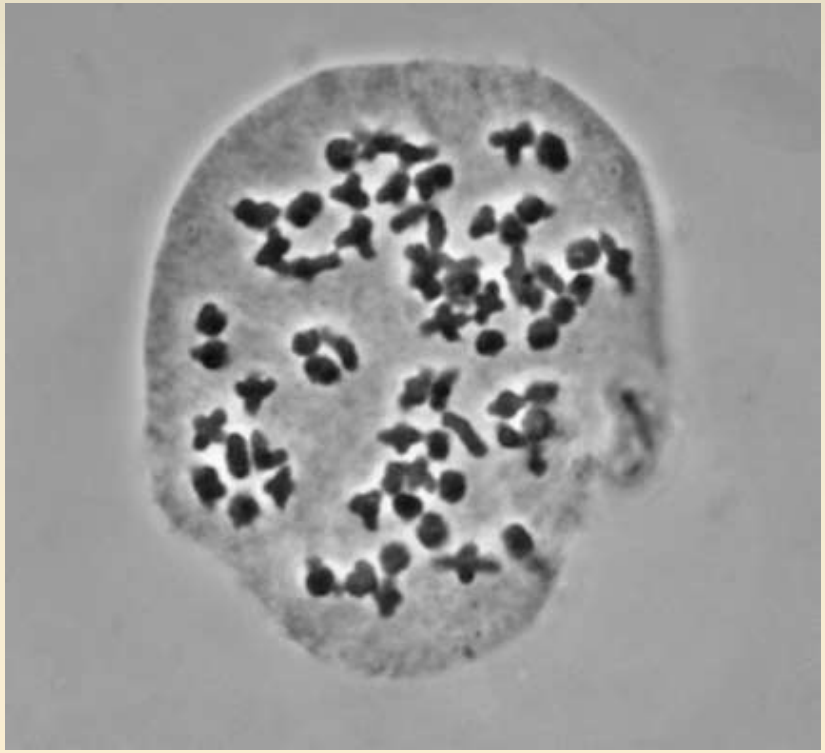
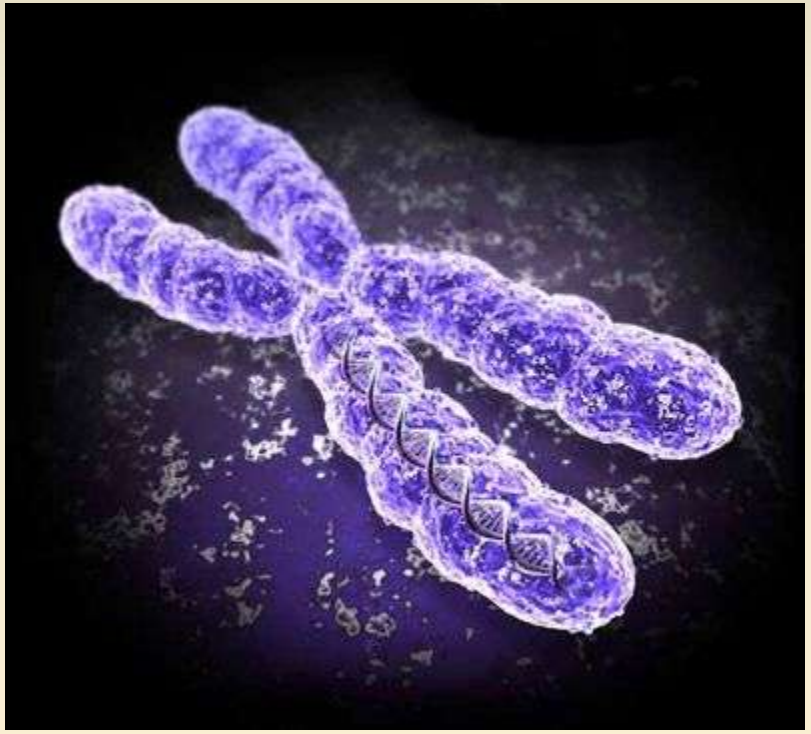
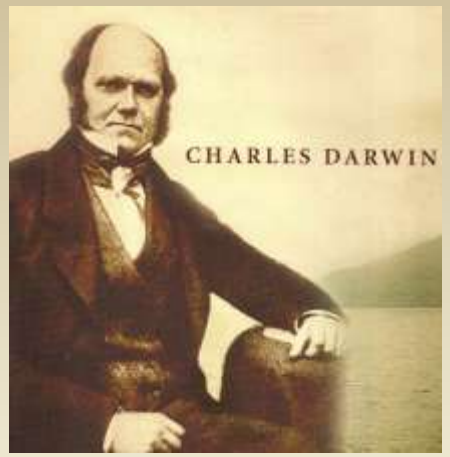
Sources of Genetic Variation







"Preservation of Favored Races in the Struggle for Life"
= Natural Selection

1. There is **variation** in morphology, function or behavior between individuals.
2. Some traits are more **adaptive** than others.
3. Traits are **heritable**.
4. Individuals that are more **"fit"** live to reproduce or **reproduce more**.
5. Less adaptive traits become less common in populations

Measuring Genetic Variation in Natural Populations

- Phenotypic Variation
  - anatomy
  - biochemistry
  - physiology
  - development
  - behavior

In most cases, one cannot infer a genotype just from the inspection or identification of a particular phenotype

- Genotypic Variation
  - alleles
  - loci
  - chromosomes
  - genomes

Indirect evidence: proteins

Direct evidence: DNA

Overview

Natural selection acts on existing phenotypic variation.

Mutations are necessary for evolution

multiple alleles, gene duplications, alterations in chromosome number, transposable elements, and modification of regulation all contribute to variation

What is a mutation?

Mutations are changes made to an organism's genetic material.

These changes may be due to errors in replication, errors during transcription , radiation, viruses and many other things.

Mutations can occur within a specific gene (small scale), as well as to the chromosome as a whole (large scale).

Mutations

Any change in the DNA sequence of an organism is a mutation.

Mutations are the source of the altered versions of genes that provide the raw material for evolution.

Most mutations have no effect on the organism, especially among the eukaryotes, because a large portion of the DNA is not in genes and thus does not affect the organism's phenotype.

Of the mutations that do affect the phenotype, the most **common effect of mutations is lethality**, because most genes are necessary for life.

Only a small percentage of mutations causes a visible but non-lethal change in the phenotype.

Are mutations always bad?

Favorable mutations present organisms with an advantage over others and ensure their survival. These mutations will accumulate in a population.

Less favorable mutations are removed from the gene pool through natural selection.

Organisms with these mutations will not survive.

Mutations as a Source of Genetic Variation

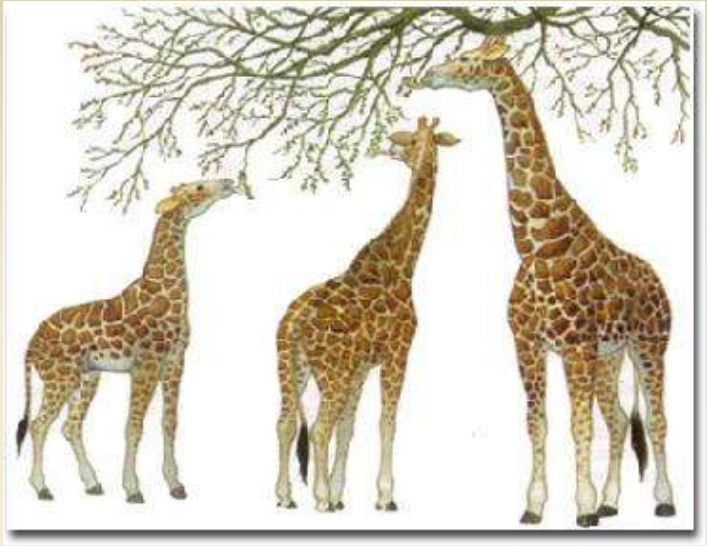
- Mutations are normally expressed at one of two levels of gene activity
  - Changes within a gene product, for example, in the amino acid constitution of a particular protein
  - Changes in the regulation of a gene or its product
- Mutations may affect the amount or rate at which a gene product is produced, or whether or not the protein is produced at all or at what points in the life of the cell

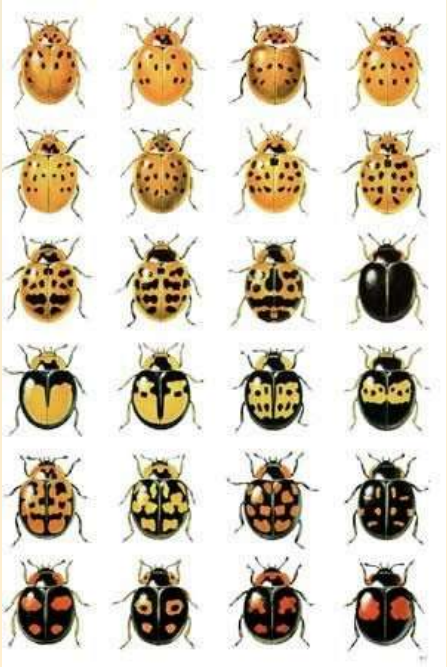
Evolutionary Impact of Mutations

All mutation events increase genetic variation in populations and give natural selection the raw material from which to generate adaptive evolutionary changes

Both the mutational processes and their rates or frequencies are diverse

Evolution is driven by the combination of both these processes, mutation and selection





Evolutionary Impact of Mutations

It is important to remember that **most of mutational processes lead to decreased adaptation** most of the time

Most mutations are harmful; most chromosome rearrangements are harmful; most changes in ploidy are harmful

However, when you take the long view, when there are so many species, so many individuals, **and so much time** (3.5 billion years), **even low frequency events**, such as beneficial mutations, beneficial chromosomal rearrangements, beneficial changes in genome ploidy can occur and when they do, natural selection will be there as the mechanism to see that they are preserved and spread

THE ORIGIN OF GENETIC VARIATION

Categories of mutations:

I. Changes in the karyotype

A. Aneuploidy (loss of one or more of the normal complement of chromosomes, or a major part of one)

B. Polyploidy (multiplication of normal chromosome complements)

II. Chromosome rearrangements

A. Duplications and deletion

B. Inversions

C. Translocations

III. Gene mutations

A. Point mutations

B. Gene conversions

C. Methylation (epigenetic changes)

Some Milestones in Genetics

1838 – Cell Theory, M.J. Schleiden and others (Schwann)

1842 – Chromosomes first seen by Nageli

1865 – Charles Darwin, Pangenesis theory, blending inheritance

1865 - Gregor Mendel discovers, by crossbreeding peas, that specific laws govern hereditary traits. Each traits determined by pair of factors.

1869 - Friedrich Miescher isolates DNA for the first time, names it nuclein.

1882 – **Walther Flemming** describes threadlike 'chromatin' in the nucleus that turns red with staining, studied and named **mitosis**. The term 'chromosome' used by Heinrich Waldeyer in 1888.

1902 – Mendel's work rediscovered and appreciated (DeVries, Corens, etc)

1903 – **Walter Sutton**, the chromosomal theory of inheritance, chromosomes are the carriers of genetic information

1944 - Avery, MacLeod and McCarty show DNA was the genetic material

1953 - James Watson and Francis Crick discover the molecular structure of DNA: a double helix with base pairs of A + T and C + G.

1955 - human chromosome number first established

1999 - The first complete sequence of a human chromosome (22) was published.

2004 - Complete sequencing of the human genome was finished by an international public consortium. **Craig Venter** etc.

Matthias Jakob Schleiden - 1838 proposes that cells are the basic structural elements of all plants.

Cell Theory

1. All living organisms are composed of one or more cells
2. The cell is the basic unit of structure and organization of organisms
3. All cells come from pre-existing cells

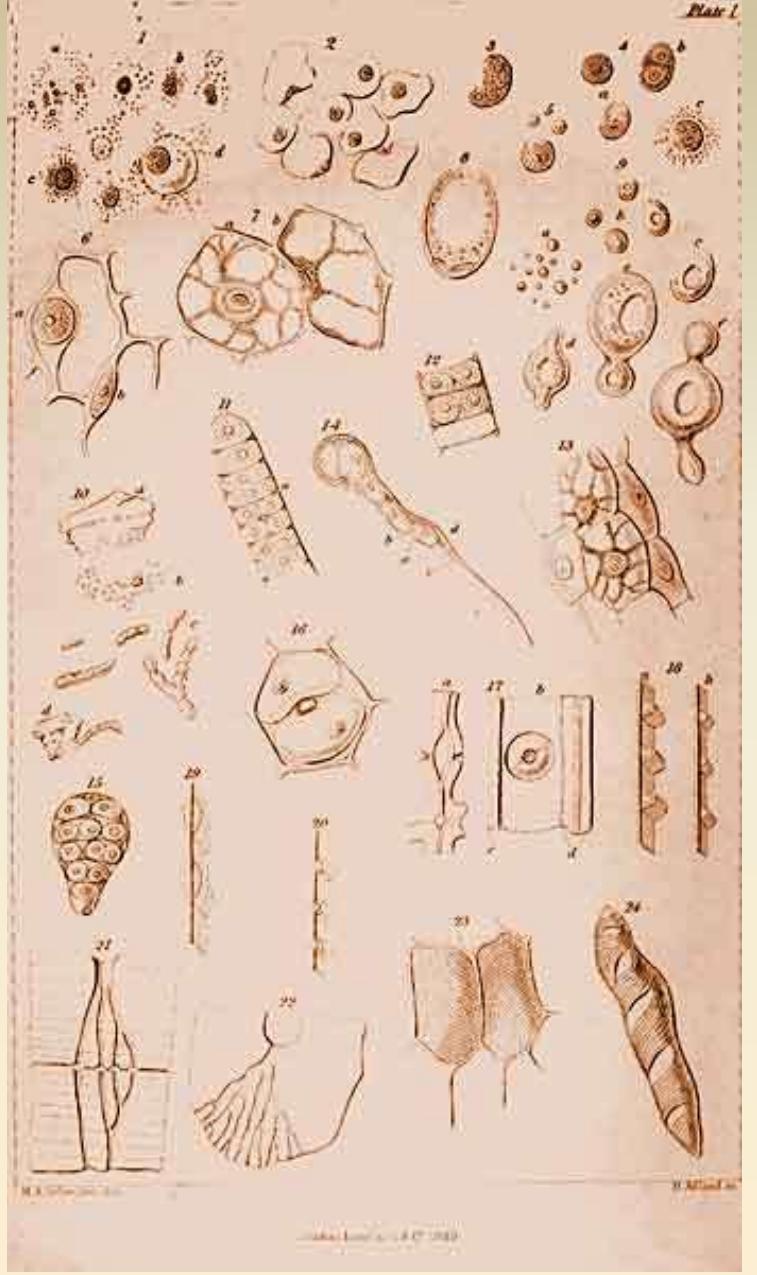
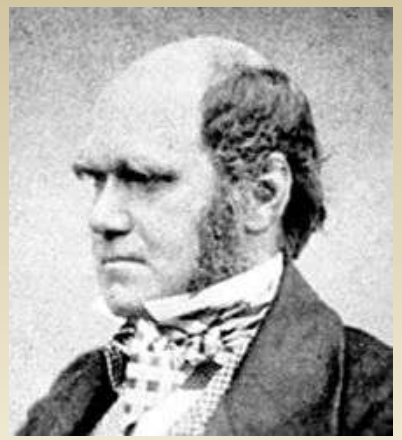
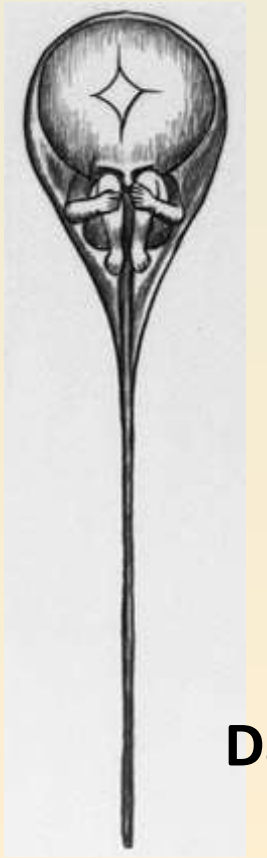
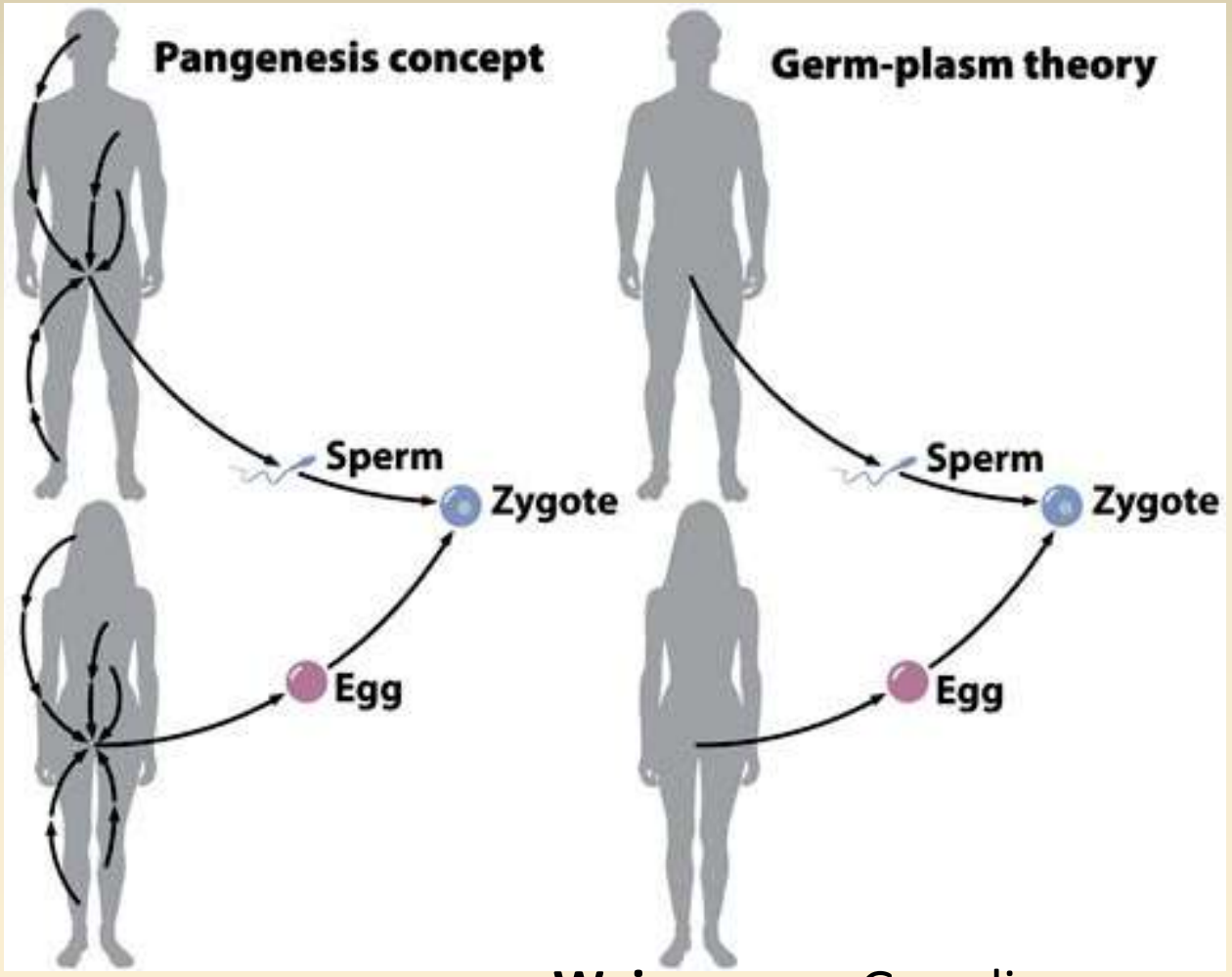


Plate 1 from J. M. Schleiden, Principles of Scientific Botany, 1849, showing various features of cell development

Darwin – 1865 - How does heredity work?



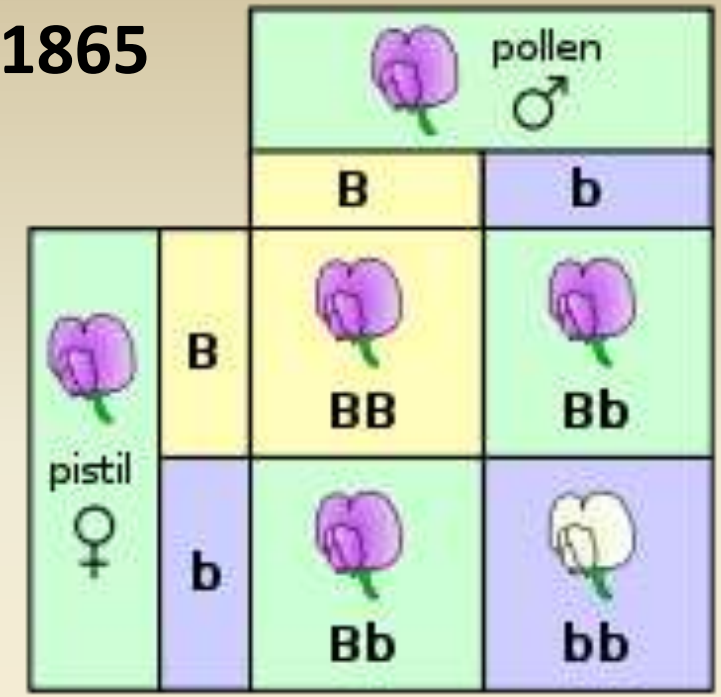




Darwin - Pangenesis

Weismann – Germline - significance of meiosis for reproduction and inheritance - 1890

Mendel's Pea Experiments - 1865



FIRST LAW:

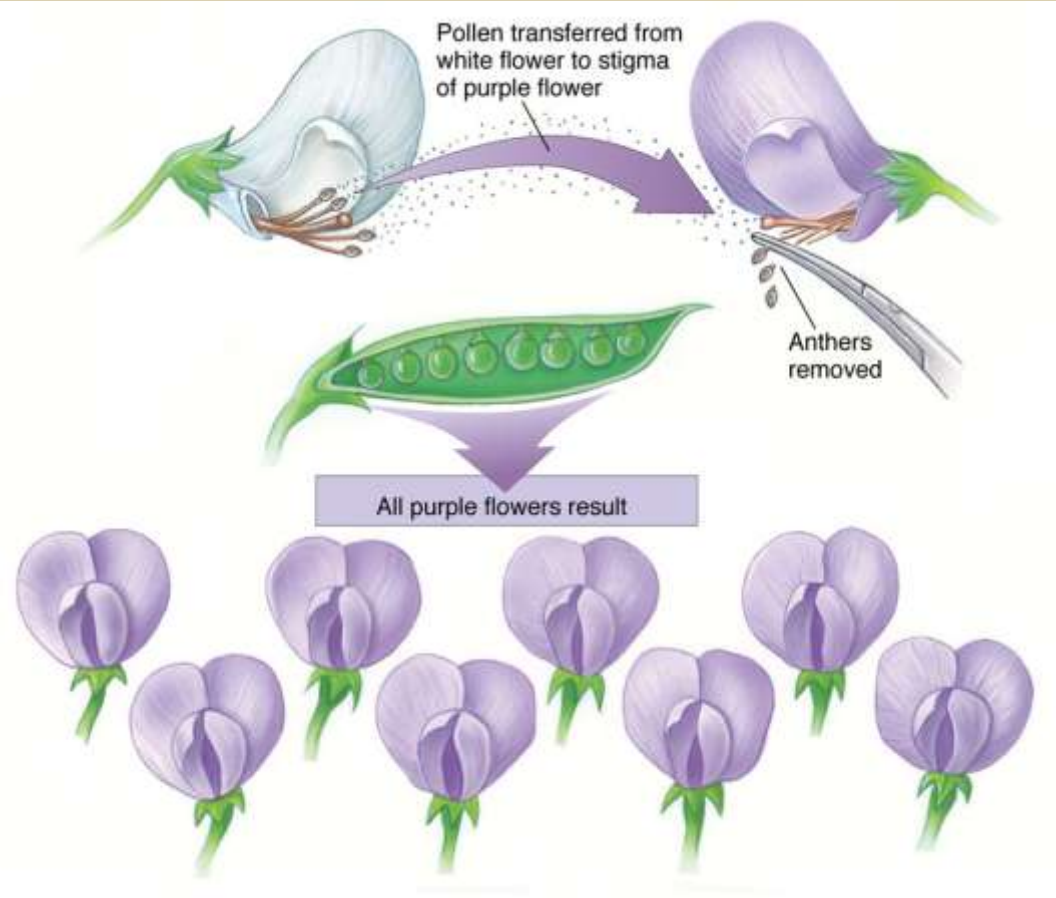
1. Each trait due to a **pair of hereditary factors** which
2. **segregate during gametogenesis**

SECOND LAW:

3. Multiple sets of hereditary factors **assort independently**

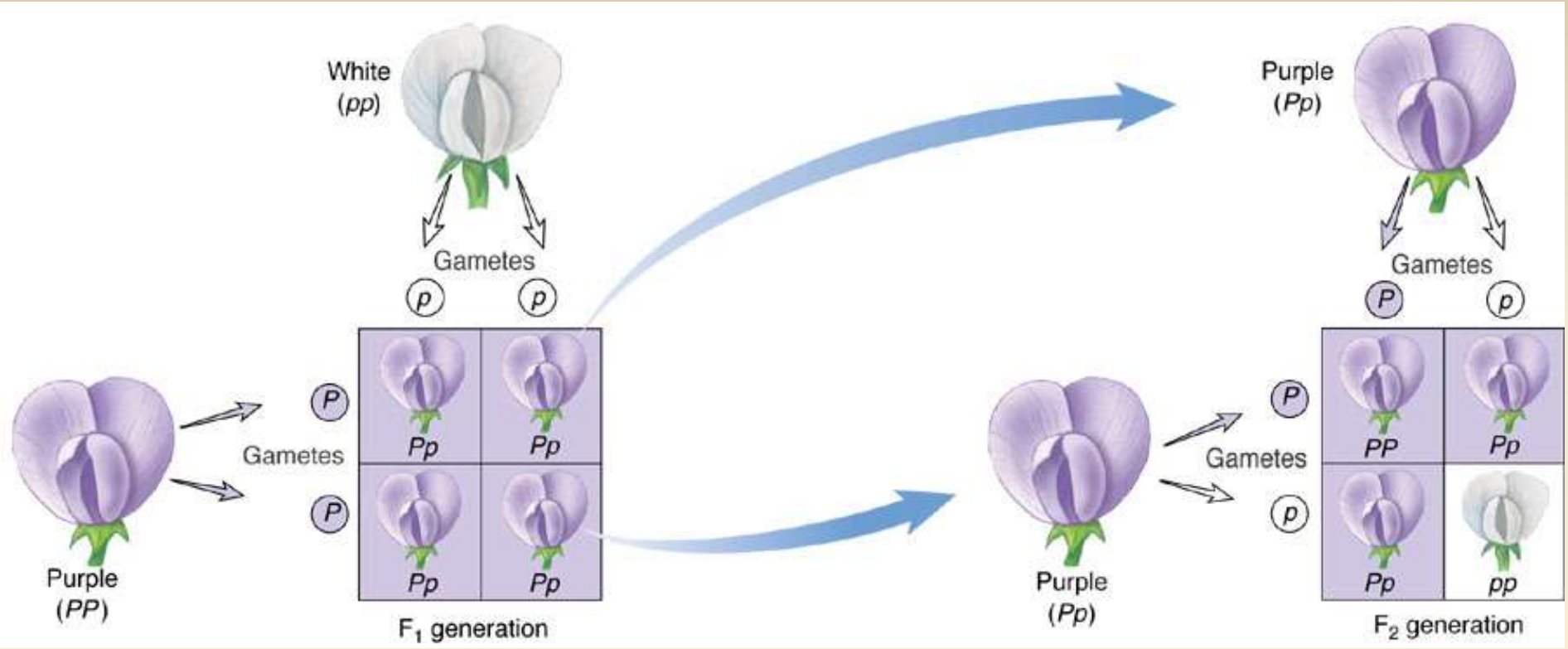
Mendel's work with peas showed that the "blending" explanation was wrong

Mendel's experimental method



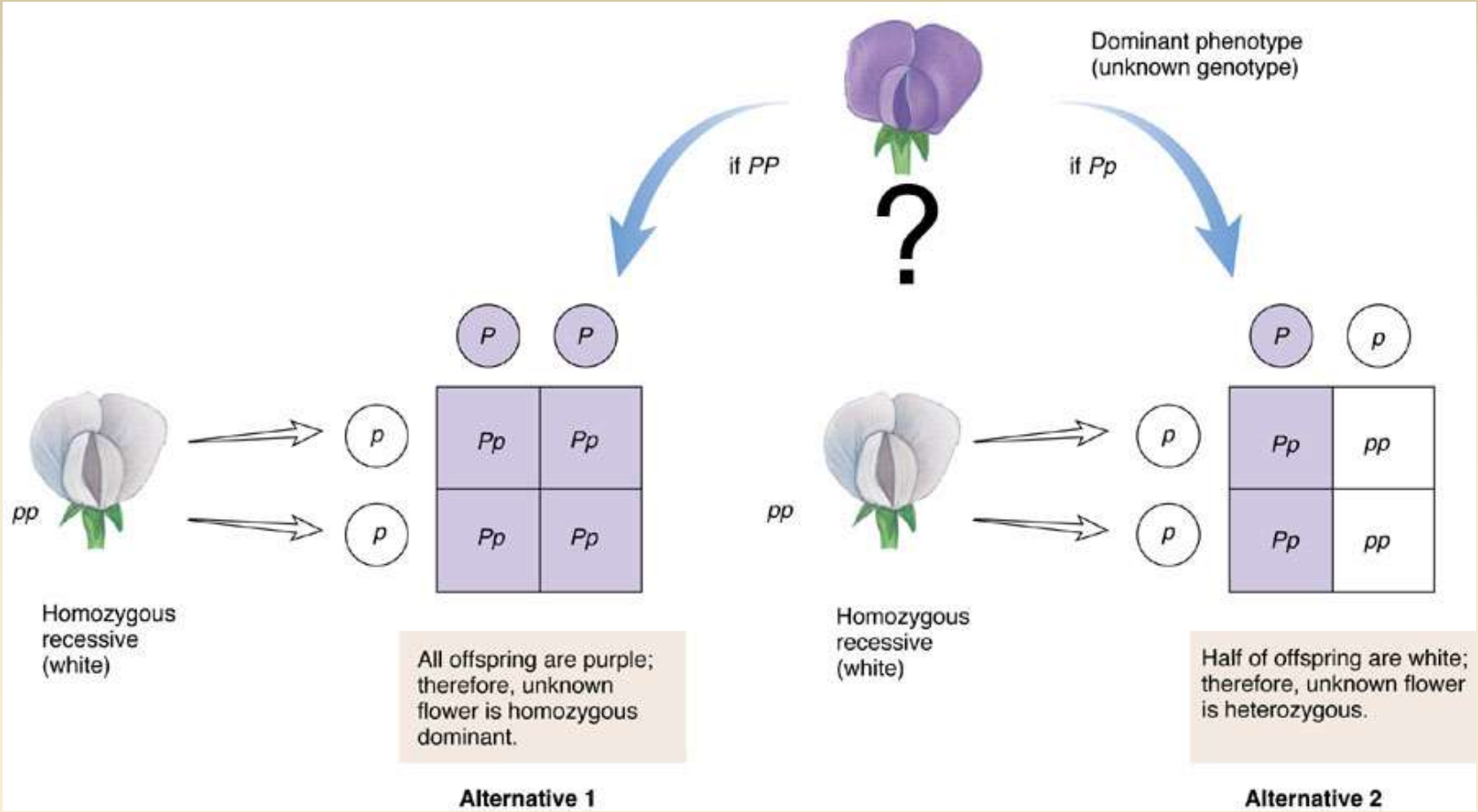
- In this experiment of a cross between true breeding white- and purple-flowered plants, Mendel pried open the surrounding petals of the purple-flowered plant and removed the male part, thus preventing self-fertilization. Then he dusted the anther with pollen he had selected from the white-flowered plant. The resulting seeds were planted and grew, all producing purple flowers.

Independent segregation — single trait, flower color



- Mendel's cross of pea plants for flower color started with true breeding white-flowered (recessive) and purple-flowered (dominant) plants. All F1 offspring of this cross were purple-flowered, and genetically heterozygous (Pp). When these were crossed, the resulting F2 offspring averaged 3 purple- for every 1 white-flowered plant, a 3:1 phenotypic ratio. However, the ratio of genotypes is 1:2:1 (1PP: 2Pp : 1pp).

Testcross



- By just looking at a dominant phenotype, for example, this plant with purple-flowers, you would not know if it was homozygous or heterozygous for the dominant allele. To determine its genotype, Mendel performed a testcross. In this illustration, the dominant phenotype (unknown genotype) was crossed with a plant known to be homozygous recessive, for example, the white-flowered plant. If all offspring are purple (Alternative 1), then the unknown flower is homozygous dominant; if offspring are half and half, purple and white (Alternative 2), then the unknown flower is heterozygous.

