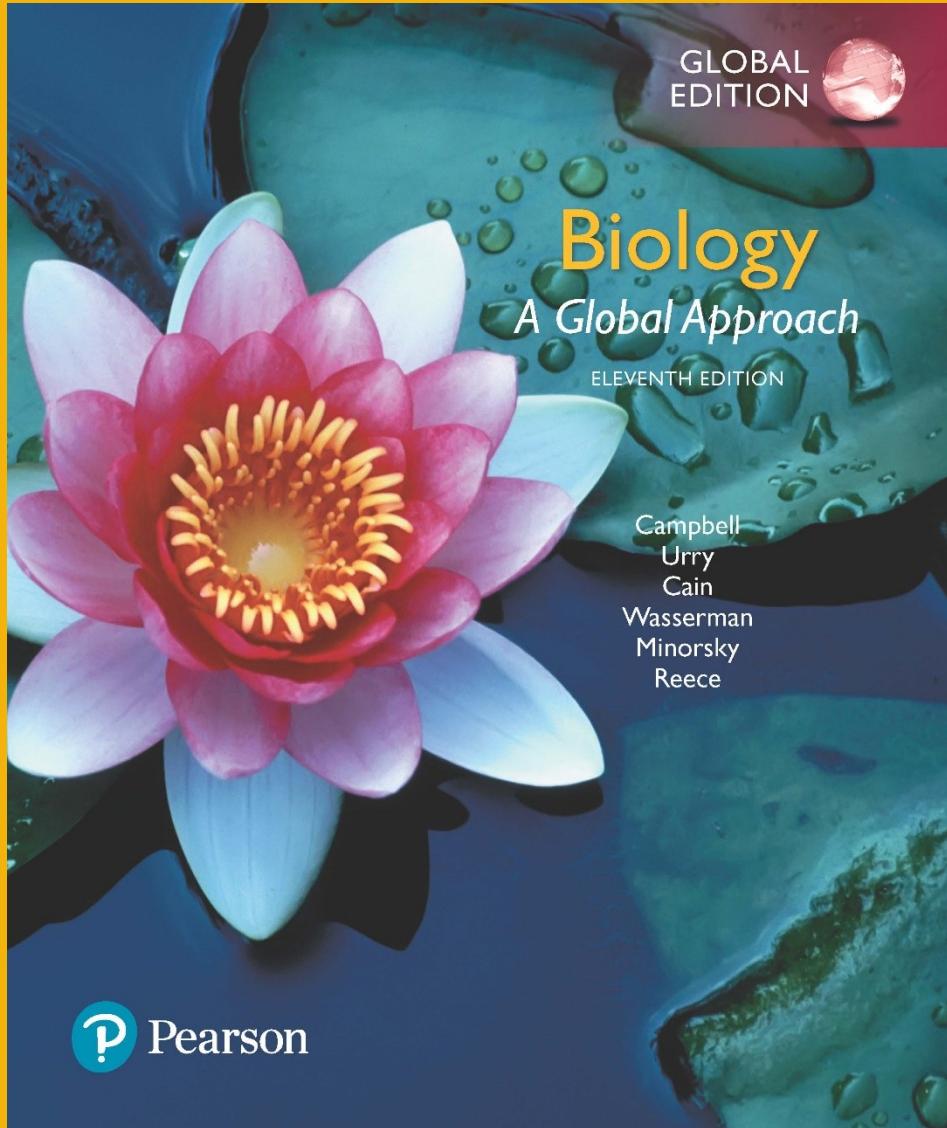


RECAP from Biology 4



Chapter 14

Mendelian Genetics

Lecture Presentations by
Nicole Tunbridge and
Kathleen Fitzpatrick

Figure 13.8

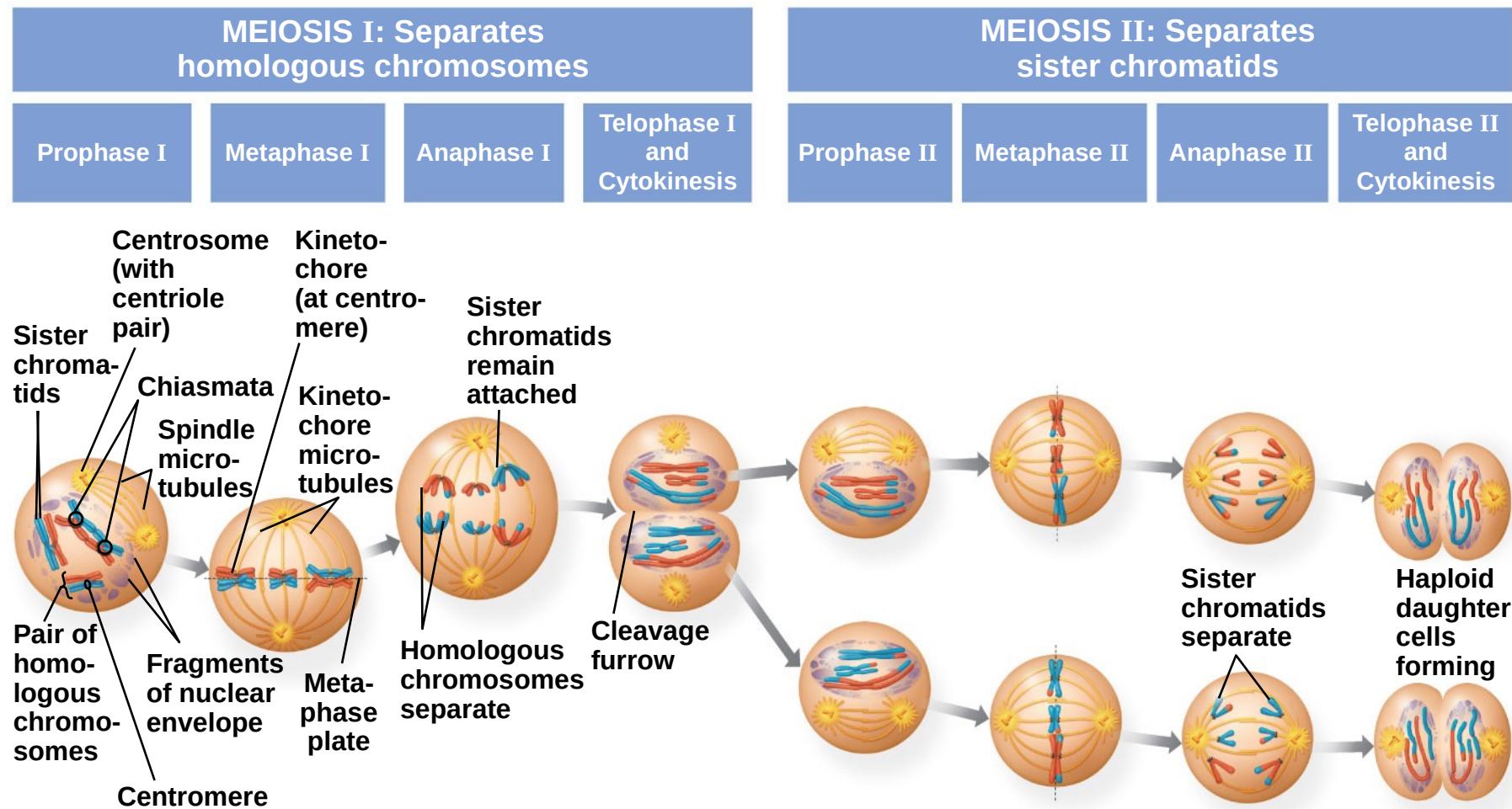


Figure 13.7

Prophase I of meiosis

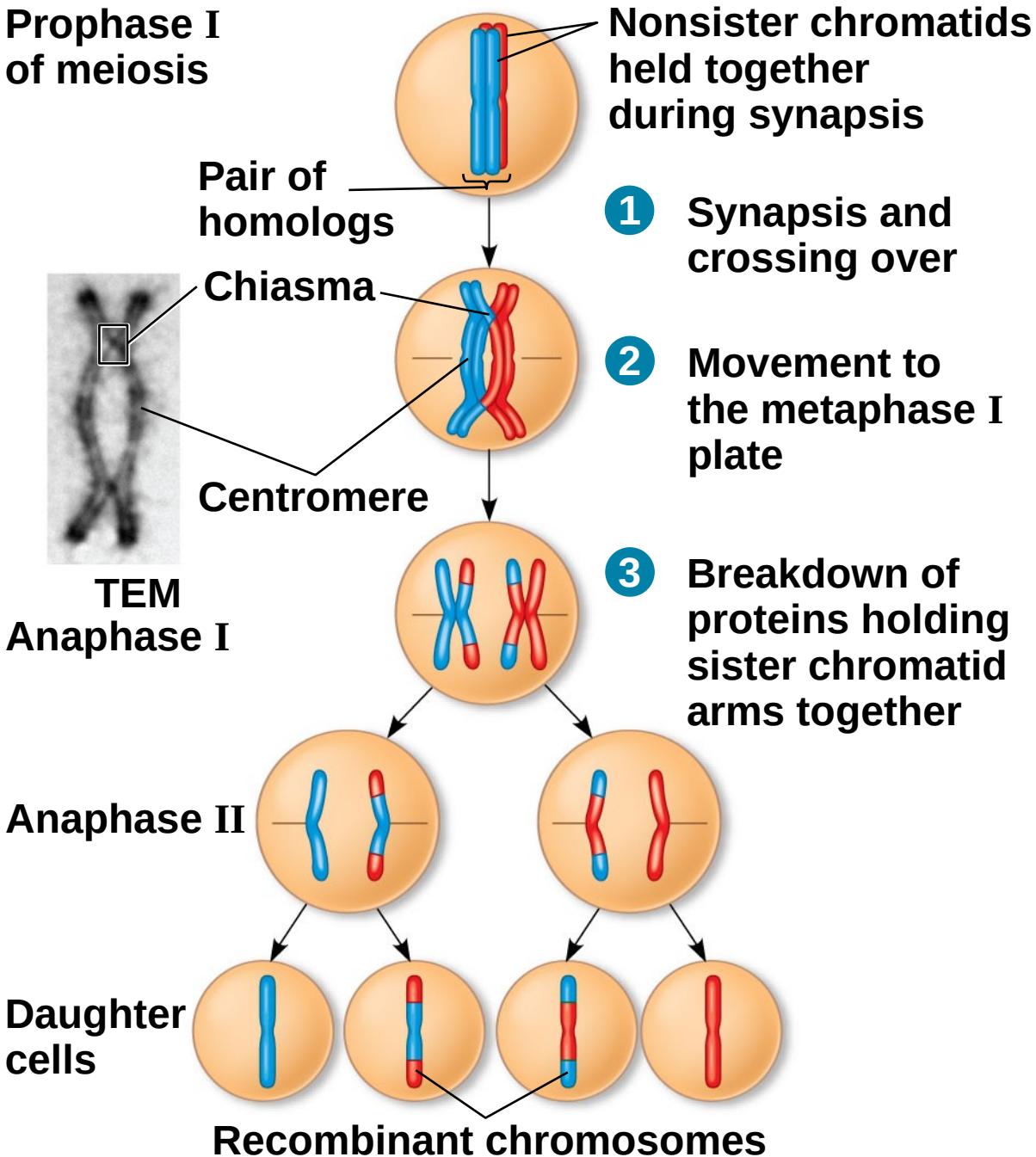
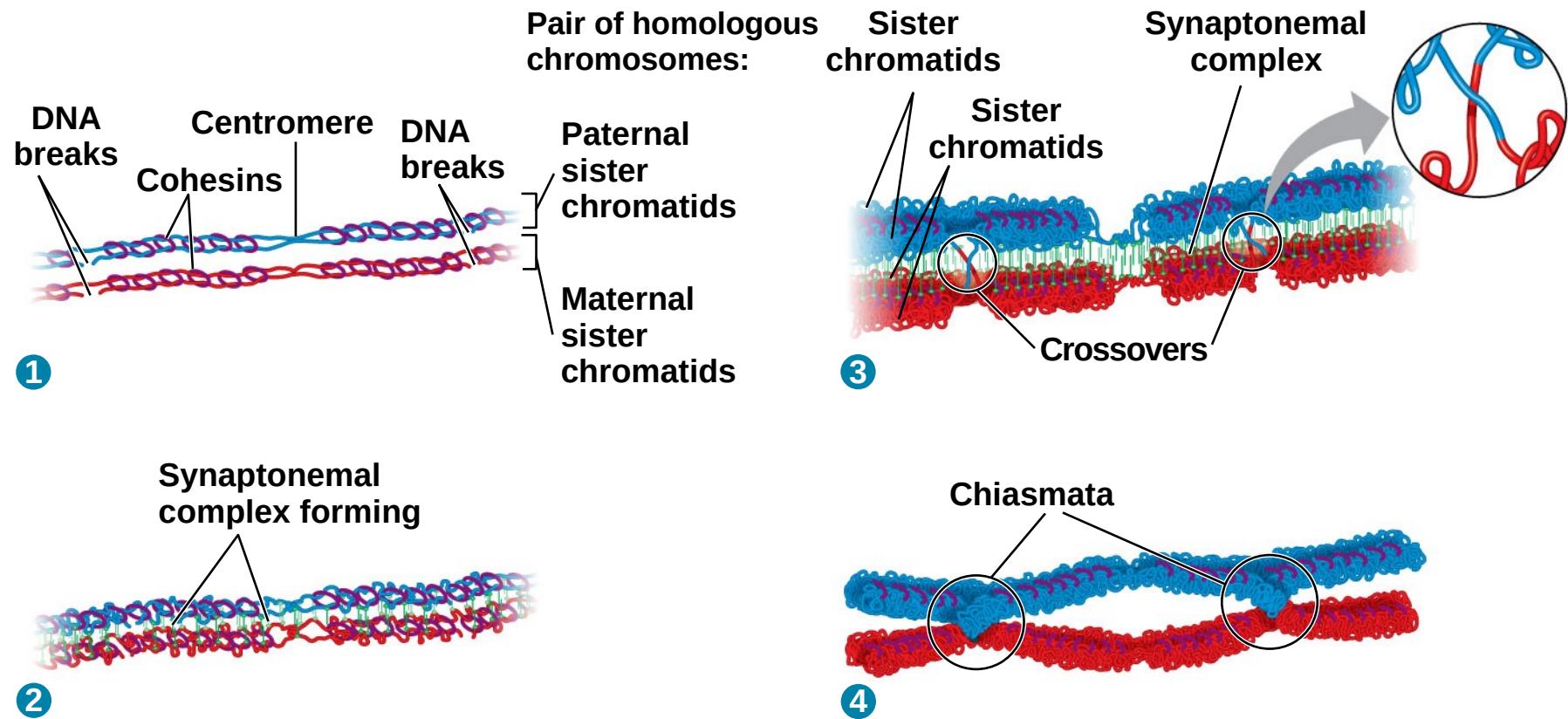
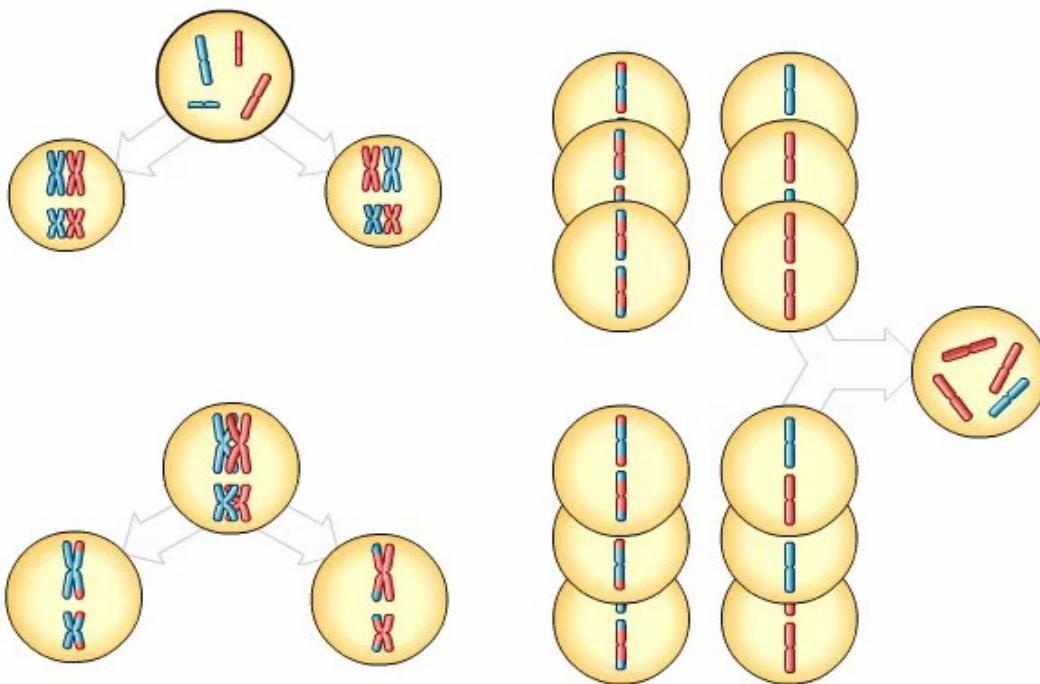


Figure 13.9





Mendel's laws

Mendel's laws

- **Law of Segregation of genes (the "First Law")**
 - During gamete formation, the alleles for each gene segregate from each other so that each gamete carries only one allele for each gene.
- **Law of Independent Assortment (the "Second Law")**
 - Genes for different traits can segregate independently during the formation of gametes.
- **Law of Dominance (the "Third Law")**
 - Some alleles are dominant while others are recessive; an organism with at least one dominant allele will display the effect of the dominant allele

An **allele** is a variant form of a given gene

GLOBAL
EDITION



Concepts of Genetics

ELEVENTH EDITION

William S. Klug • Michael R. Cummings
Charlotte A. Spencer • Michael A. Palladino



ALWAYS LEARNING

PEARSON

Chapter

5



Chromosome Mapping in Eukaryotes

*Lecture Presentation by
Dr. Cindy Malone,
California State University Northridge*

Chapter 5 Contents

- 5.1 Genes Linked on the Same Chromosome Segregate Together
 - 5.2 Crossing Over Serves as the Basis of Determining the Distance between Genes in Chromosome Mapping
 - 5.3 Determining the Gene Sequence during Mapping Requires the Analysis of Multiple Crossovers
 - 5.4 As the Distance between Two Genes Increases, the Results of Mapping Experiments Become Less Accurate
 - 5.5 *Drosophila* Genes Have Been Extensively Mapped
Continued
-

