CHROMOSOME MAPS

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INTRODUCTION

Chromosome maps are essential tools in genetics, providing a visual representation of the arrangement and organization of genes along chromosomes. These maps have evolved significantly, from early cytological studies to advanced genomic assemblies, enabling a deeper understanding of genetic structures and functions. The following sections outline key aspects of chromosome mapping.

- Historical Context
- The concept of chromosome mapping emerged from Sutton's chromosomal theory of inheritance in 1903, which established that genes reside on chromosomes.
- Morgan's experiments with Drosophila identified specific gene loci, reinforcing the role of chromosomes as carriers of genetic information(Xu, 2022).

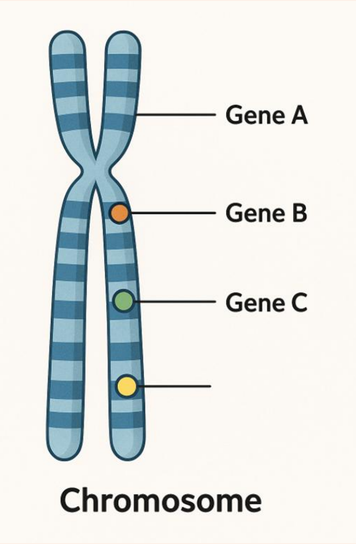
Linkage Groups and Crossing Over

- **Mendel’s laws of inheritance:**
  - **Law of Segregation**
  - **Law of Independent Assortment**
- Mendel’s pea plant experiments showed independent assortment, but some exceptions exist.
- Sutton, Morgan, and Bridges proved that genes are located on chromosomes (**Chromosome Theory of Inheritance**).

Law	Definition
Law of Segregation	During gamete formation, pairs of hereditary factors (alleles) separate so that each gamete carries only one allele from each pair.
Law of Independent Assortment	During gamete formation, different pairs of hereditary factors assort independently of each other, so the inheritance of one trait does not affect the inheritance of another.

• Linkage Groups

- Genes located on the same chromosome form a **linkage group**.
- Genes in a linkage group tend to be inherited together.
- Number of linkage groups = haploid chromosome number.
- Linkage explains exceptions to Mendel's second law (El-Masry, 2008) .



• Evidence for Linkage

•Bateson and Punnett (1905–1908): experiments with *Lathyrus odoratus* showed deviation from independent assortment ratios.

•Parental phenotypes appeared more frequently than recombinant phenotypes.

•This indicated that genes were linked.

- **Results of F2 Generation:**
- Traits studied: Flower color (Purple × Red) and pollen shape (Long × Round).
- **Results:**
  - Expected Mendelian ratio (9:3:3:1) was **not observed**.
  - **Parental combinations** (Purple–Long, Red–Round) appeared more frequently.
  - **Recombinants** (Purple–Round, Red–Long) appeared much less frequently.

Test Cross & Conclusion

- In a test cross (F1 × recessive parent):
  - Parental combinations were more frequent.
  - Recombinants were less frequent.
- **Conclusion:**
  - The genes were **linked**, not assorting independently.
  - This was the **first evidence of genetic linkage**.

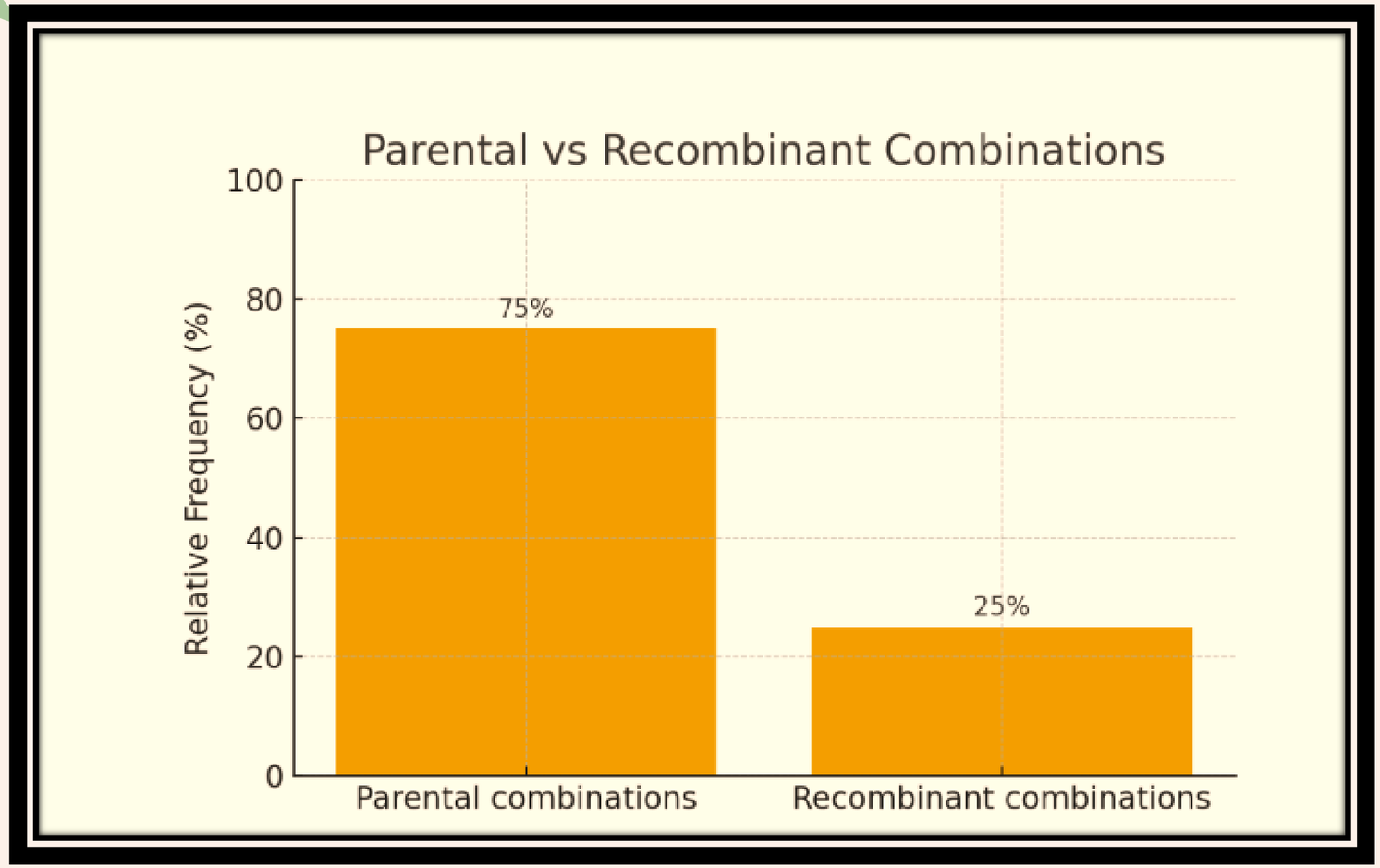

Parental vs Recombinant Combinations
Relative Frequency (%)
100
80
60
40
20
0
75%
25%
Parental combinations
Recombinant combinations

Table (6-1): Phenotypic forms and the obtained ratios in the F2 generation

Phenotype	Observed (Count/Ratio)	Expected (Count/Ratio)	
Pink Long (R- L-)	296 / 0.933	240 / 0.563	
Pink Round (R- ll)	19 / 0.045	80 / 0.188	
Red Long (rr L-)	27 / 0.063	80 / 0.188	
Red Round (rr ll)	85 / 0.199	27 / 0.062	

Table (6-2): Expected vs. Observed Ratios in the F1 generation

Phenotype	Genotype	Expected Ratio	Observed Ratio
Pink Long	Rr Ll	0.25	0.437
Pink Round	Rr ll	0.25	0.063
Red Long	rr Ll	0.25	0.063
Red Round	rr ll	0.25	0.437

• Morgan’s Discovery & Chromosome Theory

• Morgan (1911) found some gene pairs in *Drosophila melanogaster* did not follow independent assortment.
• Genes are arranged linearly on chromosomes; each gene has a fixed location.
• **Coupling (cis)**: two dominant or two recessive genes on the same chromosome.
• **Repulsion (trans)**: one dominant and one recessive gene on the same chromosome.
• New gene combinations require gene transfer between chromosomes.