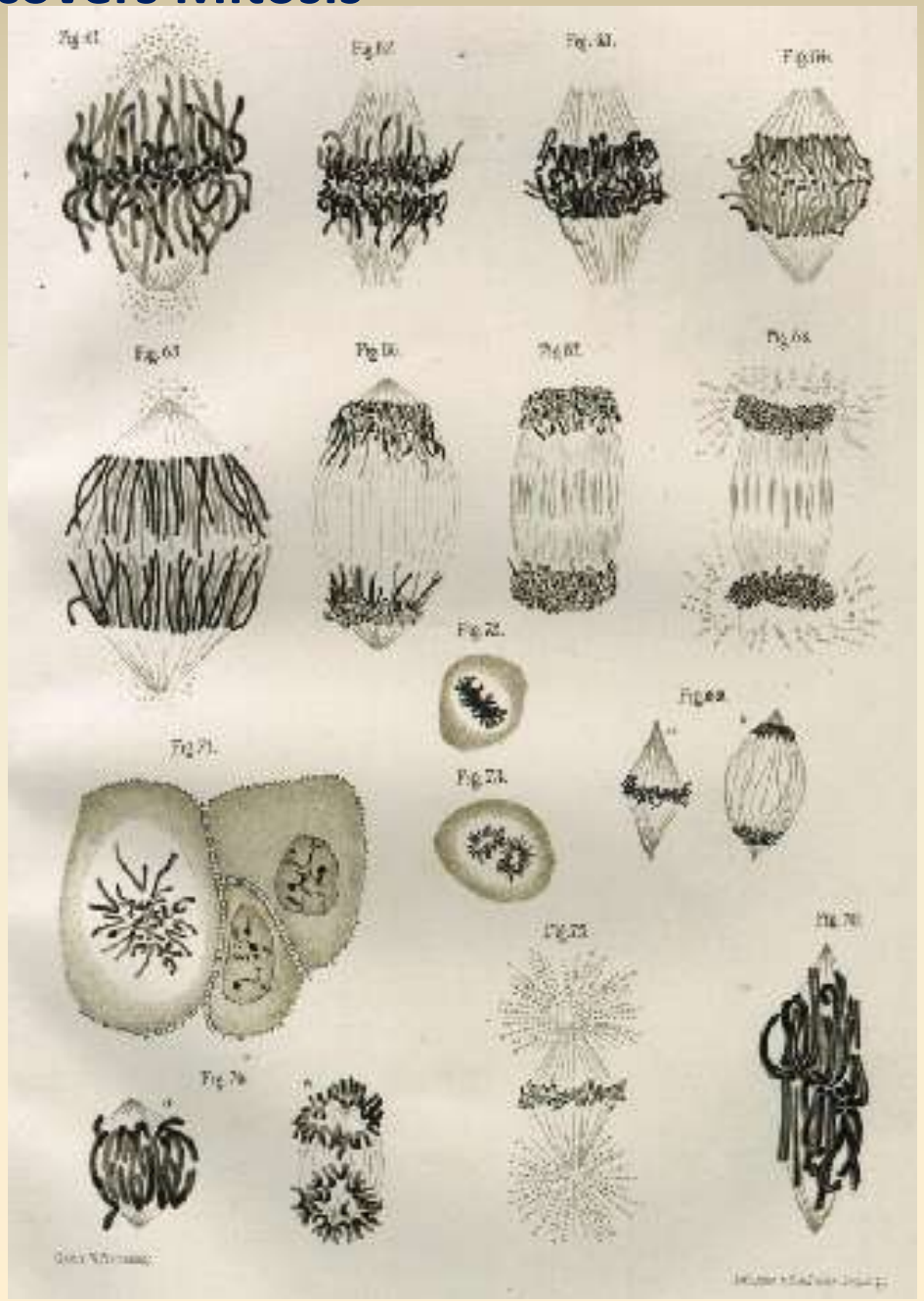
Among the most important principles of heredity are that

(1) The flow of information from genotype to phenotype is unidirectional; and

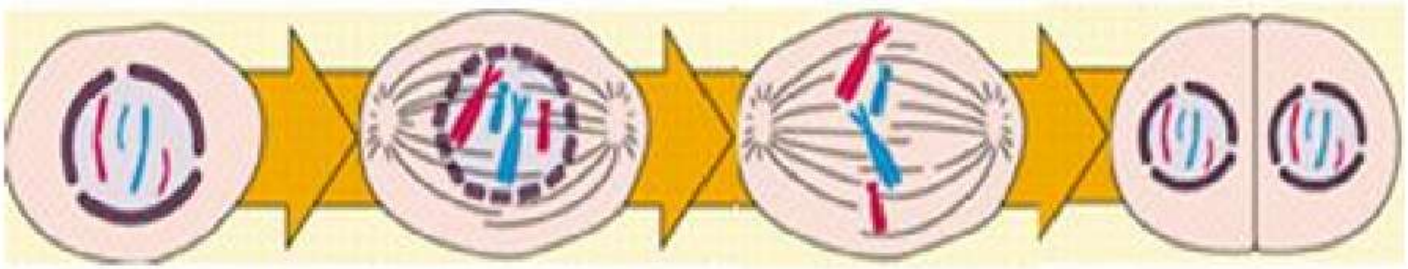
(2) The units of heredity retain their identity from generation to generation.

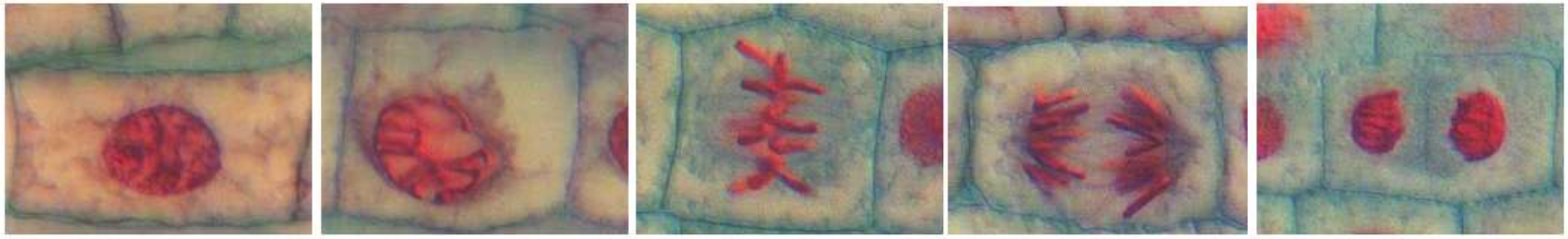
It was Mendel's exceptional contribution to show that biological characteristics were inherited by means of **discrete units, later called genes,** that remained undiluted in the presence of other genes.

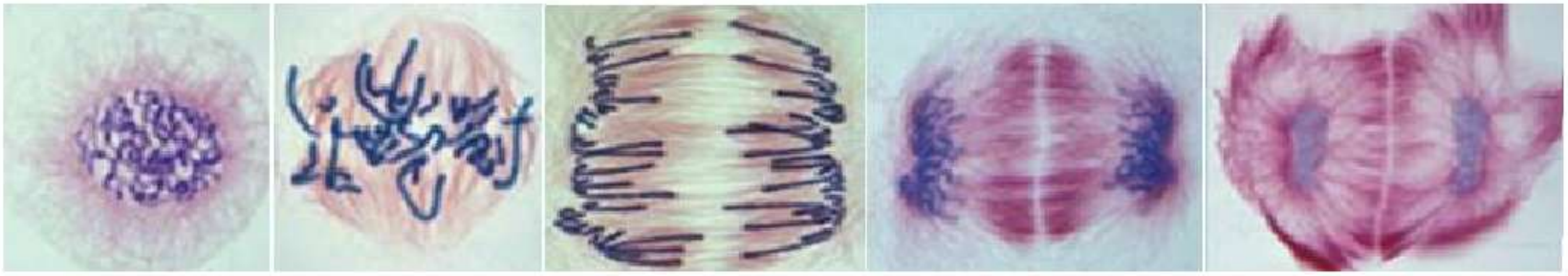
Walther Flemming – 1882 – Discovers Mitosis

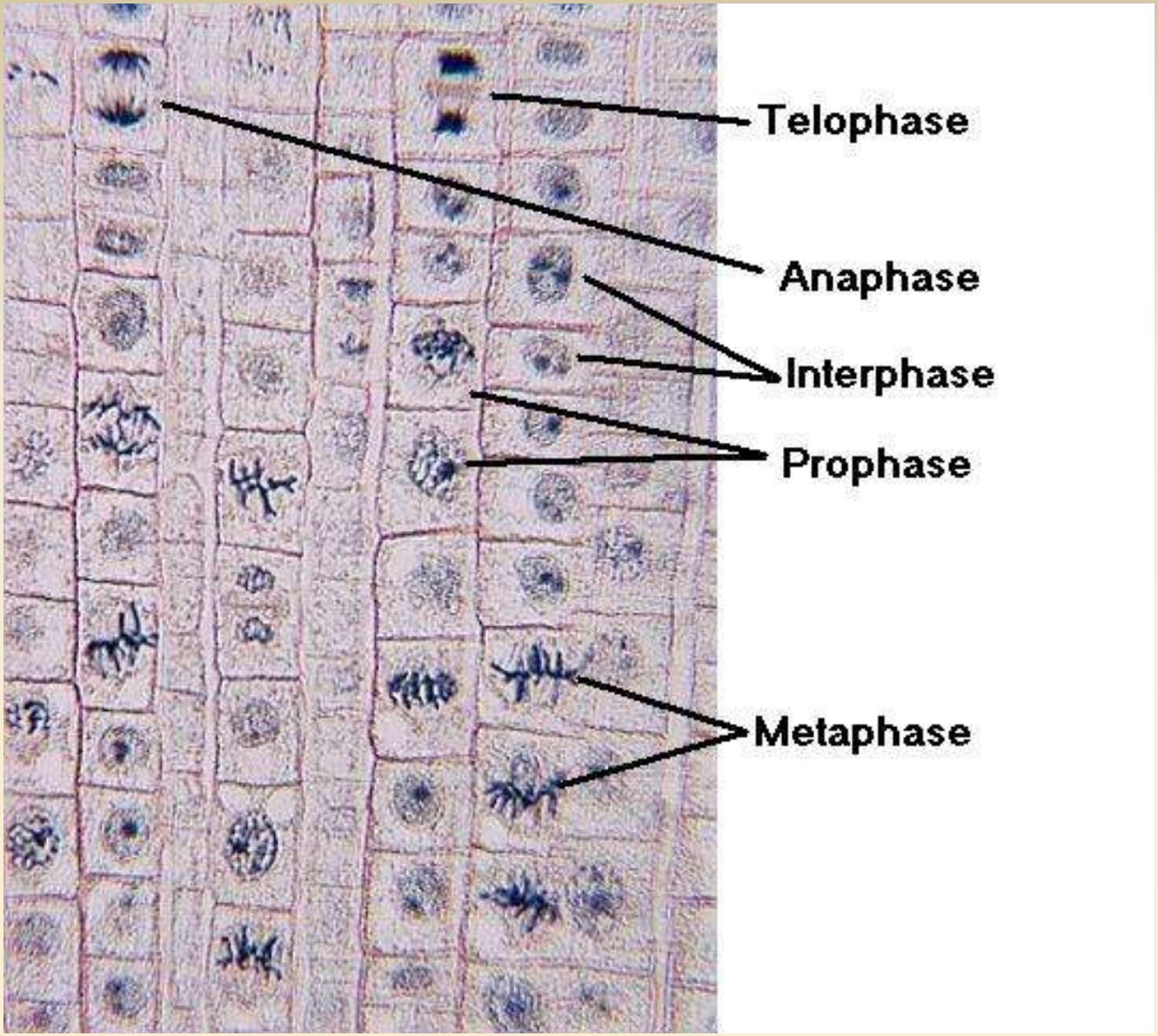


Mitosis in Plants and Animals

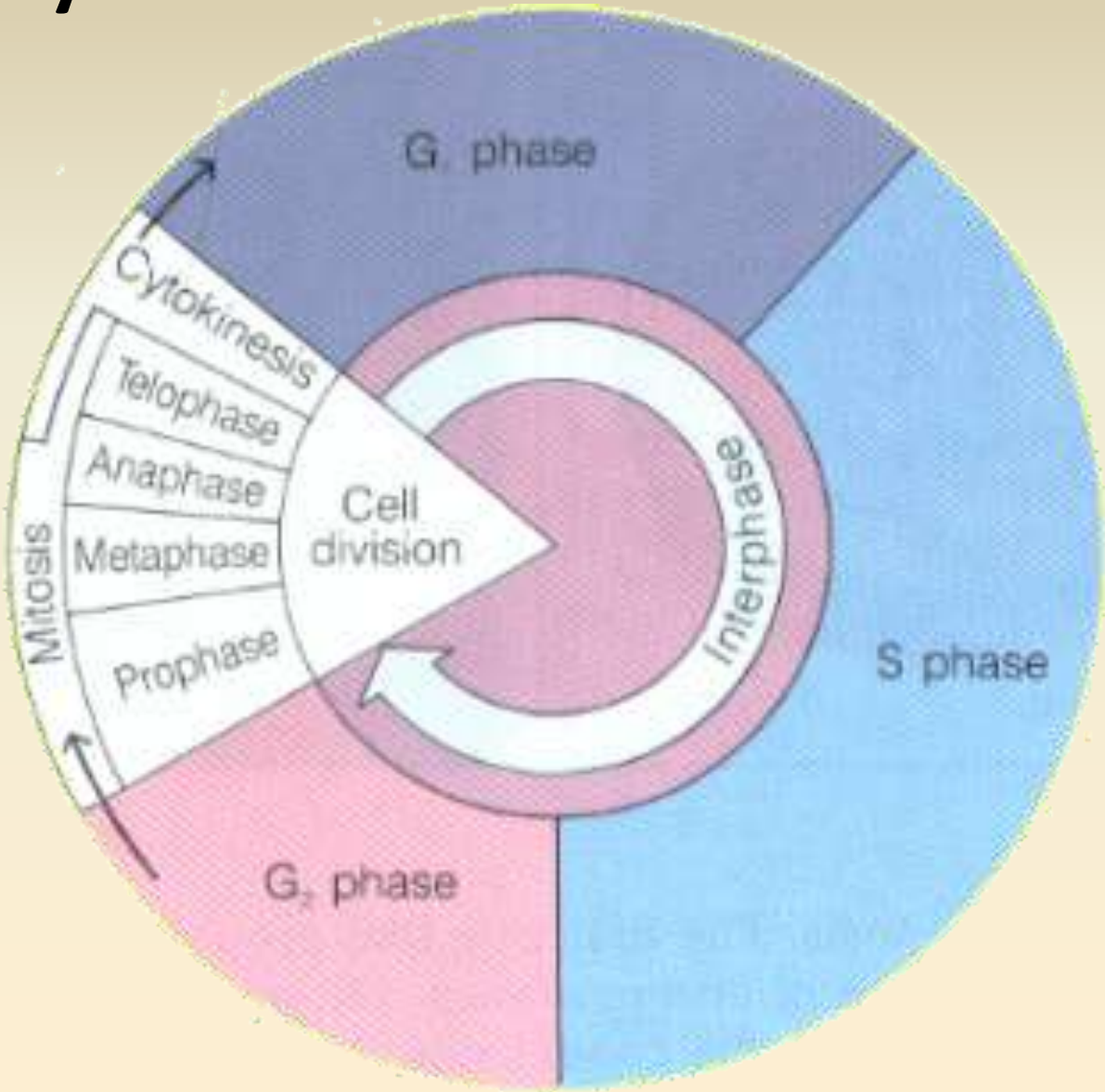




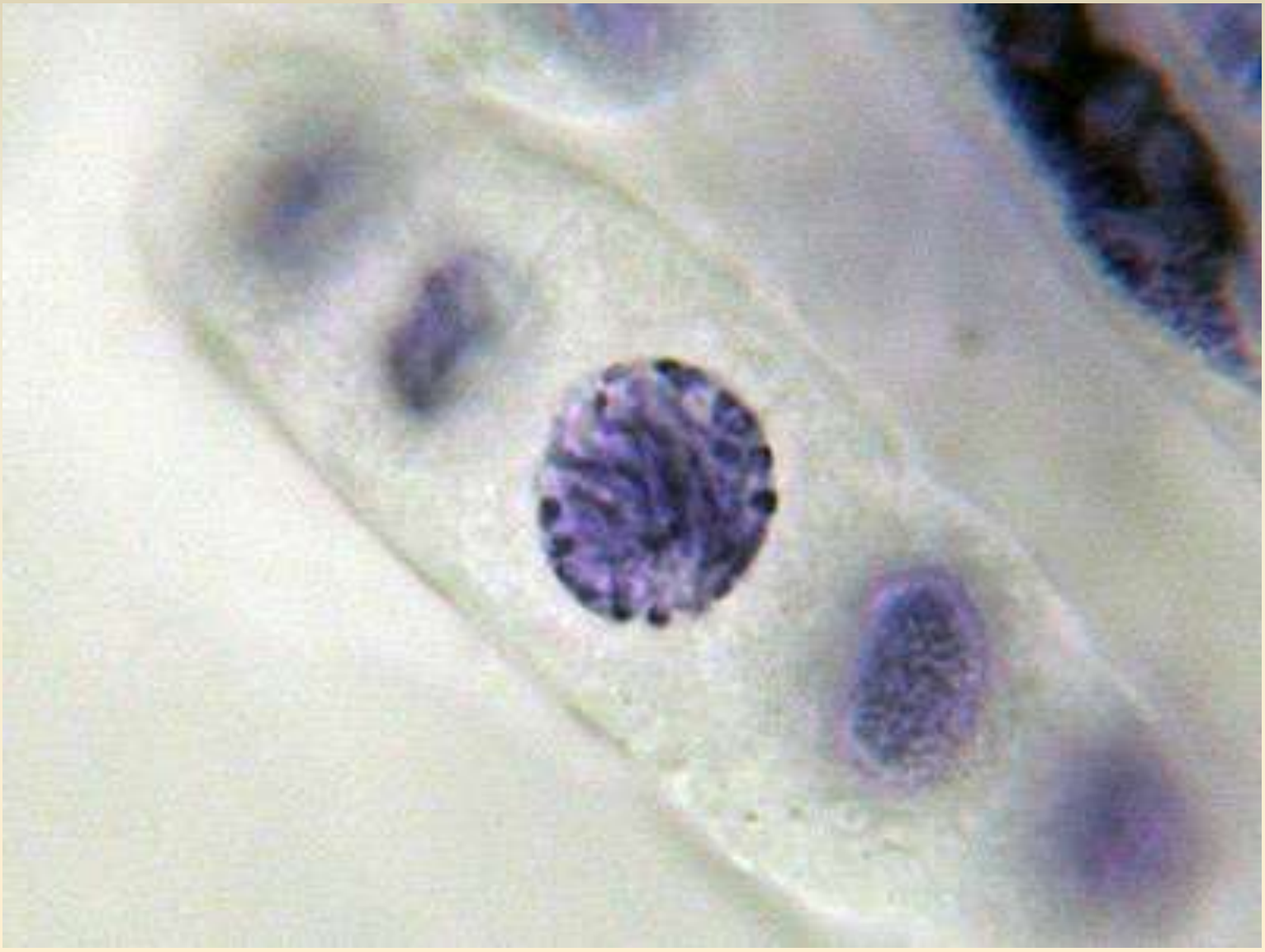



Telophase
Anaphase
Interphase
Prophase
Metaphase

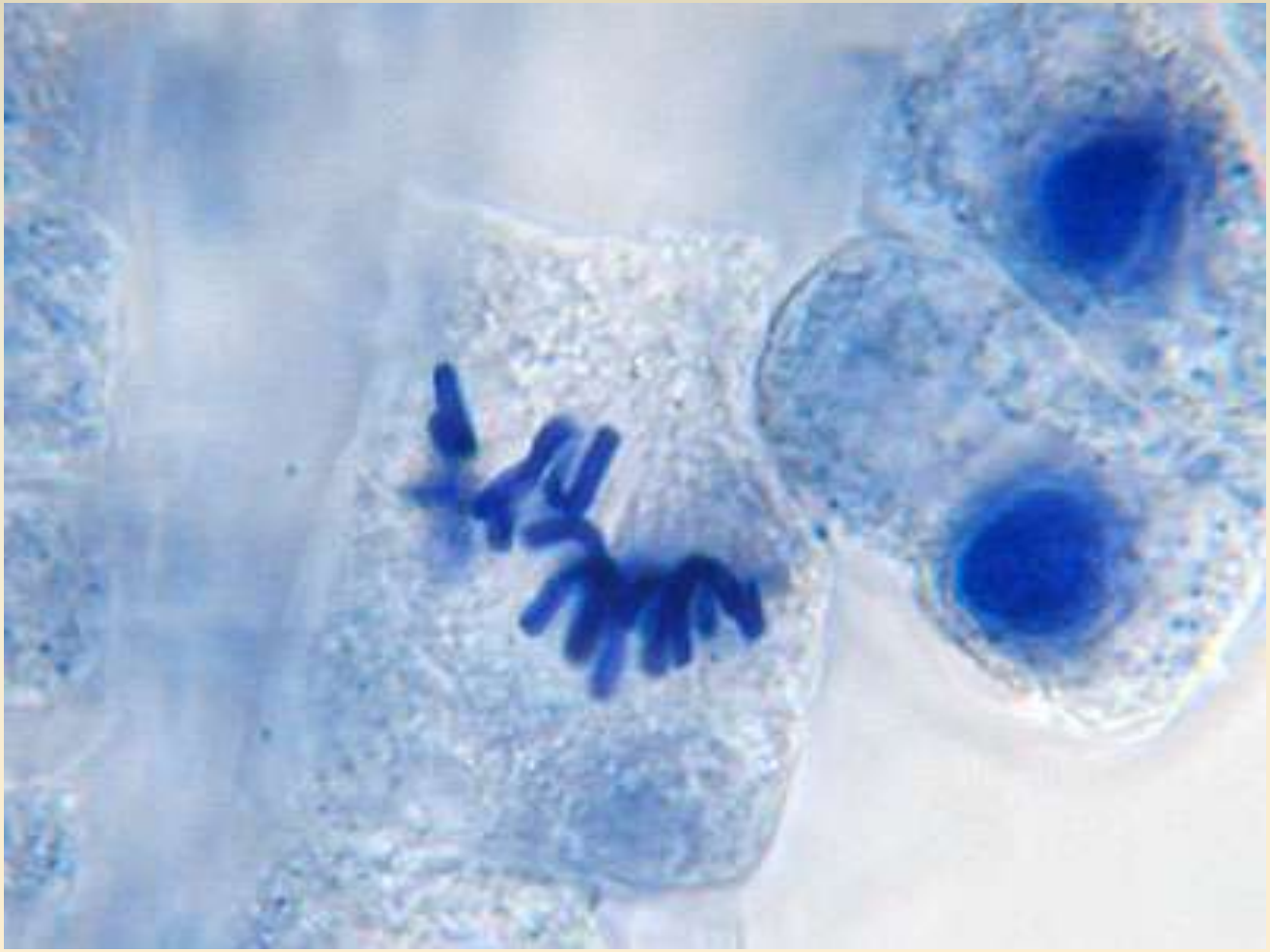
Cell Cycle


G1 phase
S phase
G2 phase
Interphase
Cell division
Mitosis
Prophase
Metaphase
Anaphase
Telophase
Cytokinesis

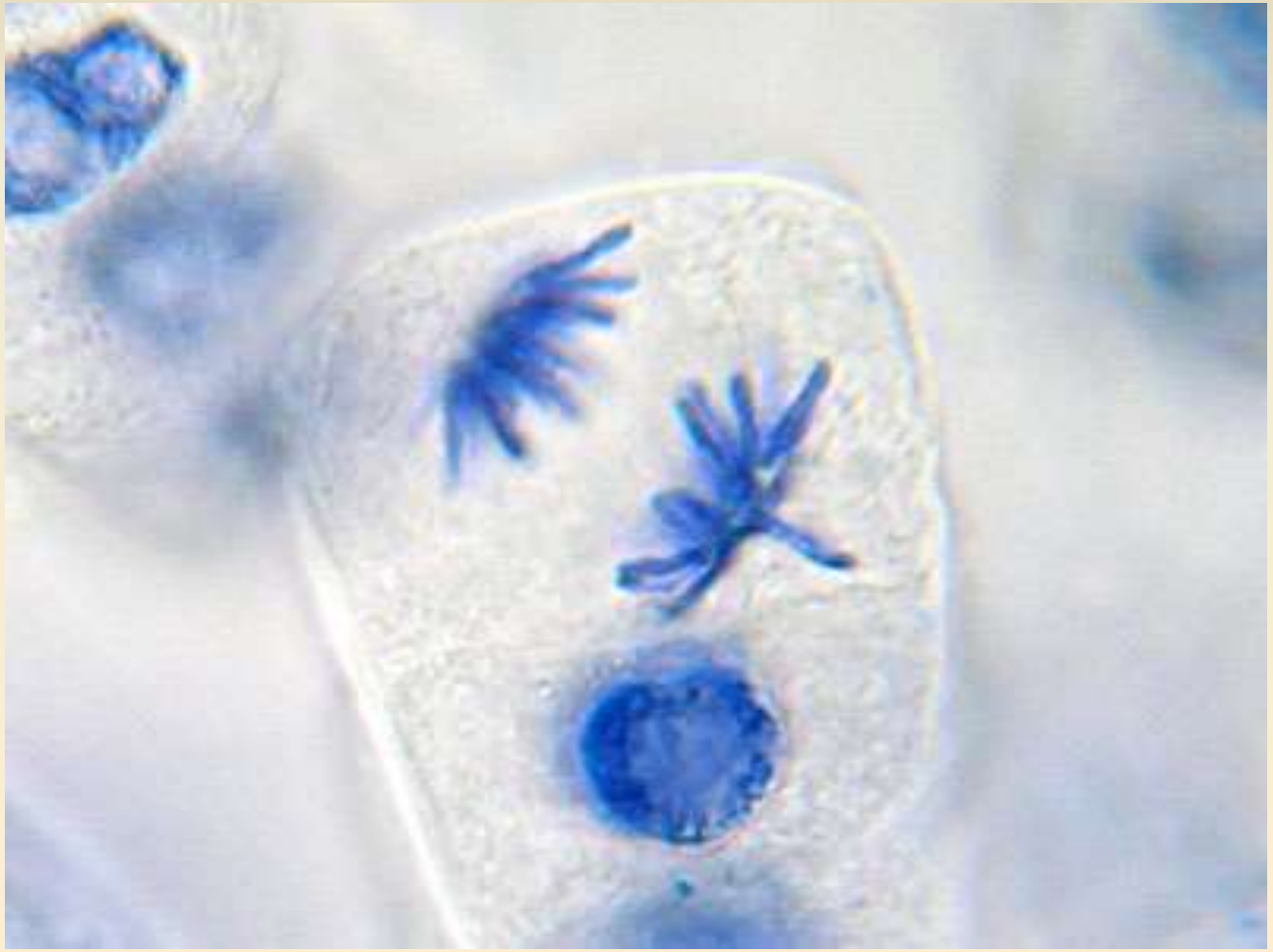
Prophase: the chromosomes begin to condense, while around the nucleus spindle fibers develop



Metaphase: the chromosomes line up along the equatorial plane of the cell



Anaphase: the chromosome pairs divide and the two groups migrate to opposite poles of the cell.



Telophase - a nuclear membrane forms, the chromosomes disperse and can no longer be distinguished. The spindle fibers dissolve. A new cell wall forms and the two cells separate.

The Problem

Mitosis produces two cells with the same number of chromosomes as the parent cell.

Mitosis of a **diploid** cell (**2n**) produces two diploid daughter cells.

If two diploid cells went on to participate in sexual reproduction, their fusion would produce a tetraploid (**4n**) **zygote**.

The Solution: Meiosis – reduction division

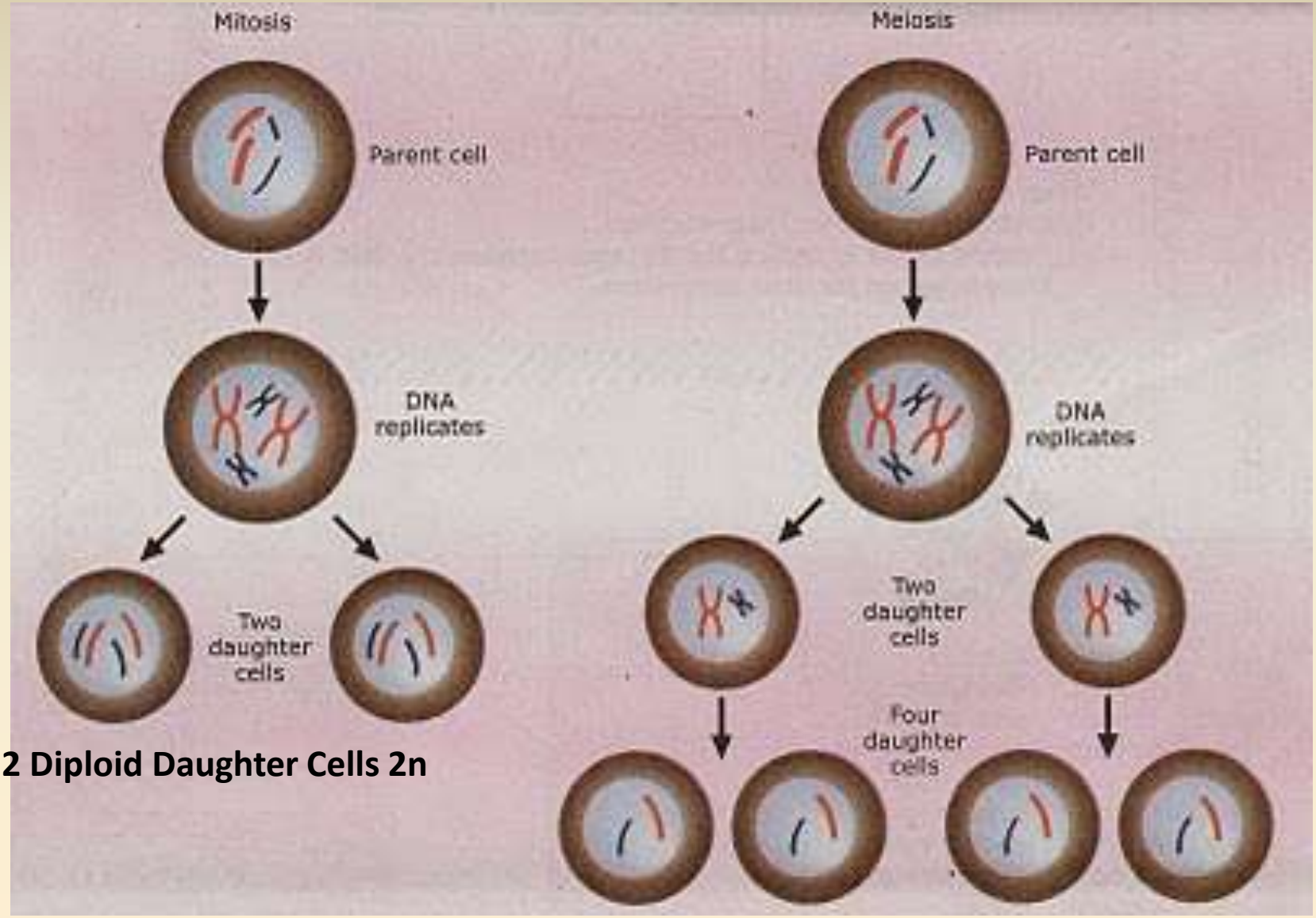
Meiosis is a process of cell division in **eukaryotes** characterized by:

- two consecutive divisions: **meiosis I** and **meiosis II**
- no DNA synthesis (no S phase) between the two divisions
- the result: 4 cells with half the number of chromosomes of the starting cell, e.g., **2n** → **n**

How did this evolve?

Mitosis

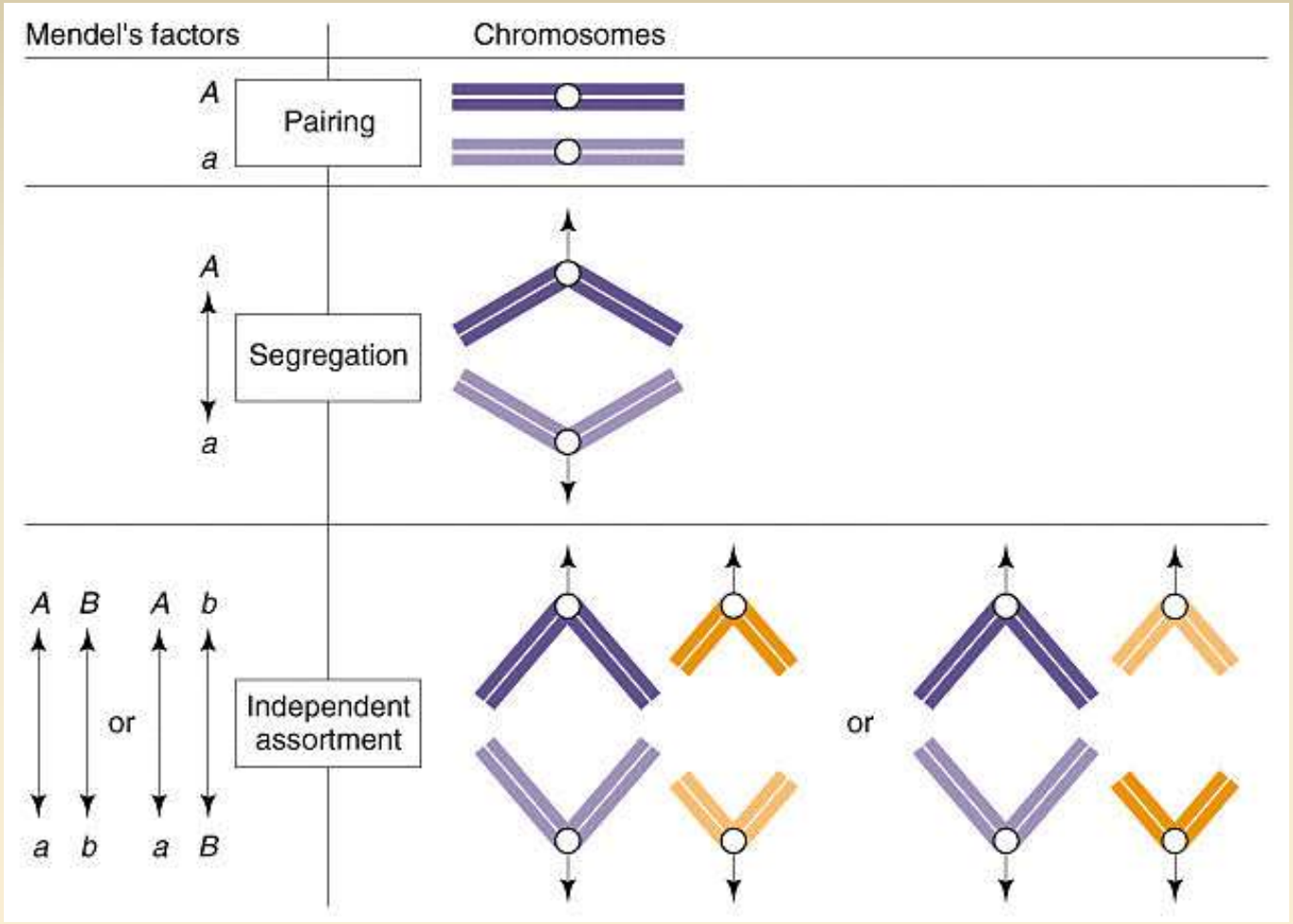
Meiosis



2 Diploid Daughter Cells 2n

4 Haploid Gametes 1n

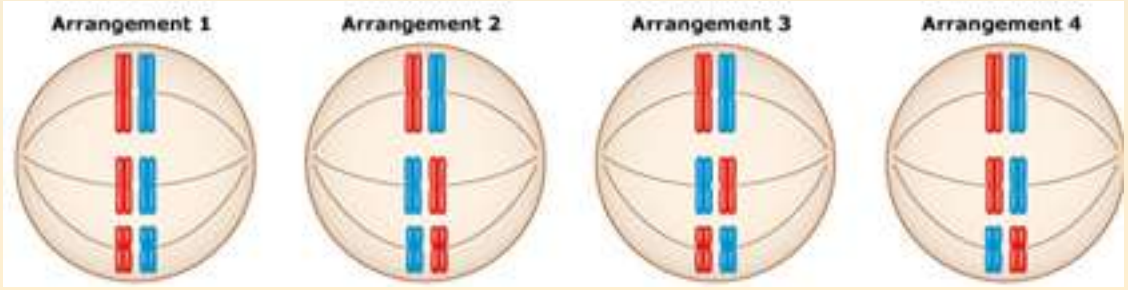
Walter Sutton – Chromosome Theory of Inheritance - 1903



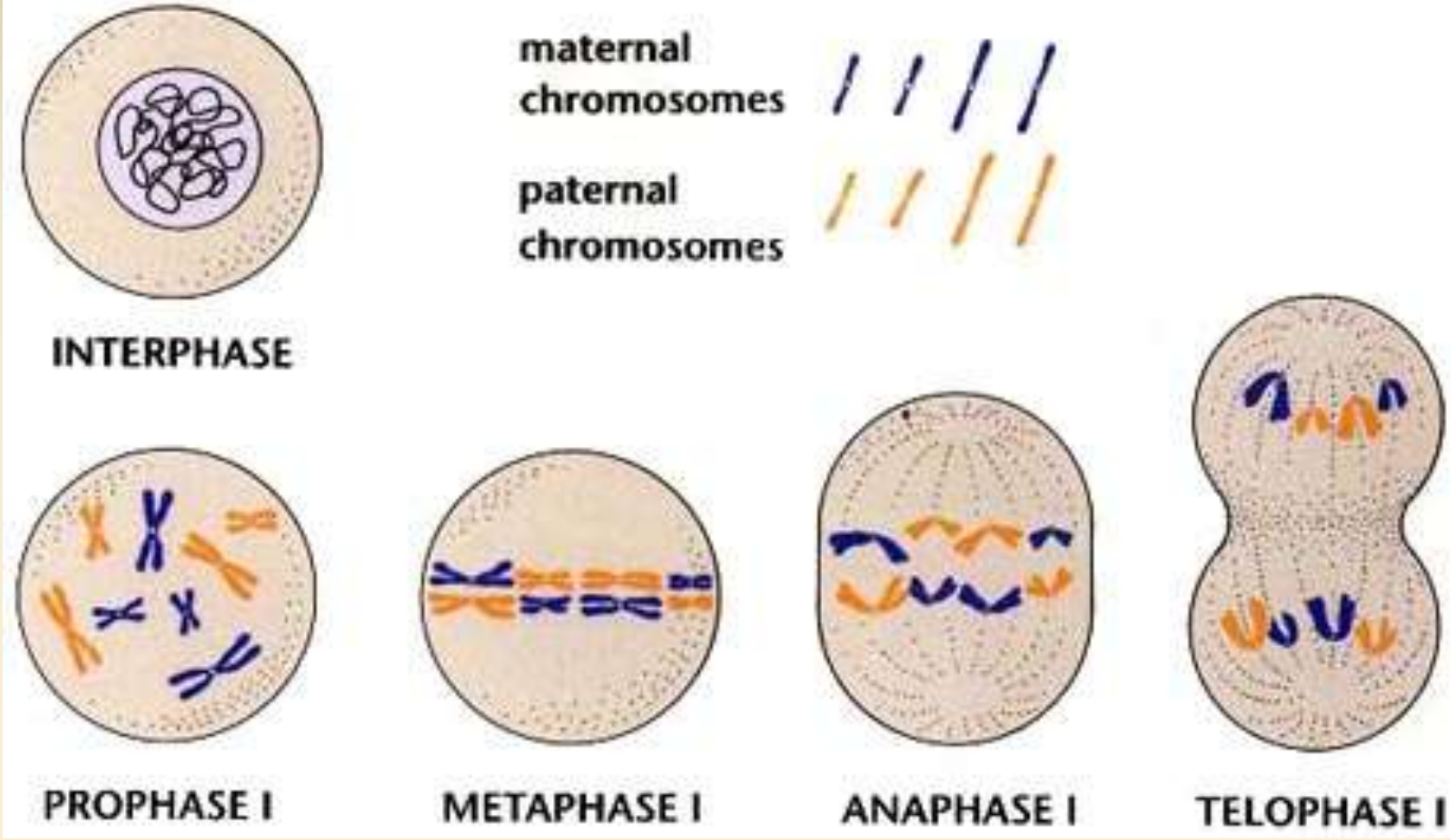
Sutton – "Chromosomes behave like Mendel's genetic factors…."

