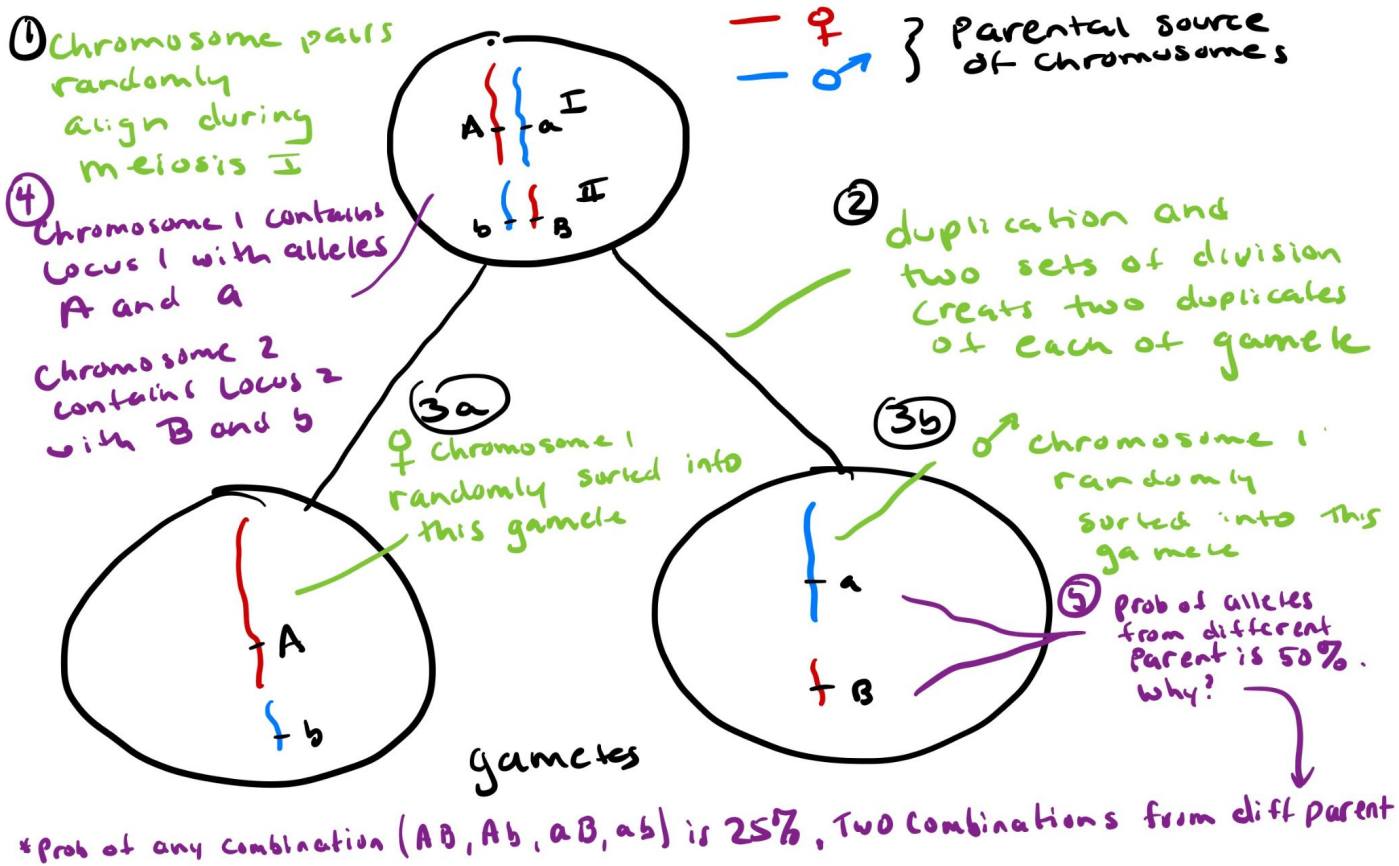
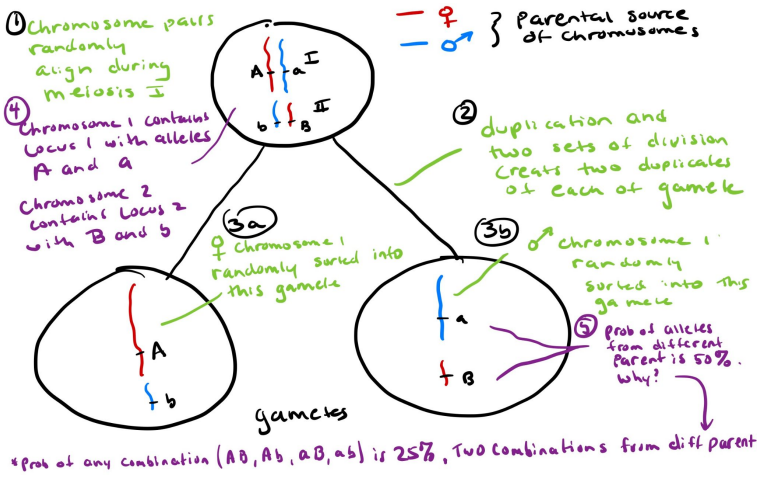
Independent inheritance and evolution of alleles on different chromosomes is due to the random alignment of maternal and paternal chromosomes in Meiosis I



