Evolution at multiple loci

- Linkage
- Sex

- Quantitative genetics

Linkage

Figure 7.1 A pair of linked loci

- Linkage can be physical or statistical, we focus on physical - easier to understand
- Because of recombination, Mendel develops law of independent assortment
- But loci do not always assort independently, suppose they are close together on the same chromosome

Haplotype - multilocus genotype

- Contraction of ‘haploid-genotype’
  - The genotype of a chromosome (gamete)
- E.g. with two genes A and B with alleles A and a, and B and b
- Possible haplotypes
  - AB; Ab; aB, ab
- Will selection at the A locus affect evolution of the B locus?

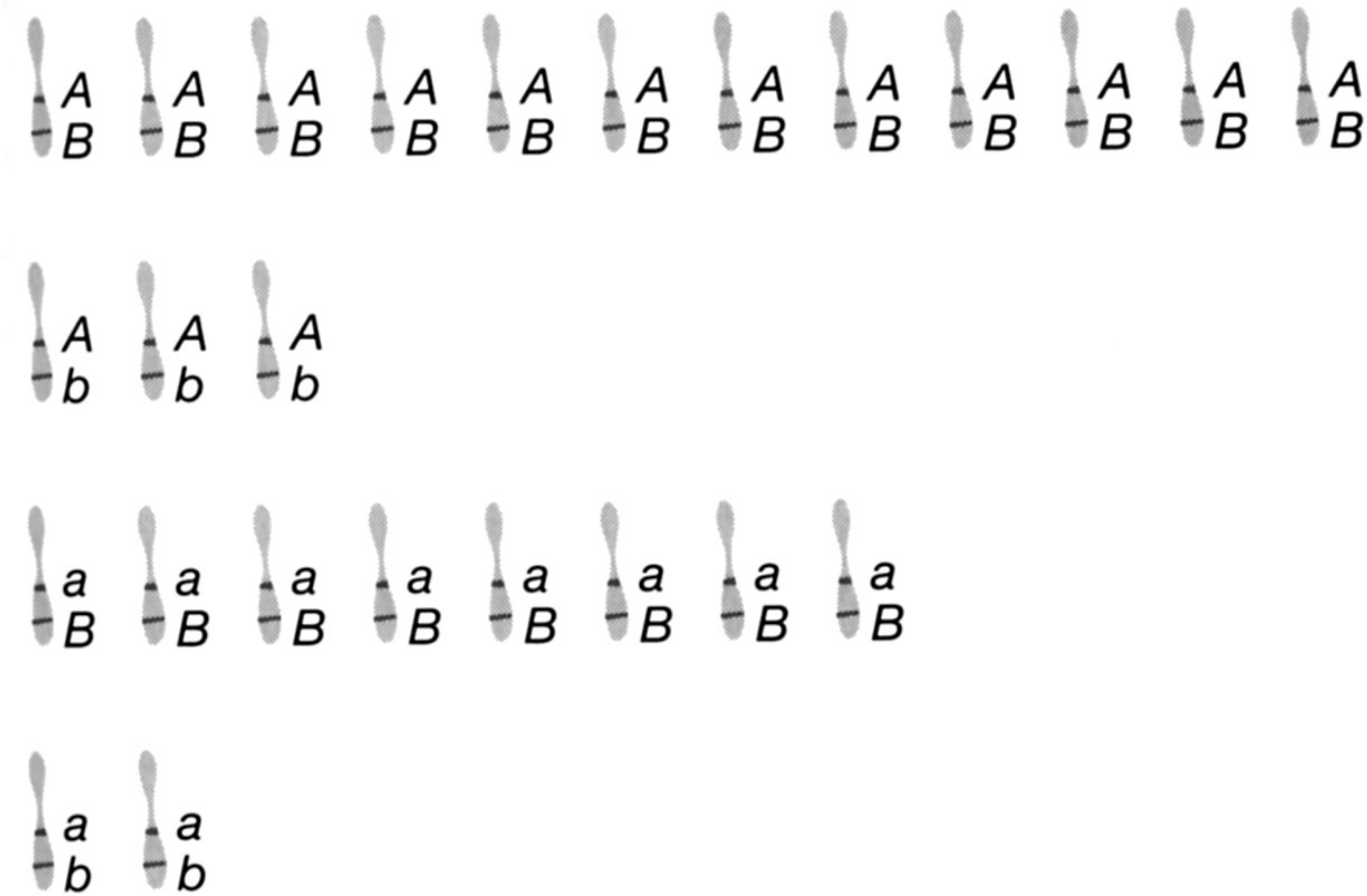
Chromosome (haplotype) frequency v. allele frequency

- Example, suppose two populations have:
  - A allele frequency = 0.6, a allele frequency 0.4
  - B allele frequency = 0.8, b allele frequency 0.2
- Are those populations identical?
- Not always!