•Crossing Over

•During meiosis (pachytene stage), homologous chromosomes pair and form a **bivalent**.

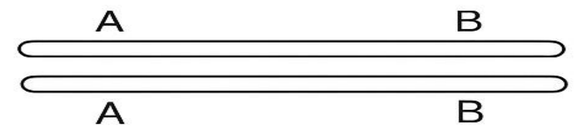
•Four chromatids twist; tension causes breakage of non-sister chromatids.

•Broken parts rejoin → **crossing over** → exchange of chromosome segments.

•Results: new gene combinations + parental types.

•Linkage strength depends on gene distance:

- Close genes → complete linkage.
- Far genes → more crossing over (El-Masry, 2008) .



Homologous Chromosomes



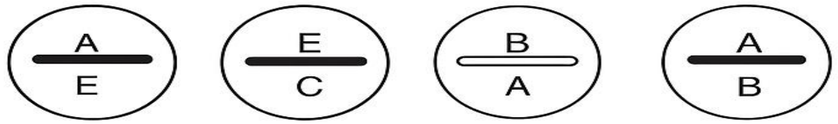
Formation of Nonsister Chrom tids for each Chromosome



Break and Crossover



New Recombinant Chromosomes



Calculations

Figure 6-1: A diagram illustrating the steps of break and fusion between non-sister chromatids in a non-bloc crossing over chromatid

- **Definition and Importance of Linkage:**
- **Linkage:** The tendency of genes located on the same chromosome to be inherited together in the parental combinations at a certain rate across generations.
- Linkage occurs only if genes are on the same chromosome.
- **Relation to gene distance:** The greater the distance between genes, the higher the probability of **genetic crossing over**, leading to more new genetic combinations in the offspring.

Maize Experiment and Genetic Distance Measurement

- A test cross in maize showed deviation from independent assortment.
- Results: parental combinations appeared at a higher frequency (96.4%) compared to recombinant types (3.6%).
- **Crossing over rate calculation**:

$$3.6\% = 100 \times \frac{\text{Number of Recombinants}}{\text{Total Offspring}} = \text{Crossing Over}\%$$

Genetic distance between genes: 3.6 map units.

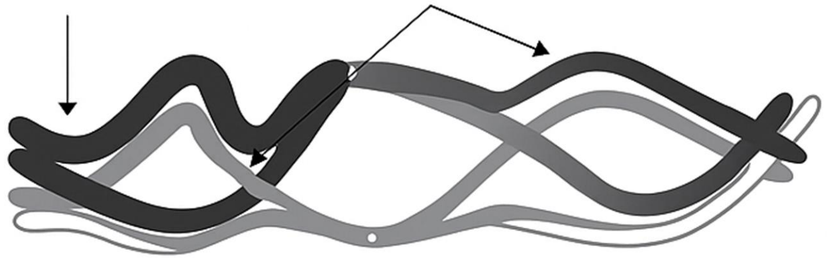
Sex Differences in Linkage and Crossing Over

- In most organisms, crossing over occurs in both sexes.
- **Exceptions:** In male *Drosophila*, crossing over is rare or absent.
- This is due to the absence of **chiasmata** during meiosis in male germ cells.
- In other species, such as the silkworm (*Bombyx mori*), crossing over may occur only in one sex.
- Linkage and crossing over are key for understanding **genetic distribution and variation**.

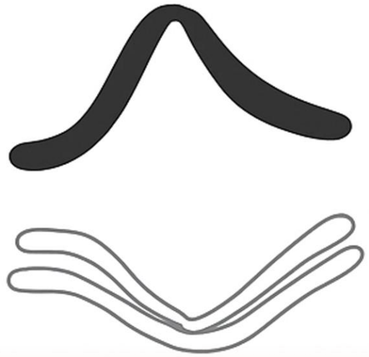
The Chiasma Theory

- Proposed by **Janssens (1909)**.
- The **Chiasma Theory** explains the relationship between **chiasmata** and **crossing-over**.
- According to this theory, **chiasmata** are the **direct result** of **crossing-over**.
- Crossing-over occurs **in the same region** where chiasmata are formed.
- It involves a **break and rejoining** of non-sister chromatids in the **bivalent** during the **pachytene stage** of meiosis.
- Thus, the theory is based on the **exchange of segments** between **non-sister chromatids** within a **bivalent chromosome unit**.

Chiasma Sites



According to Chiasma Theory, crossing-over takes place between non-sister chromatids in the Diplotene stage and is cytologically distinguished as chiasmata.



"In Metaphase I, homologous chromosomes separate after breakage and rejoining at the chiasma sites resulting in crossing-over."

Chiasma Formation

- During the **pachytene stage**, crossing-over occurs between **non-sister chromatids**.
- In the **diplotene stage**, this process appears cytologically as **chiasmata**.
- In the **metaphase I** stage, homologous chromosomes separate after **breakage and rejoining** at the chiasmata regions.
- This separation results in **genetic recombination** (crossing-over).

The Belling Theory (1931)

- Proposed by **Belling (1931)**.
- Also known as the **Chromomere Theory**.
- Suggests a link between **chromatid formation** and **genetic crossing-over**.
- Belling proposed that chromosomes are composed of small chromatin granules called **chromomeres**, connected by **thin threads**.

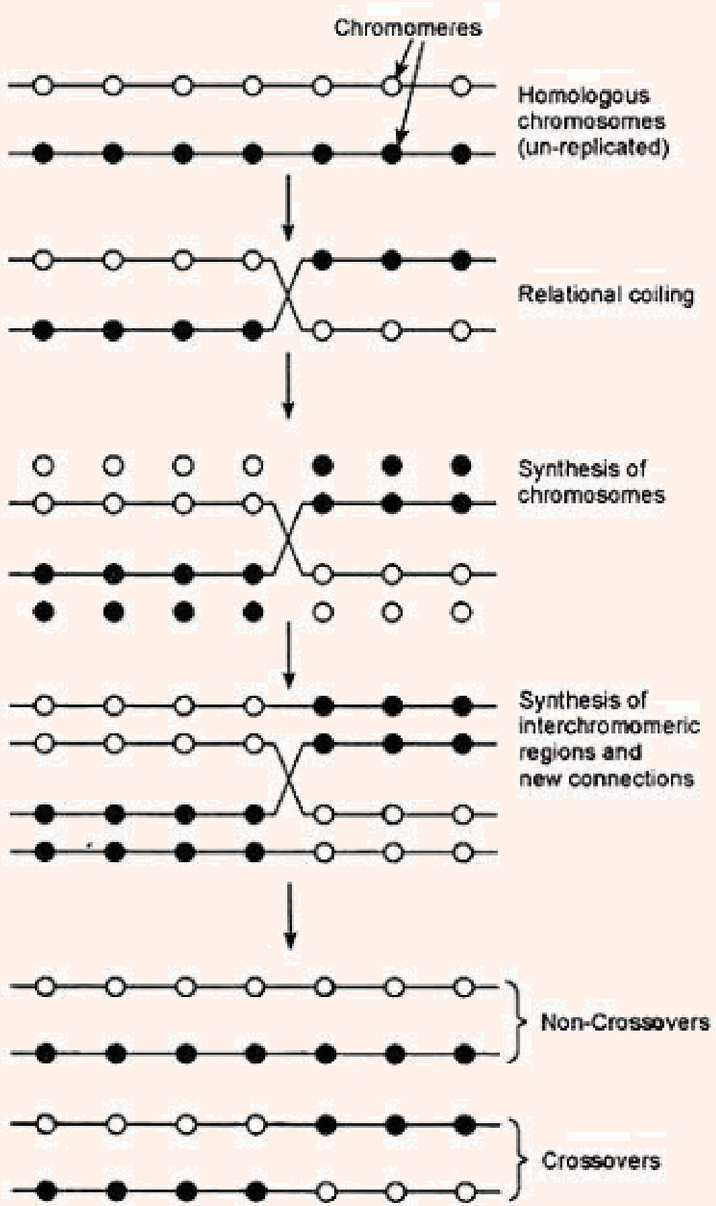


Fig. 11.6. Simplified model of Belling's hypothesis of crossing over.