Chapter 5 Contents

- 5.6 Lod Score Analysis and Somatic Cell Hybridization Were Historically Important in Creating Human Chromosome Maps
 - 5.7 Chromosome Mapping Is Now Possible Using DNA Markers and Annotated Computer Databases
 - 5.8 Crossing Over Involves a Physical Exchange between Chromatids During Mitosis
 - 5.9 Exchanges Also Occur between Sister Chromatids
 - 5.10 Did Mendel Encounter Linkage?
-

Linkage, Crossing Over, and Mapping

- Chromosomes are the unit of transmission in meiosis, not genes
 - **Linked genes** can not undergo independent assortment
 - Frequency of **crossing over** on a single chromosome is proportional to distance between them
 - Crossing over results in **recombination**
 - **Chromosome maps:** Indicate relative location of genes on chromosome
-

5.1 Genes Linked on the Same Chromosome Segregate Together

Section 5.1: Meiotic Consequences

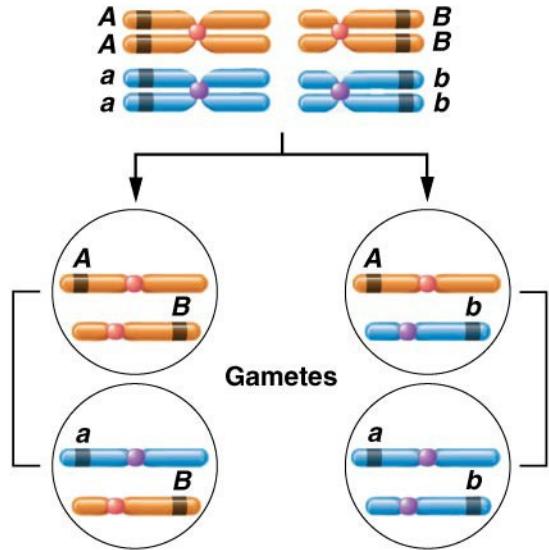
- **Meiotic consequences**
 - Independent assortment
 - No linkage exhibited
 - Linkage without crossing over
 - **Complete linkage**
 - Linkage with crossing over
 - Generates recombinant (crossover) gametes

Section 5.1: Complete Linkage and Crossing Over

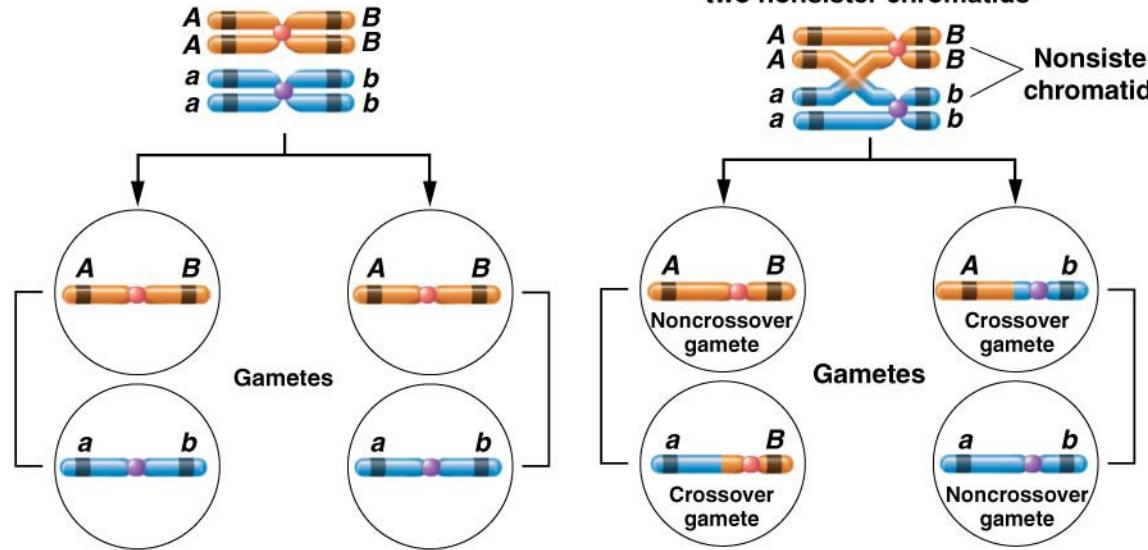
- **Complete linkage**
 - No crossing over between two genes
 - Produces **parental** (non-crossover) gametes

- **Crossing over**
 - Occurs between two nonsister chromatids
 - Both parental and recombinant (crossover) gametes are produced (**Figure 5-1**)

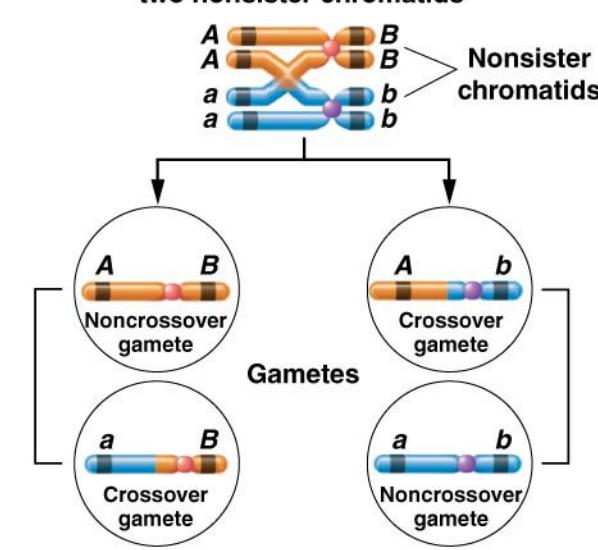
(a) Independent assortment: Two genes on two different homologous pairs of chromosomes



(b) Linkage: Two genes on a single pair of homologous chromosomes; no exchange occurs



(c) Linkage: Two genes on a single pair of homologous chromosomes; exchange occurs between two nonsister chromatids



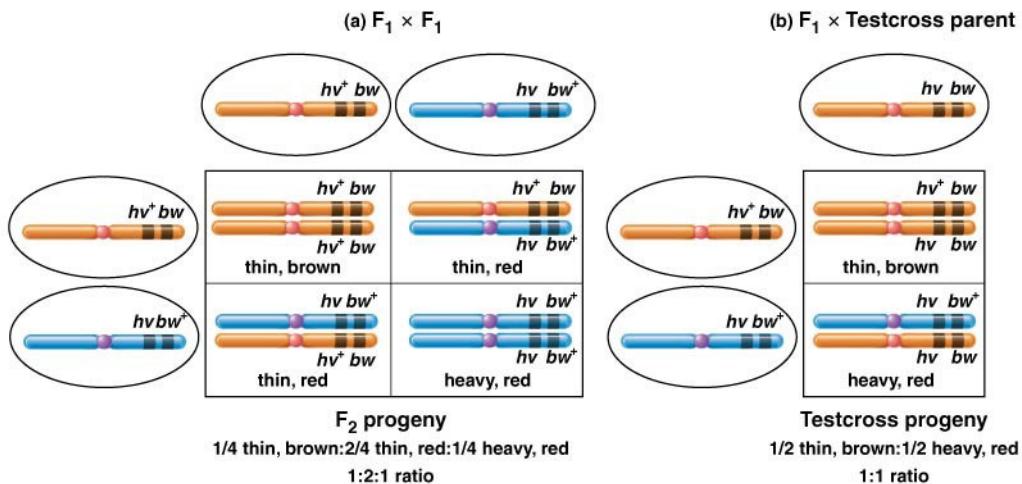
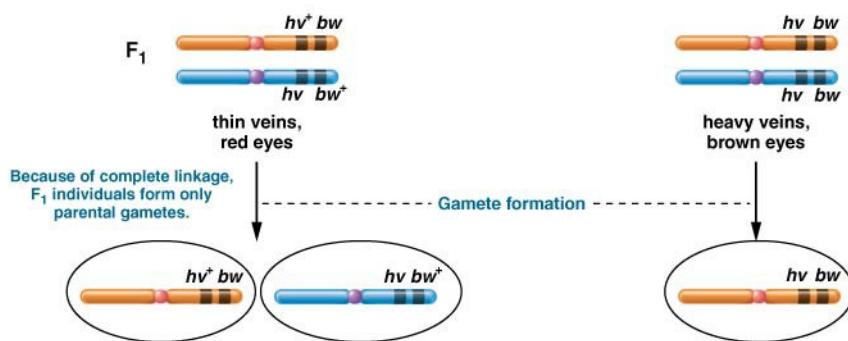
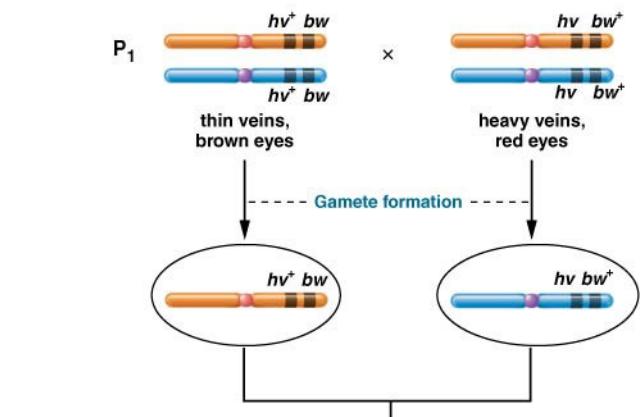
Results of gamete formation when two heterozygous genes are:

- A: on two different pairs of chromosomes
- B: on the same pair of homologous (no exchange)
- C: on the same pair of homologous (exchange)

Section 5.1: Linkage Ratio and Groups

- **Linkage ratio**
 - Complete linkage between two genes due to close proximity
 - Unique F_2 phenotypic ratio results (**Figure 5-2**)
- **Linkage group**
 - Genes on the same chromosome are part of a **linkage group**
 - Number of linkage groups should correspond to haploid number of chromosomes

