# Introduction to Genetics and Evolution

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Overview

Brief History – Charles Darwin on Natural Selection
Mendelian Inheritance and Cell Division
- Laws of Inheritance
- Codominance
- Sex Linked Genes
- Non-Mendelian Inheritance
- Continuous Variation
- Modern Synthesis

Forces of Evolution
Hardy-Weinberg Equilibrium
Detecting Molecular Variation

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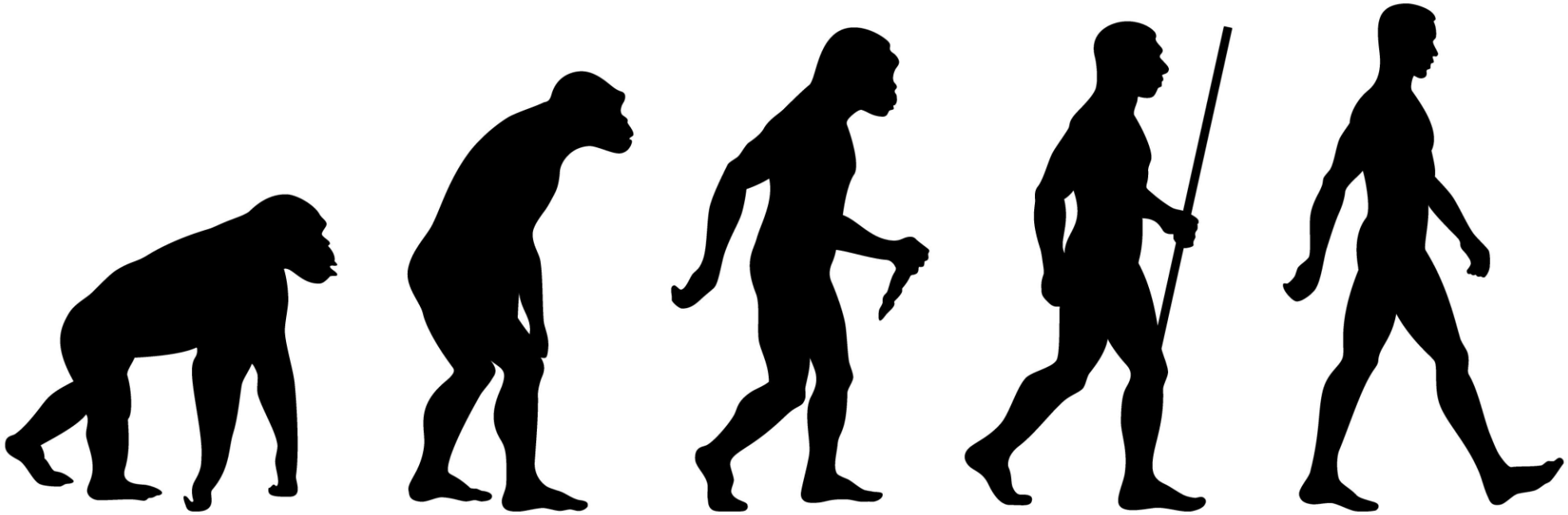

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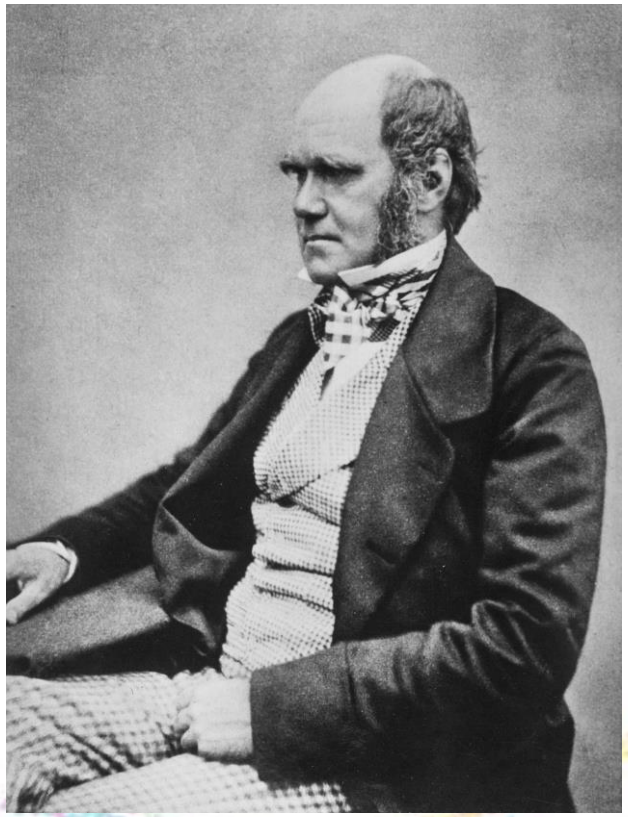
# Charles Darwin: Natural Selection



The theory of evolution **by natural selection** is the process by which organisms change over time as a result of changes in heritable trait. ("On the Origin of Species" in 1859)

Natural selection as the mechanism of change.

https://www.genome.gov/about-genomics/fact-sheets/A-Brief-Guide-to-Genomics

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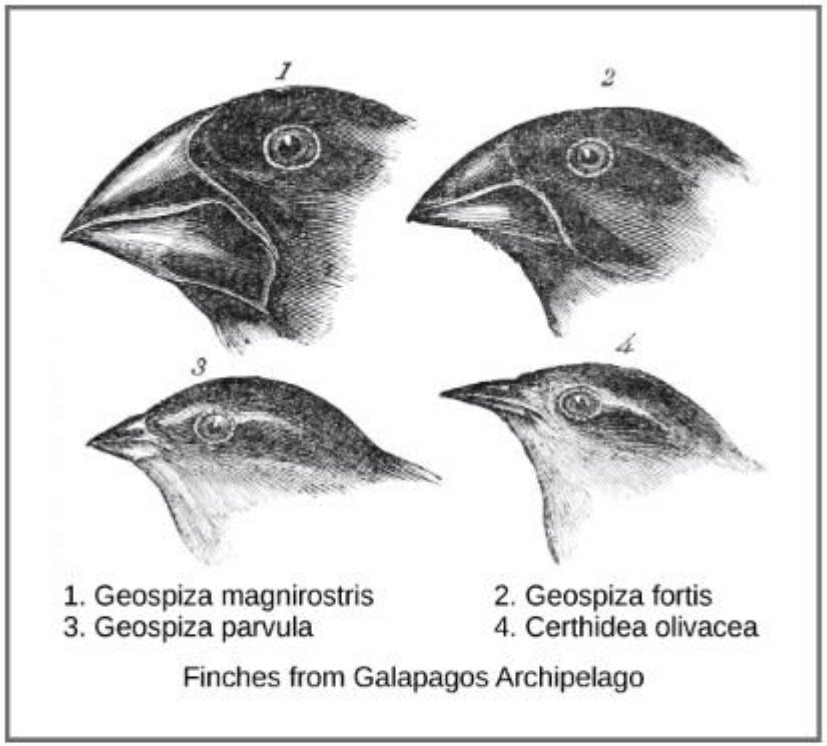
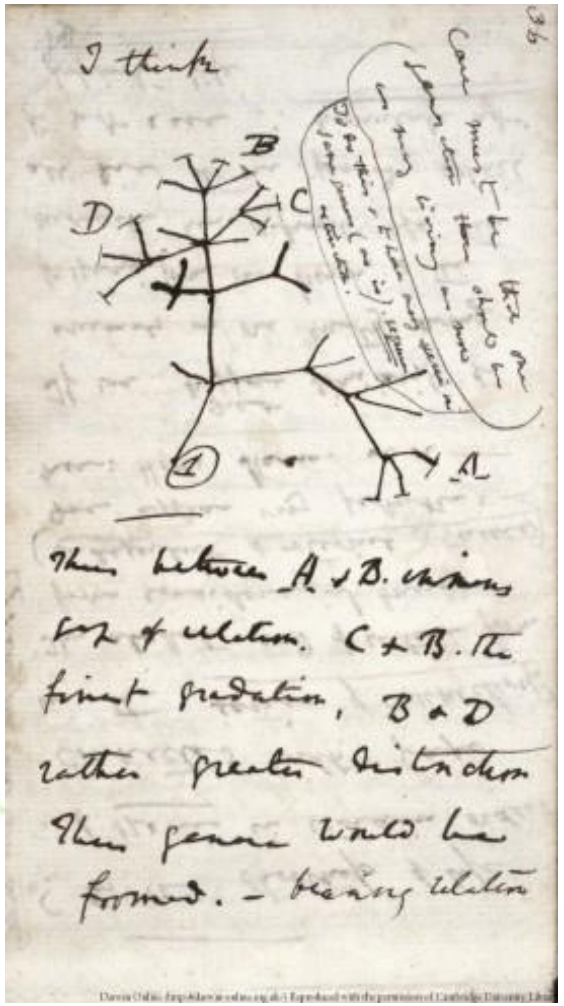



Finches from Galapagos Archipelago

**Beak Shape Among Finch Species**: Darwin observed that beak shape varies among finch species. He postulated that the beak of an ancestral species had adapted over time to equip the finches to acquire different food sources.

