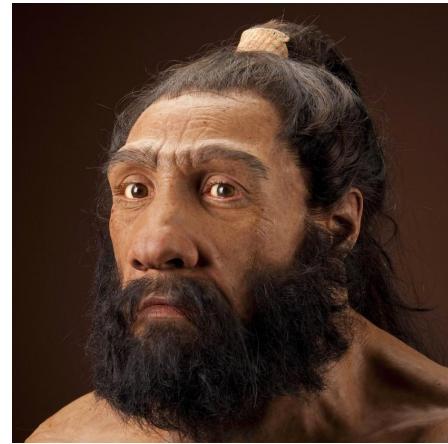
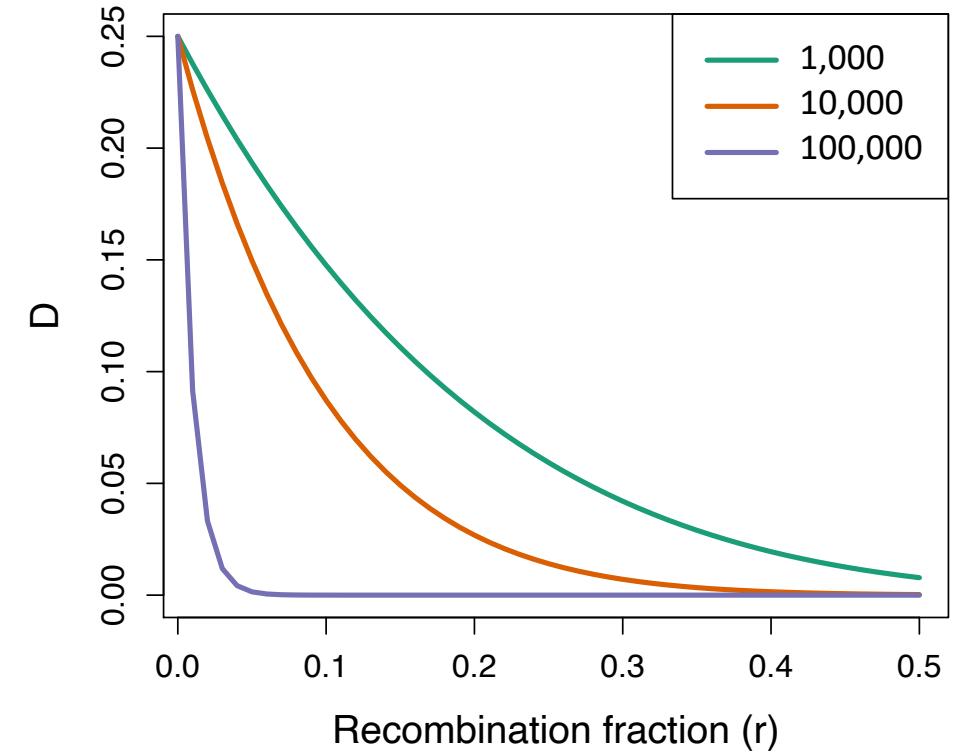
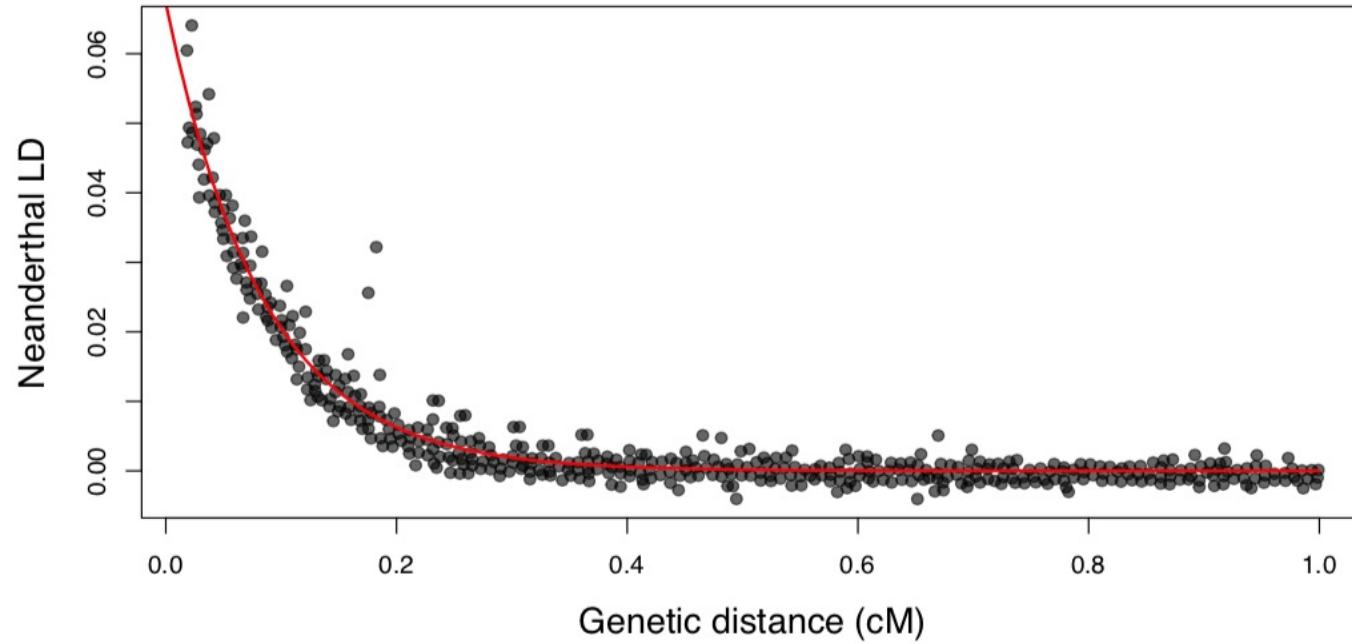
- Past bottlenecks

