Week 1 – Genetics of Breeding Populations

Quick review: Definitions, Mendel laws and linkage

Forces that contribute to changes in allele frequency

Evolutionary forces: mutation, random genetic drift and natural selection

Breeding forces: artificial selection and inbreeding

Inbreeding

Consequences of inbreeding

Inbreeding coefficient

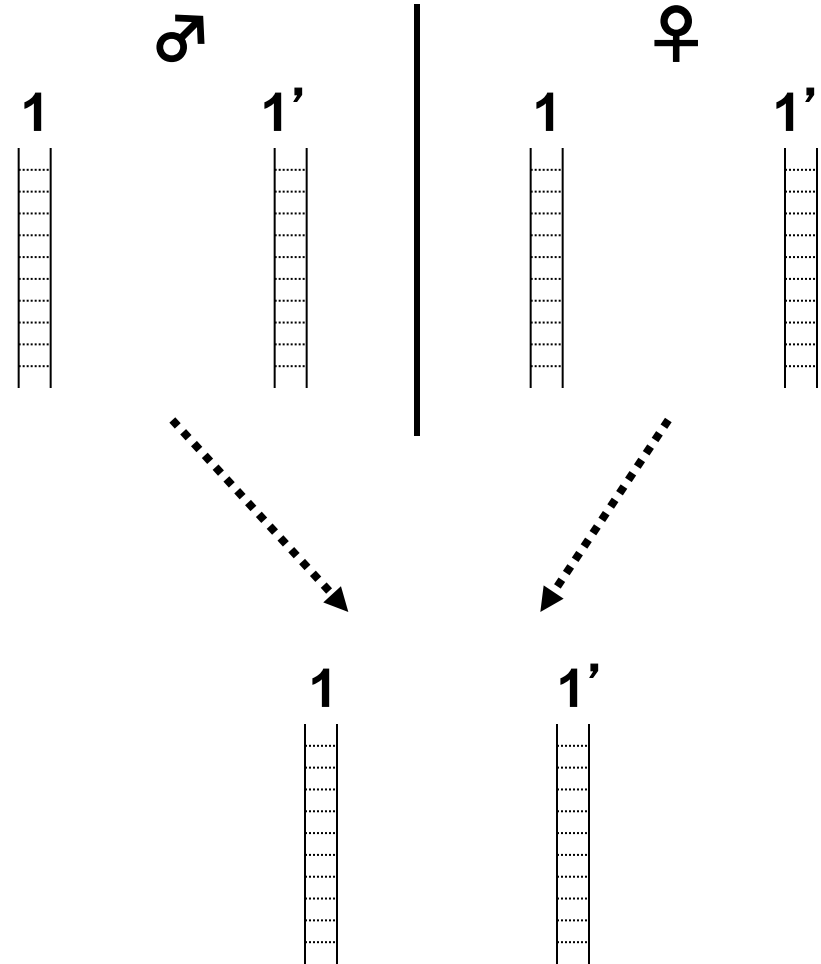Calculating the inbreeding coefficient from pedigrees (take-home exercise)

Inbreeding under regular mating systems

Calculating the inbreeding coefficient from molecular data (in-class demo)
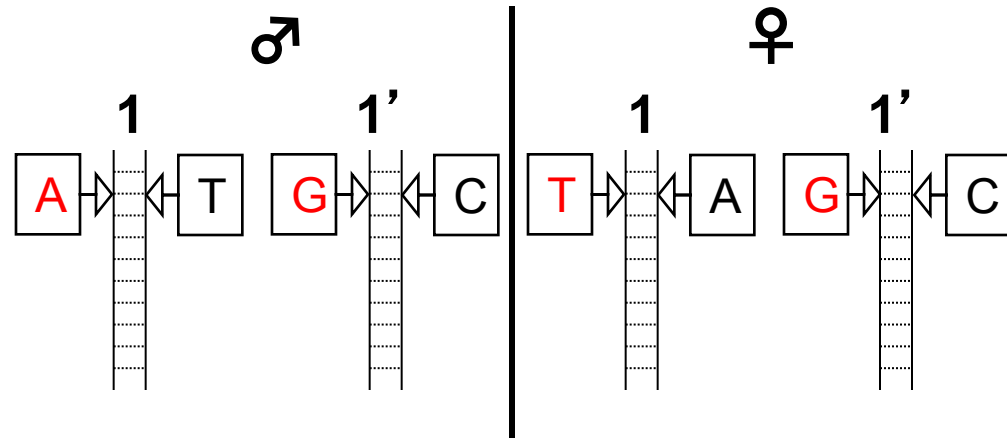
Allele, genotype and haplotype

