Linkage, Crossing over & Linkage Maps

- Tendency of genes to remain together in their original combination during inheritance is called **linkage**

- **Linked genes** are those genes which are transmitted together and fail to assort independent of each other thus violating Mendel's law of independent assortment

- All genes located on a given pair of chromosomes constitute a group referred to as **linkage group**

- Number of linkage groups = Haploid number of chromosomes for a species

- The phenomenon of linkage was firstly reported by Bateson and Punnet in 1906.

- T H Morgan put forth the theory of linkage and concluded that coupling and repulsion were two phases of single phenomenon, linkage.

- Linkage is generally classified on the basis of three criteria

(i) Crossing over

(ii) Genes involved and

(iii) Chromosomes involved

A) Linkage on the basis of Crossing over:

(i) Complete Linkage:

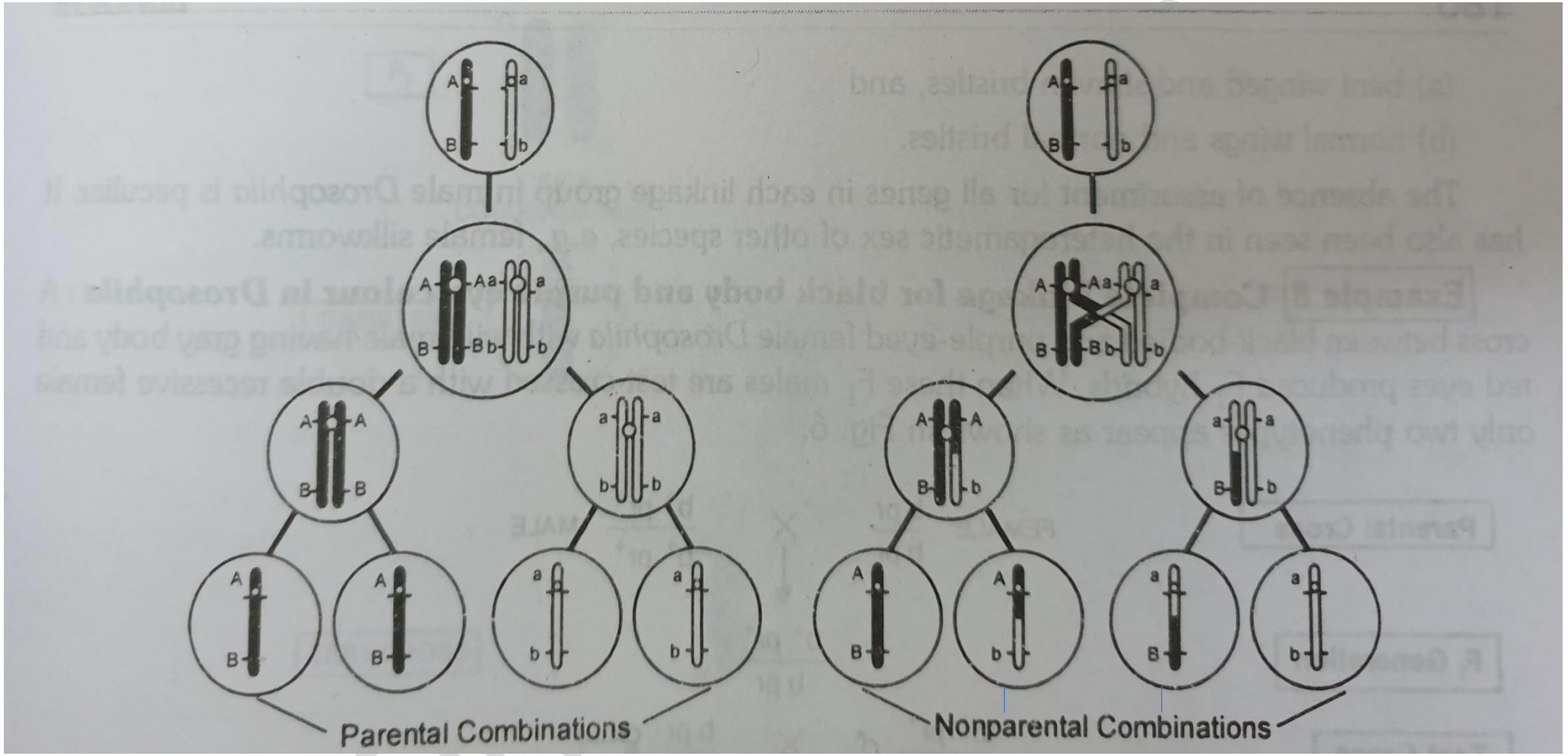
- The linked genes are transmitted together to the offspring and only parental combinations of genes appear.
- When genes are very closely placed in the chromosome they are always transmitted together and show complete linkage.
- It is known in case of males of Drosophila where there is complete absence of recombinant types due to absence of crossing over.

(ii) Incomplete Linkage:

- Linkage is incomplete when new or nonparental combinations of linked genes are also formed. It means linked genes separate in certain cases as a result of crossing over.
- Homologous chromosomes undergo breakage and reunion during meiosis at the

time of gamete formation. As a result of exchange, crossover gametes or recombinant gametes are formed along with non-crossover gametes.