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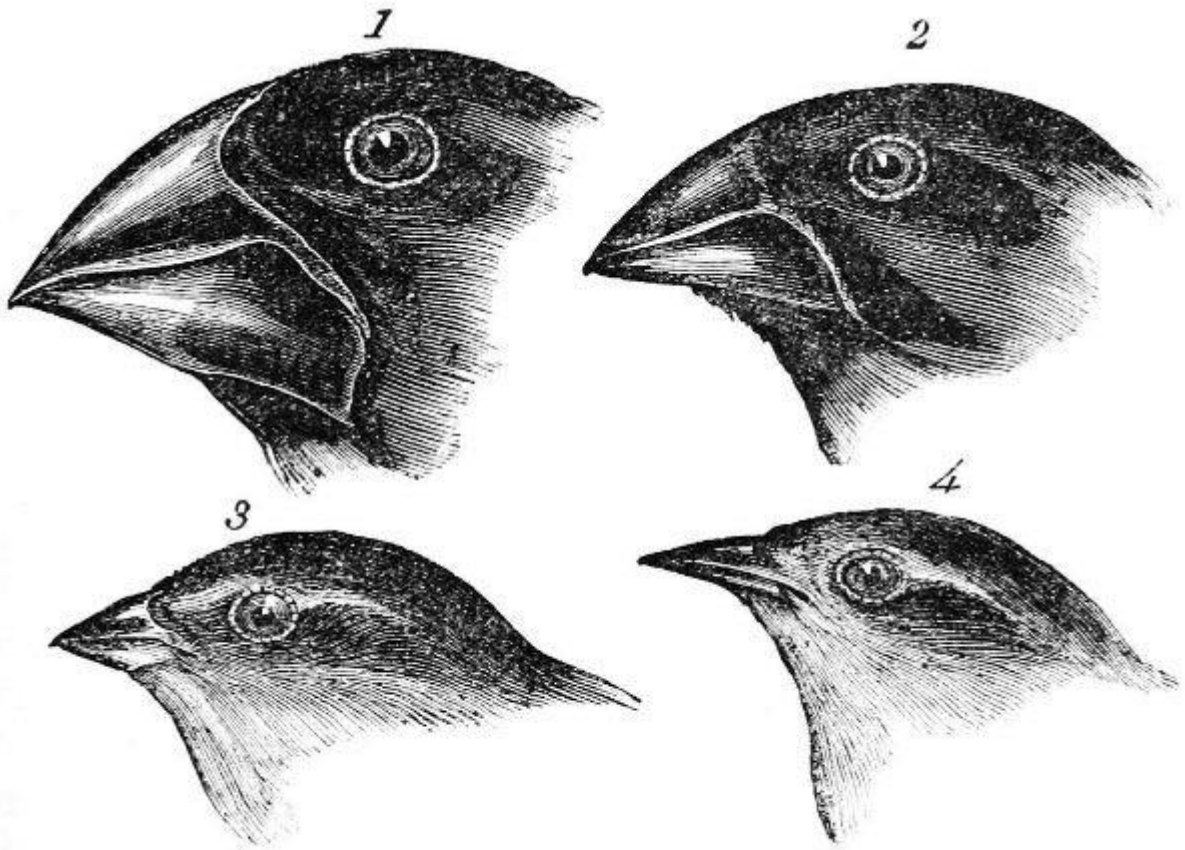
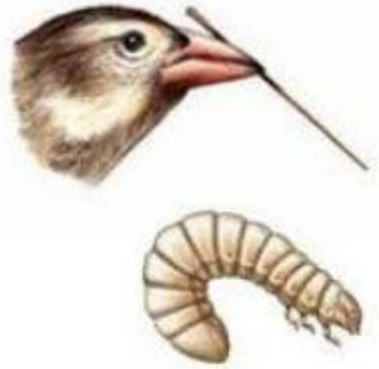



1. Geospiza magnirostris.
2. Geospiza fortis.
3. Geospiza parvula.
4. Certhidea olivacea.

Large ground finch (seeds)

Cactus finch
(cactus fruits and flowers)

Vegetarian finch (buds)



Woodpecker finch (insects)

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# Discrete Variation: Mendelian Inheritance

Principles of Mendelian inheritance (1866)

There exist hereditary factors, one of which is dominant. Each individual has two factors for each trait, one from each parent.

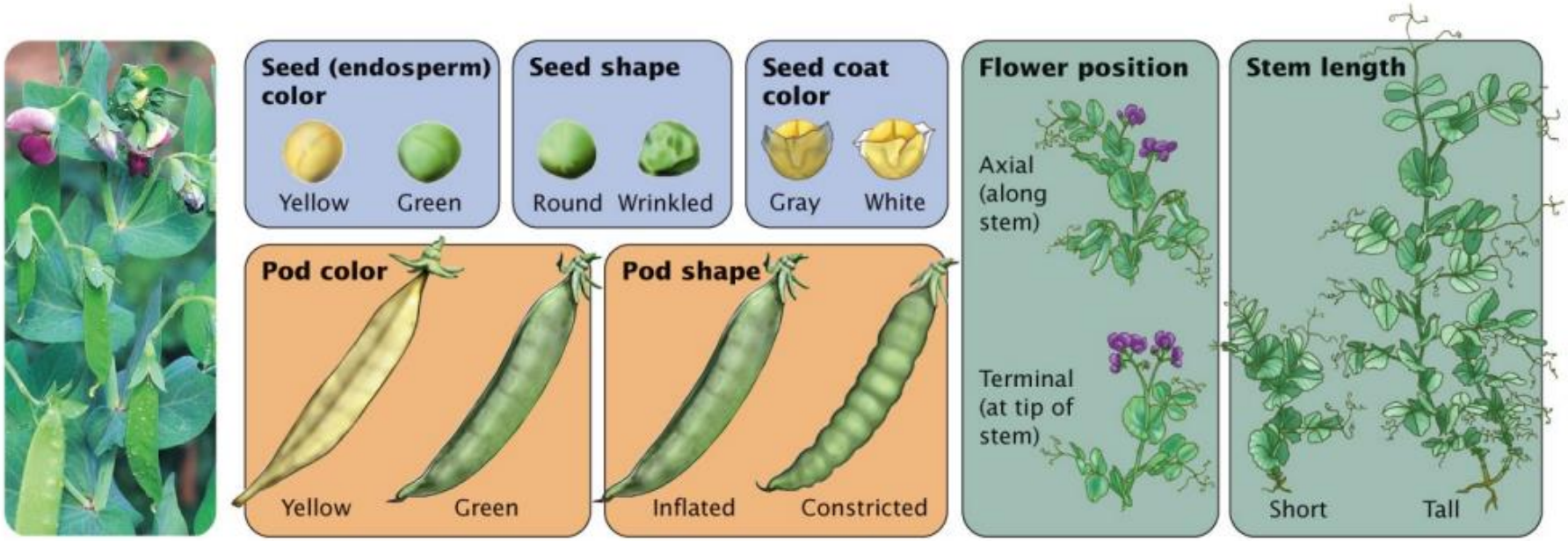


Fig_03-01 *Genetics, Second Edition* © 2005 W.H. Freeman and Company

https://www.genome.gov/about-genomics/fact-sheets/A-Brief-Guide-to-Genomics

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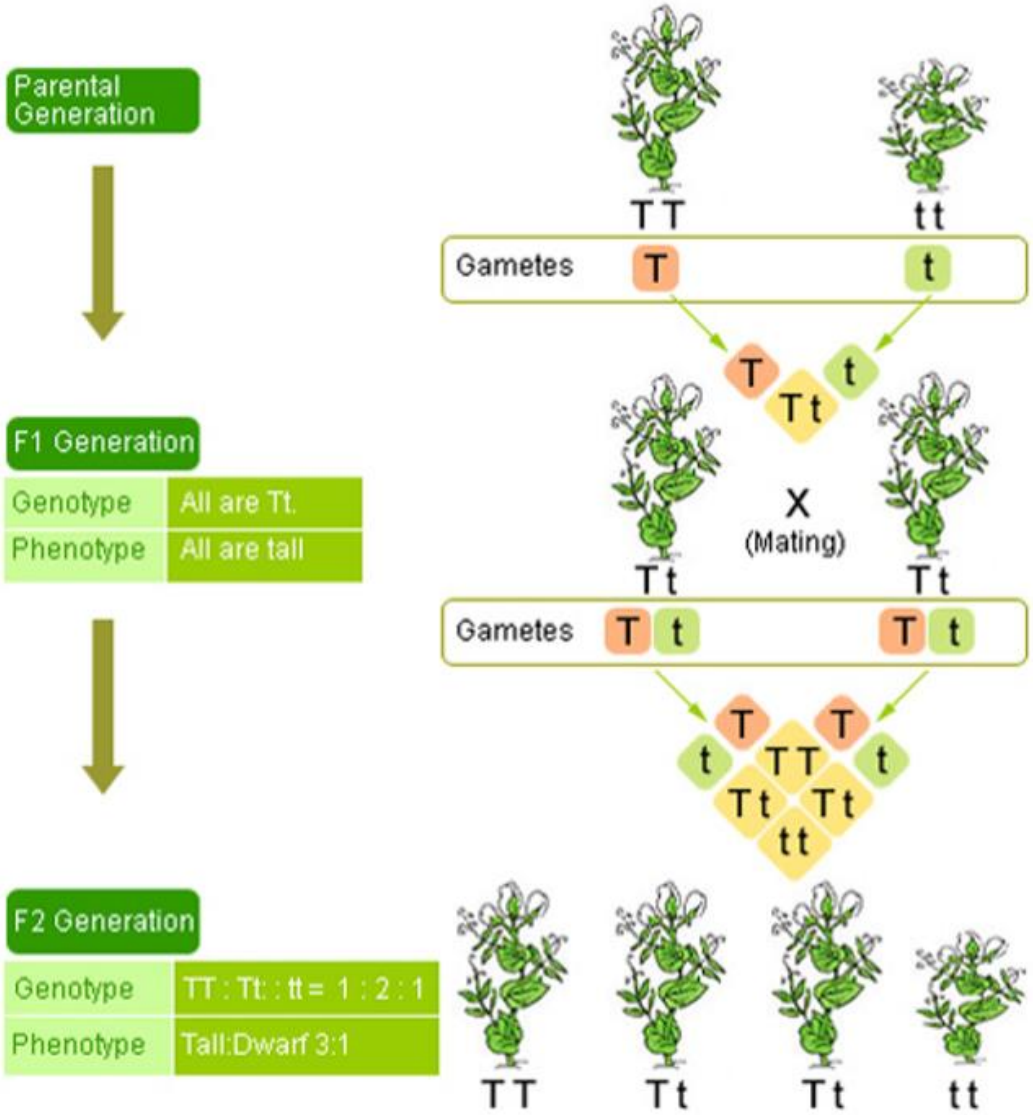


Law's of Inheritance

Law of Dominance: recessive alleles will always be masked by dominant alleles.