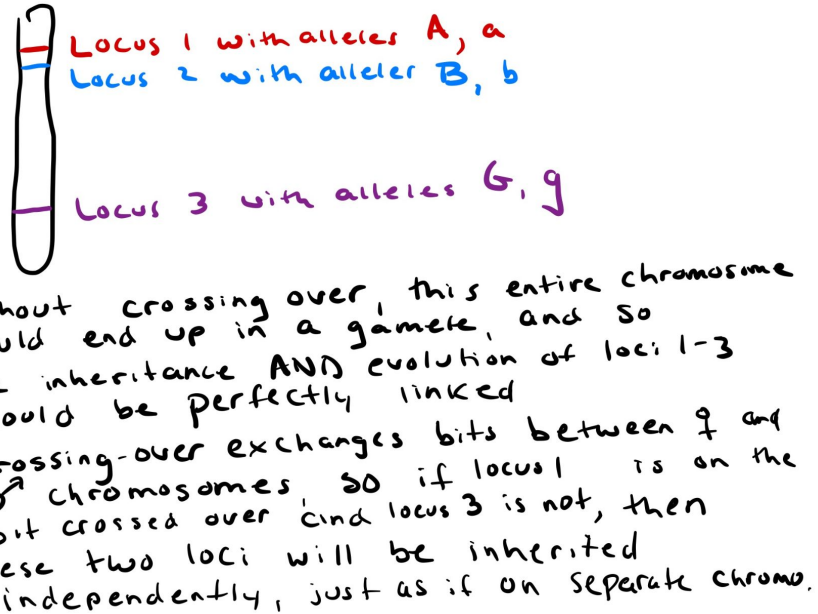
BIO 217 Linkage Equilibrium



1. Maternal and paternal chromosomes of a pair align randomly in meiosis 1. This is key!
2. Because of this, alleles on loci on two different chromosomes are inherited and evolve independently
    a. knowing the genotype at the A locus on chromosome 1 in a gamete offers zero information about the genotype of the B locus on chromosome 2. We have zero predictability
    b. this is Mendel's Law of Random Assortment
3. If there were no random alignment (and assortment), one gamete would get all of the maternal chromosomes and the other would get all the paternal chromosomes.
    a. Then, knowing the genotype at the A locus on chromosome 1 we'd have perfect predictability of the genotype at the B locus on chromosome 2

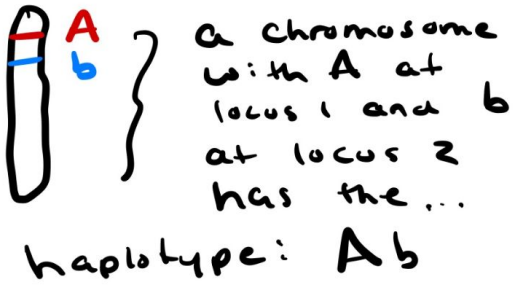
BIO 217 Linkage Equilibrium

Independent inheritance and evolution of alleles on the same chromosomes is due to crossing over between maternal and paternal chromosomes in Meiosis I



But, this crossing over isn't perfect. Loci that are closer together (physically linked) are less likely to separate during crossing over. These loci are in **linkage disequilibrium**.

BIO 217 Linkage Equilibrium



haplotypes (haploid genotype) are multilocus chromosomal genotypes

Linkage Equilibrium occurs when the haplotypes are a random combination of the alleles at each locus in the gene pool.

HWE - random mating!

LE - random combining!