- Incomplete linkage has been observed in maize, pea and *Drosophila* female

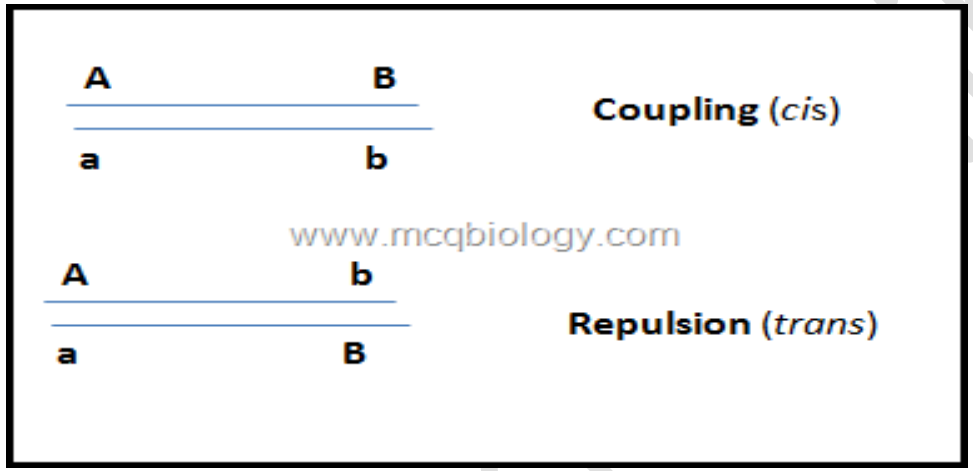


Difference between Complete & Incomplete Linkage

B) Linkage on the basis of Genes Involved:

- Coupling phase: The type of linkage arrangement when two dominant genes are on the same chromosome and the two recessive genes are on the other member of the chromosome pair (designated as AB/ab).

- Repulsion phase: The type of linkage arrangement when one dominant and one recessive gene are on the same chromosome and one recessive and one dominant are on the other member of the chromosome pair (designated as Ab/aB)



C) Linkage on the basis of Chromosomes:

(a) Autosomal linkage: It refers to linkage of those genes which are located in autosomes (other than sex chromosomes).

(b) Allosomal linkage / sex linkage: It refers to linkage of genes which are located in sex chromosomes i.e. either ‘X’ or ‘Y’ (generally ‘X’)

Characteristics of Linkage

- Linkage involves two or more genes which are located in same chromosome in a linear fashion.
- Linkage reduces variability.
- Linkage usually involves those genes which are located close to each other.
- The strength of linkage depends on the distance between the linked genes. Lesser the distance, higher the strength and vice versa.
- Linkage can be determined from test cross progeny data.

Linkage groups

- Linkage group refers to a group of genes which are present in one chromosome. In other words, all those genes which are located in one chromosome constitute one linkage group.
- The number of linkage groups is limited in each individual. The maximum number of linkage groups is equal to the haploid chromosome number of an organism.
- For example there are ten linkage groups in corn (2n = 20), seven in garden pea (2n = 14), seven in barley (2n =14), four in *Drosophila melanogaster (2n = 8) and 23 in man (2n = 46).*

Detection of linkage

- Linked genes are used for mapping. They are found by looking for deviation from the frequencies expected from independent assortment i.e. presence of linkage b/w two genes modifies the 9:3:3:1 ratio that is expected under independent assortment

- Test cross is the most common method of detecting the linkage. In this method, an individual heterozygous for the two genes under consideration (Aa/Bb) is crossed to a homozygous recessive parent (aa/bb) and the phenotypic ratio of test cross progeny is examined.

- If the phenotypic ratio of test cross progeny shows 1:1:1:1 ratio of parental and recombinant genotypes, it indicates absence of linkage.

- If the frequency of parental types and recombinant types deviate

significantly from the normal dihybrid test cross ratio of 1:1:1:1, it reveals presence of linkage between two genes under study.

No Linkage: Independent Assortment

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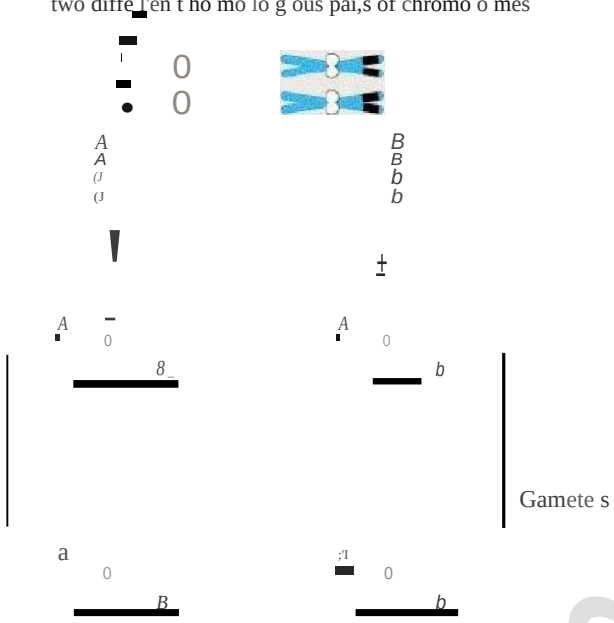