Chromomere Structure and Crossing-Over

- During chromosome duplication, new chromatids form by aligning **new chromomeres** opposite their counterparts on the original chromosome.
- Initially, these chromomeres are **not connected** by thin threads.
- Later, threads form to connect them.
- During this process, **interchange** or **overlapping** occurs between **non-sister chromatid chromomeres**, leading to **crossing-over**.
- Cytologically, this process appears as **chiasmata regions**.

Illustration Explanation

- (a) Chromosomes consist of **chromomeres** that stain intensely.
  - Black chromomeres → paternal chromosome
  - White chromomeres → maternal chromosome
- (b) **Paternal and maternal chromomeres twist** and exchange positions.
- (c) **New chromomeres** are arranged according to the new sequence after exchange.
- Thin threads later form to connect these chromomeres into a **new chromatid**.

The Replicative Exchange Theory (Copy-choice Hypothesis)

- Proposed by **Lederberg (1955)** to update **Belling's Chromomere Theory**, especially after the discovery of the **DNA molecular structure** and its genetic significance.
- This theory links **crossing-over** with the **DNA replication process** itself.
- During **DNA synthesis**, each new strand is normally built using its **complementary old strand** as a **template**.
- However, during **crossing-over**, at certain regions, the **new strand** switches and uses the **opposite old strand** from the other DNA molecule as a **template**, instead of its own.
- At the same time, the **reverse process** occurs on the other DNA molecule.

DNA Replication and Crossing-Over Process

- **(a)** During DNA replication, the **double helix unwinds**, and each old strand acts as a **template** to form a new complementary strand.
- **(b)** The synthesis of new strands begins on both old strands **almost simultaneously**.
- **(c)** The **new strands exchange** their **template strands** (old ones) during replication, leading to **reciprocal crossing-over**.
- **(d)** This exchange continues **several times** along the DNA molecule, resulting in **multiple crossing-over regions** along the DNA arms.

The Replicative Exchange Theory (Replication–Selection Hypothesis)

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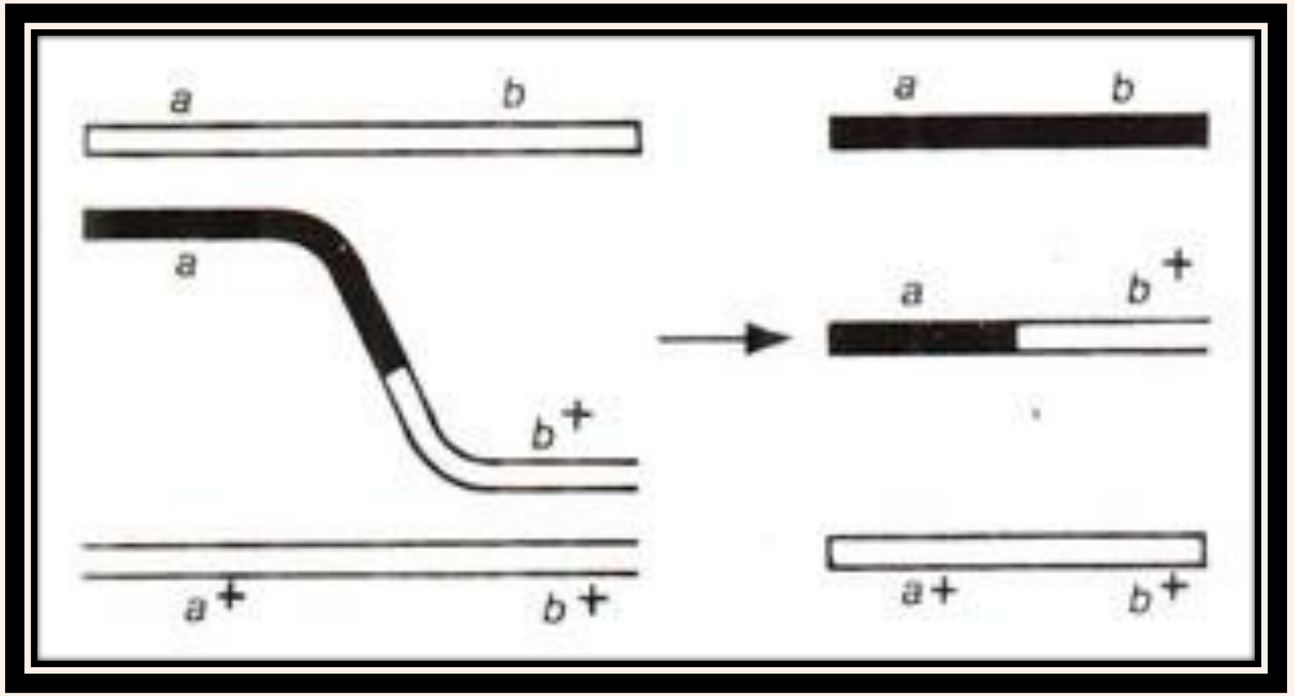


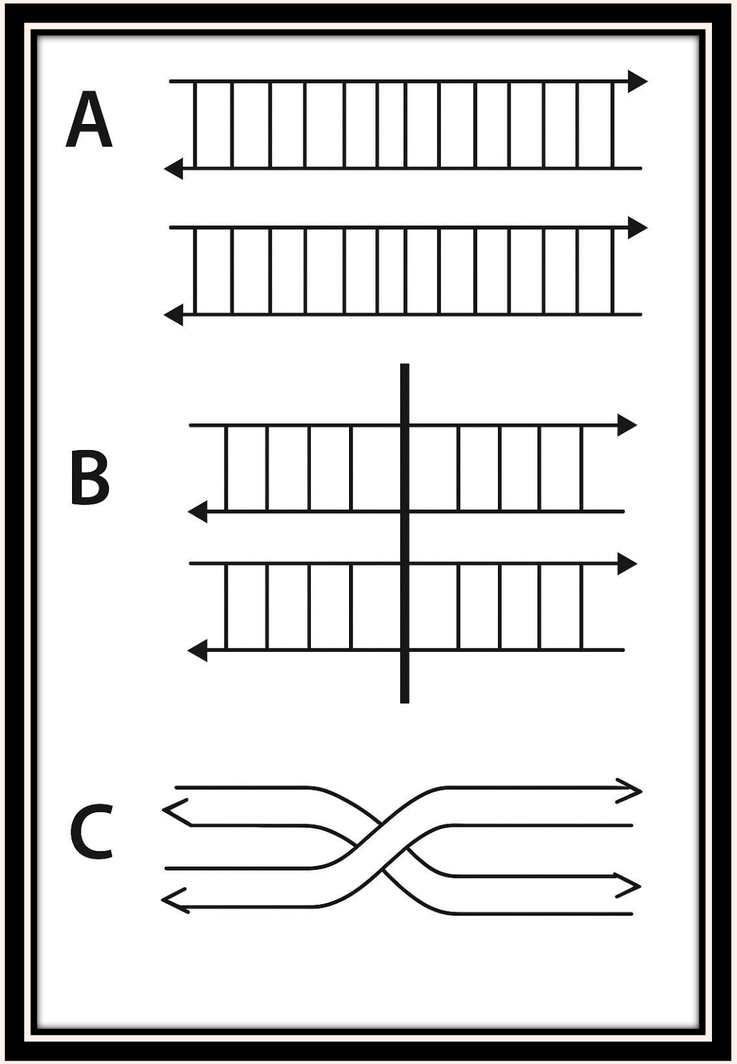
Fig Mechanism of genetic recombination based on copy choice mechanism.