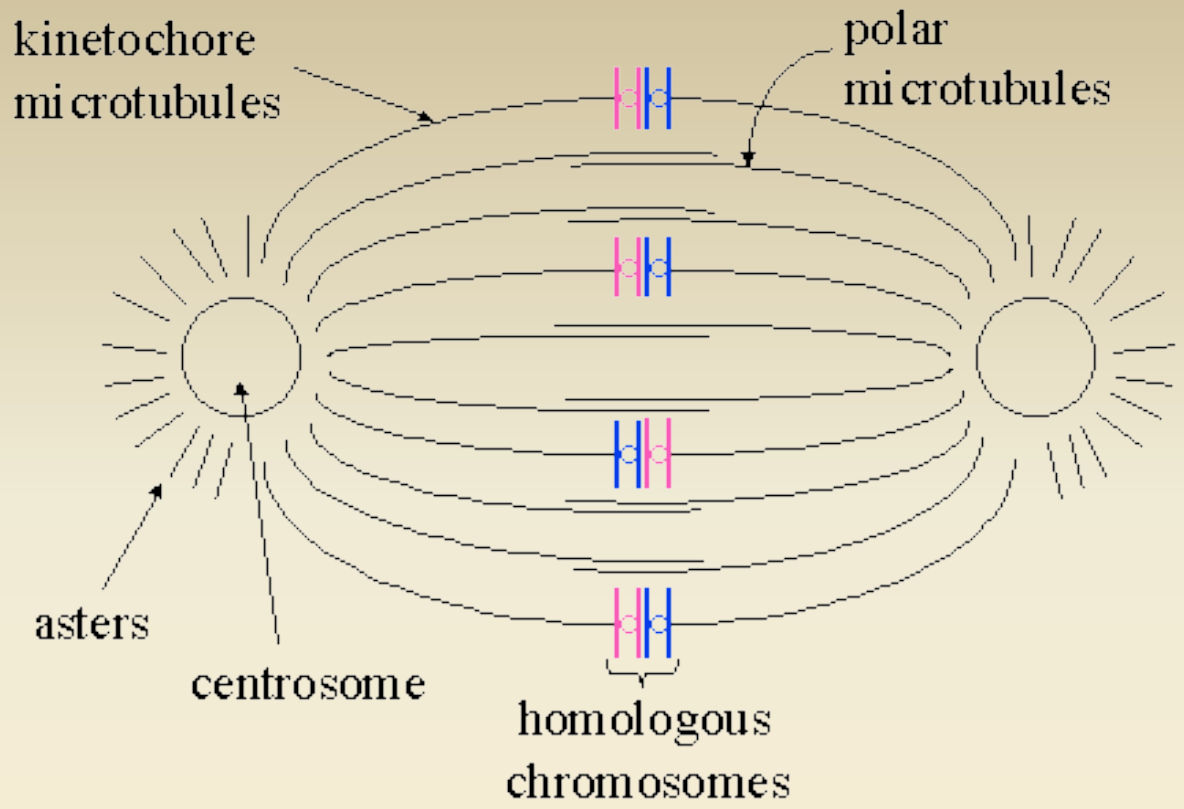
Sutton - Possible combinations of chromosome pairs at metaphase I

Chromosomes.		Combinations in Gametes.	Combinations in Zygotes.
Somatic Series.	Reduced Series.		
2	1	2	4
4	2	4	16
6	3	8	64
8	4	16	256
10	5	32	1,024
12	6	64	4,096
14	7	128	16,384
16	8	256	65,536
18	9	512	262,144
20	10	1,024	1,048,576
22	11	2,048	4,194,304
24	12	4.096	16,777,216
26	13	8,192	67,108,864
28	14	16,384	268,435,456
30	15	32,768	1,073,741,824
32	16	65,536	4,294,967,296
34	17	131,072	17,179,869,184
36	18	262,144	68,719,476,736



First Division of Meiosis



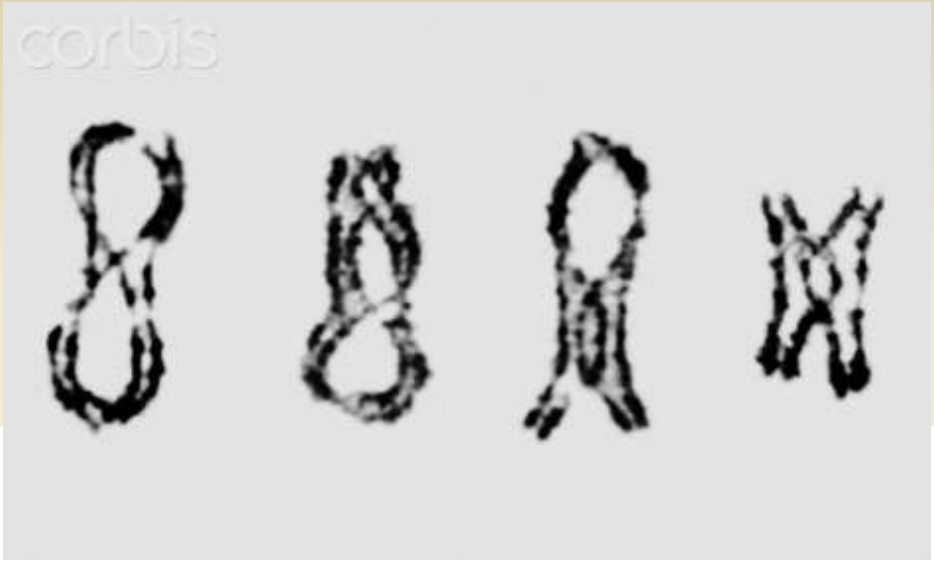


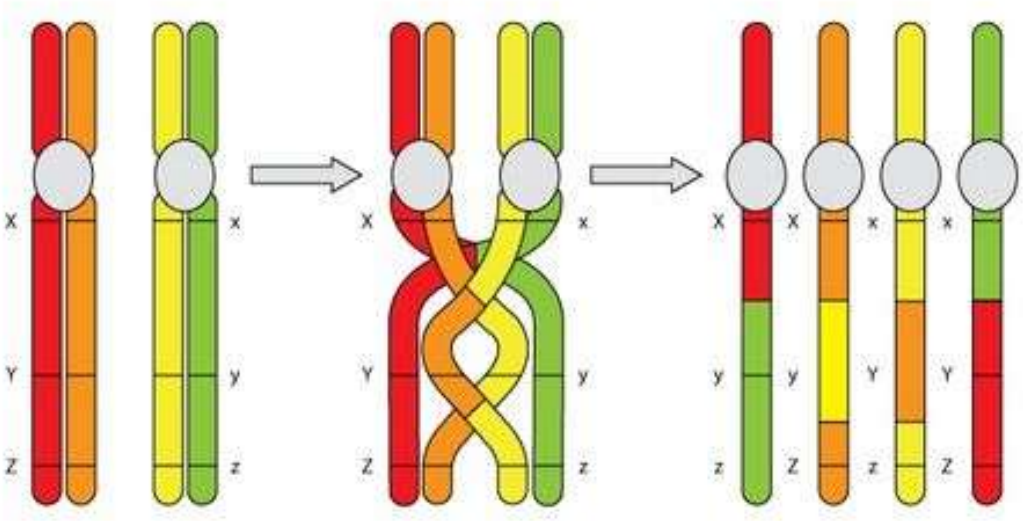
Bivalents (tetrads) become aligned in the center of the cell and are attached to spindle fibers.

Independent assortment refers to the random arrangement of pairs of chromosomes

For each chromosome pair, the chromosome that is on the left (maternal or paternal) is determined randomly. As can be seen, there are several alignment possibilities

Chiasma and Crossing Over





Basic Definitions

gene - basic unit of heredity; codes for a specific trait

locus - the specific location of a gene on a chromosome (locus - plural loci)

chromosome - elongate cellular structure composed of DNA and protein - they are the vehicles which carry DNA in cells

chromatid - one of two duplicated chromosomes connected at the centromere

centromere - region of chromosome where microtubules attach during mitosis and meiosis

diploid (2n) - cellular condition where each chromosome type is represented by two homologous chromosomes

haploid (n) - cellular condition where each chromosome type is represented by only one chromosome

homologous chromosome - chromosome of the same size and shape which carry the same type of genes

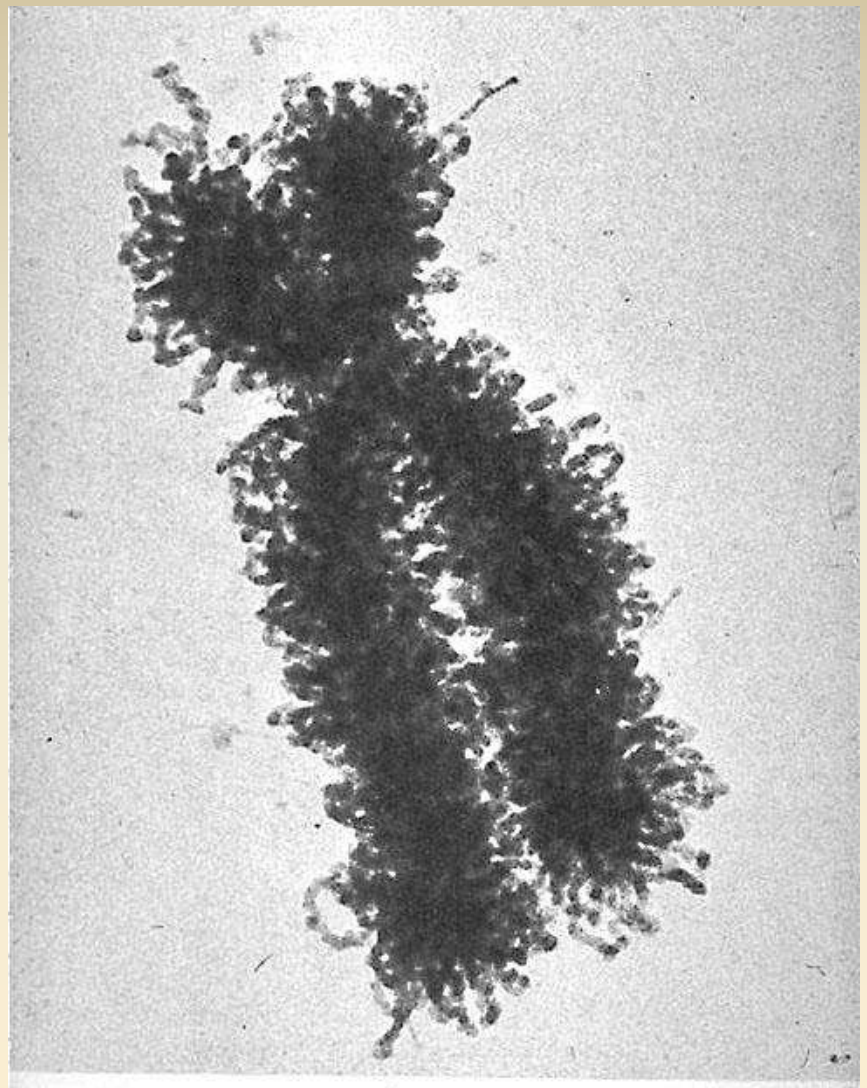
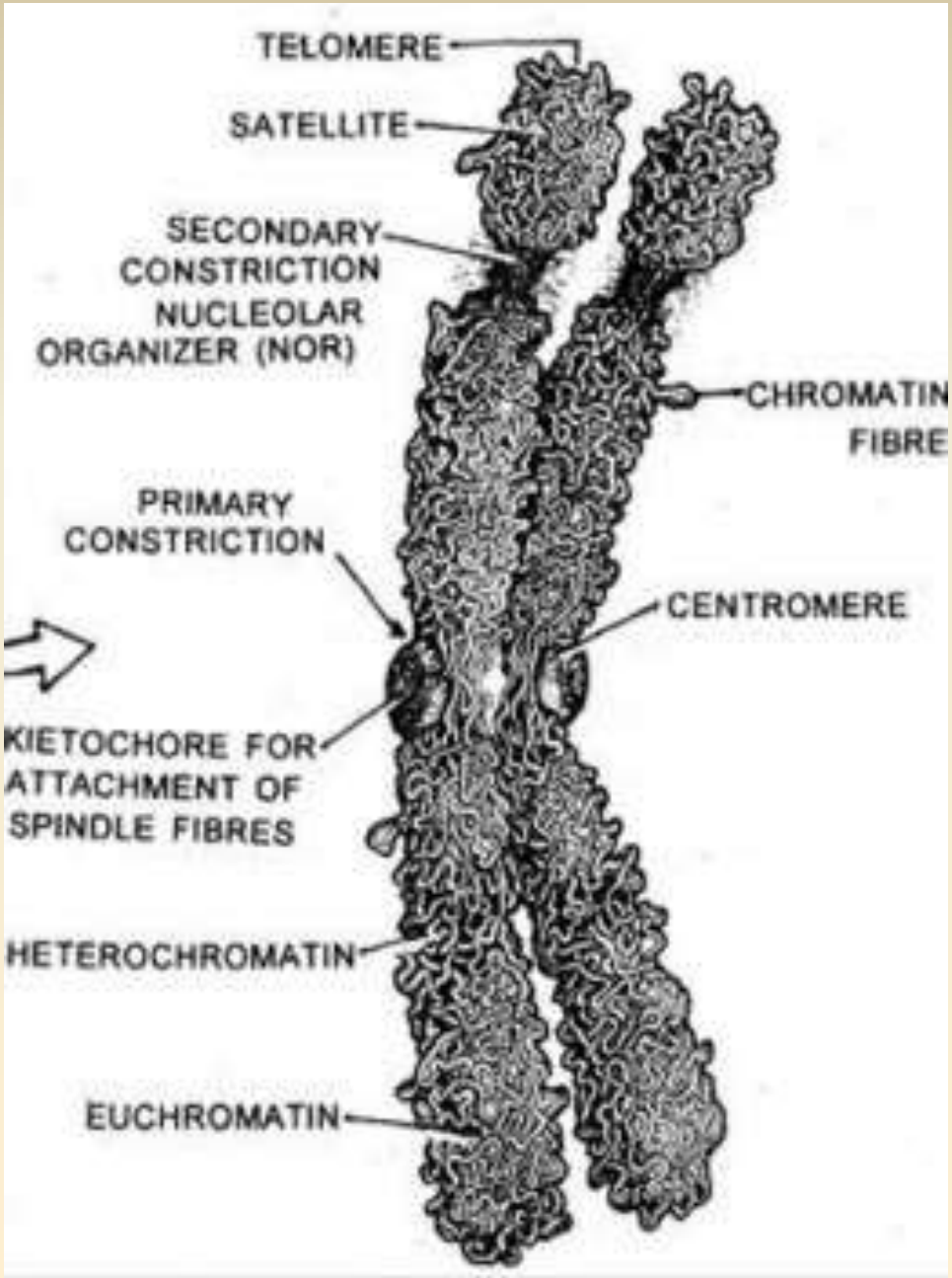
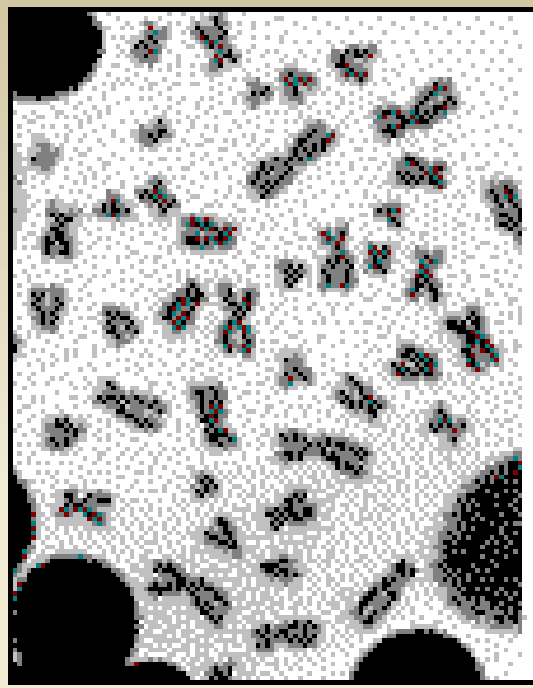
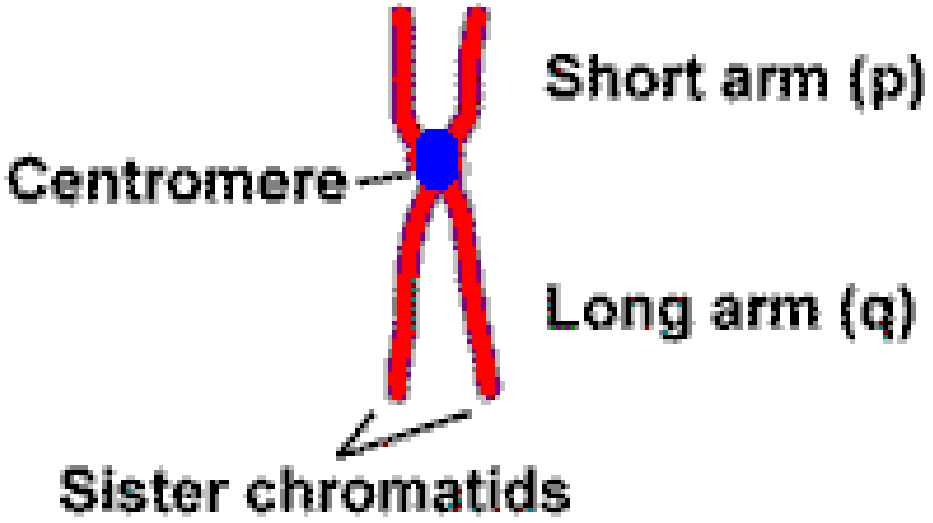


FIGURE 1-14
An electron micrograph of a human chromosome. Chromosome XII from a HeLa cell culture. (Courtesy of Dr. E. Du Praw.)





Metaphase Chromosome



Centromeric position and arm length

Metacentric Submetacentric Acrocentric Telocentric

Alterations in Chromosome Number

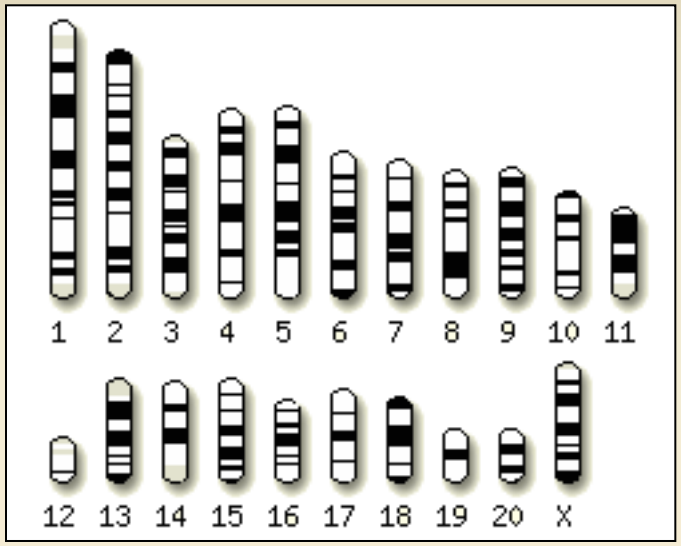
Karyotype - How many chromosomes there are, and their size and shape.

Aneuploidy: gain or loss of one chromosome or a small number of chromosomes

Polyploidy: one or more extra sets of chromosomes

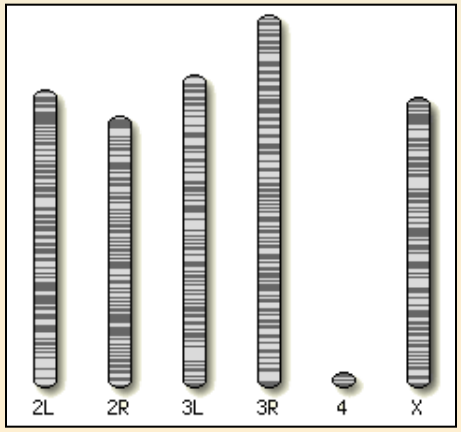
Karyotype - How many chromosomes there are, and their size and shape. They are usually species-typical.

Rat

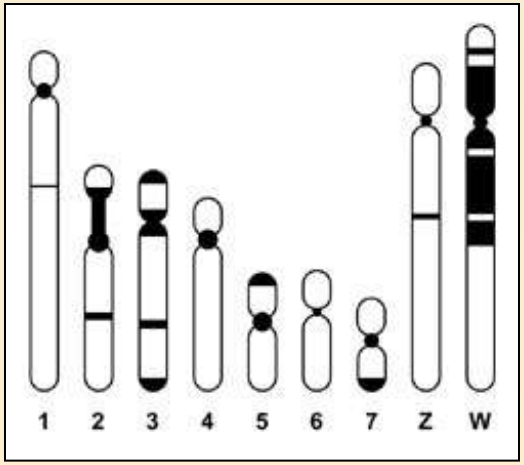


rice

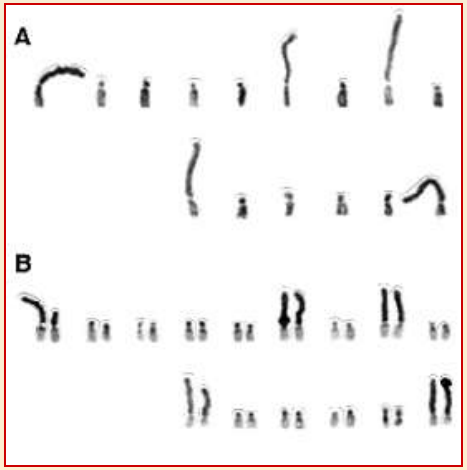
Drosophila fruit fly

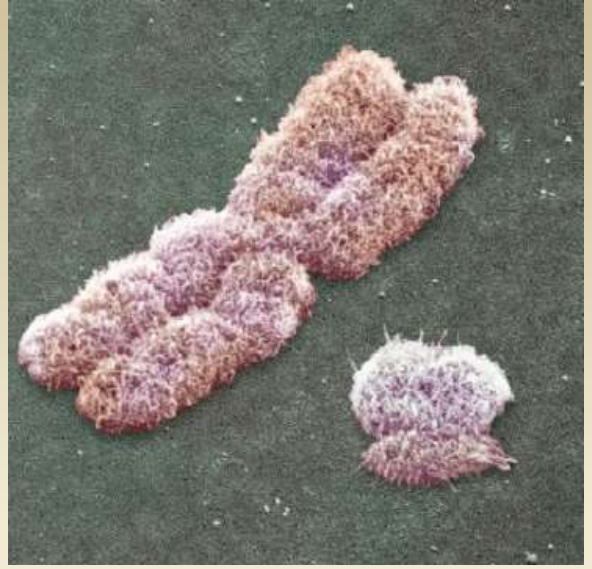


Schistosoma parasite



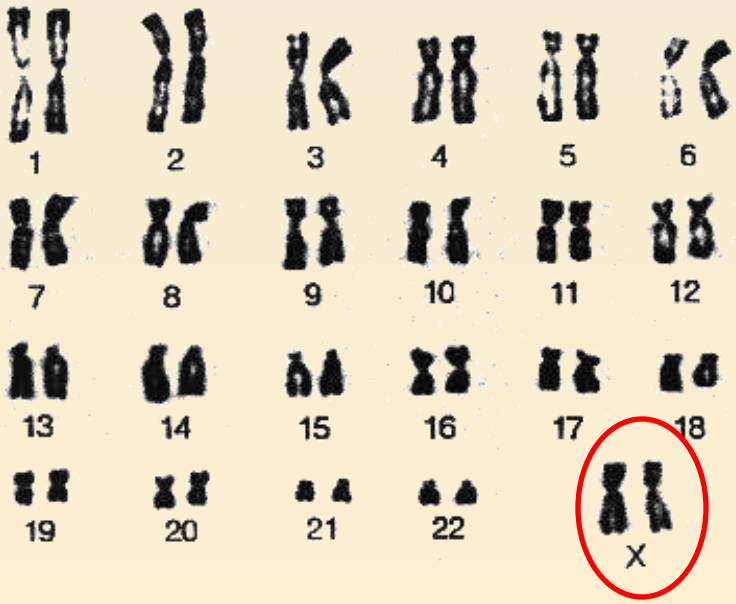
wasp



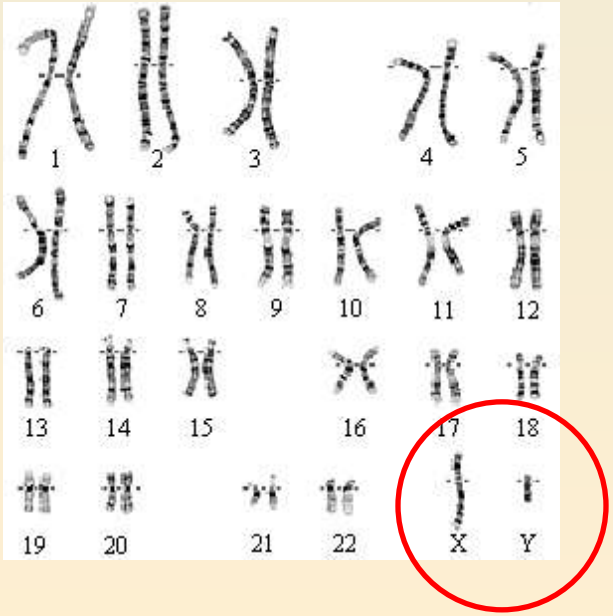


Sex Chromosomes – X, Y

Normal human female karyotype



Normal human male karyotype



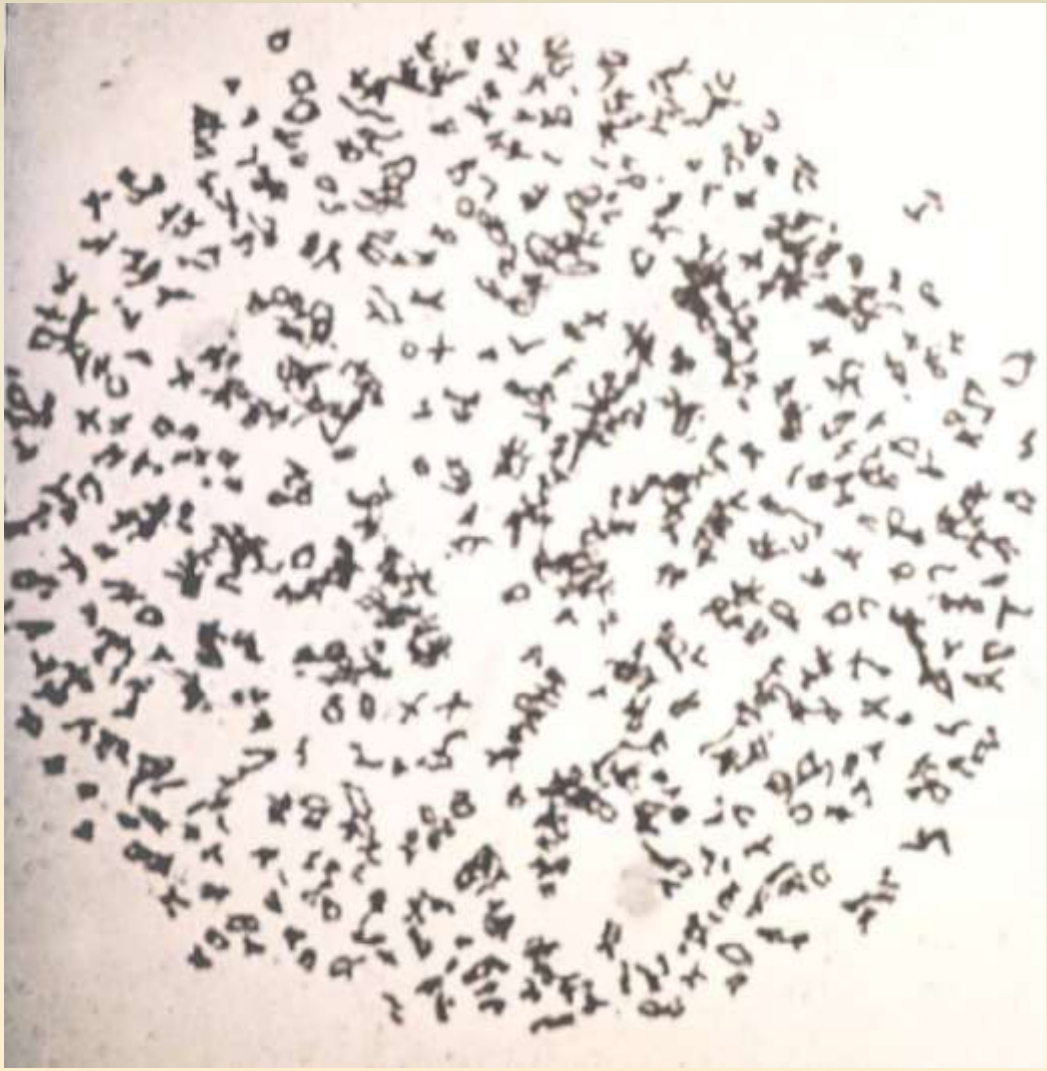
Variations in Chromosome Number

The suffix **-ploidy** refers to the number of haploid chromosome sets. Thus, haploid = 1 set, diploid = 2 sets, triploid = 3 sets,etc.

The suffix **-somy** refers to individual chromosomes. Thus, trisomy = having 3 copies of a chromosome, and monosomy = having 1 copy of a chromosome. Down syndrome, the most common from of mental retardation in humans, is caused by trisomy-21, 3 copies of chromosome 21.