Homologous chromosomes

Each individual inherits one copy (haploid) of each chromosome from its parents to form a diploid organism. They form pairs of **homologous chromosomes**.
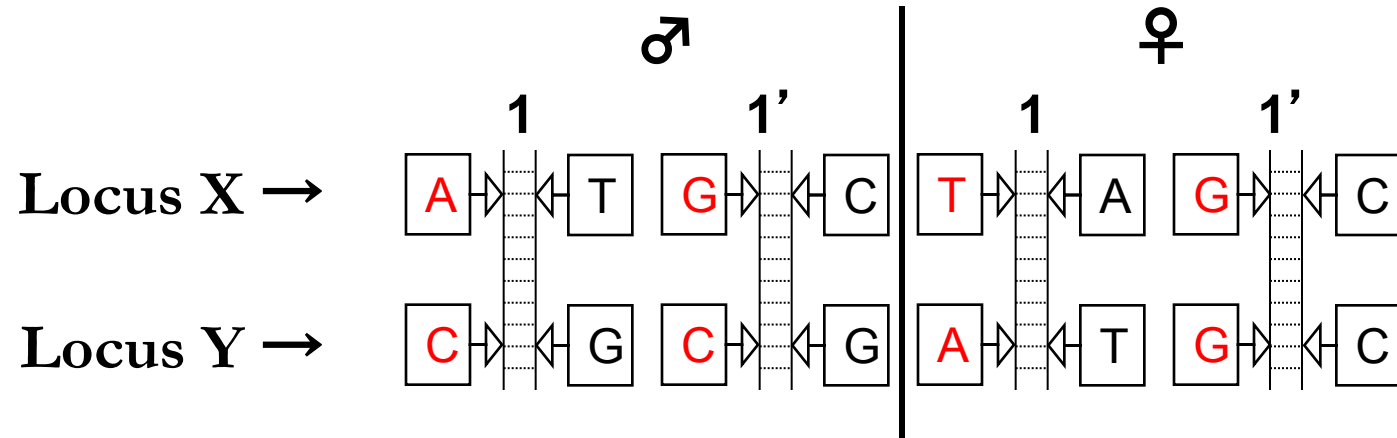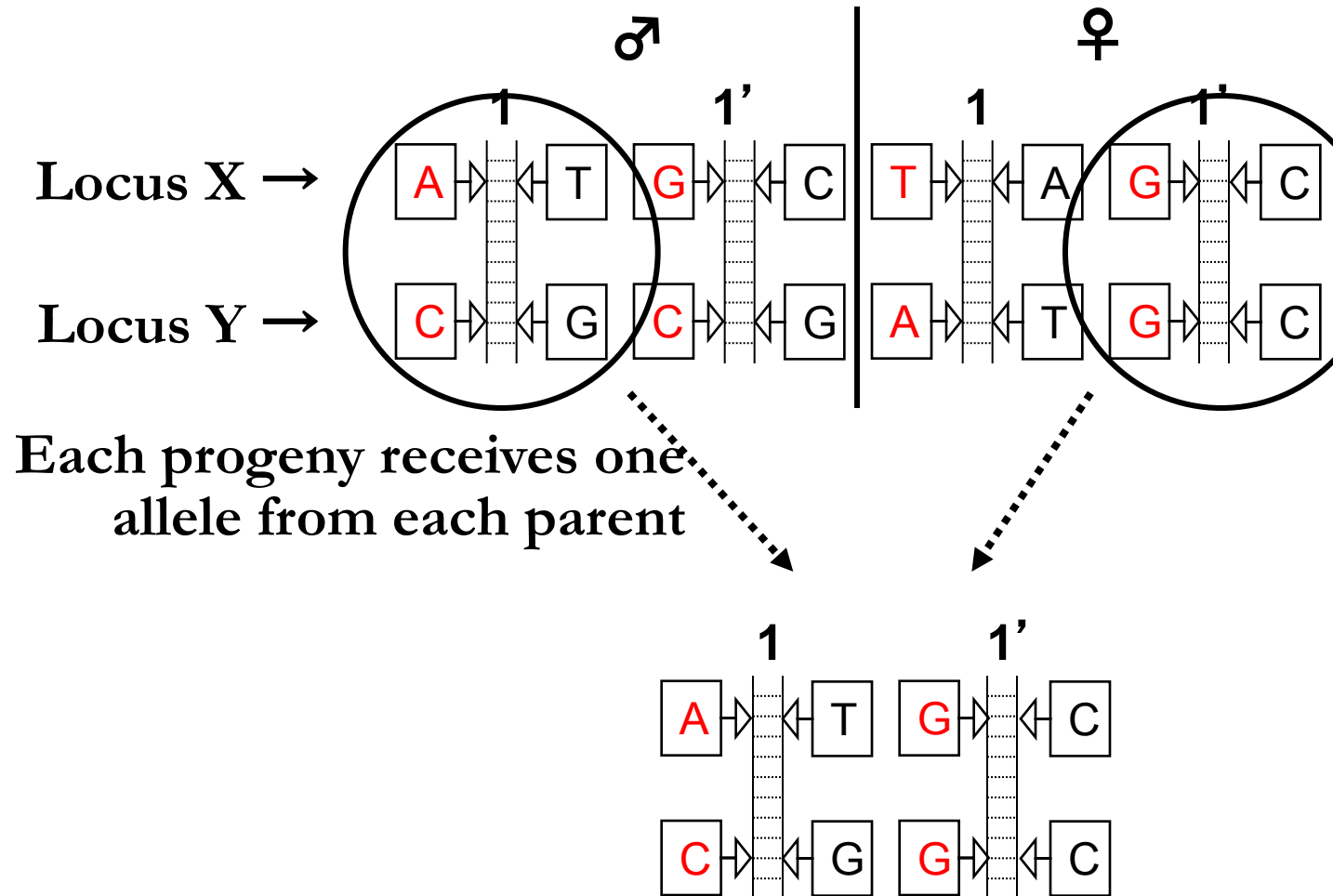
♂   ♀

1   1'   1   1'

1   1'

Alleles

♂   ♀

1   **1'**   **1**   **1'**

Locus X ⟶

♂ **alleles A and G**
♀ **alleles T and G**

A ⊳ ◁ T   G ⊳ ◁ C   T ⊳ ◁ A   G ⊳ ◁ C

Two loci

♂ | ♀

1 | 1' | 1 | 1'

Locus X → A–T G–C T–A G–C

Locus Y → C–G C–G A–T G–C

Segregation of alleles – more on this later

♂ | ♀

1 **1'** **1** **1'**

Locus X → A—T G—C | T—A G—C

Locus Y → C—G C—G | A—T G—C

Each progeny receives one allele from each parent
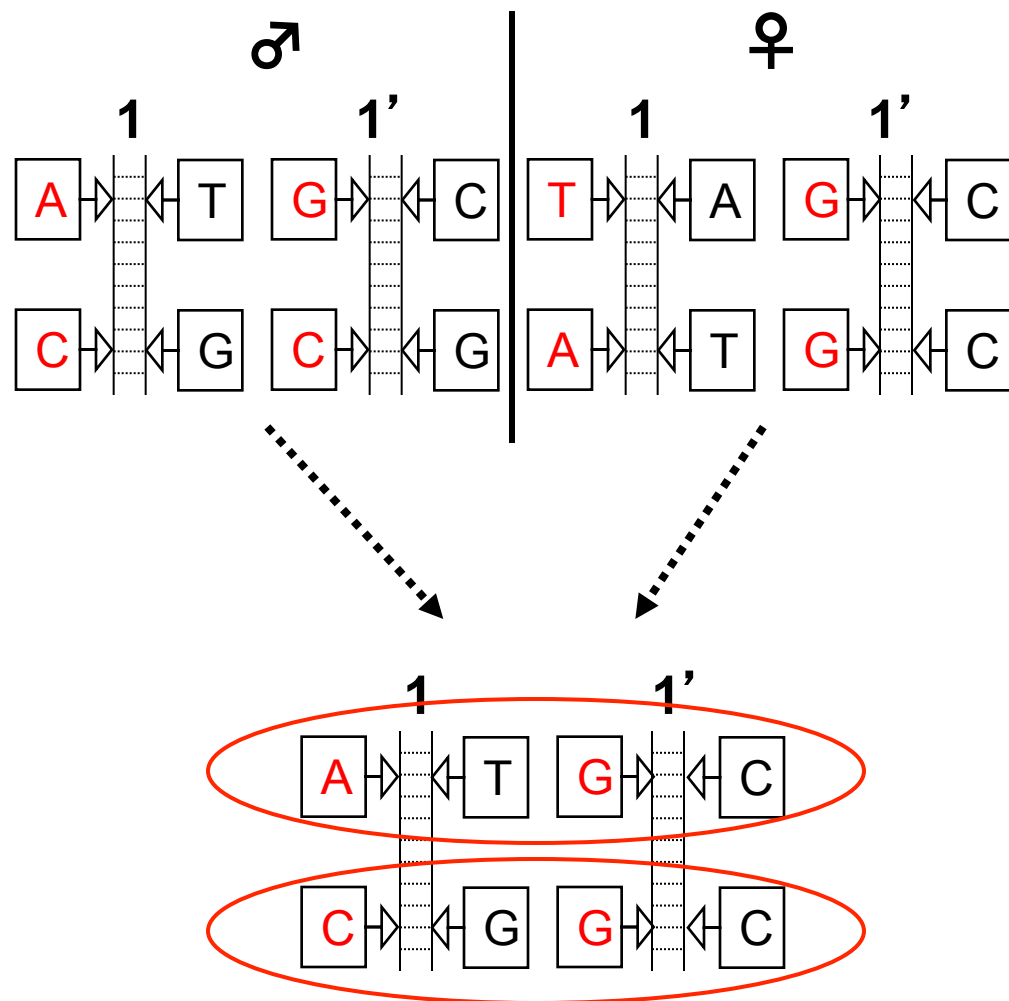
1 **1'**

