

Genetic Variation

Populations exposed to selection often evolve rapidly. Alleles that confer increased survival and reproductive ability in the new conditions rapidly increase in frequency, while alleles that were common decrease in frequency.

How does the genetic variation arise?

One of the central tenets of the modern model of evolution is that variation does not arise in response to need. Instead, genetic variation is present in natural populations before it is exposed to selection, in the form of rare alleles. New sources of selection results in an increase in allele frequencies that confer high fitness.

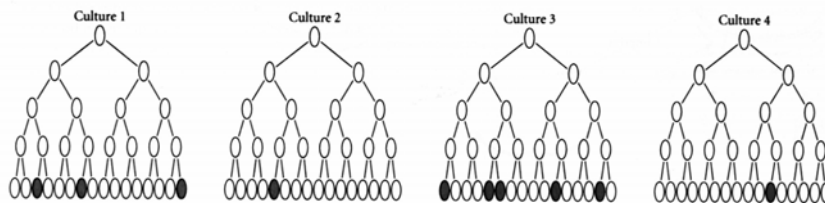
An alternative view is that new alleles that confer high fitness arise in response to exposure to selection. This is the “Neo-Lamarckian” view.

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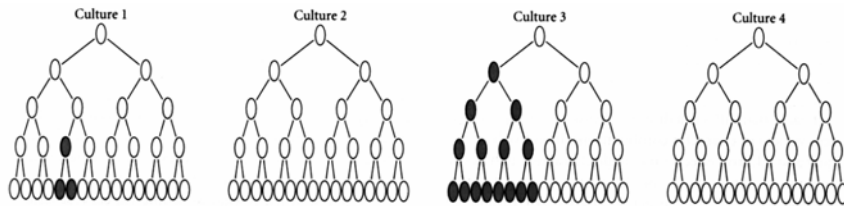
Two different experiments with bacteria originally provided evidence that variation does not arise in response to need.

Luria and Delbruck looked at variation among bacteria for resistance to a phage. They reasoned that if variation arises in response to need, the incidence of new resistance in cultures of originally nonresistant bacteria should not vary greatly among independent cultures.

They started multiple cultures of nonresistant bacteria, allowed them to multiply, and then exposed the bacteria to phage to test for resistance. Under the hypothesis that variation arises in response to need, they would expect all variation to arise after exposure. As a result they'd expect little variation in the number of resistant colonies among cultures. Their expectation:



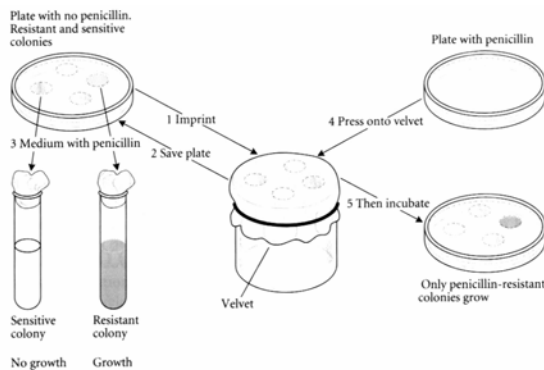
Under the hypothesis that variation arises randomly, not in response to need, resistance could appear in any generation, and thus some cultures would have many resistant bacteria (as a result of early mutation) and some cultures would have none (as result of no mutation). They expected great variation in the number of resistant colonies among cultures:



This is what Luria and Delbrück found.

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In the second experiment, **Joshua and Esther Lederberg** used **replica plating** to determine if penicillin resistance in bacterial colonies was present before exposure to penicillin or only arose after exposure to penicillin. They cultured nonresistant bacteria and then exposed them to penicillin. Their technique allowed them to determine if the original colonies from which the resistant bacteria were derived were resistant before exposure to penicillin.



Their results showed that resistance did not arise during exposure to penicillin. Resistance arose in the culture before exposure to penicillin.