Results of a cross involving two genes located On the same chromosome and demonstrating complete linkage



5.2 Crossing Over Serves as the Basis of Determining the Distance between Genes in Chromosome Mapping

Section 5.2: Crossing Over and Chiasmata

- **Chiasmata**

- Synapsed chromosomes in meiosis wrap around each other
- X-shaped intersections with points of overlap
 - Points of genetic exchange

Section 5.2: Chiasma

- Percentage of offspring resulting from recombinant gametes depends on distance between two genes on same chromosome
- Two genes located close to each other along a chromosome are less likely to have **chiasma**

Section 5.2: Sturtevant and Mapping

- Sturtevant
 - Compiled data from crosses
 - Recombination frequencies between linked genes are **additive**
 - Frequency of exchange is estimate of relative distance between two genes

Cross data compiled by Sturtevant, demonstrating recombinant phenotypes, which are either miniature(m) or white (w) mutant

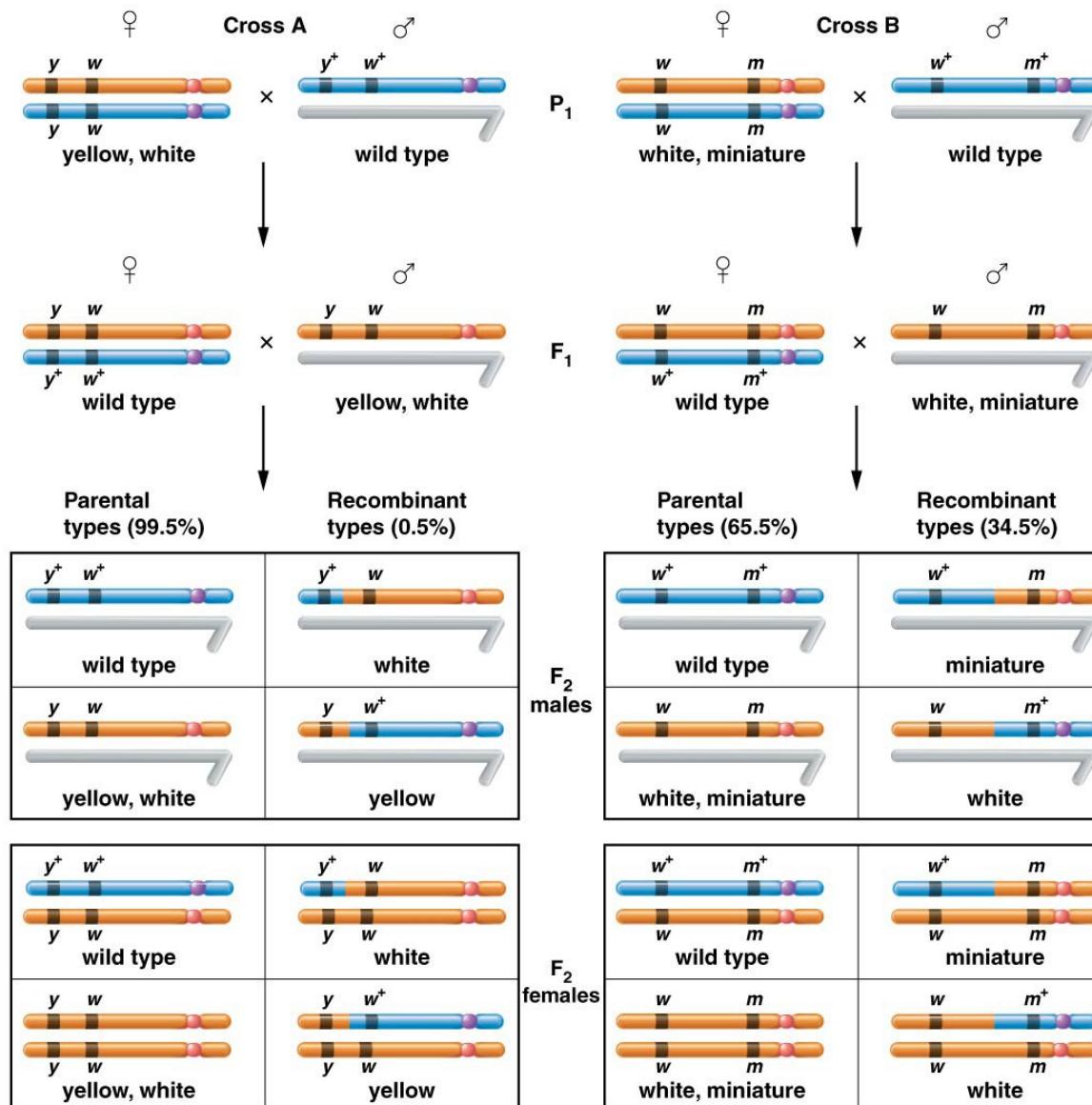
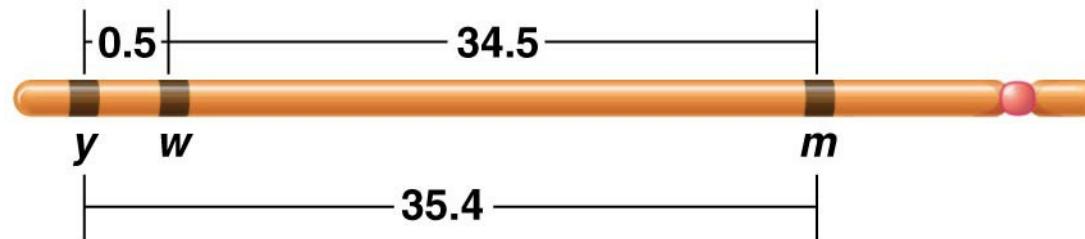


Figure 5-3

Section 5.2: Map Units

- **Map unit (mu)**

- 1 percent recombination between two genes on chromosome
- Also called **centimorgans (cM)**
- Relative distances, not exact ones



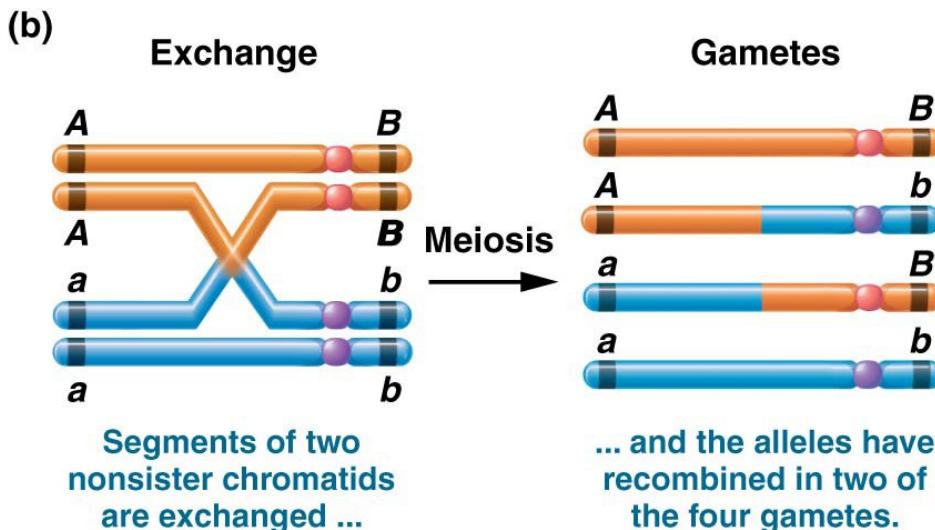
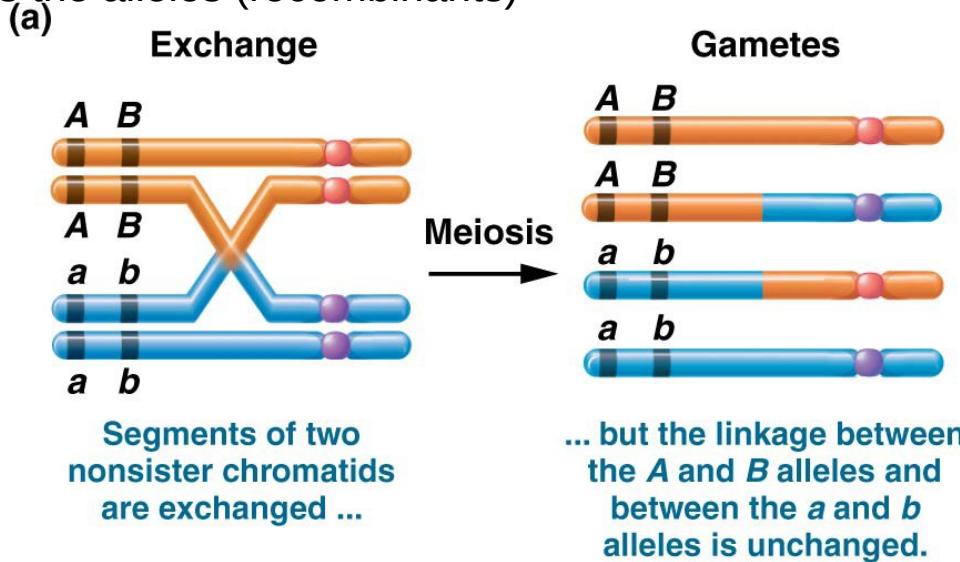
Section 5.2: Single Crossovers