Linkage (dis)equilibrium

- Loci are in equilibrium if:
  - Proportion of B alleles found with A alleles is the same as b alleles found with A alleles; and
- Loci in linkage disequilibrium if an allele at one locus is more likely to be found with a particular allele at another locus
  - E.g., B alleles more likely with A alleles than b alleles are with A alleles

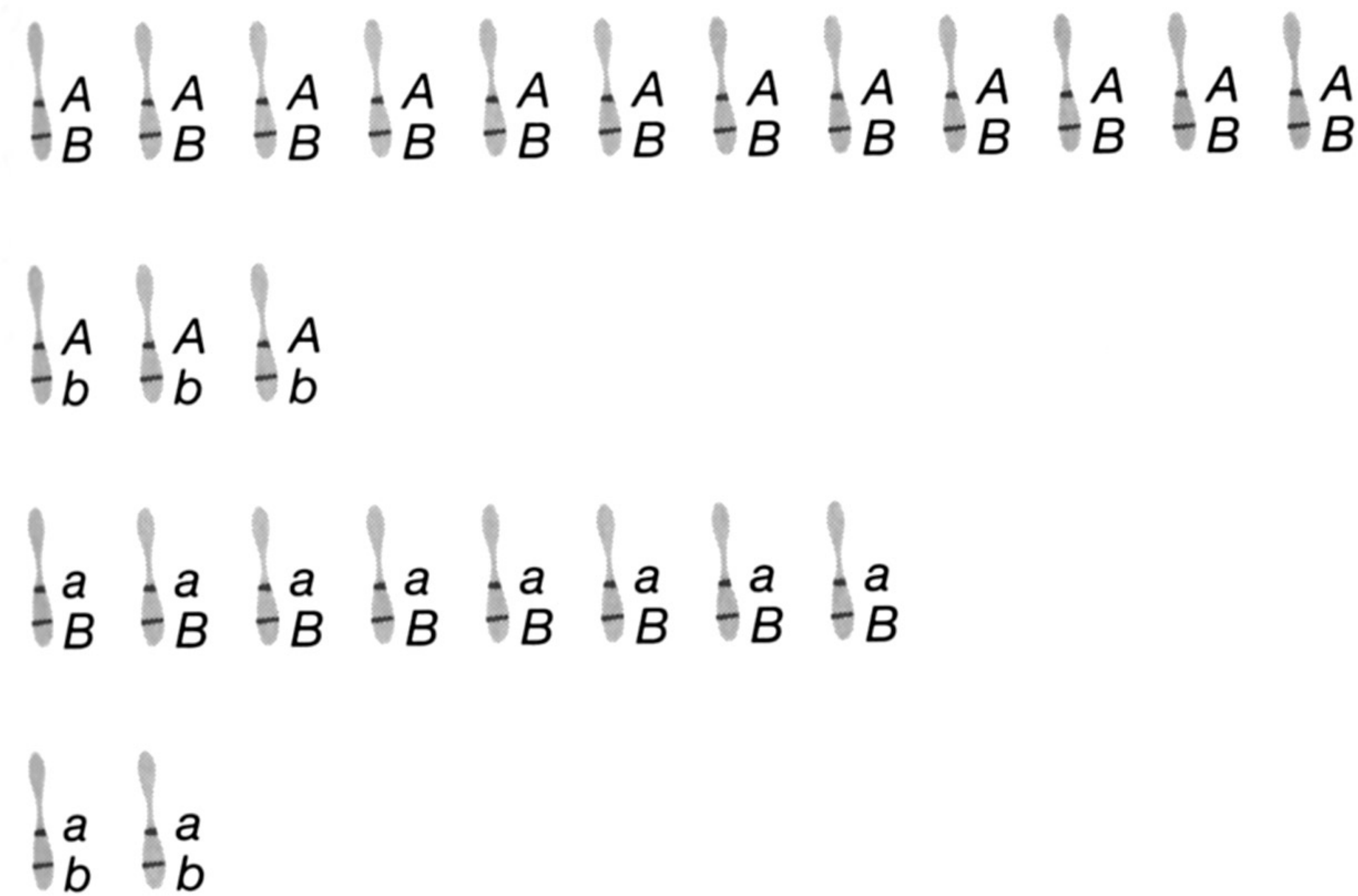
