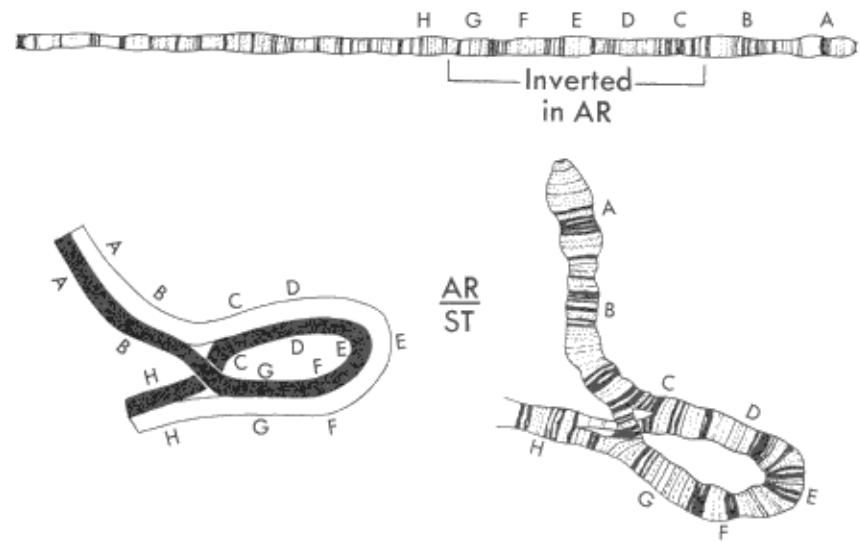
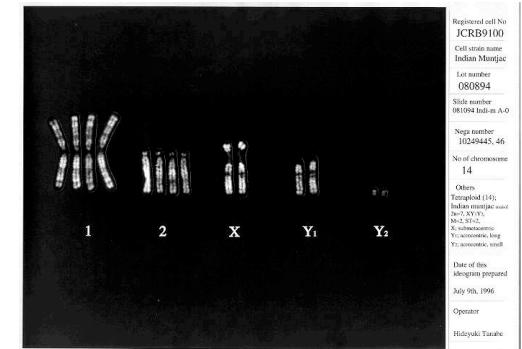


Section 16

Variation in Chromosome Number and Structure

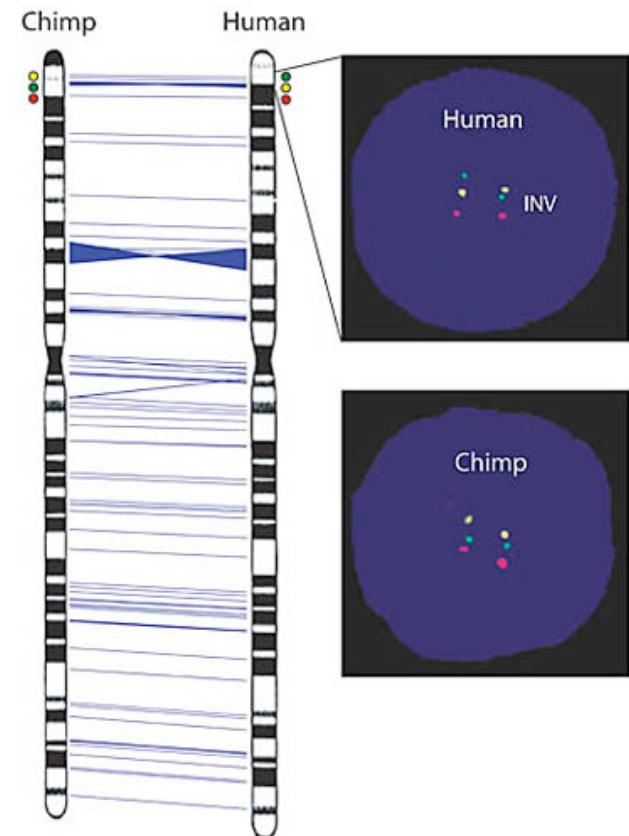
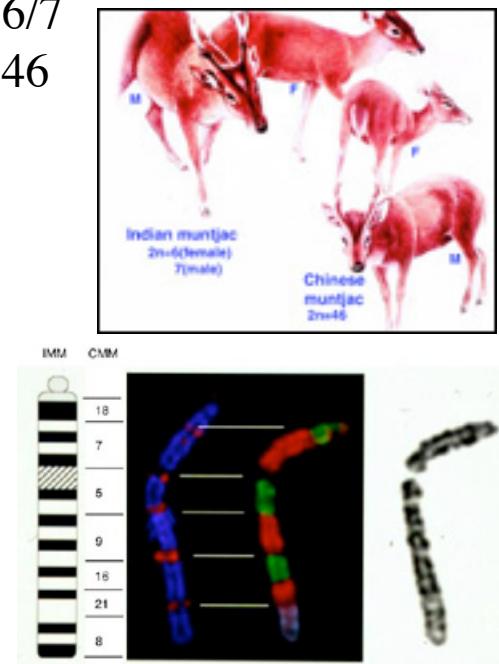
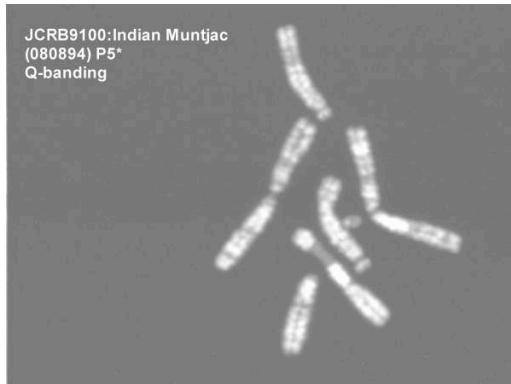


- The karyotype can change due to rare events.
- Changes are inherited.