LD is variable in humans

- Different histories for different populations

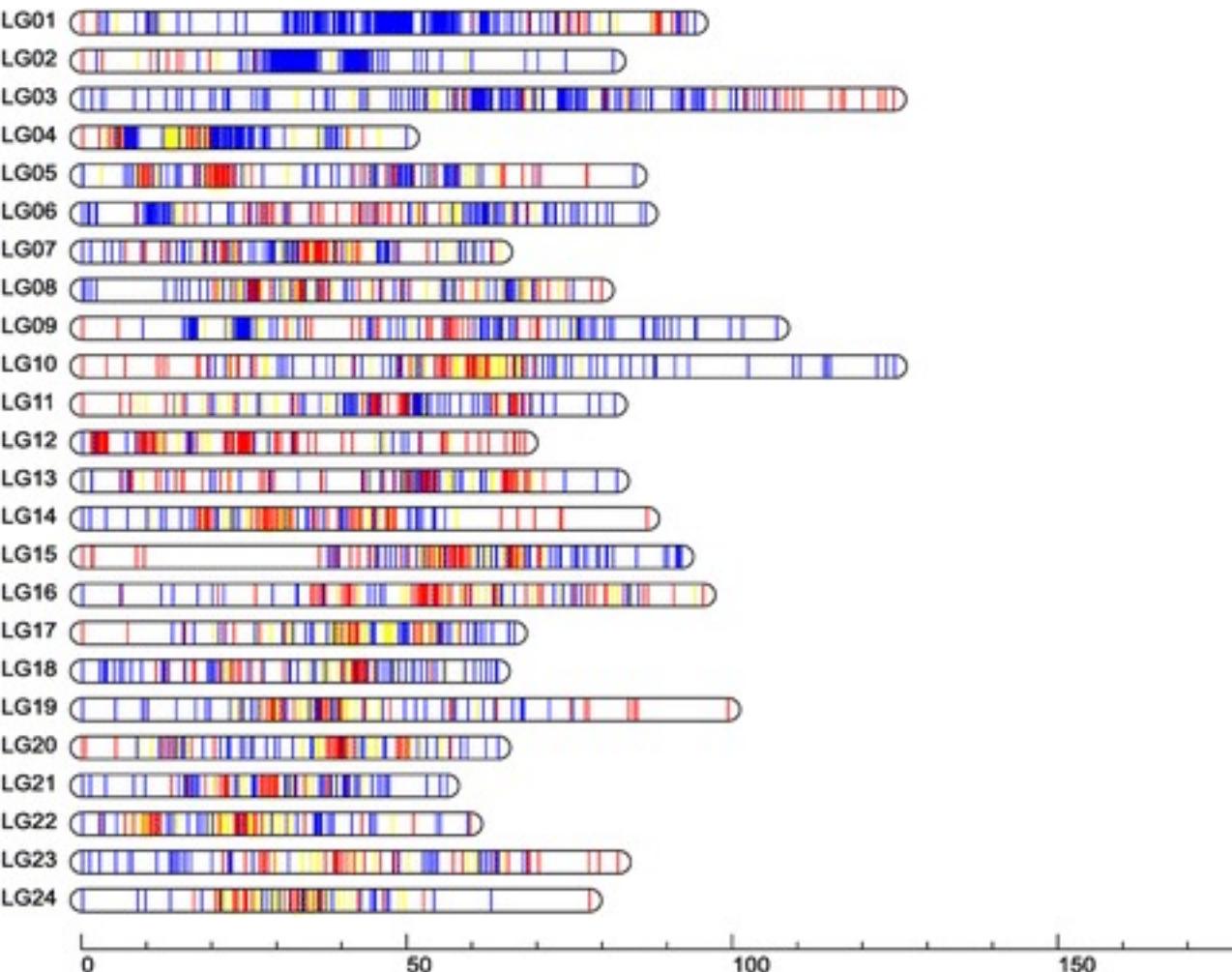


LD decay can tell us timing of hybridization

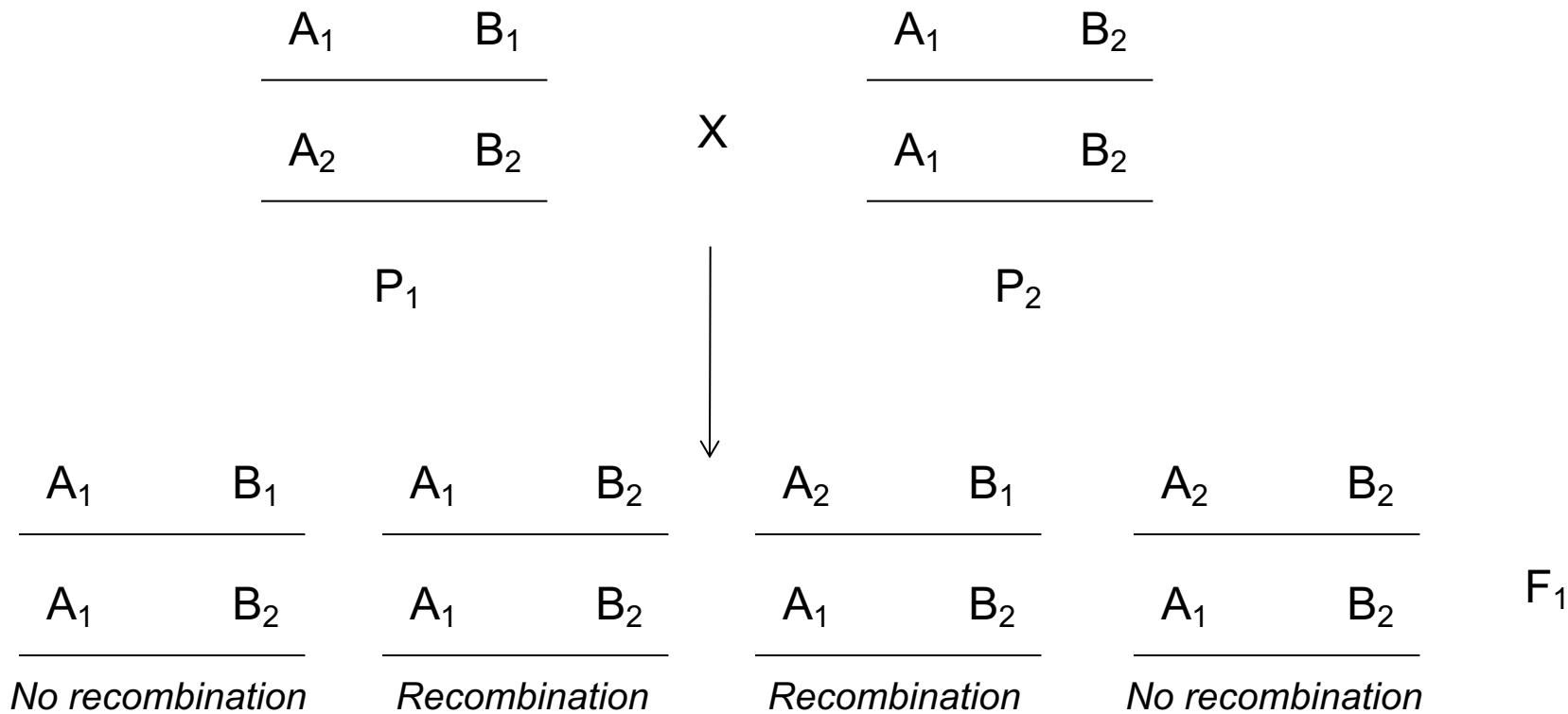


Linkage mapping

- Recombination rate: increases with physical distance between loci
- *linkage map*,
 - 'map' that indicates the position of loci relative to each other
 - Useful to e.g. locate specific loci, assemble a genome, or study recombination
- centiMorgans (cM)
 - The distance for 1 crossover in the intervening interval in every 100 products of meiosis
 - rate of crossover events at meiosis