The Polarone Theory (1964)

- The **Polarone Theory** is one of the **latest theories** explaining how **crossing-over** occurs at the **DNA level**.
- Proposed by a scientist in **1964**, this theory suggests that **DNA replication is almost completed before crossing-over occurs**, in contrast to the **Replication–Selection (Copy Choice) Theory**.
- According to this model, **each chromatid** consists of a **single double helix of DNA** surrounded by histone proteins arranged in an orderly structure.
- Therefore, in a **bivalent** (a pair of homologous chromosomes), which contains **four chromatids**, there are **four independent DNA molecules**, one for each chromatid.
- However, **crossing-over** always occurs between **two non-sister chromatids** out of the four.

Steps of Crossing-Over According to the Polarone Theory

- **(a)** Each chromatid is represented by a **single DNA helix**. Pairing occurs between **two non-sister chromatids** with their arms aligned.
- **(b)** A **symmetrical break** occurs at a specific site on the **DNA molecules** of the non-sister chromatids.
- **(c) Rejoining (recombination)** occurs between the broken arms, where each arm reattaches to the corresponding segment of the opposite chromatid in the same orientation.
- This theory concludes that **crossing-over takes place after DNA replication**, through a **breakage and rejoining process** at specific chromosomal regions.
- Thus, the **Polarone Theory** is considered the **most accurate** among the four theories, as it provides a **mechanistic explanation** for the crossing-over event.



Unequal Crossing Over

Unequal crossing over refers to cases where exchange occurs between **non-sister chromatids** that are **not perfectly aligned**.

Normally, the exchange happens between **corresponding loci** on homologous chromosomes, ensuring that the **number of genes** remains constant regardless of how many times crossing over occurs.

This precise alignment guarantees accurate gene pairing before recombination, maintaining the chromosomal gene balance.

However, in certain cases, recombination occurs between **unequal segments** of non-sister chromatids, leading to **unequal exchange** of genetic material.

Genetic Consequences and Frequency:

When unequal crossing over takes place, one chromatid **loses a segment** of the chromosome containing one or more genes (**deficiency**), while the other chromatid **gains an extra copy** of the same segment (**duplication**).

This process can lead to **structural chromosomal variations**, affecting gene dosage and sometimes causing genetic disorders.

However, such unequal exchanges are **relatively rare**.

If the recombination mechanism were less precise in aligning homologous genes, the **frequency of duplications and deficiencies** would be much higher than what is actually observed.

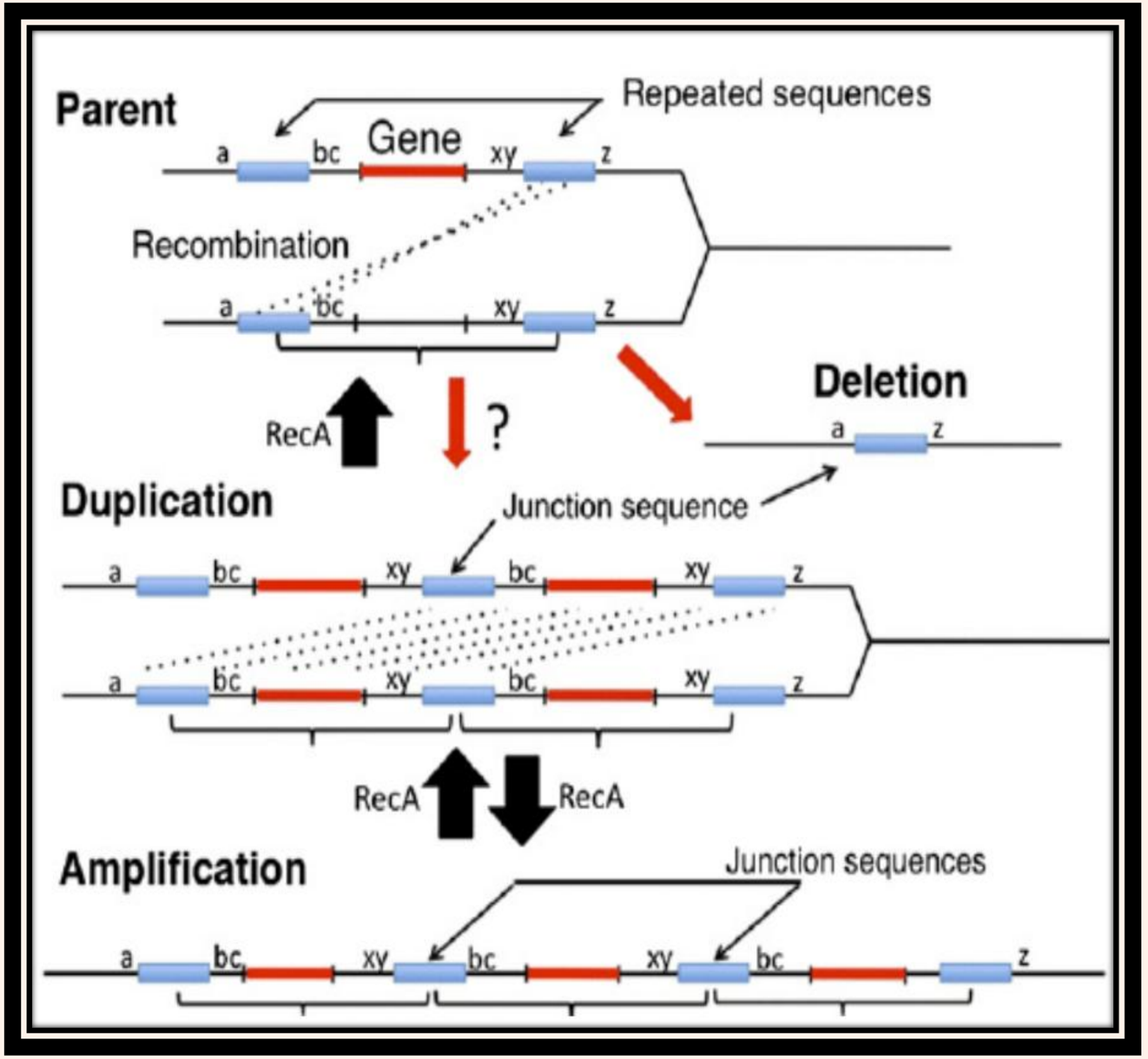


Fig. Duplication by unequal crossing over. This conventional view of duplication formation involves standard recombination events between separated sequence elements embedded in nonhomologous surrounding sequence (top).

