INTRODUCTION TO MEDICAL GENETICS

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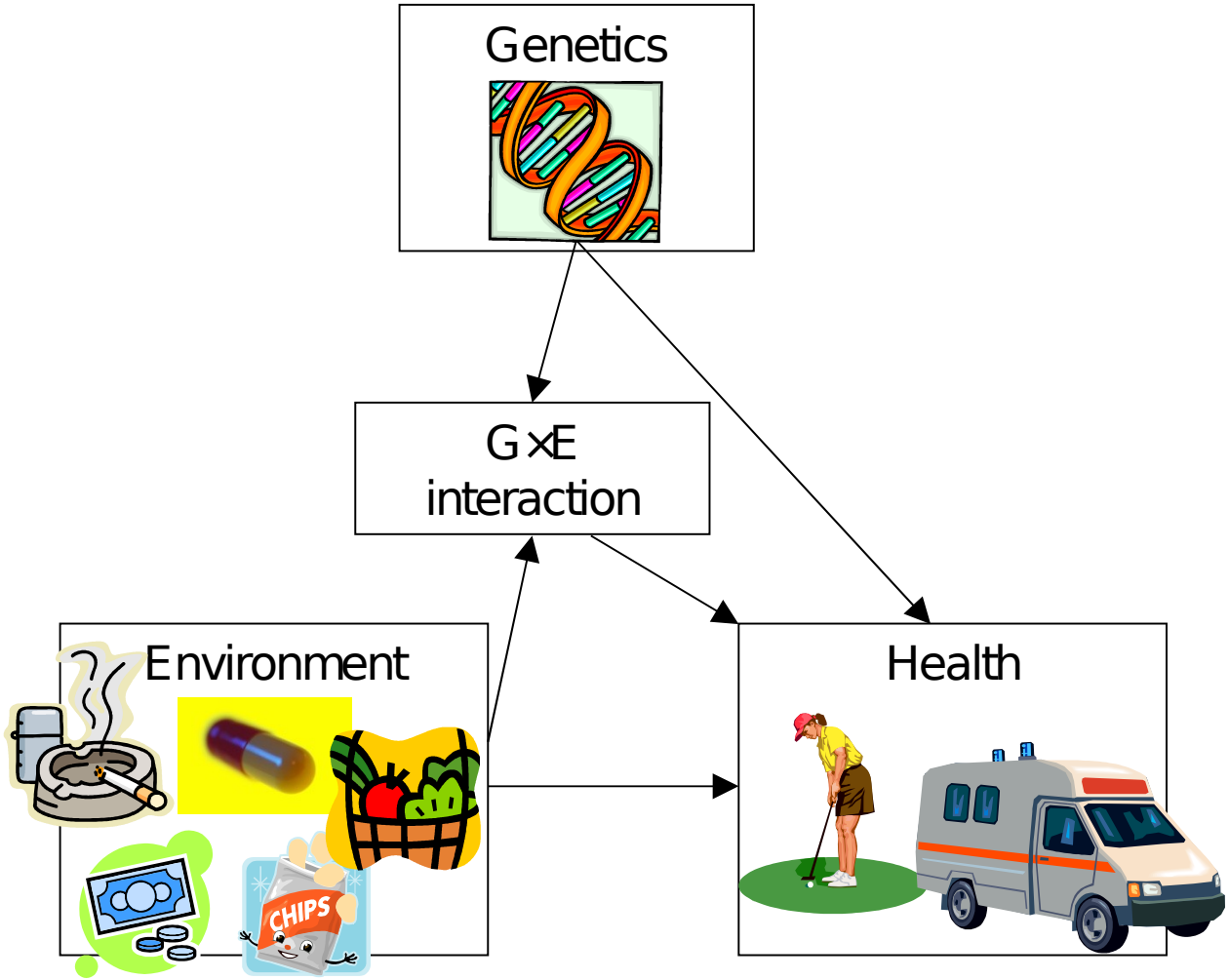
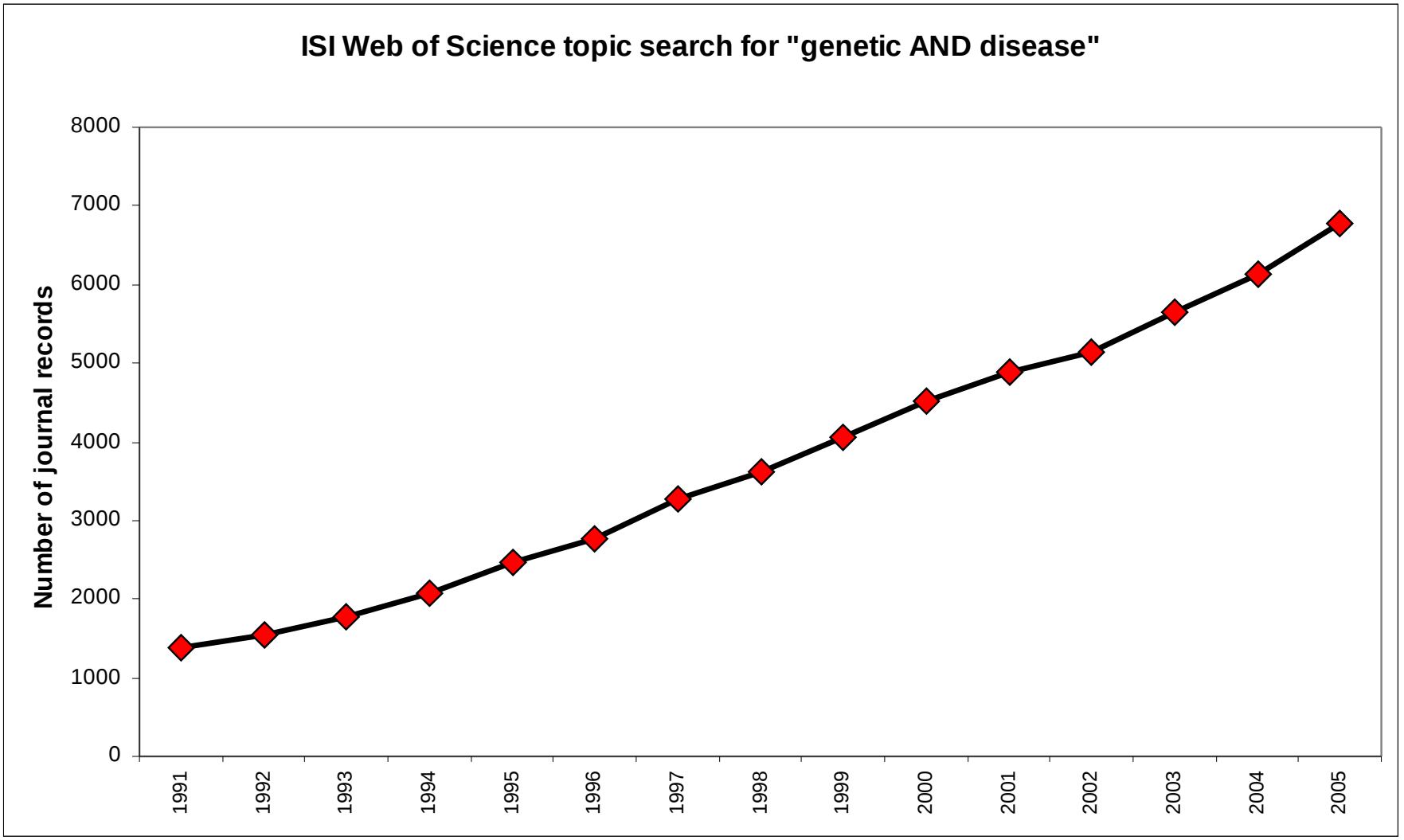
What is Genetics?

