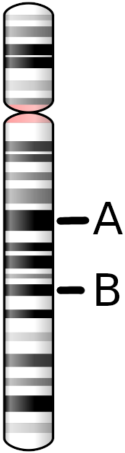
Linkage equilibrium and disequilibrium

Evolution at 2 loci

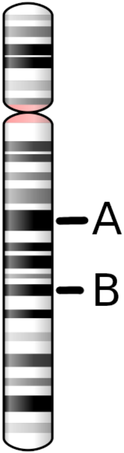


Locus A and B have 2 alleles

- Locus A
  - $Fr(A) = p$
  - $Fr(a) = q$

[1] Image: Public Domain

Evolution at 2 loci

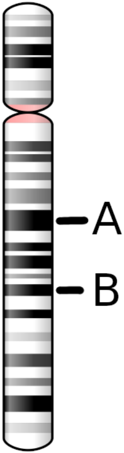


Locus A and B have 2 alleles

- Locus A
  - $Fr(A) = p$
  - $Fr(a) = q$
- Locus B
  - $Fr(B) = s$
  - $Fr(b) = t$

[1] Image: Public Domain

Evolution at 2 loci



Haploid chromosomal genotypes, "haplotypes"

- 4 haplotypes AB, Ab, aB, and ab

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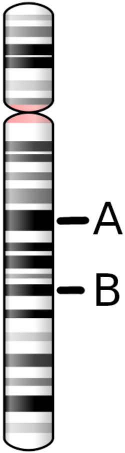

Haploid chromosomal genotypes, "haplotypes"

- 4 haplotypes AB, Ab, aB, and ab
- Expected frequencies
  - $Fr(AB) = ps$
  - $Fr(Ab) = pt$
  - $Fr(aB) = qs$
  - $Fr(ab) = qt$
- Above are in *linkage equilibrium*

[1]Image: Public Domain

Evolution at 2 loci

Linkage equilibrium: 2 loci in a population are in linkage equilibrium if an allele present at one locus of the haplotype is independent of the allele present at the other locus.

Linkage disequilibrium: 2 loci in a population are in linkage disequilibrium when there is a non-random association between a haplotype's allele at one locus and its allele at the other locus.

Evolution at 2 loci

Linkage equilibrium: Because loci are independent, knowing the allele at the one locus is of no use in predicting the allele at the other.

Linkage disequilibrium: If we know the haplotype's allele at 1 locus it provides a clue about the allele present at the other.

Coefficient of linkage disequilibrium

Coefficient of linkage disequilibrium (D) is a measure for quantifying the deviation of the population haplotype frequencies from linkage equilibrium, i.e., for quantifying the degree of linkage disequilibrium,

$$D = g_{AB}g_{ab} - g_{Ab}g_{aB}.$$

In the above, g_{AB}, g_{ab}, g_{Ab}, and g_{aB} are the *observed* frequencies of AB, ab, Ab, and ab haplotypes, respectively.

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Equilibrium: $ga_{AB} = ps$, $ga_{ab} = qt$, $ga_{Ab} = pt$, $ga_{aB} = qs$, so $D = psqt - ptqs = 0$.

Disequilibrium: $ga_{AB} \neq ps$, $ga_{ab} \neq qt$, $ga_{Ab} \neq pt$, $ga_{aB} \neq qs$, so $D \neq 0$.

Recombination between loci decreases D

How rapidly does linkage disequilibrium (D) decay with recombination?

- D_0 initial linkage disequilibrium
- D_n linkage disequilibrium in generation n
- r rate of recombination between 2 loci $(0 \leq r \leq 0.5)$

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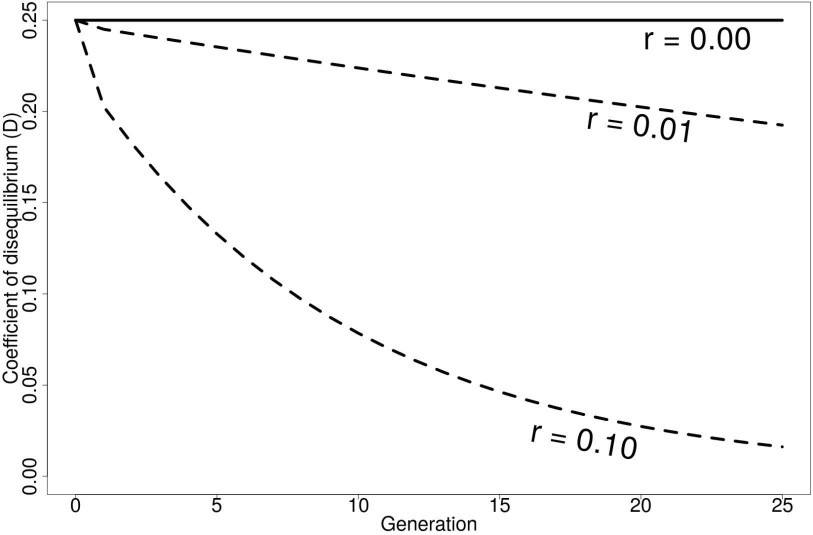
$$D_n = D_0 \left(1 - r\right)^n$$

Note each $(1 - r)$ is a generation of recombination.

What eliminates linkage disequilibrium

With sexual reproduction and random mating (recombination), linkage disequilibrium decays over time.



Sexual recombination eliminates linkage disequilibrium

1. The higher the rate of recombination the faster initial linkage disequilibrium is eliminated.
2. For tightly linked genes with low rates of recombination between them (e.g., $r = 0.01$), disequilibrium can persist for many generations.
3. Even if 2 loci are linked on the same chromosome, they will not necessarily be in linkage disequilibrium.
4. Conversely, due to effects of selection, mutation, and gene flow, two loci may exhibit linkage disequilibrium even if determined by physically unlinked genes.