A—T G—C

C—G G—C

Genotype

Describes the alleles at one locus.
One allele is received from each parent.
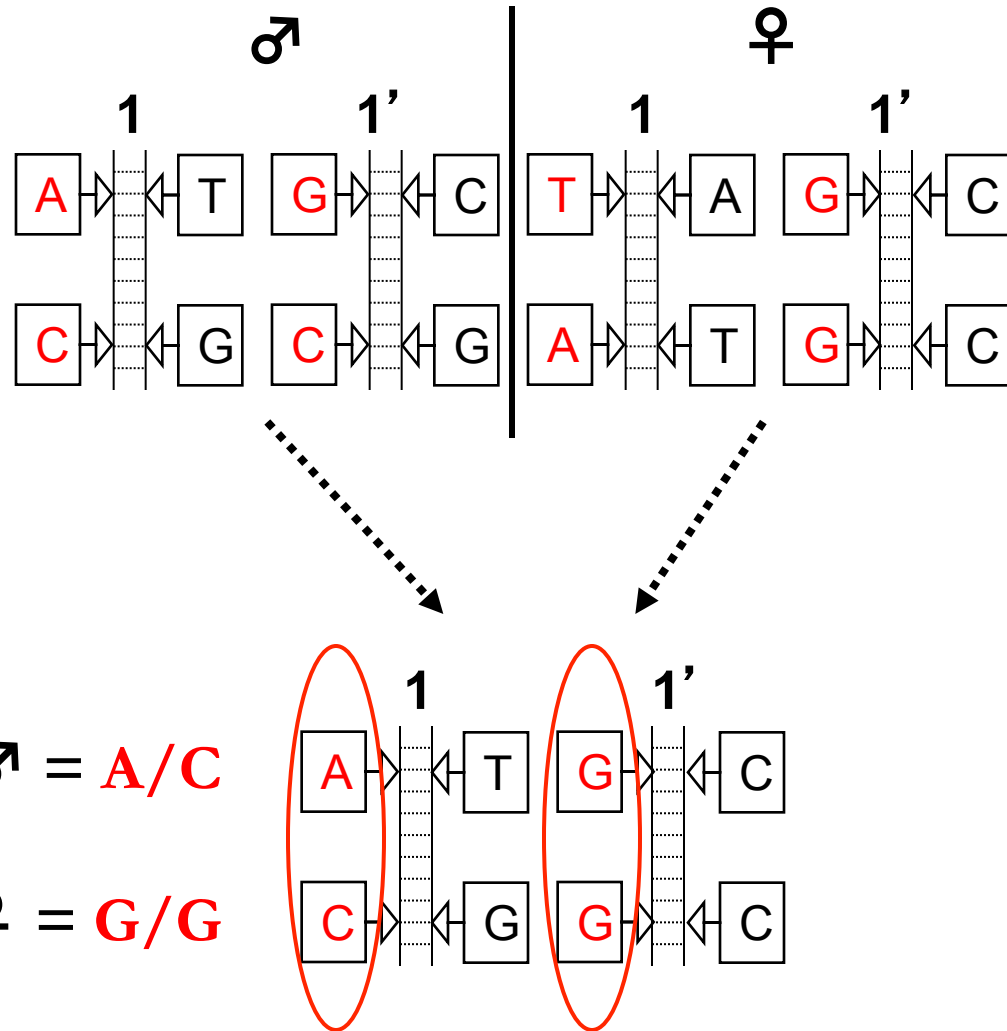The combination of alleles from both
parents form a genotype.

♂ ♀

1 **1'** **1** **1'**

A T G C T A G C

C G C G A T G C

1 **1'**

Locus X = A/G

A T G C

Locus Y = C/G

C G G C

Haplotype

Describes the alleles at multiple loci.
Combination of alleles at all loci
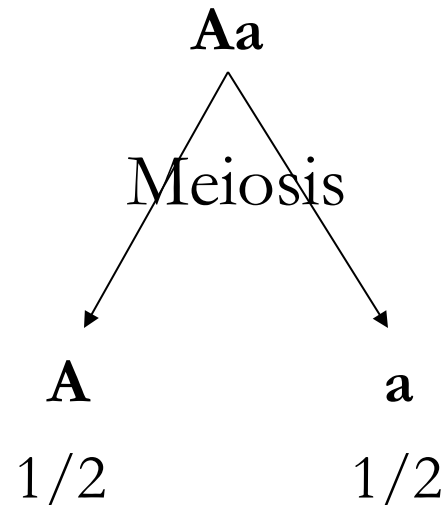received from each parent.

Haplotype inherited from ♂ = A/C

Haplotype inherited from ♀ = G/G

Segregation – Mendel's First Law

When an individual produces gametes during meiosis, alleles separate (i.e. segregate), and gametes receive, at an equal proportion, one member of the pair of alleles.

When fertilization occurs, pairs are reestablished by receiving one copy from each parent.

This is referred to as Mendel's first law, or the **Law of Segregation**.

Aa

Meiosis

A   **a**

1/2   1/2

Segregation – Mendel's First Law

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	A	A
a	Aa	Aa
a	Aa	Aa

F_1

	A	a
A	AA	Aa
a	Aa	aa

Dominant in F1	Recessive in F1	Dominant	Recessive	Total	Ratio
Spherical	Wrinkled seeds	5,474	1,850	7,324	2.96 : 1
Yellow	Green seeds	6,022	2,001	8,023	3.01 : 1
Purple	White flowers	705	224	929	3.15 : 1
Inflated	Constricted pods	882	299	1,181	2.95 : 1
Green	Yellow pods	428	152	580	2.82 : 1
Axial	Terminal flowers	651	207	858	3.14 : 1
Tall	Dwarf stems	787	277	1,064	2.84 : 1

Independent assortment – Mendel's Second Law

During gamete formation the segregation of the alleles of one allelic pair is independent of the segregation of the alleles of another allelic pair.

This is referred to as Mendel's Second Law or the **Law of Independent Assortment.**
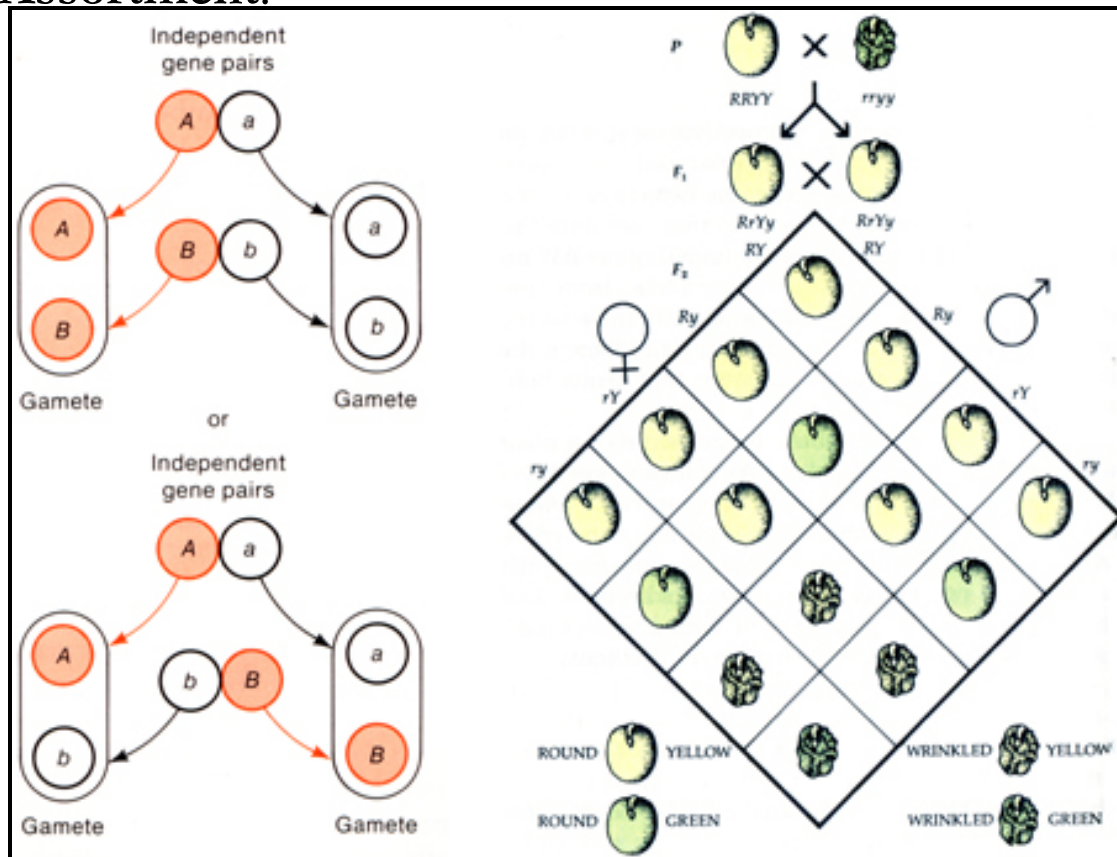
However, there is not always independent assortment.