Importance of genetics





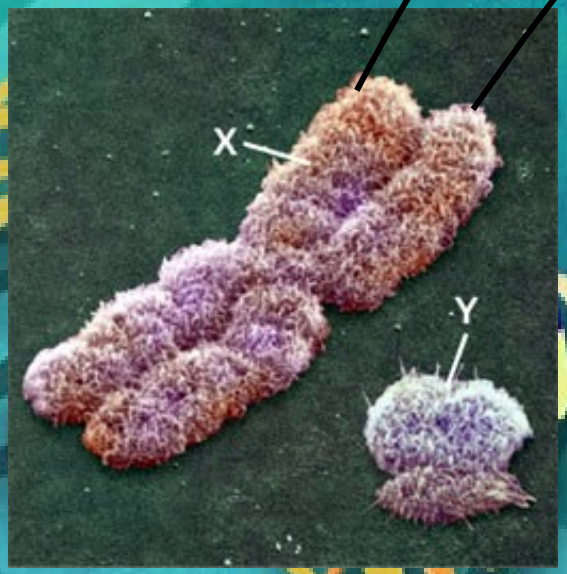
Branches of genetics

- Medical Genetics.
- Plant genetics.
- Population genetics.
- Cytogenetics.
- Molecular genetics.
- Oncogenetics.
- Nutrogenetics.

Genome Size

Species	Size in bps
Amoeba dubia	670,000,000,000
Homo sapiens	3,400,000,000
Drosophila melanogaster	180,000,000
Mycoplasma genitalium	580,000
Human immunodeficiency virus	9,750

DNA the Molecule of Life



cell

chromosomes

Chromosome

Locus

Allele

Homozygous Alleles

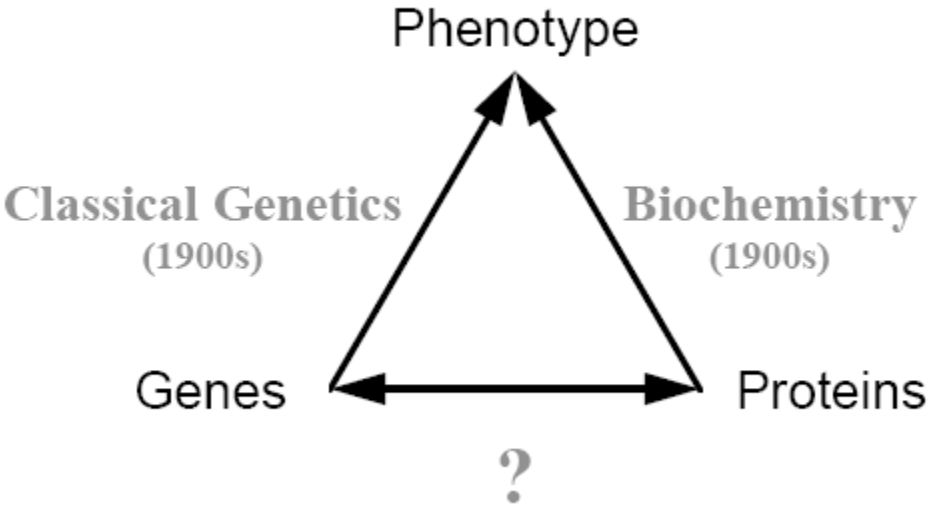
Heterozygous Alleles

Locus – *location of a gene/marker on the chromosome.*

Allele – *one variant form of a gene/marker at a particularlocus*

Genome and genes

- **Gene**: basic unit of genetic information. Genes determine the inherited characters.
- **Genome**: the collection of genetic information.
- **Chromosomes** :storage units of genes.
- **DNA** : is a nucleic acid that contains the genetic instructions specifying the biological development of all cellular forms of life



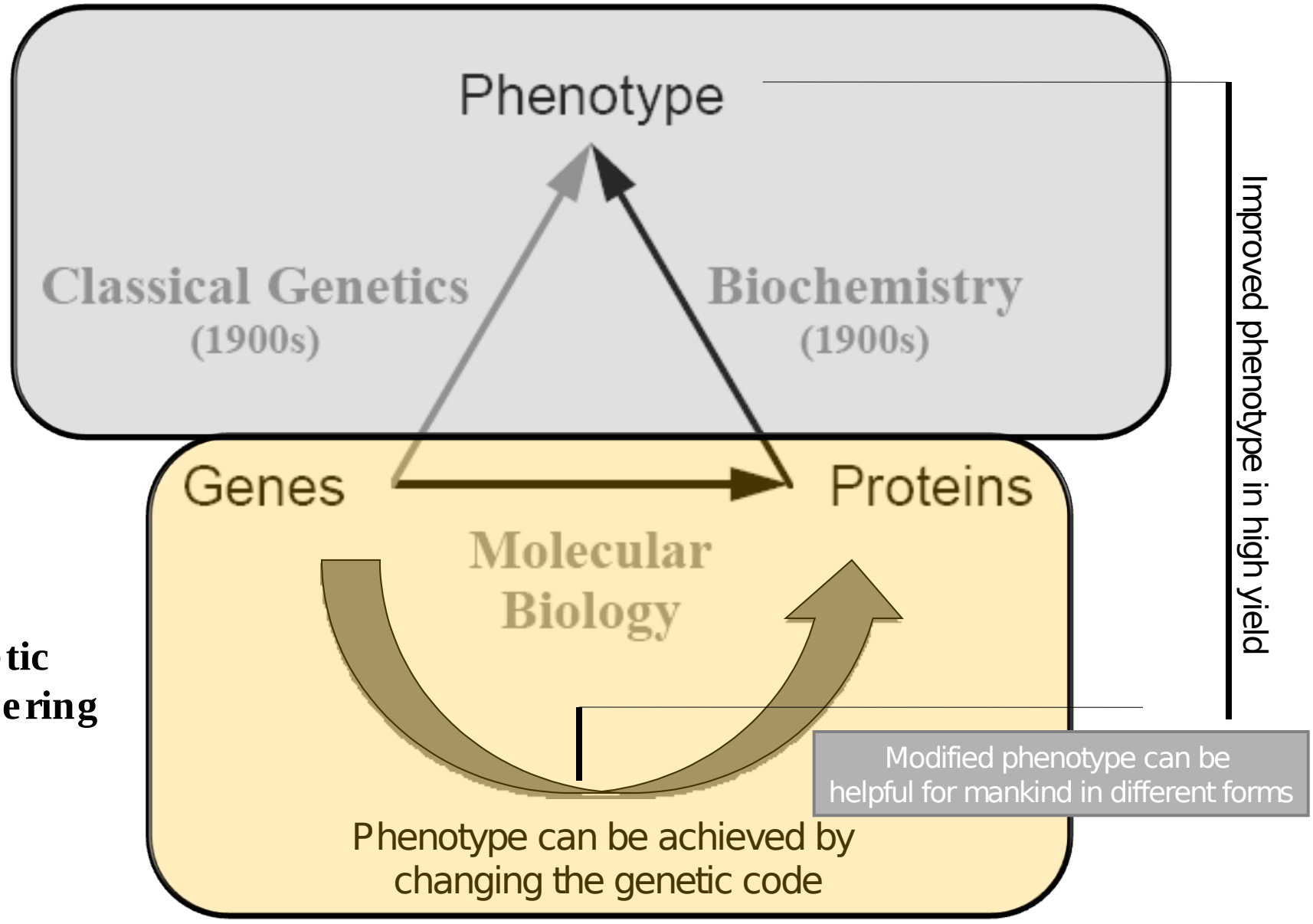
The ***phenotype*** ***of an organism denotes its external appearance*** ***(size, color,*** intelligence, etc.).