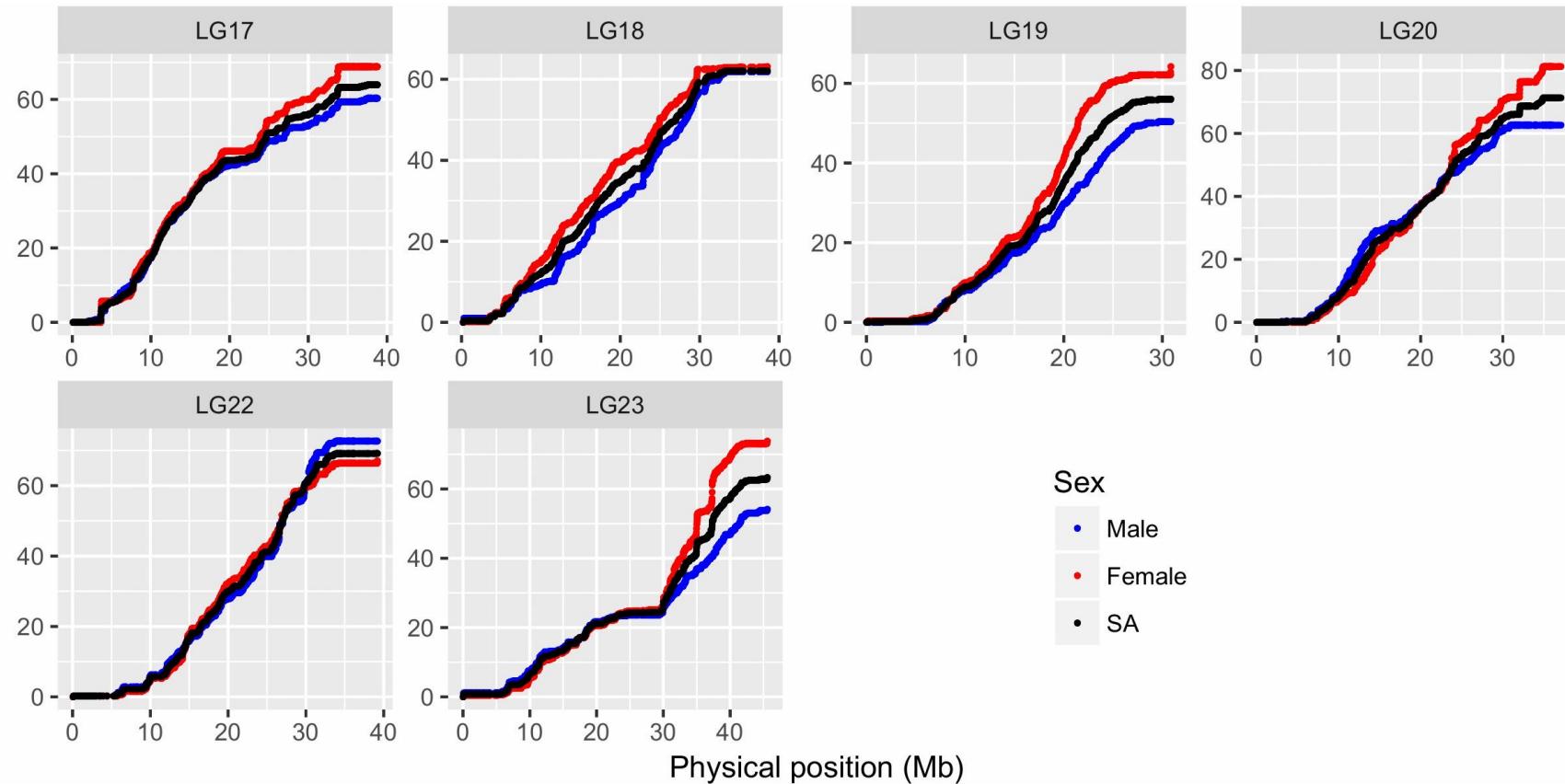


Markers that are heterozygous in one parent and homozygous



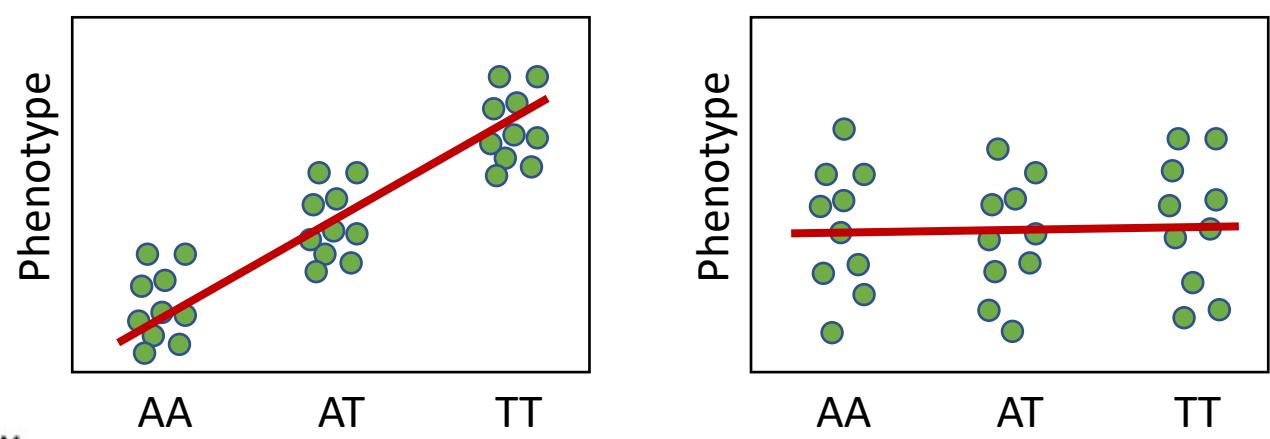
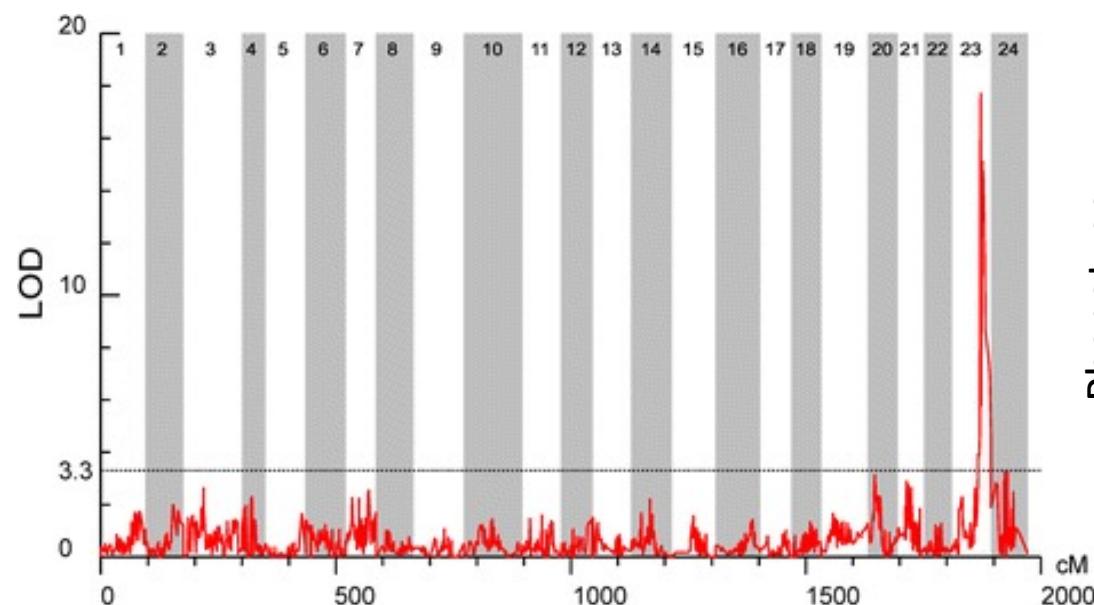
