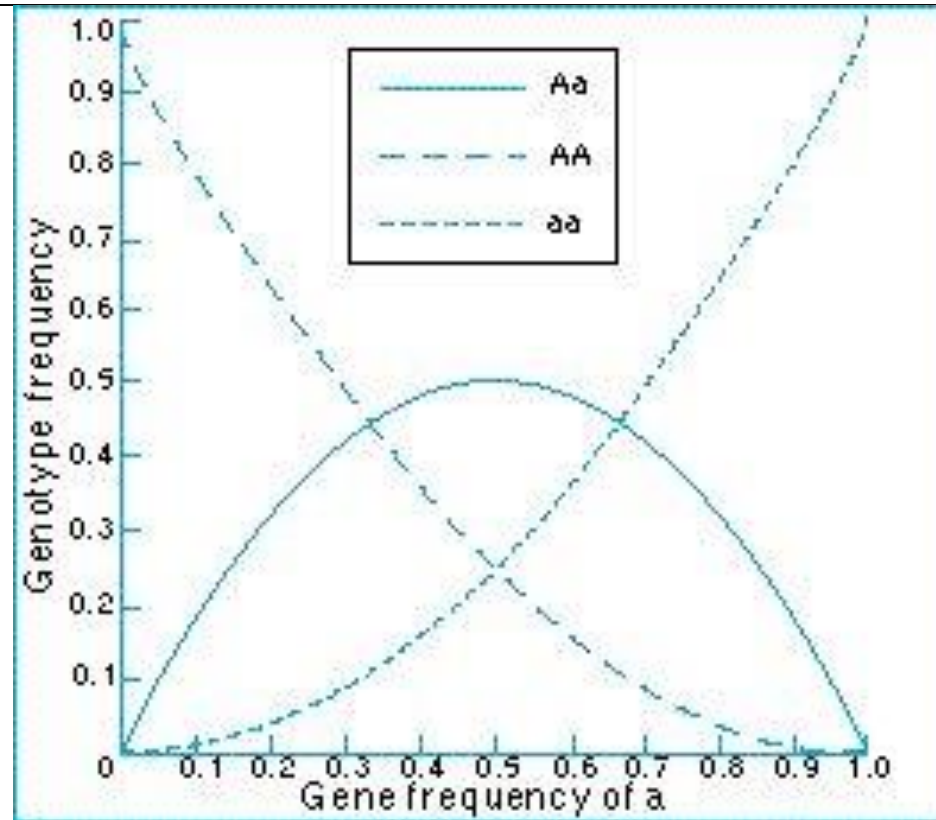


Hardy-Weinberg equilibrium

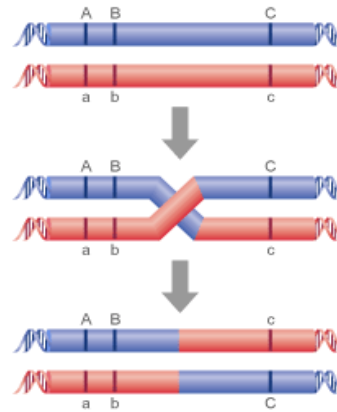


After a generation of random mating:

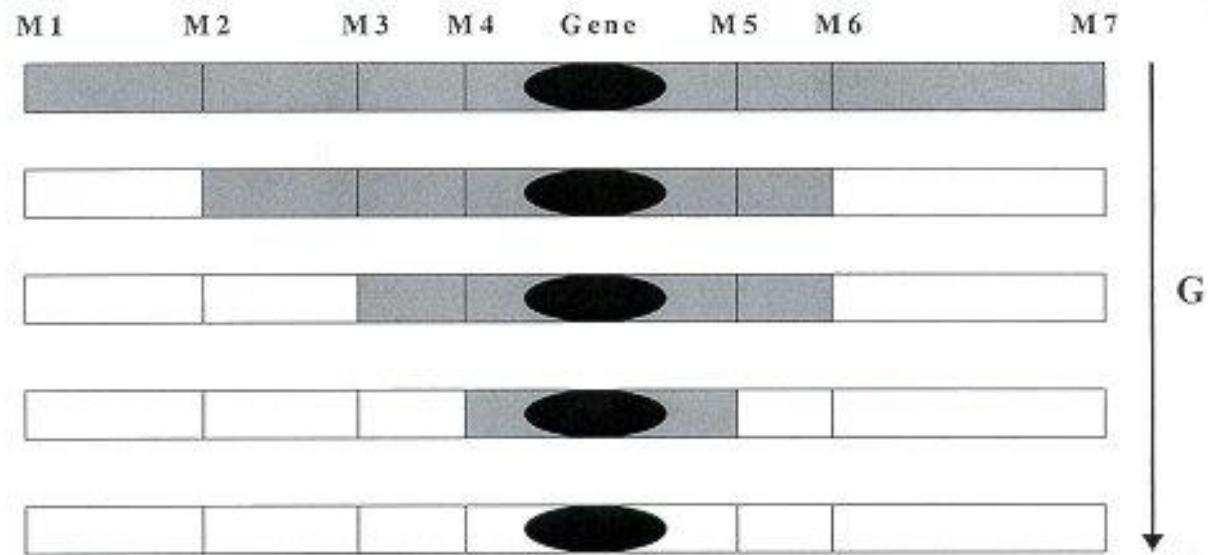
Genotype	AA	Aa	aa
Frequency	p^2	$2pq$	q^2