Linkage without Recombin ation

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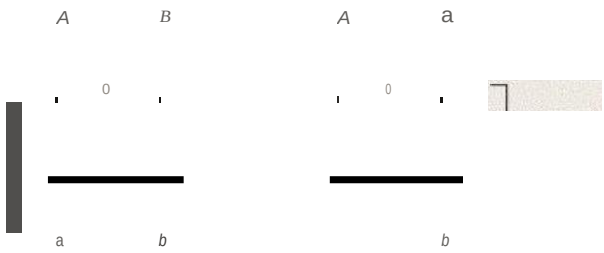
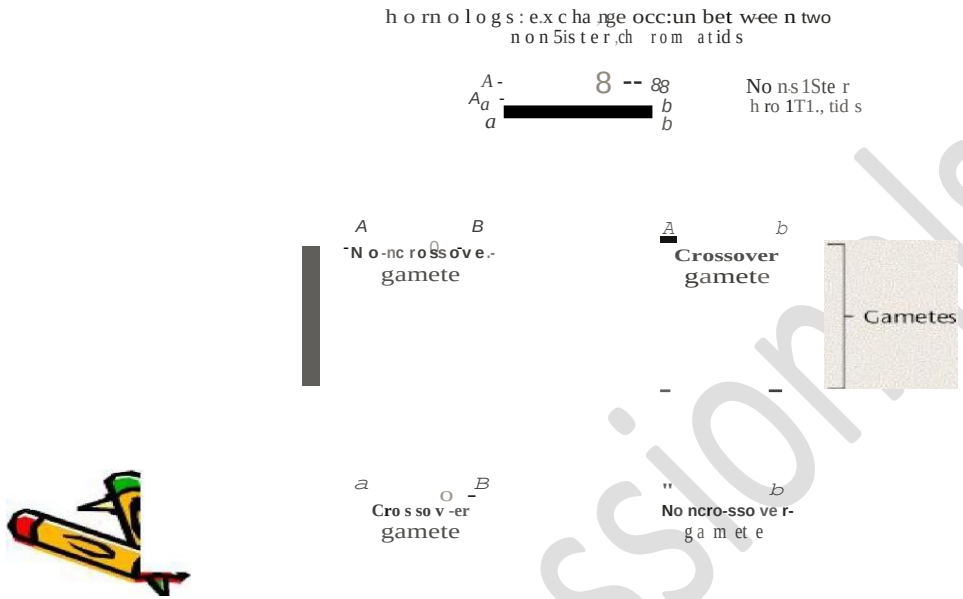


Linkage witb Recombinati

(c) Linkageb e tw e-en t wo genes on a sig le pair of



Parental Cross	**AABB**	×	**aabb**
	AB/AB		ab/ab
Gametes	(AB)	↓	(ab)
F_1		AB/ab	(Heterozygous)
Test Cross		AB/ab ×	aabb (Homozygous recessive)

A. In Case of Independent Assortment

	F_1 Gametes	F_2 Offspring	Types of Combinations	Percentage	
(i)	AB × ab	AB/ab	Paternal Types	25	100
(ii)	ab × ab	ab/ab		25	
(iii)	Ab × ab	Ab/ab	Recombinant Types	25	
(iv)	aB × ab	aB/ab		25	

B. In Case of Complete Linkage

	F_1 Gametes	F_2 Offspring	Types of Combination	Percentage	
(i)	AB × ab	AB/ab	Parental	50	100
(ii)	ab × ab	ab/ab		50	

A. When genes are present on separate chromosomes, they show independent assortment
B. When genes are present on same chromosomes, they show linkage

Crossing Over

- The reciprocal exchange of segments (therefore, of genes) between non-sister chromatids of the homologous chromosomes is referred to as crossing over.

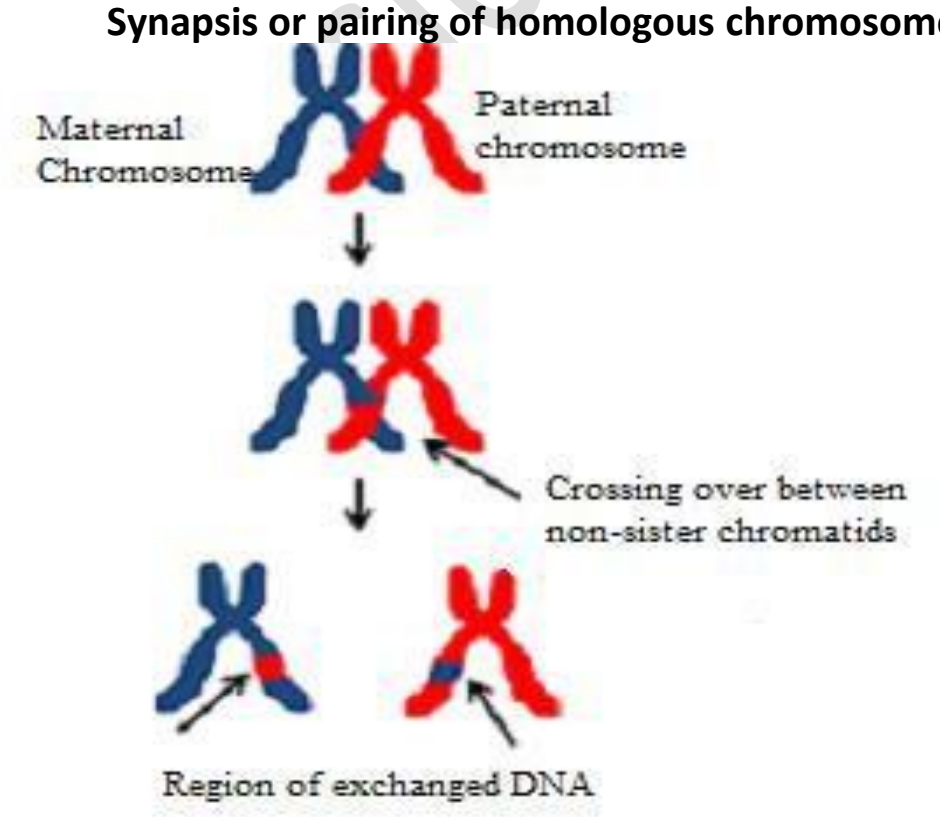
- Crossing over occurs in Prophase-I of meiosis during Pachytene stage.