Classical genetics ***showed that genes control the*** transmission of phenotype from one generation to the next.

Biochemistry showed that within one generation, *proteins had a determining effect on* phenotype.

WHAT IS A RELATION BETWEEN A GENE & A PROTEIN ?

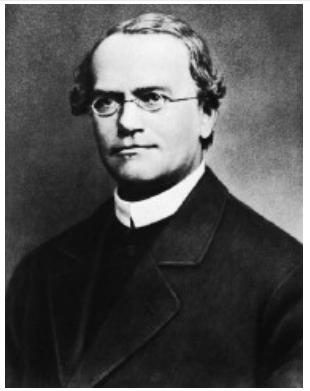
Biotechnology



Genetic Engineering

Mendel Inheritance

Australian monk who formulated fundamental law of heredity in early 1860s.

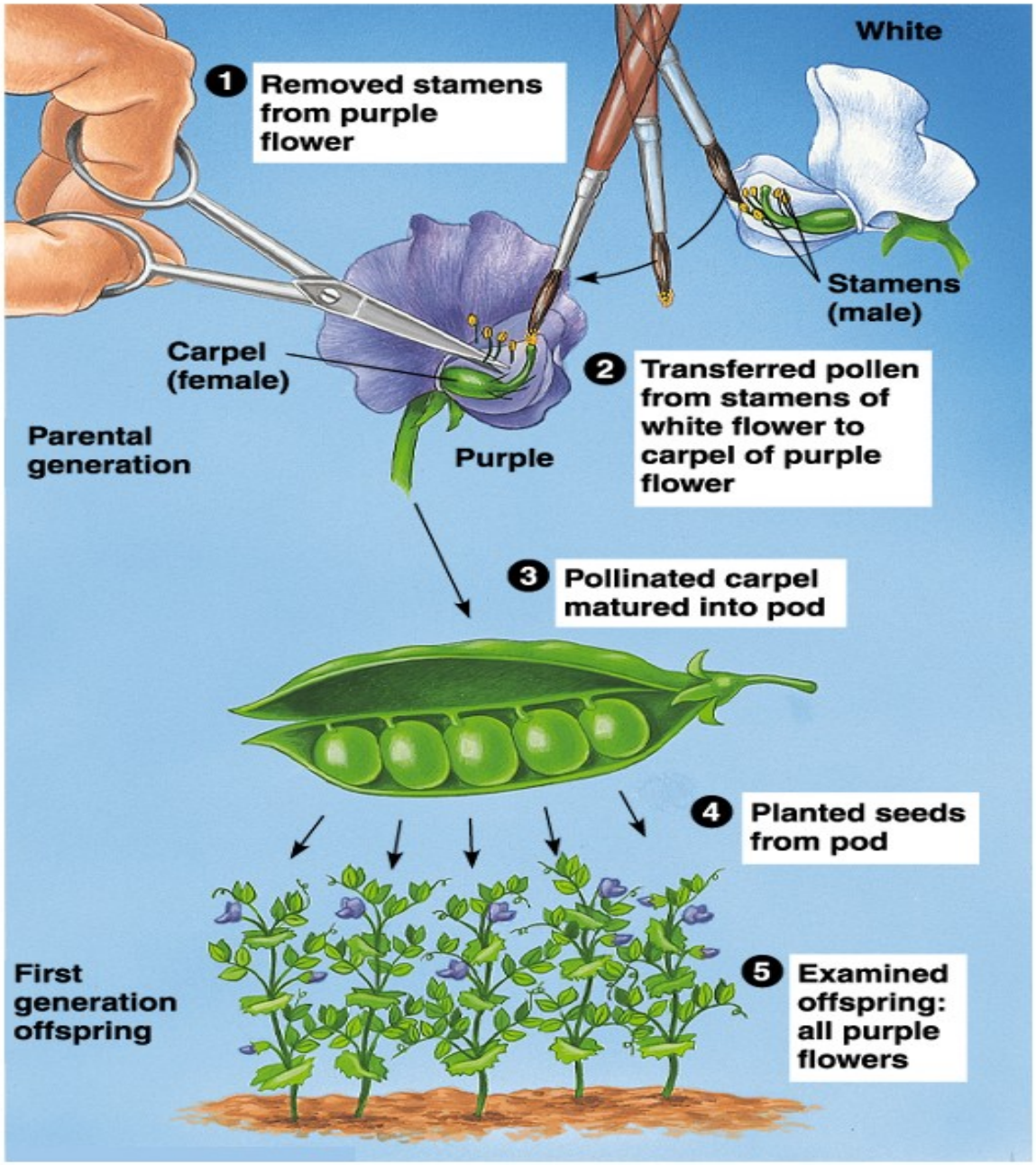


Gregor Mendel
(1822-1884)