Instead, genes can be linked in chromosomes, in which case they may not segregate independently in the progeny.

More on this later.

Hardy-Weinberg Equilibrium (HWE)

A population in **HWE** is a population of:
1.   A diploid organism;
2.   Which reproduces sexually;
3.   Allele frequencies are equal in males and females;
4.   Random mating;
5.   Generations are non-overlapping;
6.   Population size is infinite;
7.   Mutation, migration and selection are non-existent.

As a result, the allele and genotype frequencies are stable from generation to generation and the genetic properties of the population never change.

The genotype frequencies of the offspring produced by random mating depend only on the allele frequencies of the parents.

Linkage and Linkage Disequilibrium

Consider two genetic loci, with two alleles each:

Locus	Allele	Frequency		Locus	Allele	Frequency
A	A1	p_1		B	B1	q_1
	A2	p_2			B2	q_2

If these loci are randomly associated (**i.e. in equilibrium**), we would expect the **haplotype** frequency to be:

Locus A

		A1 (p_1)	A2 (p_2)
Locus B	B1 (q_1)	A1B1 (p_1q_1)	A2B1 (p_2q_1)
	B2 (q_2)	A1B2 (p_1q_2)	A2B2 (p_2q_2)

So, what would be the gamete frequencies in a hypothetical population, that has the alleles A1 and A2 (locus A) and B1 and B2 (locus B) at the following frequencies:

Locus	Allele	Obs. Freq.
A	A1	0.25
	A2	0.75
B	B1	0.50
	B2	0.50

Gamete Type (Haplotype)	Expected frequencies
A1B1	$P_{11} = 0.25*0.50 = 0.125$
A1B2	$P_{12} = 0.25*0.50 = 0.125$
A2B1	$P_{21} = 0.75*0.50 = 0.375$
A2B2	$P_{22} = 0.75*0.50 = 0.375$

At **linkage equilibrium**, the allele frequency at the loci A and B are uncorrelated:

$$f(A1B1) * f(A2B2) = f(A1B2) * f(A2B1)$$

$$P_{11} * P_{22} - P_{12} * P_{21} = 0$$

$$0.125 * 0.375 - 0.125 * 0.375 = 0$$

Gamete Type (Haplotype)	Expected frequencies
A1B1	$P_{11} = 0.25*0.50 = 0.125$
A1B2	$P_{12} = 0.25*0.50 = 0.125$
A2B1	$P_{21} = 0.75*0.50 = 0.375$
A2B2	$P_{22} = 0.75*0.50 = 0.375$

Therefore, the alleles of the loci A and B are randomly associated and the **coefficient of linkage disequilibrium D** is 0.

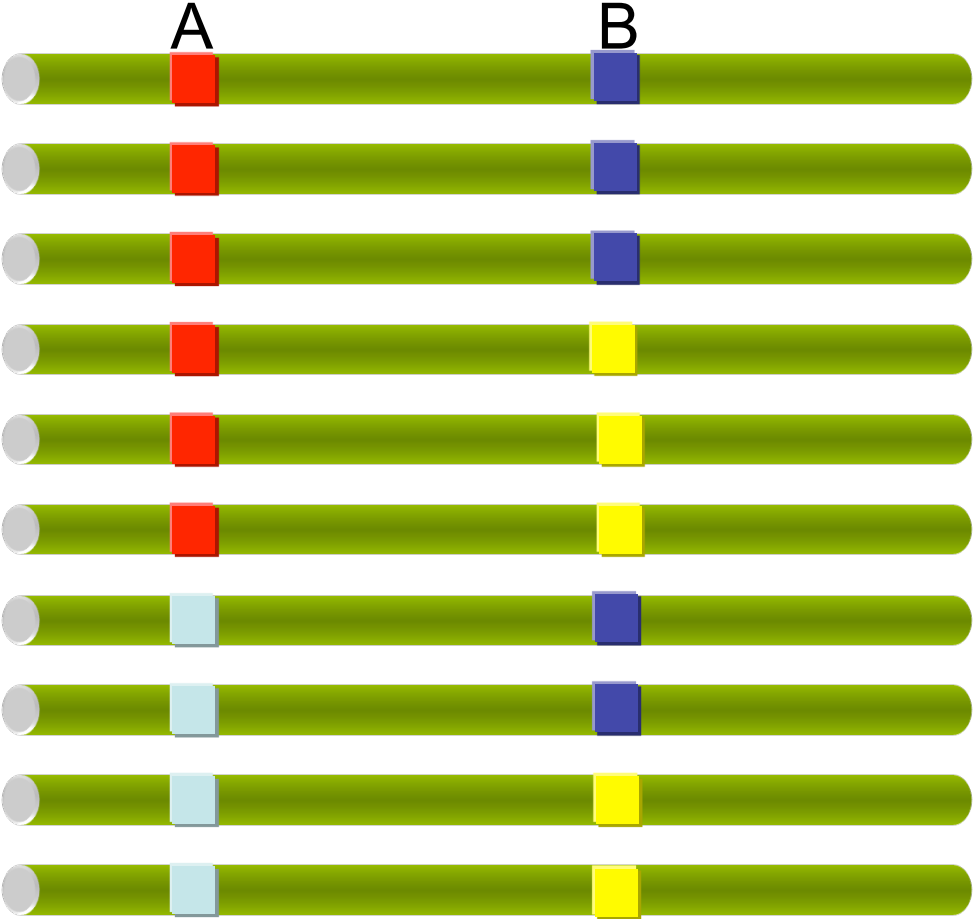$$D = P_{11} * P_{22} - P_{12} * P_{21}$$