BIO 217 Linkage Equilibrium

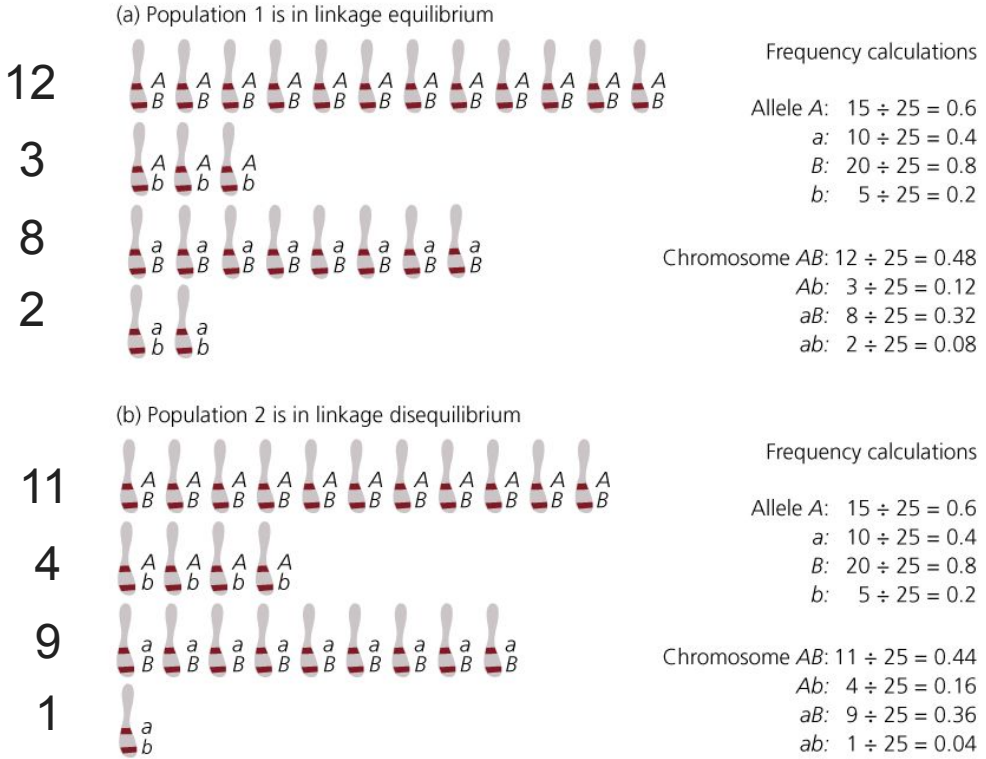


Figure 8.2 Populations with identical allele frequencies, but different chromosome frequencies

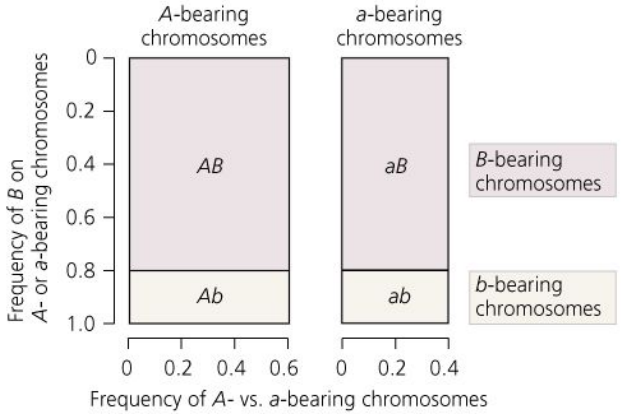
(a) In population 1 the frequency of allele *B* among A-bearing chromosomes (12 of 15, or 0.8) is the same as it is among a-bearing chromosomes (8 of 10, or 0.8). (b) In population 2 the frequencies of *B* among *A*-bearing versus a-bearing chromosomes are different (11 of 15, or 0.73, versus 9 or 10, or 0.9). Population 2 is said to be in linkage disequilibrium.

Linkage Equilibrium/Disequilibrium

							allele frequencies			
AB	Ab	aB	ab	N	D	D	P_A	P_B	B on A	B on a
12	3	8	2	25	0.000	0.000	0.6	0.8	0.8	0.8
11	4	9	1	25	-0.040	-0.040	0.6	0.8	0.733	0.900

BIO 217 Linkage Equilibrium

(a) Population 1 is in linkage equilibrium



(b) Population 2 is in linkage disequilibrium

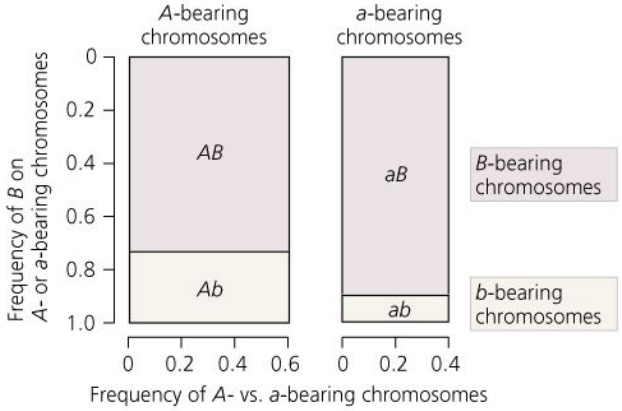


Figure 8.3 A graphical representation of populations with id

Coefficient of Linkage Disequilibrium

					allele frequencies					
AB	Ab	aB	ab	N	D	D	P_A	P_B	B on A	B on a
12	3	8	2	25	0.000	0.000	0.6	0.8	0.8	0.8
11	4	9	1	25	-0.040	-0.040	0.6	0.8	0.733	0.900

$D = P_{AB}P_{ab} - P_{Ab}P_{aB}$

The expected frequency under Linkage Equilibrium

$D = P_{AB} - P_A \cdot P_B$

Compare to HWE:

freq. of $AA = p^2 = P_A \cdot P_A$

$Aa = 2pq = 2P_A \cdot P_B$

$aa = q^2$

} expected f

What creates Linkage Disequilibrium?

1. Selection!
2. Drift!
3. Admixture!

What reduces Linkage Disequilibrium?