Consequently:

- The karyotype can vary somewhat within a species.
- The karyotype evolves.
- Different species, and less often different individuals within a species, have different numbers of chromosomes and different arrangements of genes on the chromosomes.

Indian Muntjac $2N = 6/7$
 Chinese Muntjac $2N = 46$



VARIATIONS IN CHROMOSOME NUMBER

Variations in chromosome number include euploidy (varying numbers of complete chromosome sets) and aneuploidy (partial chromosome sets).

Euploids have varying numbers of complete chromosome sets; varieties include diploid, haploid, auto- and allopolyploid, polytene. Aneuploids have partial chromosome sets.

Ploidy of organism = number of chromosome sets

Euploid: multiples of complete sets

haploid N A B C

diploid 2N A A B B C C

polyploid > 2N

triploid 3N A AA B B B C C C

tetraploid 4N A A A A B B B B C C C C

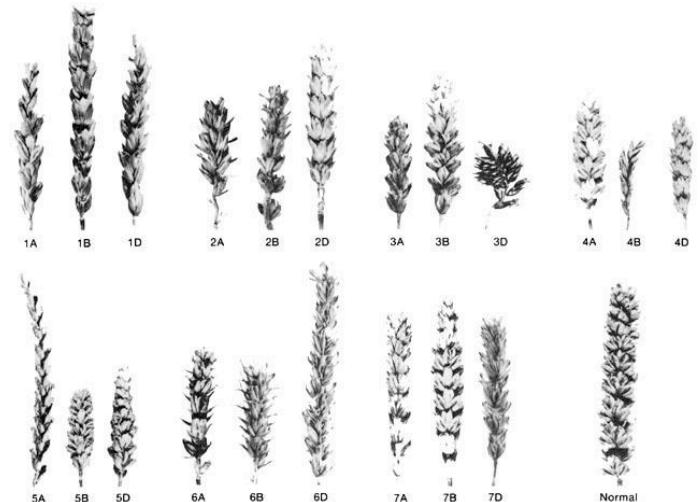
Aneuploids: diploid \pm partial set

monosomic 2N - 1 A A B B C monosomic C

trisomic 2N + 1 A A A B B C C trisomic A

Aneuploidy important because:

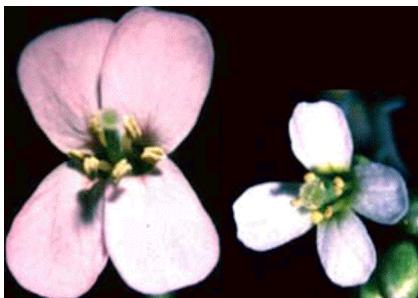
- genetic tool
- results in genetic defects



Polyplody important because:

- plant evolution polyploidization -> new species, especially in grasses
- plant breeding polyploidization -> new useful variety

Bread wheat (*Triticum aestivum*) is allotetraploid with diploid chromosome sets from 3 different parent species, each of which had $2N = 14$, so total in wheat is 42.