Chromosome Number

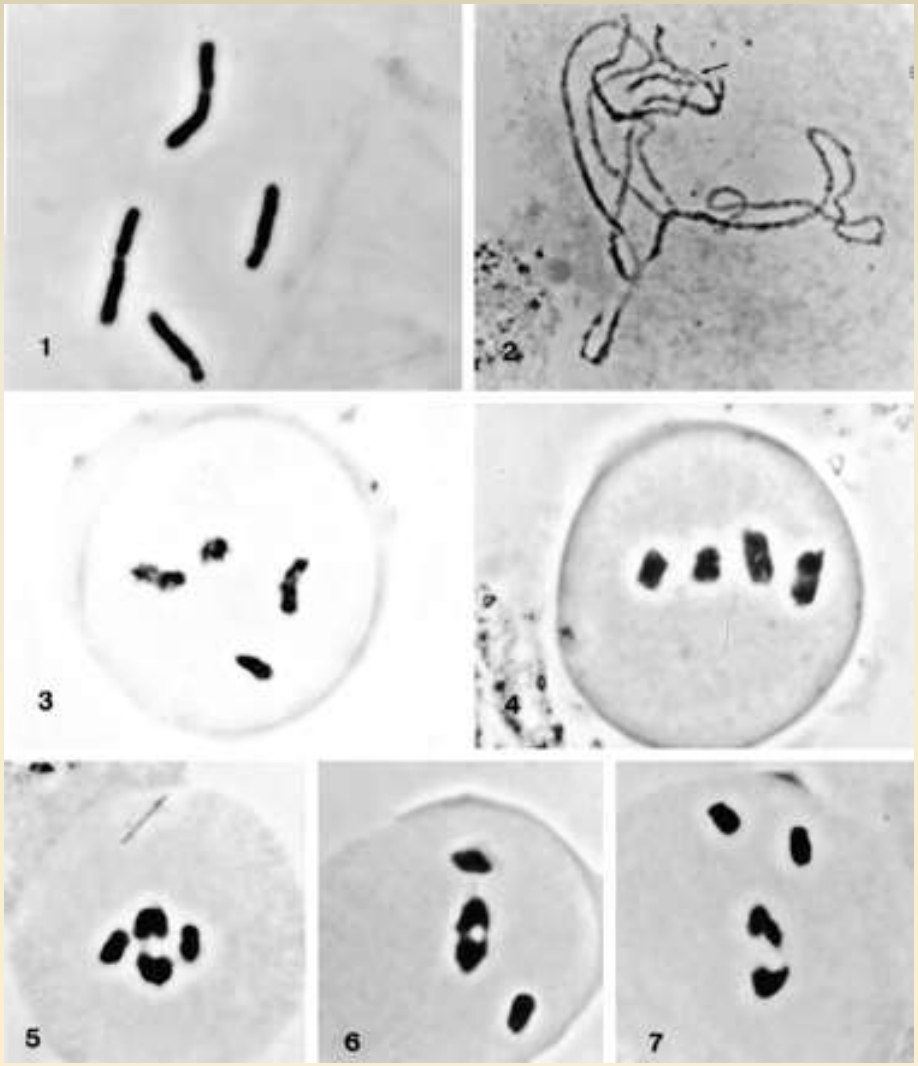
***Ophioglossum reticulatum* - 2N = 96X = 1440**



Ophioglossaceae
Botrychium virginianum

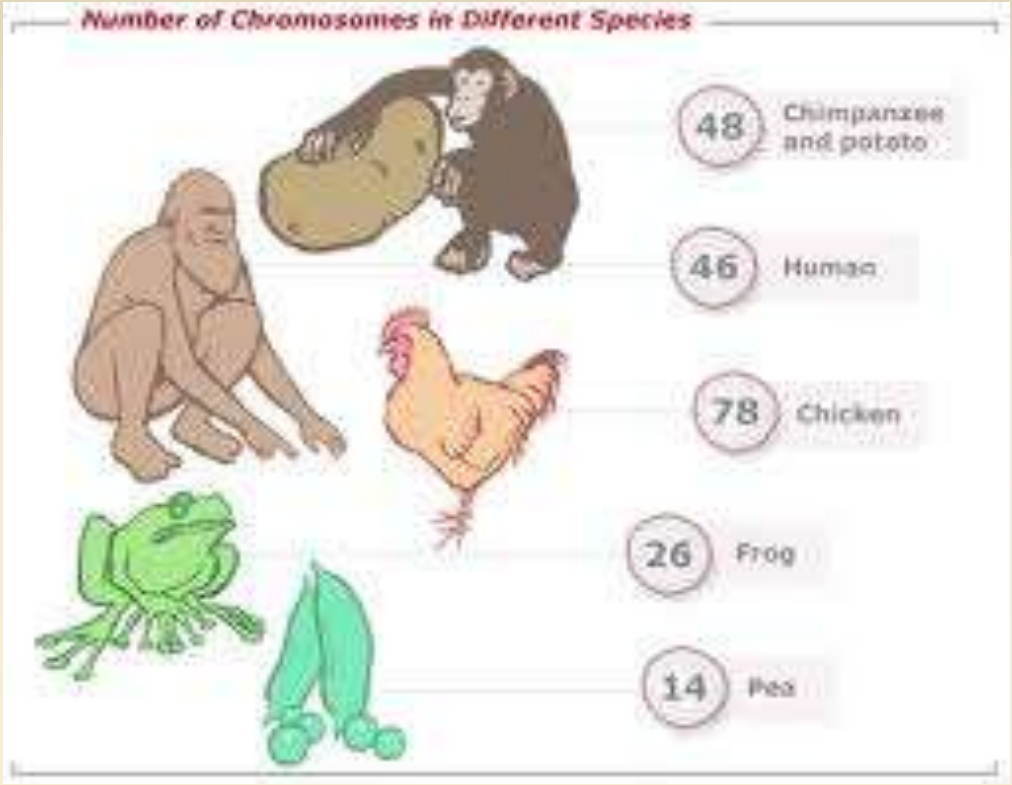
Haplopappus (Machaeranthera) gracilis (Asteraceae)

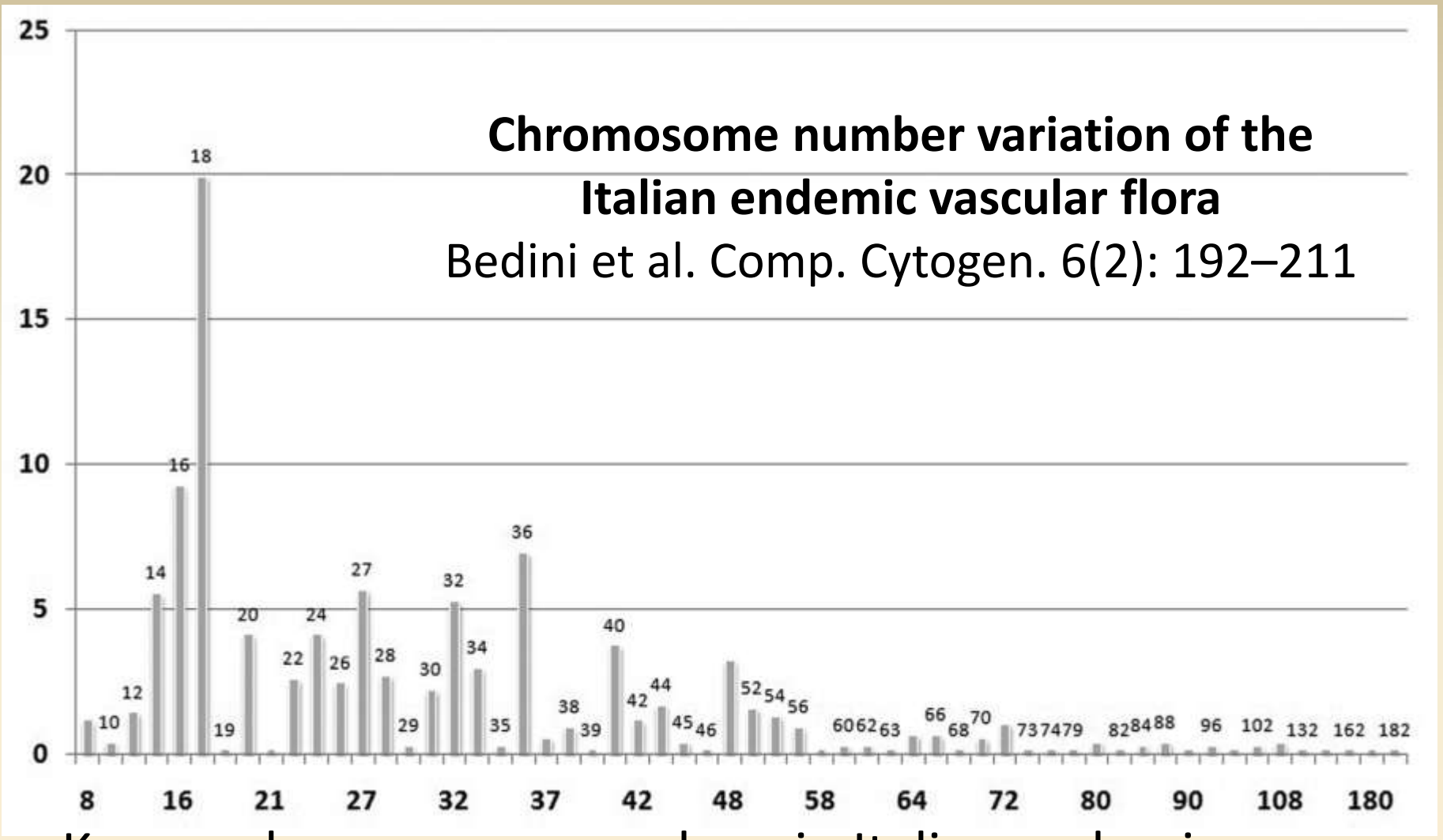
2N = 2X = 4



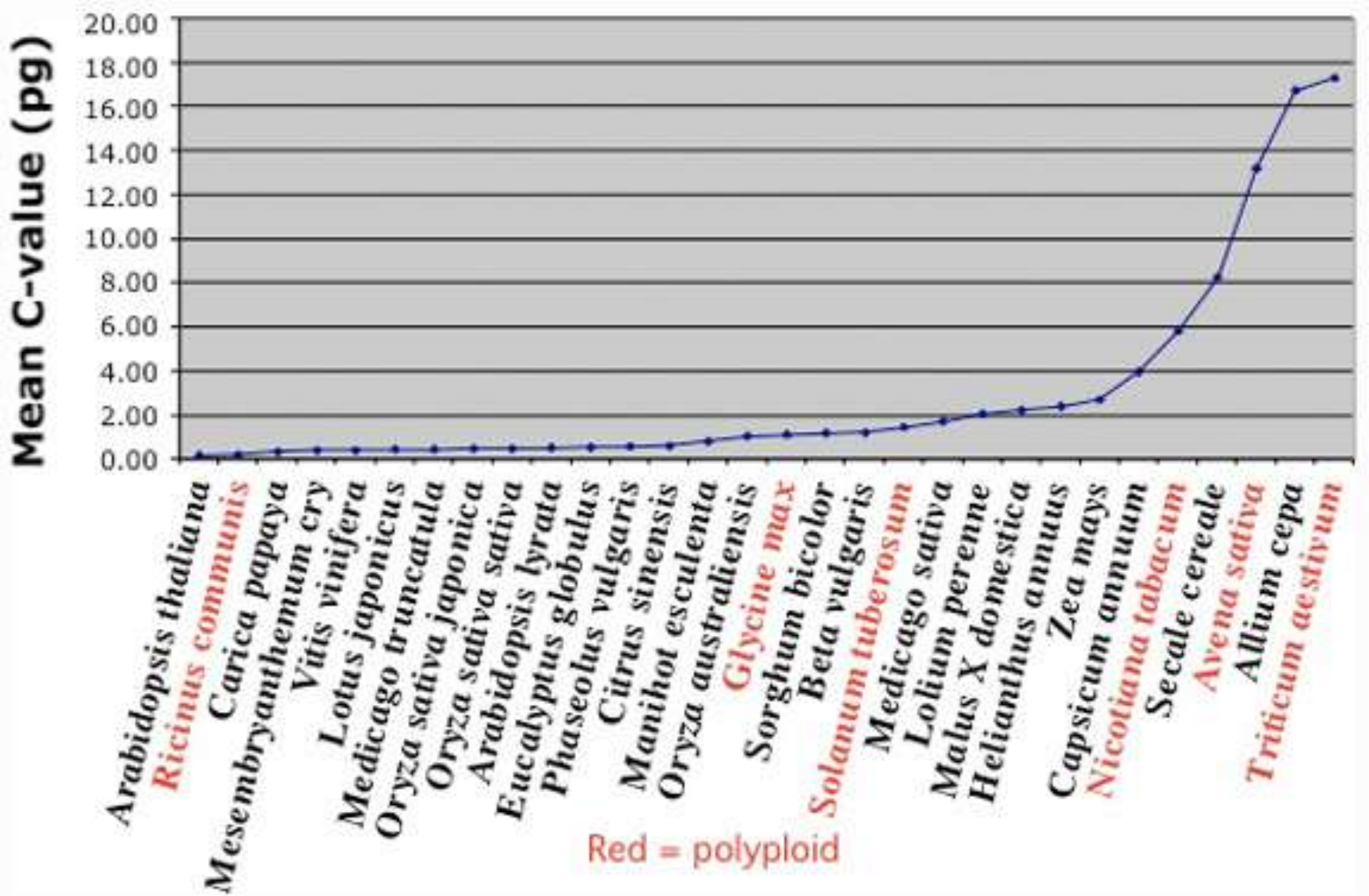
Chromosome number in Animals
Number low, Polyploidy very rare

Common Name	Species	Diploid number
Animals (2n)		
Human	*Homo sapiens*	46
Monkey	*Macaca mulatta*	42
Dog	*Canis familiaris*	78
Cat	*Felis domesticus*	38
Mouse	*Mus musculus*	40
Frog	*Rana pipiens*	26
Fruit fly	*Drosophila melanogaster*	8
Flatworm	*Planaria torva*	16





Known chromosome numbers in Italian endemics range from 2n = 8 to 2n = 182. **Mean chromosome number for Italian endemics is 2n = 30.68** 20.27 (median: 2n = 26, mode: 2*n* = 18).

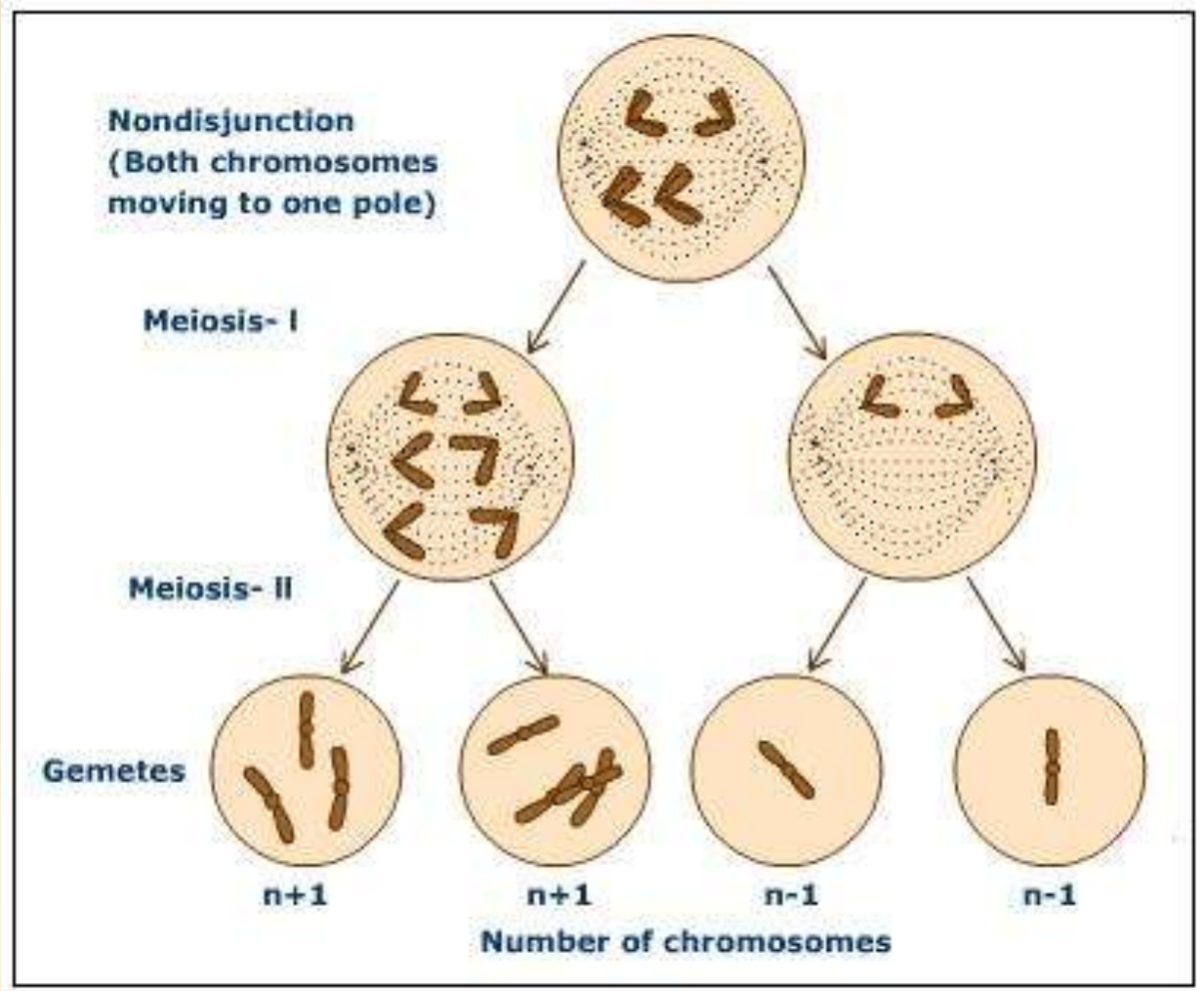


C-Values – amount of DNA in cell

Aneuploidy

Arises by Nondisjunction

Nondisjunction - failure of homologues or chromatids to separate during meiosis



Aneuploidy

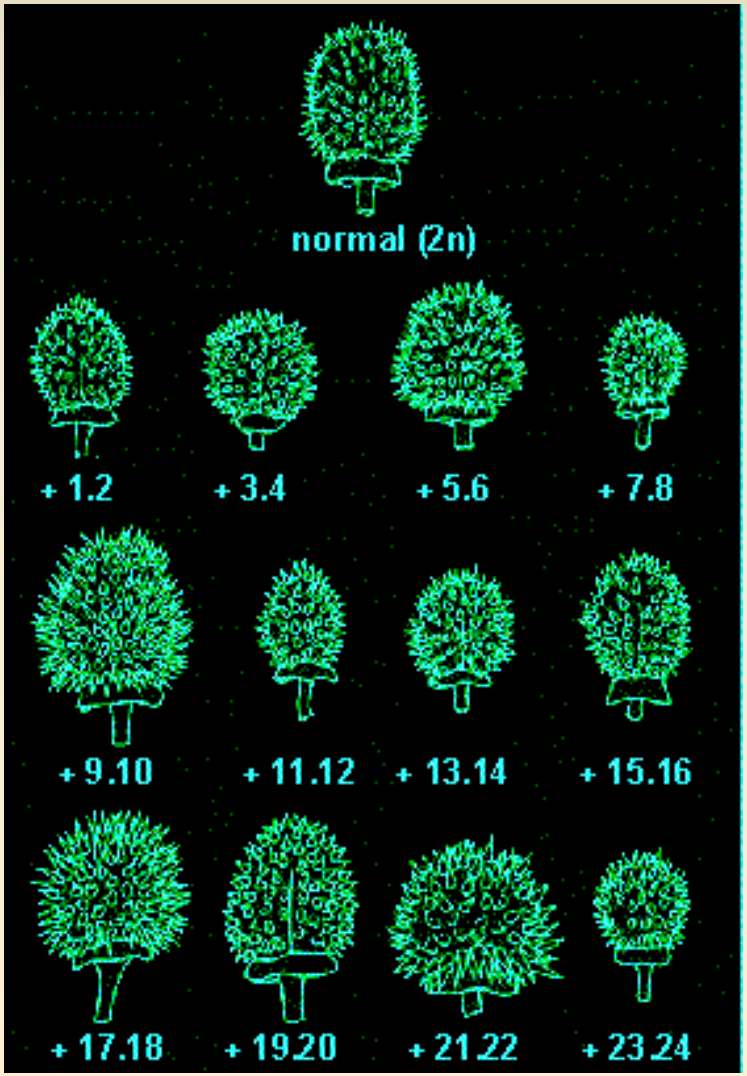
In general, **organisms need a balanced number of chromosomes**.

Having an extra chromosome (trisomic) or missing a chromosome (monosomic) is usually lethal. The chromosomes in this case are unbalanced, not equal numbers of all types. This condition is called "aneuploid".

Most diploids **don't survive as haploids**, because they are usually heterozygous for recessive lethal alleles. Similarly, making an organism homozygous at most genes (through repeated matings between close relatives) is usually lethal. Heterozygosity helps diploid organisms cope with different environmental conditions.

Aneuploidy in Plants - *Datura*

A gain or loss of one or more chromosomes, e.g. 2N -1, 2N + 1, 2N + 2, etc. The most common cases are trisomies (sing. trisomy) where a single additional chromosome is present.



Fruits of *Datura*-
Plants On top: Control plant (2n)

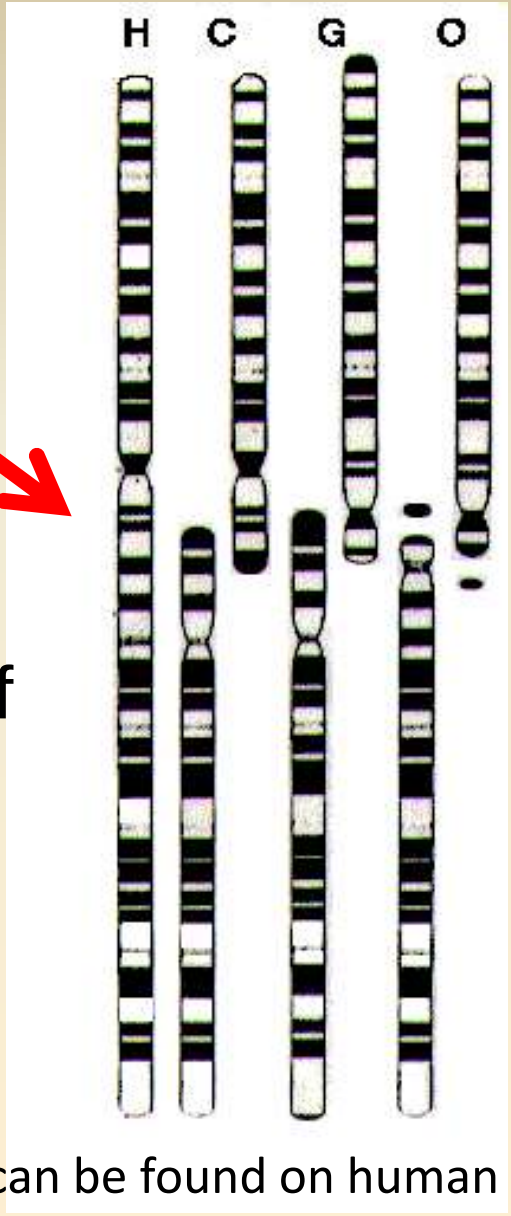
Below: Mutants that are characterized by **one additional chromosome** each.

Loss of one or more chromosomes usually has more severe consequences

Aneuploidy occurred in the lineage leading to human from their common ancestor with the great apes (chimps, gorillas, and orangutans).

Homologous chromosomes are aligned in this karyotype.

Human chromosome #2 is a fusion of 2 different chromosomes in the other species, including the loss of the terminal fragments of both chromosomes.



Remnants of a second, presumably inactive centromere can be found on human chromosome 2. Chromosome 2 also has telomere sequences not only at both ends but also in the middle

Aneuploid Series - well known in plants

Carex - long and nearly continuous series from n=6 to n=56

Crepis – series n=6-5-4-3

Nicotiana – series n=12-11-10-9

Aneuploidy in *Claytonia virginica*

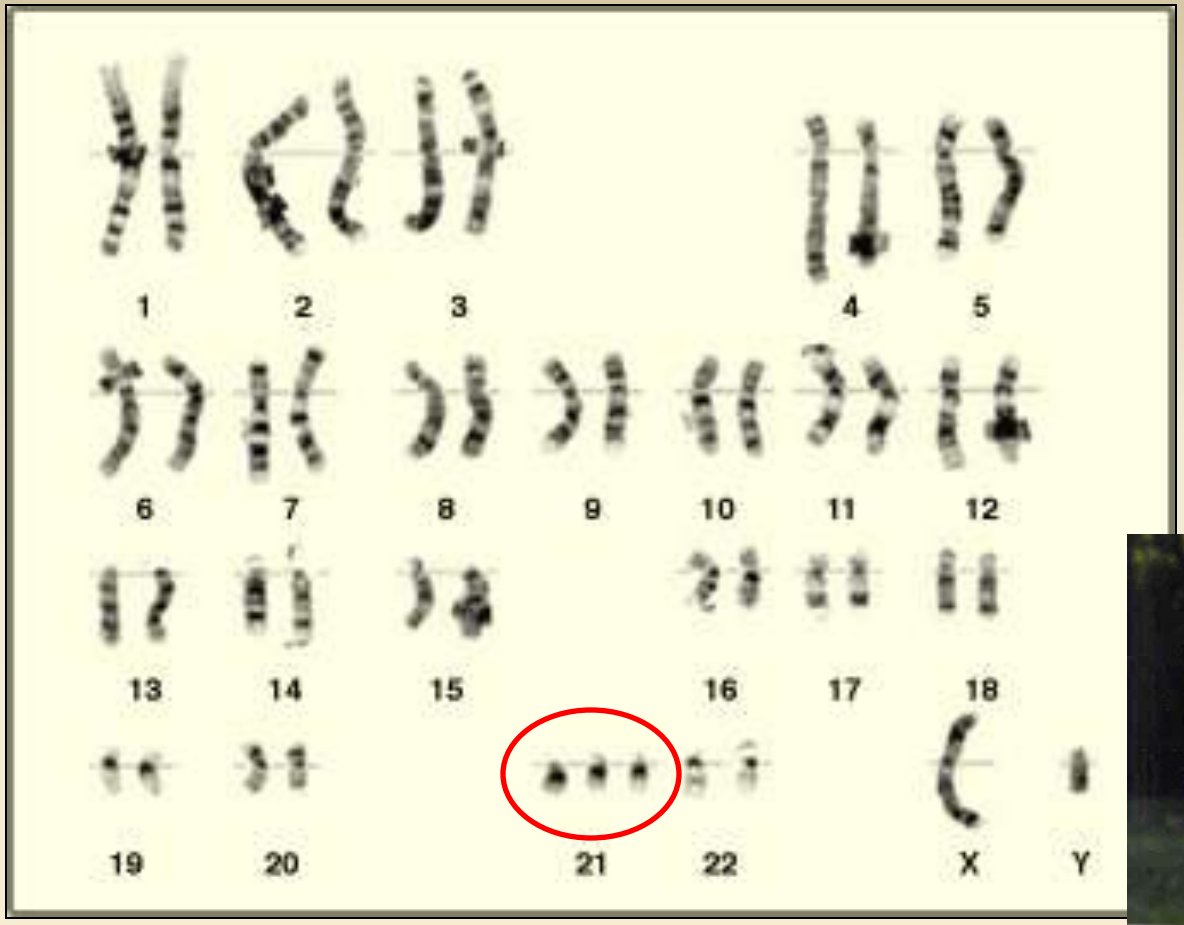
FIGURE 19.2 Variation of diploid chromosome numbers in populations throughout the range (enclosed area) of *Claytonia virginica* (Portulacaceae). (Redrawn from Lewis, Oliver, and Suda 1967:154)

Walter Lewis (1970, 1971), MBG.
Plants have different chromosome numbers in different parts of their ranges and even within same population. and within one individual from year to year.

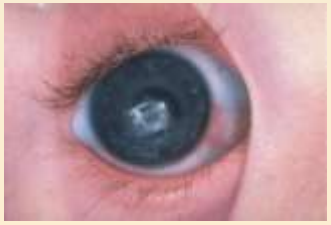
"I would argue that if an organism does not take its chromosome number seriously, there is no reason why the systematist should" (Walter Lewis).

Trisomy 21

Down Syndrome



Physical Features



Eye fold

Palm Crease

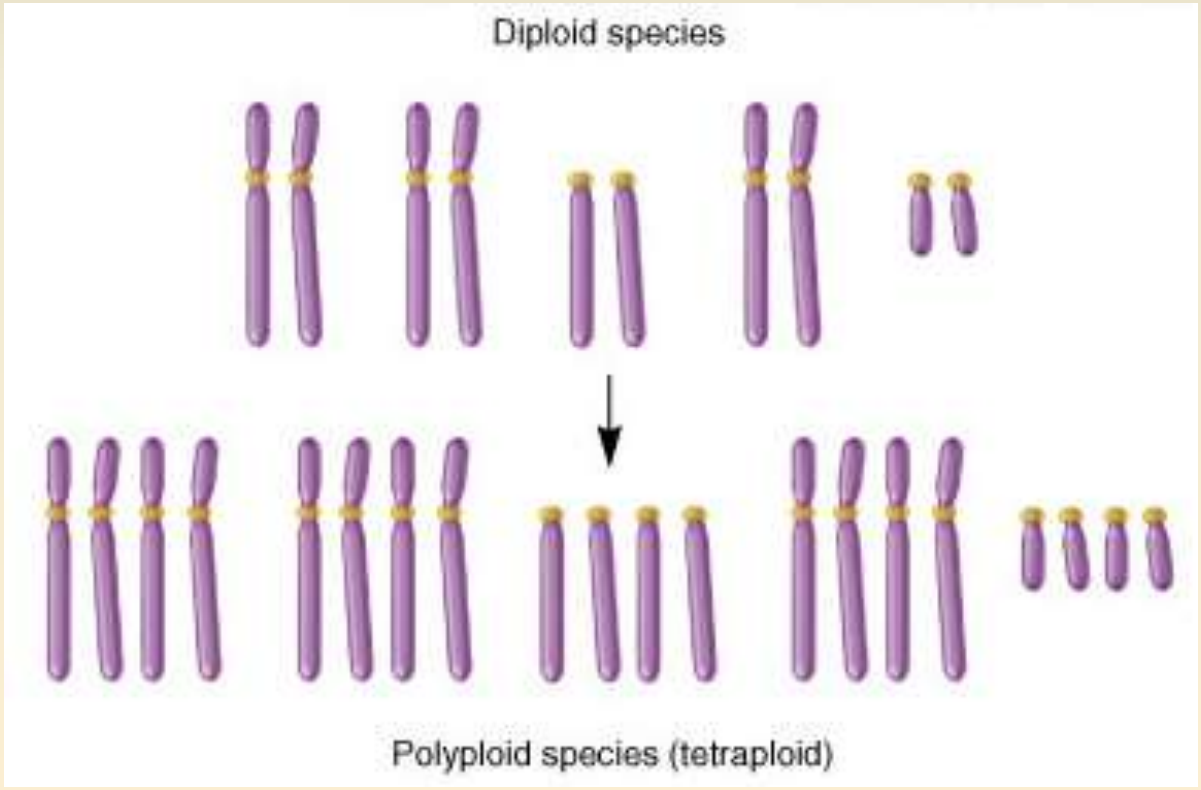
Human Chromosomal Aneuploids

Autosomal Aneuploids

Down Syndrome	Trisomy 21
Edward Syndrome	Trisomy 18
Patau Syndrome	Trisomy 13

Polyploidy

Polyploidy occurs when all the chromosomes are present in three or more copies or whole sets.



Polyploidy is common in plants and rare in animals.

Polyploidy

Polyploidy occurs when there are more than two homologous sets of chromosomes

Most multicellular eukaryotic organisms are normally diploid.

Polyploidy may occur due to abnormal cell division, i.e., **nondisjunction events**

Polyploidy is most **commonly found in plants**. Half of all angiosperms (flowering plants) and almost all ferns are polyploid.

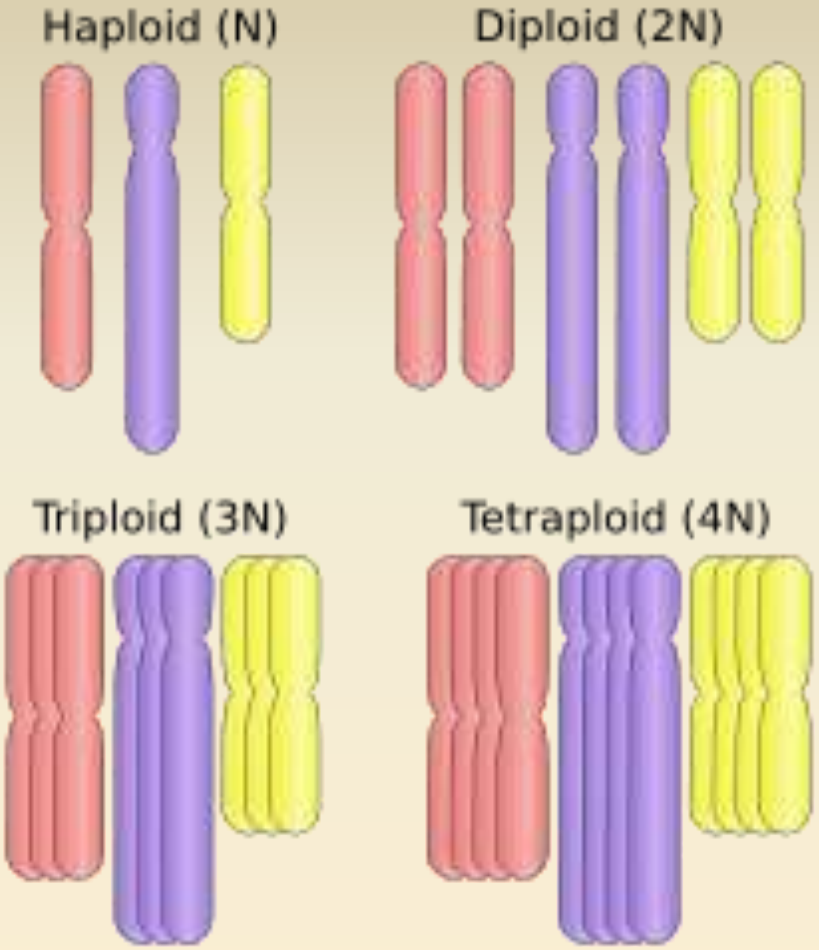
Polyploidy occurs in some animals, such as goldfish, salmon, and salamanders, but is especially common among ferns and flowering plants, including both wild and cultivated species.

Polyploidy

Genes in polyploid chromosome sets are free to develop new functions through natural selection and evolution.

Polyploidy is a key source of genetic variation.