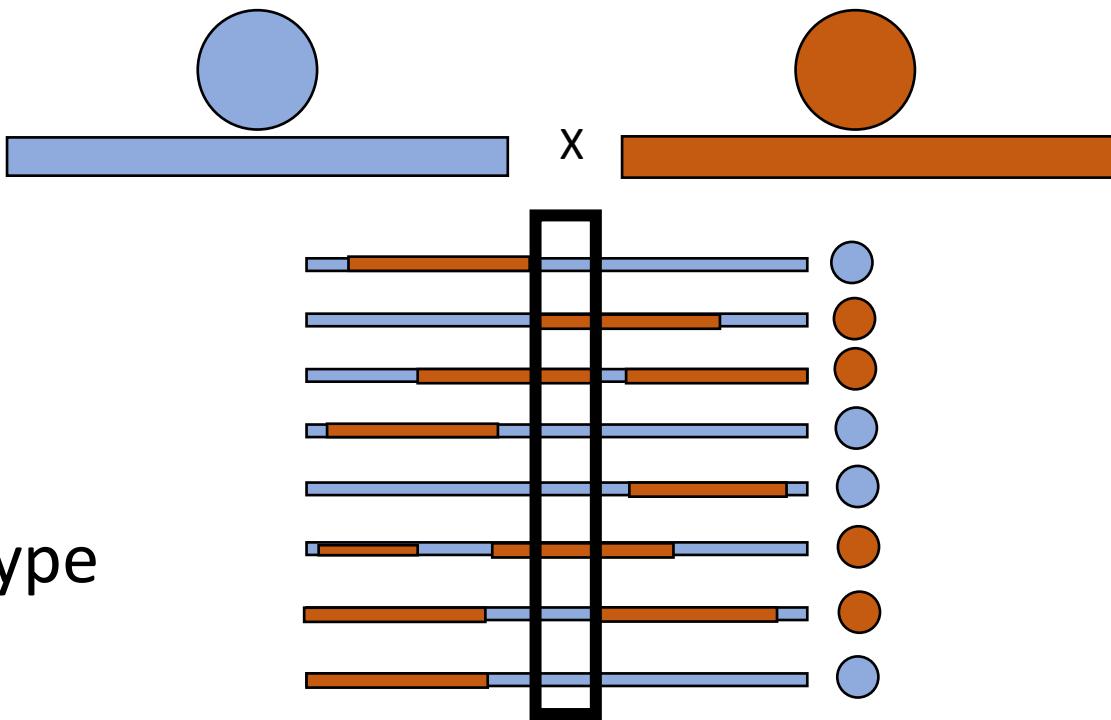
The proportions of these four cases in the progeny provide an estimate of recombination frequency between A and B in P₁