Linkage and linkage disequilibrium

- Linkage:



Origin of linkage disequilibrium (LD)



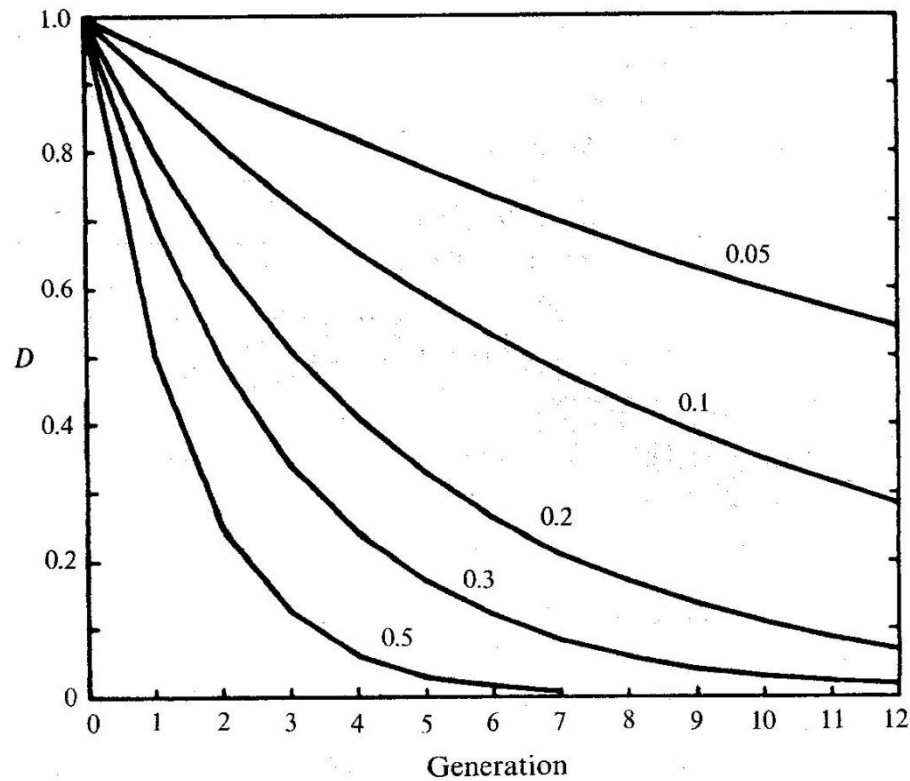
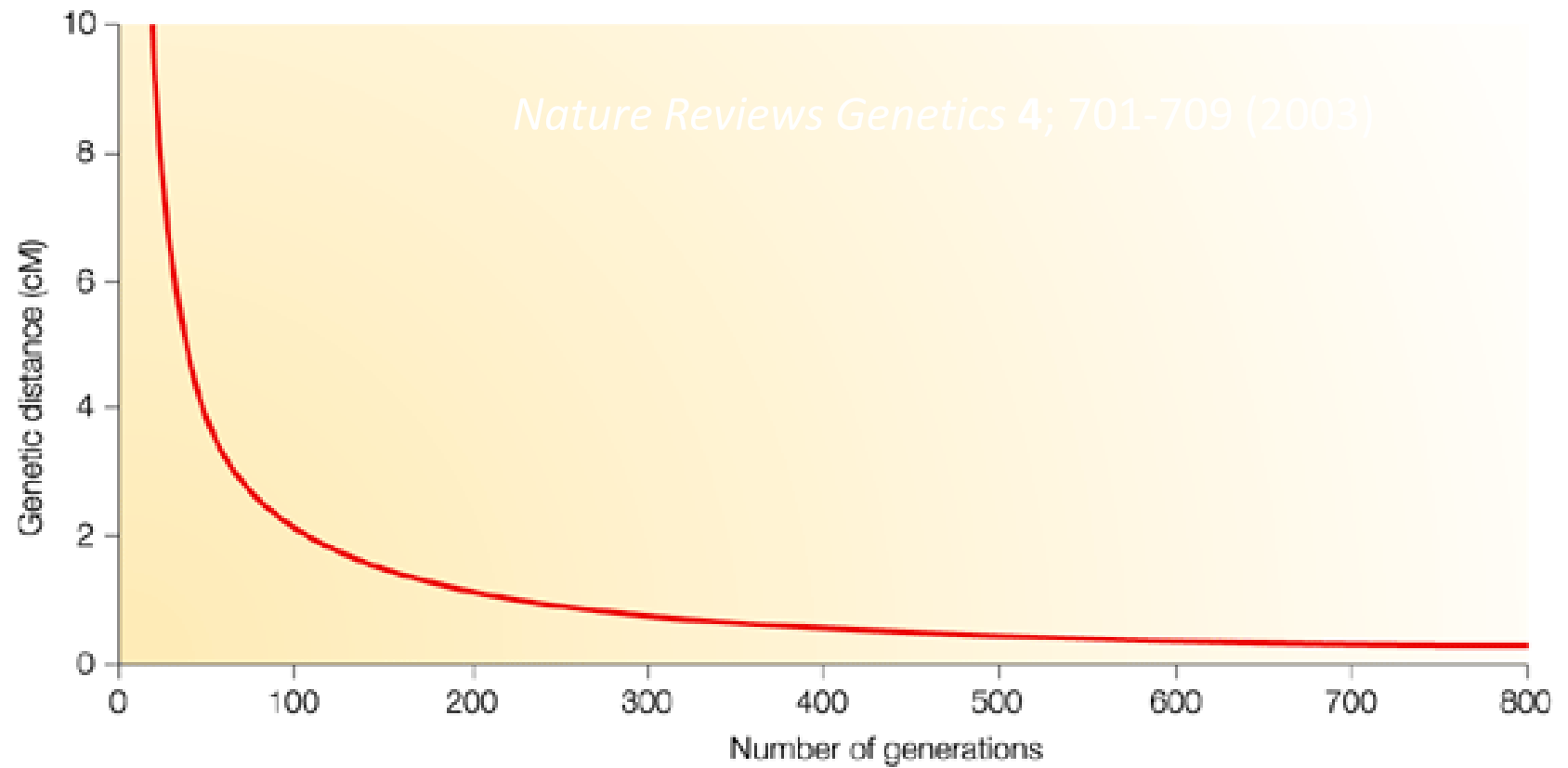
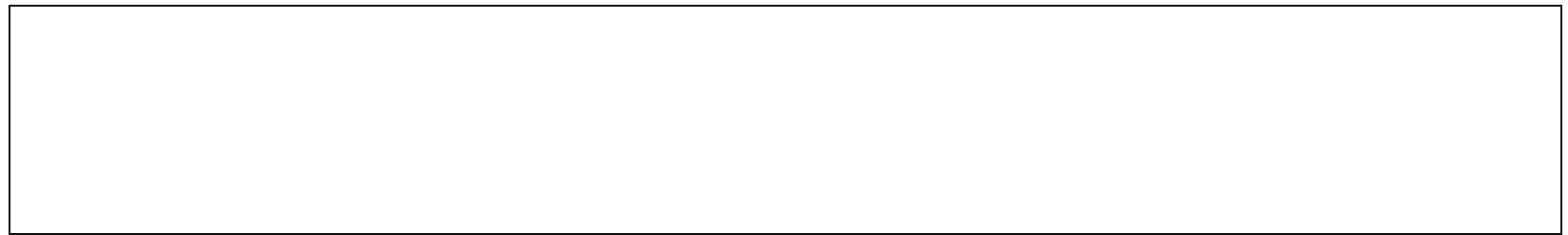


Fig. 1.3. Approach to equilibrium under random mating of two loci, considered jointly. The graphs show the amount of disequilibrium, D , relative to the disequilibrium in generation 0. The five graphs refer to different degrees of linkage between the two loci, as indicated by the recombination frequency shown alongside each graph. The graph marked 0.5 refers to unlinked loci.