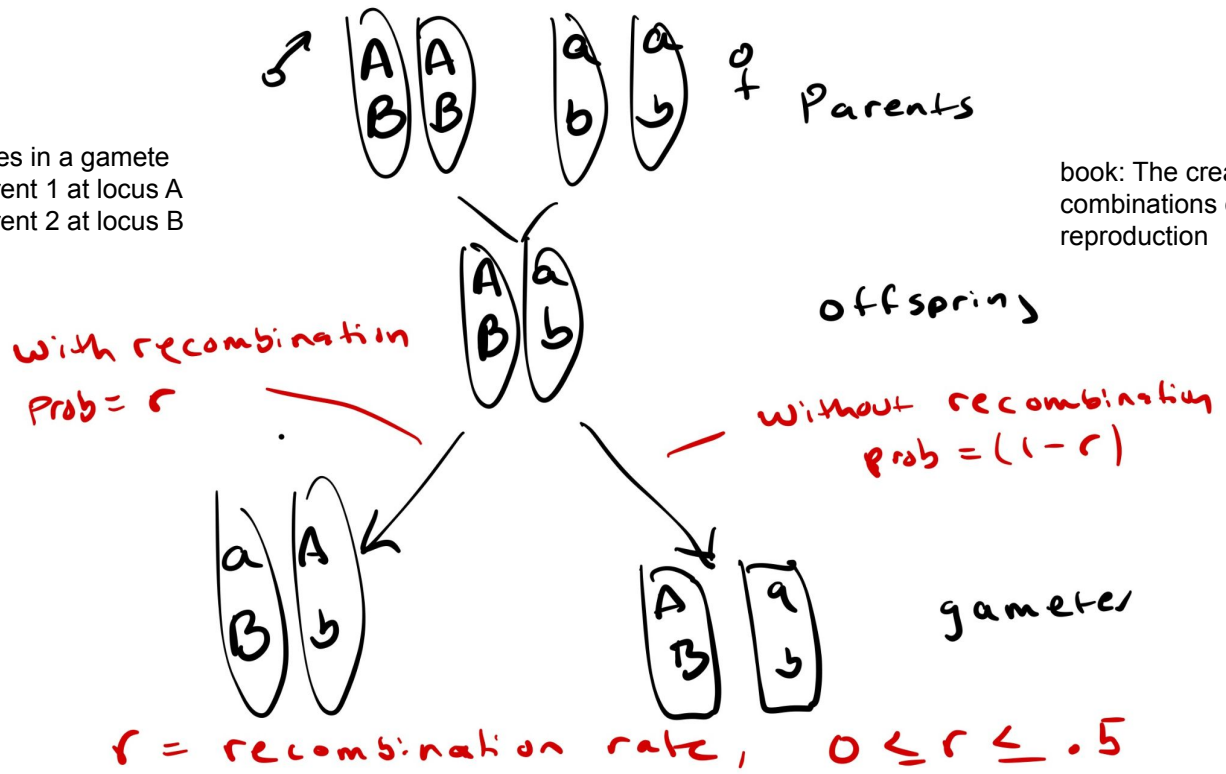
1. Sex!