Polyploidy – multiple sets of chromosomes



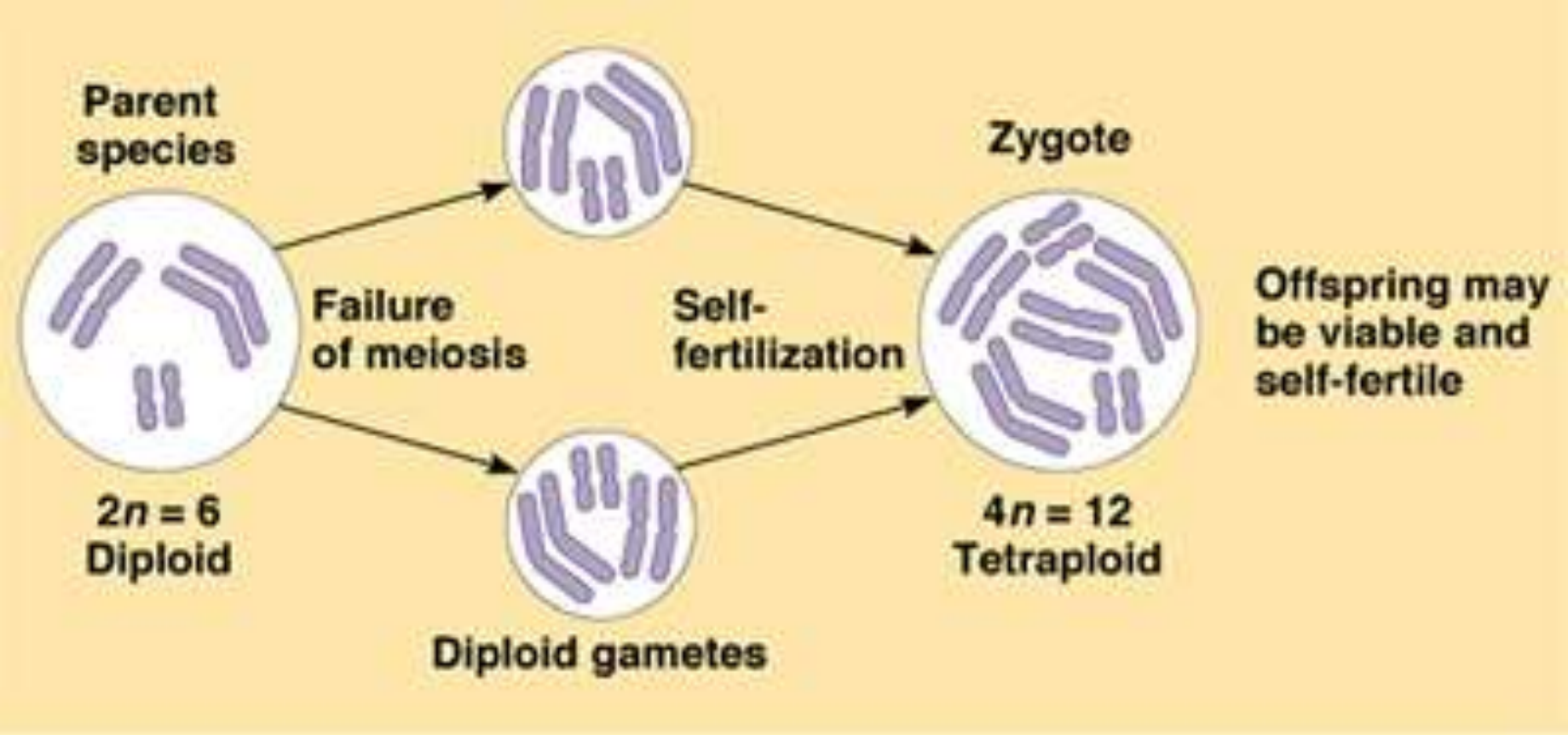
Diploid – 2 sets
Triploid – 3 sets (watermelon)
Tetraploid – 4 sets (cotton)
Hexaploids – 6 sets (wheat)

Autopolyploids: polyploids composed of multiple sets of chromosomes from the same species

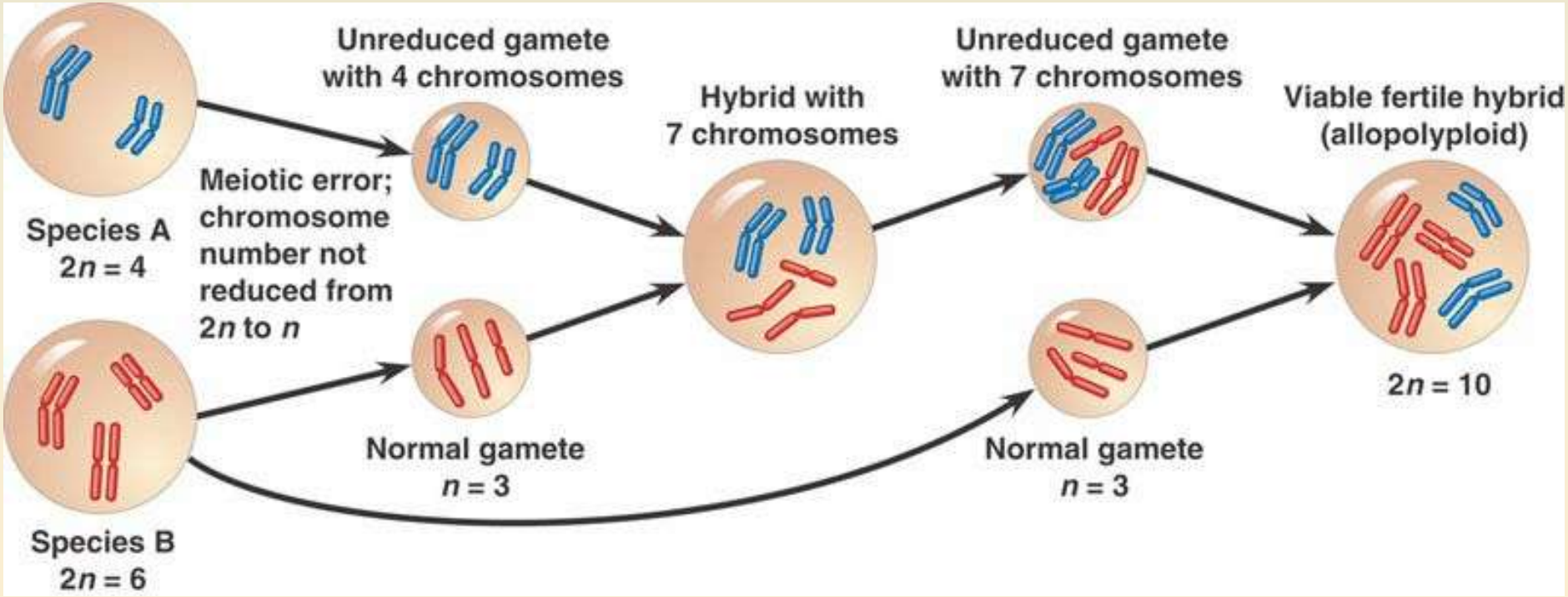
Allopolyploids: polyploids that are a new species, composed of multiple sets of chromosomes from closely related species

Autopolyploids: polyploids composed of multiple sets of chromosomes from the same species

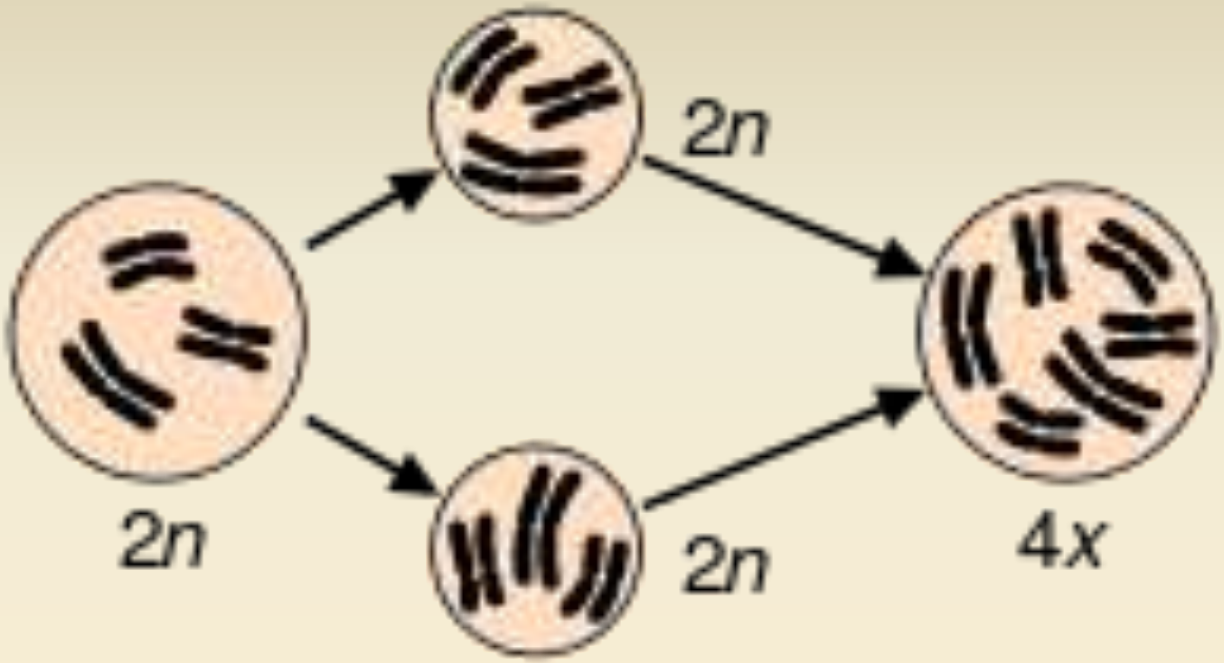
Nondisjunction - chromosomes fail to separate after duplication, resulting in unreduced gametes



Allopolyploids: composed of multiple sets of chromosomes from closely related species, probably common in speciation, formation of new species



Tetraploids – 4 sets of chromosomes



Failed meiosis, gametes 2N

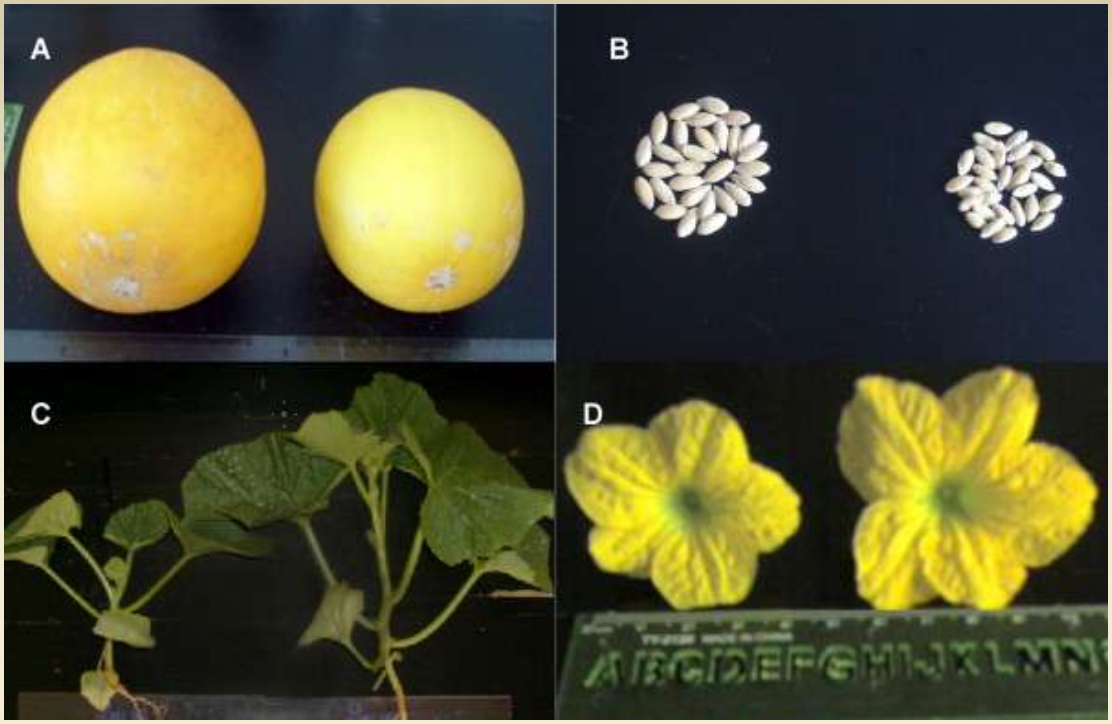
Tetraploid crops: apple, durum or macaroni wheat, cotton, potato, cabbage, leek, tobacco, peanut, Pelargonium (potted Geranium)

Autopolyploids are often large and healthier that the original diploids.

Thus, autopolyploids are commonly found in fruits and vegetables.

For instance, commercial chrysanthemums and daylilies are usually tetraploid

Some Tetraploid Fruits



Muskmelon – tetraploid and diploid compared

Passiflora

Raspberries

Allopolyploidy	**Banana & plantain, blackberry & raspberry, blueberry, tart cherry, European plum, strawberry**
	***Triploidy*: banana and plantain, apple, pear**
	***Tetraploid* : tart cherry, raspberry, blackberry, blueberry, kiwifruit (*Actinidia sinensis*)**
	***Hexaploid*: European plums, kiwifruit (*A. deliciosa*)**
	***Octaploid:* strawberry**

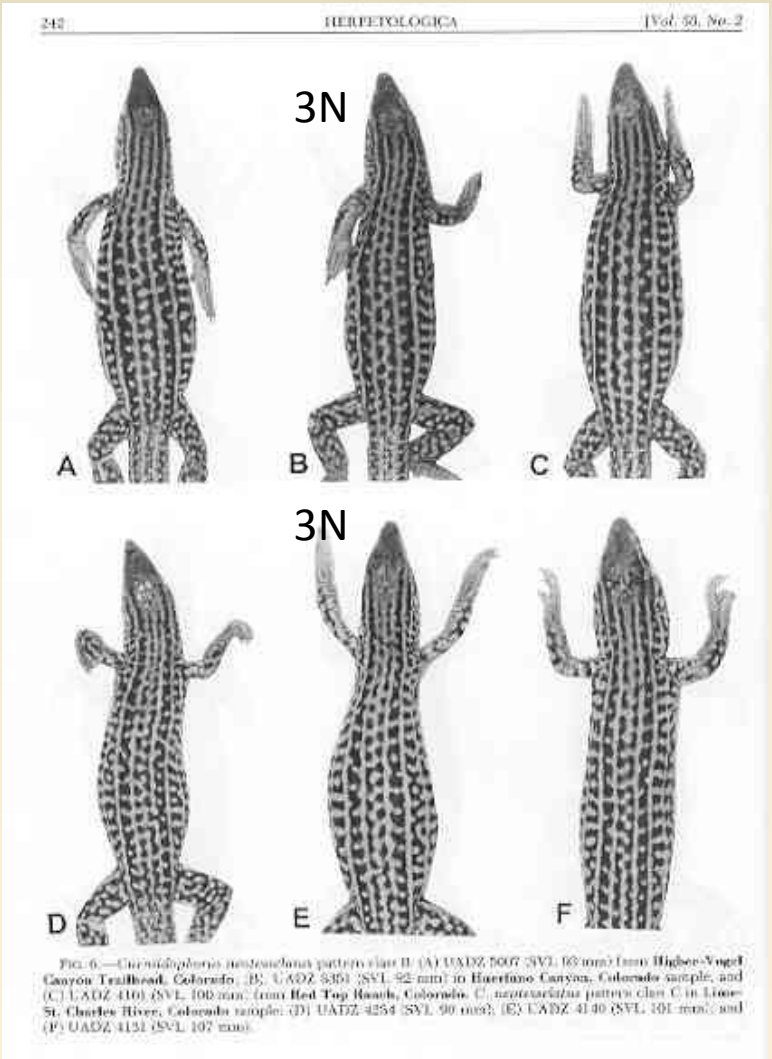
Triploidy – 3 sets

- In some circumstances, a diploid gamete fertilizes a normal haploid gamete

- Then a triploid individual is the result

- At meiosis, sets of 3 like chromosomes have great mechanical difficulty in the close alignment of **synapsis**

checkered whiptail lizard



Triploid crops: apple, banana, citrus, ginger, watermelon

Musa acuminata (Asian Banana)	X	*Musa balbisiana* (Asian Banana)	=	*Musa X paradisiaca* (Hybrid Banana)
AA (fertile)		BB (fertile)		AAB or ABB (etc.) (sterile)

Origin Of Triploid Banana From Asian Parents

A = one haploid set of chromosomes from *M. acuminata*

B = one haploid set of chromosomes from *M. balbisiana*

Triploids – 3 sets of chromosomes

Triploid organisms are usually sterile. Triploidy is a common way of making seedless fruit, such as in watermelons. Recall that the seed is a multicellular organism, many cell divisions after fertilization.

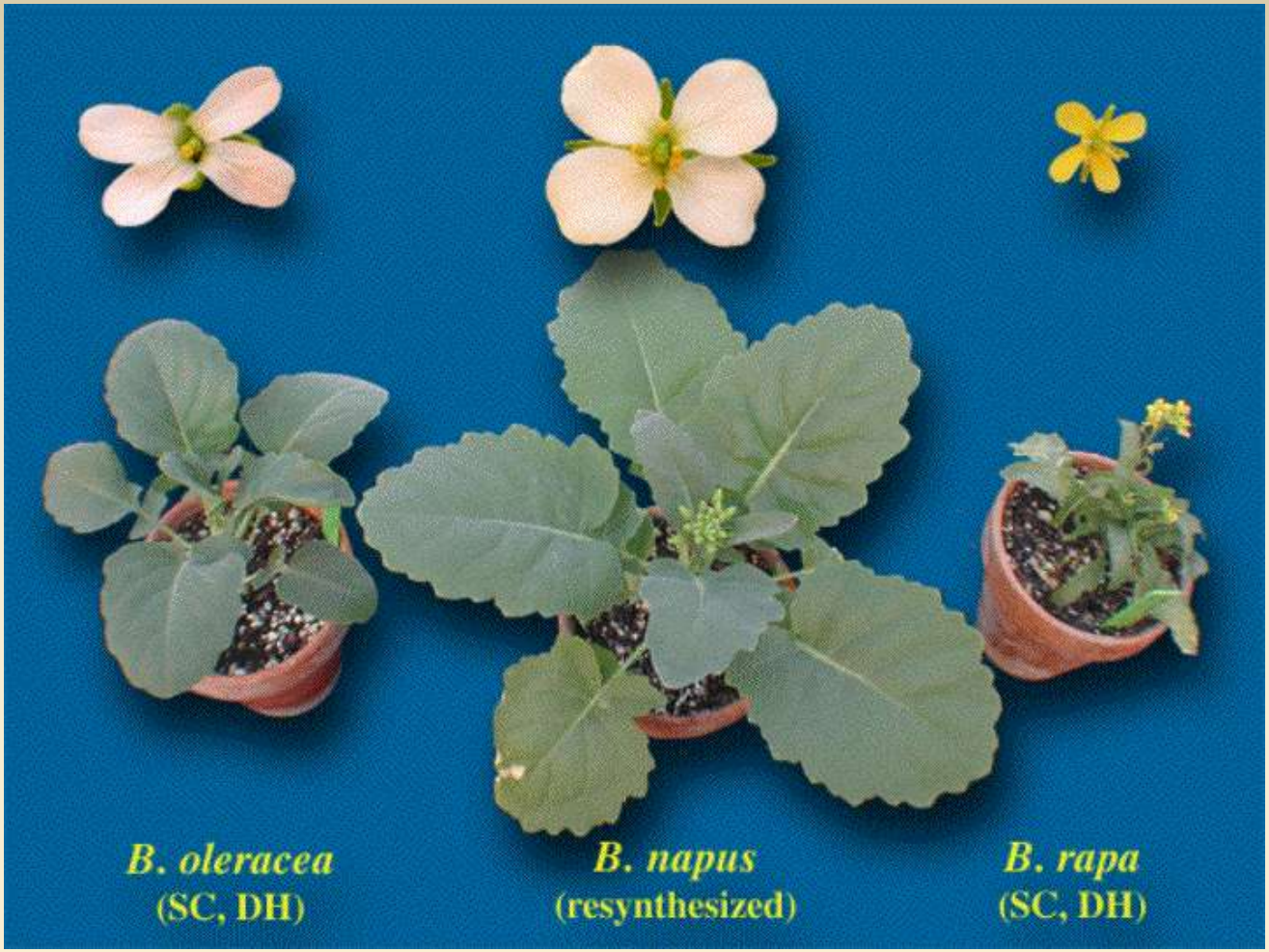
The reason triploids are sterile can be found in metaphase and anaphase of meiosis 1. Homologues pair up in metaphase of M1, then they are pulled to opposite poles in anaphase.

In triploids, there are 3 members to each set of homologues. They line up as triples at metaphase. In anaphase, 1 homologue goes to the upper pole, and one homologue goes to the lower pole. The third homologue goes randomly to either pole.

The result is that each cell after M1 has 1 copy of some chromosomes and two copies of other chromosomes. This is an aneuploid condition, which nearly always results in dead embryos.

In humans, triploid fetuses are the result of dispermy, fertilization of an egg by two sperm simultaneously. Triploid humans usually die before or just after birth. About 15% of spontaneous abortions are due to triploidy.

Hybrid Vigor - resynthesized *Brassica napus*



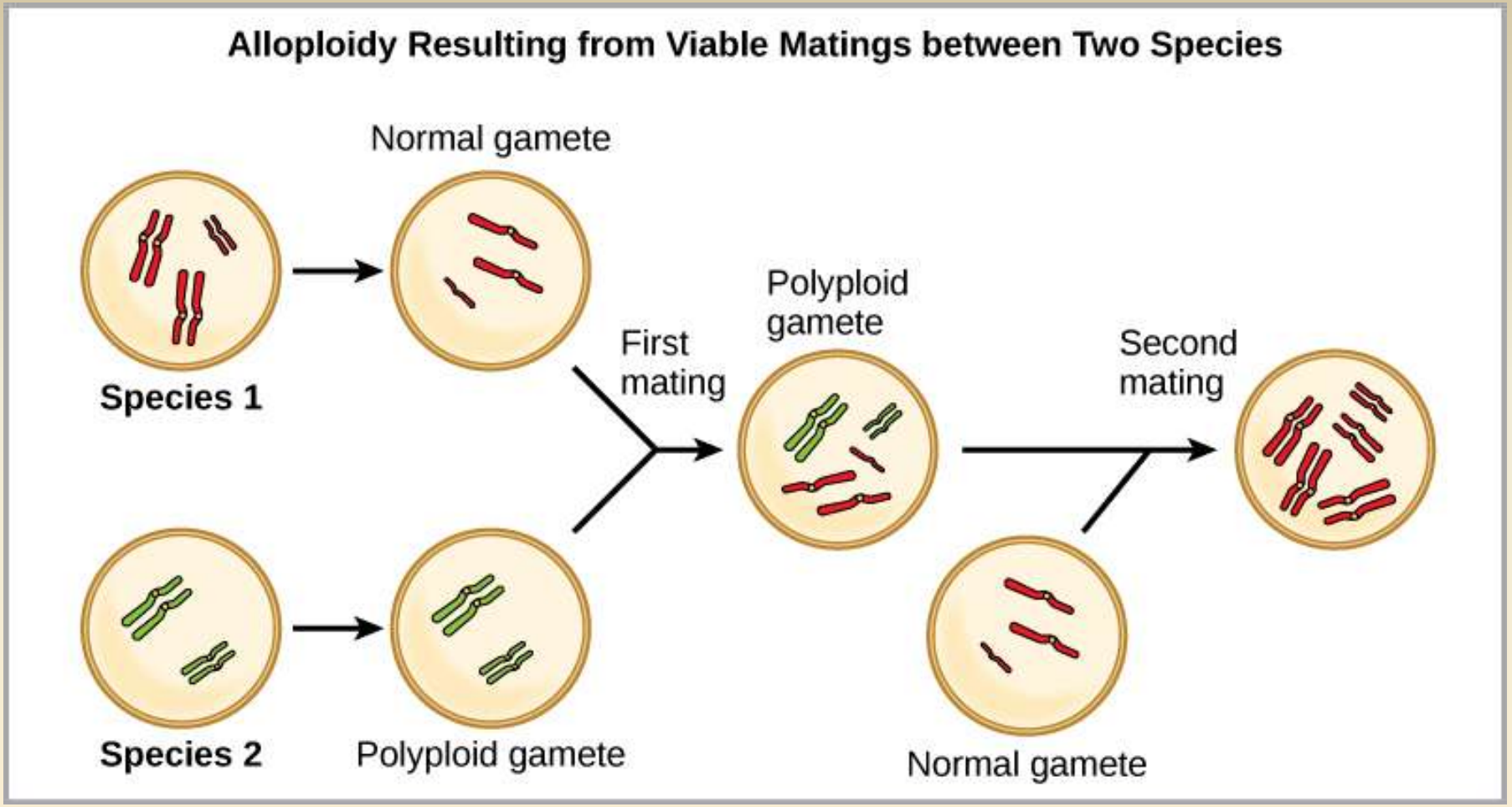
An example of an allopolyploid that shows hybrid vigor over its diploid progenitors is resynthesized *Brassica napus*.

Allopolyploidy

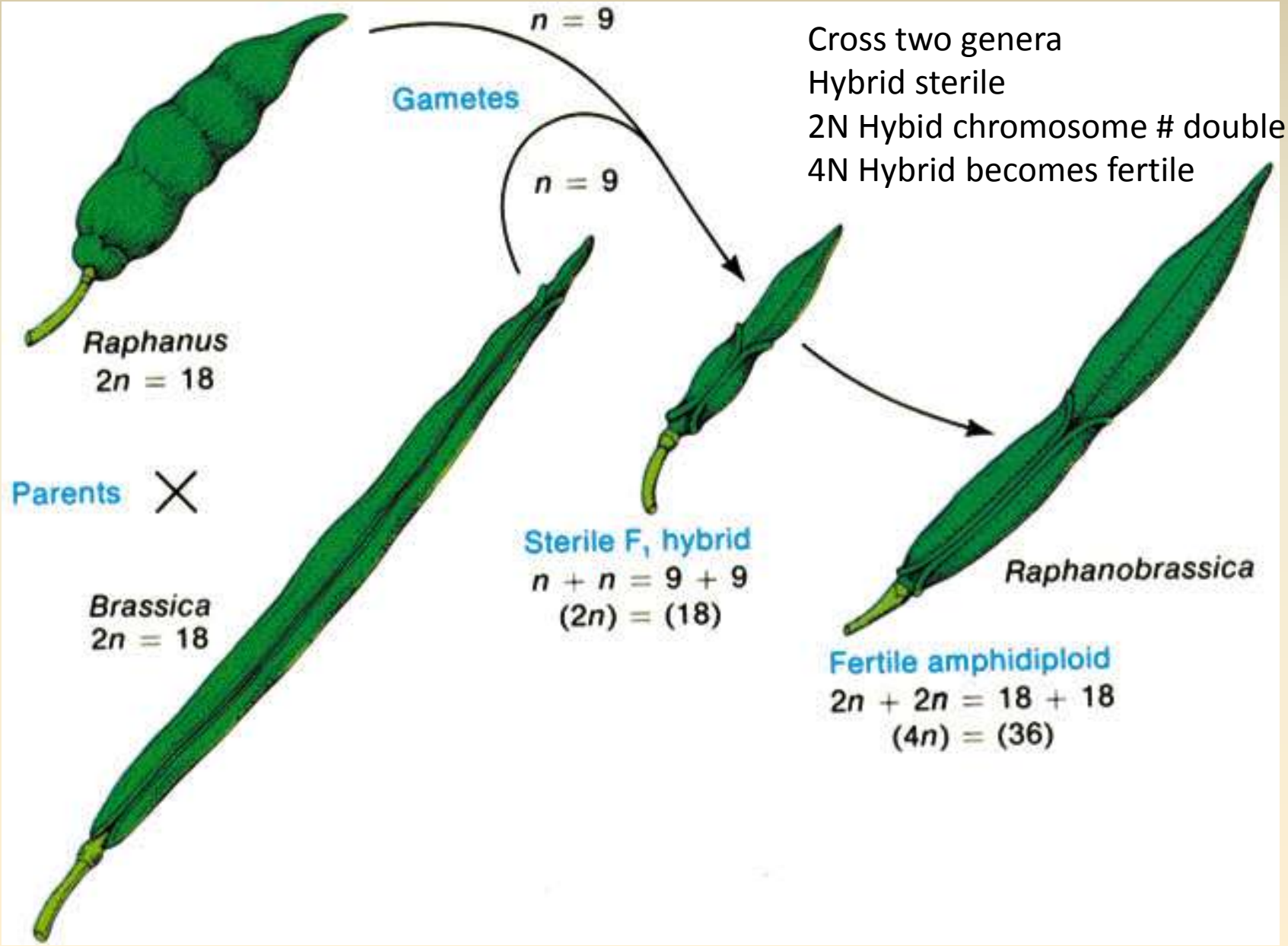
Cross-fertilization of different species, followed by polyploidy, was responsible for the development of many crop plants e.g. wheat.

Initial cross-fertilization produces sterile offspring, because chromosomes cannot pair up during meiosis.

If a sterile plant undergoes polyploidy and self-fertilization a new species can develop essentially immediately.


Alloploidy Resulting from Viable Matings between Two Species
Normal gamete
Species 1
First mating
Polyploid gamete
Second mating
Species 2
Polyploid gamete
Normal gamete

Raphanobrassica – allopolyploid created in lab



Cross two genera
Hybrid sterile
2N Hybid chromosome # double
4N Hybrid becomes fertile

The Evolution of Wheat

- At least 30,000 years ago, in the Fertile Crescent of southwest Asia, a natural hybrid formed between two grasses, *Triticum monococcum* (wild einkorn) and a species of *Aegilops* (goat grass)

Hybrid wheat

The Evolution of Wheat

- Later, tetraploid *Triticum sps.* hybridized with a diploid species *to* yield modern hexaploid wheat

Polyploidy and “Instant Speciation”

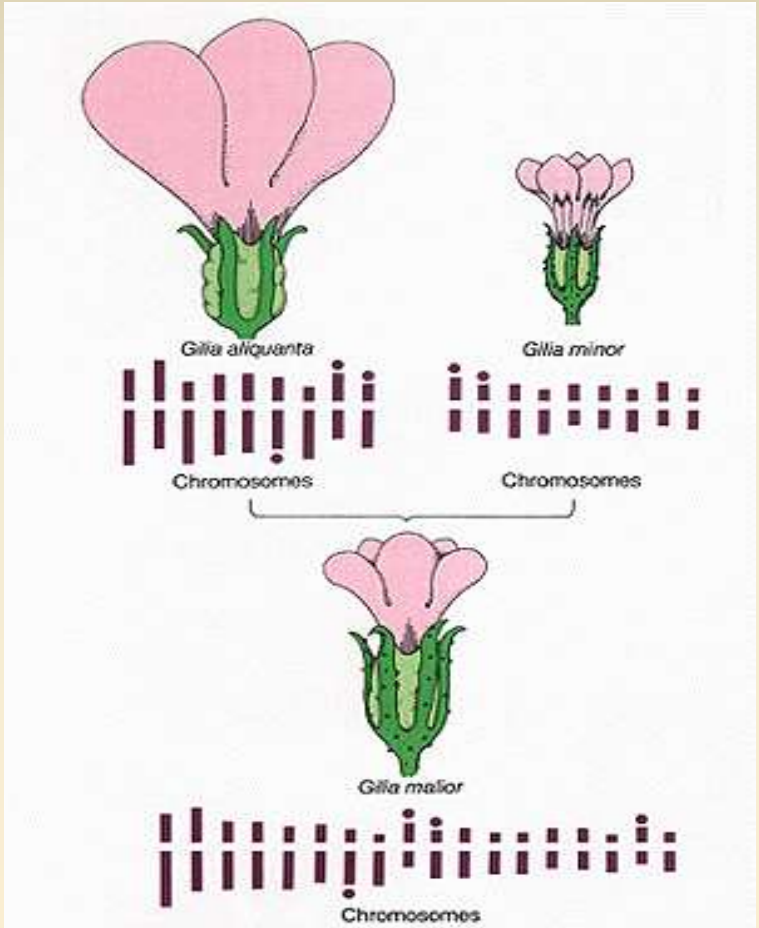
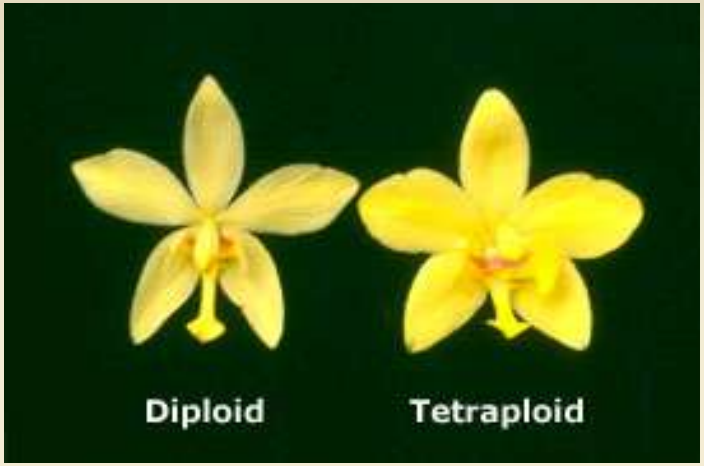


Figure 40-8 INSTANT SPECIATION: POLYPLOIDY IN *Gilia*.
Plants can form "instant species" through polyploidization, the duplication of an entire set of chromosomes. *Gilia malior*, for example, occasionally undergoes allopolyploidization, the doubling of chromosomes from two parent plants of different species. The 18 chromosomes in *G. malior* are no longer exact copies of the 9 from each parent species, reflecting changes in the chromosomes subsequent to the "speciation" event.

Polyploidy is very common in plants, and is thought to have resulted in “instant speciation” in many cases.

The reason that this may be successful in plants is that many plants are capable of self-fertilization, and therefore would not experience the chromosomal incompatibilities with themselves that would make them sterile in back-crosses with either parent.

Parthenogenesis and Apomixis



Many polyploid plants can avoid the troubles of mechanical conflicts in meiosis by **reproducing asexually** with various vegetative means of reproduction

Again, this permits a single individual to multiply into a population of like individuals

Polyploid individuals are often large and hardy

Parthenogenetic Species

Komodo dragon

Bonnethead shark

Water flea

Bynoe's gecko

Warramaba virgo grasshopper

Mulga trees

In what organisms does parthenogenesis occur?

- Occurs in many types of plants
- Few Vertebrates
  - komodo dragons
  - mole salamanders
  - hammerhead sharks
  - some reptiles
  - some amphibians
  - some fish
  - rarely in birds
- Invertebrates
  - water fleas
  - aphids
  - some bees
  - some scorpians
  - many others
- Can be artificially induced (even in mammals)

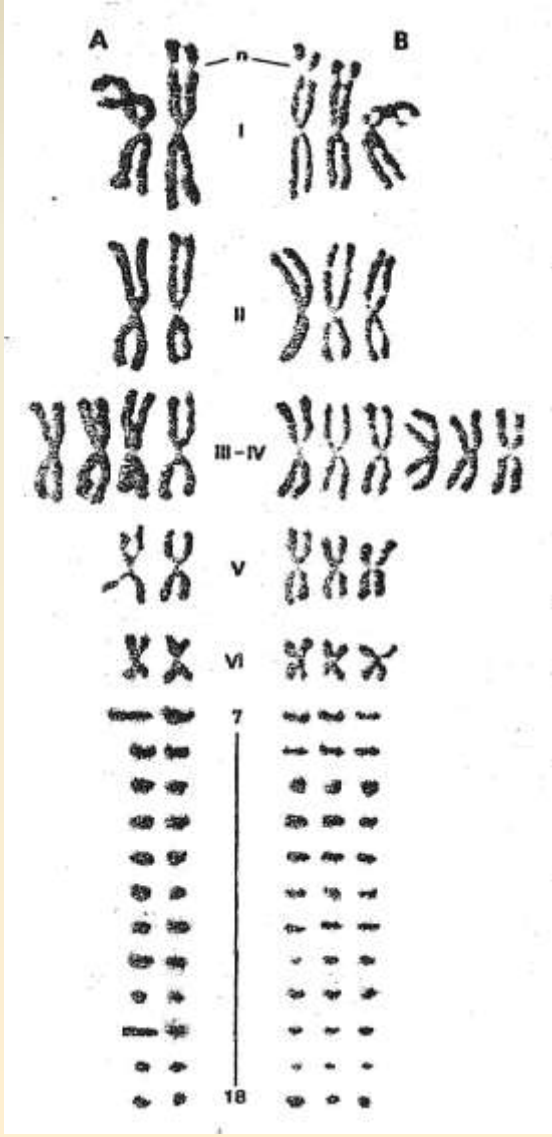
Polyploidy in Animals

Polyploid animal taxa include earthworms and flatworms, which can self-fertilize, and some other groups including insects that can reproduce asexually (parthenogenesis).