The Stage at Which Crossing Over Occurs (Neurospora Experiment)

•Genetic crossing-over occurs during **meiosis** between homologous chromosomes.
•Two hypotheses were proposed:
1.Crossing-over happens **before chromosome duplication**.
2.Crossing-over happens **after chromosome duplication**.
•Experiments using the fungus **Neurospora** showed that all meiotic products are contained in a single ascus, allowing observation of the crossing-over process.
•Results demonstrated that crossing-over takes place **after the chromosomes have duplicated into chromatids**.
•The same conclusion was confirmed in **Drosophila (fruit flies)**, where new genetic combinations appeared only when crossing-over occurred after duplication.

Evidence from *Drosophila melanogaster:*

Similar results were confirmed in *Drosophila melanogaster*.
Researchers studied females with **attached X chromosomes (XXY)** to track how crossing over influences X-linked traits (like eye color).
During meiosis, the attached X chromosomes move together to one pole, and the Y chromosome moves to the opposite pole.
If fertilized normally, the offspring are females with red eyes (XX), unless **crossing over** occurs, which can produce new phenotypes (different eye colors).
This provided clear evidence that **crossing over occurs after chromosomal duplication**, since recombinant traits appeared only in that condition.

Cytological Basis of Crossing Over

- To confirm genetic recombination, scientists needed **cytological evidence** showing physical chromosome exchange.
- Between **1929–1931**, studies proved that **genetic crossing over** is always accompanied by a **cytological (chromosomal) crossover**.
- Two key experiments provided final proof:
  - **Creighton & McClintock (1931)** – in *maize (corn)*
  - **Stern (1931)** – in *Drosophila melanogaster (fruit fly)*

Key Experiments

Creighton & McClintock (Maize):

•Used chromosome 9, one with a **knob and translocation**, the other normal.

•Linked genes:

- **C/c** – aleurone color
- **Wx/wx** – endosperm type

•When recombination occurred, **genetic exchange** always matched **physical exchange** between chromosomes.

Conclusion: Genetic crossover = physical chromosome exchange.

Stern (Drosophila):

•Marked **X chromosomes** with visible structural differences.

•Used genes for **eye color (cr)** and **eye shape (B)**.

•Recombinant offspring showed that **crossing over** caused **exchange of chromosome parts**.

Gene Mapping and Chromosomal Maps

A **chromosomal map** is a diagram that shows the **linear arrangement of genes** on a chromosome and the **distances** between them based on **recombination frequencies**.

- Every organism has a specific number of chromosomes, each carrying a set of genes.
- Each gene has a fixed position on a chromosome, but distances between genes vary, allowing the creation of chromosomal maps.
- **Crossing Over:**
- Crossing over is the exchange of segments between non-sister chromatids during meiosis, producing new gene combinations.
- The **recombination frequency** between two genes is used to estimate the ,**chromosomal distance**:
  - 1 map unit (cM) = 1% recombination frequency.
  - The probability of crossing over increases with the distance between genes.

Measurement Unit:

- The **centiMorgan (cM)** is the unit of chromosomal distance.
- **1 cM = 1% recombination** between two genes.
- Example: 5% recombination → distance = 5 cM.

•Gene Order:

•Three genes (e.g., A, B, C) can be ordered on a chromosome by comparing recombination frequencies.

•The gene appearing in the least frequent double crossover classes is **in the middle**.

•Example:

- •If recombination frequencies are: A–B = 6%, A–C = 9%, B–C = 3% → the correct order is **B – A – C**.

•Three-Point Cross:

•Used to determine the positions of three linked genes on the same chromosome.

•Phenotypic classes:

- •**Parental types:** >50% of offspring.
- •**Single crossovers:** <50%.
- •**Double crossovers:** least frequent.

Determining Gene Order:

- Gene order is determined by **crossing-over percentages**.
- The **middle gene** has the lowest double-crossing frequency.
- **Three-point cross** method is used for precise mapping.

1.Calculating Chromosomal Distances:

1. Distance between two genes = (Number of recombinant individuals ÷ Total offspring) × 100
2. Expected double crossover = (recombination frequency in region 1) × (recombination frequency in region 2)
3. **Coefficient of coincidence (C.O.C):**
    1. = Observed double crossovers ÷ Expected double crossovers
    2. C.O.C = 1 → no interference; C.O.C = 0 → complete interference.

2.Practical Example in Maize (Corn):

1. Three linked genes on chromosome 9:
    1. Grain color (C/c)
    2. Endosperm type (Sh/sh)
    3. Grain shape (Wx/wx)
2. Analysis of single and double crossovers gives the gene order:

   C – Sh – Wx
    1. Distances: Sh–C = 3.5 cM, Sh–Wx = 18.1 cM
    2. Stronger linkage between C and Sh than Sh and Wx.

3.Importance of Chromosomal Maps:

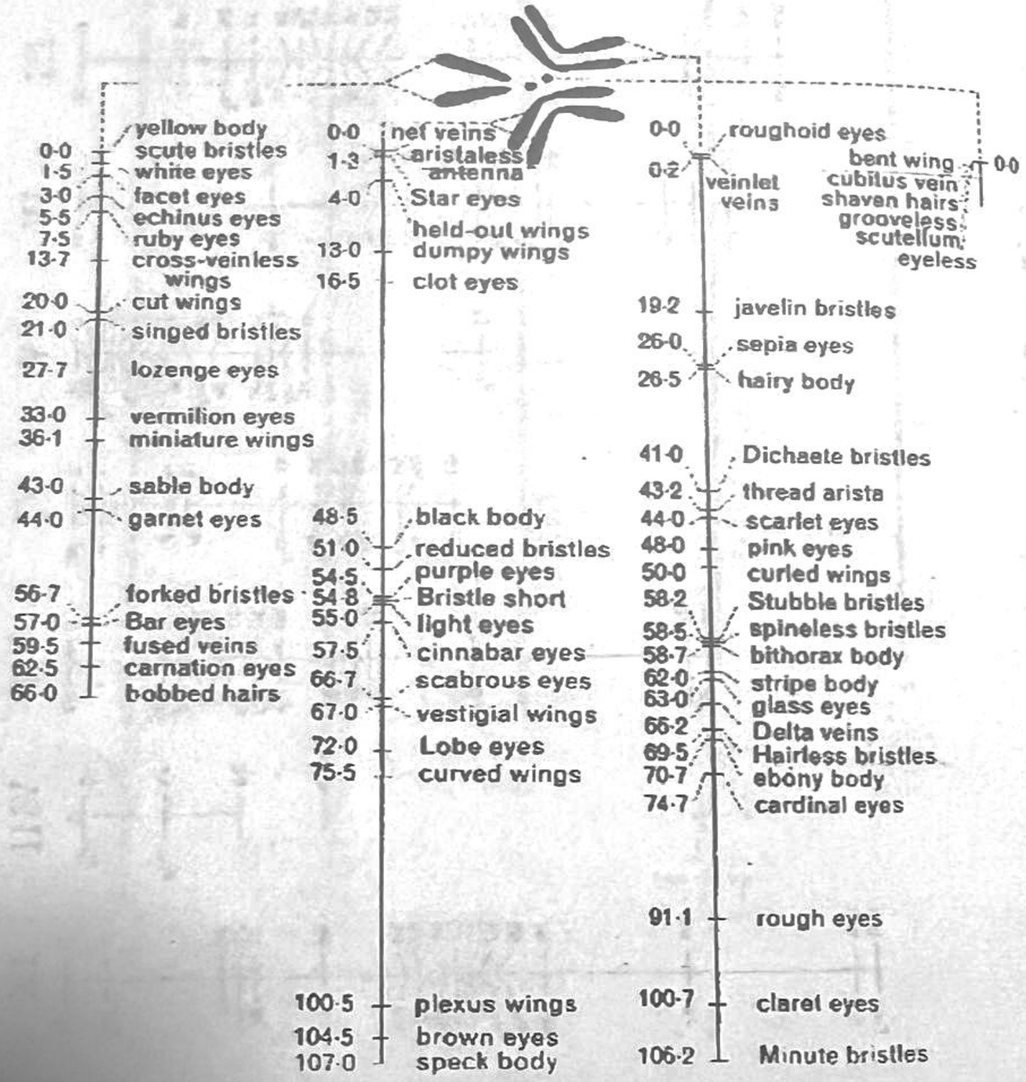
1. Show gene order and distances.
2. Help study linked traits.
3. Allow construction of linkage maps for many organisms, e.g., **Drosophila melanogaster**.