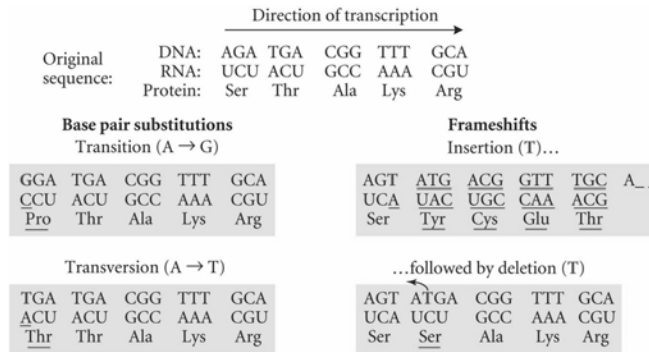
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Mutation - the alteration of a region of DNA or chromosome; and altered state of a region of DNA or chromosome

Types of mutations:

base pair substitution - a single base pair change in DNA, also called a **point mutation**

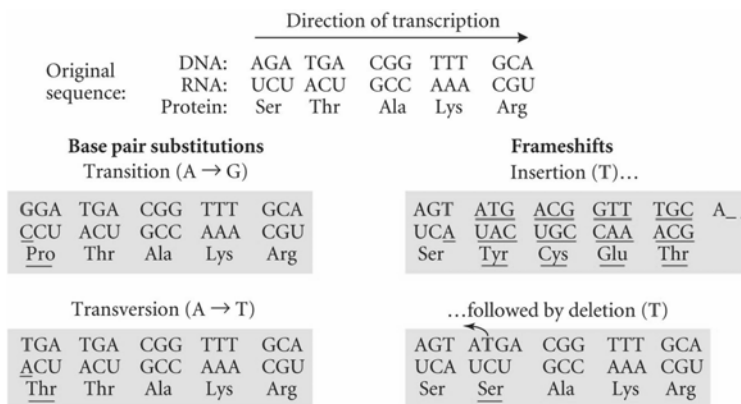
Point mutations can result in single amino acid changes or no change in amino acid - synonymous mutation.



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Nonsynonymous mutations may have small or large effects on the properties of the protein product of the gene.

A single base pair addition or deletion is a **frameshift mutation** - the result is a change in reading frame of RNA product of the gene and many amino acid changes in the protein product - usually results in a nonfunctional protein product.



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Recombination can also result in sequence changes

Intragenic recombination

Sequence 1: AT**G**GATCGATCGATGC
TACCTAGCTAGCTACG

Sequence 2: ATCGATCGAT**G**GATGC
TAGCTAGCTAC**C**TACG

Sequence 3: AT**G**GATCGAT**G**GATGC
TACCTAGCTAC**C**TACG

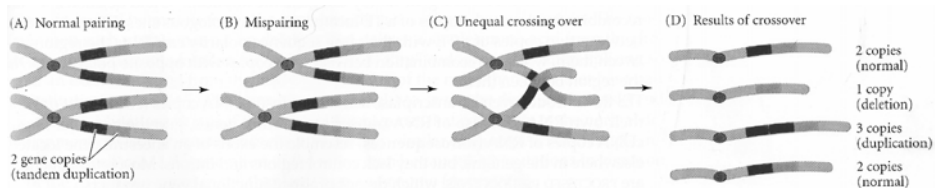
The amino acid changes resulting from the original two point mutations are combined in a single protein as a result of recombination.

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Unequal crossing-over results in sequence duplications and deletions.

Unequal crossing-over usually occurs in regions where there are tandem repeats.

The result can be a reduction in the number of repeats or an increase in the number of repeats.



High numbers of tandem repeats make a region liable to unequal crossing-over and additional duplications.

It can give rise to gene families (multiple copies of variants of a single gene) and new functional genes.