BIO 217 Linkage Equilibrium

Recombination

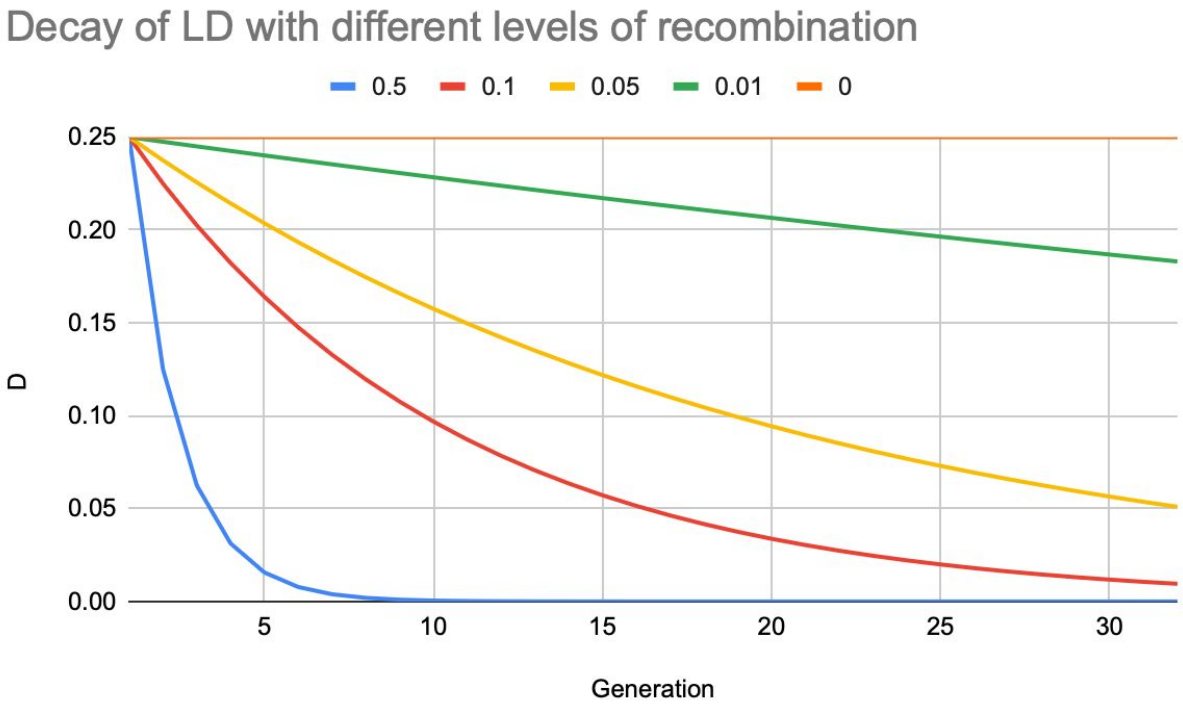
A process that combines in a gamete

1. Allele from parent 1 at locus A
2. Allele from parent 2 at locus B

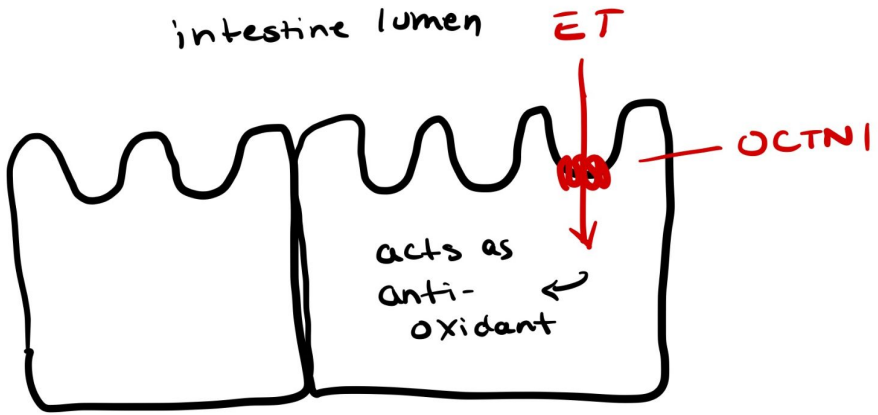


book: The creation of new combinations of alleles during sexual reproduction

1. Remember: genotype frequencies go back to HWE with one generation of random mating
2. Something similar happens with LE, but it takes many generations of random combination events through either crossing over or independent assortment.



LD can lead to misidentification of gene associated with phenotype due to **genetic hitchhiking** –
Ergothioneine role in Crohn's disease



ET - Ergothioneine (metabolite of fungi)

fungus → ET —(absorb in root)→ Plant → animal

LD can lead to misidentification of gene associated with phenotype due to **genetic hitchhiking** – Ergothioneine role in Crohn's disease

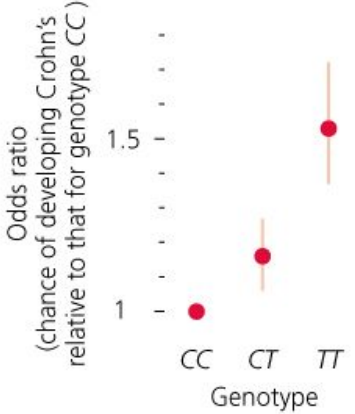
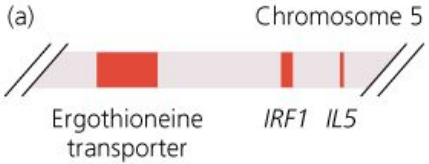


Figure 8.10 Ergothioneine transporter genotype is statistically associated with the risk of Crohn's disease
Whiskers show 95% confidence intervals. Redrawn from Wang et al. (2011).



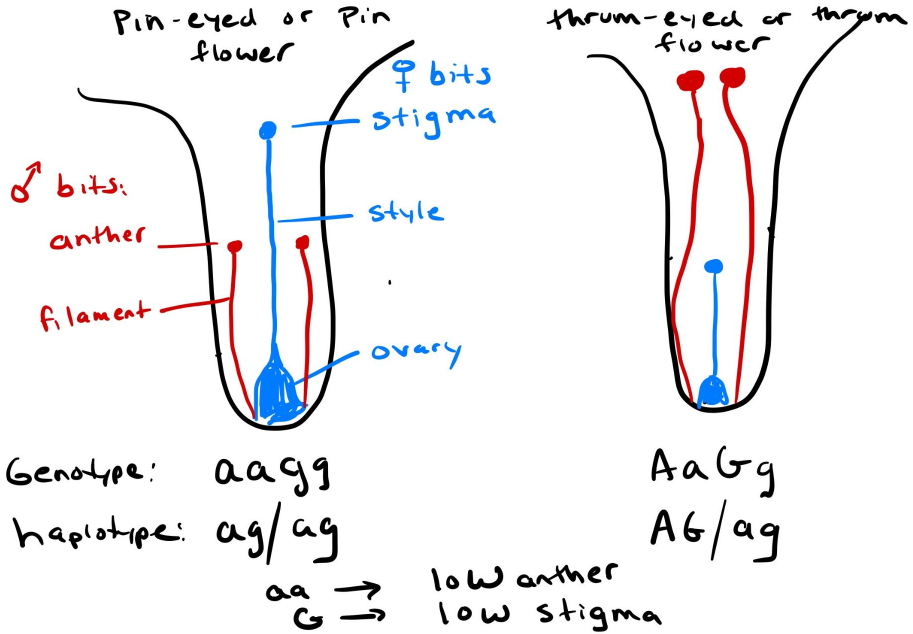
(b)