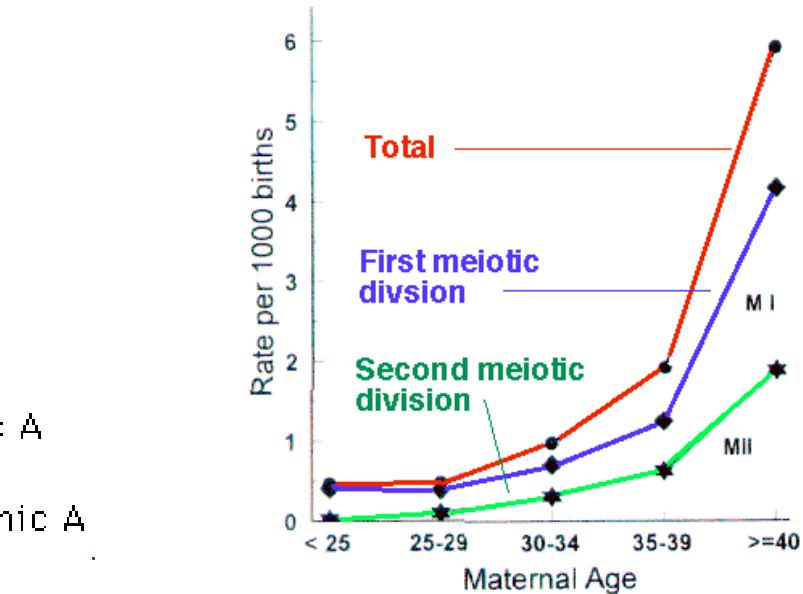
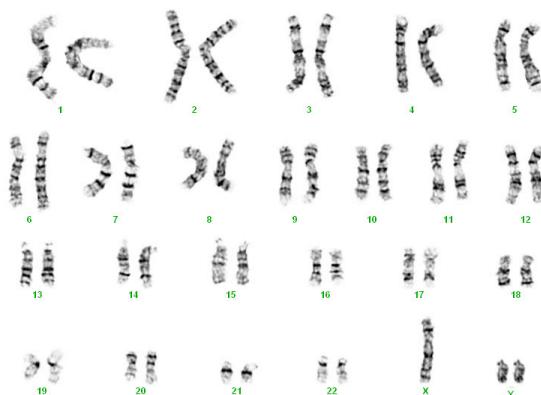
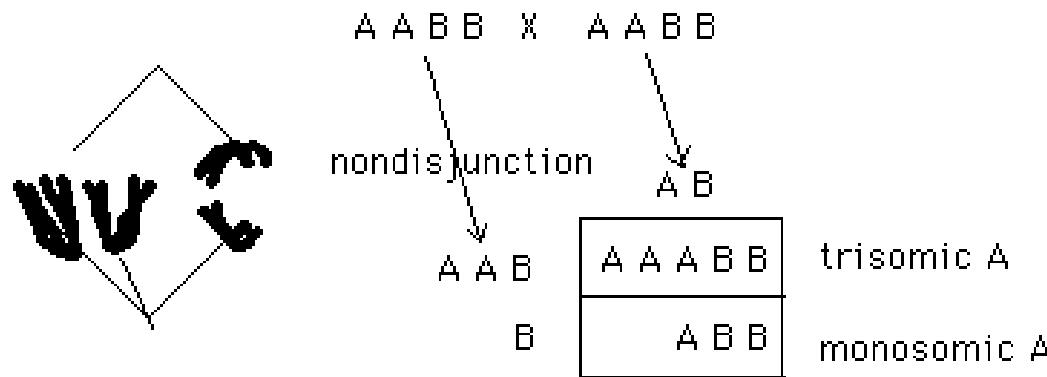
Variations in chromosome number are usually caused by errors in mitosis, meiosis, or fertilization.

Errors in mitosis, meiosis, or fertilization cause polyploidy. E.g.:

(a) 2 sperm + 1 egg --> 3N

(b) Failure of anaphase separation in mitosis in germ line --> 4N gametocyte --> 2N gametes. Can be induced with agents that block spindle formation or dissolve spindle.

Aneuploids result from nondisjunction.



3. Changes in chromosome number often cause abnormalities in gene expression (and hence the phenotype) and in meiosis.

Gene dosage effects: aneuploidy results in unbalanced genomes and abnormal development; hence aneuploidy is usually lethal or detrimental.

Embryo with one extra or one too few chromosome has **unbalanced genome --> abnormal development**. Genome evolved to work with two functional copies of each gene. If have too few or too many of some genes, those make too much or too little gene product, and may upset metabolic pathways; e.g. if some enzymes are too abundant, may make too much product.

Aneuploidy in humans is common medical problem.
Occurs in ca. 3.5% of all embryos.

Aneuploidy for large chromosome in humans usually causes unbalance for one or many important genes, usually lethal --> stillbirth. Accounts for ca. 20% of all stillbirths.

Aneuploidy for small chromosomes maybe viable. E.g. Down's syndrome = trisomy 21. (Or part of 21, attached to another chromosome.)

Causes of trisomy 21:
≈ 75% female MI or MII nondisjunction
≈ 25% male MI or MII "

Female eggs arrested in prophase of MI at birth. Eggs age --> increasing frequency of nondisjunction with increasing maternal age, especially > 45 years.

Meiosis in aneuploids and autopolyploids may be abnormal because of problems with synapsis, resulting in sterility. Don't have time to cover in course, can omit corresponding sections of reading.

VARIATIONS IN CHROMOSOME STRUCTURE

Also called chromosomal mutations (OK when they first occur), chromosomal abnormalities or aberrations (not strictly applicable because sometimes ≥ 2 different structures are present in population in high frequency; can't say that either one is aberrant or abnormal).

Changes in chromosome structure occur in both prokaryotes and eukaryotes. We will focus on eukaryotes.

1. Transposable elements = TEs AKA “jumping genes”

Transposition:

- TE moves to new location
- rare event; frequency is on order of mutation rate or somewhat higher, but not so frequent that they interfere with mapping
- duplicative transposition puts a copy of the TE in the new position, leaving the old one behind; nonduplicative transposition moves the TE.

1 2 3 4 5 6 7 8 9 10 --duplicative transposition--> 1 2 3 4 5 6 7 8 9 2 10

--non-duplicative transposition--> 1 3 4 5 6 7 8 9 2 10

- Duplicative transposable elements can spread in genome even if they are of no selective advantage to the organism, and even if they are mildly detrimental. Sometimes called **selfish DNA**.



Transposable elements were first discovered by Barbara McClintock (first woman elected to National Academy of Science).in maize; Nobel Prize.

Mechanisms:

- Some have transposase gene -> transposase protein which cuts TE out and inserts in target sequence.
- Retrotransposons transcribed to make RNA copy, then reverse transcriptase makes DNA copy of the RNA, and DNA is integrated into target sequence.

The act of transposition itself may cause rearrangements of adjacent sequences.

TE inserted in gene or in controlling sequences can make gene inactive, just like a mutation.

