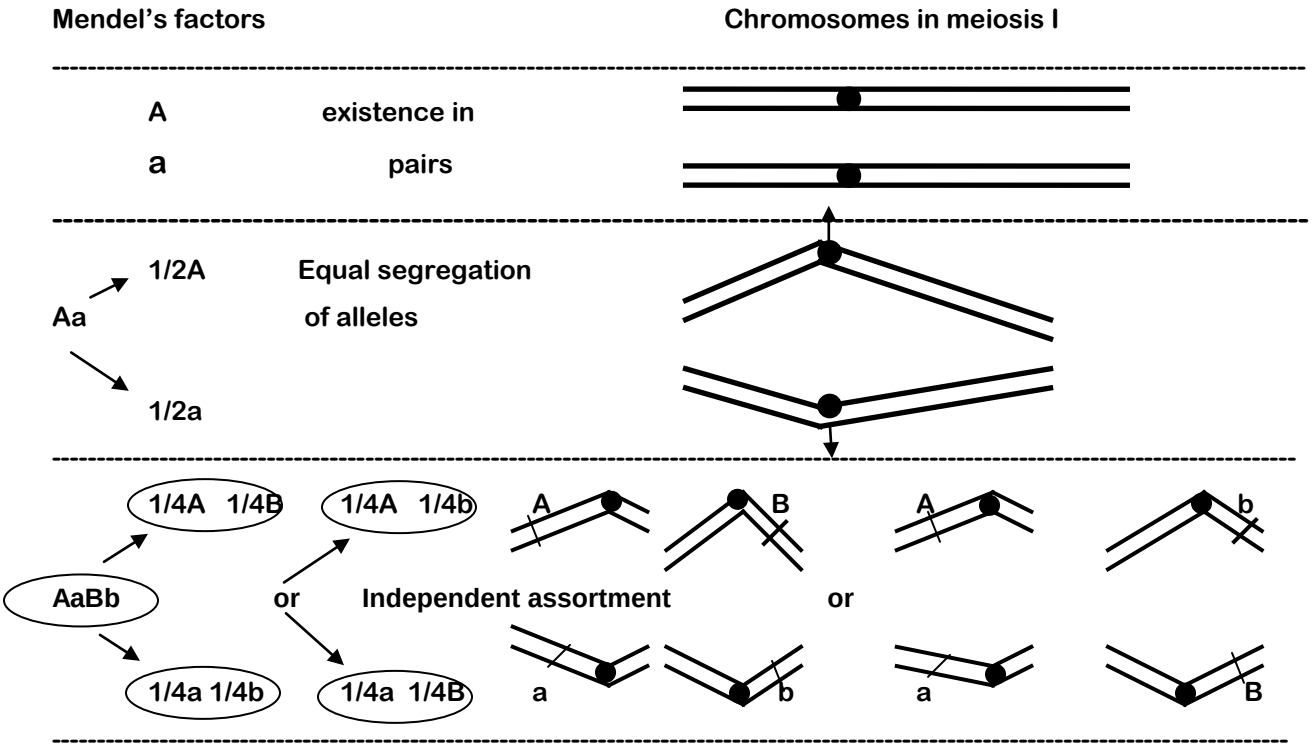
Lecture 3 Chromosomes and Sex Determination

1. Sex chromosomes
2. Sex linkage
3. Chromosome nondisjunction
4. Sex determination
5. Sex-linked traits in humans

Chromosome theory of heredity comes from the understanding of **the parallel behavior of Mendel's factors and chromosomes:**

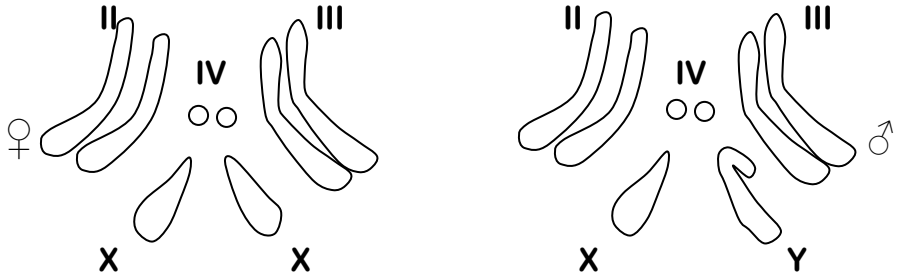
- alleles are in pairs - so are chromosomes;
- alleles of a gene segregate equally into gametes - so do chromosome homologs;
- different allelic pairs segregate independently - so do different homologous pairs of chromosomes.