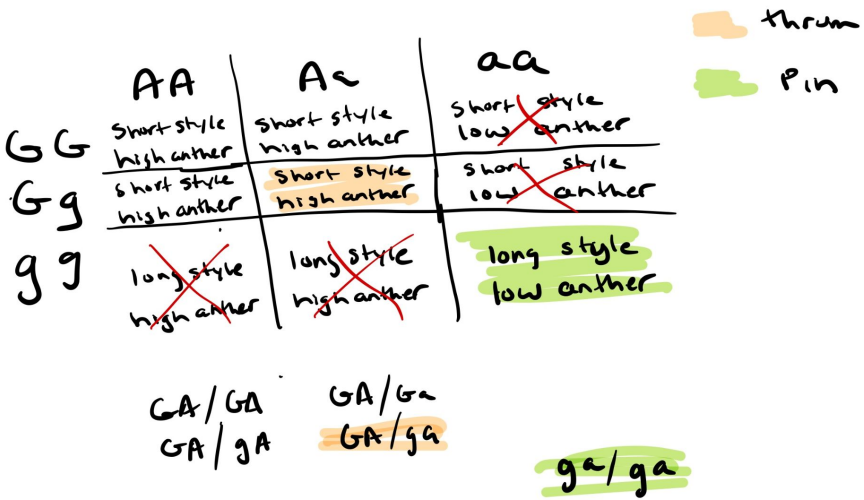
Haplotype	Frequency among Cases	Controls
L503F no recombination	0.374	0.324
L503F recombination	0.107	0.102

Figure 8.12 Recombination breaks the association between *L503F* and Crohn's disease
(a) Map of chromosome 5 near the ergothioneine transporter gene. (b) The association between Crohn's and *L503F* chromosomes in which there has not been recombination between the ergothioneine transporter gene and *IL5* is statistically significant ($p = 2.6 \times 10^{-8}$). The association between Crohn's and *L503F* chromosomes in which there has been recombination is not significant ($p = 2.1$). From Huff et al (2012).

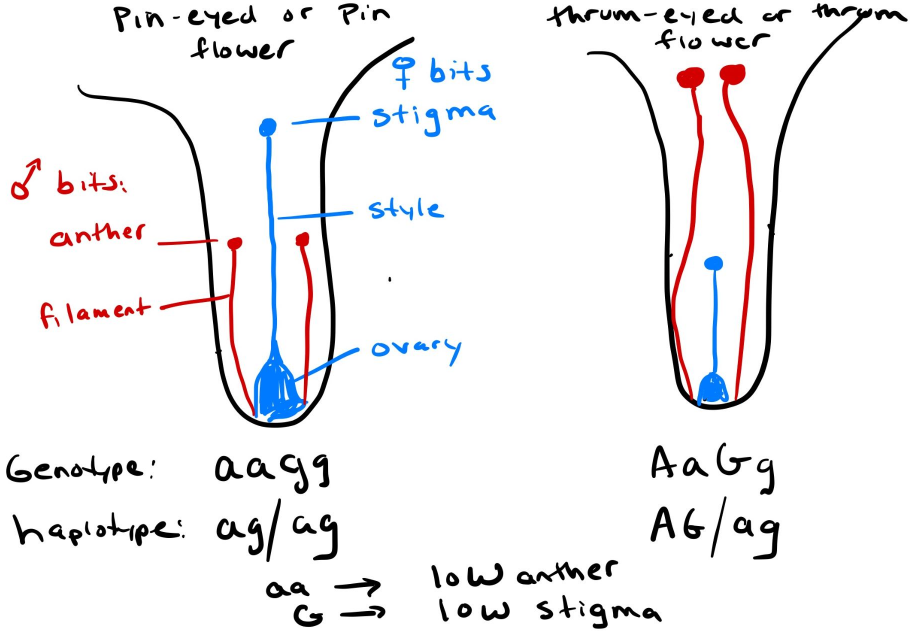
Selection **for** Linkage Disequilibrium – distyly in *Primula*