In contrast to polyploid plants, **polyploid animals are often malformed** and do not experience normal development

Karyotype studies of still born humans and domestic animals such as cows, horses, sheep, goats, cats, and dogs reveal that many of the **naturally aborted fetuses** were polyploids

Polyploidy reptiles and fish



In vertebrates, polyploidy is thought to be lethal in all birds and mammals. However, it is known to occur rarely in reptiles, typically in association with female-only parthenogenetic species (left). In contrast, polyploidy is quite common in fishes (above).

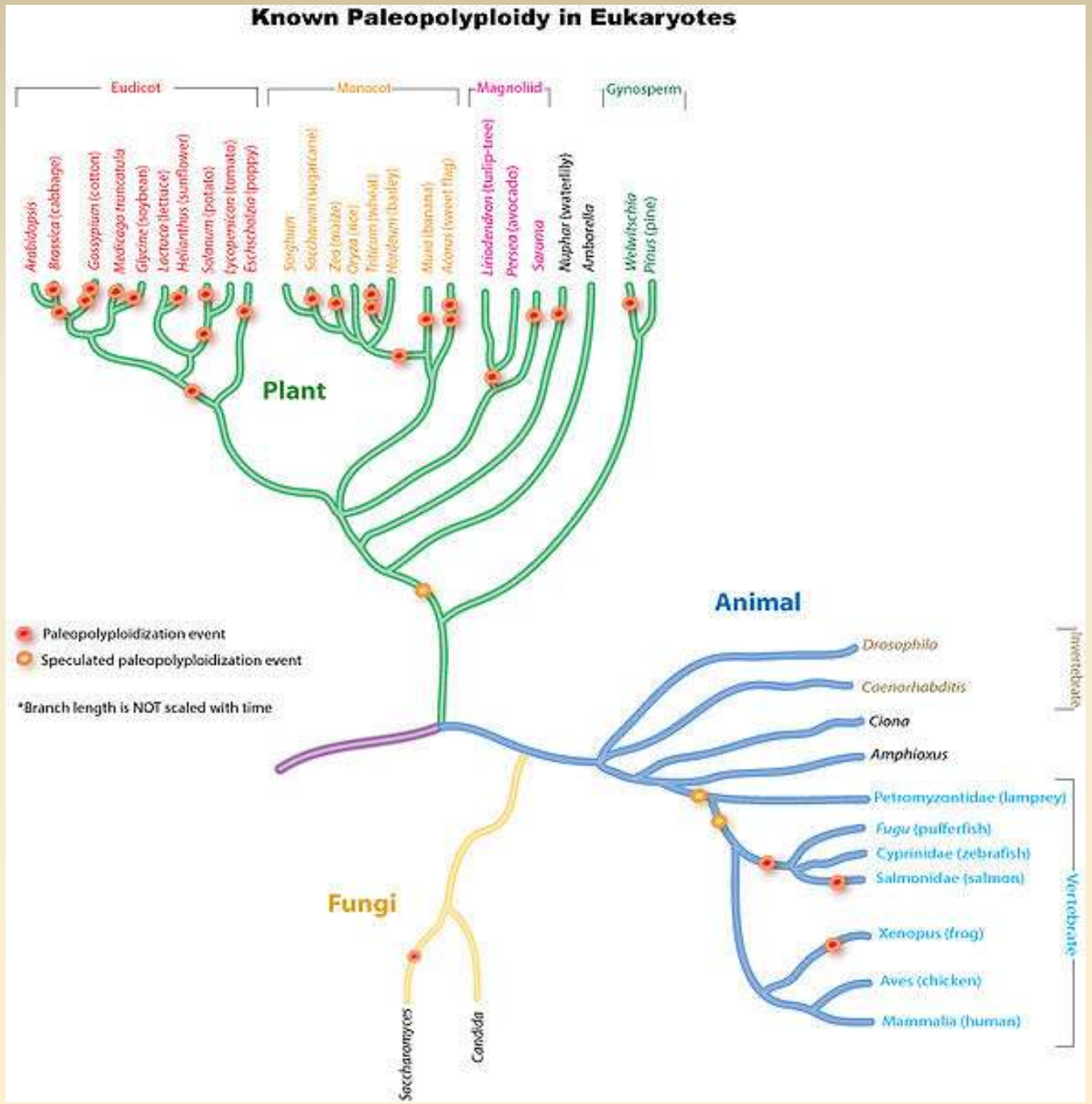
Parthenogenesis

Parthenogenesis means producing offspring from unfertilized eggs. If the egg cells have not undergone meiosis, the offspring are diploid. Some fish and shrimp reproduce by parthenogenesis. It is generally not very successful over the long term, because there is no way to remove randomly occurring mutations.

However, bdelloid rotifers, simple animals containing about 1000 cells, apparently have been reproducing parthenogenically for up to 40 million years. There is no sign of DNA recombination between individuals in this group.

Many plants can reproduce vegetatively, by taking a cutting from the plant body and causing it to develop roots. This ability makes it very easy to develop unusual genetic lines of plants: they never have to undergo meiosis and fertilization. For instance, commercial potatoes are propagated vegetatively, through "eyes" on the tubers.

Next Generation Sequencing reveals **ancient polyploids**



Chromosome Alterations

Chromosome Alterations

Potentially the largest phenomena capable of contributing to the pool of mutations

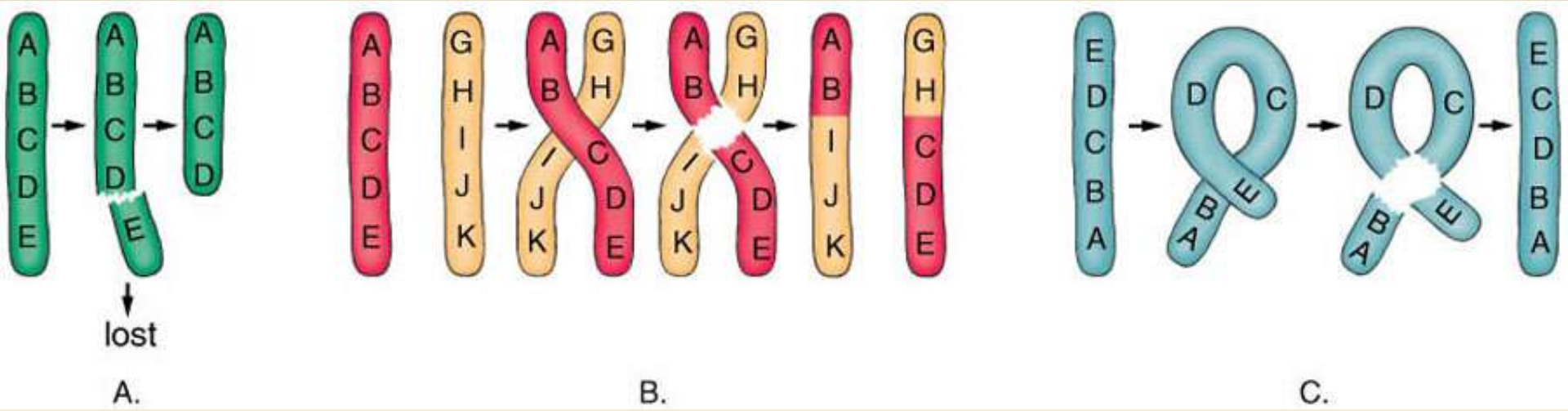
Some chromosome changes affect only gene order and organization

Others alter the amount of DNA available

Others alter blueprints, eliminate genes, or add copies of genes

Others influence linkage groups of genes

Chromosomal Rearrangements

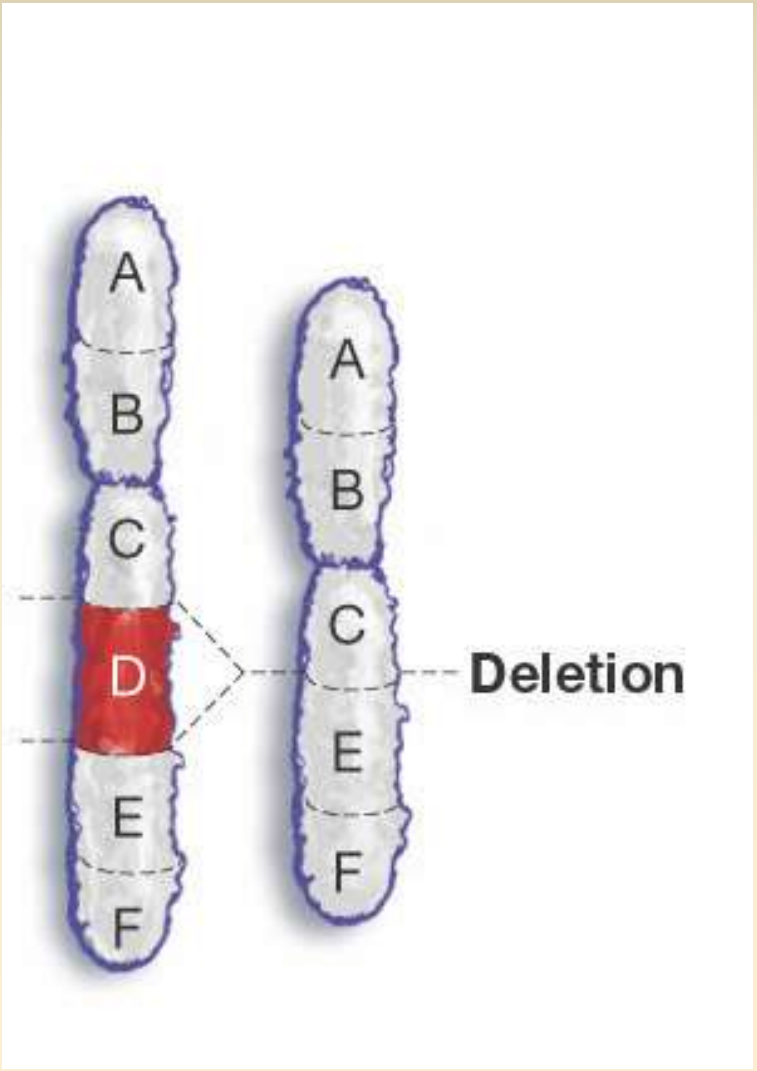


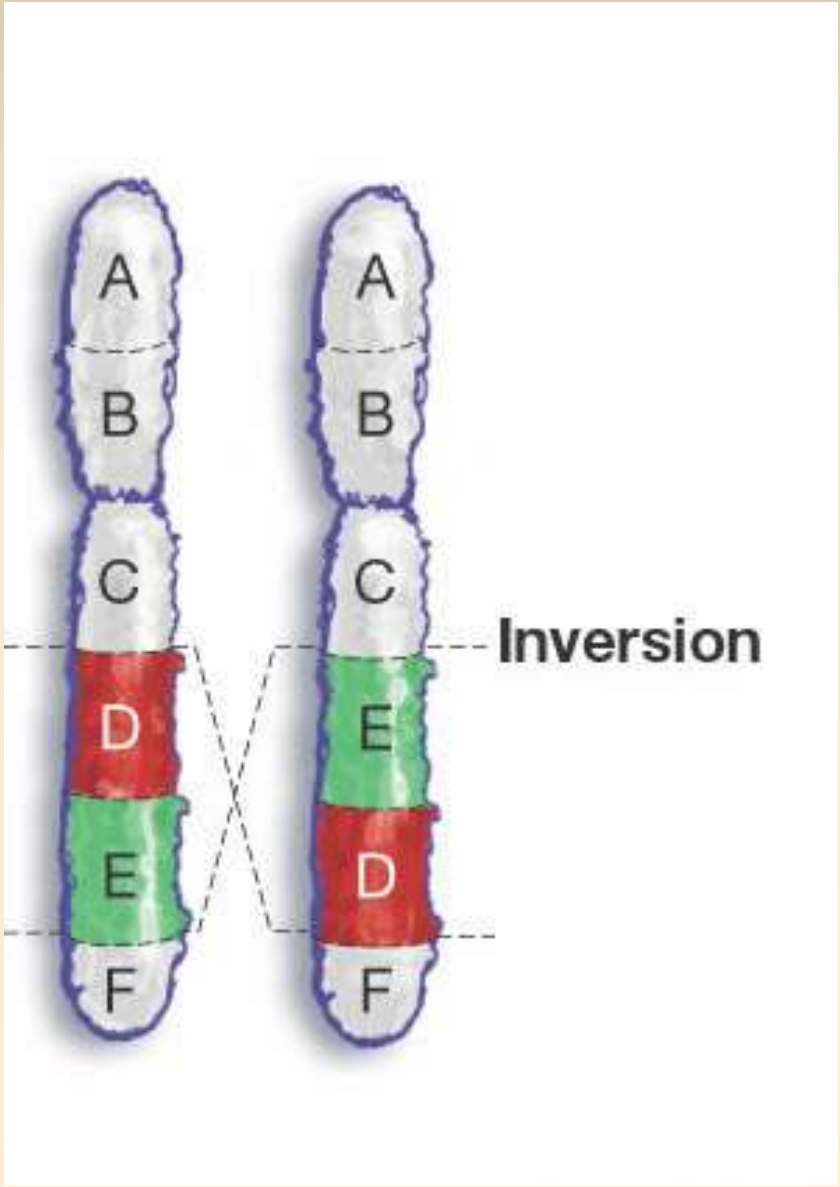
a) **Deletion:** Part of a chromosome breaks off and is lost

b) **Translocation:** Part of a chromosome detaches and becomes attached to another

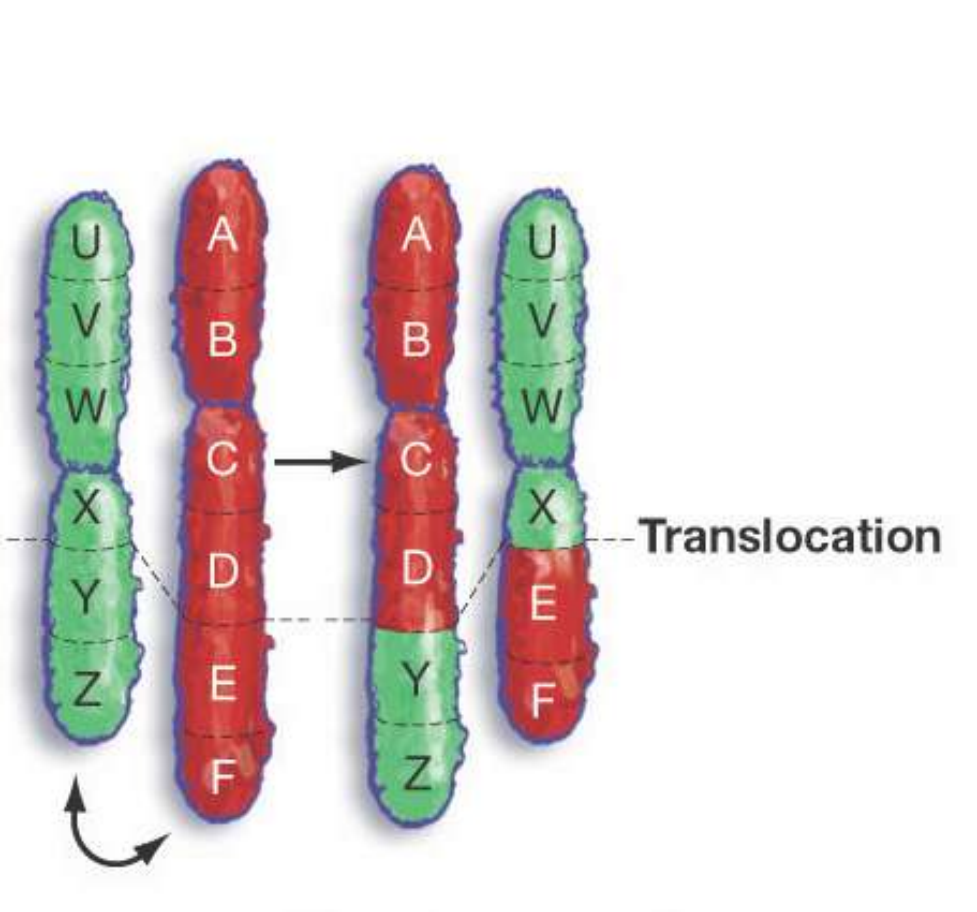
c) **Inversion:** Part of a chromosome becomes switched around within the chromosome

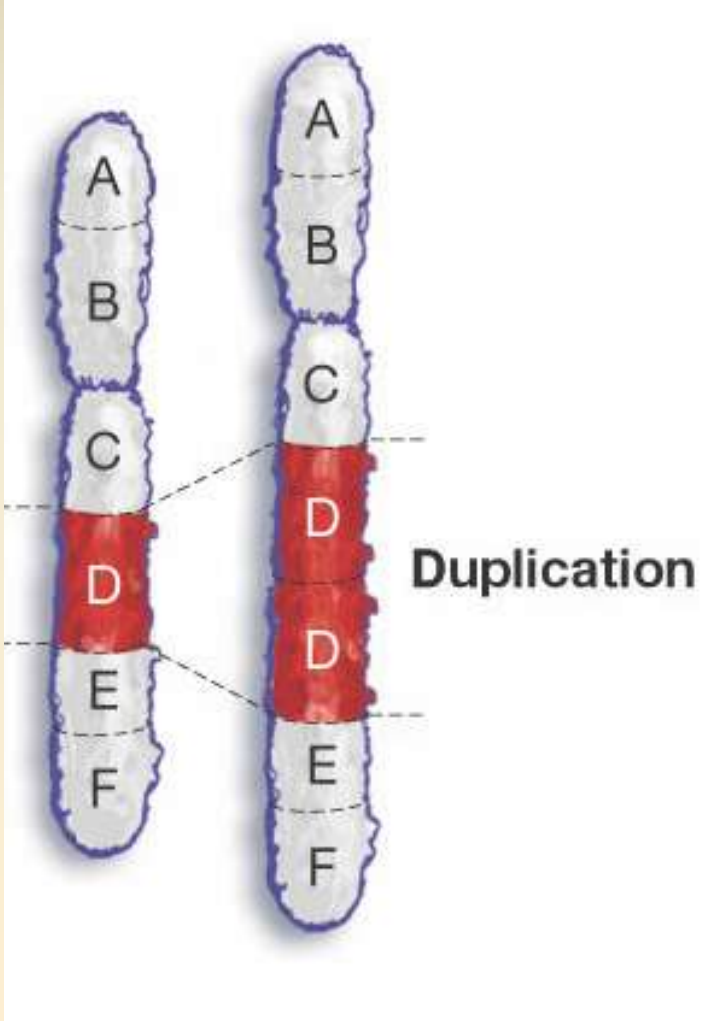
Chromosome Structural Changes





Chromosome Structural Changes





Prophase I – where structural changes take place

When the chromosomes first become visible they are already doubled, each homologue having been duplicated during the preceding S phase.

Each dyad consisting of two sister chromatids held together by a protein complex.

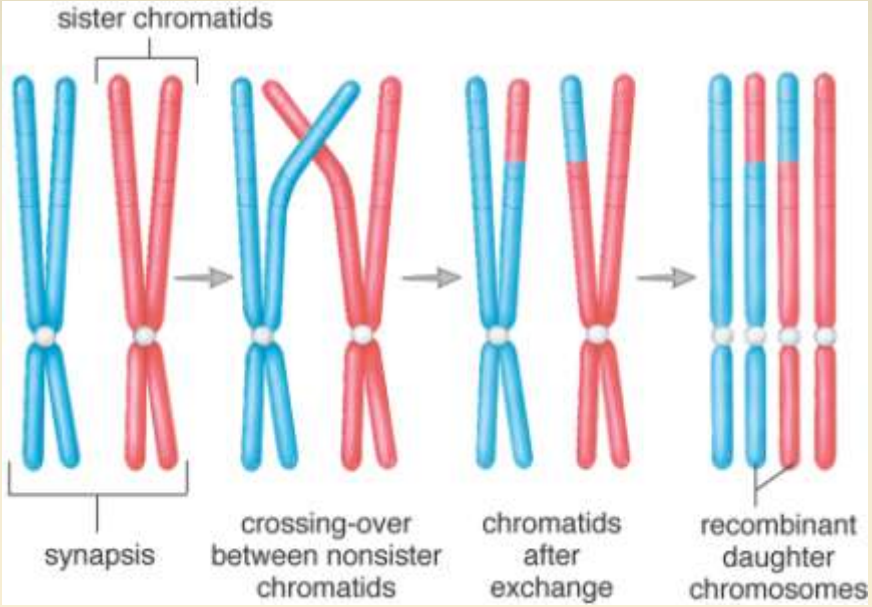
Pairing: Each pair of homologous dyads align lengthwise with each other.

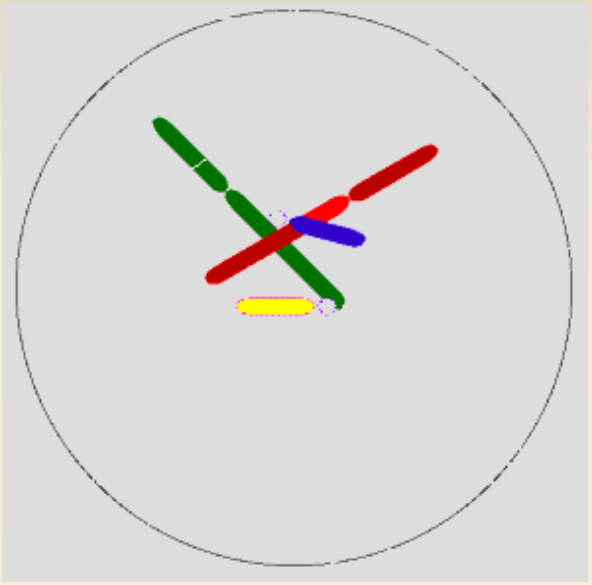
Result: a **tetrad**. These structures are sometimes referred to as **bivalents** because at this stage you cannot distinguish the individual sister chromatids under the microscope.

The two homologous dyads are held together by one or more **chiasmata** (sing. = chiasma) which form between two **nonsister** chromatids at points where they have crossed over.

the **synaptonemal complex** (SC), a complex assembly of proteins (including cohesin)

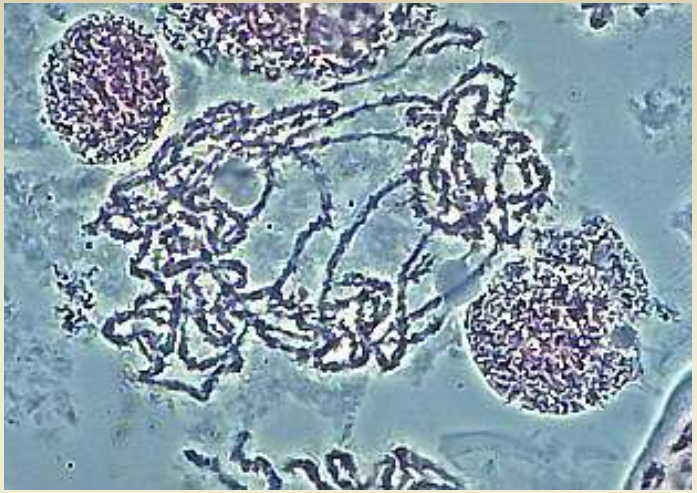
Crossing Over and Recombination





- During meiosis, chromosomes duplicate and homologous pairs synapse
- Chromatids exchange homologous sections carrying alleles, producing recombinant daughter chromosomes with a different combination of alleles

Meiosis I - Prophase

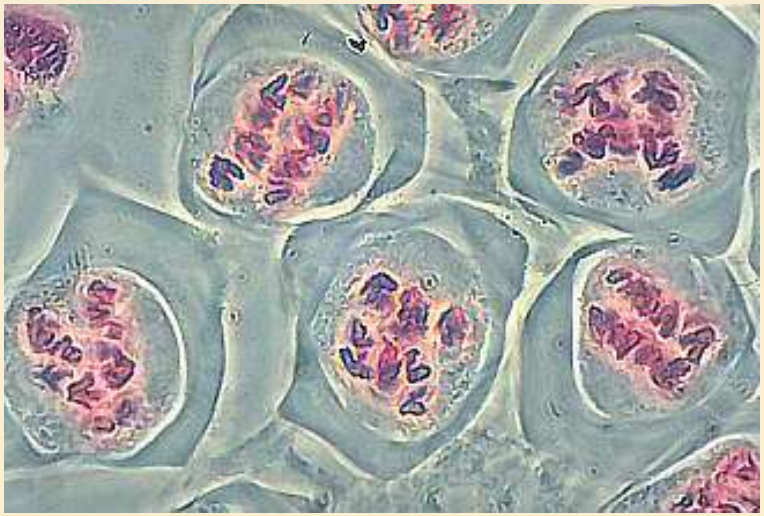


Zygotene / pachytene (the homologous chromosomes can be recognized as thin double strands).

Diplotene (the bivalents can be seen as clear double strands).

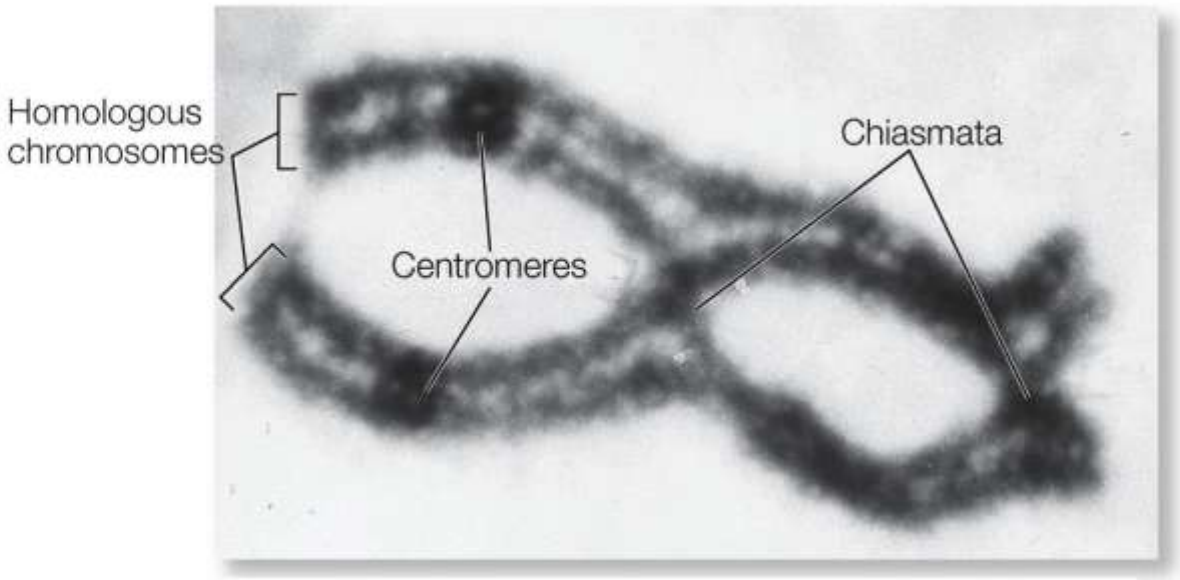
Meiosis I

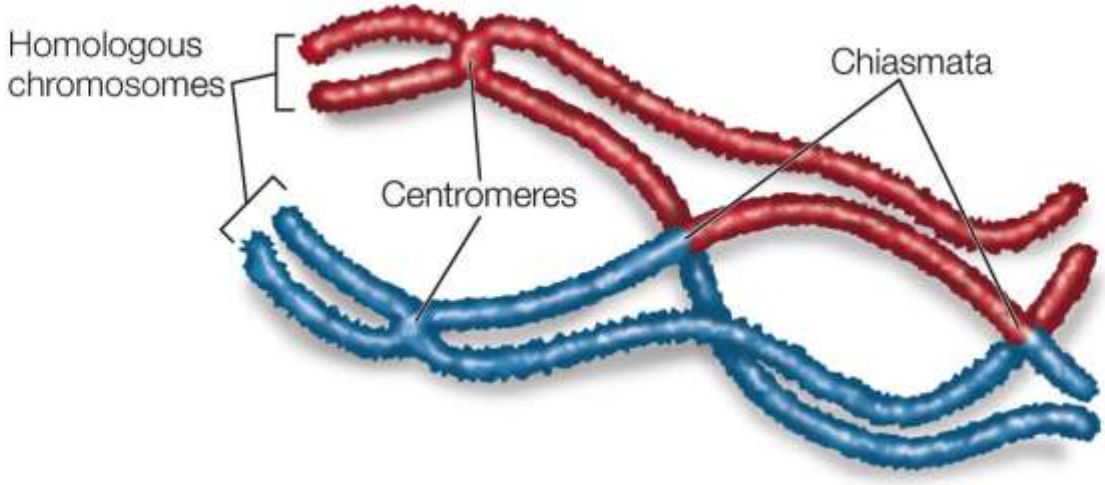
Metaphase I: side view of all seven bivalents in the equatorial plane. Both series of centromers are already stretched towards the poles.



Diakinesis (The homologous chromosomes are drawn to opposite poles. All seven bivalents contain chiasmata.).

Crossing over introduces genetic variability.





***LIFE 8e*, Figure 9.17**

Unequal Crossing-Over

During meiosis, synapsed chromosomes occasionally pair out of register with each other

Cross-over then occurs between non-homologous sections

As a result, **genes are duplicated on one chromosome, and deleted on the other**.

Chromosomes with gene duplications provide new possibilities for gene function in eukaryotic evolution

Equal and Unequal Crossing-Over

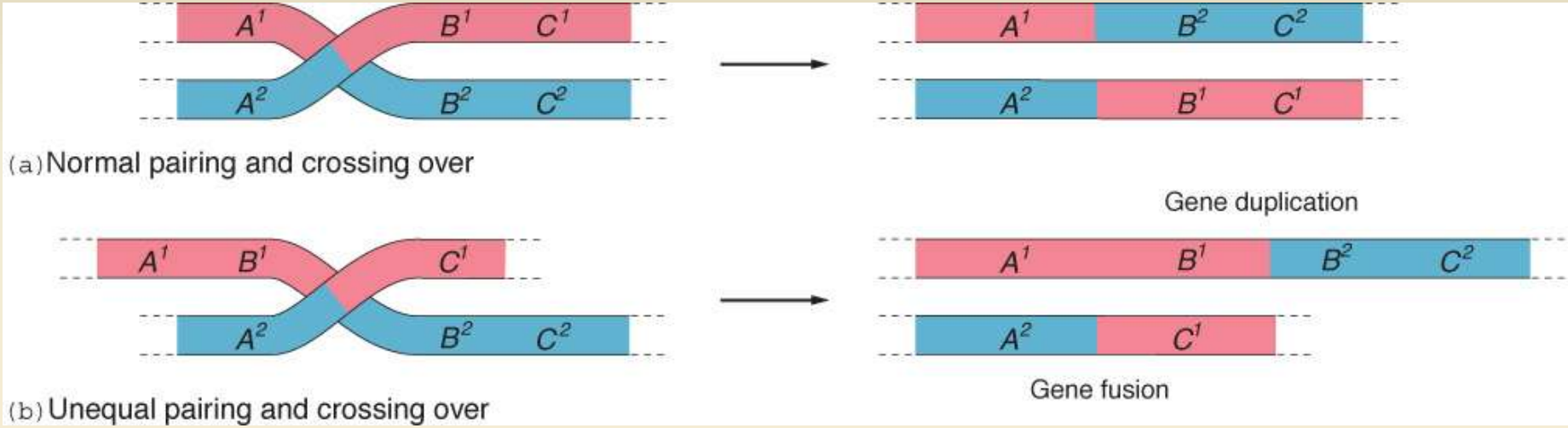


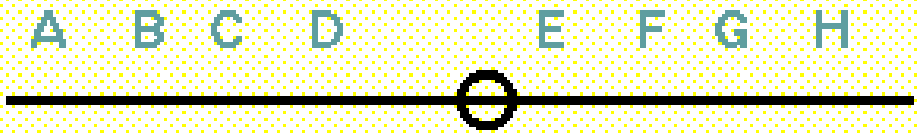
Figure 04: Equal and unequal crossing-over for three gene segments on a chromosome

Equal Crossing-Over provides new arrangements of alleles on chromosomes but has little potential for new variation

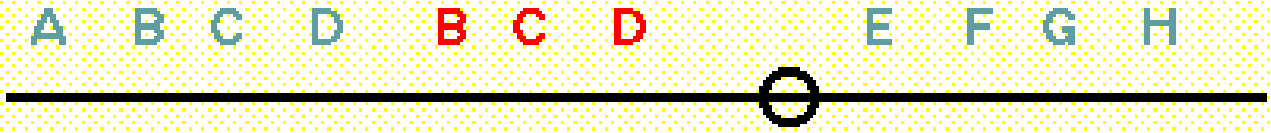
Variation could occur if the break and repair occurred within a gene, instead of between genes as illustrated

Types of Duplications

Normal chromosome

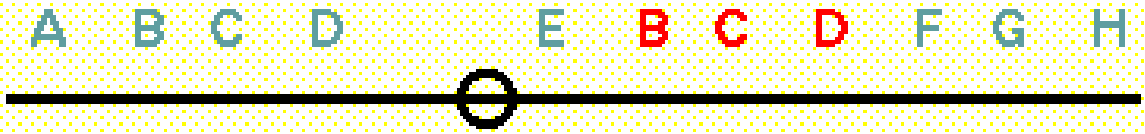


Tandem duplication

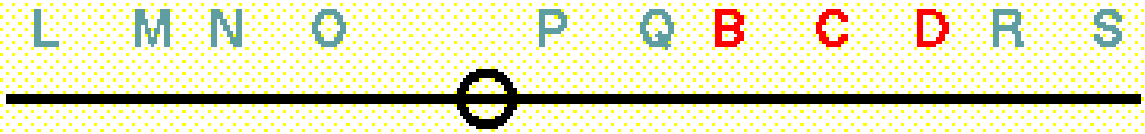


Reverse tandem duplication

Duplication on a different arm



Non-homologous (displaced) duplication



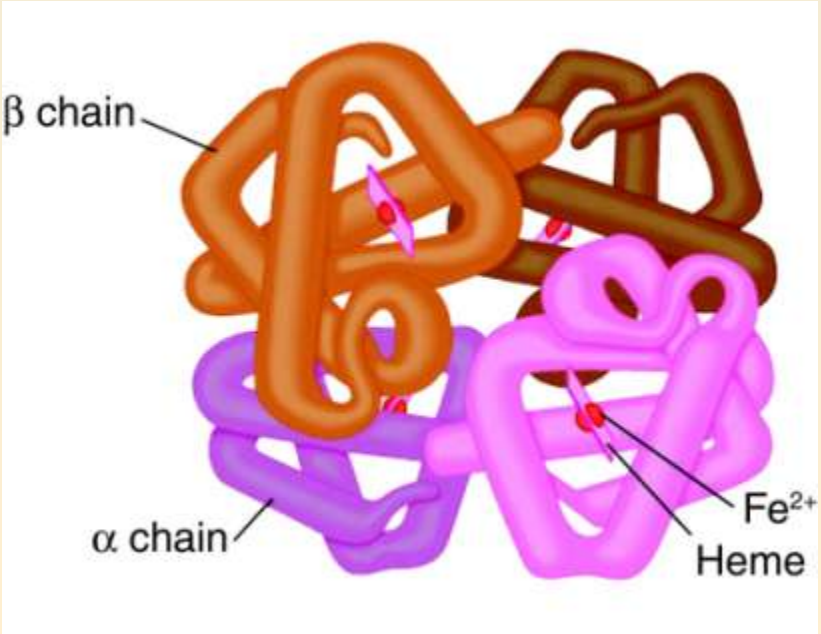
Globin genes

- Human globin genes are examples of products of gene duplication.