At **linkage disequilibrium**, there is a correlation between allele frequency at the loci A and B. Consequently:
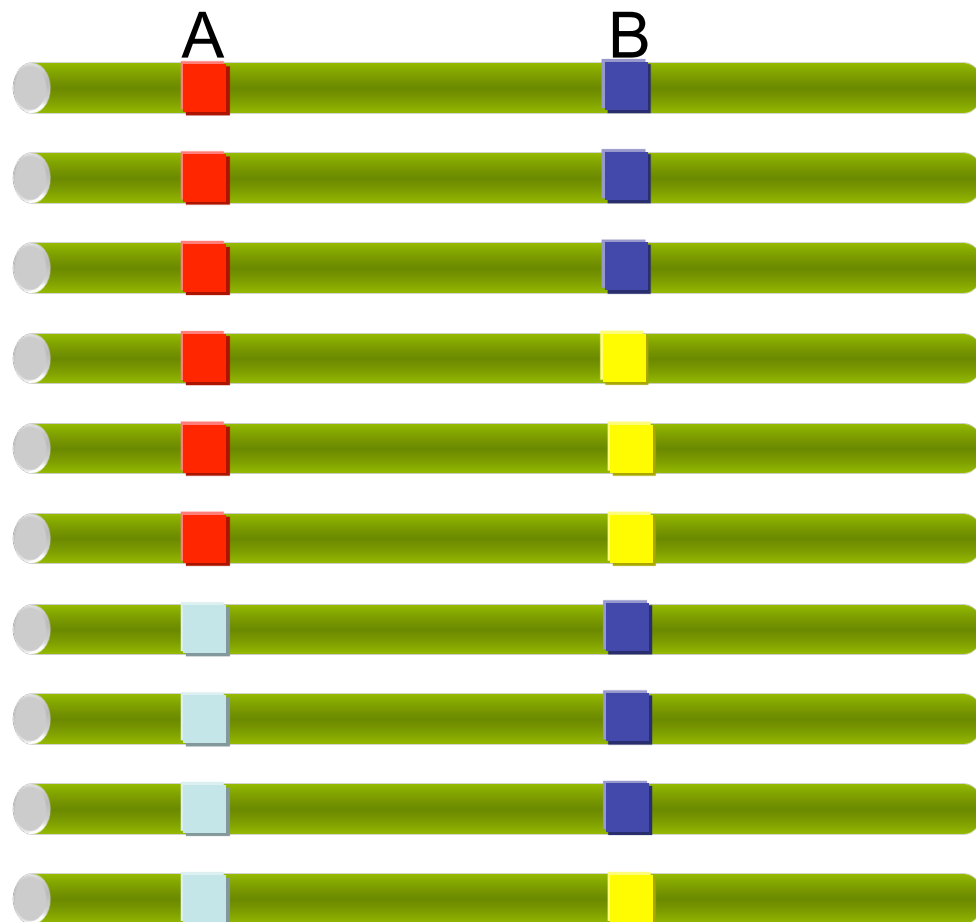
$$f(A1B1) * f(A2B2) \neq f(A1B2) * f(A2B1)$$

$$P_{11} * P_{22} - P_{12} * P_{21} \neq 0$$

As a result, the **coefficient of linkage disequilibrium D** differs from 0.

$$D = P_{11} * P_{22} - P_{12} * P_{21} \neq 0$$

Week 1 – Quick review

	B1	B2
A1	0.3	0.3
A2	0.3	0.1

$P_{A1} = 0.6$ $P_{B1} = 0.6$

$P_{A2} = 0.4$ $P_{B2} = 0.4$

Turn in on September 4.

Rate of recombination

- Linkage disequilibrium decays over time because of recombination.
- The rate of recombination defines (in part) how fast LD will decay.
- Let's consider the gametes formed by an individual with genotype A1B1/A2B2.

A1   **A2**

B1   **B2**

Gametes

A1   **A2**

B1   **B2**
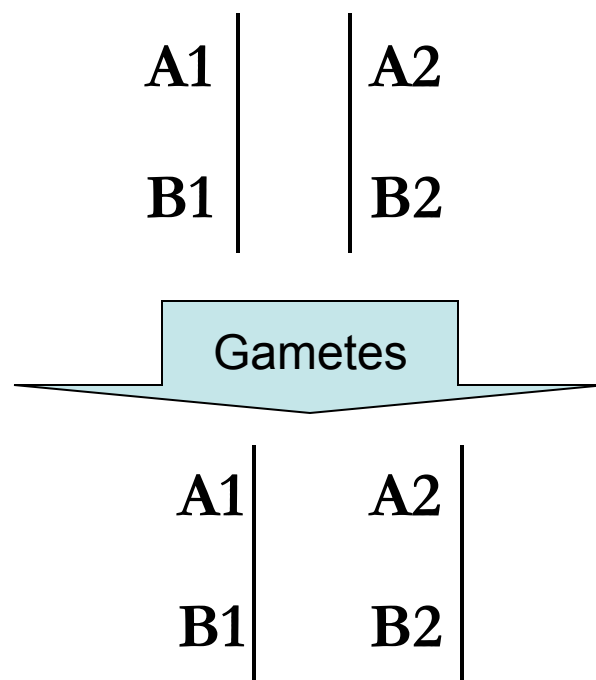
- A different allele combination may be created if recombination occurs between the loci A and B.

A1 | | A2

B1 | | B2

Gametes

A1 | A2

B2 | B1
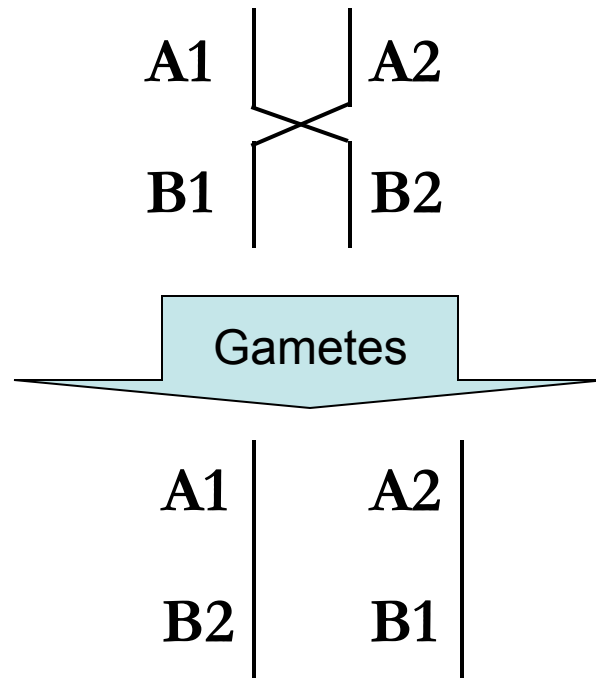
Two levels of Equilibrium:

Between the alleles at a given locus
(Hardy-Weinberg Equilibrium)
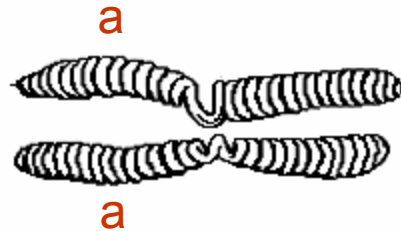
$$P_{aa} = p_a p_a$$

Between alleles at two different loci

(Linkage Equilibrium – more on this later)

$$P_{aB} = p_a p_B$$

Forces that contribute to changes in allele frequency

Evolutionary forces

mutation

random genetic drift

natural selection

Breeding forces

artificial selection

inbreeding

Mutation

Mutations are the ultimate source of genetic variation.