Linkage Disequilibrium

- 2 SNPs
SNP A and SNP B
- 2 Alleles each
A1, A2, B1 and B2
- 4 possible haplotypes
A1B1, A1B2, A2B1, A2B2
- $D = p_{11} - p_{A1}p_{B1}$
 $= p_{11}p_{22} - p_{12}p_{21}$

		SNP B	
		p_{B1}	p_{B2}
SNP A	p_{A1}	p_{11}	p_{12}
	p_{A2}	p_{21}	p_{22}

r^2

- r^2 is the correlation coefficient for a 2X2 table

$$r^2 = \frac{D^2}{p_{A1}p_{A2}p_{B1}p_{B2}}$$

- If $p_{A1} = p_{B1}$
Max $r^2 = 1$, Min $r^2 = 0$
- If $p_{A1} \neq p_{B1}$
Max $r^2 < 1$, Min $r^2 = 0$

SNP B

		p _{B1}	p _{B2}
SNP A	p _{A1}	p ₁₁	p ₁₂
	p _{A2}	p ₂₁	p ₂₂

D'

- D' normalizes D to the maximum possible D given p_{A1} and p_{B1}
- For all comparisons
Max $D' = 1$, Min $D' = -1$

$$D' = \frac{D}{D_{\max}}$$

SNP B

SNP A

	p_{B1}	p_{B2}
p_{A1}	p_{11}	p_{12}
p_{A2}	p_{21}	p_{22}

Perfect Linkage Disequilibrium

- Genotype information is completely redundant
- Allele frequencies are identical
- Only two haplotypes exist: A1B1 and A2B2
- $|D'|=1, r^2 = 1$

		SNP B	
		p_{B1}	p_{B2}
SNP A	p_{A1}	p_{11}	0
	p_{A2}	0	$1-p_{11}$

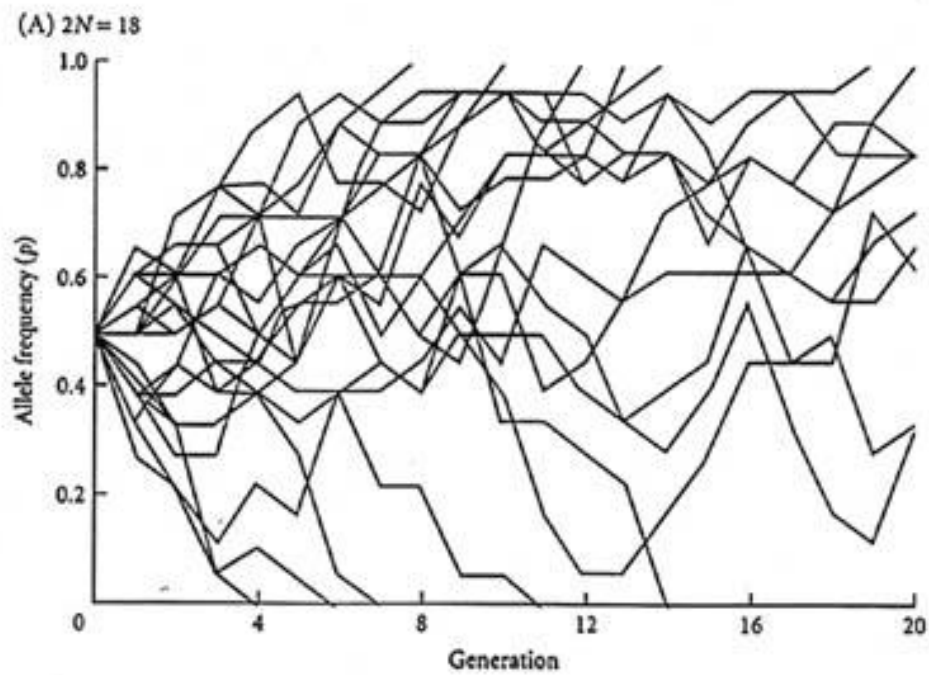
Complete Linkage Disequilibrium

- Genotype information is not completely redundant
- Allele frequencies are not identical
- Three haplotypes exist: A1B1, A1B2 and A2B2
- No recombination detected
- $|D'|=1$, $r^2 < 1$