If transposon excises cleanly, gene activity can be restored.

The copies of a transposable element are sites of homology at which crossing-over can occur within a chromosome and between homologous or nonhomologous chromosomes --> changes in chromosome structure. Crossing-over probably in interphase.

2. Repeats = repeated sequences

Repeats are segments of DNA that are present two or more times in the genome of an organism.

(1) Many short repeats arise in the course of evolution due to mutations, just by chance:

(2) Short (simple sequence) tandem repeats arise by replication slippage:

ATTCG –replication--> ATTTCG

ATGATGATG ↔ ATGATGATG

Some human hereditary defects are due to increases in number of tandem repeats; e.g.

Myotonic muscular dystrophy

Some regions of chromosomes are rich in short tandem repeats, notably centromeres.

These are the bane of DNA sequencers; this is why a large part of the human genome still hasn't been sequenced.

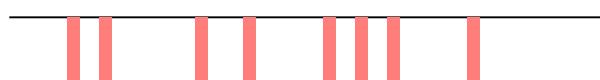
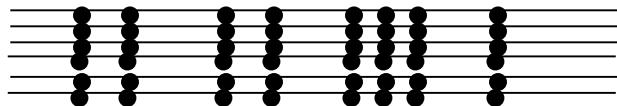
(3) Longer repeated sequences arise by duplicative transposition.

Polytene Chromosomes

Some insects, including *Drosophila*:

During differentiation of some tissues (salivary glands, Malpighian tubules, etc.)
cells go through repeated S phases (e.g. 10) without mitosis --> polyplloid or
polytene nuclei.

Polytene chromosomes: all copies held tightly together and in alignment.



Stain, see bands where DNA is more concentrated.

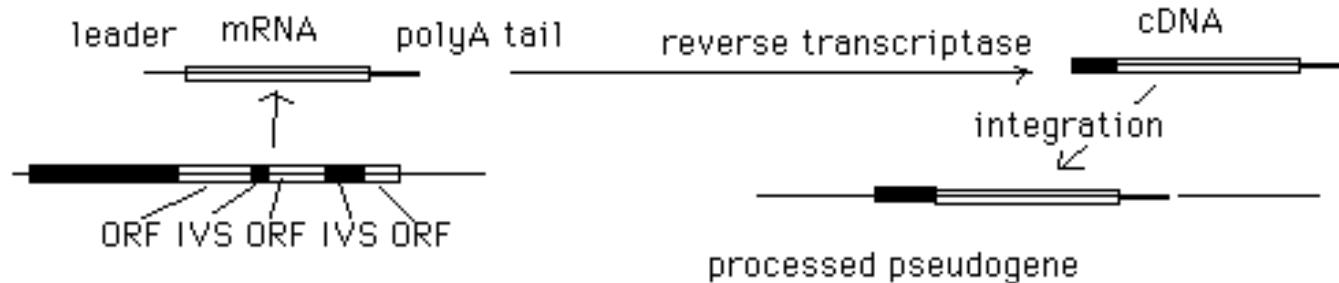
PHYSICAL LANDMARKS!

3. Duplication = process of duplicating a segment (usually a whole gene or genes); also used to denote the repeated copies

1 2 3 4 5 6 --duplication--> 1 2 3 4 5 4 5 6

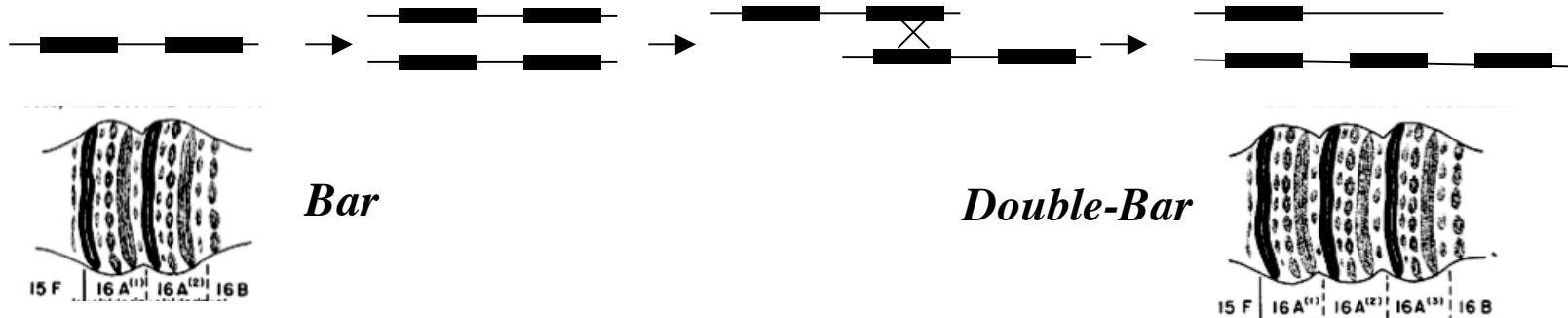
Might be called *dup45*

- (1) Duplications can arise by duplicative transposition.
- (2) Duplications can occur via processed pseudogenes:



- (3) Duplication can occur via unequal crossing-over between existing repeats, usually in sister chromatids produced by replication of a chromosome.