The rate at which mutations occur (u = mutation rate per nucleotide site per generation) defines how much genetic diversity there will be within and between species.
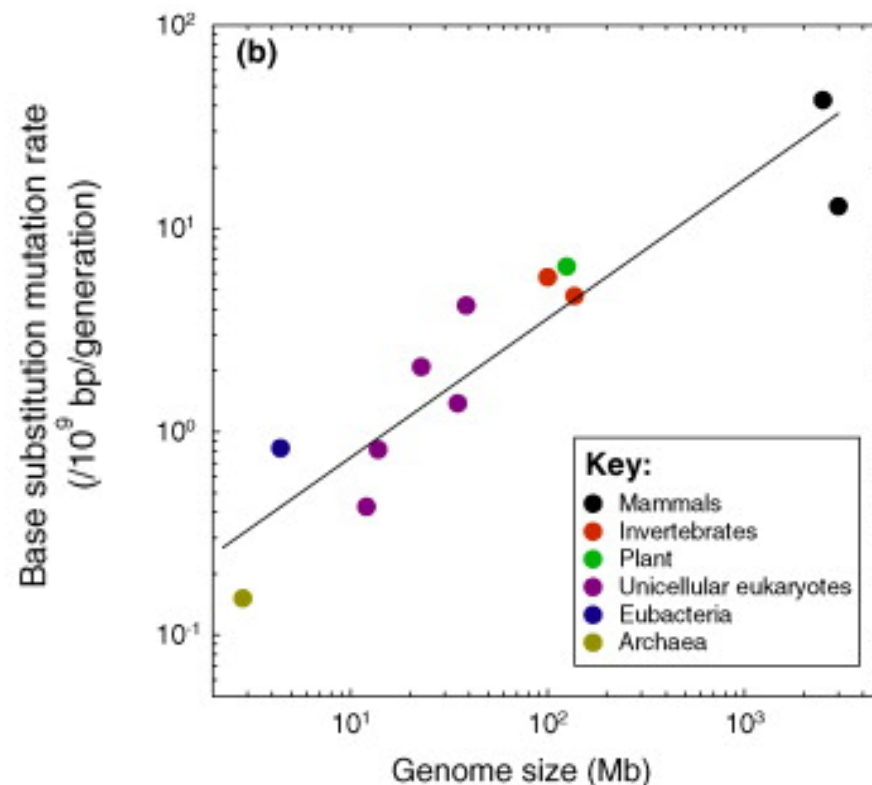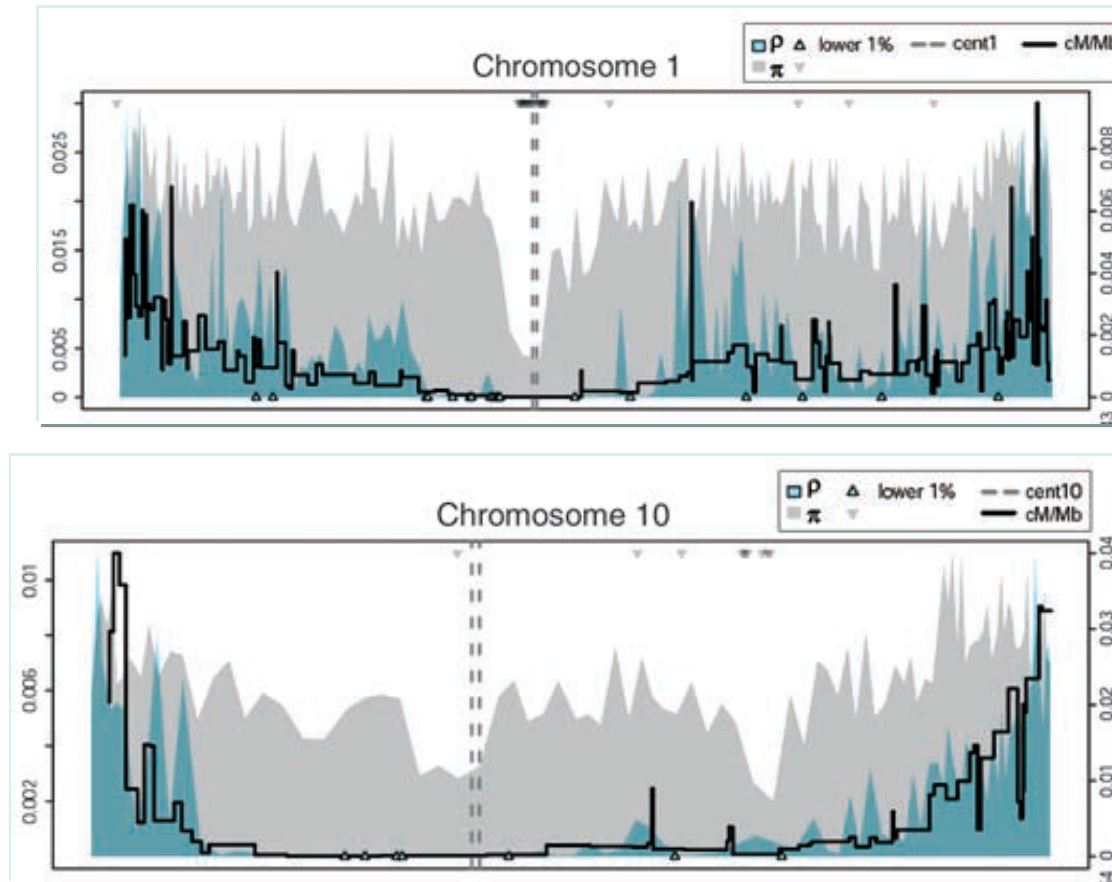
Mutation rates in the maize genome (commercial lines)

Random Genetic Drift

Populations (natural and breeding) undergo cycles of population growth and reduction.

Random genetic drift arises in all populations from the effect of sampling (but is more significant in small populations).

Generally, from one generation to another, most genes will remain at the frequency of the original population. However, by chance, alleles at some genes will drift towards fixation.

(A)

$2N = 18$

Allele frequency (p)

Generation

(B)

$2N = 100$

Allele frequency (p)

Generation
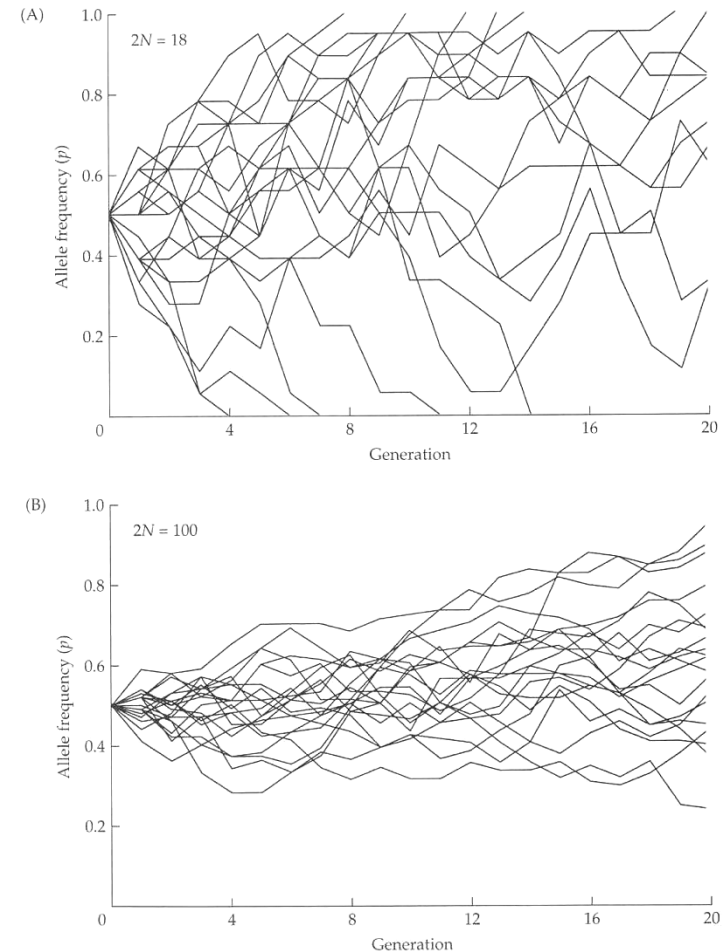
Neutral theory of evolution – The balance of mutation and genetic drift

The natural theory of evolution was proposed to explain the large genetic variation that was observed in natural populations. The theory makes some assumptions:

- Most alleles are **selectively neutral**
- Genetic variation observed in natural populations results from the balance of **mutation** and **genetic drift**