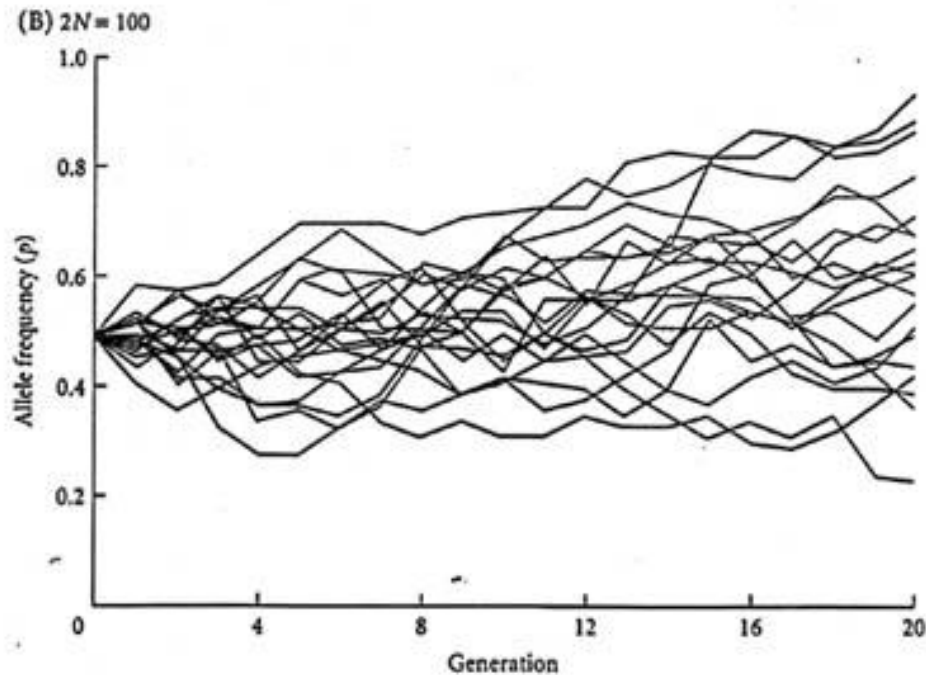
		SNP B	
		p_{B1}	p_{B2}
SNP A	p_{A1}	p_{11}	p_{12}
	p_{A2}	0	$1-p_{11}-p_{12}$