Equilibrium - alleles



A locus, A allele p = 15/25 = 0.6 a allele q = 1-p = 0.4

B locus, B allele p = 20/25 = 0.8; b allele q = 1-p = 0.2

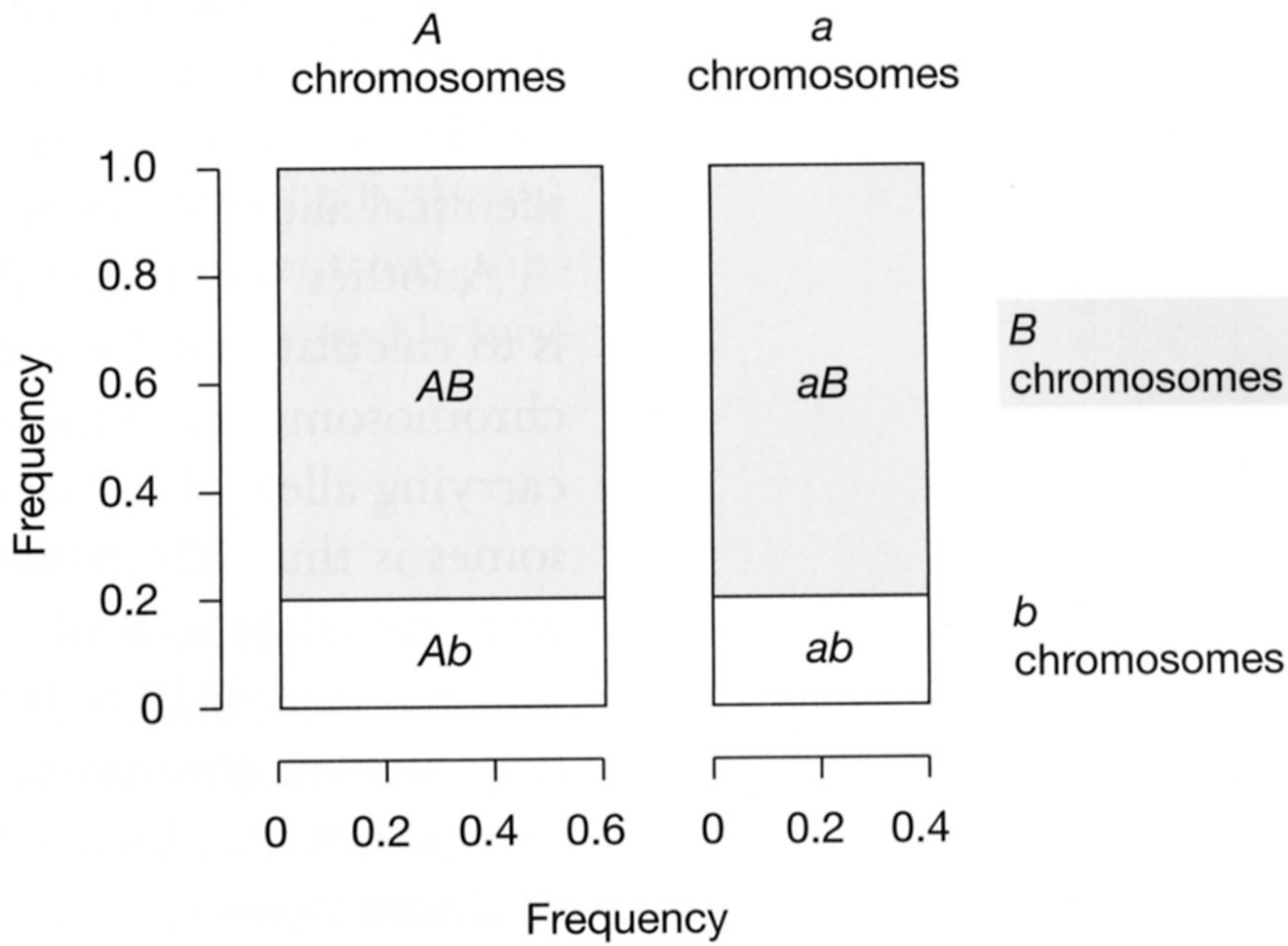
Equilibrium - haplotypes



Allele B with allele A = 12; A without B = 3 times; AB 12/15 = 0.8

Allele B with allele a = 8; a without B = 2 times; aB 8/10 = 0.8

Equilibrium graphically

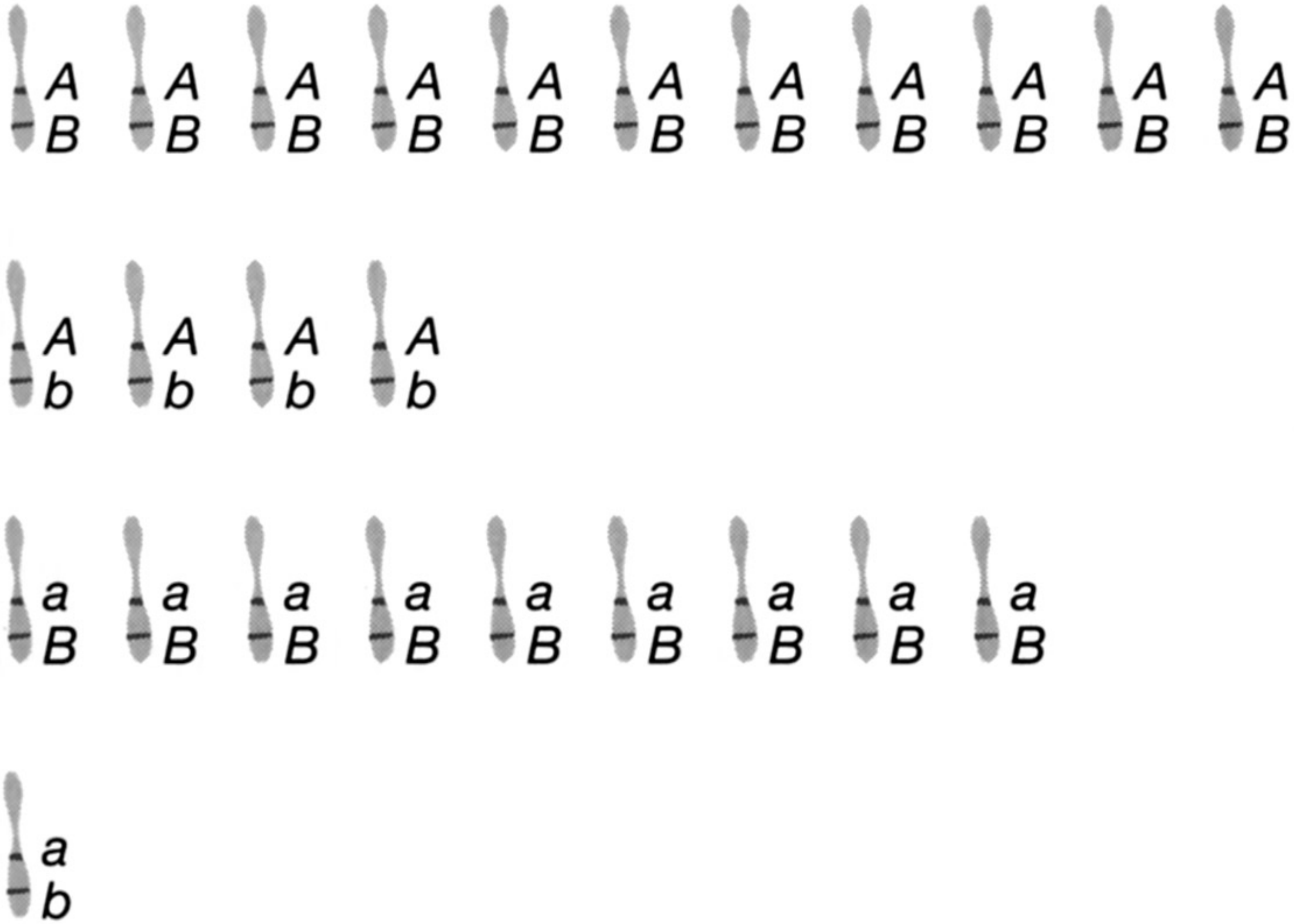