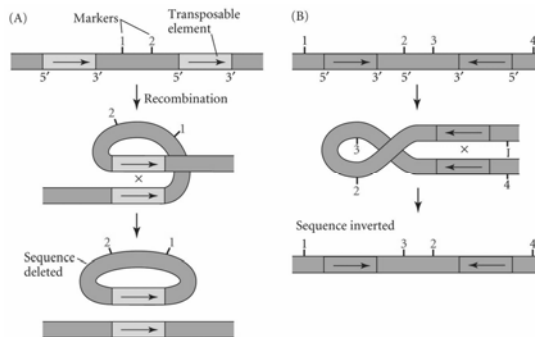
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Transposable elements - sequences of DNA that can be inserted into regions of the genome

Insertion of a sequence of bases into a functional gene or the regulatory region of a functional gene can destroy normal functioning of that gene.

Transposable elements can result in the movement of neighboring genes that were not initially part of the transposable elements.

Recombination between transposable elements can result in deletions or inversions of base pair sequences.



Examples of mutations:

Sickle-cell anemia - a single base pair substitution that results in a single amino acid change in the β chain of Hb

Precocious puberty - a single amino acid change in the gene for the receptor for luteinizing hormone results in males that show signs of puberty as early as age 4.

Cystic fibrosis - a fatal disease that occurs in 1 in ever 2500 births among northern Europeans is due to a mutation in a chloride ion channel protein. Different mutations account for the same condition: a deletion of 3 base pairs results in the deletion of a single amino acid, a conversion of an arginine codon into a stop codon, an alteration in a splicing enzyme has resulted in the deletion of an exon from the mRNA transcribed from the gene.

Retinitis pigmentosa - a degenerative disease of the retina - can be caused by mutations in at least 8 different genes.

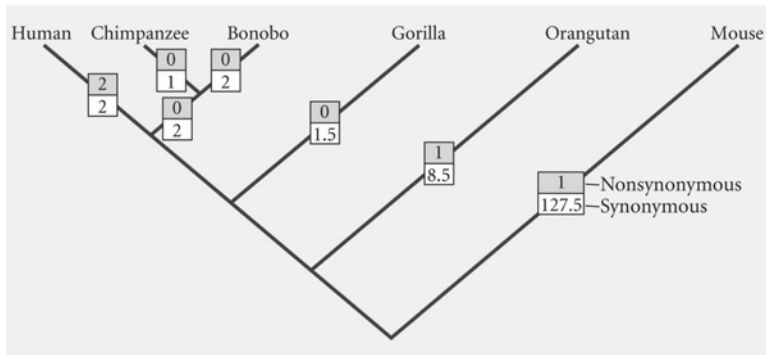
Hemophilia - caused by mutations in two different genes for blood clotting proteins. The mutations can be base pair substitutions, small deletions, small duplications. Twenty percent of the cases of hemophilia A are caused by an inversion of a long sequence of bases within one of the genes.

Huntington's disease - a fatal neurological disorder - is due to an excessive number of repeats of the sequence CAG - normal forms of the genes have 10 to 30 repeats, mutants have more than 75

Although most mutations are have deleterious effects on the encoded protein some have beneficial effects and have been important in evolution

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FOXP2 - encodes a transcription factor - mutations in this gene can cause severe speech and language disorders. Humans differ from chimpanzees at two base pairs that result in nonsynonymous amino acid changes. The amount of change in this gene is unusually high relative to synonymous changes in the gene suggesting the gene may have been important in the evolution of human speech abilities.



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Estimating Mutation Rates

Mutation rates can be estimated by their appearance in laboratory stocks or by counting the number of offspring born in each generation with genetic disease caused by a dominant allele - these are likely to be underestimates of the frequency of point mutations because synonymous mutations will have the same phenotypic effect.