- **Single crossover (SCO)**
 - Occurs between two nonsister chromatids
 - Recombination is observed in 50% of gametes
 - In genes 50 map units apart, crossing over can be expected between 100% of tetrads

Two examples of single crossover between two non-sister chromatids and the gametes subsequently produced

A: exchange does not alter the linker arrangement (parental gametes only)

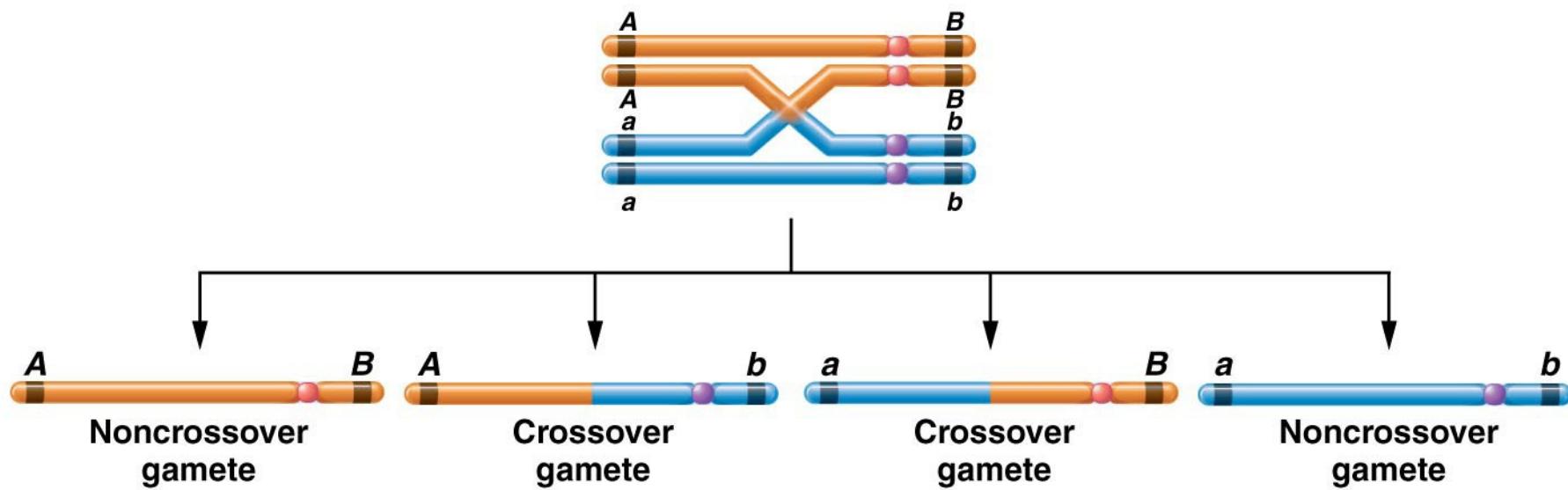
B: the exchange separates the alleles (recombinants)



Section 5.2: Single Crossovers

- Single exchange between two nonsister chromatids in tetrad stage
 - Two noncrossover (parental) gametes produced
 - Two crossover (recombinant) gametes produced
- **Figure 5-6**

The consequences of a single exchange between two non-sister chromatids occurring in the tetrad stage. Two non-crossover (parental) and two crossovers (recombinant) gametes are produced



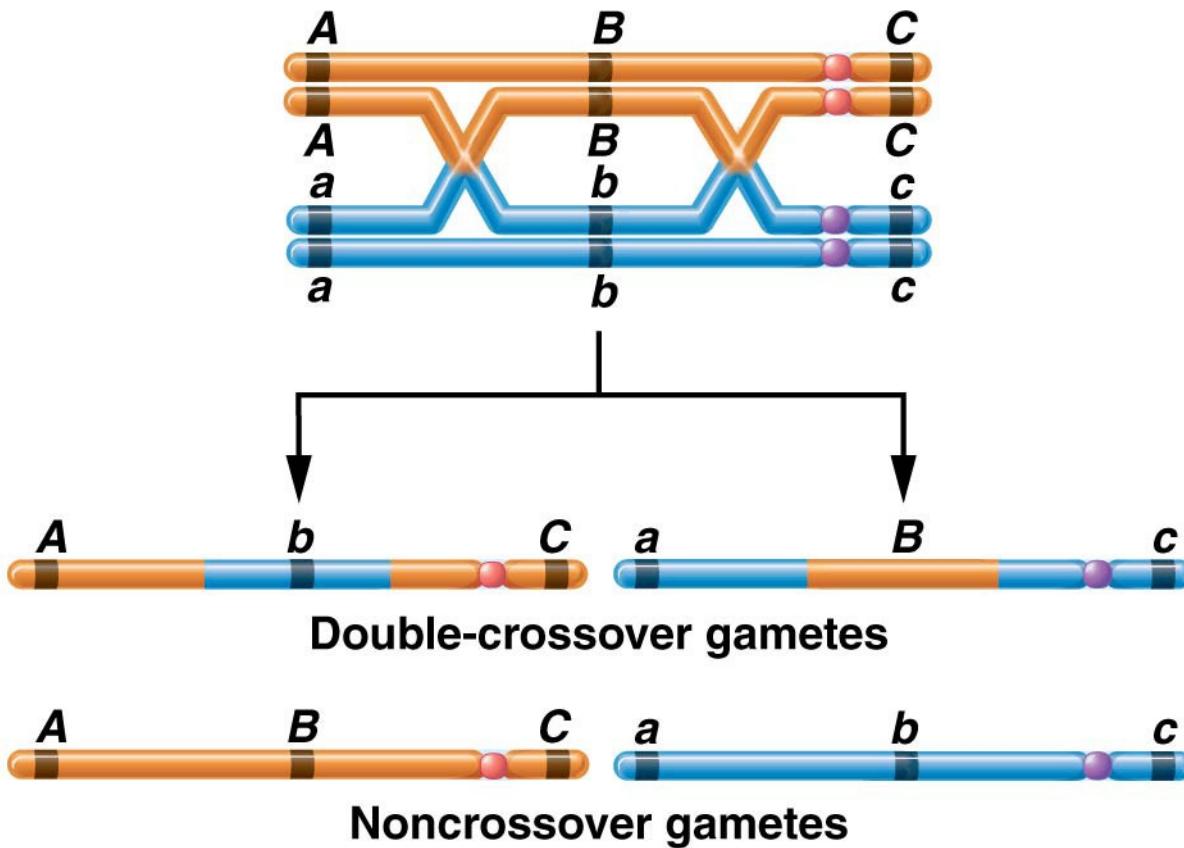
5.3 Determining the Gene Sequence during Mapping Requires the Analysis of Multiple Crossovers

Section 5.3: Multiple Exchanges

- **Single crossover**
 - Used to determine distance between two linked genes

- **Double crossover**
 - Double exchanges of genetic material
 - Used to determine distance between three linked genes
 - Genes must be heterozygous for two alleles

Consequences of a double exchange occurring between two non-sister chromatids.

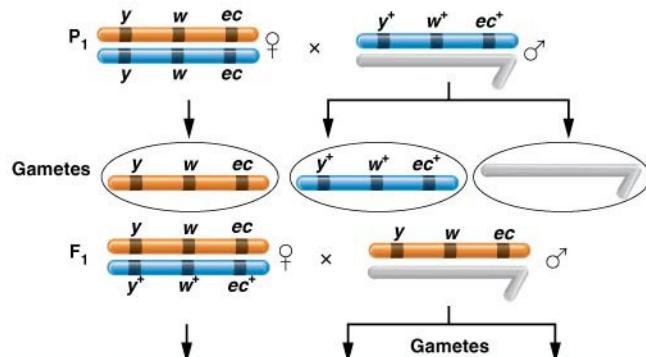


Section 5.3: Frequencies

- Expected frequency of double-crossover gametes is lower than that of either single-crossover gamete class and if three genes are close together along one chromosome

Section 5.3: Three-Point Mapping

- **Three criteria of three-point mapping**
 - Parent must be heterozygous for all three genes under consideration
 - Phenotypic class must reflect genotype of gametes of parents
 - Sufficient number of offspring must be produced for representative sample
- **Figure 5-8**



A three-point mapping cross involving the yellow (*y*), white (*w*) and echinus (*ec*) genes in fruit flies