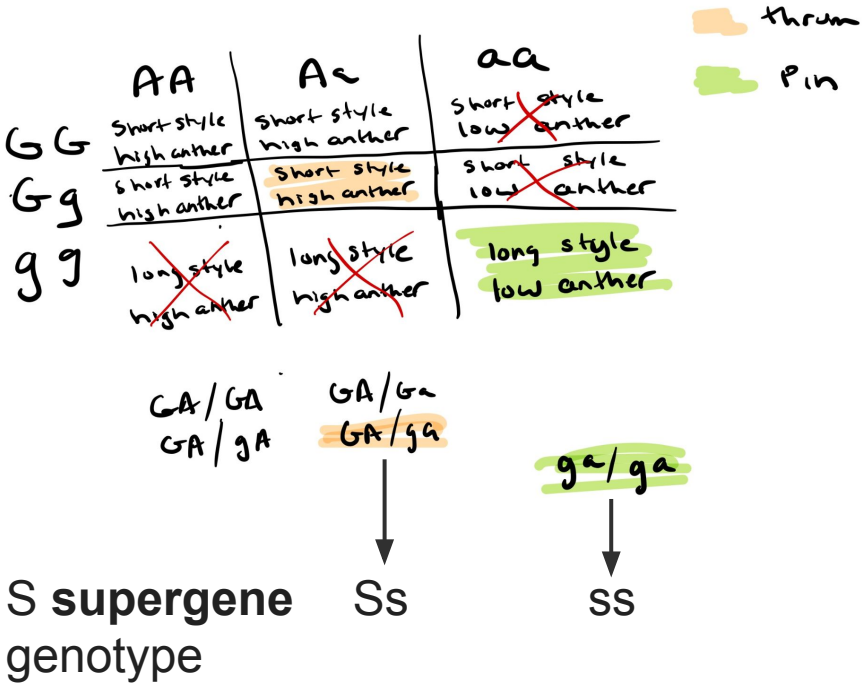
Selection **for** Linkage Disequilibrium – distyly in *Primula*





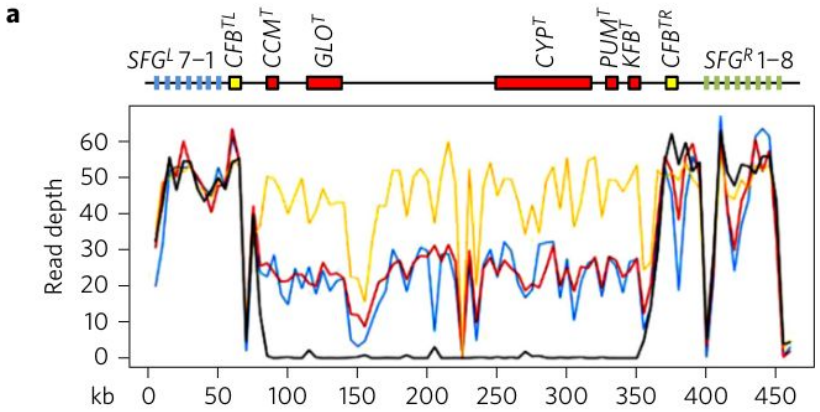
Selection **for** Linkage Disequilibrium – distyly in *Primula*

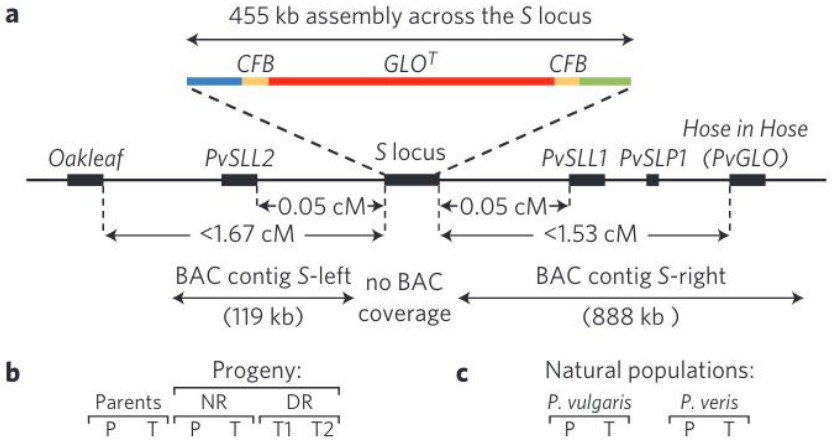




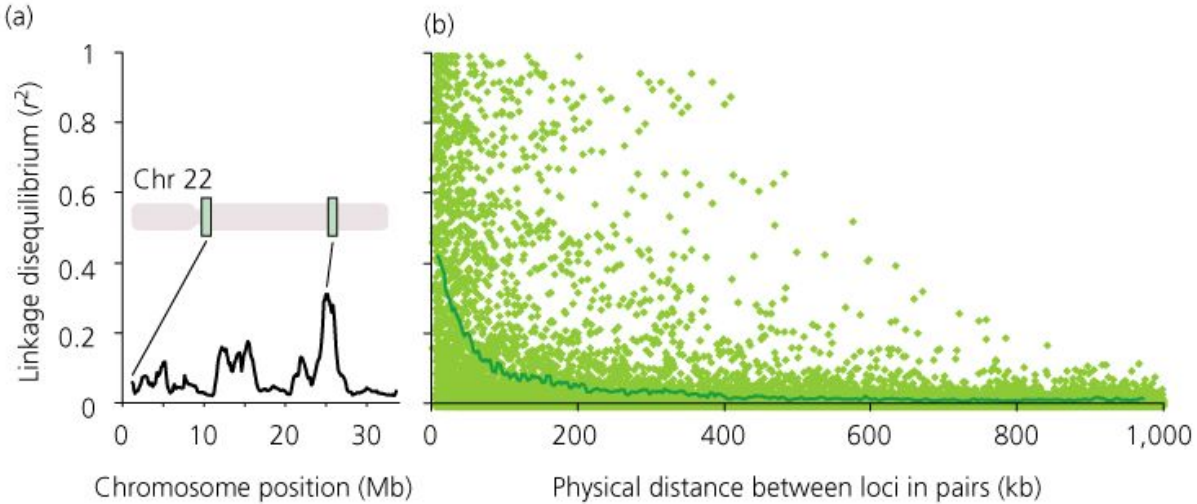
Selection **for** Linkage Disequilibrium – distyly in *Primula*