Steps to Make a Chromosomal Map

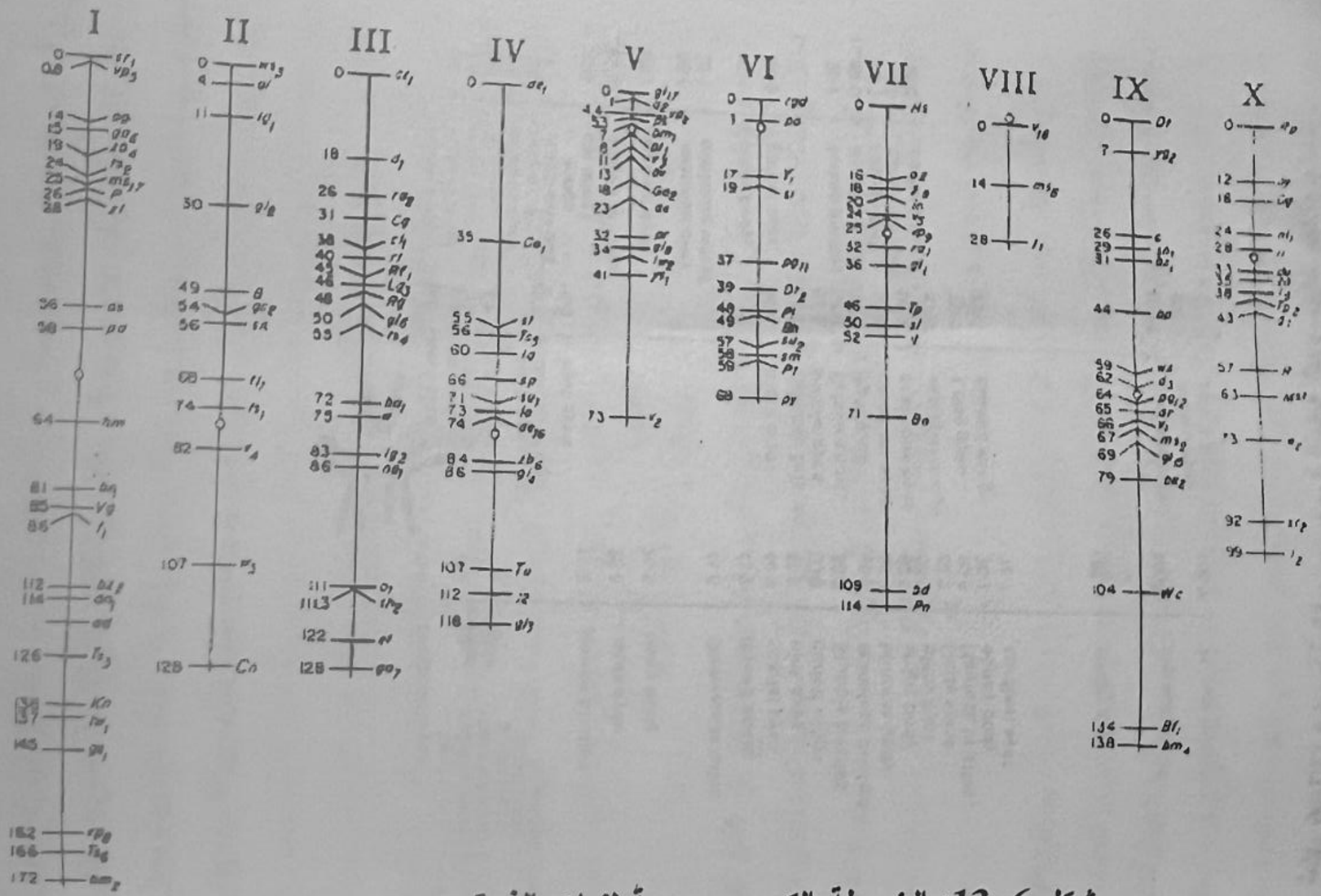
1. Perform test crosses.
2. Count **single and double crossovers**.
3. Identify middle gene based on lowest double-cross percentage.
4. Convert recombination percentages to **cM**.
5. Draw chromosome with gene positions.

Chromosomal Map Examples:

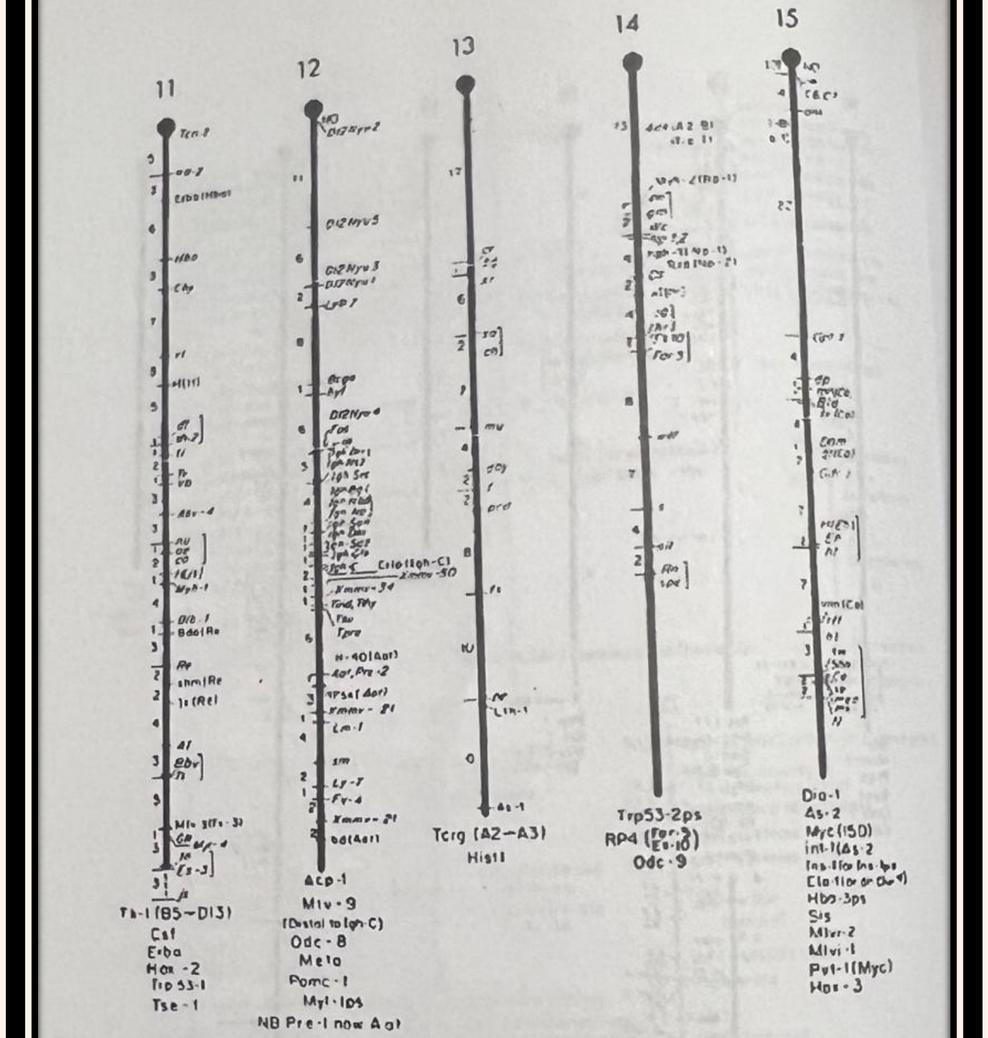
- **Drosophila melanogaster:** 4 chromosome pairs, hundreds of genes mapped.
- **Maize (Zea mays):** 10 chromosome pairs, gene mapping for kernel traits.
- **Mouse:** 20 chromosome pairs, used in molecular genetics studies.