Origin of female gametes	Gametes	<i>y</i> <i>w</i> <i>ec</i>	<i>y</i> <i>w</i> <i>ec</i>	F ₂ phenotype	Observed number	Category, total, and percentage
NCO <i>y</i> <i>w</i> <i>ec</i> <i>y⁺</i> <i>w⁺</i> <i>ec⁺</i>	① <i>y</i> <i>w</i> <i>ec</i>	<i>y</i> <i>w</i> <i>ec</i>	<i>y</i> <i>w</i> <i>ec</i>	<i>y</i> <i>w</i> <i>ec</i>	4685	Non-crossover
	② <i>y⁺</i> <i>w⁺</i> <i>ec⁺</i>	<i>y⁺</i> <i>w⁺</i> <i>ec⁺</i>	<i>y</i> <i>w</i> <i>ec</i>	<i>y⁺</i> <i>w⁺</i> <i>ec⁺</i>	4759	9444 94.44%
SCO <i>y</i> <i>w</i> <i>ec</i> <i>y⁺</i> <i>w⁺</i> <i>ec⁺</i>	③ <i>y</i> <i>w⁺</i> <i>ec⁺</i>	<i>y</i> <i>w⁺</i> <i>ec⁺</i>	<i>y</i> <i>w⁺</i> <i>ec⁺</i>	<i>y</i> <i>w⁺</i> <i>ec⁺</i>	80	Single crossover between <i>y</i> and <i>w</i>
	④ <i>y⁺</i> <i>w</i> <i>ec</i>	<i>y⁺</i> <i>w</i> <i>ec</i>	<i>y</i> <i>w</i> <i>ec</i>	<i>y⁺</i> <i>w</i> <i>ec</i>	70	150 1.50%
SCO <i>y</i> <i>w</i> <i>ec</i> <i>y⁺</i> <i>w⁺</i> <i>ec⁺</i>	⑤ <i>y</i> <i>w</i> <i>ec⁺</i>	<i>y</i> <i>w</i> <i>ec⁺</i>	<i>y</i> <i>w</i> <i>ec⁺</i>	<i>y</i> <i>w</i> <i>ec⁺</i>	193	Single crossover between <i>w</i> and <i>ec</i>
	⑥ <i>y⁺</i> <i>w⁺</i> <i>ec</i>	<i>y⁺</i> <i>w⁺</i> <i>ec</i>	<i>y⁺</i> <i>w⁺</i> <i>ec</i>	<i>y⁺</i> <i>w⁺</i> <i>ec</i>	207	400 4.00%
DCO <i>y</i> <i>w</i> <i>ec</i> <i>y⁺</i> <i>w⁺</i> <i>ec⁺</i>	⑦ <i>y</i> <i>w⁺</i> <i>ec</i>	<i>y</i> <i>w⁺</i> <i>ec</i>	<i>y</i> <i>w⁺</i> <i>ec</i>	<i>y</i> <i>w⁺</i> <i>ec</i>	3	Double crossover between <i>y</i> and <i>w</i> and between <i>w</i> and <i>ec</i>
	⑧ <i>y⁺</i> <i>w</i> <i>ec⁺</i>	<i>y⁺</i> <i>w</i> <i>ec⁺</i>	<i>y⁺</i> <i>w</i> <i>ec⁺</i>	<i>y⁺</i> <i>w</i> <i>ec⁺</i>	3	6 0.06%
<p>Map of <i>y</i>, <i>w</i>, and <i>ec</i> loci</p> <p>Distance: <i>y</i> to <i>w</i> = 1.56, <i>w</i> to <i>ec</i> = 4.06</p>						

Section 5.3: Noncrossover

- **Noncrossover F_2 phenotypes**
 - Occur in greatest proportion of offspring

- **Double-crossover (DCO) phenotypes**
 - Occur in the smallest proportion

Section 5.3: Reciprocal Classes

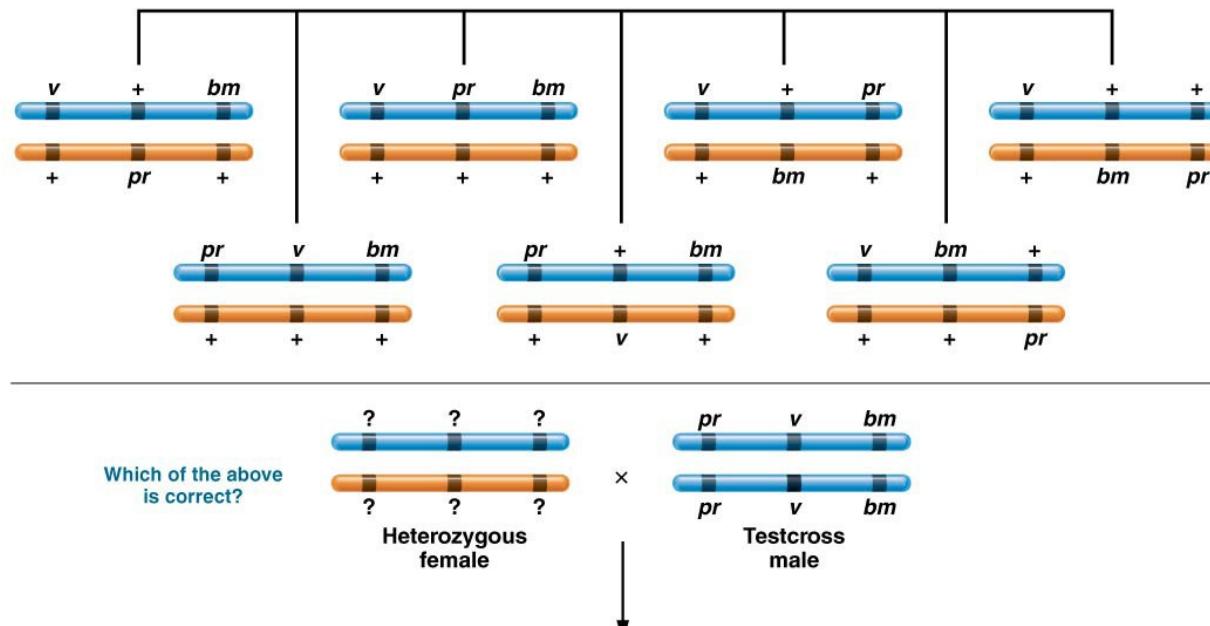
- **Reciprocal classes of phenotypes**
 - F_2 phenotypes complement each other
 - Derived from heterozygote
 - Have wild type and mutant for all three genes

Section 5.3: Determining Gene Sequence

- **Determining gene sequence:**
 - **Method 1** based on three possible arrangements of genes
 - **Method 2** uses three possible arrangements
 - Also considers double-crossover event
- **Figure 5-10 and Figure 5-11**

A: Some possible alleles arrangements and gene sequences in a heterozygotes female.
B: The data form a three-point mapping cross, where the female is testcrossed, provide the basis for determining which combination of arrangement and sequence is correct

(a) Some possible allele arrangements and gene sequences in a heterozygous female



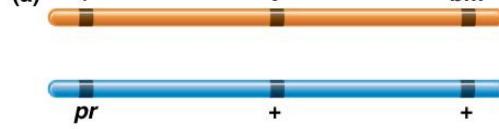
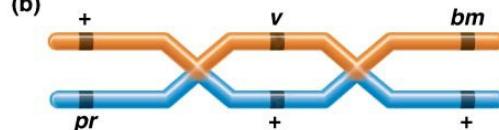
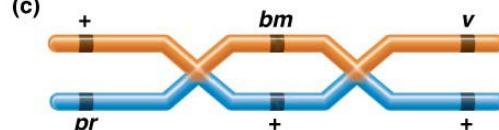
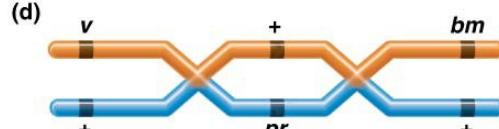
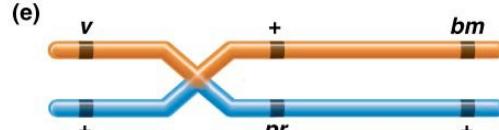
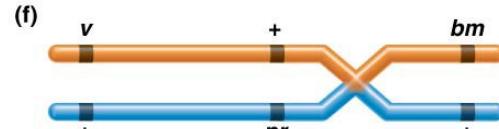
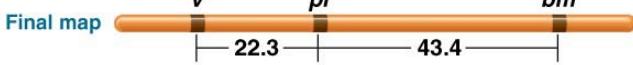
(b) Actual results of mapping cross*

Phenotypes of offspring	Number	Total and percentage	Exchange classification
<i>+</i> <i>v</i> <i>bm</i>	230	467 42.1%	Noncrossover (NCO)
<i>pr</i> <i>+</i> <i>+</i>	237		
<i>+</i> <i>+</i> <i>bm</i>	82	161 14.5%	Single crossover (SCO)
<i>pr</i> <i>v</i> <i>+</i>	79		
<i>+</i> <i>v</i> <i>+</i>	200	395 35.6%	Single crossover (SCO)
<i>pr</i> <i>+</i> <i>bm</i>	195		
<i>pr</i> <i>v</i> <i>bm</i>	44	86 7.8%	Double crossover (DCO)
<i>+</i> <i>+</i> <i>+</i>	42		

* The sequence *pr* – *v* – *bm* may or may not be correct.