Theories of inheritances

Reshuffling of genes from generation to generations

He studied mathematics at University of

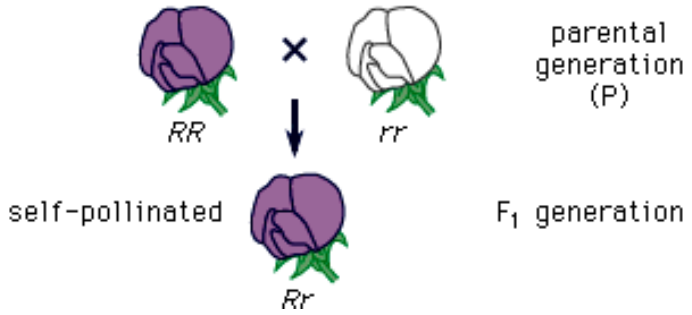


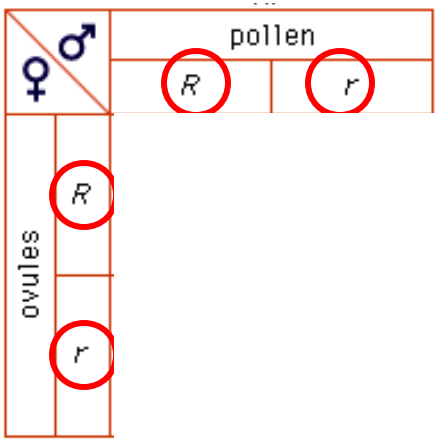
One trait inheritance

- Mendel performed cross-breeding experiments between true breeding plants (homozyous).
- Choose varieties that differed in only one trait (monohybrid).
- Performed crosses:
- Parental generation = P
- First generation offspring = F1 (1st filial)
- Second generation offspring = F2 (2nd filial)

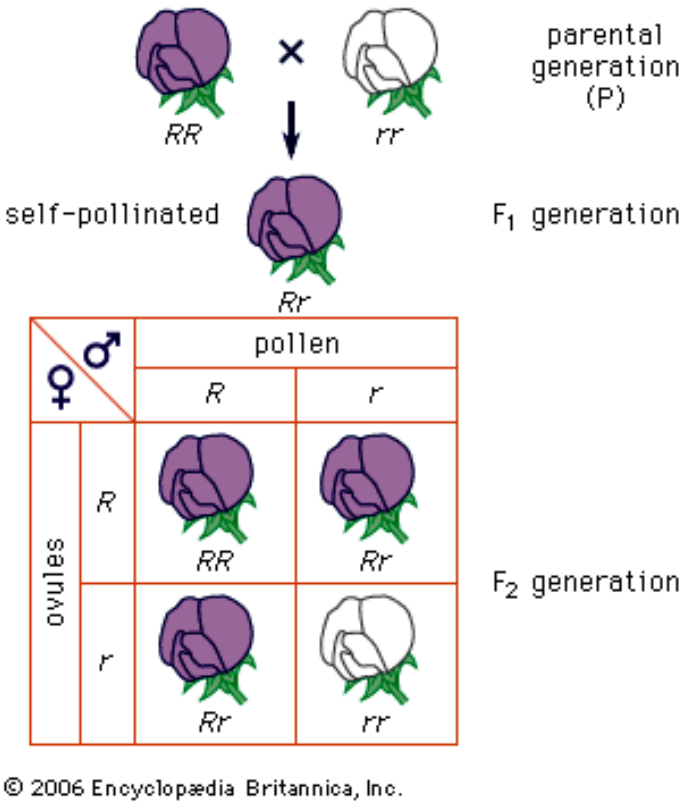
Law of segregation

- Each individual has two factors for each trait.
- The factors separate when gametes form.
- A gamete contains only one of two factors.
- Fertilization = new individual with 2 factors for each trait.





Genotype Vs Phenotype



Genotype

Refers to the alleles an individual receives

Genotypic frequency

Frequency of specific allelic recombination

RR : Rr : rr

1 :2 : 1

Phenotype

Refers to the physical appearance of the individual

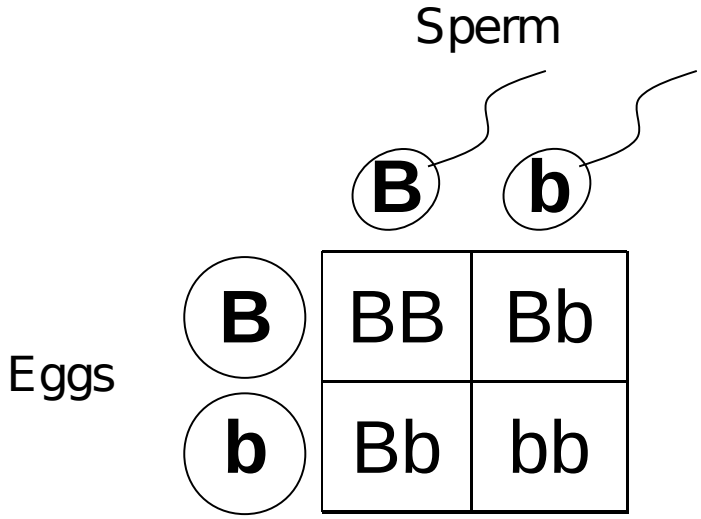
Phenotypic frequency

Round : Oval

3 : 1

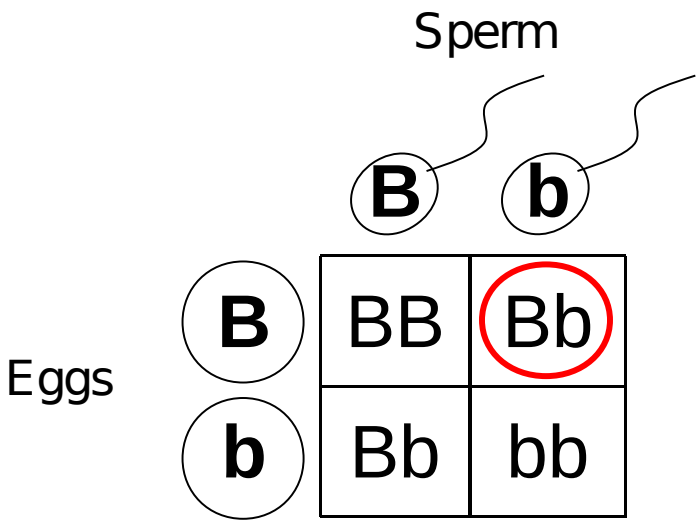
Modern genetics and Law of segregation

- E.g. if you have one allele for brown eyes (B) and one for blue eyes (b), somatic cells have Bb and each gamete will carry one of B or b chosen randomly



Mendel's law of dominance

- If your two alleles are different (*heterozygous*, e.g. Bb), the trait associated with only one of these will be visible (dominant) while the other will be hidden (recessive). E.g. B is dominant, b is recessive.