- Globin gene family contains two major gene clusters (alpha and beta) that code for the protein subunits of hemoglobin.

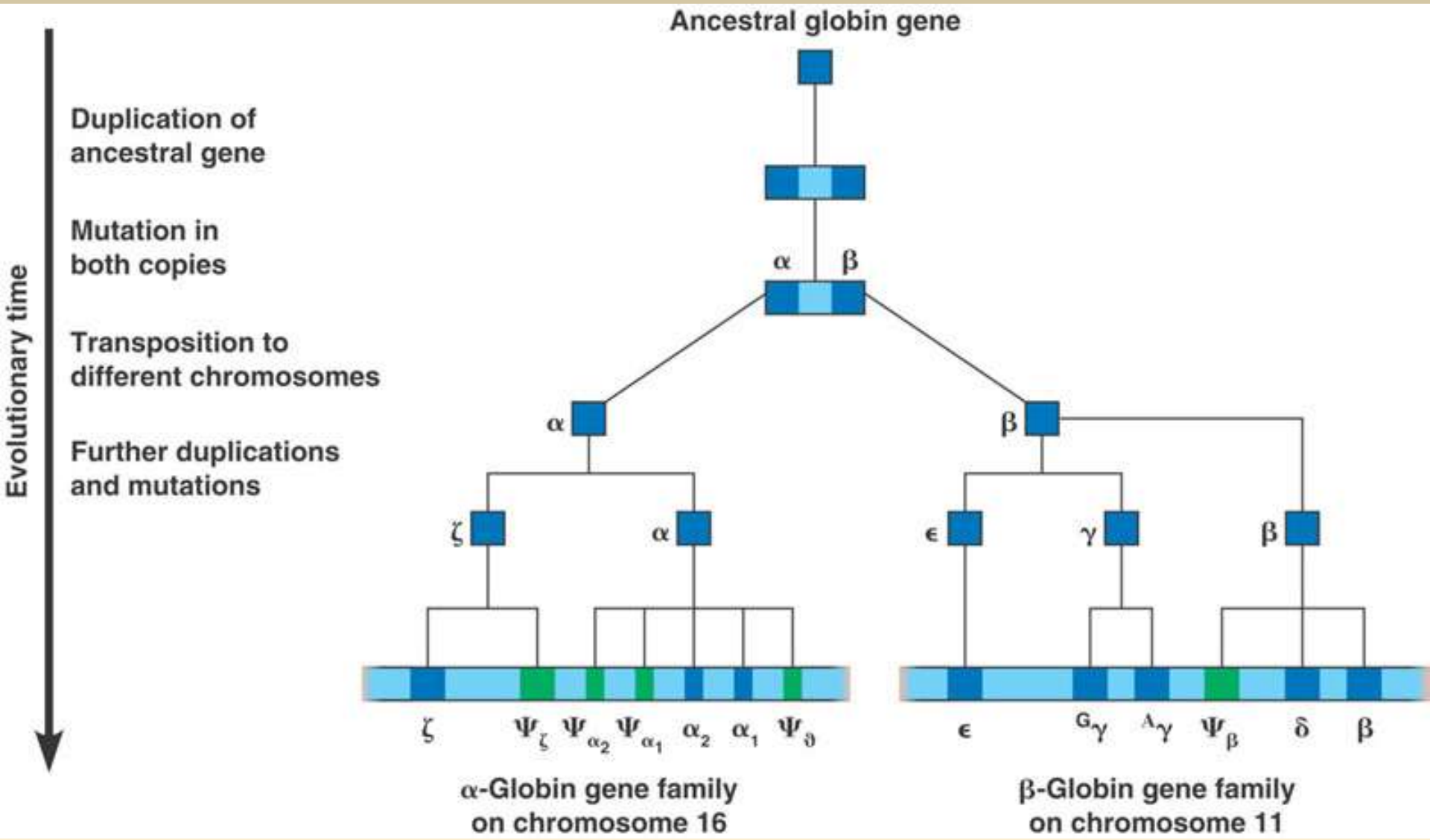
Globin genes

- Hemoglobin (the oxygen-carrying molecule in red corpuscles) consists of an iron-binding heme group and four surrounding protein chains (two coded for by genes in the Alpha cluster and two in the Beta cluster).



Globin genes

- Ancestral globin gene duplicated and diverged into alpha and beta ancestral genes about 450-500 mya.
- Later transposed to different chromosomes and followed by further subsequent duplications and mutations.



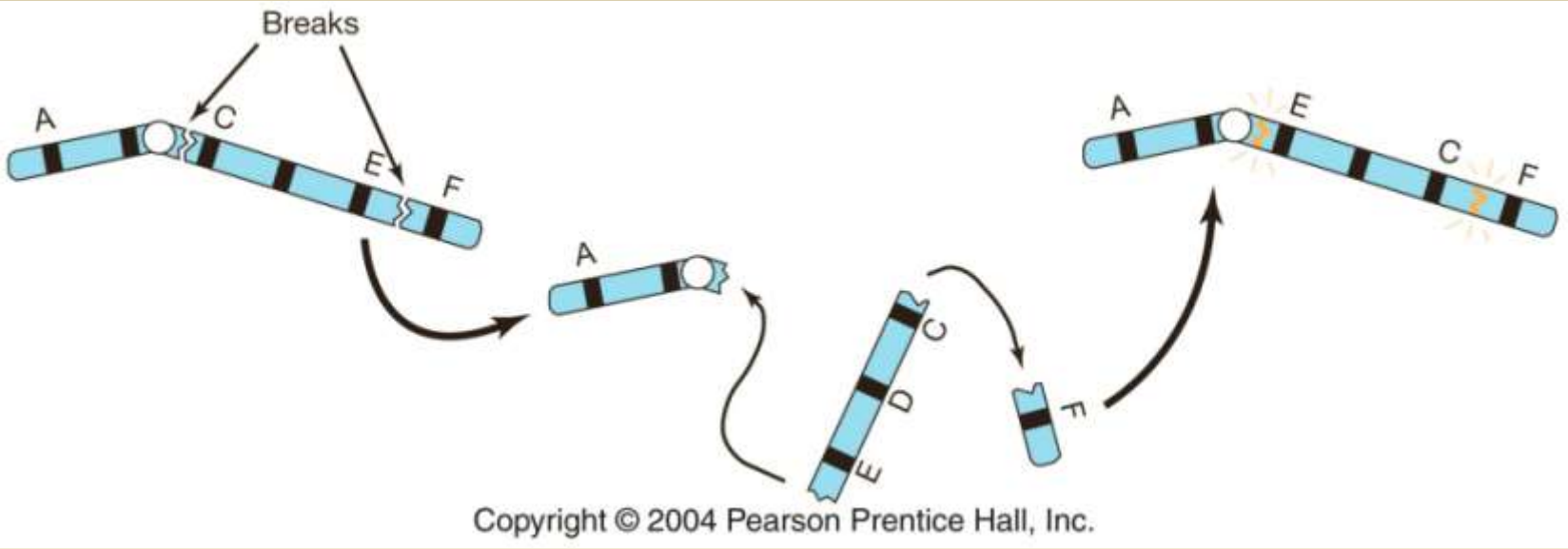
From Campbell and Reese Biology 7th ed.

Inversions

A chromosome inversion occurs when a section of chromosome is broken at both ends, detaches, and flips.

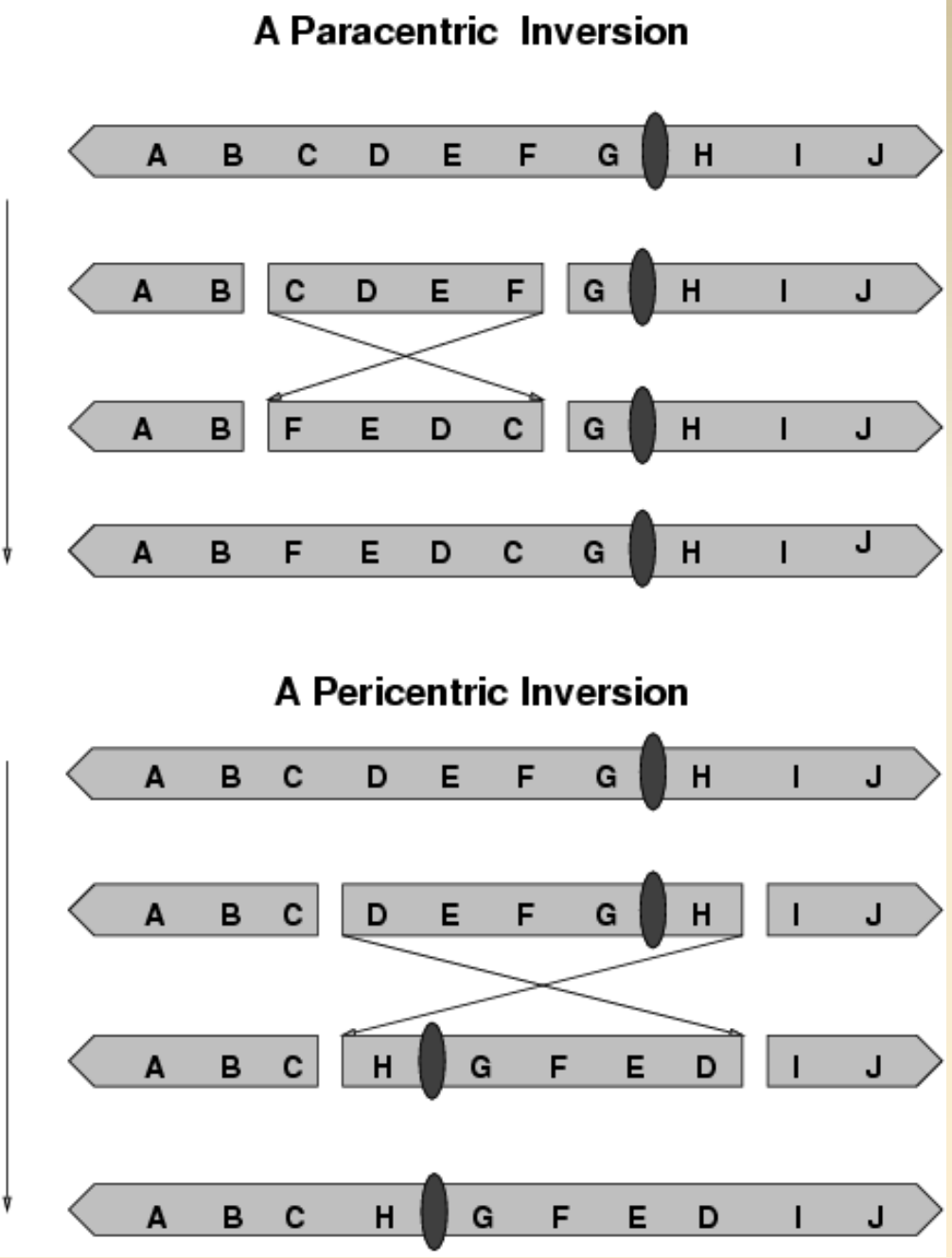
Inversion alters the ordering of genes along the chromosome.

Chromosome Inversion



Two breaks occur in a single DNA strand but the improper repair reverses the sequence of the loci on one chromosome

The inversion has not altered the individual gene blueprints, just their arrangement along the arm of the chromosome



Paracentric inversion: the inverted chromsome piece **does not** include Centromere.

Pericentric inversion: the inverted chromsome piece **does** include Centromere.

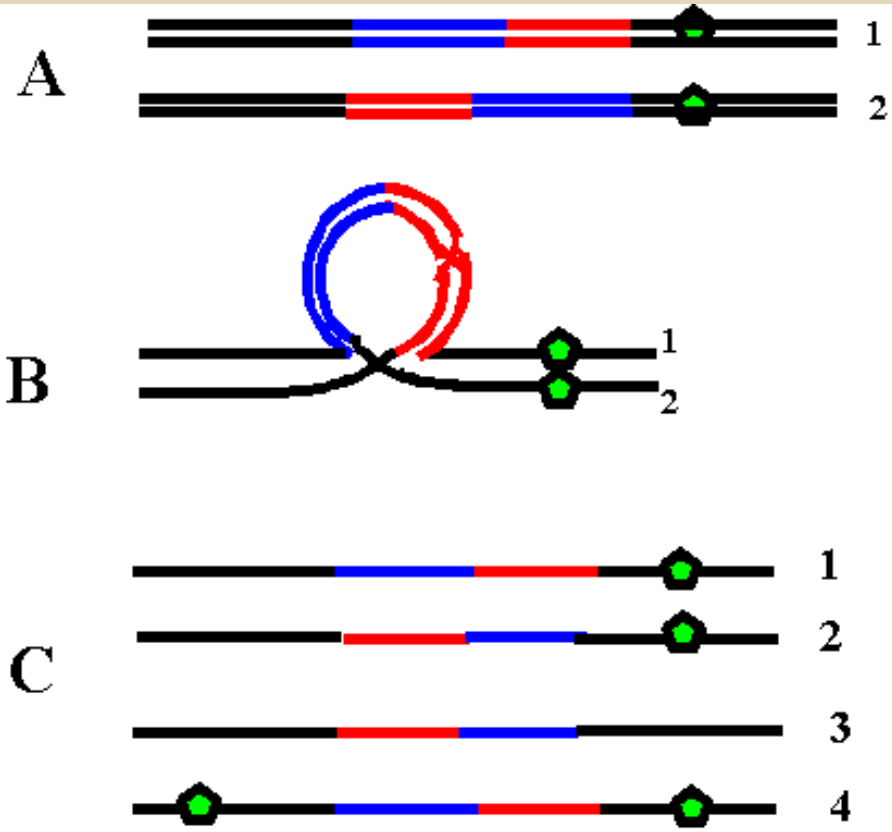
Inversions

Inversion affects linkage (linkage is the likelihood that genes on a chromosome are inherited together i.e., not split up during meiosis).

Inverted sections cannot align properly with another chromosome during meiosis and crossing-over within inversion produces non-functional gametes.

Genes contained within inversion are inherited as a set of genes also called a “supergene”

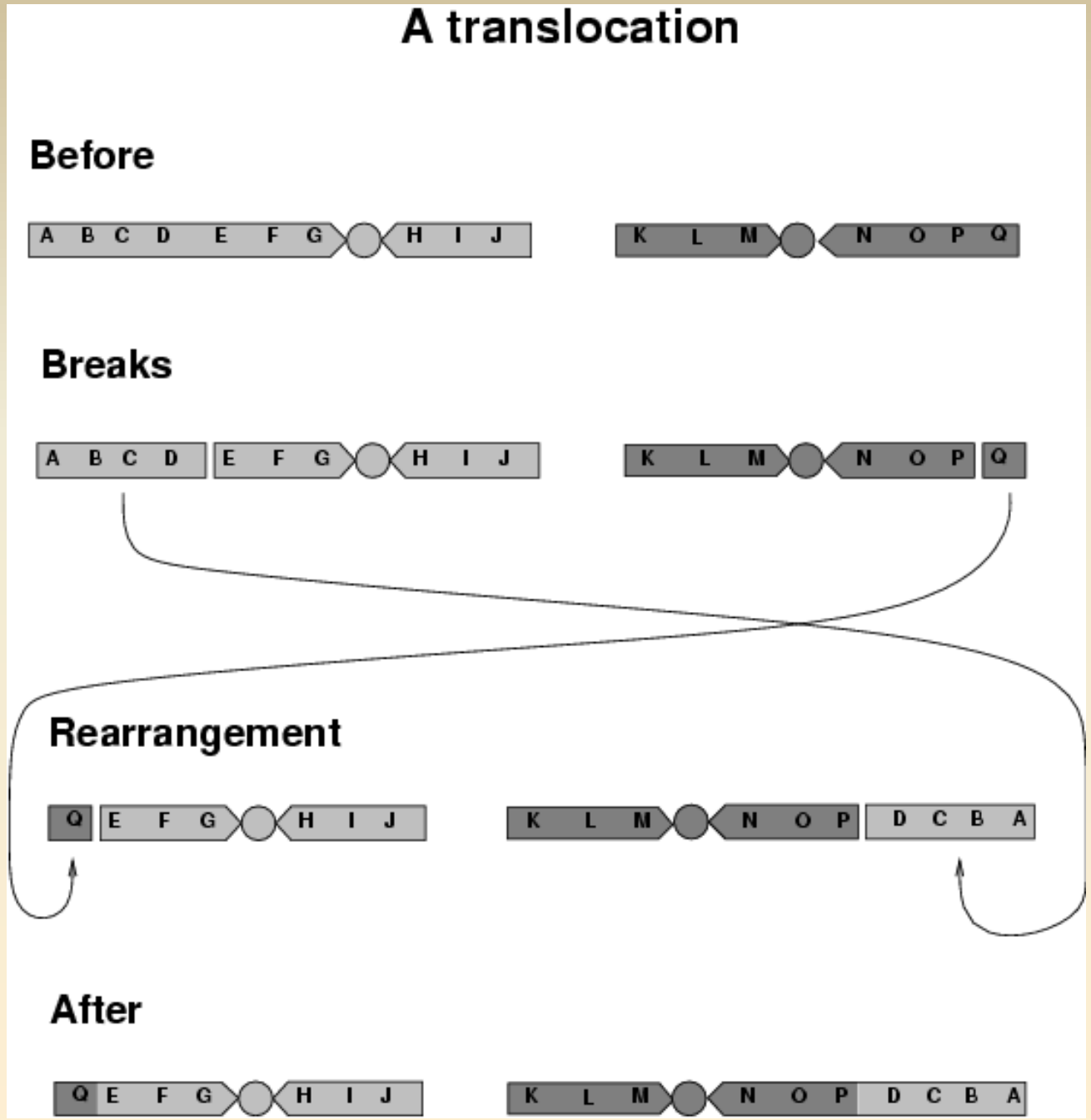
Inversion heterozygote needs to **form a loop** with one chromosome so the chromosome pairs can align in meiosis.



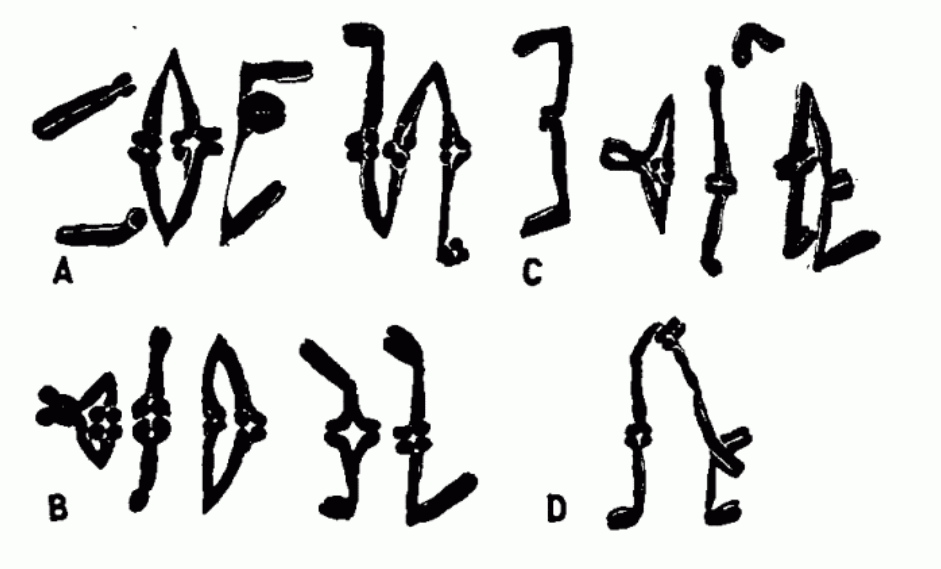
Paracentric inversion going through meiosis, with a recombination within the inversion

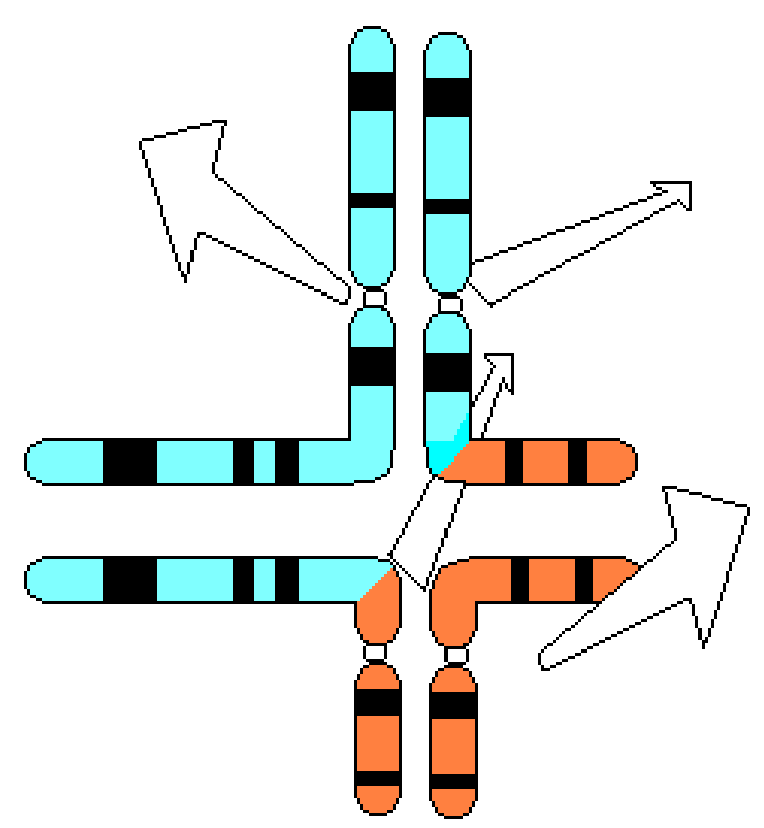
Of the four gametic products, one is normal, one has the inversion, one has an acentric chromosome, and one has a dicentric chromosome. The acentric chromosome cannot survive. The dicentric chromosome may be pulled apart during mitosis, with a random loss or gain of genetic material

A translocation

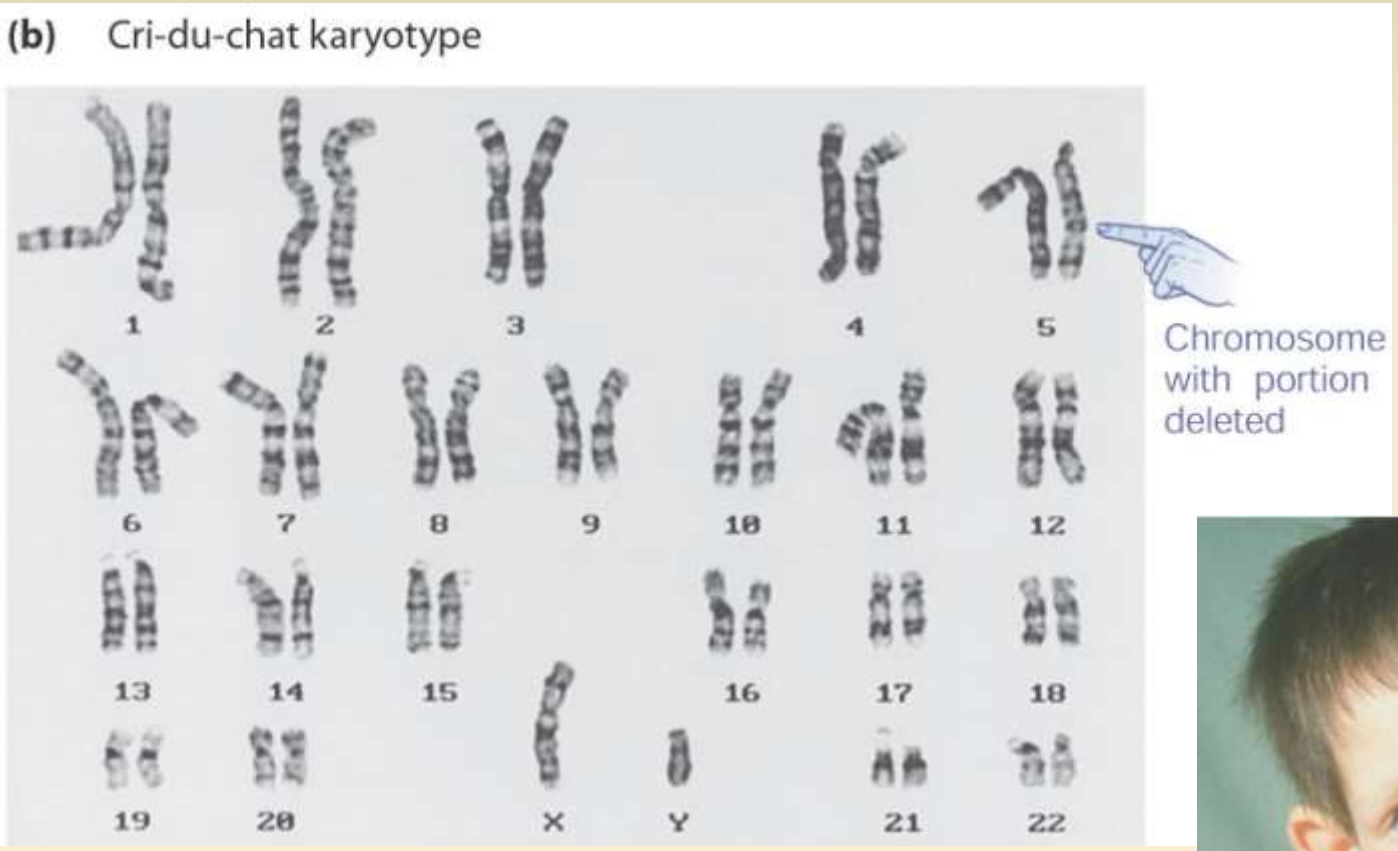


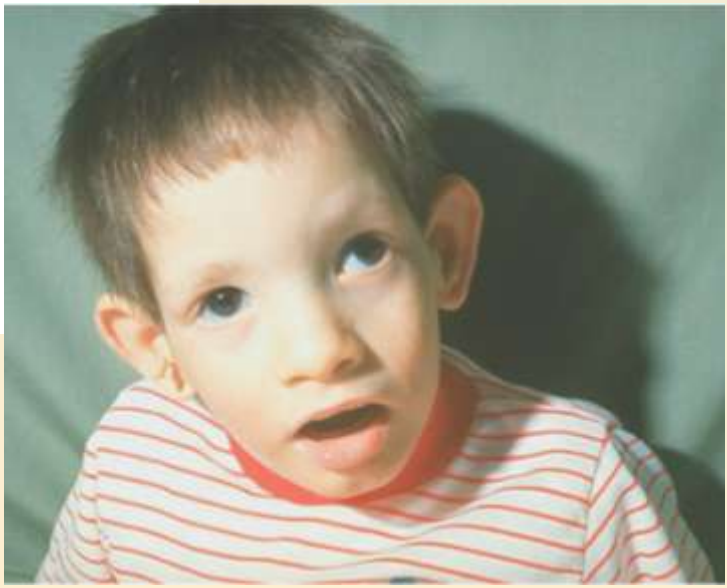
Translocation heterozygotes can still pair up their chromosomes, forming a cross. But half of their gametes will not contain all genes and some are duplicated.



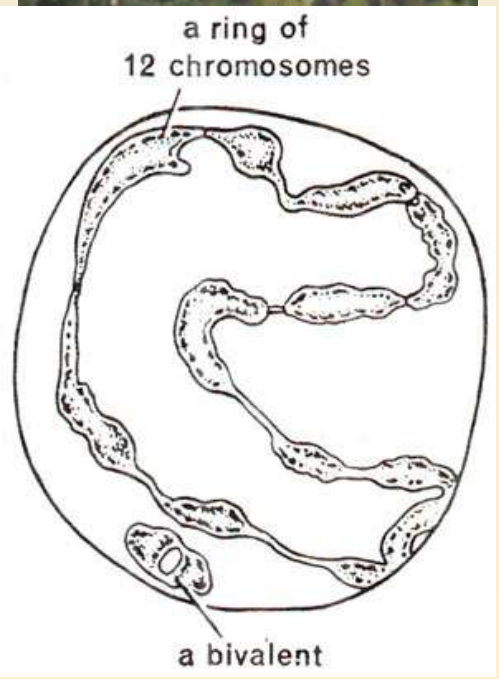


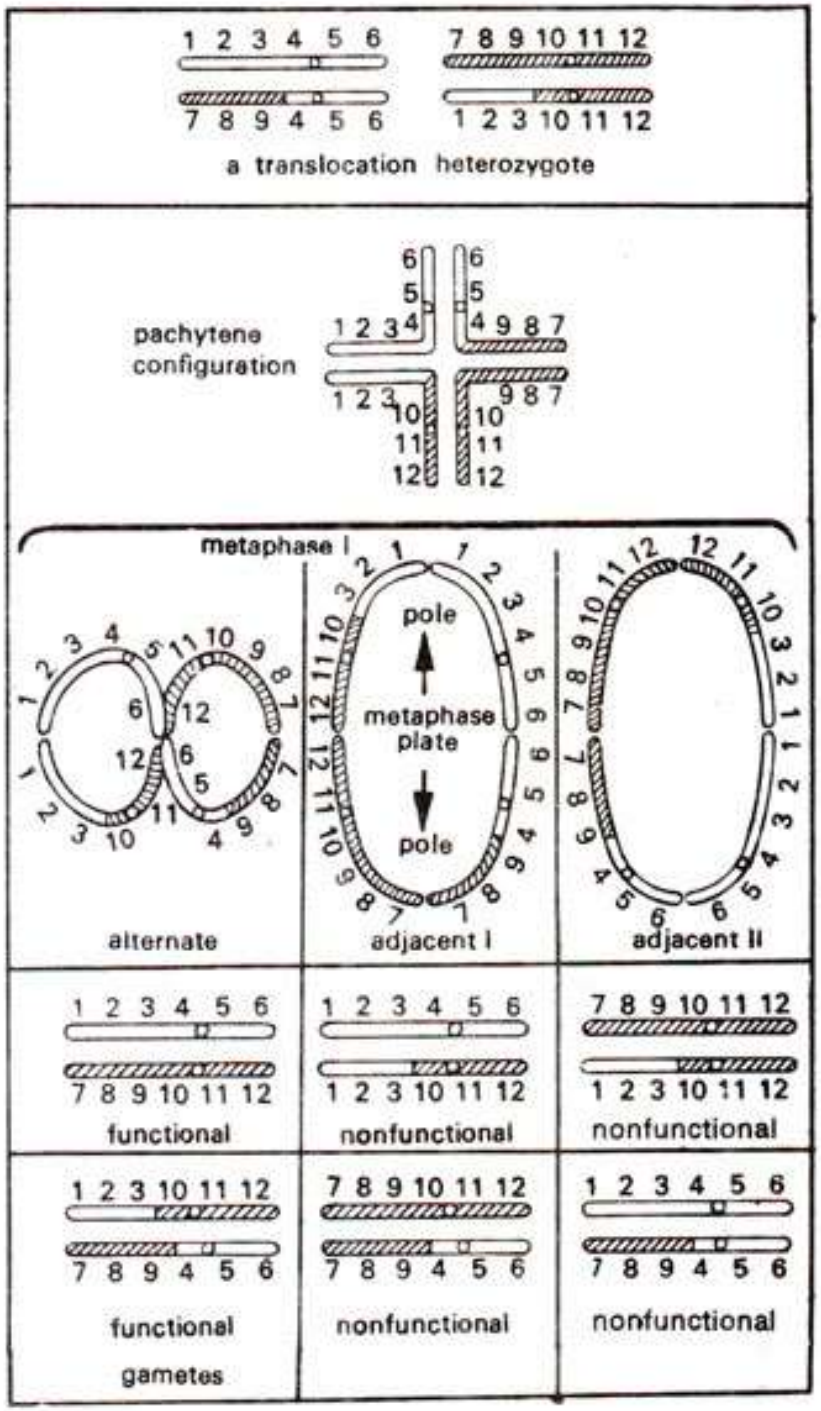
Cri-du-Chat Syndrome – a Debilitating Disorder Caused by Chromosome Deletion, Loss of the Short Arm of One Copy of Chromosome 5



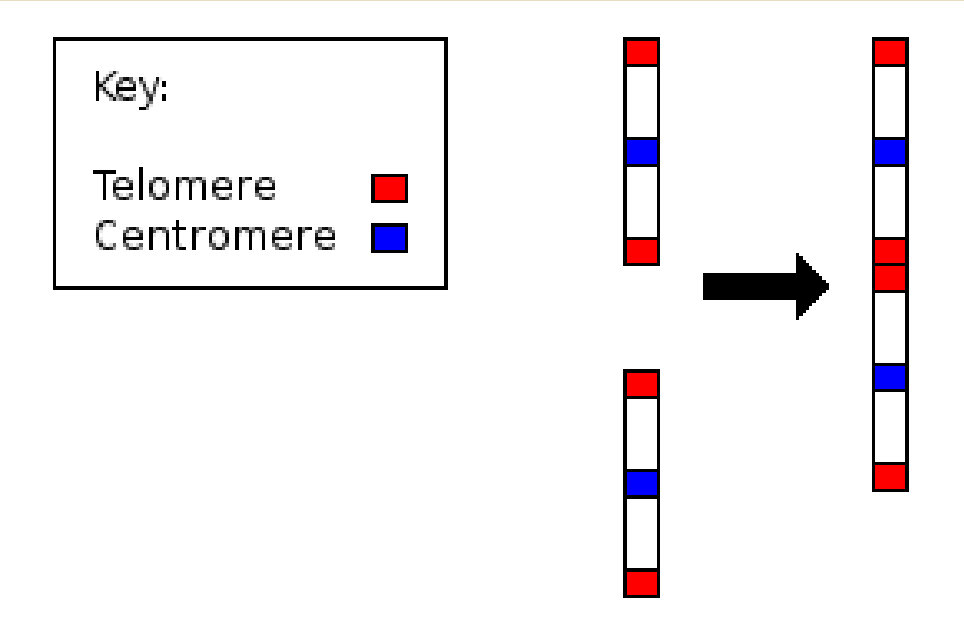


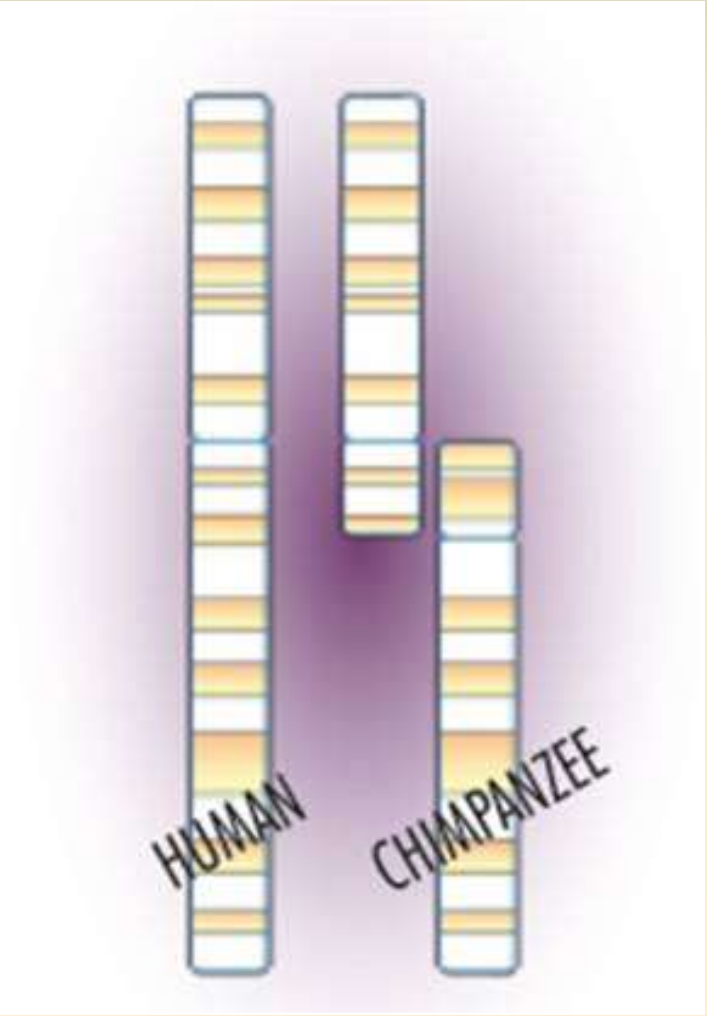
Oenothera Ring Chromosomes





Chromosome Fusion





Mutations

Types of Mutations

- Point mutation
  - Synonymous – no change in a.a.
  - Nonsynonymous – change a.a.
- Frame-shift mutation
- Stop mutation
- Chromosome Fusion
- Trinucleotide Repeats

What causes Mutations?