Physical vs. genetic maps

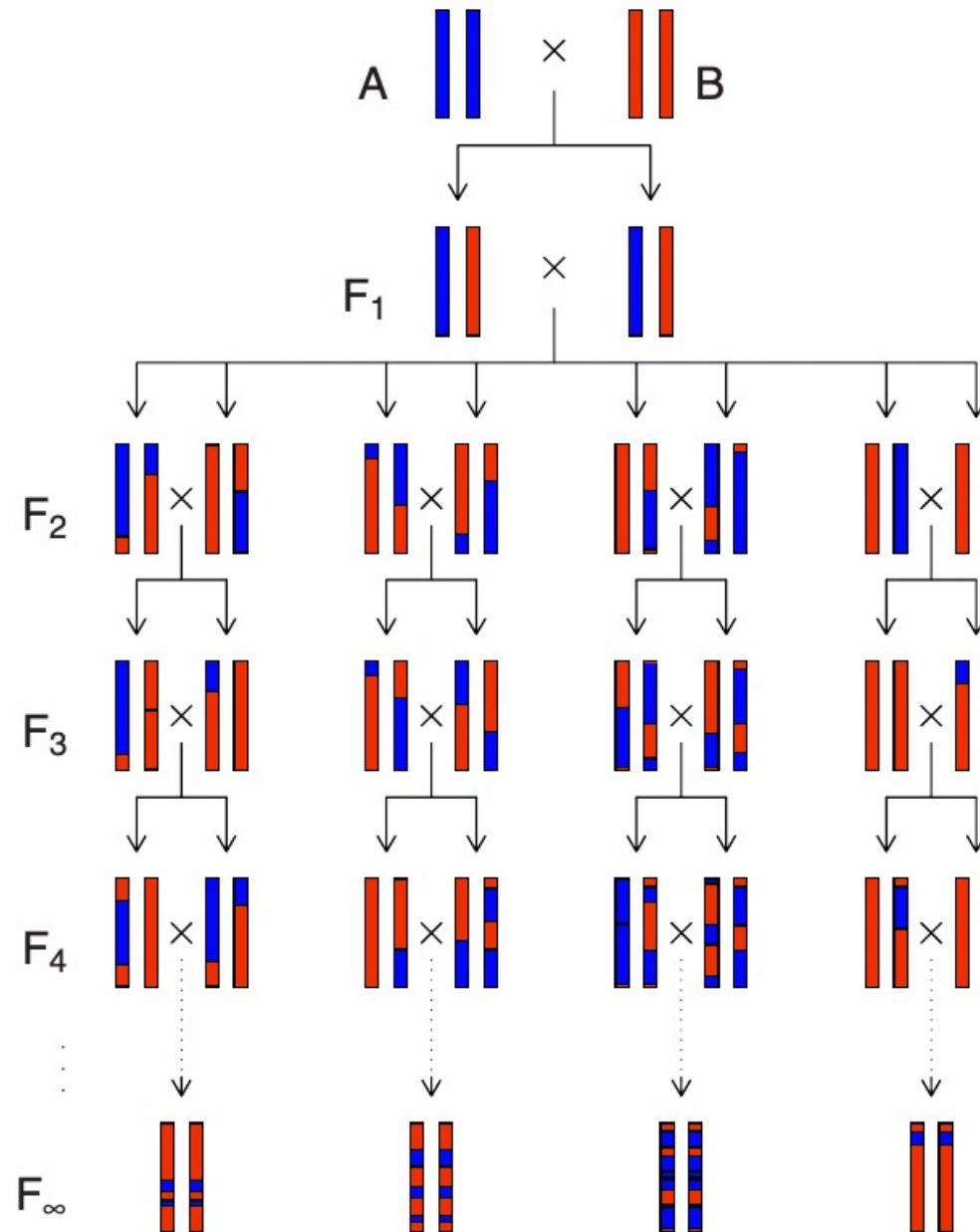


QTL mapping

- Linking genetic variation to phenotypic variation
- Artificially generating linkage
- Look for associations with phenotype