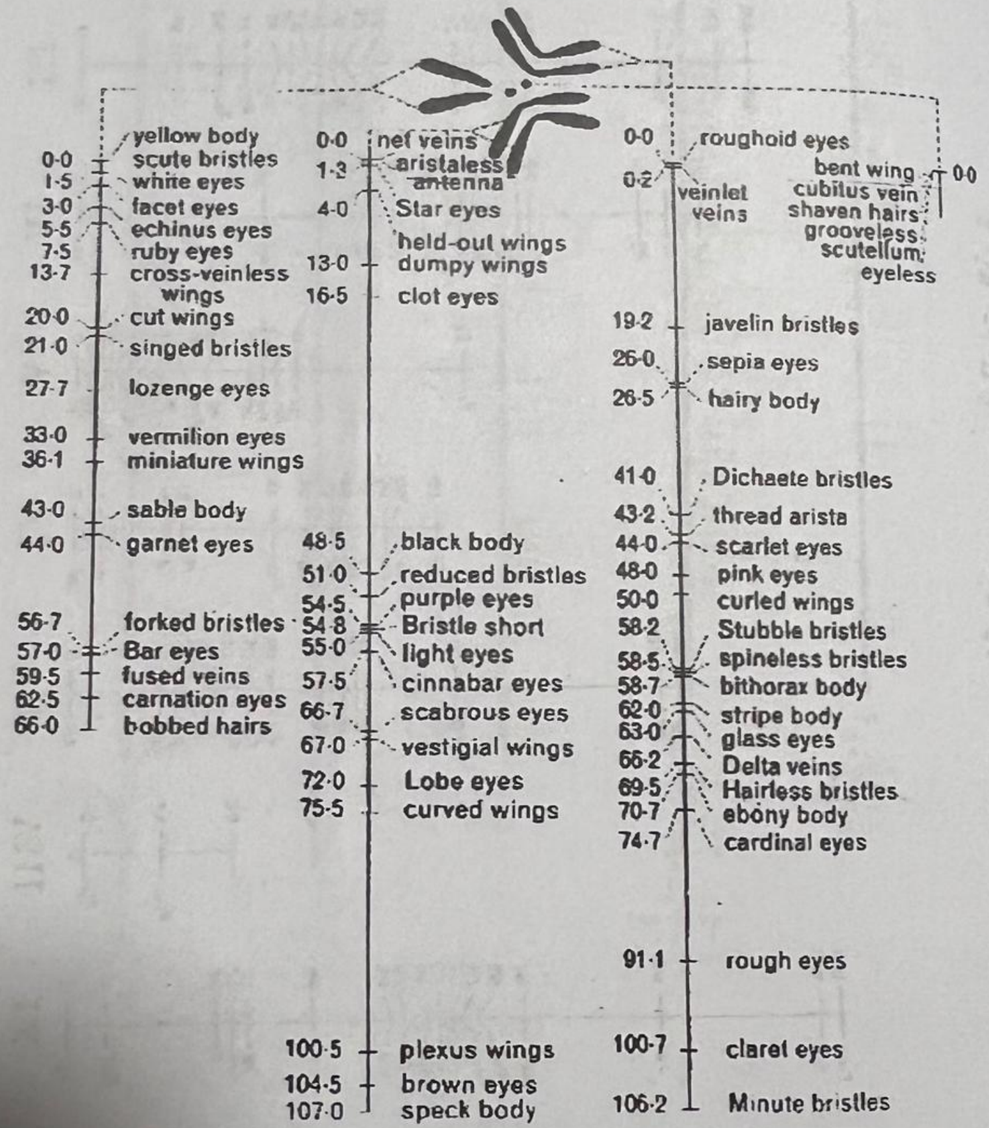
شكل 6-12: الخريطة الكروموسومية لذبابة الدروسوفلا ميلانوجاستر.



شكل 6-13: الخريطة الكروموسومية لنبات الذرة.



تابع شكل 6–14: الخريطة الكروموسومية للفأر.



شكل 6-12: الخريطة الكروموسومية لذبابة الدروسوفلا ميلانوجاستر.