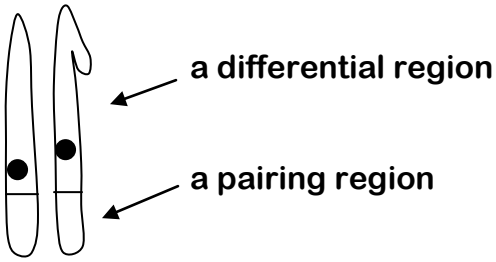
In addition:

- **number of chromosomes in organism is constant (except for gametes);**
- **number of chromosomes is species-specific;**
- **sperm cells are just small bags with a nucleus filled with chromosomes, almost w/o cytoplasm;**
- **phenotypic differences b/w sexes correlate with chromosome morphology and number;**
- **AND MOST IMPORTANTLY: transmission of distinct traits was correlated with transmission of morphologically distinct chromosomes - sex chromosomes**

1. Sex chromosomes. In *Drosophila* there are 4 pairs of chromosomes:



Females (and in humans) are XX, males are XY. Other three pairs are called autosomes.



Females produce only X-chromosome containing gametes (homogametic sex), while males (heterogametic sex) produce 1/2 gametes with X, and 1/2 with Y (by the law of Equal Segregation). Therefore, in the progeny, if gametes are fused at random, 1/2 is XX (♀), and 1/2 is XY (♂).

Y-chromosomes have a paternal mode of inheritance (from fathers to sons).

2. Sex linkage. In 1909 Thomas Morgan, experiments with *Drosophila*:

P ♀ red eyes X ♂ white eyes

F_1 all red eyes

F_2 3 red (2 ♀ :1 ♂) : 1 white (1♂).

Morgan's interpretation:

Original wild type (red-eyed) females are X^+/X^+.

Males are mutant and hemizygous for X chromosomes: X^w/Y.

P: X^+/X^+ ♀ crossed with X^w/Y ♂

Gametes X^+ ½ X^w ½ Y

F1: X^+/X^w and X^+/Y (all red-eyed)

F2:

	X^+	Y (male gametes)
X^+	X^+/X^+ 1/4 red ♀	X^+/Y 1/4 red ♂
X^w	X^w/X^+ 1/4 red ♀	X^w/Y 1/4 white ♂

Thus explaining why all white-eyed flies are males.

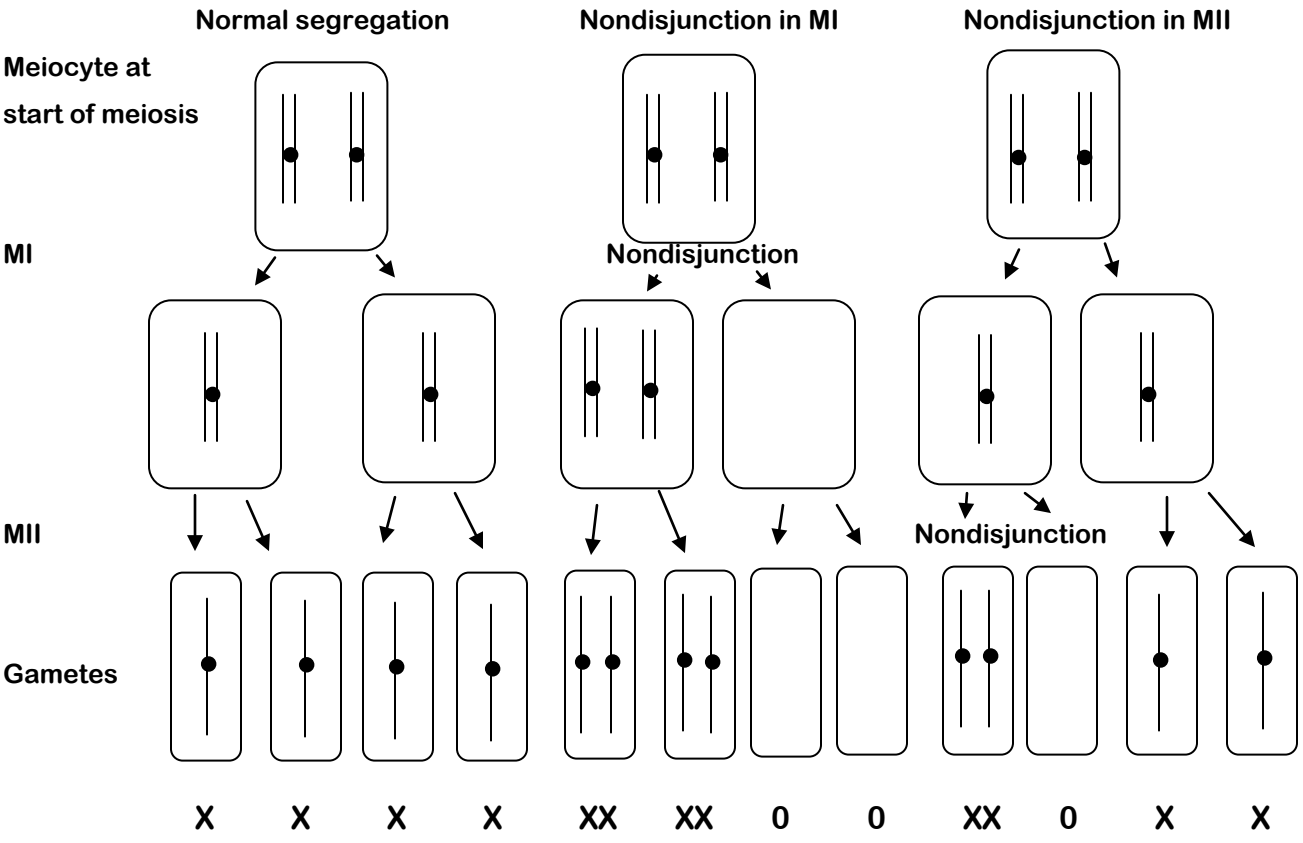
Reciprocal cross:

P:	X^w/X^w	x	X^+/Y
	white ♀		red ♂
F1:	X^w/X^+	and	X^w/Y
	Red ♀		white ♂
F2:	¼ X^w/X^w		¼ X^w/Y
	white ♀		white ♂
	¼ X^+/X^w		¼ X^+/Y
	red ♀		red ♂

3. Chromosome nondisjunction. Experiments of Calvin Bridges:

P:		X^wX^w ♀	x	X^+Y ♂		
F1	most:	X^wX^+	and	X^wY		
	1/2000:	white	and	red	("exceptional" progeny)	

The Bridges' idea is that two homologous X chromosomes did not move to the opposite poles during Anaphase I of meiosis: nondisjunction



Interpretation of Bridges' experiments:

P: X^w/X^w x X^+/Y

Nondisjunction gametes: X^w/X^w 0 **Normal gametes:** X^+ Y

Fusion:

female gametes	X^+	Y (male gametes)
X^w/X^w	~~$X^w/X^w/X^+$~~ dies	$X^w/X^w/Y$ white female
0	$X^+/0$ sterile red male	~~0/Y~~ dies

4. Sex determination. In *Drosophila* sex determined but by the ratio of the X chromosomes to autosomal chromosomes (AA):

X per 3 pairs of autosomes = male

XY per 3 pairs of autosomes = male

XX per 3 pairs of autosomes = female

XXY per 3 pairs of autosomes = female

Humans:

X0: Turner syndrome. Nondisjunction in either parent.

X → X0

0 → X0

XXY: Kleinfelter syndrome. Nondisjunction can happen in the mother or father:

XX → XXY (Y)

X → XXY (XY)

XYY-syndrome. Non-disjunction of Y chromosome in MII (father).

XXX-syndrome.

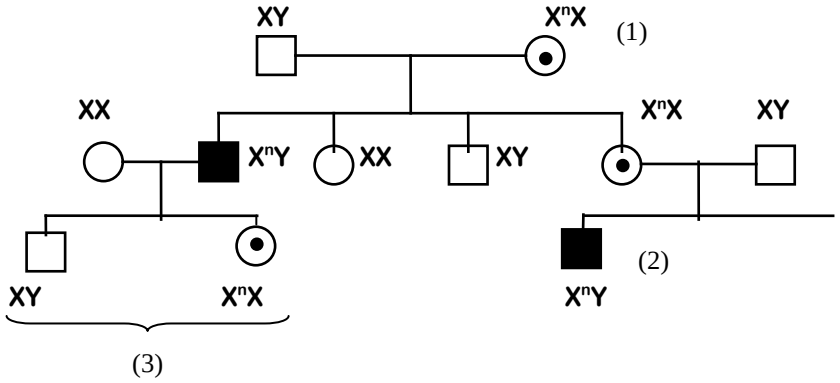
5. Sex-chromosome linked traits in humans.

A number of recessive mutations are X-linked. Their transmission is described by the following rules:

(1) Homogametic sex (females) can be carriers of many recessive disorders.

(2) Heterogametic sex (males) expresses the respective phenotype because they are hemizygous for X-chromosome. They receive their X from the mother.

(3) Sons of affected males are free of the disease allele. But daughters become carriers.



Examples of X-linked recessive traits:

hemophilia - inability of blood to clot, caused by defective Factor VIII;

Duchenne's muscular dystrophy - fatal, death by early adulthood;

red-green color blindness;

testicular feminization syndrome (androgen insensitivity) – the individuals are XY but develop as females (sterile)

X-linked dominant characters: the pattern of inheritance is like X-linked recessive, but heterozygous females express the trait. Examples: faulty teeth enamel, trombopathy (severe bleeding due to interference in the blood platelets formation)

Y-linked: all Y-genes are hemizygous, expressed phenotypically:

maleness itself; hairy ears; sterility