Classic case: Bar eye mutation is actually a duplication of several bands. Sturtevant & Bridges. Unequal crossing-over between sister chromatids or homologous X chromosomes (in females) → double-Bar and wild type..



Red-green colorblindness can result from this process, as described in textbook.

Ribosomal RNA genes in eukaryotes are present in long tandem arrays which vary in number.

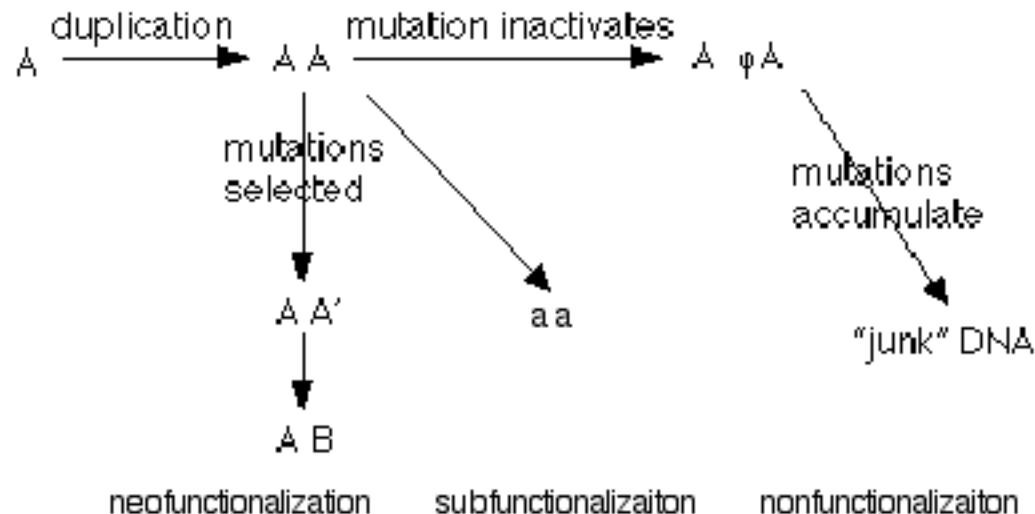
Duplications are important in the evolution of new genes.

Duplication → 2 copies of a gene in a genome.

Diploids have two genomes, so diploid initially heterozygous for duplication and has 3 copies.

Sexual reproduction can produce individuals with 4 copies.

We will just track the fate of two copies.



Most often, pseudogene diverges further so eventually not recognizable as related to gene. Contributes to "junk" DNA, unique or repeated sequences with no detectable function. Eventually deleted.

Duplicate can also acquire mutations that turn it into a gene with similar function, e.g. (binding protein duplicates, one copy --> hemoglobin (blood), other copy --> myoglobin (

e.g. human globins: example of clustered multigene family.

α	alpha	major adult
β	beta	major adult
γ	gamma	fetal
δ	delta	infant, minor adult
ϵ	epsilon	embryonic
ζ	zeta	embryonic
φ	psi	pseudogene

chromosome 16 α family _____ ζ_2 ζ_1 $\varphi\alpha_1$ α_2 α_1 _____

chromosome 11 β family _____ φb_2 ϵ _____ $G\gamma$ $A\gamma$ φb_1 δ _____ β _____

When we discuss molecular evolution, will see how we can trace the evolution of all of these genes in detail from a single ancestral gene. That gene duplicated to give myoglobin and globin genes; the latter duplicated to form α and β globin genes; and each of those duplicated further.

4. Deletion = loss of a segment of DNA, and the result of that loss.

(1) Deletions arise by unequal crossing-over (together with duplication).

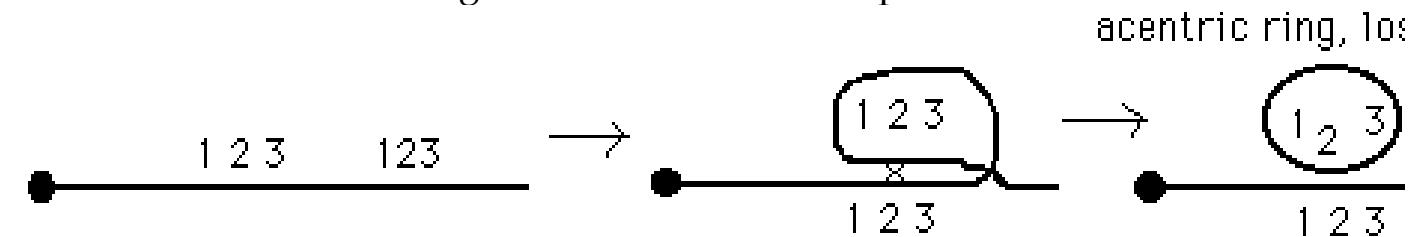
(2) Deletions arise by intrachromosomal crossing-over between direct repeats.

deletion = deficiency

1 2 3 4 5 6 --deletion--> 1 2 3 6 Might be called *def45*.