TABLE 8.2 Spontaneous mutation rates of specific genes, detected by phenotypic effects

Species and locus	Mutations per 100,000 cells or gametes
<i>Escherichia coli</i>	
Streptomycin resistance	0.00004
Resistance to T1 phage	0.003
Arginine independence	0.0004
<i>Salmonella typhimurium</i>	
Tryptophan independence	0.005
<i>Neurospora crassa</i>	
Adenine independence	0.0008-0.029
<i>Drosophila melanogaster</i>	
Yellow body	12
Brown eyes	3
Eyeless	6
<i>Homo sapiens</i>	
Retinoblastinoma	1.2-2.3
Achondroplasia	4.2-14.3
Huntington's chorea	0.5

Mutation rates can be estimated indirectly by counting the number of differences between two descendants of a common ancestor and counting the number of generations since their origin. This method assumes that no selection has been involved in the change in allele frequency with each species.

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Mutation rates can be estimated by assuming that deleterious mutations are removed by selection.

The forward mutation rate ($A \rightarrow a$) is given the symbol μ .

The reverse mutation rate ($a \rightarrow A$) is given the symbol ν .



Without mutation, deleterious dominant alleles should be removed by selection until they are absent from the population. So the mutation rate is equal to the observed frequency of the deleterious dominant alleles (p) in the population.

$$\nu = p$$

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Deleterious recessive mutations will be removed from the population very slowly once they become rare. The rate of removal is

$$\Delta p = \frac{spq^2}{1 - sq^2}$$

And, when the recessive allele is rare the denominator is ~ 1 .

Deleterious recessive alleles are reintroduced by mutation at rate μ - So, in a population in which mutation adds the allele and selection removes it we should have

$$\mu p = spq^2$$

$$\mu = sq^2$$

If the deleterious recessive allele is lethal ($s=1$), the mutation rate is equal the observed frequency of homozygotes.

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TABLE 8.3 Estimates of spontaneous mutation rates per base pair and per genome

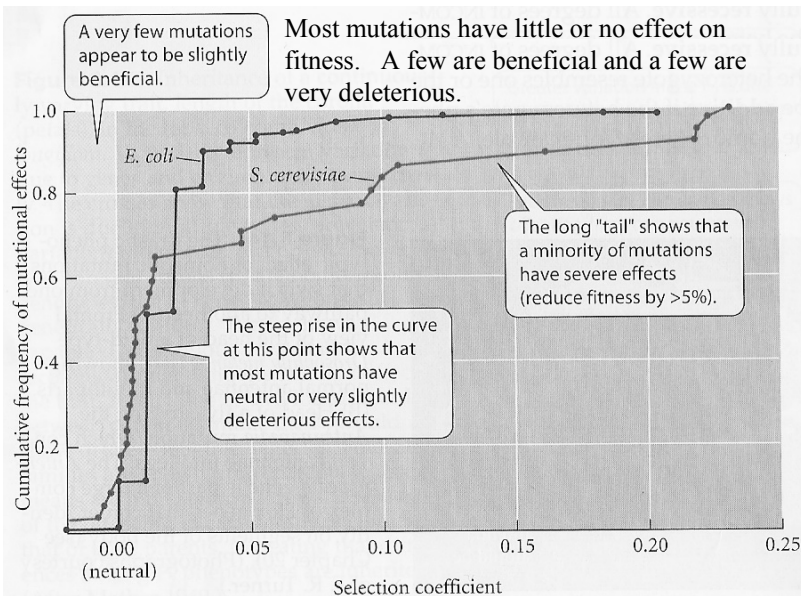
Organism	Base pairs		Mutation rate			
	in haploid genome	in effective genome ^a	per base pair per replication	per replication per haploid genome	per replication per effective genome ^a	per sexual generation per effective genome ^b
T2, T4 phage	1.7×10^5	—	2.4×10^{-8}	0.0040	—	—
<i>Escherichia coli</i>	4.6×10^6	—	5.4×10^{-10}	0.0025	—	—
<i>Saccharomyces cerevisiae</i> (yeast)	1.2×10^7	—	2.2×10^{-10}	0.0027	—	—
<i>Neurospora crassa</i> (bread mold)	4.2×10^7	—	7.2×10^{-11}	0.0030	—	—
<i>Caenorhabditis elegans</i>	8.0×10^7	1.8×10^7	2.3×10^{-10}	0.018	0.004	0.036
<i>Drosophila melanogaster</i>	1.7×10^8	1.6×10^7	3.4×10^{-10}	0.058	0.005	0.14
Mouse	2.7×10^9	8.0×10^7	1.8×10^{-10}	0.49	0.014	0.9
Human	3.2×10^9	8.0×10^7	5.0×10^{-11}	0.16	0.004	1.6

Rates of mutation of individual base pairs are low but when summed over the entire genome the effect is considerable.