Law of Segregation: each gamete receives only one copy of a gene (allele)

Law of Independent Assortment: alleles of different genes sort independently during gamete formation

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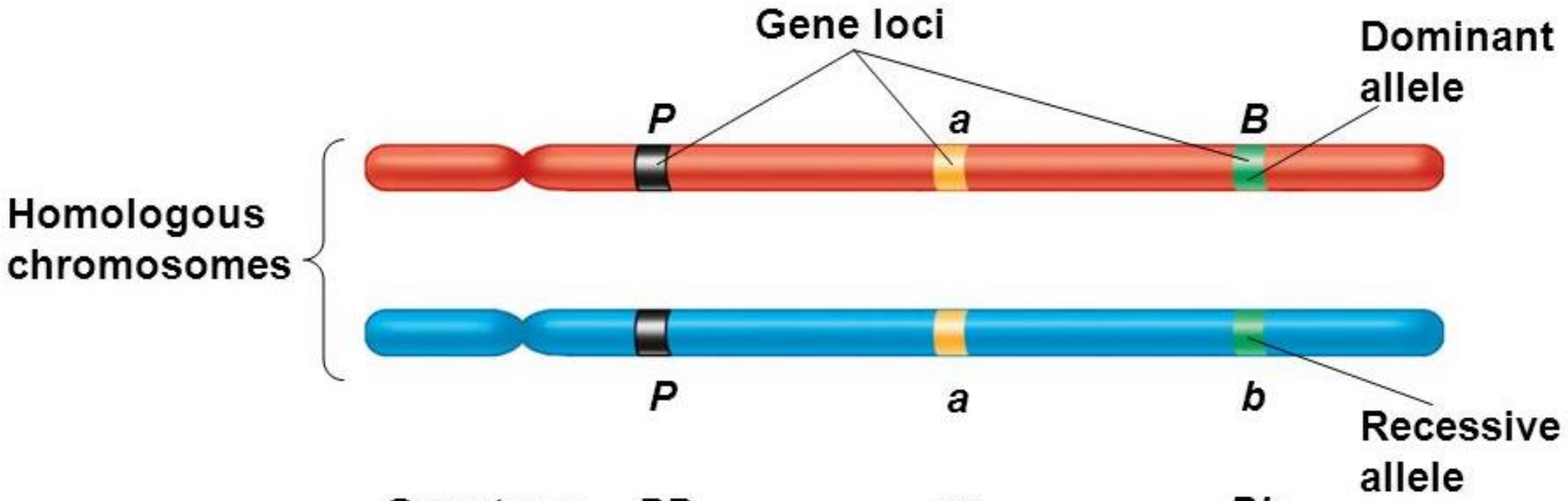



**Genotype:** ***PP*** ***aa*** ***Bb***

**Homozygous for the dominant allele**

**Homozygous for the recessive allele**

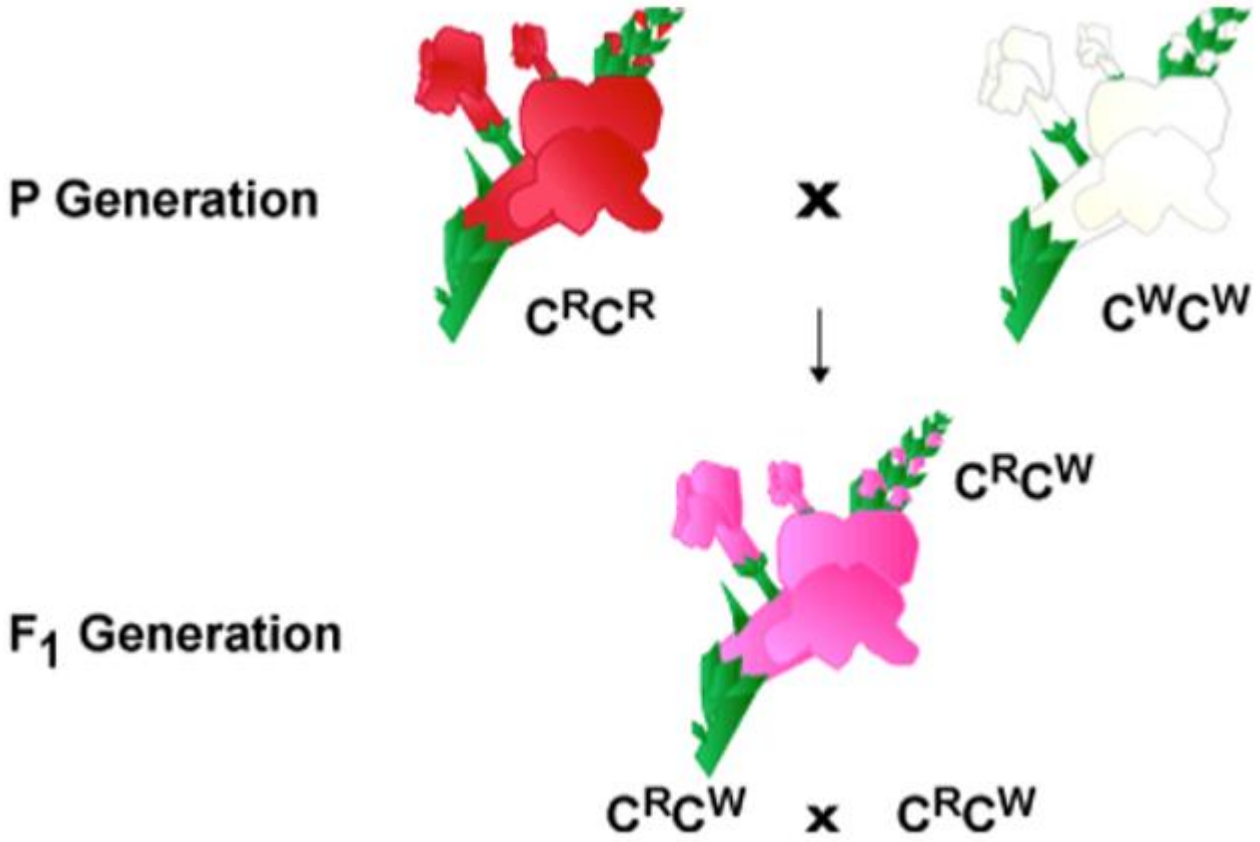
**Heterozygous, with one dominant and one recessive allele**



http://www.agilent.com/labs/features/2013_oliver.html

**Dominance may be incomplete or partial**

Codominance, Incomplete dominance
Example:  Snapdragon (Antirrhinum majus)
Incomplete dominance
Red x white = pink

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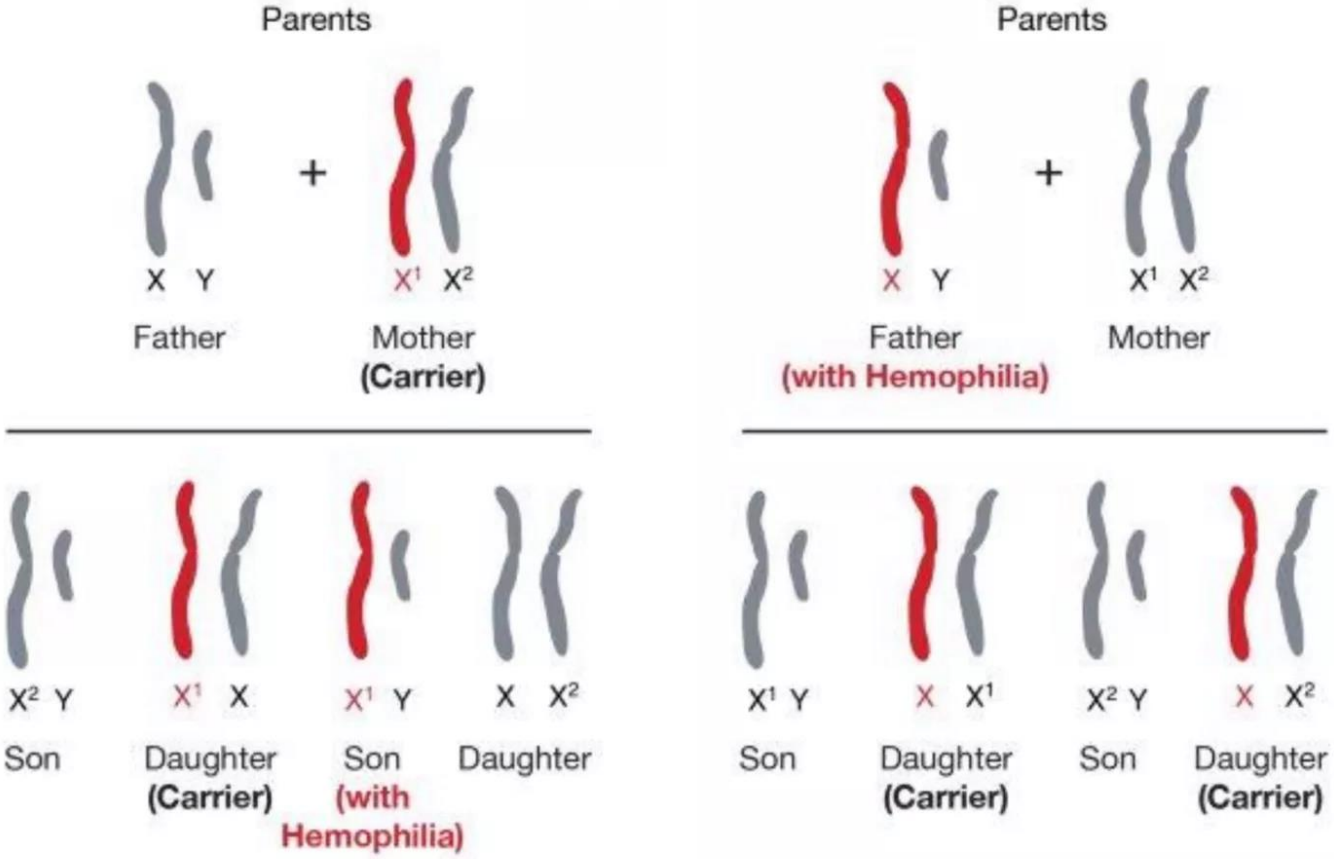
**Genes that are found on sex chromosomes are called sex-linked genes**

If a gene is located on the Y chromosome, it is a **Y-linked gene**. These genes are only inherited by males because, in most instances, males have a genotype of **(XY)**. Females do not have the Y sex chromosome. Genes that are found on the X chromosome are called **X-linked genes**.