- During prophase-I homologous chromosomes will line up with one another, forming tetrads. During this lining up, DNA sequences can be exchanged between the homologous chromosomes.

- The new combinations of DNA created during crossover provide a

significant source of genetic variation or genetic diversity.

- Gametes or individuals carrying original or parental combination of genes are referred to as parental or non-crossover or non-recombinant types.
- Gametes or individuals carrying new combination of genes arising from crossing over are called non-parental or cross-over or recombinant types



Types of Crossing Over:

- Depending upon the number of chiasmata involved, crossing over may be of three types, viz., single, double and multiple as described below:

i. Single Crossing Over:

- It refers to formation of a single chiasma between non-sister chromatids of homologous chromosomes. Such cross over involves only two chromatids out of four.

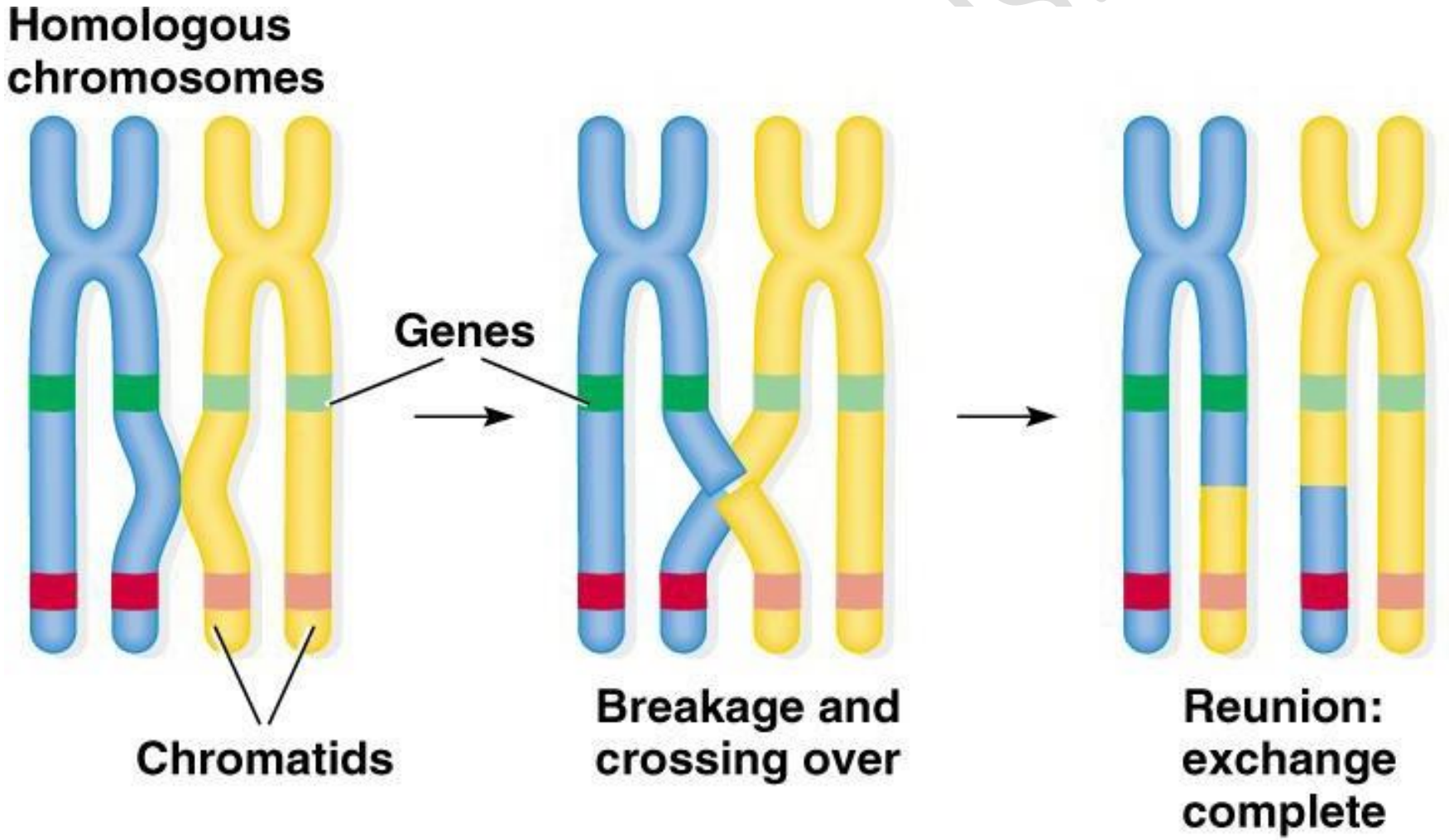
ii. Double Crossing Over:

- It refers to formation of two chiasmata between non-sister chromatids of homologous chromosomes. Double crossovers may involve either two strands or three or all the four strands.