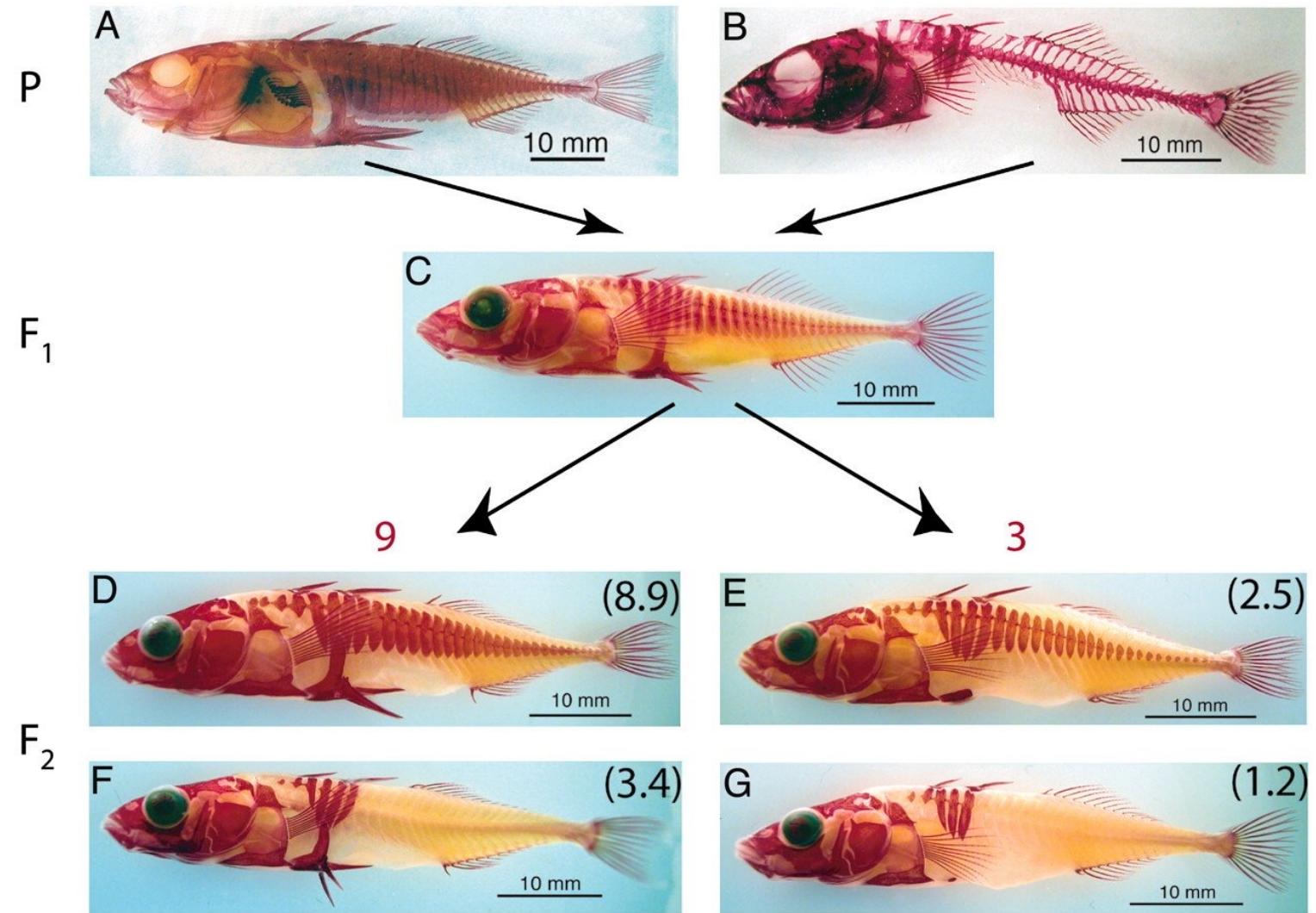


QTL mapping



From: A Guide to QTL Mapping with R/qtl

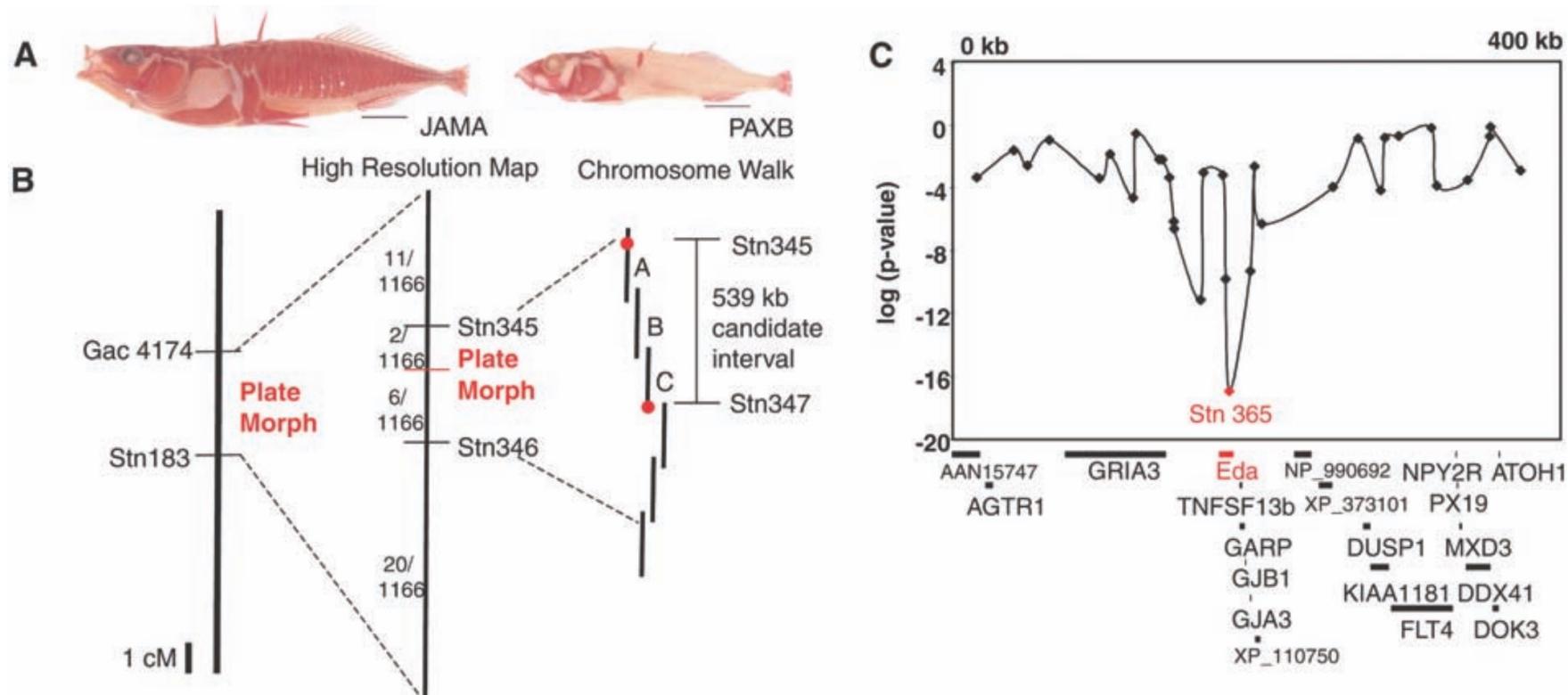
QTL mapping



Parallel genetic basis for repeated evolution of armor loss in Alaskan threespine stickleback populations