Genotypic frequency: BB : Bb : bb
1 : 2 : 1

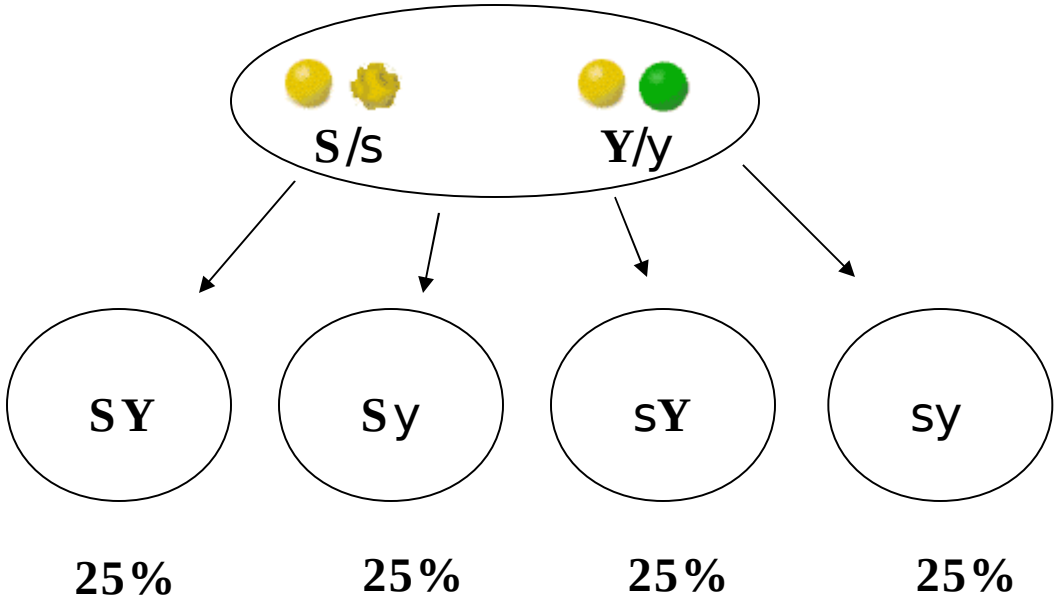
Phenotypic frequency:
Brown : Blue
3 : 1

ominant allele: The allele which is always visible phenotypically or through its action

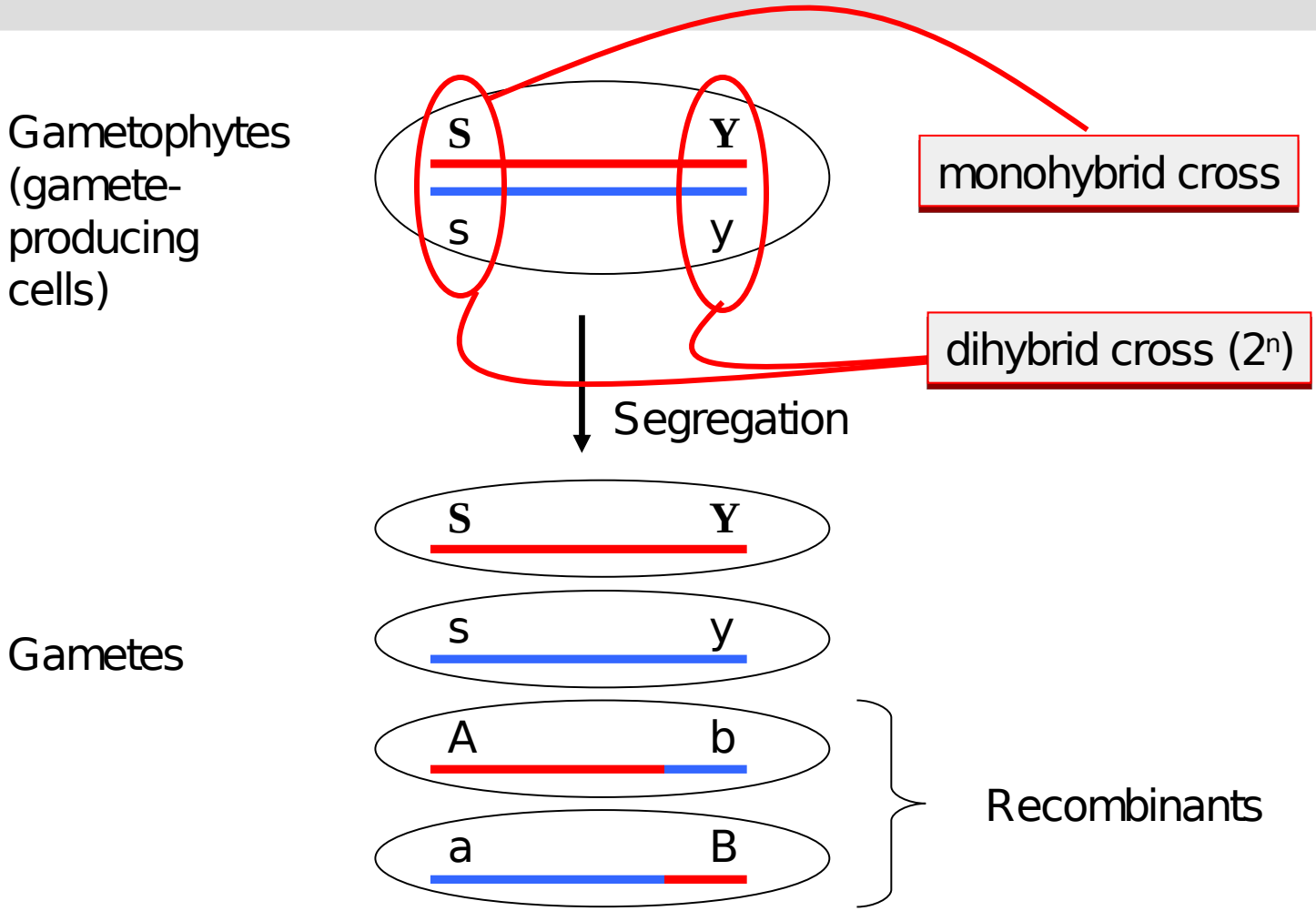
ecessive allele: The allele which is only visible phenotypically if no dominant allele is prese

Mendel's law of independent assortment

- Knowledge of which allele has been inherited at one locus gives no information on the allele has been inherited at the other locus