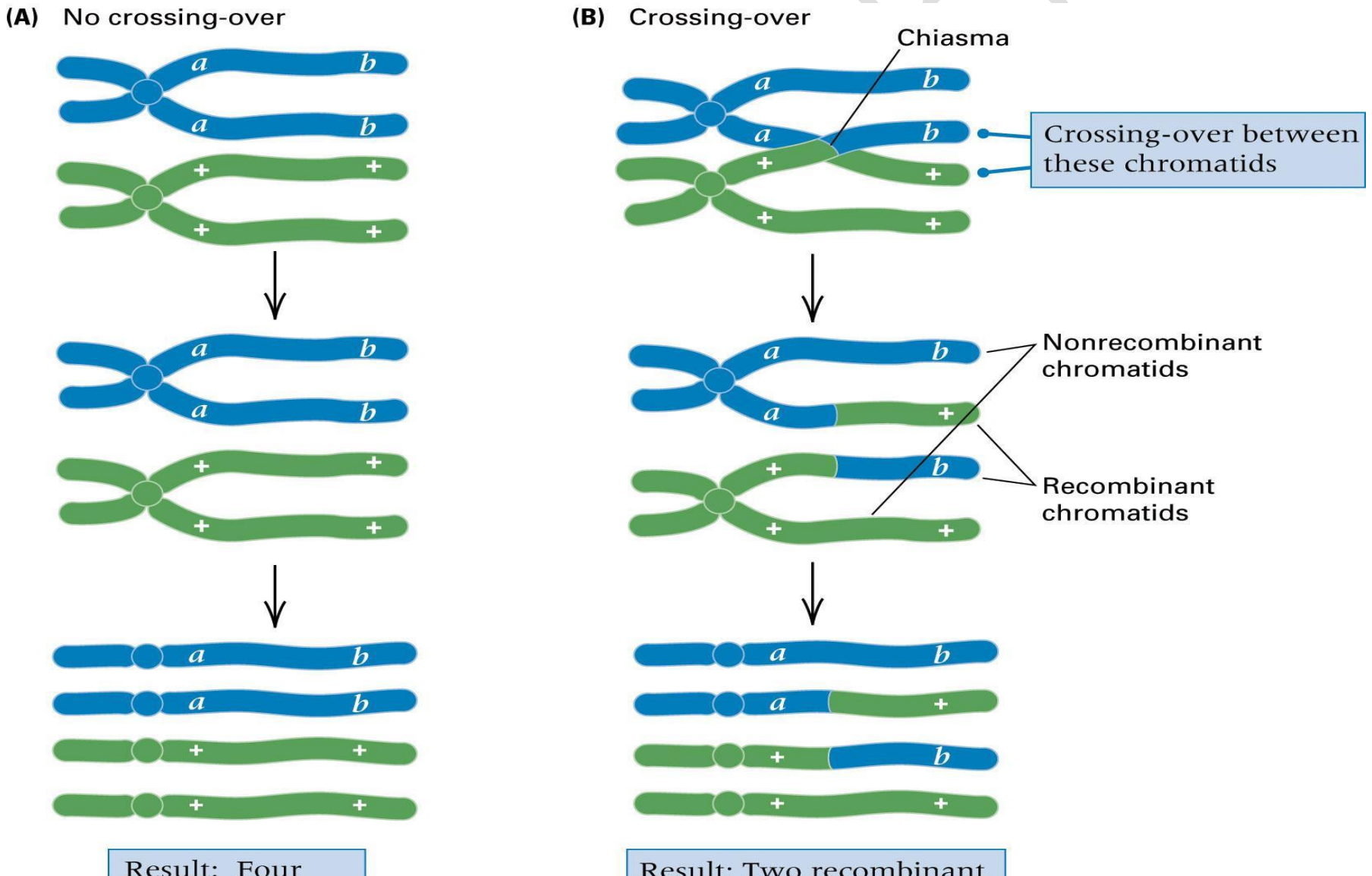
iii. Multiple Crossing Over:

- Presence of more than two crossovers between non-sister chromatids of homologous chromosomes is referred to as multiple crossing over. Frequency of such type of crossing over is extremely low.