William A. Cresko*,†, Angel Amores*, Catherine Wilson*, Joy Murphy*, Mark Currey*, Patrick Phillips†, Michael A. Bell‡,
Charles B. Kimmel*, and John H. Postlethwait*§

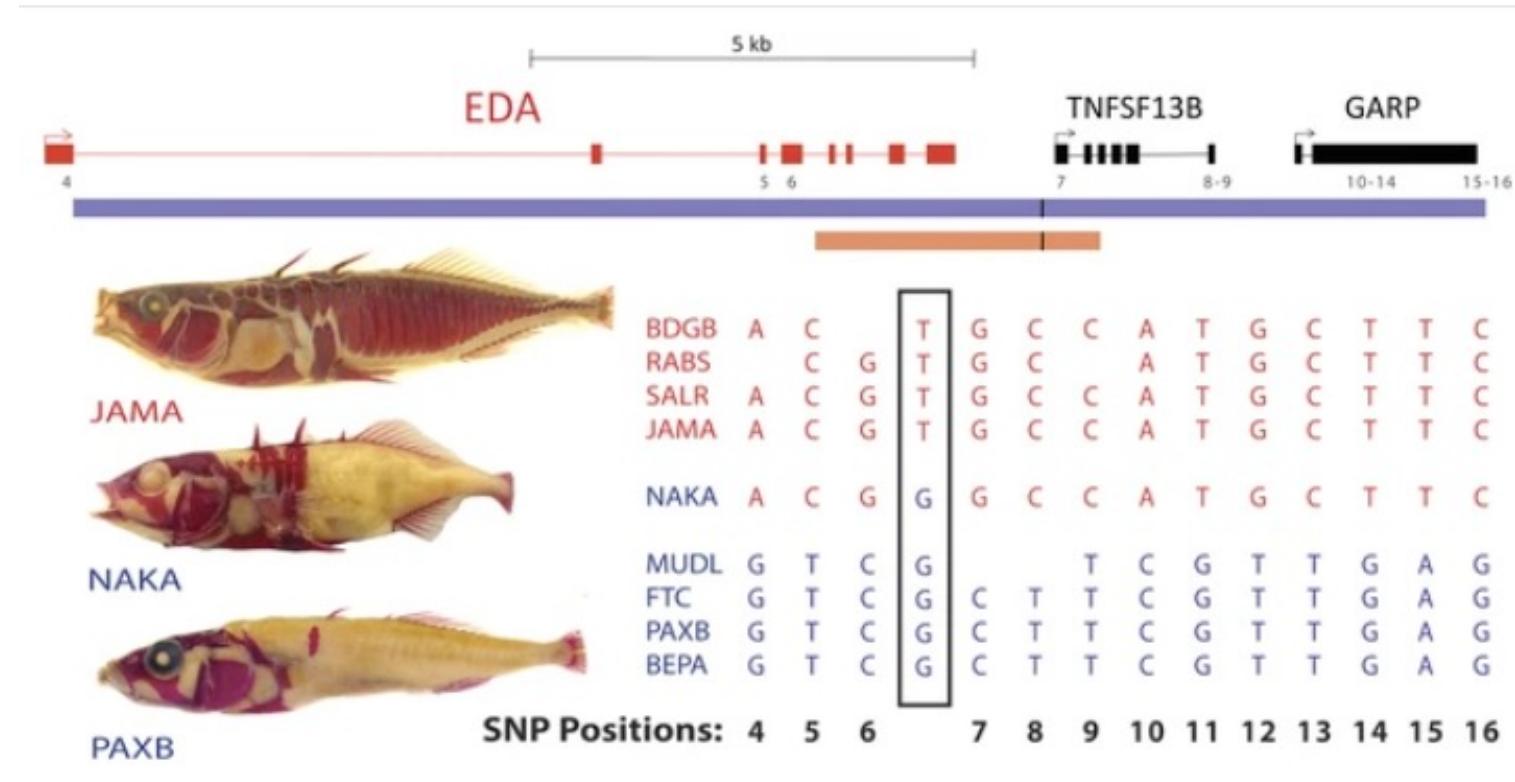
QTL mapping



**Widespread Parallel Evolution in
Sticklebacks by Repeated Fixation
of Ectodysplasin Alleles**

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Jeremy Schmutz,³ Richard M. Myers,³ Dolph Schlüter,⁴
David M. Kingsley^{1,2}

QTL mapping



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PAPER FOR NEXT WEEK

ORIGINAL ARTICLE

MOLECULAR ECOLOGY WILEY

Founder effects shape linkage disequilibrium and genomic diversity of a partially clonal invader

Ben A. Flanagan^{1,2}  | Stacy A. Krueger-Hadfield^{1,3}  | Courtney J. Murren¹  |
Chris C. Nice⁴ | Allan E. Strand¹ | Erik E. Sotka¹ 