Some lines of evidence indicate that the Neutral Theory is essentially a reasonable model: (1) most mutations have no visible functional effect, and (2) at the inferred mutation rates, if mutations had functional effects, organisms would not survive.
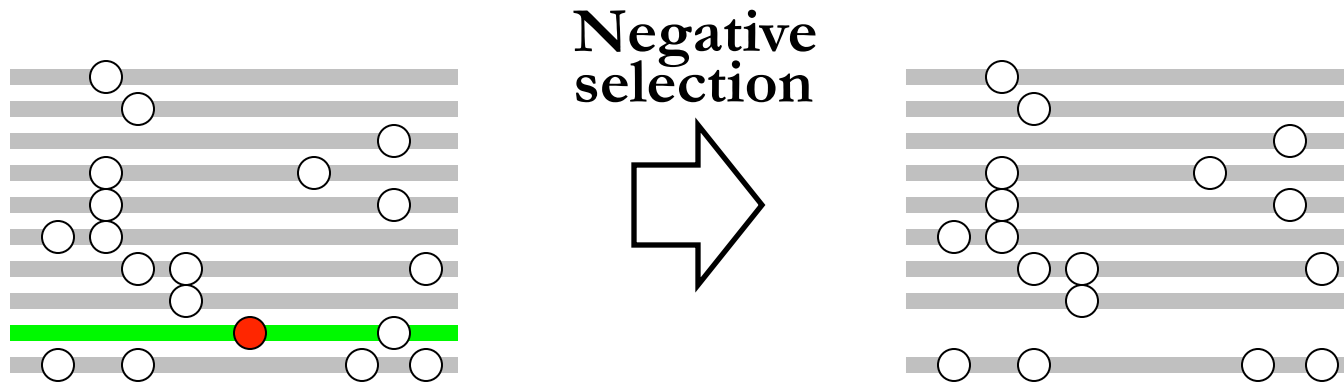
Natural Selection

When individuals contribute different numbers of offspring to the next generation, this difference may be due to variable viability (i.e. survival) and fertility (i.e. success in generating offspring).

The *fitness* of an individual is defined as its proportional contribution of offspring to the next generation.

If differences in individual fitness are on average associated with the presence or absence of a particular gene (allele), then *selection* is said to operate on that gene. Selection can act at many stages of the life cycle:
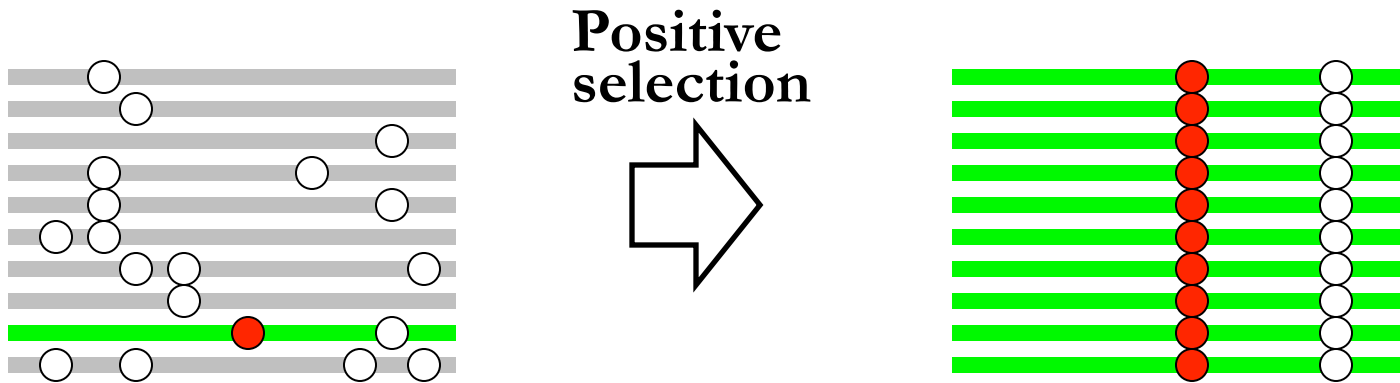
(1) zygote to adult survival: viability selection;

(2) mate choice: sexual selection;

(3) production of gametes: fecundity selection or gametic selection.