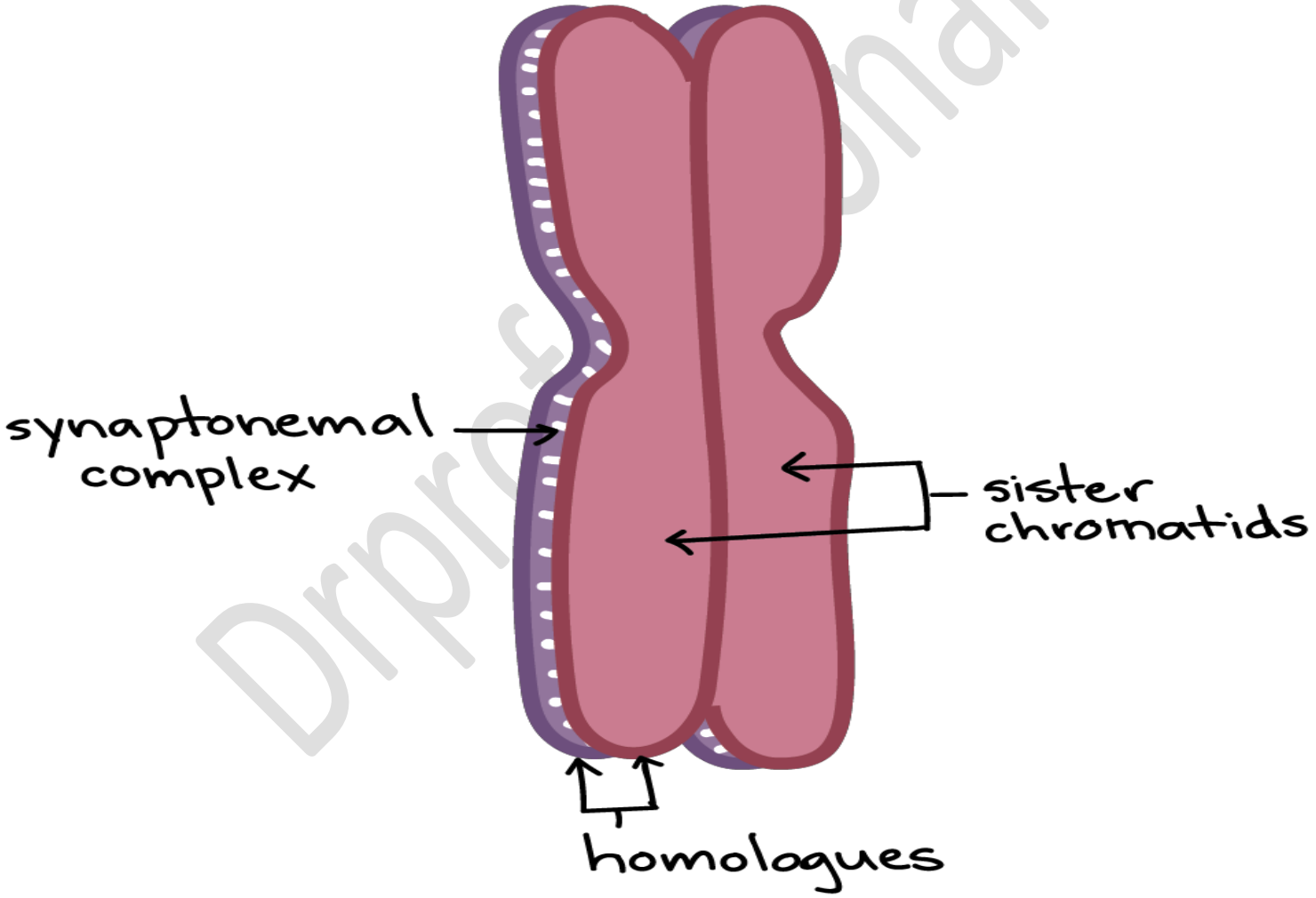
Fig. 13.2 Mechanism of crossing-over



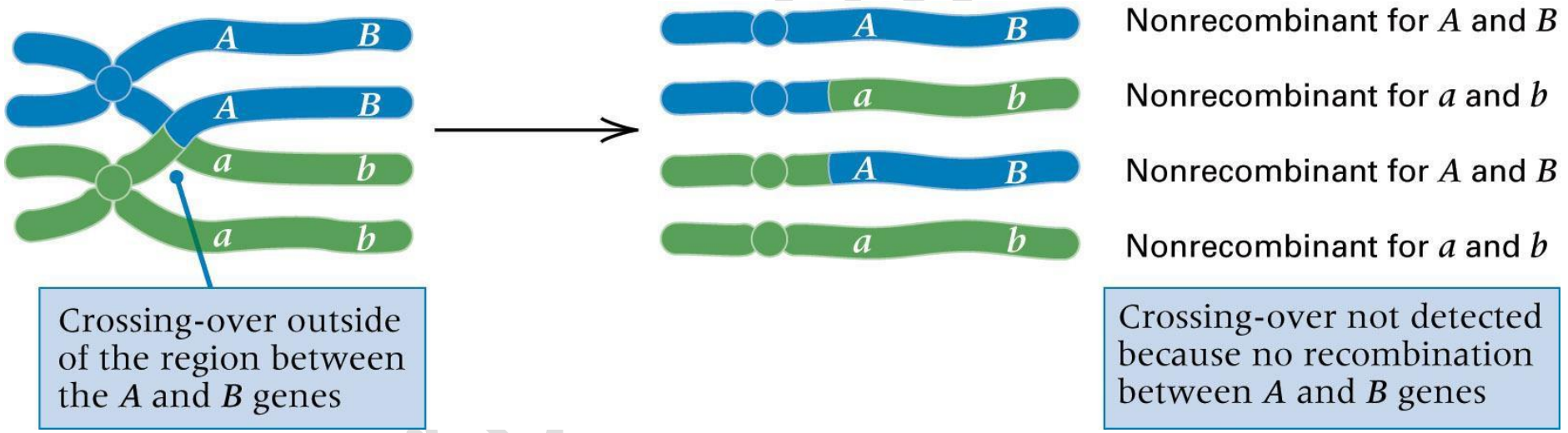
Recombinant gametes are created by recombination (crossing over) between homologous chromosomes



The synaptonemal complex (The synaptonemal complex (SC) is a protein structure that forms between homologous chromosomes (two pairs of sister chromatids) during meiosis and is thought to mediate synapsis and recombination during meiosis I in eukaryotes) holds the homologues together during crossing-over.