## Hemophilia

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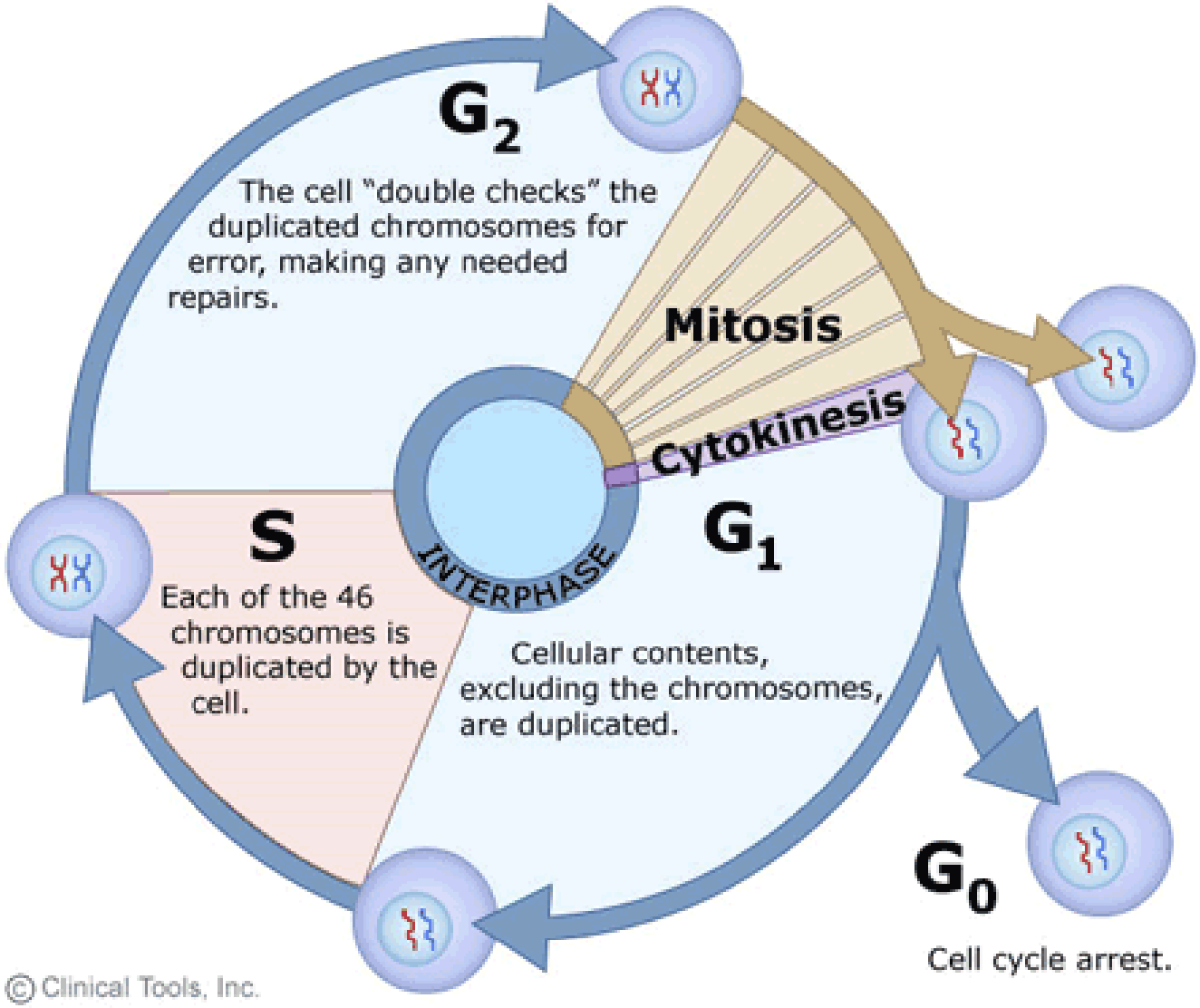
# Cell Cycle

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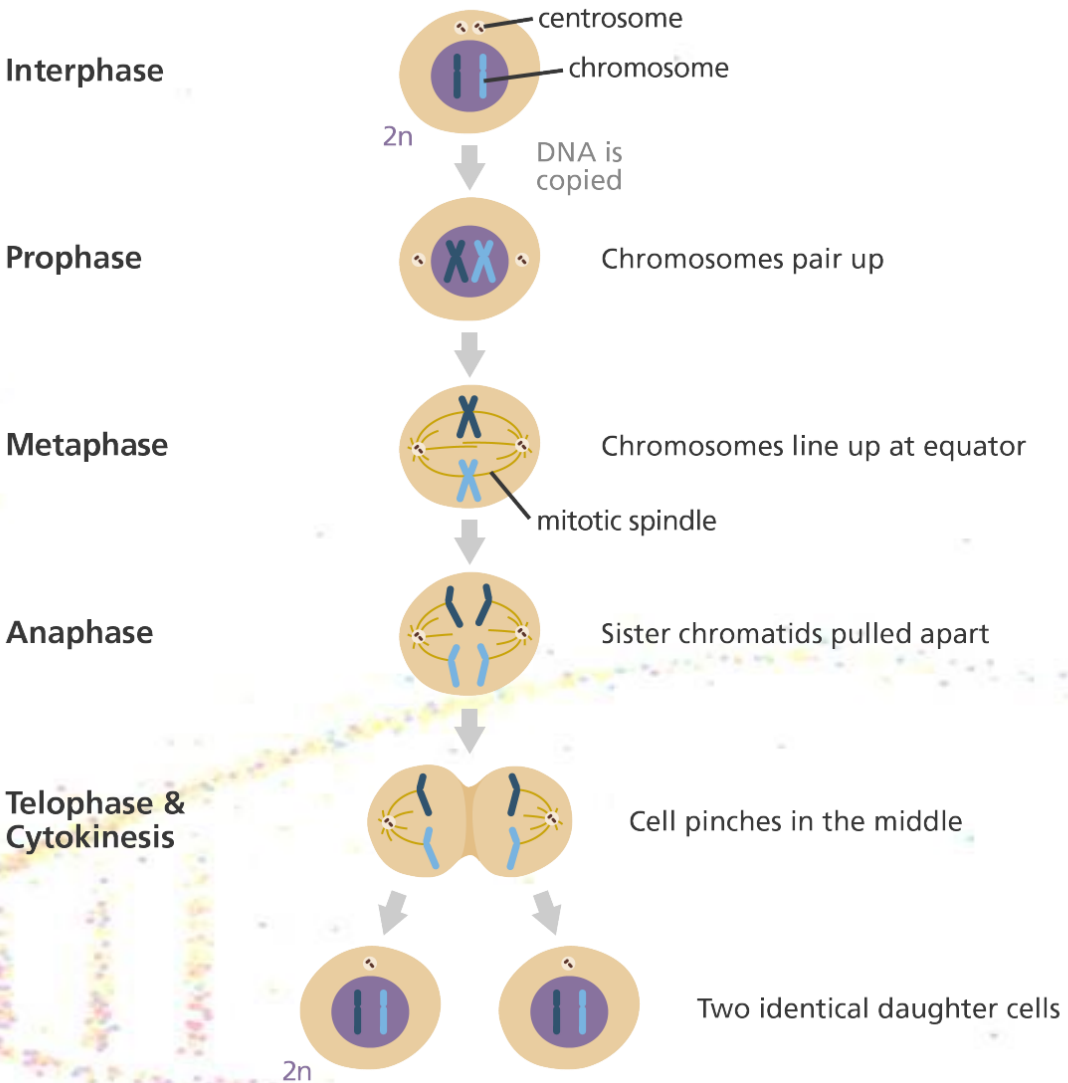
# Cell Division: Mitosis

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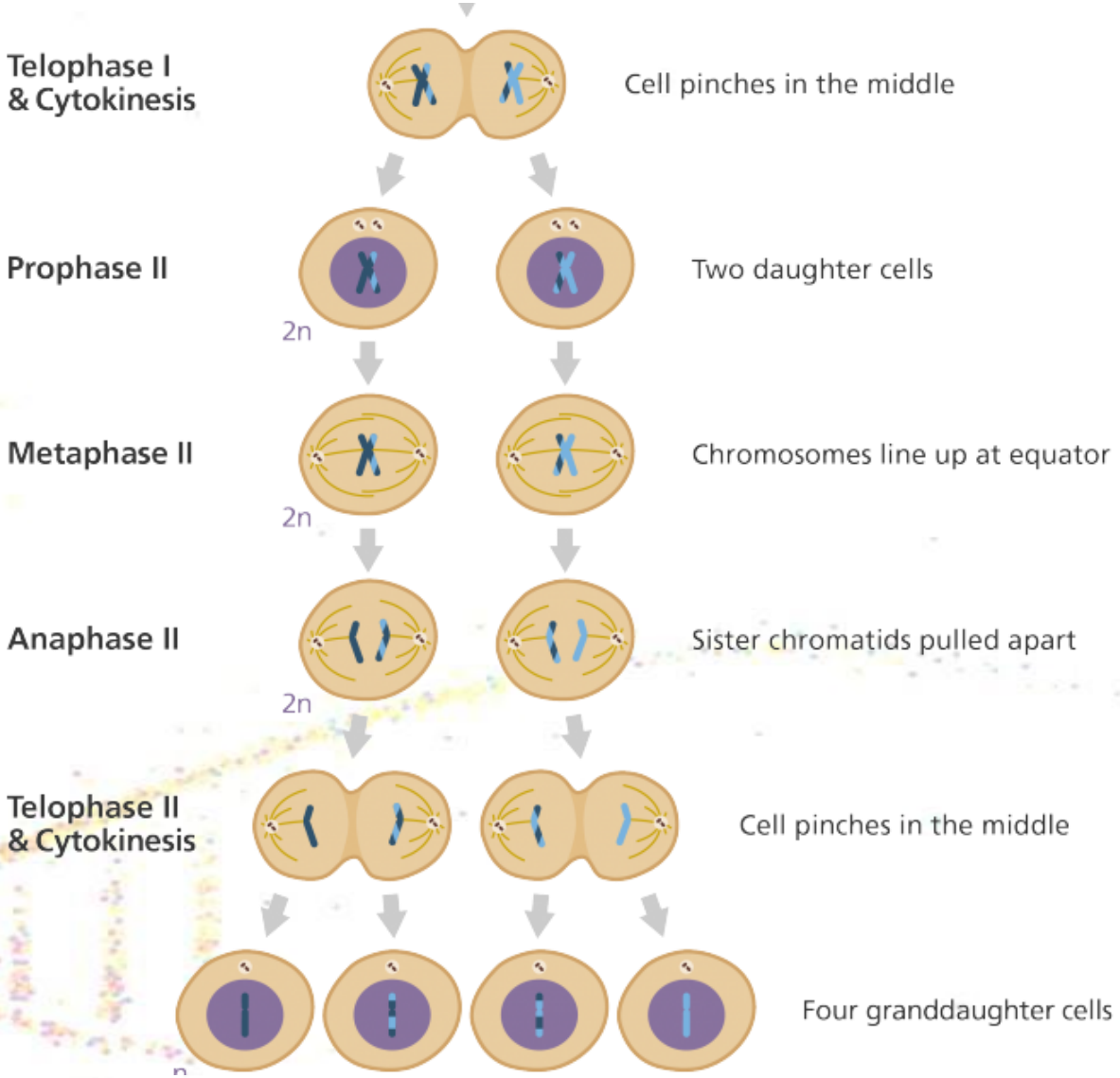
# Cell Division: Meiosis