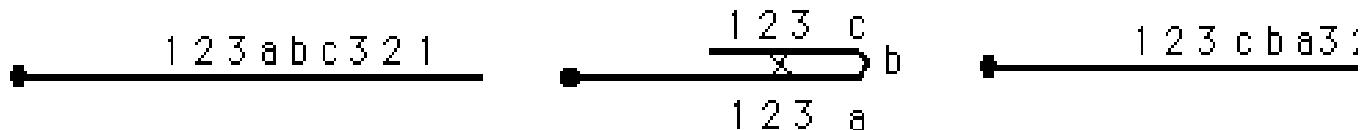
Origins of **deletions**:

Intrachromosomal crossing-over between **direct** repeats:



5. Inversions arise by intrachromosomal crossing-over between inverted repeats.

Inversions arise by intrachromosomal crossing-over between **inverted** repeats.



Inversions act as cross-over "suppressors" in inversion heterozygotes because cross-overs within the inverted region --> unbalanced genomes with duplications and deletions, hence inviable gametes and/or progeny.



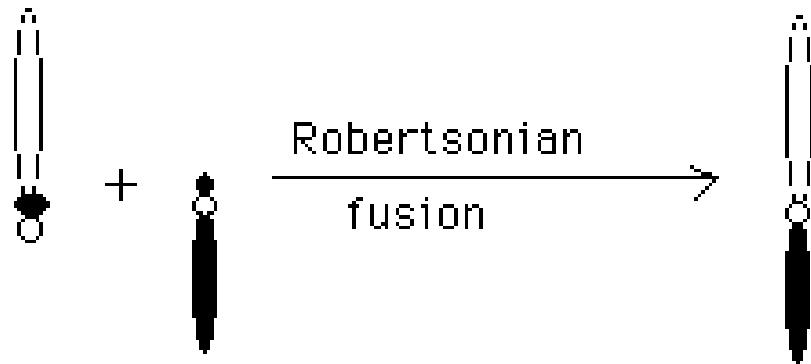
Deletion of 8p23.1
Died age 3

6. Reciprocal translocations arise by crossing-over between homologous regions on nonhomologous chromosomes.

Reciprocal translocations arise by crossing-over between homologous regions on **nonhomologous chromosomes**.

1 2 3 4 r 5 6 7 8 r 9 10 --reciprocal translocation--> 1 2 3 4 r 9 10 7 8 r 5 6

7. Robertsonian fusions change N.



Small arms are lost.

Extreme example of change in chromosome number is seen in deer. Reeve's muntjac $2N = 46$, same order of magnitude as most other deer species. Indian muntjac $2N = 6$.

Note that most rearrangements may take place by crossing-over between repeats or other homologous DNA segments (segments with similar sequence).

Duplicative transposition is a major source of such duplicated regions.

If a transposable element invades a genome, it can spread and facilitate rearrangements. Thus it can increase variation in chromosome structure and eventually lead to evolution of new gene arrangements and new phenotypes.

Transposable elements can contribute to, or even give rise to, promoters and other regulatory sequences.

Transposable elements can spread from one organism to another.

e.g. P element was transferred from *Drosophila willistoni* (or a close relative) to *Drosophila melanogaster*, probably by a parasitic mite that sucks cytoplasm from fly eggs.

The evolutionary origin(s) of transposable elements are unknown (last I heard).

Rearrangements can affect meiosis and mitosis

What happens when rearranged chromosomes synapse in meiosis I?

Textbook discusses in detail. Main point: synapsis and recombination is always between homologous chromosome regions. Centromeres segregate normally, but chromosome segments may not. Will have example(s) in practice problems.

Visible in polytene chromosomes in heterozygotes for rearrangements.

Position effect = phenotype of a gene or region of a chromosome depends on its neighbors. One obvious rationale: move gene to different position, may put under control of different set of upstream controlling sequences.

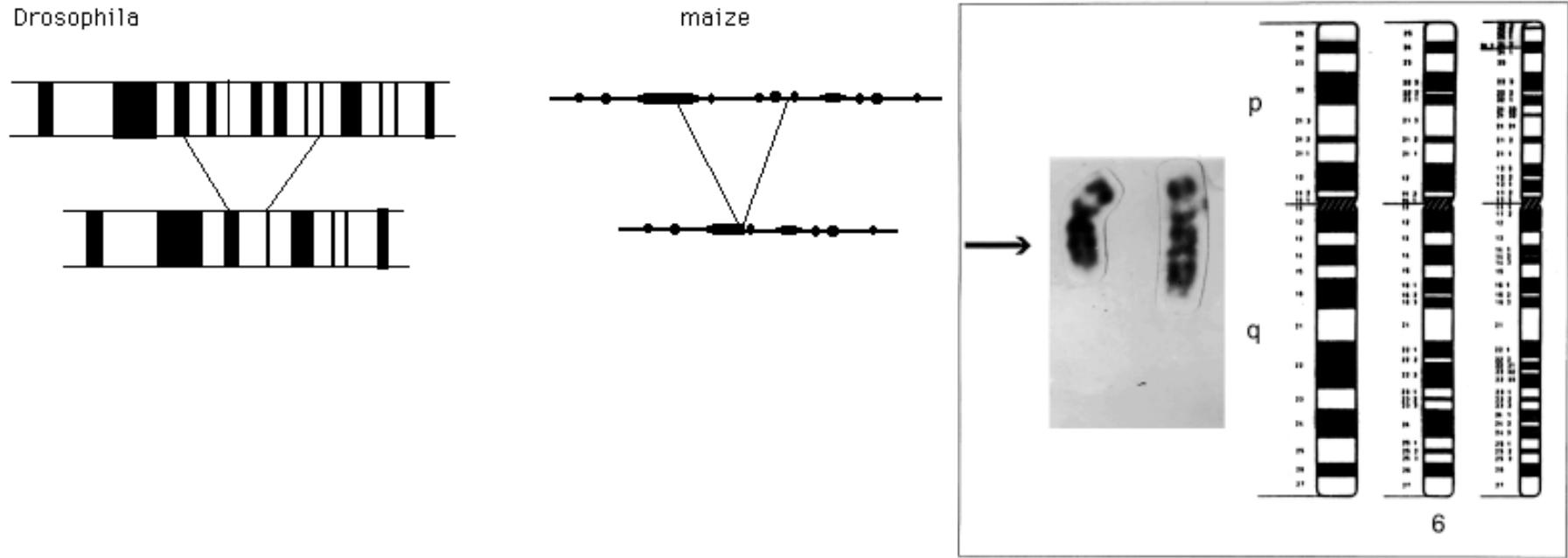
Deletions (and other structural changes) are important tools for mapping genes on chromosomes (tying linkage maps to physical maps).