Crossing over must occur between 2 genes to produce recombinant gametes



Here the crossing over did not occur between the 2 genes. As a result,

all four gametes are nonrecombinant (parental combinations)

Significance of Linkage and Crossing Over:

- Linkage b/w genes is a measure of the probability of genes being transmitted together to the progeny and could be put to practical use. For example-

Genes causing diseases expressed later in life

Gene controlling disease is closely linked to a gene that expresses early in life, the latter could be used as **marker** to identify whether an individual carries the gene for that disease before its actual onset

- Linkage reduces the possibility of variability in gametes unless crossing over occurs
- Linkage reduces the chance of recombination of genes and thus helps to hold the parental characteristics together.
- In livestock, linkage between genes can be used for selection of superior animals. For eg.- if a gene is found to be linked to a gene responsible for disease resistance

or superior performance, it can be used as a marker for identifying genetically superior animals to be used for breeding.

- One of the best example of linkage between a single-gene trait and trait of economic importance has been reported in chickens:

Blood group genotype	B_1B_1	B_1B_2	B_1B_{19}
Laying house mortality (%)	34.0	4.0	6.0

Since blood typing can be done at an early age, chicks of genotype B1B1 can be discarded at hatching.

➢ Crossing over leads to formation of new gene combinations that did not exist among the parents and thus provide a powerful mechanism for creation of genotypic variability.

➢ Frequency of crossing over is used to determine the relative distances between genes on a chromosome and thus it helps in establishment of linkage maps.

Chromosome, Gene, Genetic or Linkage Mapping:

- The assignment of relative positions to genes on chromosomes or Graphical representation of relative distances between linked genes of a chromosome is known as Chromosome, Gene, Genetic, cross over map or Linkage Mapping.

- A chromosome map indicates the relative distance between different genes on a chromosome (gene distance) and the linear sequence of genes along the chromosome (gene order).

- **Principle of Mapping:** the frequency of cross-over's or recombinants

among testcross progeny is a measure of distance between genes on a chromosome.

- Therefore, the frequency with which the cross-over or recombinant types occur among test cross progeny is used as the criterion for determining the distance between genes.
- The distance between linked genes is measured in map unit. One map unit is equal to one percent of crossing over. Thus one map unit represents the linear distance between genes on a chromosome which gives a crossover frequency of one percent.
- The distance between genes is also expressed in Morgan units as follows:

1% crossing over = 1 centiMorgan(1cM)

(A map unit, or centiMorgan, is equal to crossing over between 2 genes in 1% of the gametes)

10% crossing over = 1 deciMorgan (1dM)

100% crossing over= 1 Morgan unit (M)

Recombination frequency or Cross-over frequency

- **How often recombination occurs depends on how far apart the genes are:**
- **If genes are close together, there will be very low recombination rates.**
- **If genes are farther apart, there will be higher rates of recombination.**
- **Recombination frequency increases with increasing distances between genes**

- **No matter how far apart two genes may be, the maximum frequency of recombination between any two genes is 50 percent.**

- The distance between genes is proportional to the frequency of recombination events.

- Recombination frequency (R) = recombinant progeny/total progeny

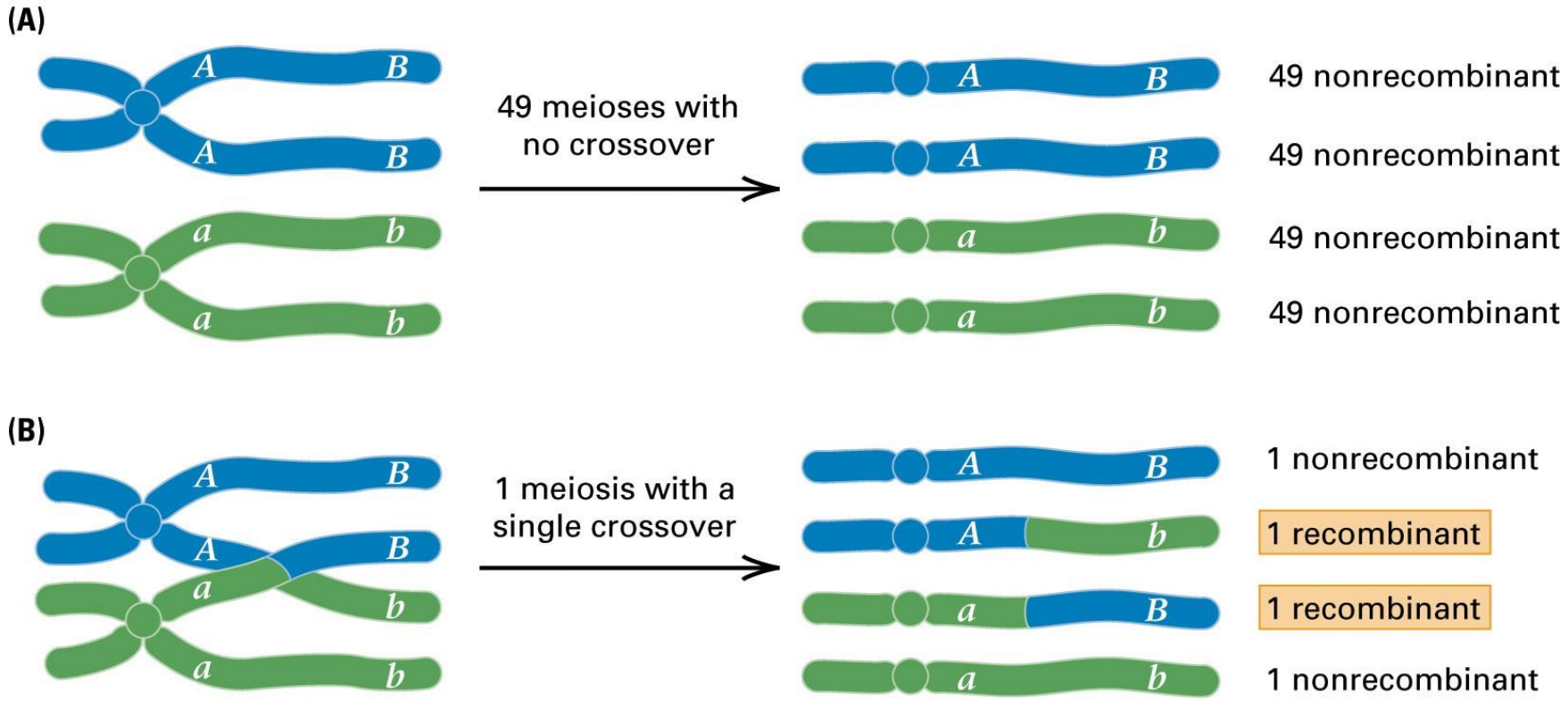
Total progeny= Total amount of recombinants + total amount of non-recombinants