Disequilibrium - alleles

A locus, A allele p = 15/25 = 0.6 a allele q = 1-p = 0.4

B locus, B allele p = 20/25 = 0.8; b allele q = 1-p = 0.2

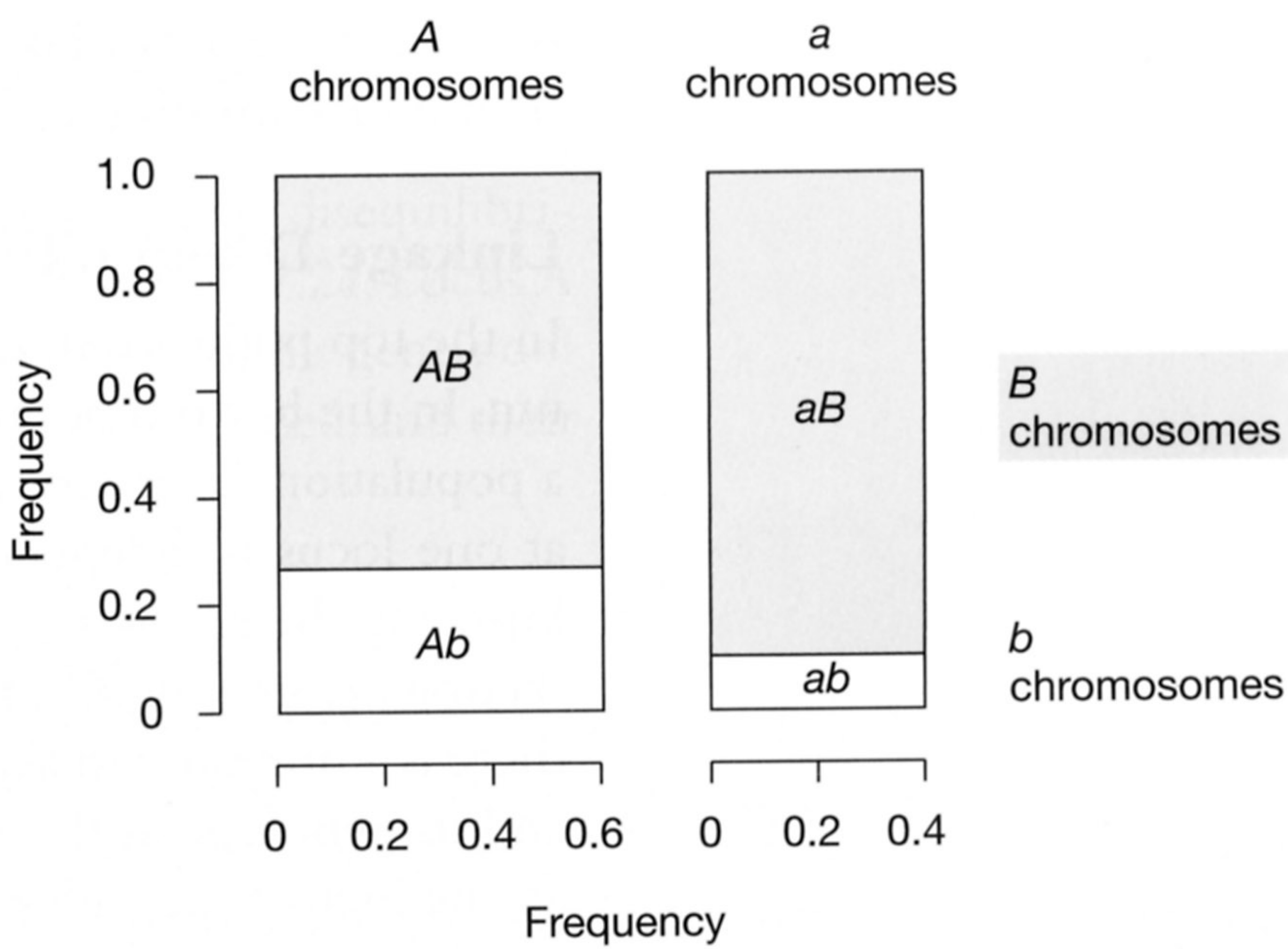
Disequilibrium - haplotypes



Allele B with allele A = 11; A without B = 4 times; AB 11/15 = 0.73

Allele B with allele a = 9; a without B = 1 times; aB 9/10 = 0.9

Disequilibrium graphically



Example recap:

- In both populations
  - A frequency = 0.6; a frequency = 0.4
  - B frequency = 0.8; b frequency = 0.2
- In the disequilibrium population
  - Allele B more likely to be found with allele a than allele A

Defining equilibrium

- Intuitive: if knowing whether or not locus 1 genotype is *A* or *a* gives you a hint as to if locus 2 genotype is *B* or *b*, then not in equilibrium
- If knowing genotype of locus 1 tells you nothing about genotype of locus 2, then loci are in equilibrium

Quick calculation

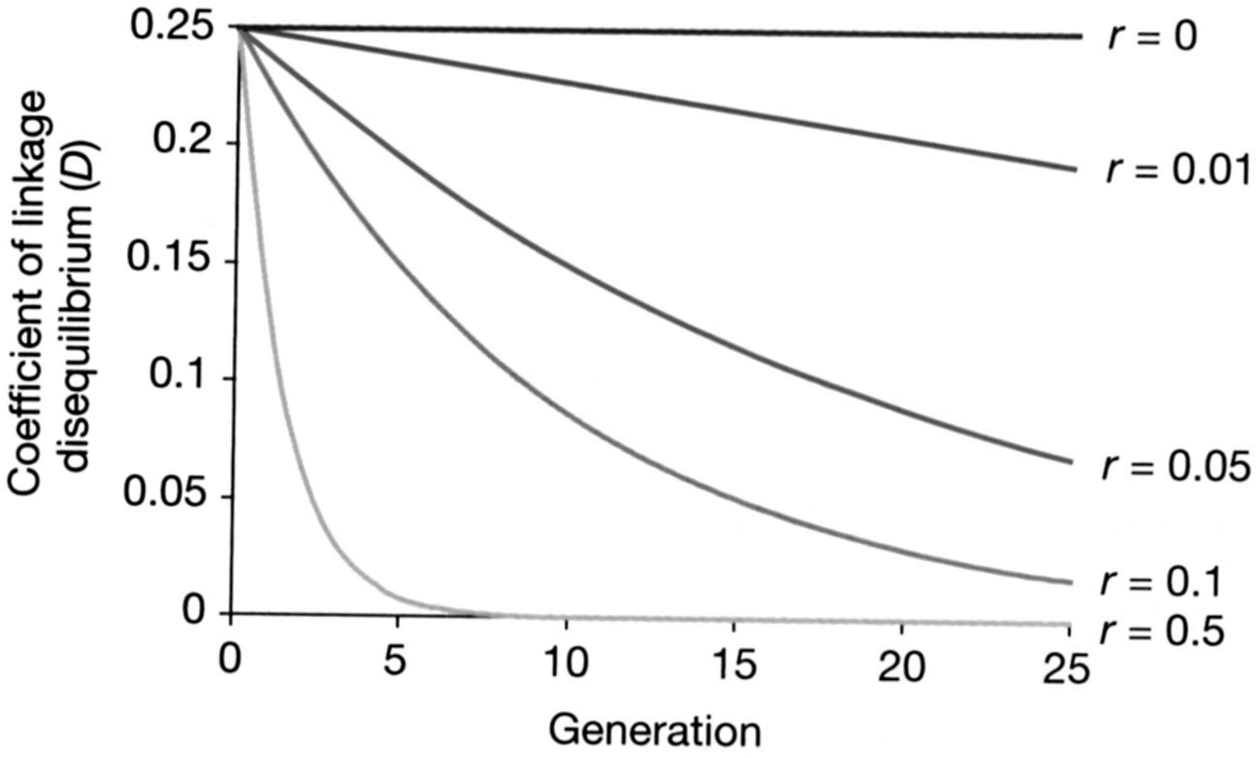
- In equilibrium if: Haplotype frequency is product of allele frequencies
- From the equilibrium example:
  - AB haplotype was 12 of 25 = 0.48
  - A frequency was 0.6; B frequency was 0.8
    - 0.6*0.8 = 0.48
  - ab haplotype was 2 of 25 = 0.08
  - a frequency was 0.4; b frequency was 0.2
    - 0.4*0.2 = 0.08