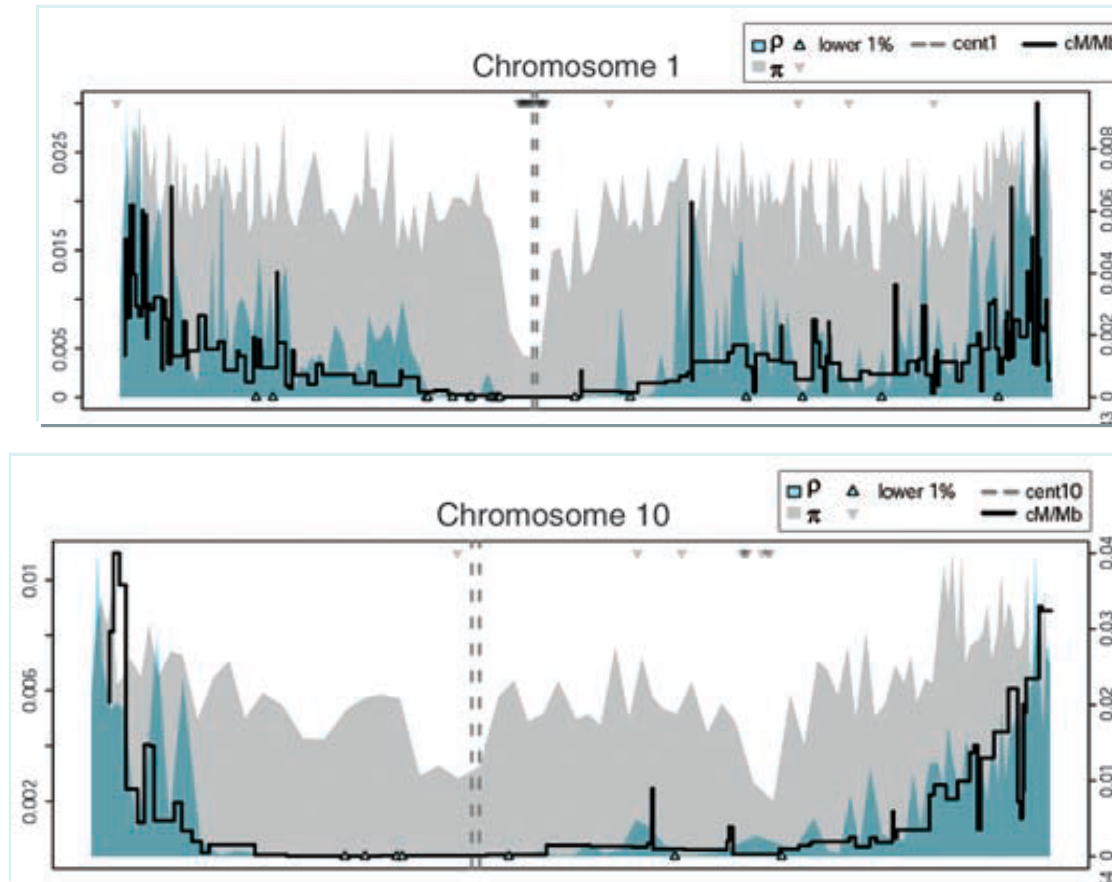# Negative or purifying selection

Negative selection

● Disadvantageous mutation

○ Neutral mutation

Positive selection

Positive selection

🔴 Advantageous mutation

⚪ Neutral mutation

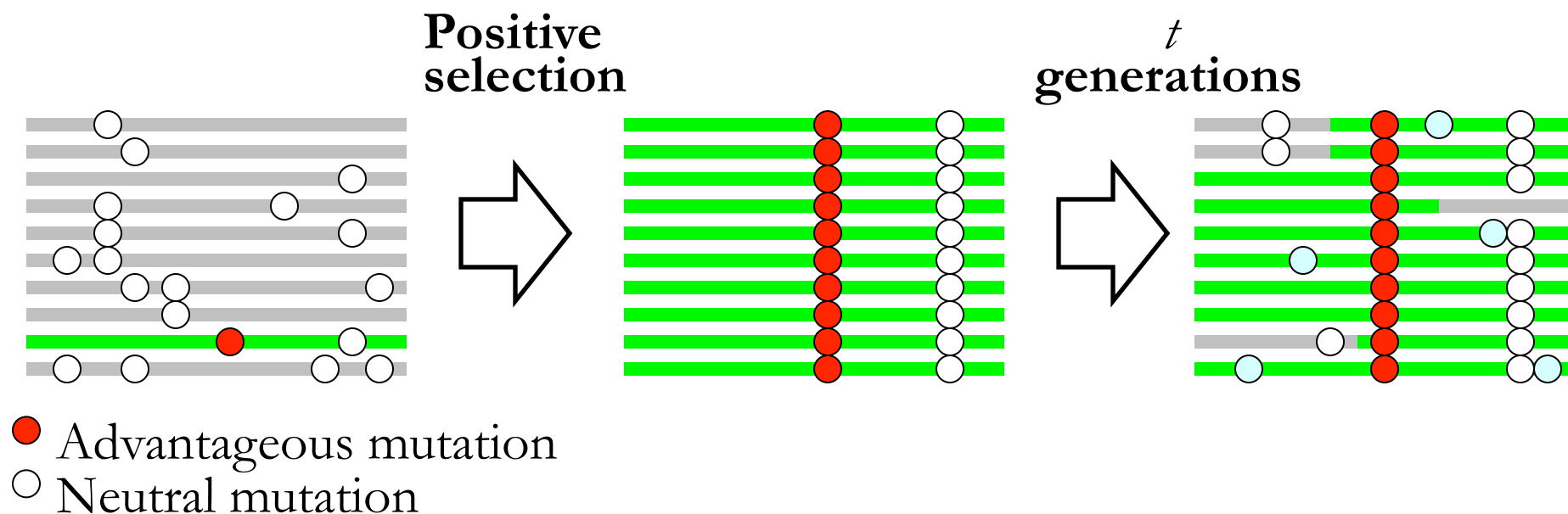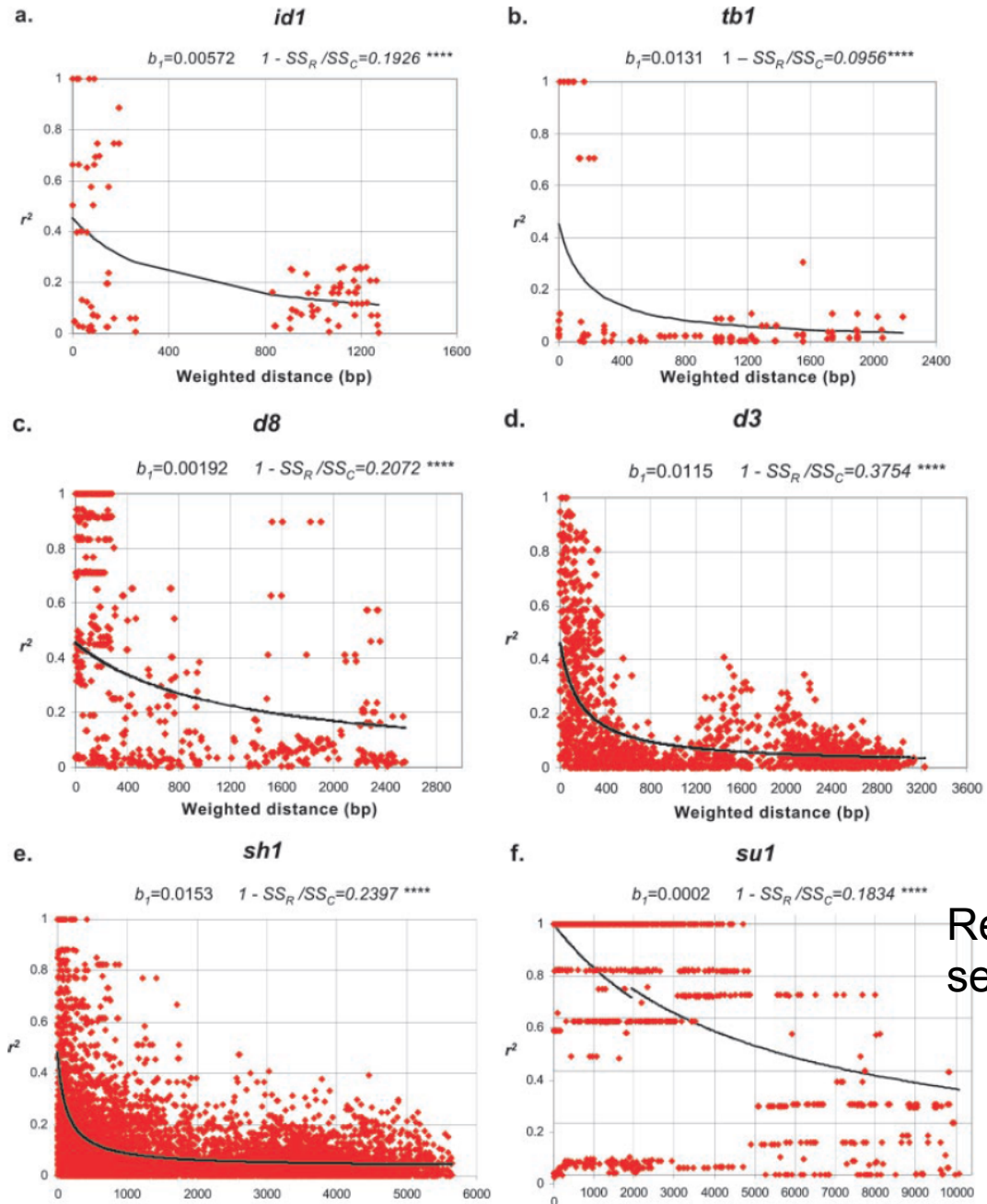# Variation in the maize genome reflects selection

Artificial Selection

When selected individuals contribute offspring to the next generation, or when selected offspring are crossed to produce the next generation, because they carry specific trait properties.

Effects of artificial selection genetic diversity and LD

- A selected genetic variant (a.k.a. allele) will lead to lower diversity and high LD around the locus that is being artificially selected
- Over time, LD will decay around the locus under selection at a rate dependent on the number of generation and rate of recombination

Positive selection

t **generations**

● Advantageous mutation
○ Neutral mutation

Examples

a. **id1** $b_1=0.00572$ $1 - SS_R/SS_C=0.1926$ ****

b. **tb1** $b_1=0.0131$ $1 - SS_R/SS_C=0.0956$ ****

c. **d8** $b_1=0.00192$ $1 - SS_R/SS_C=0.2072$ ****

d. **d3** $b_1=0.0115$ $1 - SS_R/SS_C=0.3754$ ****

e. **sh1** $b_1=0.0153$ $1 - SS_R/SS_C=0.2397$ ****

f. **su1** $b_1=0.0002$ $1 - SS_R/SS_C=0.1834$ ****

Recent selection

Remington et al. 2001 (PNAS)