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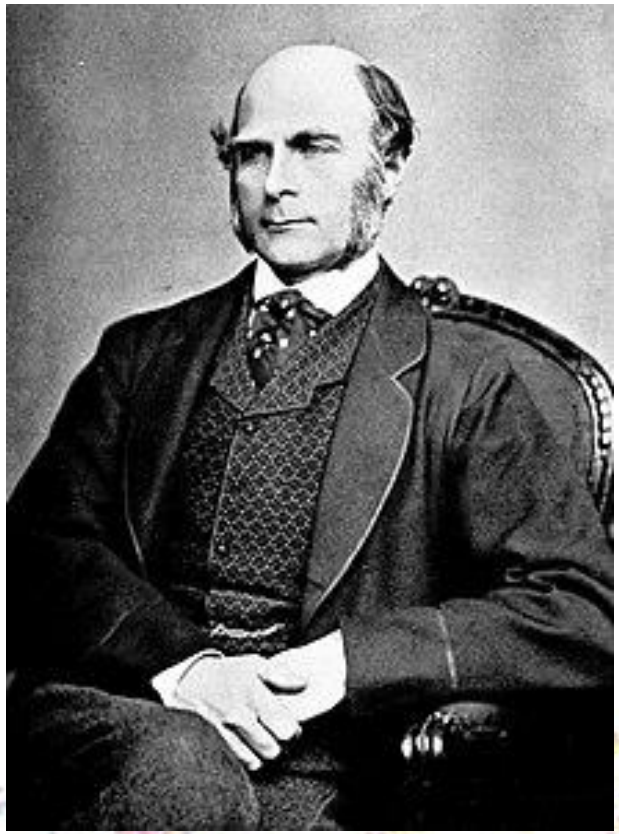
# Continuous Variation: Biometrics



Continuous variation does not show a few discrete alternative states but is found as a continuum in a population

e.g. Height in Humans, Skin color, Milk yield in cattle, IQ (intelligence quotient), Time to run 100m, Weight in humans

Sir Francis Galton

-introduced the Model for population stability and made a Statistical description of continuous traits. Continuous traits typically fit a normal distribution and they have a multifactorial inheritance meaning they are polygenic.

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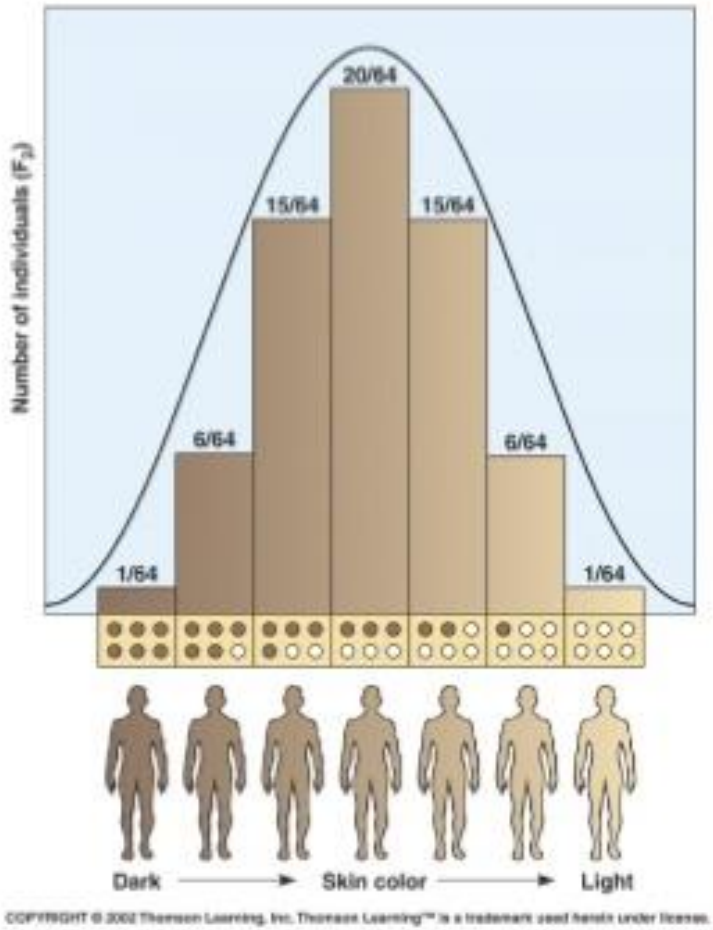
# Polygenic Traits

- The control of a trait by more than one gene
  - Skin color is controlled by at least 6 genes
- Each gene product is **additive** to the others
- The hallmark of a polygenic trait's phenotype expression is:
  - A bell curve distribution
  - A continuous distribution





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# The inheritance pattern of discrete variation (mendelian) vs continuous variation.

Are they different?

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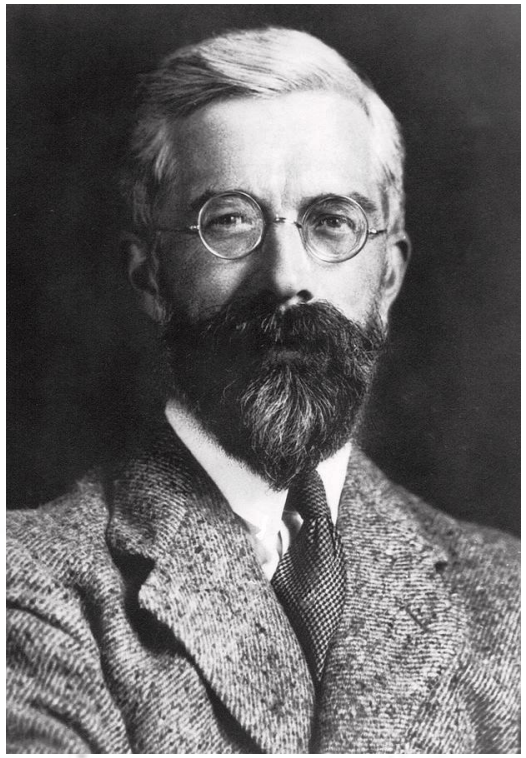
# Unifying Biometrics and Mendelian Inheritance



R.A. Fisher (1918): Biometrics meets Mendelian inheritance

- Inheritance of Continuous traits consistent with Mendelian genetics
- Additive effects of “many unblending particles of inheritance” could result in a normal distribution of the trait in a population
- Effects of genes are cumulative
- No one gene is dominant or recessive

Fisher, R. A. (1918). The Correlation between Relatives on the Supposition of Mendelian Inheritance. Transactions of the Royal society of Edinburgh, 52(02), 399-433.

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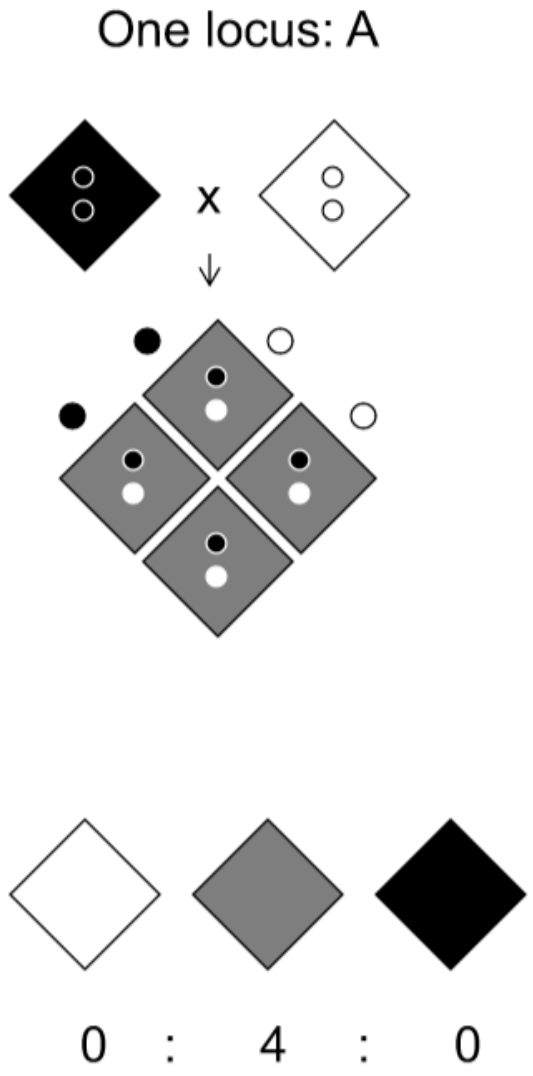
Consider a hypothetical trait:
Phenotype: Hair color

Polygenic trait
Additive effects of 2 alleles at multiple loci

‘Black’ allele
‘White’ allele

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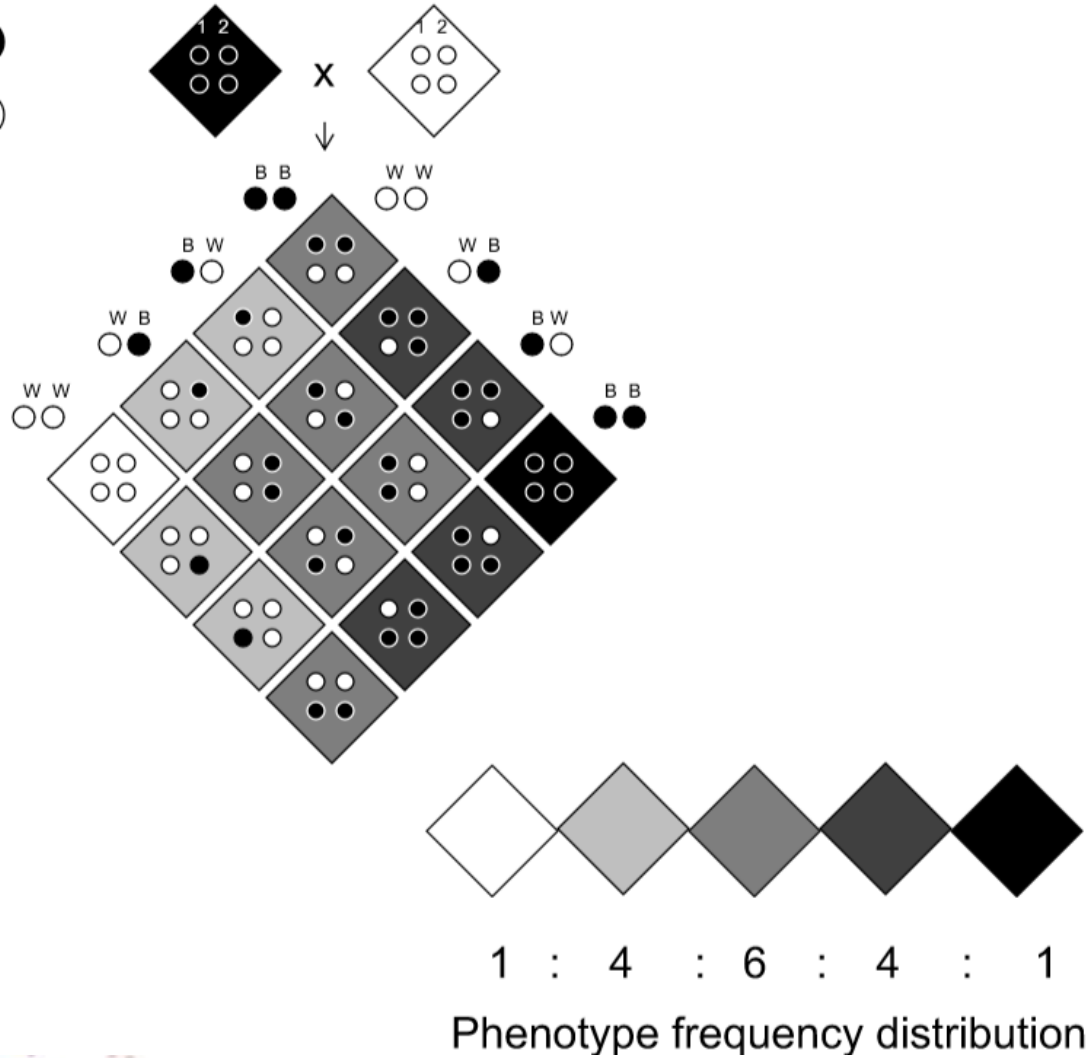
# Additive effects of 2 alleles at multiple loci