Quantifying disequilibrium

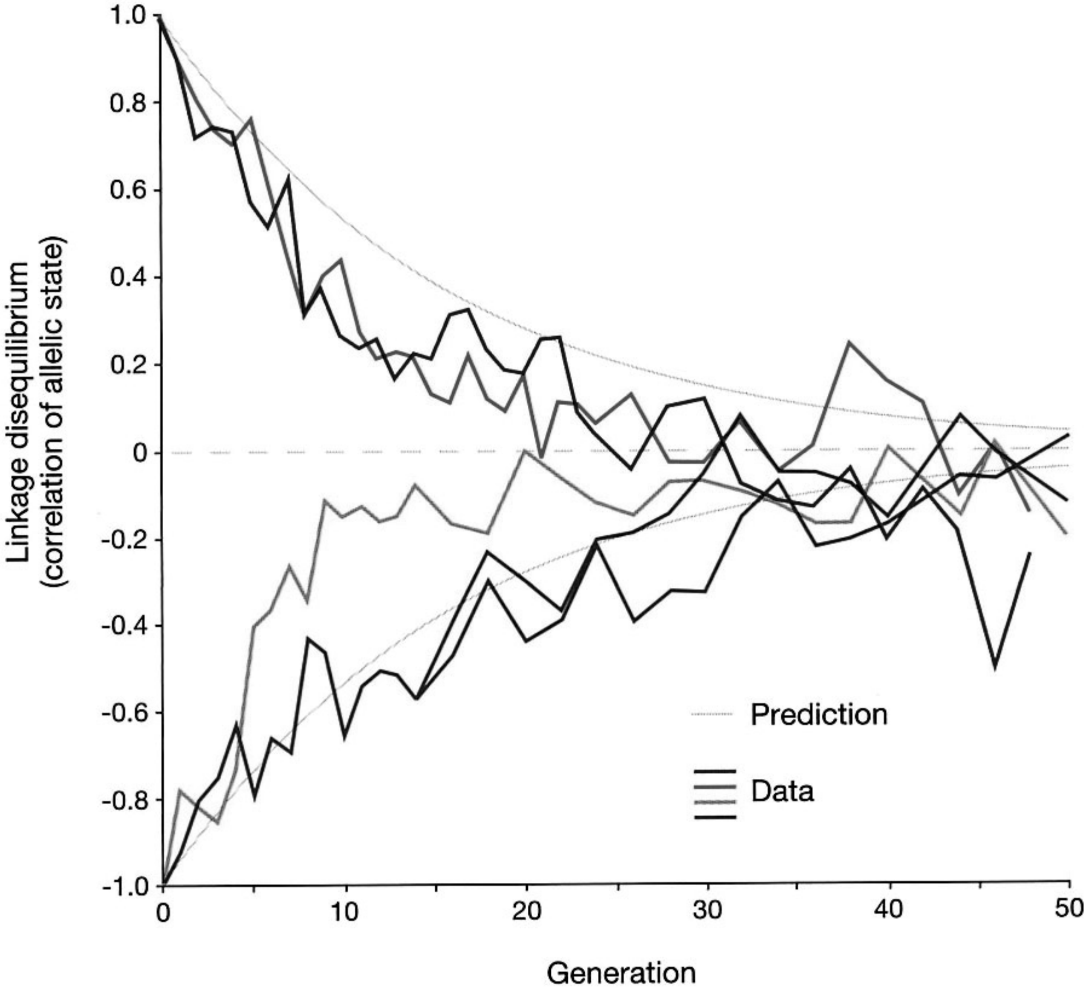
- D coefficient of linkage disequilibrium
  - $= g_{AB}g_{ab} - g_{Ab}g_{aB}$
- Ranges from -0.25 to 0.25