Mutagens

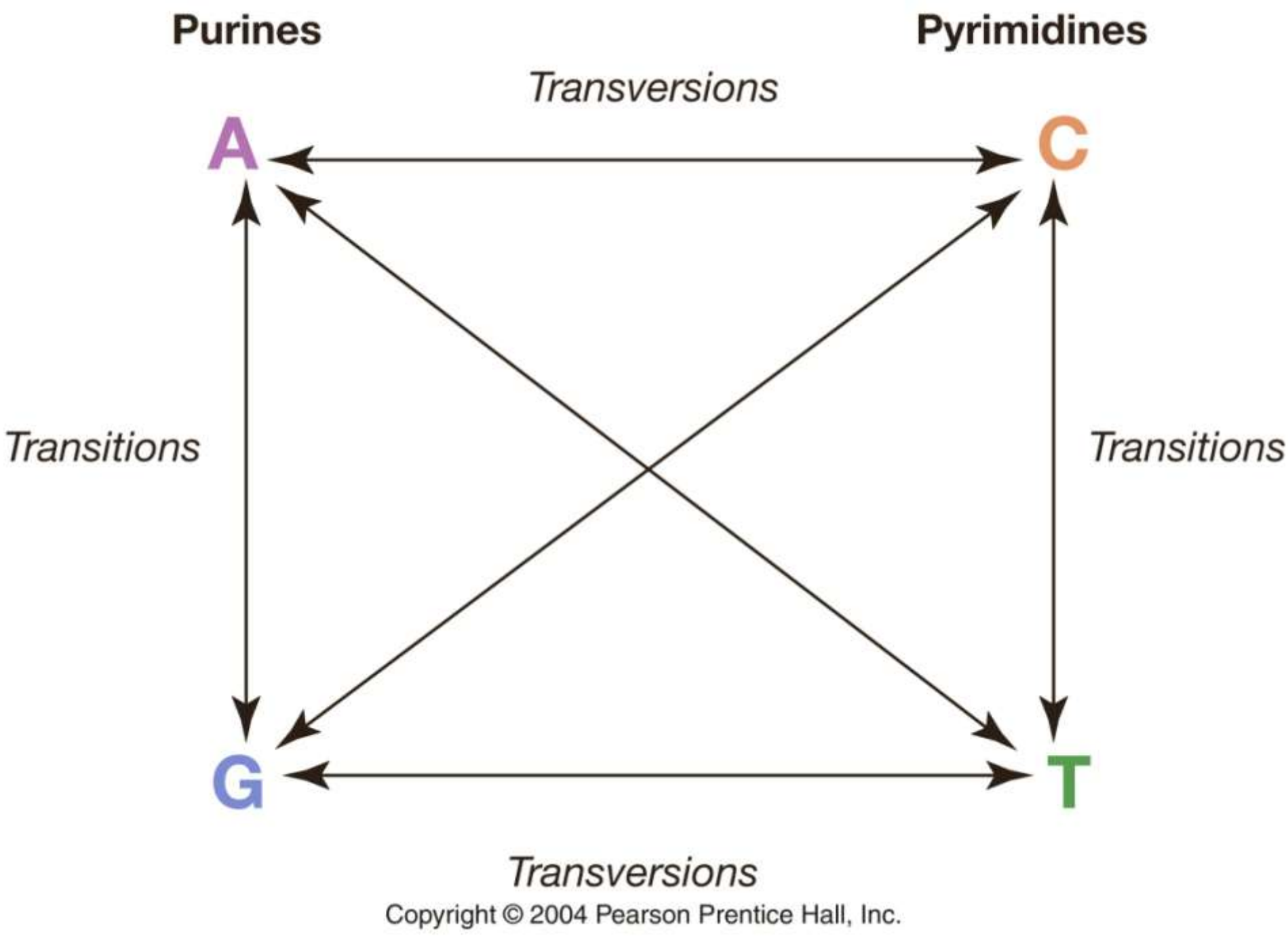
- Ultraviolet radiation
- Ionizing radiation
- Chemical mutagens

Types of mutations

A mistake that changes one base on a DNA molecule is called a *point mutation.*

Two forms:

- Transition: one pyrimidine (T or C) substituted for the other pyrimidine or one purine substituted for the other purine (A or G).
- Transversion: purine substituted for pyrimidine or vice versa



Types of mutations

Transitions more common than transversions.

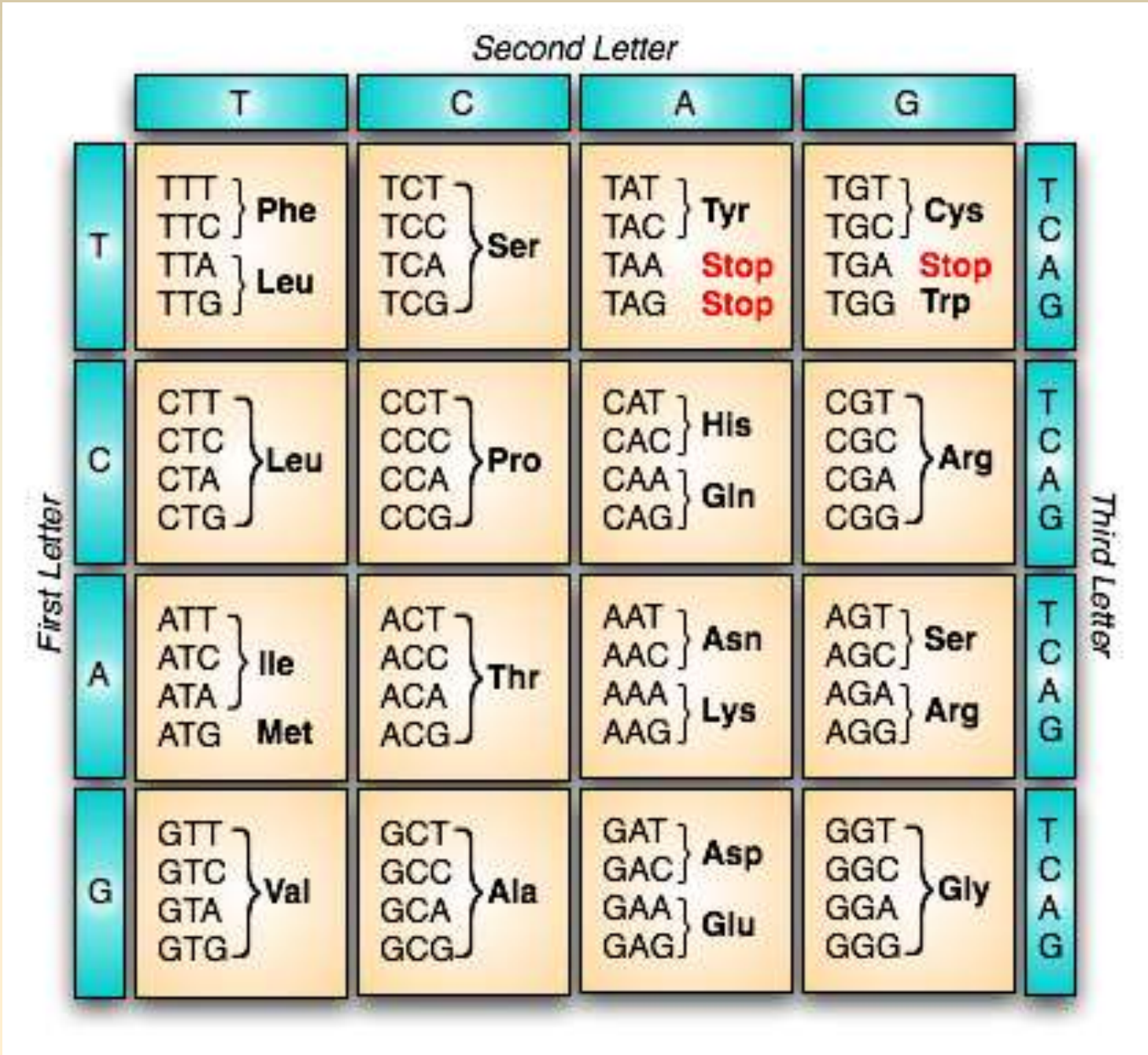
Perhaps because transitions cause less disruption to the DNA molecule and so are less likely to be noticed by DNA repair molecules.

Types of mutations

Not all mutations cause a change in amino acid coded for. These are called **silent mutations** (aka synonymous, old and new have same a.a.)

Mutations that do cause a change in amino acid are called **replacement mutations** (aka missense or nonsynonymous).

Nonsense – mutation to a stop codon, terminates protein.


Second Letter
T
C
A
G
First Letter
Third Letter
T
C
A
G
TTT TTC Phe
TTA TTG Leu
TCT TCC TCA TCG Ser
TAT TAC Tyr
TAA Stop
TAG Stop
TGT TGC Cys
TGA Stop
TGG Trp
CTT CTC CTA CTG Leu
CCT CCC CCA CCG Pro
CAT CAC His
CAA CAG Gln
CGT CGC CGA CGG Arg
ATT ATC ATA Ile
ATG Met
ACT ACC ACA ACG Thr
AAT AAC Asn
AAA AAG Lys
AGT AGC Ser
AGA AGG Arg
GTT GTC GTA GTG Val
GCT GCC GCA GCG Ala
GAT GAC Asp
GAA GAG Glu
GGT GGC GGA GGG Gly

Types of mutations

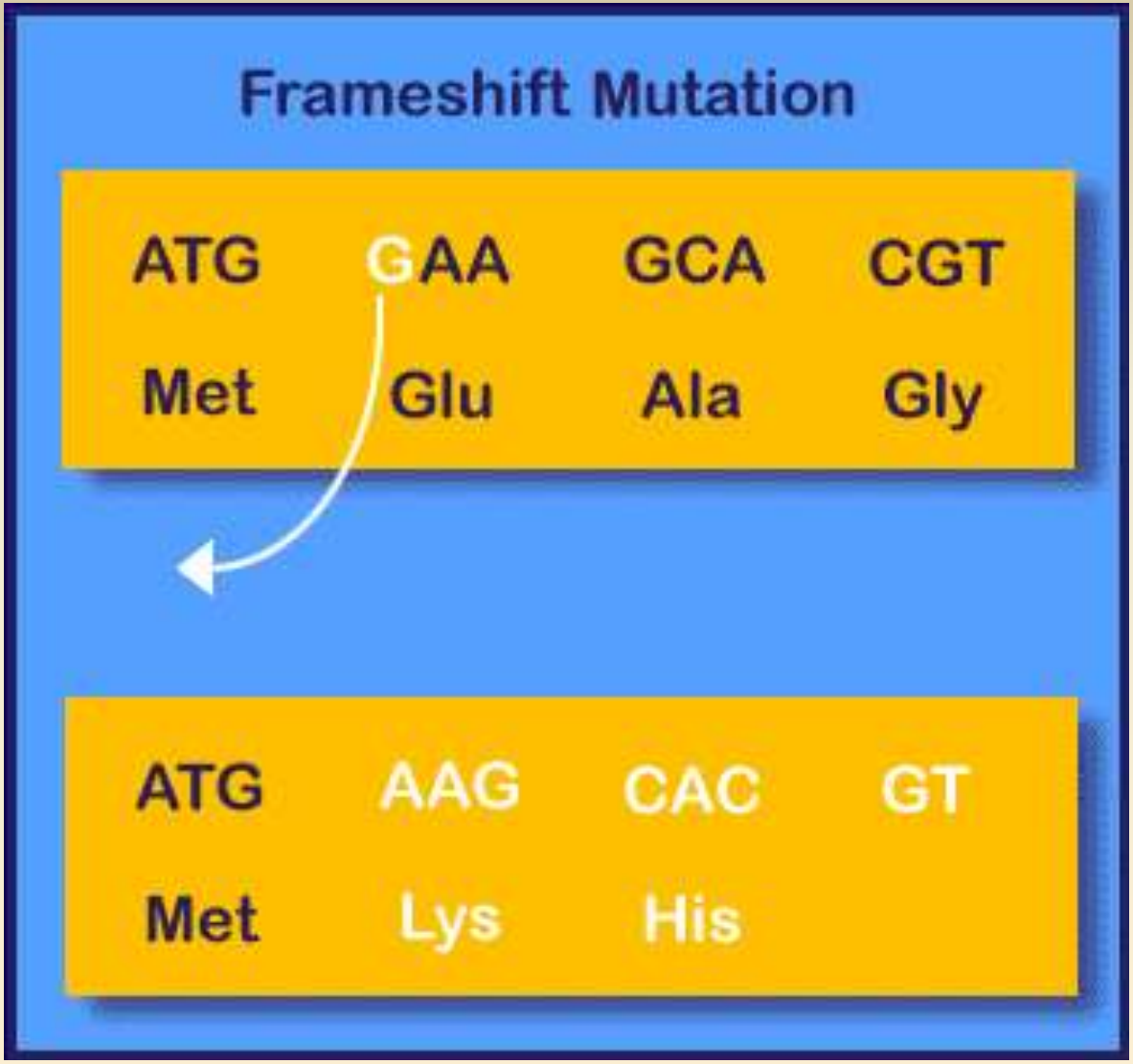
- Another type of mutation occurs when bases are inserted or deleted from the DNA molecule.
- This causes a change in how the whole DNA strand is read (a frame shift mutation) and produces a non-functional protein.

Frameshift Mutation – insertion or deletion of single base in a codon

THE CAT ATE THE RAT

THC ATA TET HER AT

THE CAT TAT ETH ERA T


Frameshift Mutation
ATG GAA GCA CGT
Met Glu Ala Gly
ATG AAG CAC GT
Met Lys His

Sickle Cell Is a Point Mutation

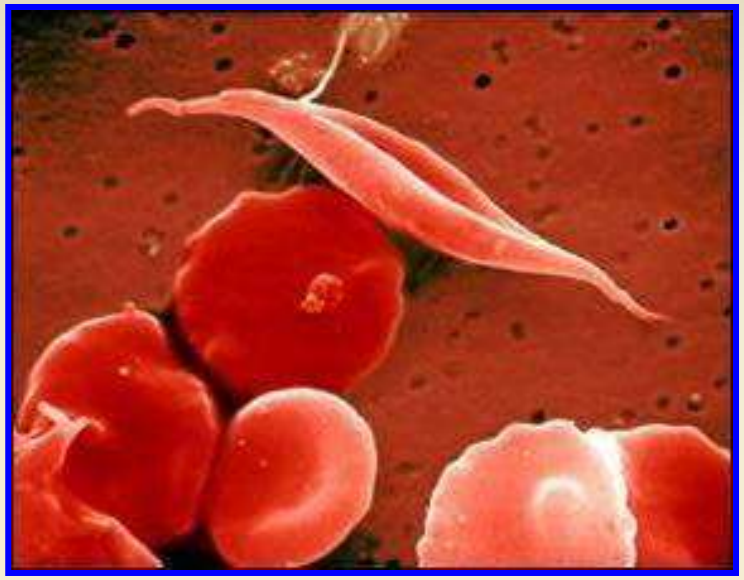
Sickle Cell is an Example of an Inborn Error of Metabolism

HBB Sequence in Normal Adult Hemoglobin (Hb A):

Nucleotide	CTG	ACT	CCT	GAG	GAG	AAG	TCT
Amino Acid	Leu	Thr	Pro	Glu	Glu	Lys	Ser
	3			6			9

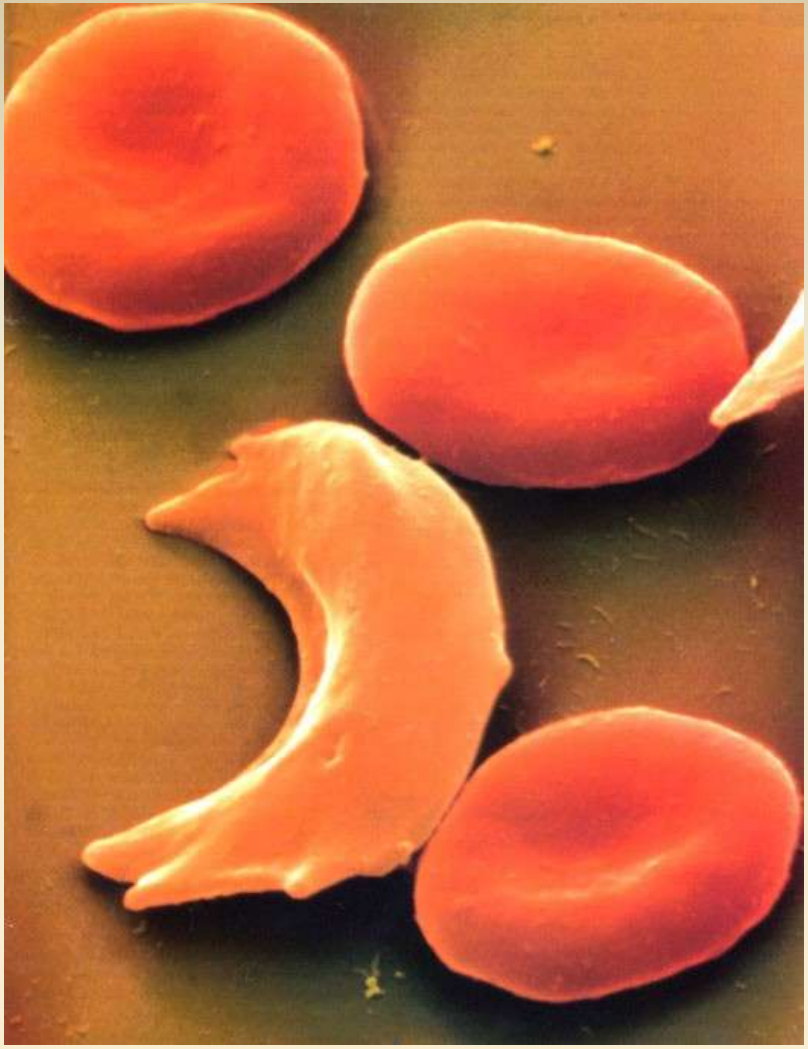
HBB Sequence in Mutant Adult Hemoglobin (Hb S):

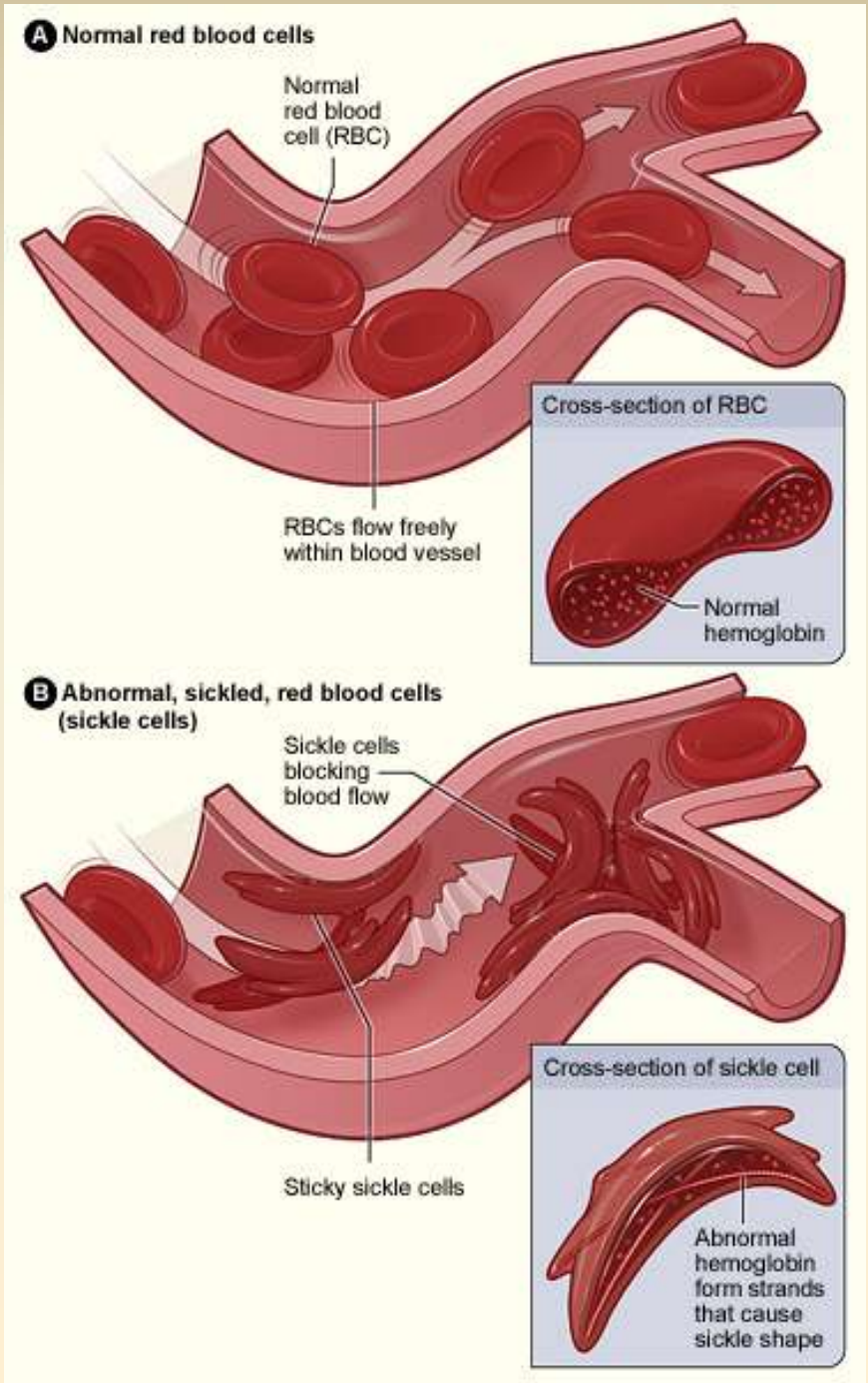
Nucleotide	CTG	ACT	CCT	GTG	GAG	AAG	TCT
Amino Acid	Leu	Thr	Pro	Val	Glu	Lys	Ser
	3			6			9

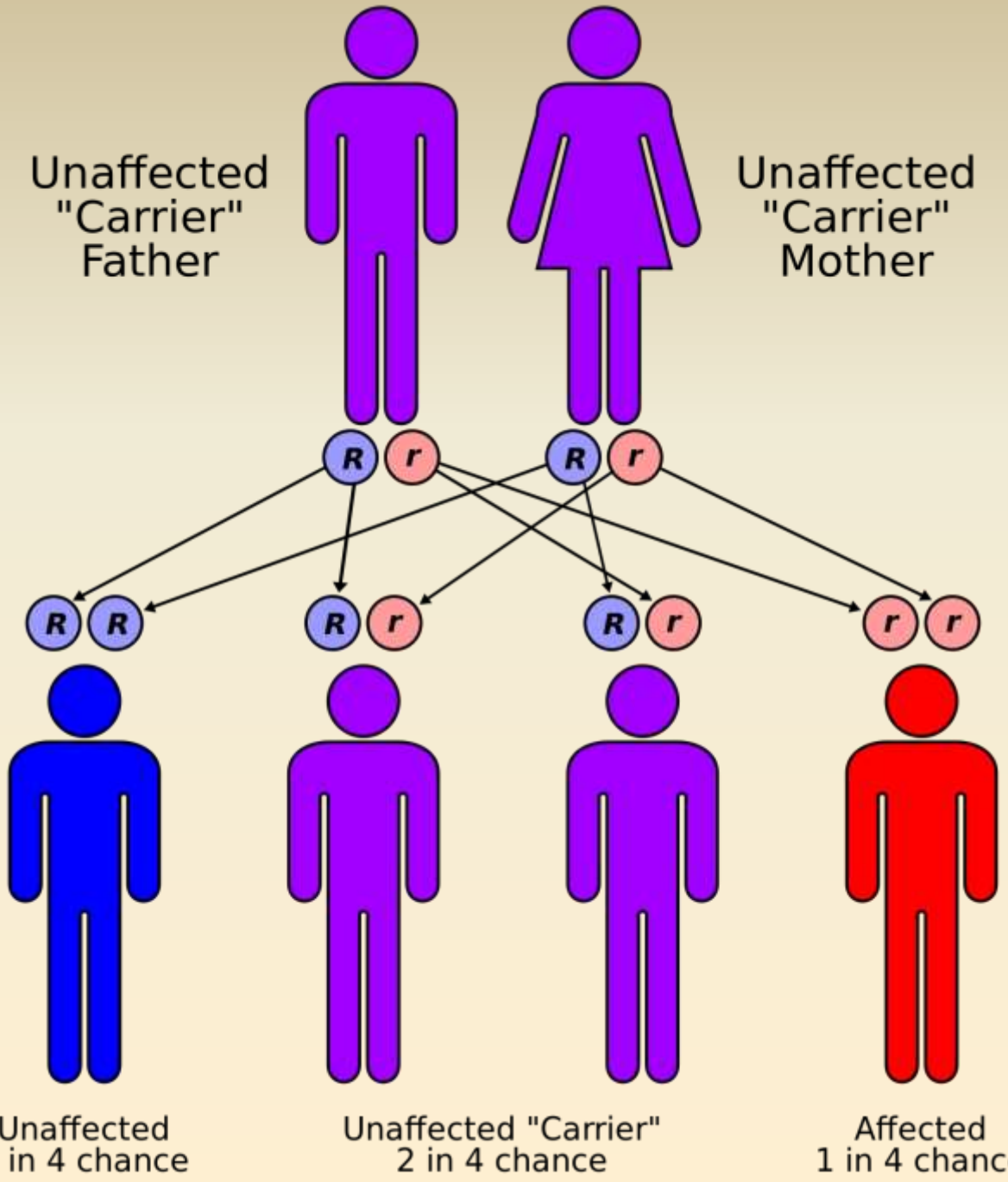


Sickle cell disease: A single base change in DNA codes via RNA for a different amino acid, **valine**

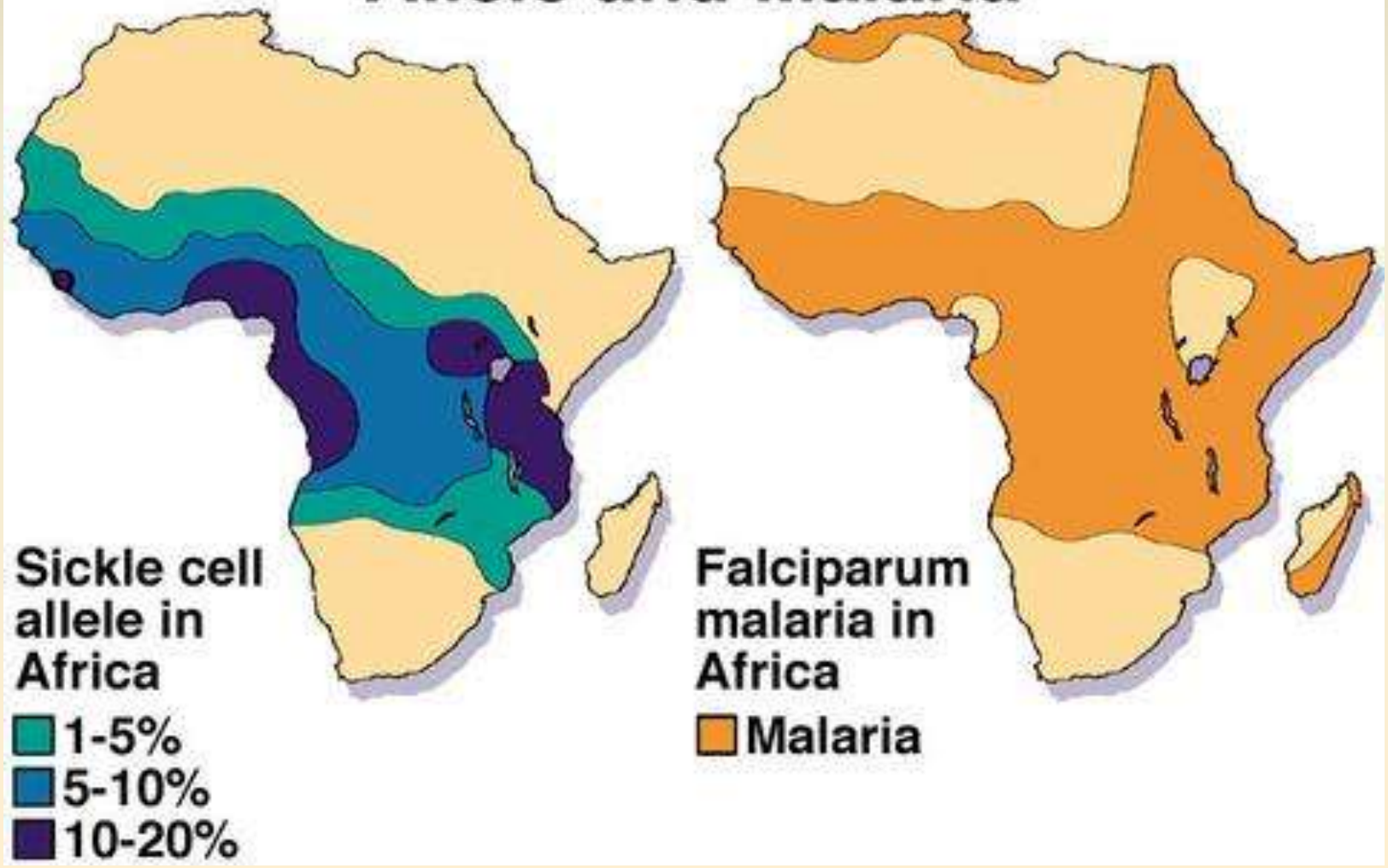
But this critical amino acid is important in proper folding of the hemoglobin molecule, which becomes defective, producing sickled red blood cells




A Normal red blood cells
Normal red blood cell (RBC)
RBCs flow freely within blood vessel
Cross-section of RBC
Normal hemoglobin
B Abnormal, sickled, red blood cells (sickle cells)
Sickle cells blocking blood flow
Sticky sickle cells
Cross-section of sickle cell
Abnormal hemoglobin form strands that cause sickle shape


Unaffected
"Carrier"
Father
Unaffected
"Carrier"
Mother
R
r
R
r
R
R
R
r
R
r
r
r
Unaffected
1 in 4 chance
Unaffected "Carrier"
2 in 4 chance
Affected
1 in 4 chance

Correlation between Sickle Cell Allele and Malaria



Trinucleotide Repeats

During replication, DNA polymerase can "stutter" when it replicates several tandem copies of a short sequence. For example, CAGCAGCAGCAG, 4 copies of CAG, will occasionally be converted to 3 copies or 5 copies by DNA polymerase stuttering.

Outside of genes, this effect produces useful genetic markers called SSR (simple sequence repeats).

Within a gene, this effect can cause certain amino acids to be repeated many times within the protein. In some cases this causes disease

Trinucleotide Repeats

For example, Huntington's disease is a neurological disease that generally strikes in middle age, producing paranoia, uncontrolled limb movements, psychosis, and death. Woody Guthrie, a folk singer from the 1930's, had this disease.

The Huntington's disease gene normally has between 11 and 33 copies of CAG (codon for glutamine) in a row. The number occasionally changes. People with HD have 37 or more copies, up to 200). The rate of copy number change is much higher in HD people--too many copies makes the repeated sequence more subject to DNA polymerase stuttering during meiosis.

Interestingly, the age of onset of the disease is related to the number of CAG repeats present: the more repeats, the earlier the onset.

Germinal vs. Somatic Mutations

Mutations can occur in any cell. They only affect future generations if they occur in the cells that produce the gametes: these are "germinal" or "germ line" mutations.

Mutations in other cells are rarely noticed, except in the case of cancer, where the mutated cell proliferates uncontrollably. Mutations in cells other than germ line cells are "somatic" mutations.

END