‘Black’ allele (B)
‘White’ allele (W)

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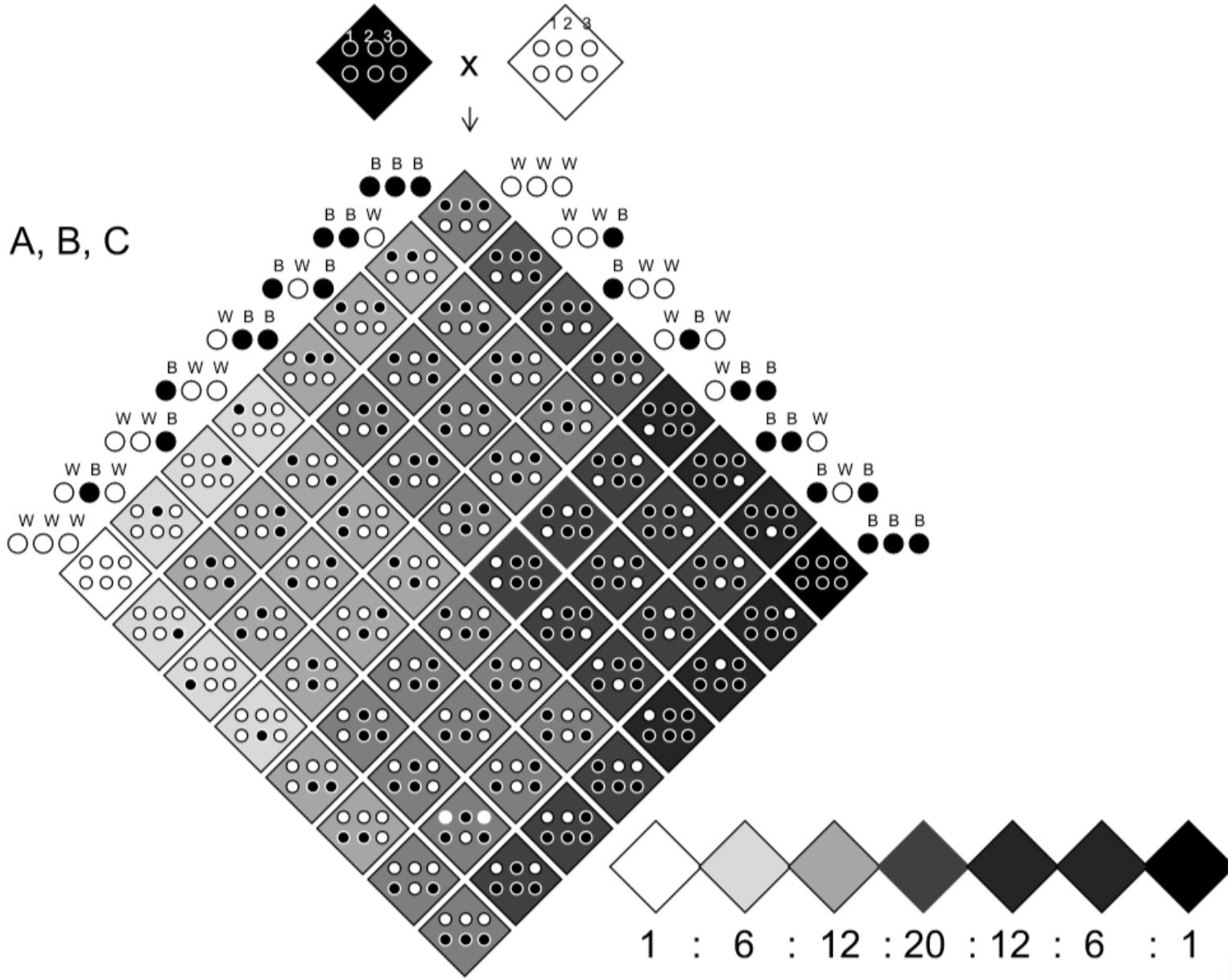
Three loci: A, B, C

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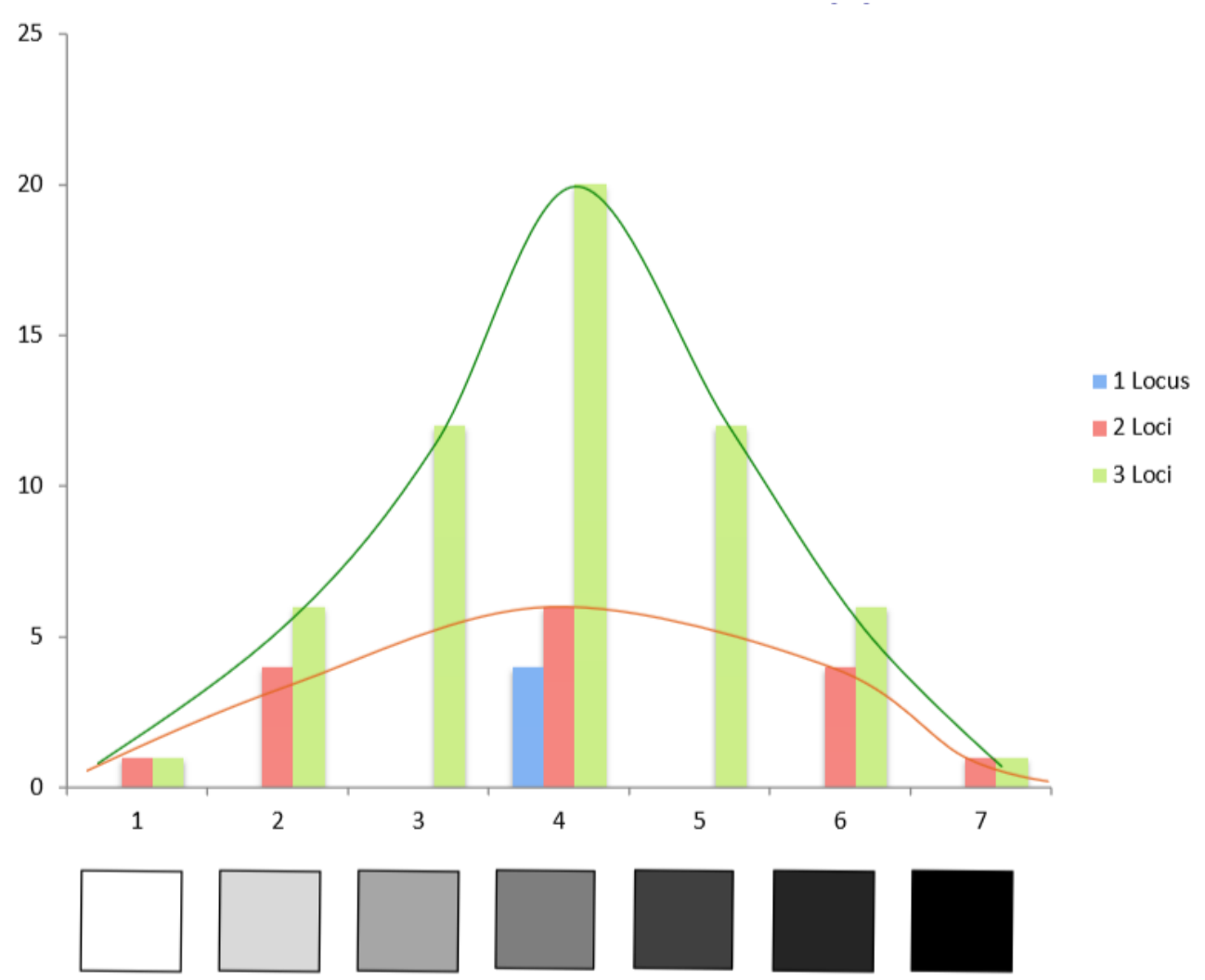


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# Modern Synthesis (Huxley, 1943)

Natural Selection
(Charles Darwin)

The Correlation between Relatives on the Supposition of Mendelian Inheritance.
(RA Fisher 1918)

Discrete Variation:
Mendelian Inheritance
(Gregor Mendel)

Continuous Variation
(Francis Galton)

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4318712/pdf/nihms622574.pdf an interesting paper to read

# Population Genetics

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**Population genetics** is the study of genetic variation within populations, and involves the examination and modeling of changes in the frequencies of genes and alleles in populations over space and time.