Relating recombination maps and physical maps of landmarks.

Can use deletions (and other structural changes) to map genes.

Can use deletions (and other structural changes) to tie linkage map to physical map of chromosome.

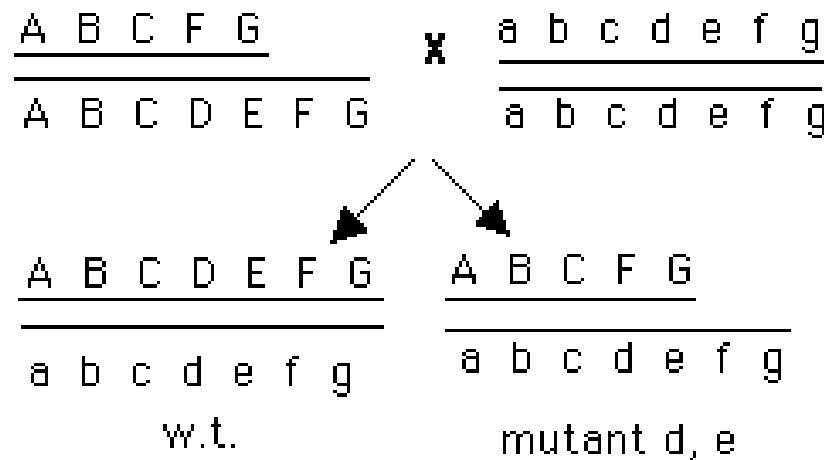
(1) Map deletion on physical map. See what landmarks are missing.



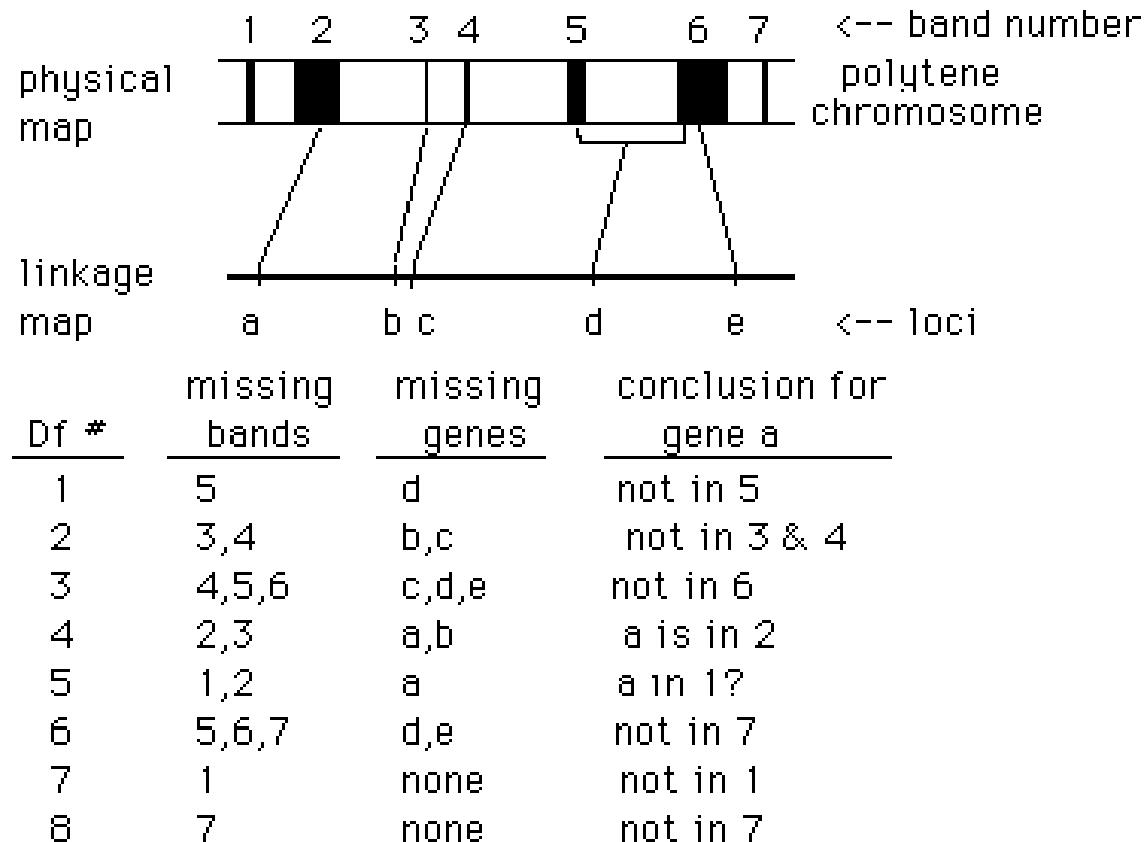
(2) Map deletions on genetic map: determine which recessive mutations are "uncovered" by deletions. An alternative way of looking at this is to see what mutations complement a deletion. If a mutation and a deletion don't complement each other, they involve the same gene.