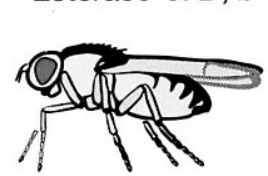
Sex, recombination, and disequilibrium

- Meiosis mixes up which alleles are with which other alleles



Experimental data,
Clegg et al. 1980



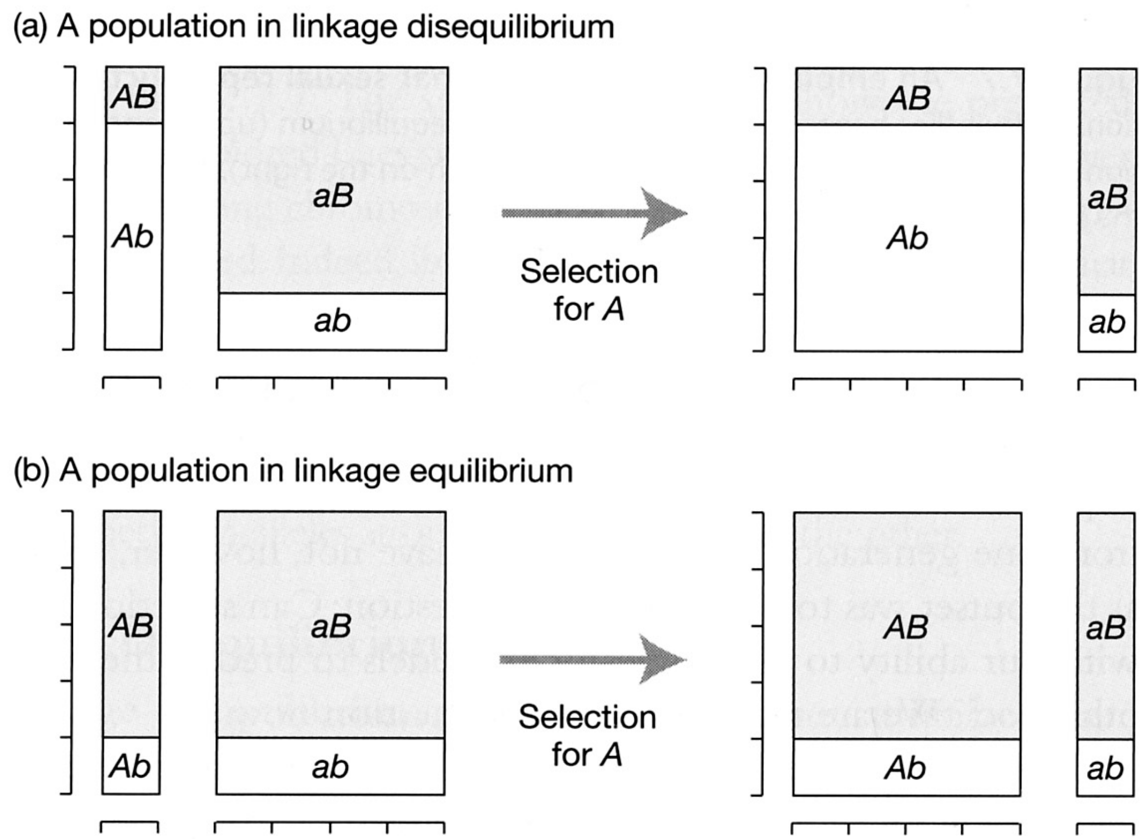


Causes of linkage disequilibrium

- Non-random mating
- Selection
- Mutations in small populations
- Inversions preventing recombination
- Immigration/emigration; population admixture

Multilocus selection

- Does selection at locus A affect evolution at locus B?
- It can, if alleles at A and B are linked



Multilocus evolution

- Selective sweep
- Hitch-hiking allele

Can selection produce a small dog with big ears?

- If body size alleles and ear size alleles are unlinked
- But less effectively if body size alleles and ear size alleles are linked, or if the same genes affect both traits (pleiotropy)

Humans and linkage

- Huttley et al surveyed over 5000 loci across 22 autosomes
- Most loci unlinked, unless under strong selection or physically linked
- Selected linked loci within immune system
  - Chromosome 6 HLA (MHC in non-humans)
- Physically linked closely paired loci
  - Probability of recombination depends on distance

Linkage and allele history

- Recall the CCR5 delta 32 mutation?
  - In homozygotes prevents entry of HIV into cells
- Frequency around 20% in Europe, 0% elsewhere
- Delta 32 allele in linkage disequilibrium with nearby loci GAAT and AFMB
- GAAT alleles and AFMB alleles non-coding and in equilibrium with each other

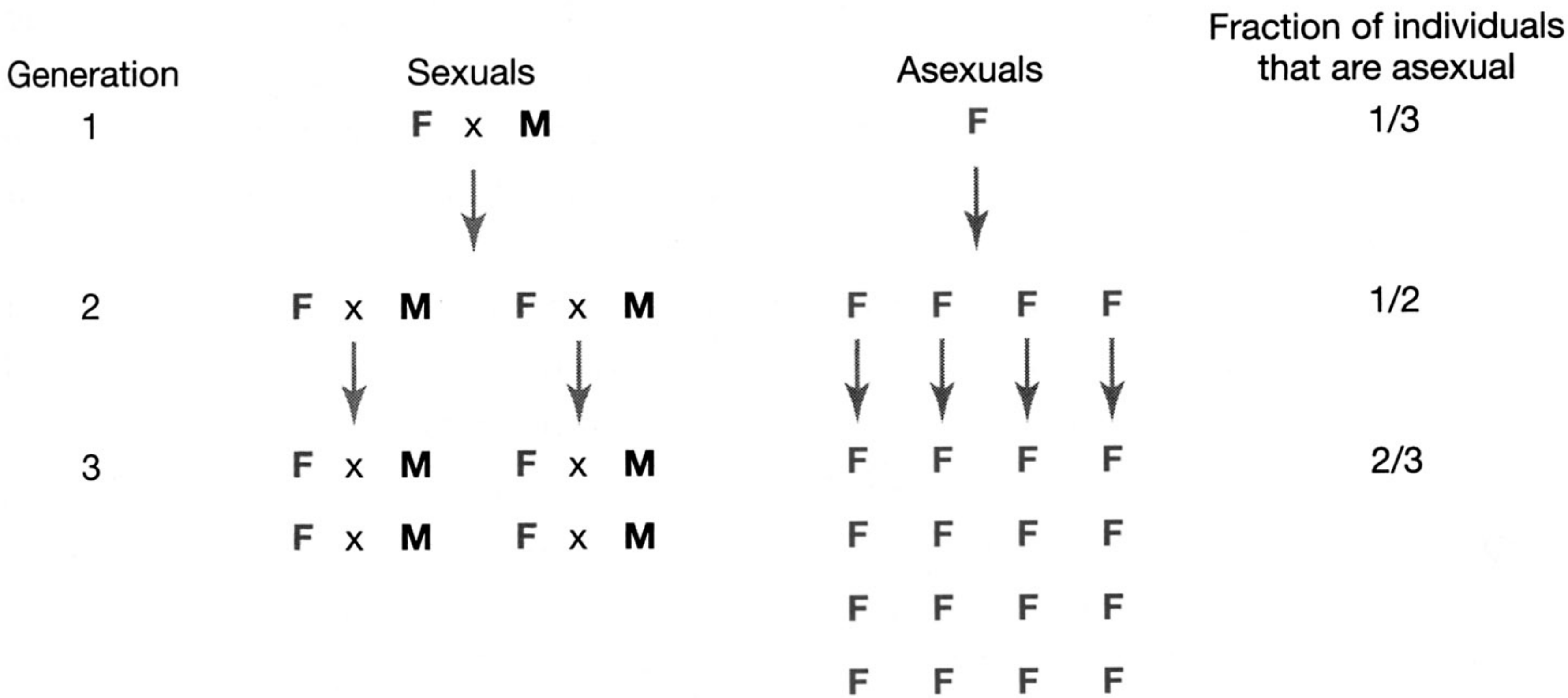
History of CCR5 delta 32 allele

- Probably arose by mutation in an individual that just happened to have allele *197* at GAAT locus and allele *215* at AFMB locus
- New delta 32 favored by selection, and brought AFMB 215 and GAAT 197 along for the ride