Mendel's law of independent assortment

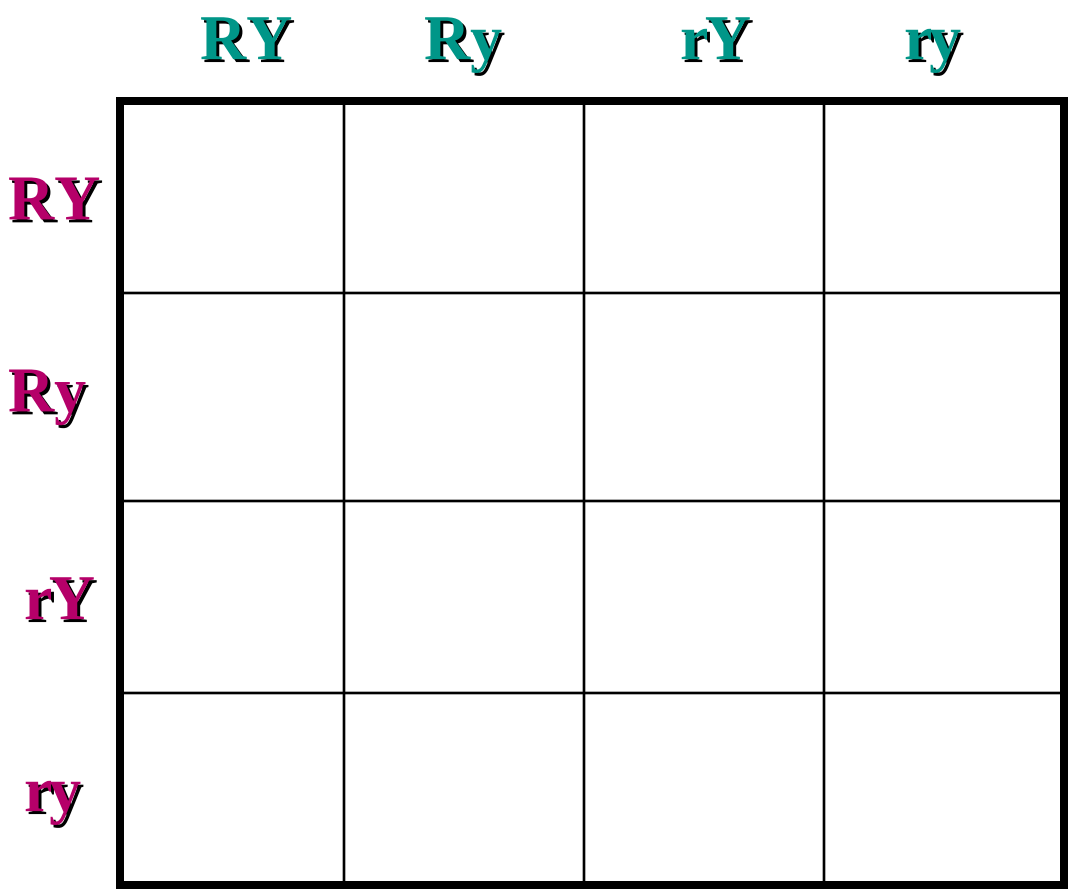


Alleles for *different* traits are distributed to sex cells (& offspring) independently of one an

Dihybrid cross

- **Traits: Seed shape & Seed color**
- **Alleles: R round**
  r wrinkled
  Y yellow
  y green

All possible gamete combinations



Dihybrid Cross

	RY	Ry	rY	ry
RY	RRYY	RRYy	RrYY	RrYy
Ry	RRYy	RRyy	RrYy	Rryy
rY	RrYY	RrYy	rrYY	rrYy
ry	RrYy	Rryy	rrYy	rryy

Round/Yellow: 9

Round/green: 3

wrinkled/Yellow: 3

wrinkled/green: 1

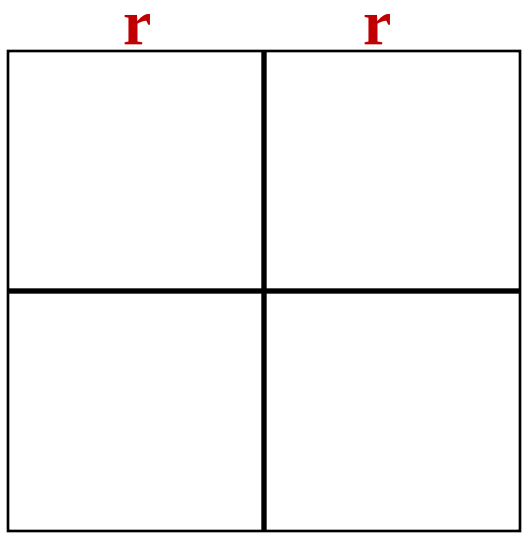
9:3:3:1 phenotypic ratio

LAW	PARENT CROSS	OFFSPRING
DOMINANCE	TT x tt tall x short	100% Tt tall
SEGREGATION	Tt x Tt tall x tall	75% tall 25% short
INDEPENDENT ASSORTMENT	RrGg x RrGg round & green x round & green	9/16 round seeds & green pods 3/16 round seeds & yellow pods 3/16 wrinkled seeds & green pods 1/16 wrinkled seeds & yellow pods