Note this is a slightly different way of using the term "complement".

Testcross a deletion heterozygote:



(3) Tie the physical map to the genetic map by using overlapping deletions.

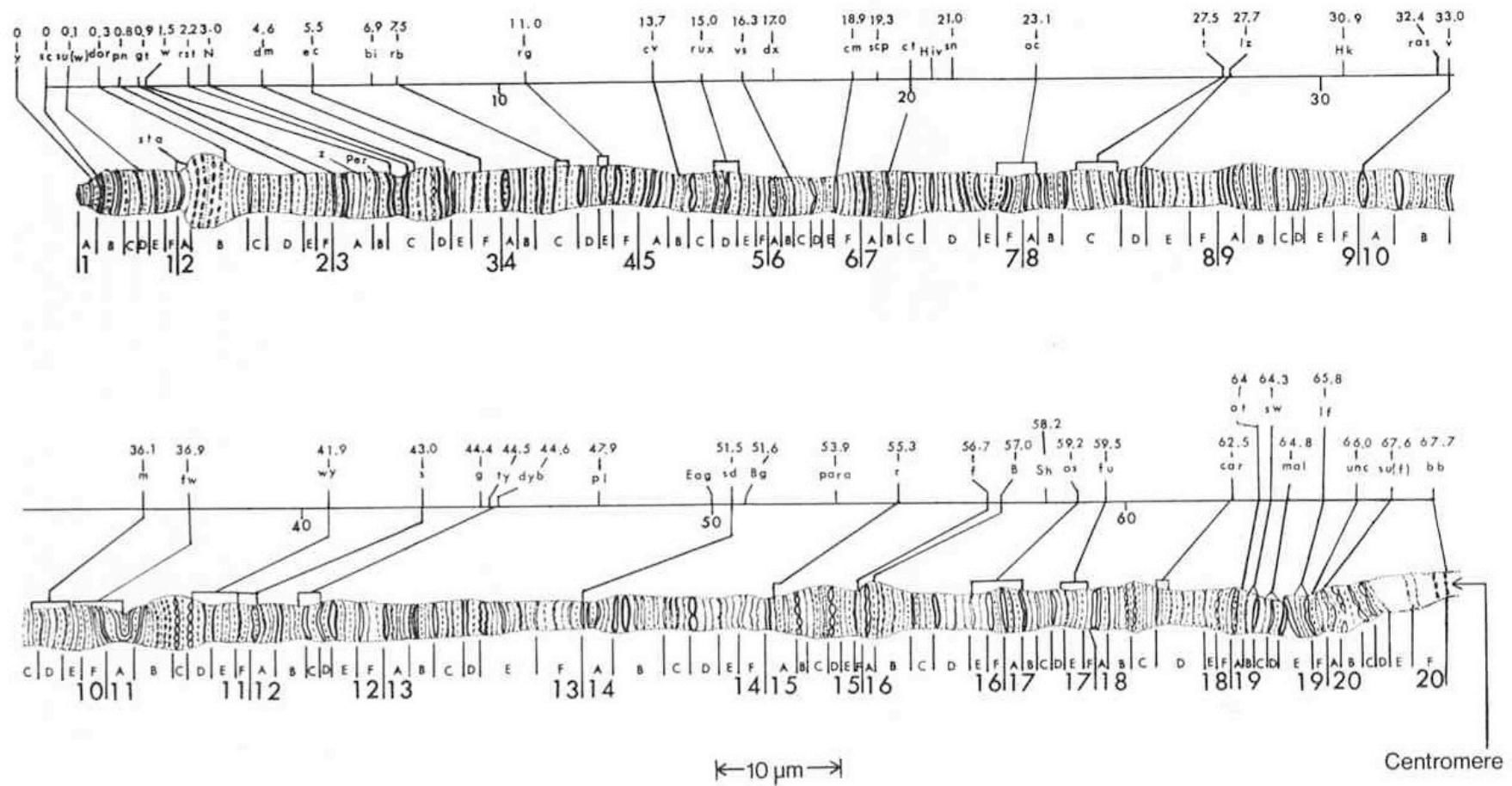


From these data, can't tell whether d is 5, 6, or both. But we know it can't be both if d is a point mutation.

Order, and sometimes the position, of genes can be determined using overlapping deletions, even without a physical map.

Physical and Genetic Maps Agree in Gene Order, Not Distances

Reason: recombination frequencies aren't uniform along chromosome.



Other Methods of Relating Physical and Genetic Maps

- FISH
- Finding genes in complete genome sequences.