Linkage breakdown

- Delta 32 still non-randomly associated with GAAT 197 and AFMB 215, but not perfect
  - Some recombination has occurred
- Back calculating based on recombination rate give estimate of delta 32 mutation appearing ca. 700 years ago (possibly 275 to 1875 years)
- Selective agent may have been bubonic plague or smallpox

What good is sex anyway?



Asexuals will win if

- Same number of offspring produced by sex and asex
- And/or
- Offspring survival not different for sex and asex

- The fact that most species are sexual suggests that one or both of these must be wrong

Sex and genetic variation

- Asexuals are clones produced by parthenogenesis; genetically identical to mom
- Sexuals have recombination; genetically variable offspring different from parents
- Linkage disequilibrium
  - If pop in equilibrium, sex has no genetic effect *on its own*
  - Either drift or multilocus selection

Sex and drift

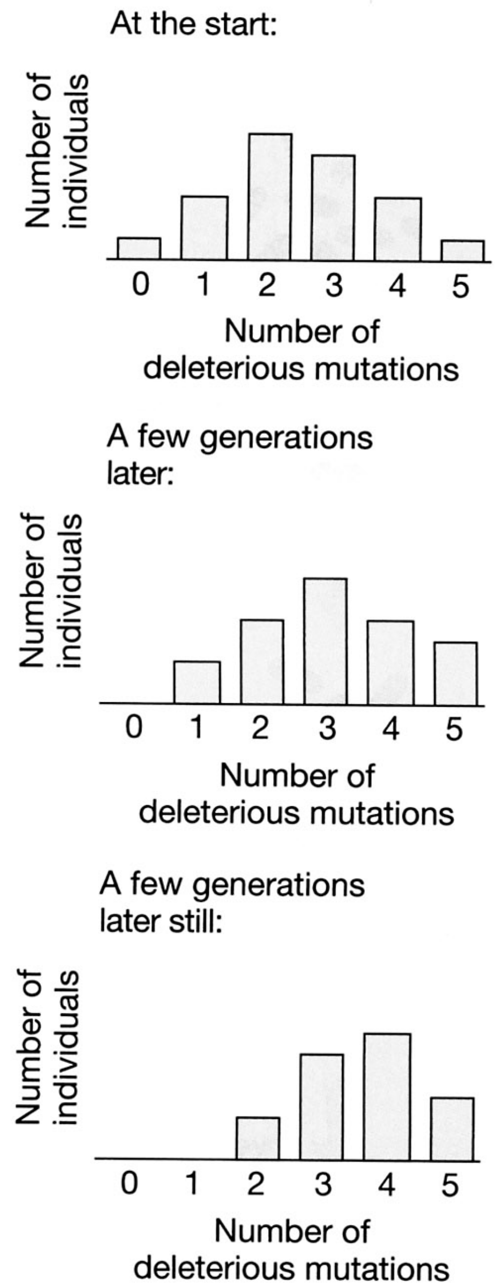
- Sex gets rid of bad mutations
- Asexual females always pass on new bad mutations
- Muller’s ratchet - mutation accumulation
- In small pops, drift can knock out the individuals with the fewest mutations (selection may knock out individuals with most mutations)

Muller's ratchet

As highest fitness groups lost by drift, average fitness declines.

Loss of highest fitness group by drift exceeds recreation by back-mutation.

Burden called **genetic load.**



Sex and Muller's ratchet

- Sex allows recreation of zero deleterious mutation subpopulation each generation by recombination
- With asexual reproduction, the zero deleterious mutation genotypes are missing (i.e. there is linkage disequilibrium)

Muller's ratchet outcomes

- Very dependent on population size
  - Small pop' affected
- Mildly deleterious mutations more likely to accrue
  - Strongly deleterious selected out
- Studies with endosymbiotic bacteria demonstrate mutation accumulation
  - But over long term
  - Short term asex strongly favored

Sex and selection

- Changing environment favors sex
- ‘best’ genotype today not ‘best’ genotype tomorrow
- Sex genes favored over asexual genes because of high fitness of *some of the* sexual genotypes in changed environment

Sex and co-evolution

- Abiotic environments (water, temperature, etc) don’t usually change fast enough for sexuals to win over asexuals
- Biotic environments do: co-evolutionary arms races
  - Evolve resistance to disease, bad for disease, disease evolves back at you
  - Red Queen Hypothesis

Do parasites favor sex?

- Lively studied snails and parasitic trematode worms
- Worms castrate snails (by eating their gonads!)
- Across 66 New Zealand lakes, the more parasites the higher proportion of males
  - Produced by sexual females