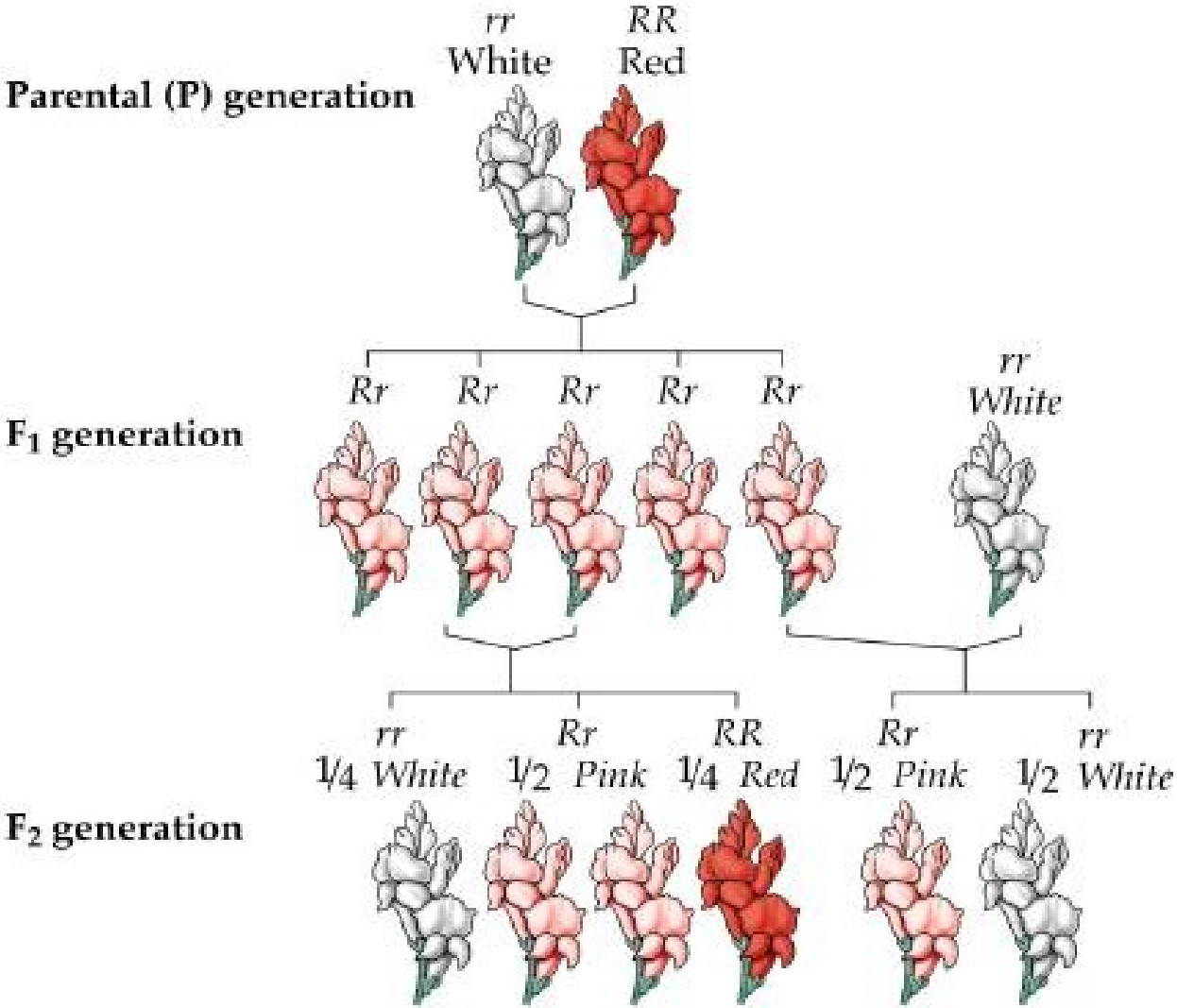
Incomplete Dominance

- **F1 hybrids** have an appearance somewhat **in between** the **phenotypes** of the two parental varieties.
- **Example: snapdragons (flower)**
- **red (RR) x white (rr)**

- **RR = red flower**
- **rr = white flower**



Incomplete Dominance



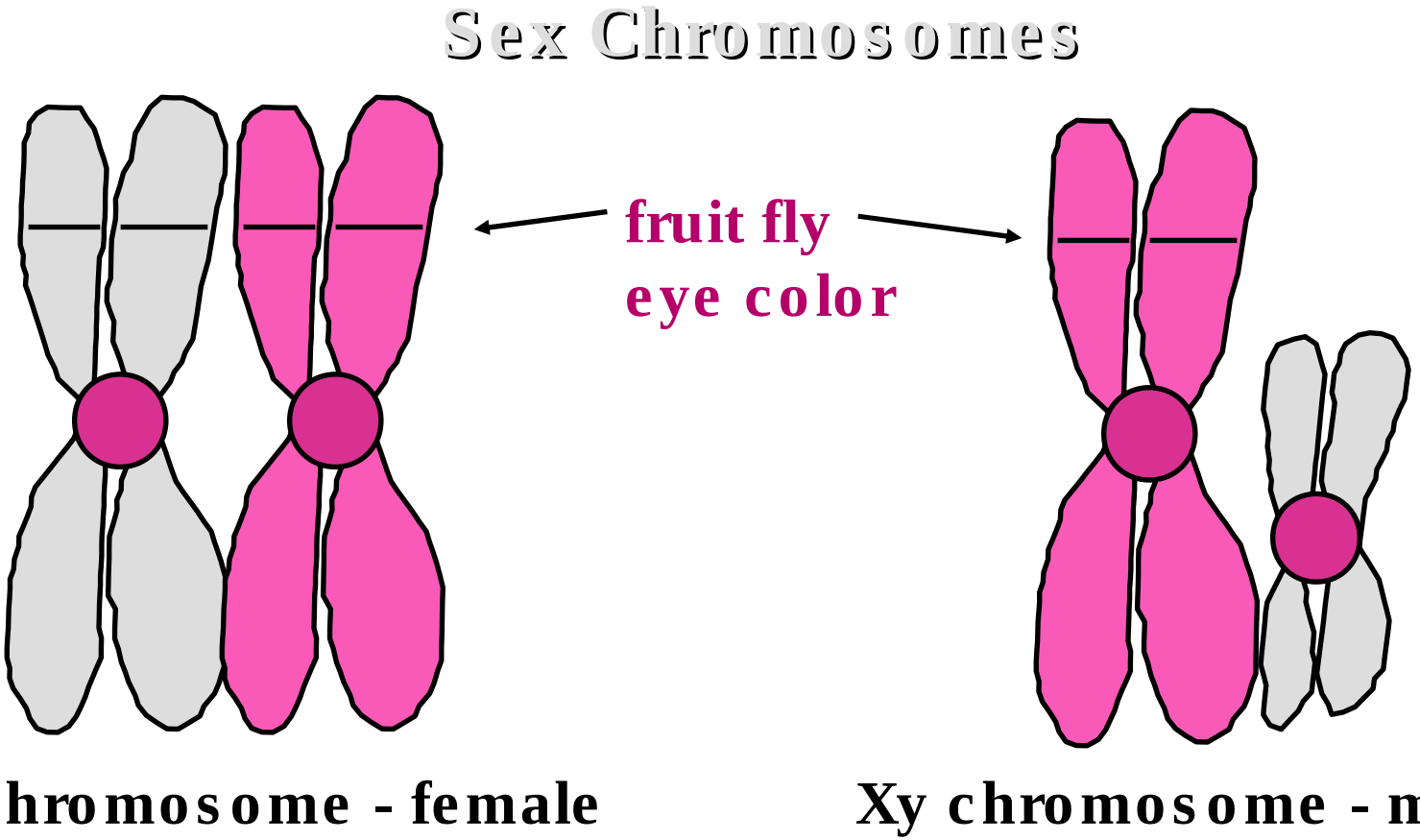
Codominance

- Two alleles are expressed (multiple alleles) in heterozygous individuals.
- Example: blood type

1. type A = I^AI^A or I^Ai
2. type B = I^BI^B or I^Bi
3. type AB = I^AI^B
4. type O = ii