Figure 5-10

Producing a map of the three genes in the cross in Figure 5-10, where neither the arrangement of alleles nor the sequence of genes in the heterozygous females parent is known

Possible allele arrangements and sequences	Testcross phenotypes	Explanation
(a) 	+ v bm and pr + +	Noncrossover phenotypes provide the basis for determining the correct arrangement of alleles on homologs
(b) 	+ + bm and pr v +	Expected double-crossover phenotypes if v is in the middle
(c) 	+ + v and pr bm +	Expected double-crossover phenotypes if bm is in the middle
(d) 	v pr bm and + + +	Expected double-crossover phenotypes if pr is in the middle <i>(This is the actual situation.)</i>
(e) 	v pr + and + + bm	Given that (a) and (d) are correct, single-crossover phenotypes when exchange occurs between v and pr
(f) 	v + + and + pr bm	Given that (a) and (d) are correct, single-crossover phenotypes when exchange occurs between pr and bm
(g)	Final map 	

5.4 As the Distance between Two Genes Increases, Mapping Estimates Become More Inaccurate

Section 5.4: Map Distance

- Expected frequency of multiple exchanges between two genes predicted from distance between them
- Genes farther apart increase the probability of undetected crossovers

Section 5.4: Interference (I)

- **Interference**
 - Inhibition of further crossover events
 - Inhibited by another crossover event nearby
 - Reduces expected number of multiple crossovers

Section 5.4: Coefficient of Coincidence

- Calculated to quantify disparities that result from interference

- **Coefficient of coincidence (C)**

$$C \propto \frac{\text{Observed DCO}}{\text{Expected DCO}}$$

- Interference:

$$I \propto 1 \} C$$

-
- How to calculate Expected DCO
 - The expected DCO is calculated using the mapping distances.
 - Expl map: $v -- 22.3 -- pr -- 43.4 -- bm$
 - Expected DCO = $22.3 * 43.3 = 9.7\%$

Section 5.4: Positive and Negative Interference

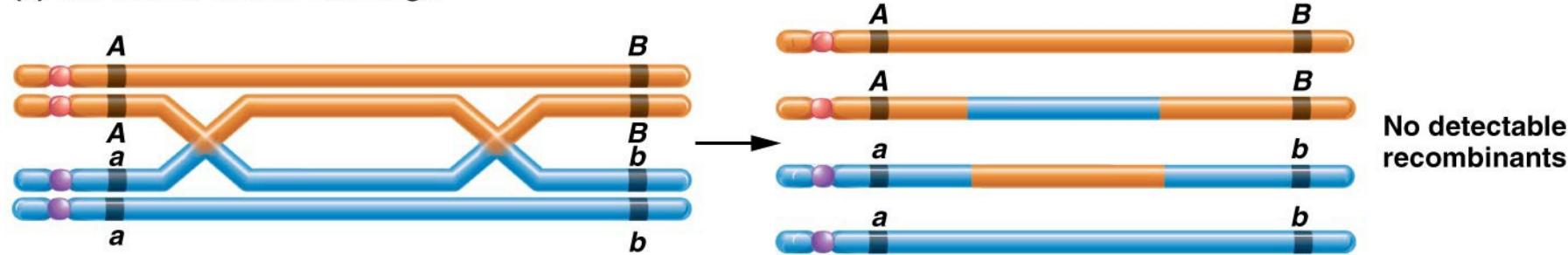
- **Interference**
 - **Complete** when no double crossovers occur
 - **Positive**: Fewer double-crossover events than expected occur
 - I is a positive number
 - **Negative**: More double-crossover events than expected occur
 - I is a negative number

Section 5.4: Figure 5-12

- Two genes close together
 - Positive interference occurs
 - Accuracy of mapping is high
- Distance between genes increases
 - Interference decreases
 - Accuracy of mapping decreases (**Figure 5-12**)

- A: a double crossover is undetected because no rearrangements of the alleles occurs
 B: The theoretical and actual percentage of recombinant chromatids versus map distance

(a) Two-strand double exchange



(b)

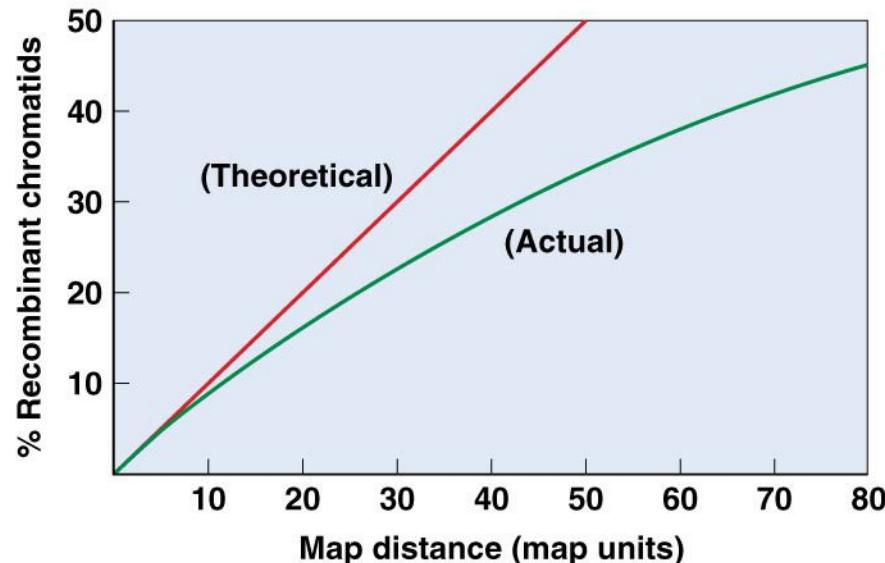


Figure 5-12

5.5 *Drosophila* Genes Have Been Extensively Mapped

Section 5.5: Map Constructs

- Large number of mutants in organisms such as
 - *Drosophila*
 - Maize
 - Mice
- Allows for construction of extensive chromosome mapping
- **Figure 5-13**

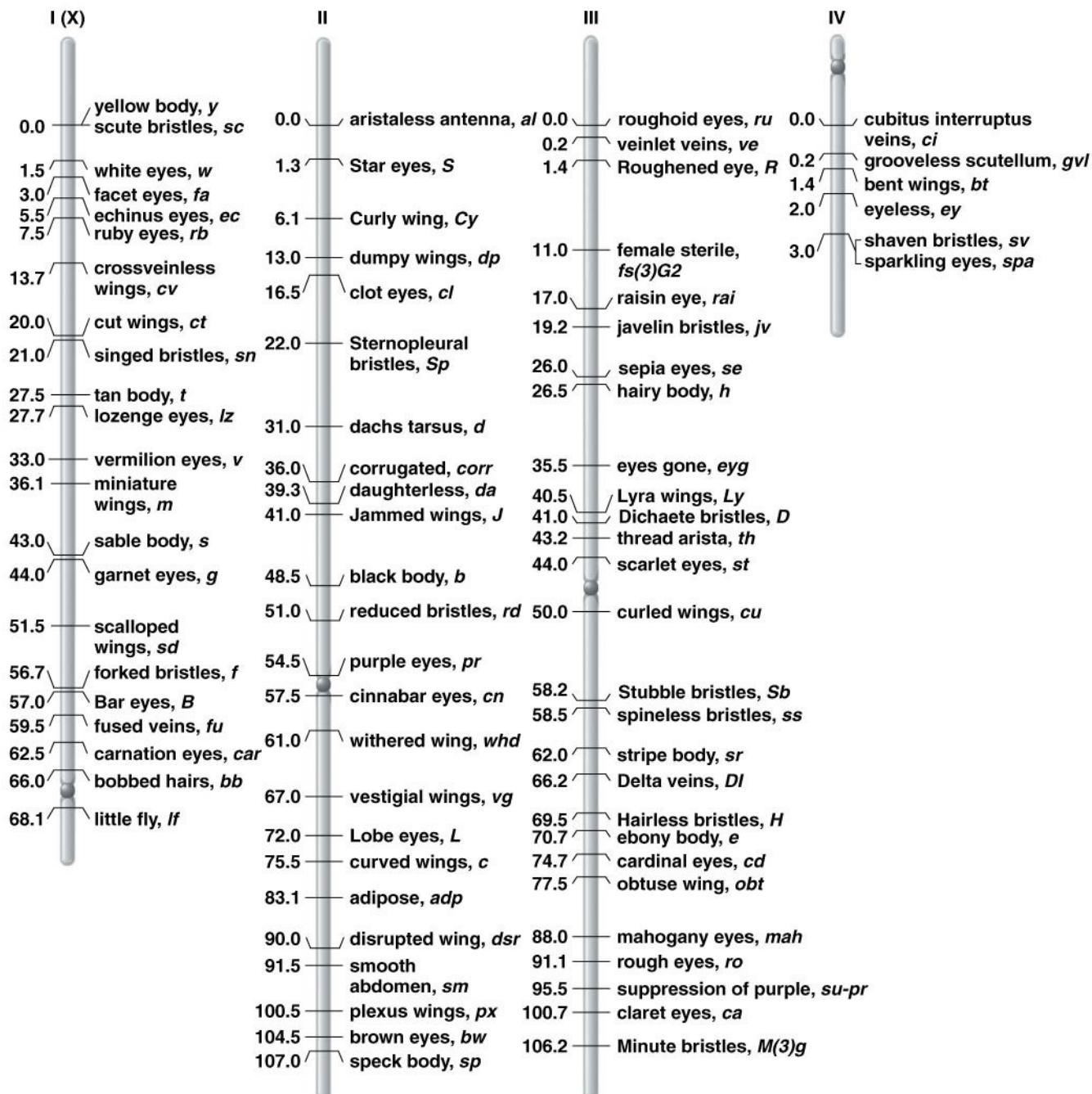


Figure 5-13

5.6 Lod Score Analysis and Somatic Cell Hybridization Were Historically Important in Creating Human Chromosome Maps

Section 5.6: Lod Score Method

- **Lod score method**
 - Relies on probability calculations
 - Demonstrates linkage between two genes when linkage analysis relies primarily on pedigrees
 - Assesses probability that pedigree with two traits reflects genetic linkage between them

Section 5.6: Lod Score

- Lod score accuracy is limited by the extent of the pedigree

Section 5.6: Somatic Cell Hybridization

- **Somatic cell hybridization**
 - Made possible the assigning of human genes to their respective chromosomes
 - Involves fusing two cells into a single hybrid cell: **heterokaryon**
- **Syndkaryon:**
 - Heterokaryons cultured *in vivo*—nuclei are fused together

Section 5.6: Synteny Testing

- **Synteny testing**
 - Presence or absence of each chromosome, with presence or absence of each gene product
 - **Figure 5-14:** Four gene products tested in relation to eight human chromosomes