NATURE PLANTS DOI: 10.1038/NPLANTS.2016.188 ARTICLES





How much linkage disequilibrium is there?



a chromosome is about 50,000 - 250,000 kb.

Figure 8.14 On human chromosome 22, most pairs of loci are in linkage equilibrium

(a) Calculations of the average linkage disequilibrium (squared correlation of allelic state) among nearby loci reveal localized peaks. (b) However, the disequilibrium between loci falls with distance. From Dawson et al. (2002).

How much linkage disequilibrium is there?

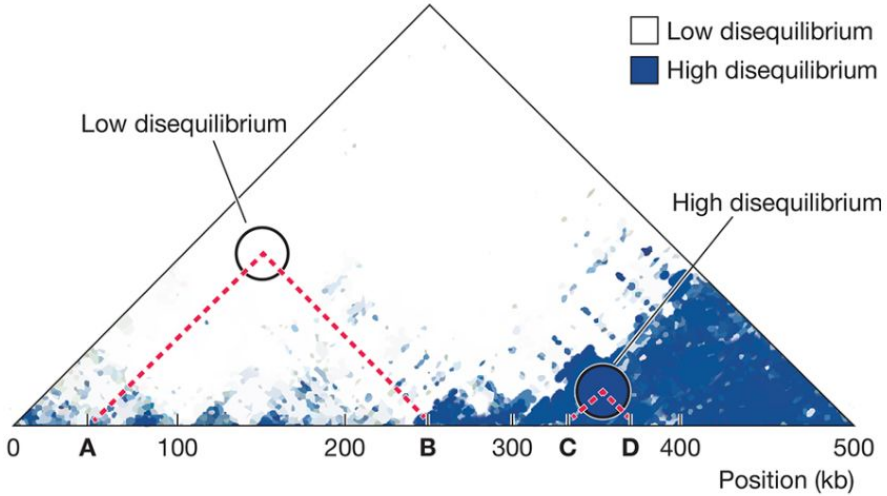


FIGURE 4.13 Linkage disequilibrium tends to be higher between pairs of DNA bases that are very close to each other on a chromosome. Shown is a region of 500 thousand base pairs (kb) of a chromosome sampled from 89 humans in eastern Asia. Sites A and B are relatively far apart (200 kb), and they have low linkage disequilibrium. Sites C and D are much closer (50 kb), and they have high linkage disequilibrium. (Based on The International HapMap Consortium. 2005. *Nature* 437: 1299–1320.) View larger image

a chromosome is about 50,000 - 250,000 kb.

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B

Phil. Trans. R. Soc. B (2012) **367**, 395–408
doi:10.1098/rstb.2011.0245

Research

Extensive linkage disequilibrium and parallel adaptive divergence across threespine stickleback genomes

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Population genomic studies are beginning to provide a more comprehensive view of dynamic genome-scale processes in evolution. Patterns of genomic architecture, such as genomic islands of increased divergence, may be important for adaptive population differentiation and speciation. We used next-generation sequencing data to examine the patterns of local and long-distance linkage disequilibrium (LD) across oceanic and freshwater populations of threespine stickleback, a useful model for studies of evolution and speciation. We looked for associations between LD and signatures of divergent selection, and assessed the role of recombination rate variation in generating LD patterns. As predicted under the traditional biogeographic model of unidirectional gene flow from ancestral oceanic to derived freshwater stickleback populations, we found extensive local and long-distance LD in fresh water. Surprisingly, oceanic populations showed similar patterns of elevated LD, notably between large genomic regions previously implicated in adaptation to fresh water. These results support an alternative biogeographic model for the stickleback radiation, one of a metapopulation with appreciable bi-directional gene flow combined with strong divergent selection between oceanic and freshwater populations. As predicted by theory, these processes can maintain LD within and among genomic islands of divergence. These findings suggest that the genomic architecture in oceanic stickleback populations may provide a mechanism for the rapid re-assembly and evolution of multi-locus genotypes in newly colonized freshwater habitats, and may help explain genetic mapping of parallel phenotypic variation to similar loci across independent freshwater populations.