Sex-linked Traits

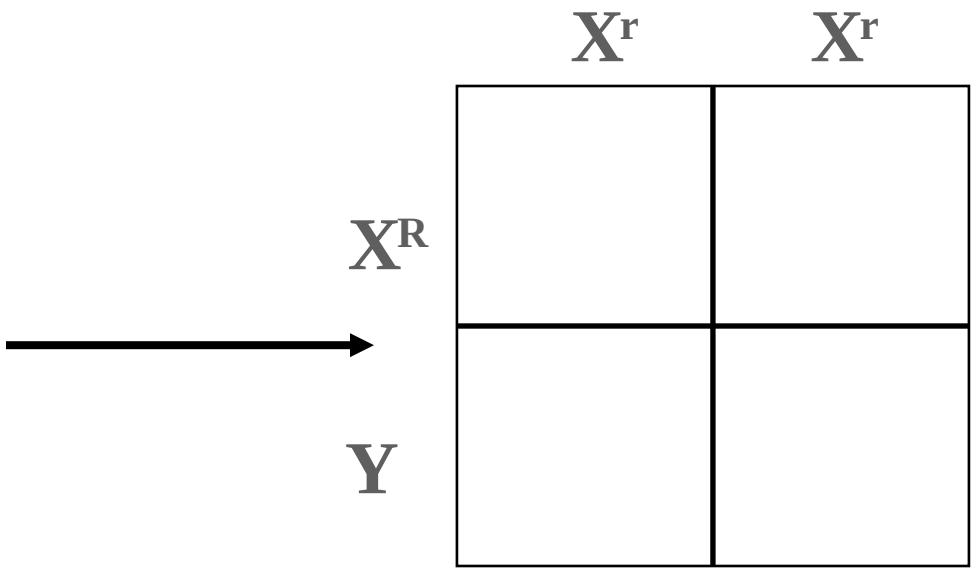
Example: Eye color in fruit flies



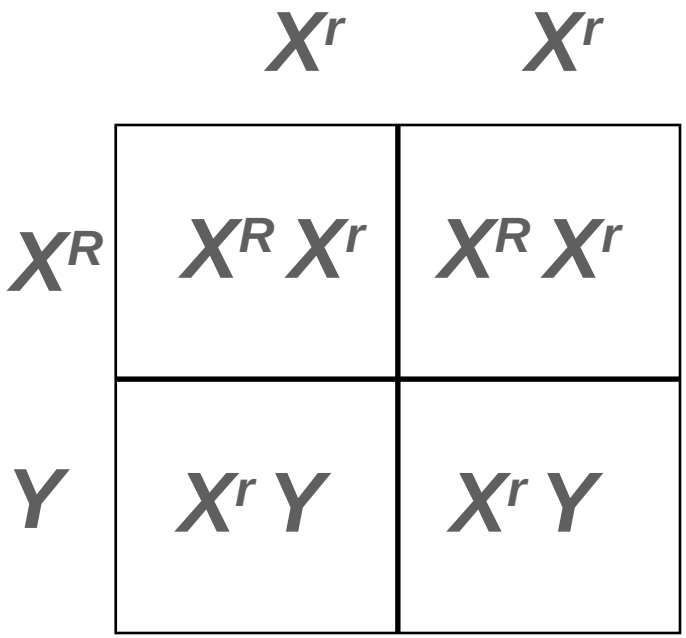
Sex-linked Traits

- Example: Eye color in fruit flies
- (red-eyed male) x (white-eyed female)

  X^RY x X^rX^r
- Remember: the Y chromosome in males does not carry traits.
- RR = red eyed
- Rr = red eyed
- rr = white eyed
- XY = male
- XX = female



Sex-linked Traits

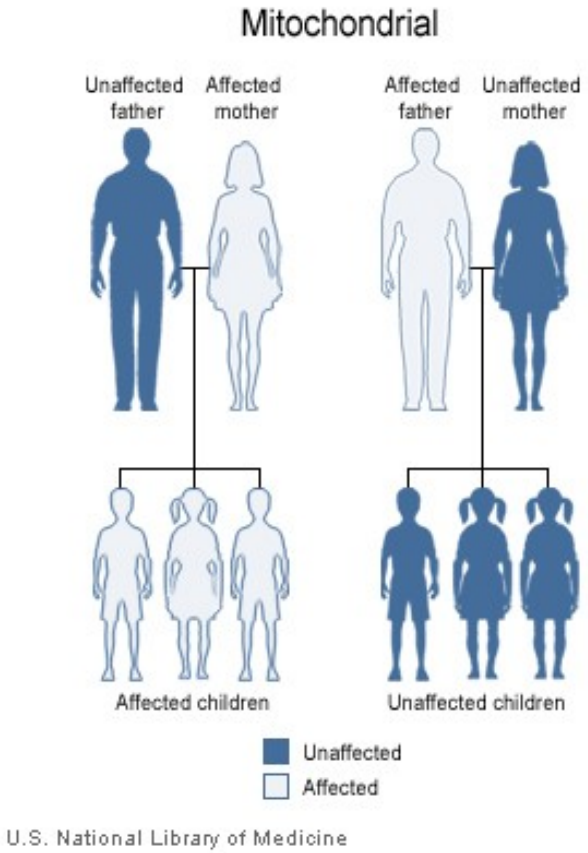


50% red eyed female

50% white eyed male

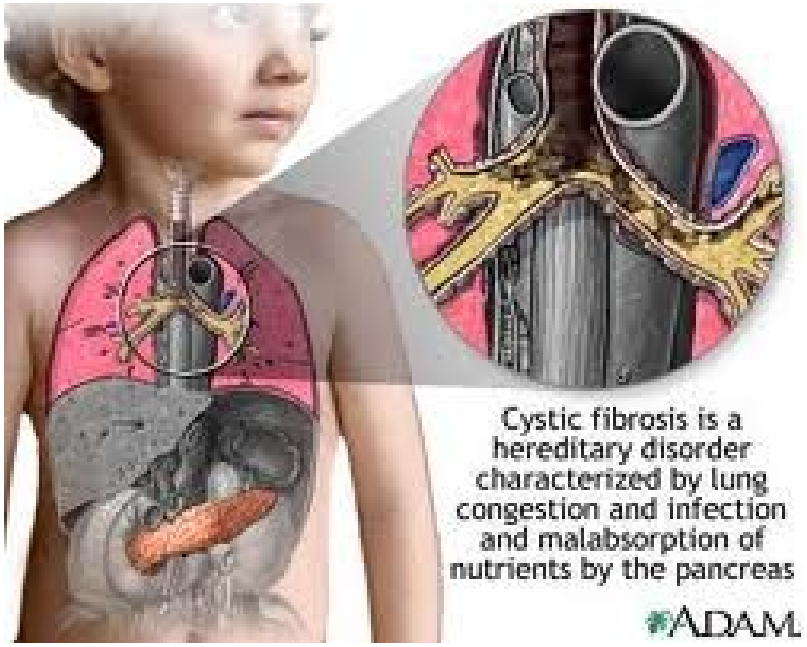
Mitochondrial inheritance

- *This type of inheritance applies to genes in mitochondrial DNA.*
- *Mitochondrial disorders can appear in every generation of a family and can affect both males and females, but fathers do not pass mitochondrial traits to their children.*
- *E.g. Leber's hereditary optic neuropathy (LHON)*



Some common genetic disorders

- ***Cystic fibrosis*** – disease affecting the mucus lining of the lungs, leading to breathing problems and other difficulties.



Some common genetic disorders

Huntington disease

- Huntington's chorea is an inherited disorder characterized by abnormal body movements called chorea, and loss of memory. There also is evidence that doctors as far back as the Middle Ages knew of this devastating disease. The incidence is 5 to 8 per 100,000. It takes its name from the New York physician George Huntington who first described it precisely in 1872.

A new study from Nancy Wexler, in Venezuela in the 1990s with a boy with Huntington's disease, suggests there may be ways to delay the onset of the disease.

Some common genetic disorders

- ***Hemophilia***
- *illness* that impair the body's ability to control bleeding.

Some common genetic disorders

- ***Fragile X syndrome*** - is a genetic condition that causes a range of developmental problems including learning disabilities and mental retardation. Usually males are more severely affected by this disorder than females. In addition to learning difficulties, affected males tend to be restless, fidgety, and inattentive. Affected males also have characteristic physical features that become more apparent with age.