A hypothetical grid of data used in synteny testing to assign genes to their appropriate human chromosomes. Three somatic hybrid cell lines have been scored for the presence of absence of human chromosomes 1 through 8, as well as for their ability to produce the hypothetical human gene products A, B and C

Hybrid cell lines	Human chromosomes present								Gene products expressed			
	1	2	3	4	5	6	7	8	A	B	C	D
23									-	+	-	+
34									+	-	-	+
41									+	+	-	+

5.7 Chromosome Mapping Is Now Possible Using DNA Markers and Annotated Computer Databases

Section 5.7: DNA Markers and RFLPs

- **DNA markers**

- Short segments of DNA with known sequence and location
- Useful landmarks for mapping
- Earliest examples of DNA markers:
 - **RFLPs and microsatellites**

Section 5.7: RFLPs and Microsatellites

- **RFLPs: Restriction fragment length polymorphisms**
 - Polymorphic sites
 - Generated when specific DNA sequences are recognized and cut by restriction enzyme
- **Microsatellites**
 - Short repetitive sequences
 - Found throughout genome

Section 5.7: SNPs

- **SNPs: Single-nucleotide polymorphisms**
 - Found throughout genome
 - Used by geneticists to identify and locate related genes
 - Used to screen for diseases
 - Example: **Cystic fibrosis**

Section 5.7: Cystic Fibrosis

- **Cystic fibrosis**

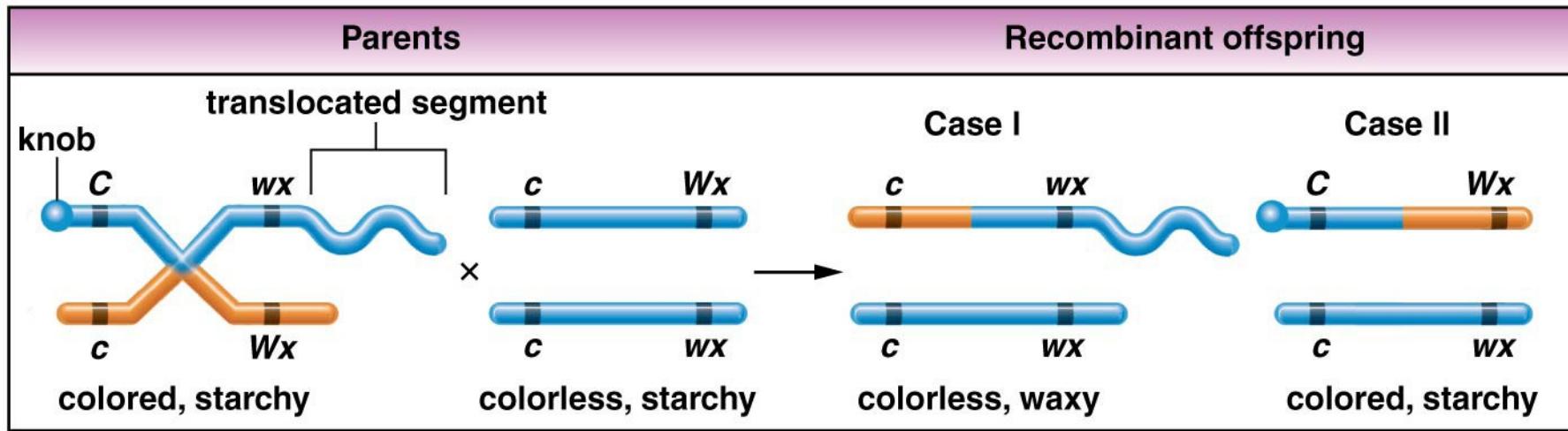
- Gene located by using DNA markers
- Life-shortening autosomal recessive exocrine disorder
- Gene causing disorder found on chromosome 7

5.8 Crossing Over Involves a Physical Exchange between Chromatids

Section 5.8: Chiasmata and Crossing Over

- Genetic mapping techniques used to study relationship between **chiasmata** and **crossing over**
- Mapping in maize
 - Used **cytological markers**
 - Established crossing over involves a physical exchange of chromosome regions (**Figure 5-15**)

The phenotypes and chromosome composition of parents and recombinant offspring in Creighton and McClintock's experiment in maize. The knob and translocated segment served as cytological marker, which established that crossing over involved an actual exchange of chromosomes arms



5.9 Exchanges Also Occur between Sister Chromatids During Mitosis

Section 5.9: Sister Chromatid Exchanges

- **Sister chromatid exchanges (SCEs)** occur during mitosis but do not produce new allelic combinations

Section 5.9: SCEs and Harlequins

- **SCEs: Sister chromatid exchanges**
 - Reciprocal exchanges similar to crossing over
 - Between sister chromatids (crossing over is between NONsisters)
- **Harlequin chromosomes**
 - Sister chromatids involved in mitotic exchanges
 - Patch-like appearance when stained and viewed under a microscope (**Figure 5-16**)

SCE between sister chromatids resulting in the formation of harlequin chromosomes

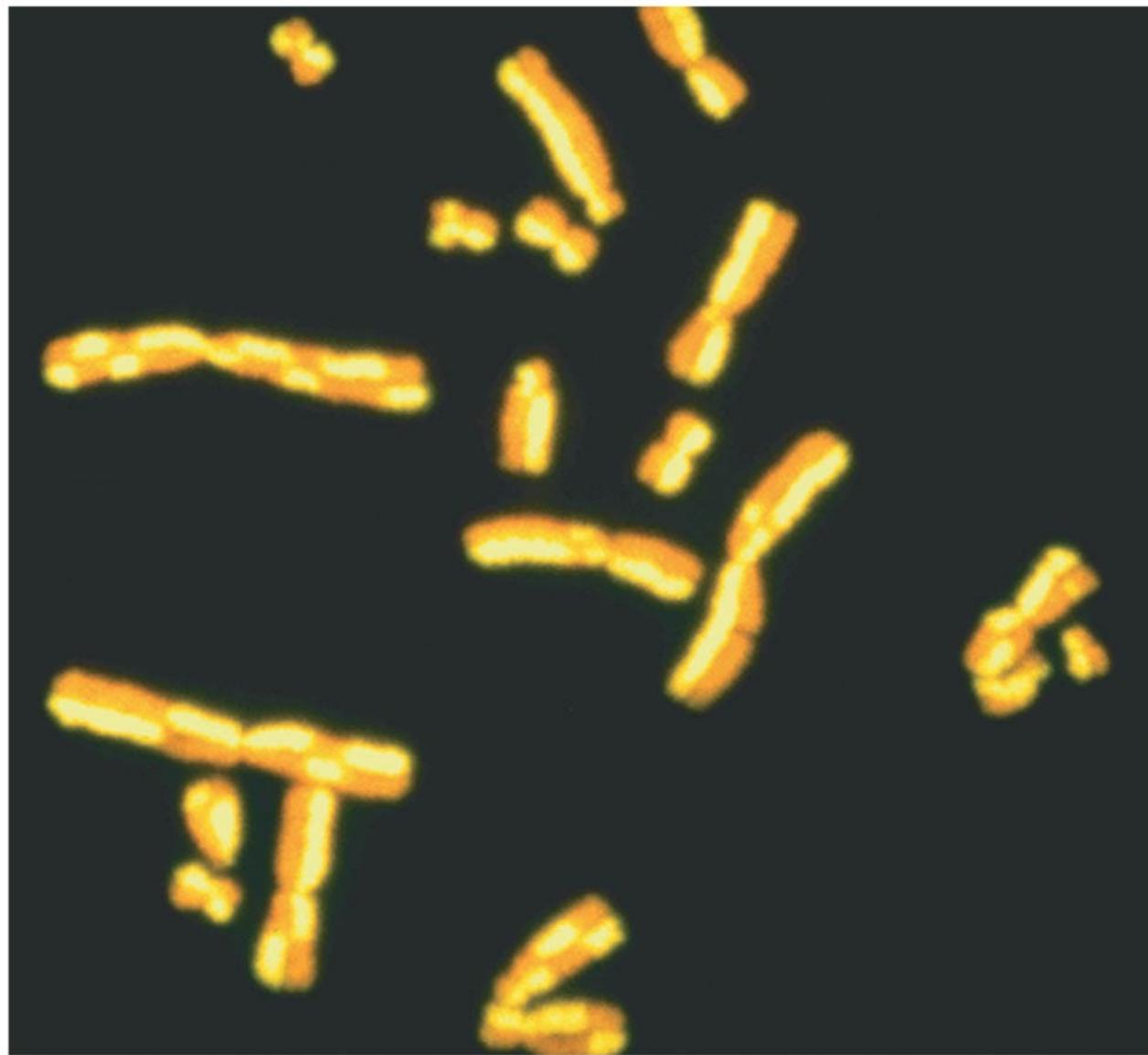


Figure 5-16

Section 5.9: Bloom Syndrome

- Agents that induce chromosome damage
 - **Viruses, X-rays, UV, mutagens**
 - Increase frequency of sister chromatid exchange in Bloom syndrome
- **Bloom syndrome**
 - Human disorder
 - Mutation in **BLM gene** chromosome 15
 - Prenatal and postnatal retardation of growth

Section 5.9: BLM Gene

- **BLM gene**
 - Encodes enzyme DNA helicase
 - DNA helicase's role is DNA replication

5.10 Did Mendel Encounter Linkage?

Section 5.10: Mendel's Garden Peas

- Mendel did not encounter linkage relationships
- If he had:
 - Might not have recognized basic patterns of inheritance
 - Might not have interpreted them correctly
- Mendel had inaccuracy in his hypothesis