Recombination can be expressed in four equivalent ways:

- Frequency of recombination (0.00-0.50)
- Percent recombination (0-50%)

- 1% recombination = 1 map unit (m.u.)
- 1 map unit = 1 centimorgan (cM)

The genetic distance between 2 genes is expressed in map units (% recombination)



(C) Frequency of recombination: $r = \frac{1 + 1}{49 + 49 + 49 + 49 + 1 + 1 + 1 + 1} = \frac{2}{200}$

$= 1$ percent $= 1$ map unit $= 1$ cM

- Cross over frequenc es can be oonve e into map un! s.
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- ge e A and gene **B** cross ove 6.0 6

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12.5 = 18.5

B

PURPOSE & USES OF GENETIC MAPPING

✓ It allows geneticists to understand the overall complexity and genetic organization of a particular species.

✓ To determine the linear order and distance of separation among genes that are linked to each other along the same chromosome.

✓ The chromosome maps display the exact location, arrangement and combination of genes in a linkage group of chromosomes.

✓ They are useful in predicting results of dihybrid and trihybrid crosses.

✓ Genetic maps are useful from an evolutionary point of view. A comparison of the genetic maps for different species can improve our understanding of the evolutionary

relationships among those species.

Interference

- The term interference was coined by Muller which refers to the tendency of one crossover to reduce the chance of another crossover in its adjacent region.

- Interference is affected by gene distance on the chromosome. Lesser the gene distance greater is the interference and vice versa.

- Sometimes, presence of recombination in one region enhances the chance of recombination in another adjacent region. This is termed as negative interference. This type of situation has been observed in some lower organisms, viz., Aspergillus and bacteriophages.

Coefficient of interference is estimated as follows:

- Coefficient of interference (%) = 1 – Coefficient of coincidence x 100
- The interference is inversely proportional to the percentage of crossing over. For instance, if the double cross overs are altogether absent, interference is cent percent.
- If the frequency of double cross overs is equal to the expected value, it means that there is no interference.

Positive interference	Negative interference
1. One crossover reduces the chance of another crossover in the adjacent region.	1. One crossover enhances the chance of another crossover in the adjacent region.

2. Observed in both eukaryotes and prokaryotes	2. Found in some lower organisms like aspergillus and bacteriophages
3. In this case coefficient of coincidence is less than one	3. In this case coefficient of coincidence is more than one

Coincidence

- Coined by Muller to explain strength, degree or intensity of interference.
- The coefficient of coincidence is the percentage ratio of observed double crossovers to the expected double crossovers.
- The greater the coincidence, lesser will be the interference and vice versa.
- Coefficient of coincidence = $\frac{\text{observed double crossovers}}{\text{expected double crossovers}}$

- The coincidence is the complement of interference. Thus, coincidence + interference=1
- When interference is complete (i.e.=1) no double cross overs are formed. It means coincidence is zero. When interference decreases, coincidence increases.
- When coincidence is one, interference is zero. It means percentage of observed and

expected double cross overs will be almost the same.

Possible types of interference and corresponding coefficient of incidence

S.NO.	Coefficient of coincidence	Frequency of double cross overs	Type of Interference
1.	0	Double CO= 0%	Absolute or Complete interference
2.	<1 (less than one)	Double CO less frequent than expected	Partial or positive interference
3.	1	Double frequency=expected frequency	None or absence of interference
4.	>1 (more than one)	Double CO more frequent than expected	Negative interference

Difference between Crossing over and Linkage

Crossing over	Linkage
1. It leads to separation of linked genes	1. It keeps the genes together
2. It involves exchange of segments between non-sister chromatids of homologous chromosomes	2. It involves individual chromosomes
3. The frequency of crossing-over can never exceed 50%	3. The number of linkage group can never be more than haploid chromosome number
4. It increase variability by forming new gene combinations	4. It reduces variability
5. Distance between two genes is directly proportional to the chance of crossing over	5. Distance between two genes is inversely proportional to the degree of linkage