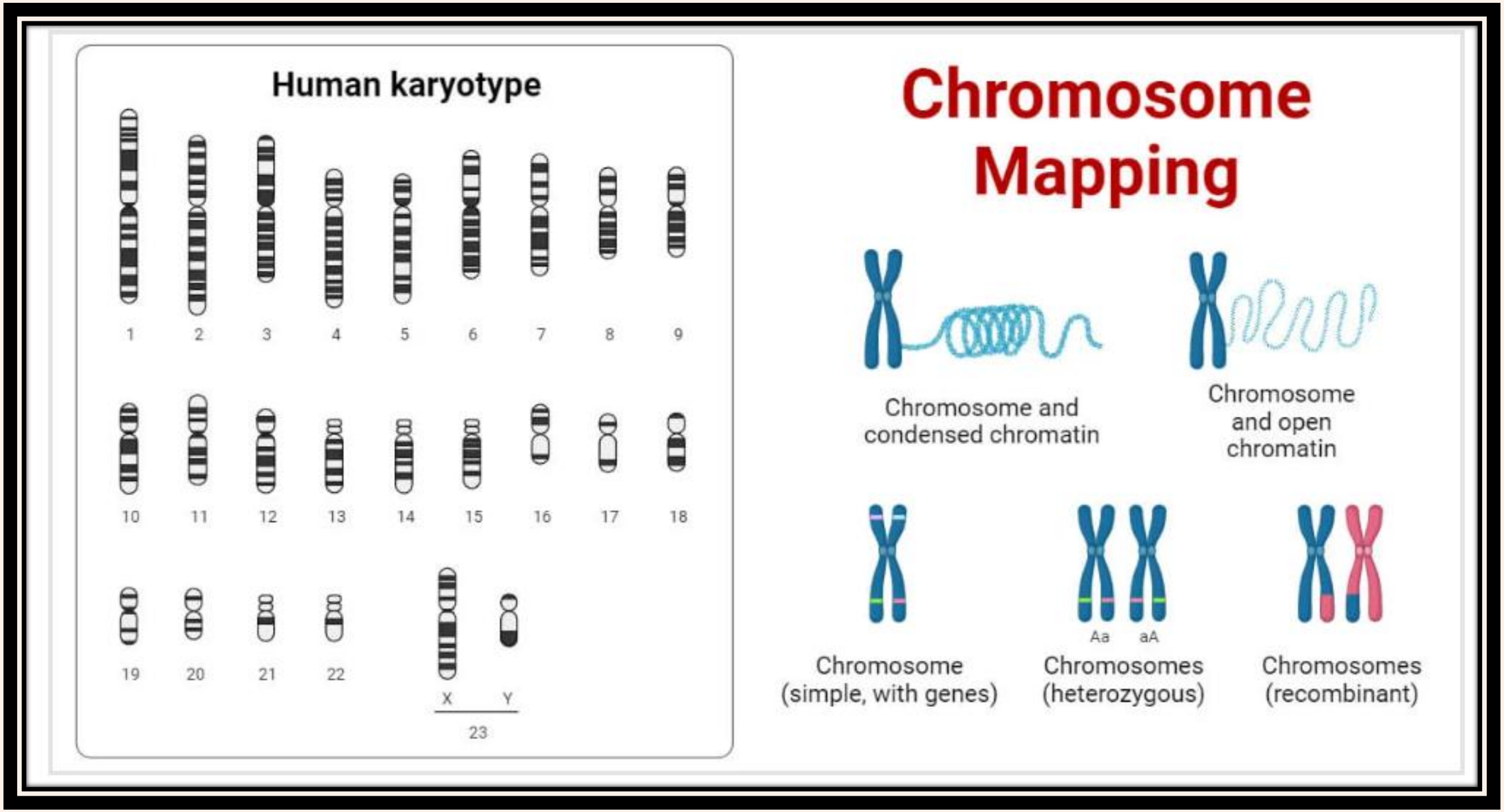


Fig. Chromosome Mapping

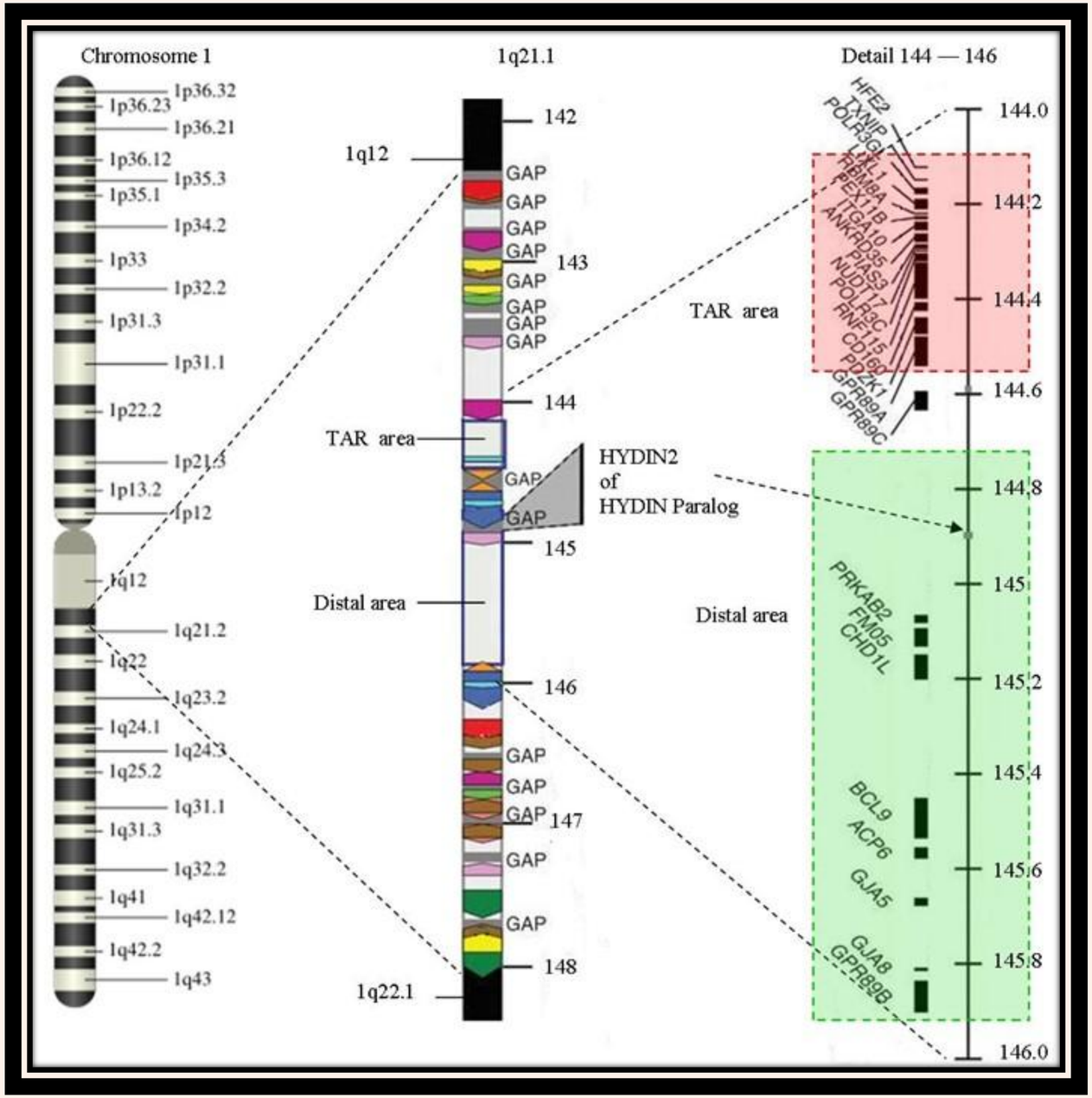


Fig A genetic map of human chromosome 1, with an enlarged section displaying the genes located within that region.

Importance of Chromosomal Maps:

1. Show gene order and distances.
2. Help study linked traits.
3. Allow construction of linkage maps for many organisms, e.g., **Drosophila melanogaster**.

- **Comprehensive chromosomal maps** play a vital role in:
  - Diagnosing **genetic disorders**
  - Developing **targeted therapies**
  - Enhancing **preventive medicine**

  (Miga and Sullivan, 2021)
- **Mapping methodologies** in mammalian cells help to:
  - Understand **nuclear organization**
  - Explore **regulation of gene expression**

  (Nastały and Maiuri, 2021)
- Despite major advances, **challenges remain** in:
  - Deciphering the **complexity of genome organization**
  - Understanding its effects on **evolutionary biology** and **medical science**

Factors Affecting Crossing Over:

1. Chromosomal Influence

•The rate of crossing over can be affected by the **relative length** of the chromosome.

•**Chromosomal abnormalities** may reduce crossing over between genes in the affected regions.

- **Inversions:** Crossing over decreases within inverted regions, inversely proportional to inversion length (shorter inversions cause greater reduction).
- **Duplications and translocations:** Also lower the frequency of crossing over.

2. Effect of Sex

- Crossing over **does not occur** in:
  - **Male Drosophila**
  - **Female silkworms**
  - **Wax moths**
- In some species, crossing over varies between sexes for autosomes.
  - Example: In the **grouse bird**, recombination rate between feather color genes was **24% in males** and **46% in females**.

3. Effect of Age

- Studies on *Drosophila melanogaster* show that crossing over **decreases with age**, especially near the **centromere**.
- In chickens, the **rate of crossing over increases with age**:
  - **1st year:** 21.9 ± 1.4%
  - **2nd year:** 36.9 ± 2.9%
  - **3rd year:** 47.6 ± 3.6%

4. Radiation

- **H. J. Muller (Nobel Prize, 1940)** found that **low doses of X-rays** increased crossing over near the **centromere** in *Drosophila melanogaster*.
- **Plough** also observed that **radium exposure** increased crossing over in the *b–pr–cn* region on the second chromosome.

5. Temperature

- Several researchers (Plough, 1917–1935; Stern, 1926; Grubard, 1932) confirmed that **temperature significantly influences recombination**.
- Crossing over **increases or decreases** when temperature deviates from the **optimal range (20–22°C)**.
- The **regions near the centromere** are most affected.
- Example (*Drosophila* chromosome II):
  - **14°C:** 9.8%
  - **22°C:** 10.9%
  - **30°C:** 11.8%

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THANK YOU