Genetic drift



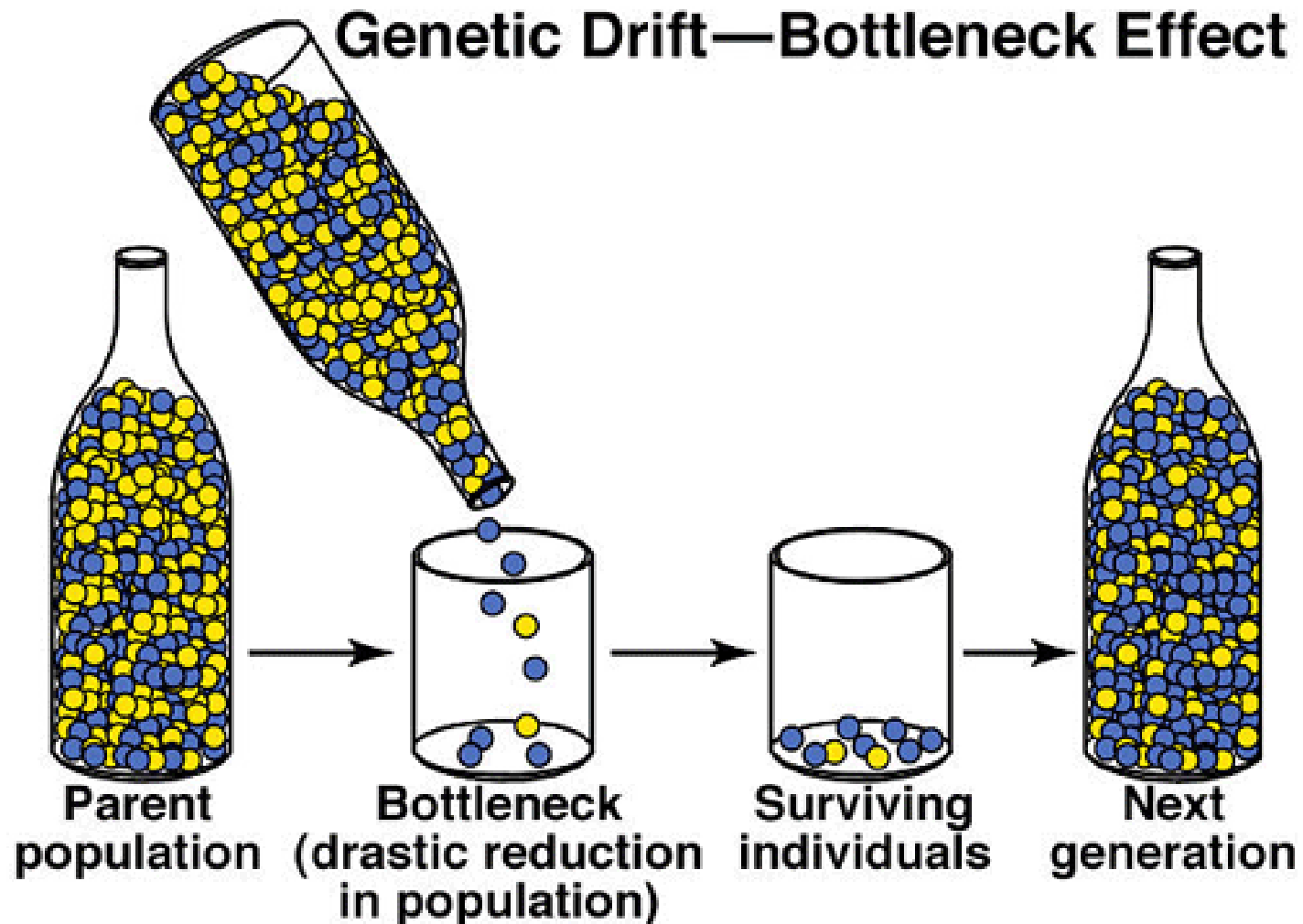


Simulation of
genetic drift in two
different
populations

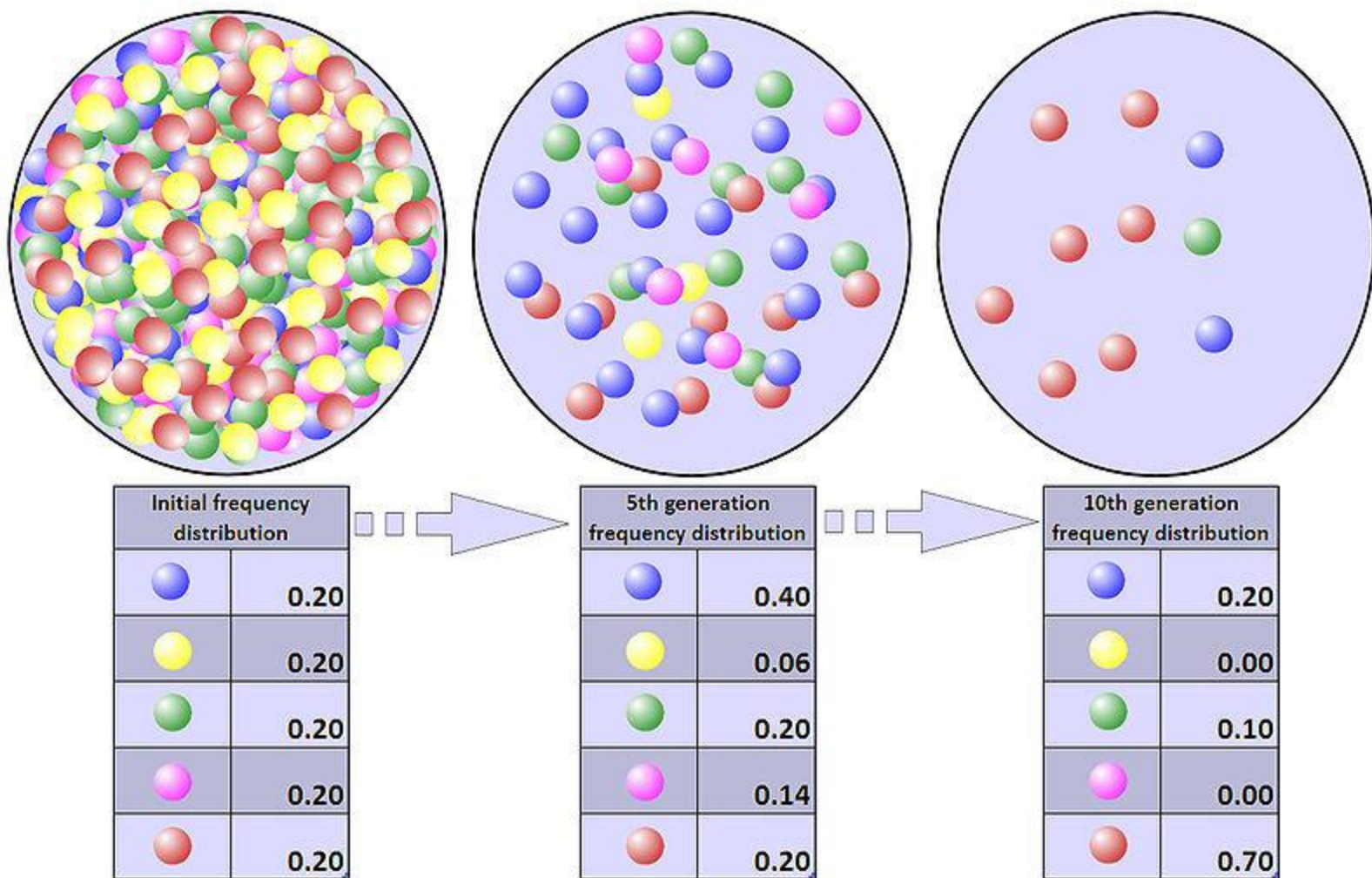


Bottleneck effect

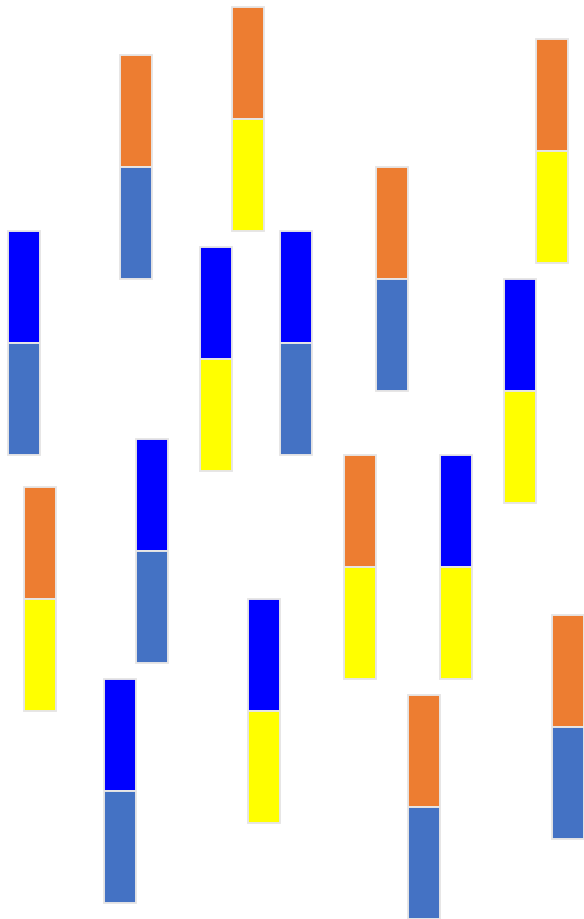
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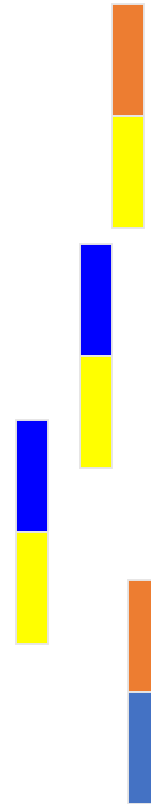
Founder effect



Founder effect can generate linkage disequilibrium



$D' = 0$



$D' = 1$, LD complete