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# Mutation

Mutation: Ultimate source of new variation

Point mutations, SNPs
Insertions, deletions = frameshift
Large-scale mutations in chromosomal structure
    Chromosomal inversions, translocations
    Transposable elements


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# Genetic Drift

Stochastic change in allele frequency due to random sampling in a finite population

Two types of Drift

- Founder Effect
- Bottleneck Effect

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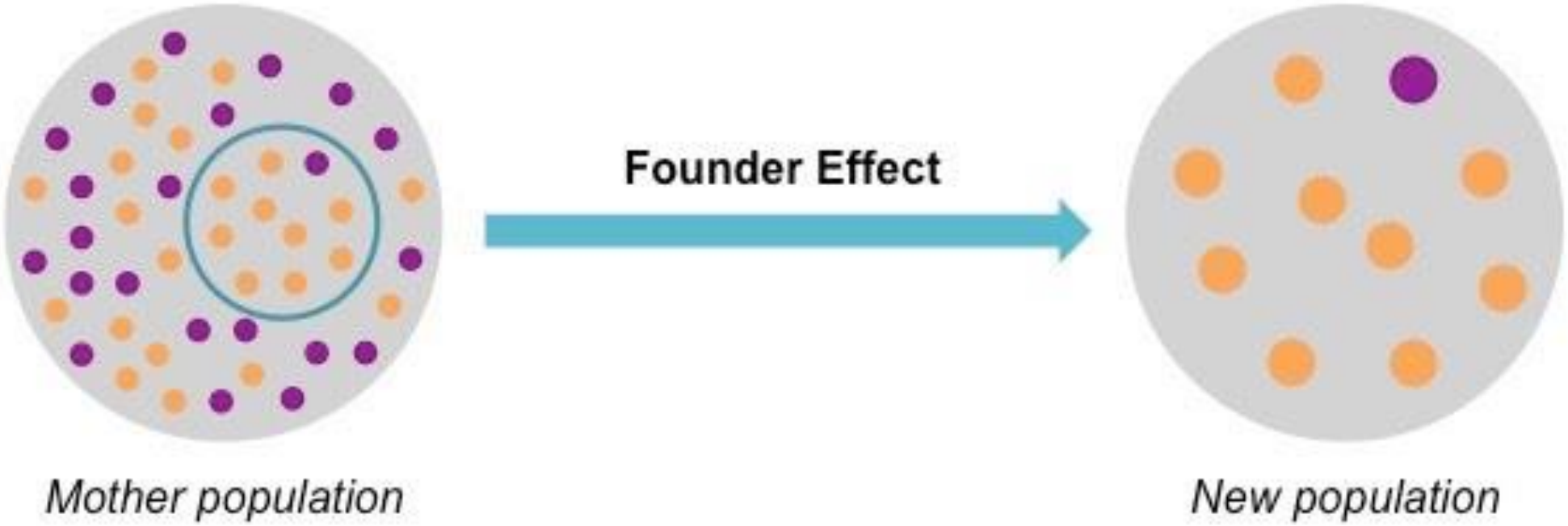
Founder Effect
Mother population
New population

# Population bottleneck

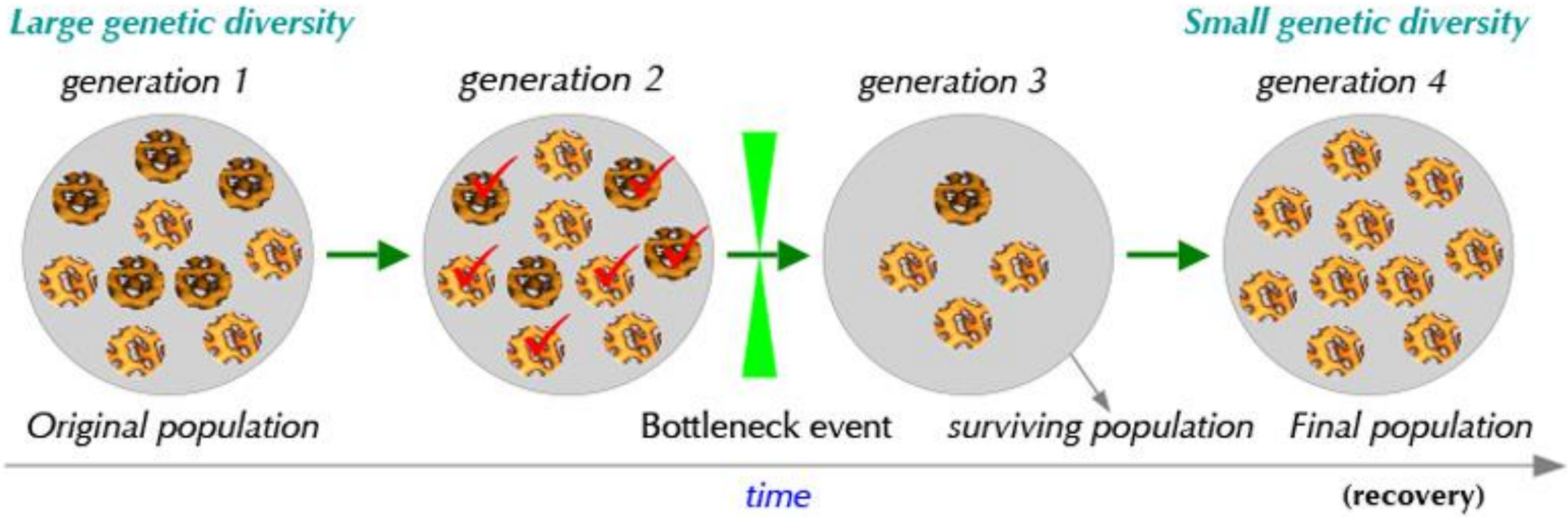


Image design: COSNET Lab

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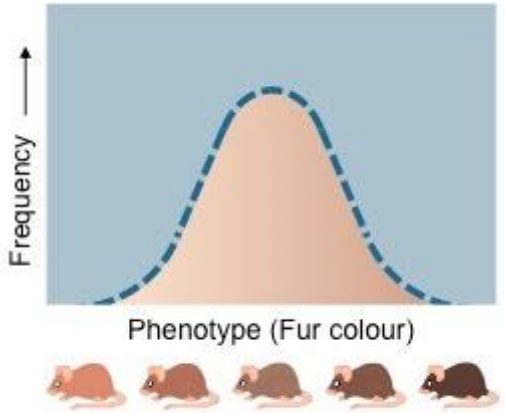
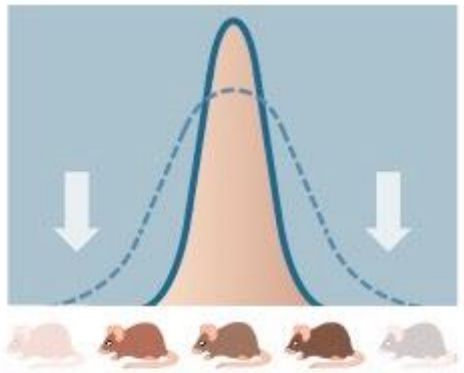
# Selection

Natural selection is the differential survival and reproduction of individuals due to differences in phenotype. It is a key mechanism of evolution, the change in the heritable traits characteristic of a population over generations.




**Normal Distribution**

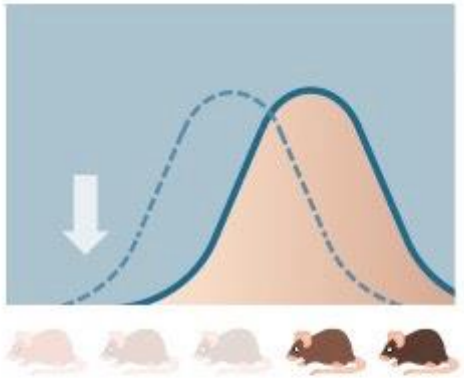
Gaussian (bell-shaped) trend



**Stabilising Selection**

Culls extreme variations

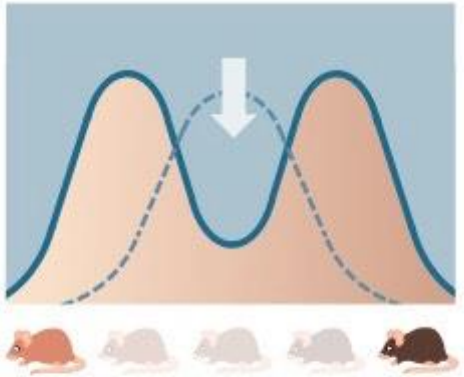
Narrows width of distribution



**Directional Selection**

Favours one extreme

Shifts distribution left / right



**Disruptive Selection**

Favours both extremes

Creates bimodal distribution

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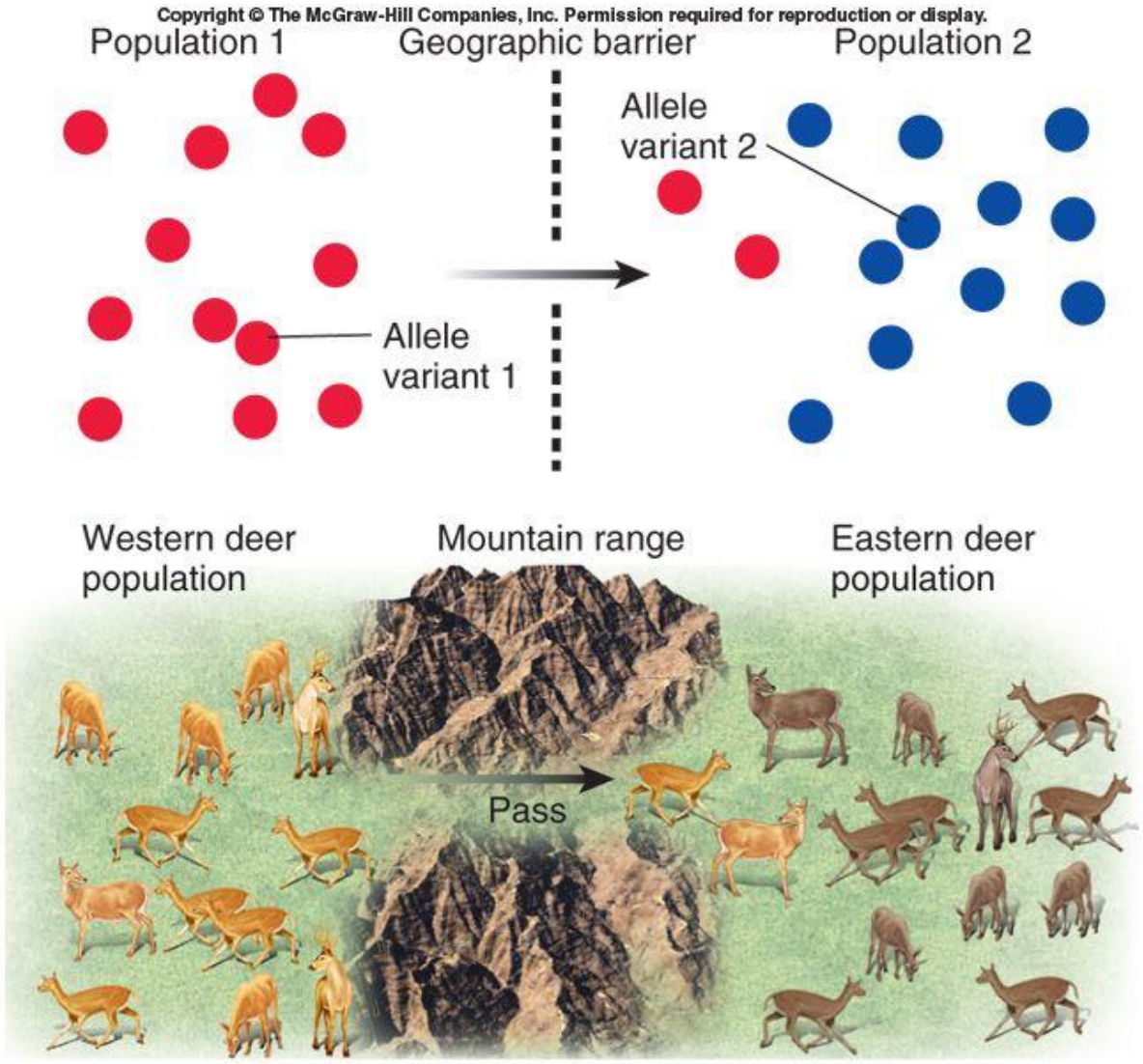
# Gene Flow

Gene flow is the movement of alleles from one genetic pool (population) to another.

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# Hardy-Weinberg Equilibrium (HWE)

Allelic frequencies will remain the same from one generation to the next with the following assumptions:

There is no mutation, no migration, no selection, population is infinitely large and randomly mating

$$(p + q)^2 = 1$$

$$p2 + 2pq + q2 = 1$$

For a diploid organism, consider a 2 allele locus (A, a), where A is dominant

Let:
*p* = frequency of allele A
*q* = frequency of allele a

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## Violations of HWE

- Small population size
- Deviations from random mating
- Assortative mating
- Disassortative mating
- Inbreeding
- Population structure
- Mutation
- Migration
- Selection

# Testing for deviations from HWE expectations:

Chi-square test: goodness of fit between observed & expected frequencies

| Genotype | Observed | Expected | |
|---|---|---|---|
| MM | 165 | | |
| MN | 562 | | |
| NN | 339 | | |
| Total | 1066 | | |

1. Calculate allele frequencies p and q (for M and N, respectively):

$$p = \frac{2 \times 165 + 562}{2 \times 1066} = \frac{892}{2132} = 0.4184$$

$$q = 1 - 0.4184 = 0.5816$$

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# Testing for deviations from HWE expectations:

Chi-square test: goodness of fit between observed & expected frequencies

| Genotype | Observed | Expected | |
|---|---|---|---|
| MM | 165 | 186.61 | |
| MN | 562 | 518.80 | |
| NN | 339 | 360.58 | |
| Total | 1066 | | |

1. Calculate allele frequencies p and q (for M and N, respectively):
2. Calculate expected number of individuals per genotype:

$MM = 0.4184^2 \times 1066 = 186.61$

$MN = 2(0.4184)(0.5816) \times 1066 = 518.80$

$NN = 0.5816^2 \times 1066 = 360.58$

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# Testing for deviations from HWE expectations:

Chi-square test: goodness of fit between observed & expected frequencies

| Genotype | Observed | Expected | |
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| MM | 165 | 186.61 | |
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| Total | 1066 | | |

1. Calculate allele frequencies p and q (for M and N, respectively):
2. Calculate expected number of individuals per genotype:
3. Calculate $X^2$

$$\chi^2 = \sum \frac{(Observed - Expected)^2}{Expected}$$

$$X^2 = \frac{(-21.6)^2}{181.61} + \frac{(43.2)^2}{518.80} + \frac{(-21.6)^2}{360.58} = 7.46$$

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# Testing for deviations from HWE expectations:

Chi-square test: goodness of fit between observed & expected frequencies

| Genotype | Observed | Expected | |
|---|---|---|---|
| MM | 165 | 186.61 | |
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| Total | 1066 | | |

1. Calculate allele frequencies p and q (for M and N, respectively):
2. Calculate expected number of individuals per genotype:
3. Calculate $X^2$
4. Determine probability of $X^2$ from $X^2$ distribution table

Degrees of freedom = 3 -1 -1

Since P < 0.05, there is significant deviation from HWE.

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# How do we detect variation?

**MARKER : Object or feature used to identify, distinguish**

| Marker Class | Level of Analysis |
|---|---|
| Morphological | Phenotype |
| Biochemical | Gene Product (Protein) |
| Molecular | DNA sequence |

**MOLECULAR MARKER**

Specific locations in the genome where variation is observed

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# DNA Markers: Location + Types of variation

1. Location
    - Nuclear DNA
    - Cytoplasmic DNA –mitochondria, chloroplast

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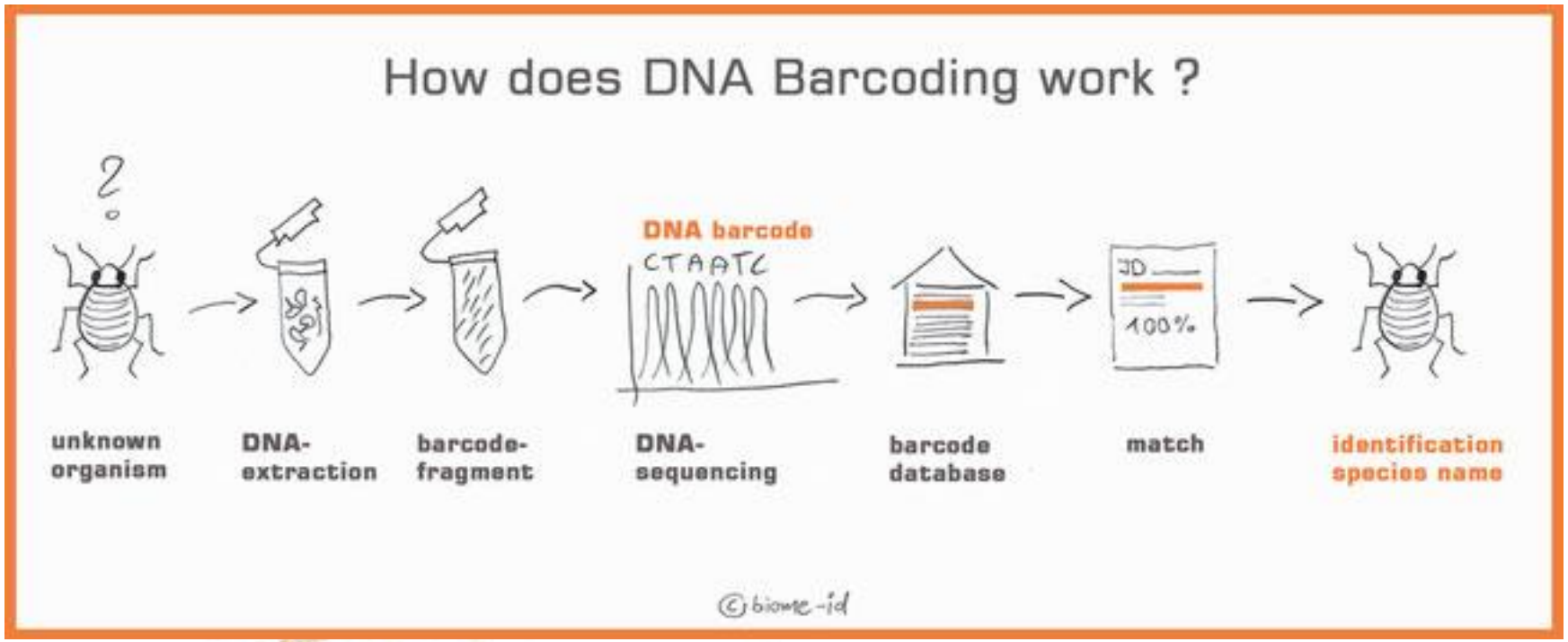
# Mitochondrial DNA marker – COI (Cytochrome oxidase I)

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# DNA Markers: Location + Types of variation

1. Location
    - Nuclear DNA
    - Cytoplasmic DNA –mitochondria, chloroplast

2. Types of Mutation
    - Point mutations
    - Insertions/Deletions
    - Sequence repeats
    - Inversions
    - Translocations

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DNA Markers:

# Types of variation

1. Point mutations – sequence change

2. Insertions/Deletions – sequence AND length change
   - Tandem repeats



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DNA Markers:

# Tandem repeats

- 2 or more nucleotides are repeated, adjacent to each other
  - Microsatellites : 2 – 6 bp units
  - Minisatellites: 10 – 100 bp units
- Change in length (length variants = alleles)

```
Allele 1   AGTCTGCACACACACACA--------TGTCAAGCT   (CA)6
Allele 2   AGTCTGCACACACACACACACA----TGTCAAGCT (CA)8
Allele 3   AGTCTGCACACACACACACACACACACATGTCAAGCT (CA)10
```

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Table 1 | **Comparison of different molecular markers**

| Marker | Advantages | Disadvantages |
|---|---|---|
| SNPs | • Low mutation rate<br>• High abundance<br>• Easy to type<br>• New analytical approaches are being developed at present<br>• Cross-study comparisons are easy; data repositories already exist | • Substantial rate heterogeneity among sites<br>• Expensive to isolate<br>• Ascertainment bias<br>• Low information content of a single SNP |
| Microsatellites | • Highly informative (large number of alleles, high heterozygosity)<br>• Low ascertainment bias<br>• Easy to isolate | • High mutation rate<br>• Complex mutation behaviour<br>• Not abundant enough<br>• Difficult to automate<br>• Cross-study comparisons require special preparation |
| Allozymes | • Cheap<br>• Universal protocols | • Requirement for fresh or frozen material<br>• Some loci show protein instability<br>• Limited number of available markers<br>• Potentially direct target of selection |
| RAPDs and derivatives | • Cheap<br>• Produces a large number of bands, which can then be further characterized individually (for example, converted into single locus markers) | • Low reproducibility<br>• Mainly dominant<br>• Difficult to analyse<br>• Difficult to automate<br>• Cross-study comparisons are difficult |
| DNA sequencing | • Highest level of resolution possible<br>• Not biased<br>• Cross-study comparisons are easy; data repositories already exist | • Still significantly more expensive than the other techniques |

RAPD, randomly amplified polymorphc DNA; SNP, single nucleotide polymorphism.