With 1.6 mutations per sexual generation in the effective genome, a population of 1 million humans will have 1.6 million new mutations in each generation. Although most will be deleterious or neutral, if only a small fraction were beneficial there would be considerable raw material for evolution.

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Mutations and Fitness



The effects of a mutation can vary among environments.

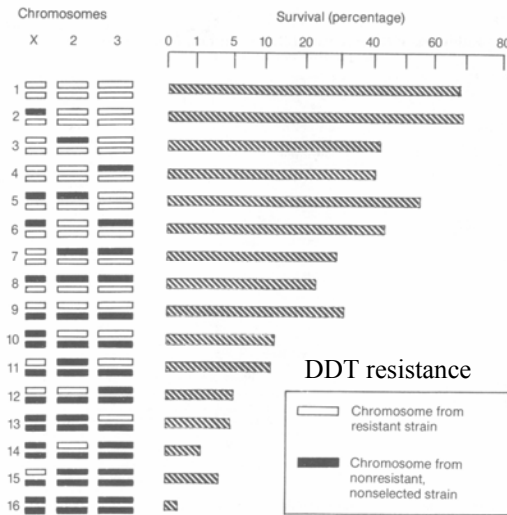
An allele that increases fitness in a cool environment may decrease fitness in a warm environment.

The sickle-cell allele confers high fitness to the heterozygote where malaria is common but is neutral in heterozygotes where malaria is not common.

Experiments with *Drosophila* showed that a mildly deleterious allele became up to 10 times more deleterious when populations were crowded and had fewer resources.

Thus, many alleles that have little or no effect on fitness in the current environment may be beneficial or harmful if the environment changes. For example, alleles for pesticide or antibiotic resistance may have little effect on fitness until the agent is applied. The same is likely true for many other mutations.

The effects of slightly beneficial mutations in different genes can be combined to produce more adaptive combinations.



Mutations in different individuals can be combined quickly in sexual species.

In asexual species combination of mutations depends upon multiple independent mutations within a genetic lineage.

Sex allows much faster adaptation through the rapid combination of slightly beneficial mutations. 19

Changes in **Karotype**

Karyotype - a description of the chromosomal constitution of and organism - number, size, shape, internal arrangement

Changes in ploidy - the number of sets of chromosomes

Aneuploidy - loss or gain of one or more chromosomes in a set - this is usually deleterious because of genic imbalance- Down's Syndrome in humans is the result of have 3 copies of chromosome 21 - trisomy 21

Polyploidy - having one or more extra sets of chromosomes
 2N - diploid, 3N - triploid, 4N - tetraploid, etc.

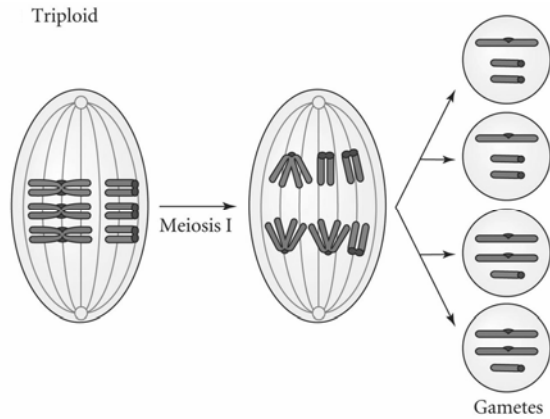
Polyloid organisms can have problems with meiosis.

An **autopolyploid** has multiple sets of chromosomes from the same species. An **allopolyploid** has multiple sets of chromosomes from different species.

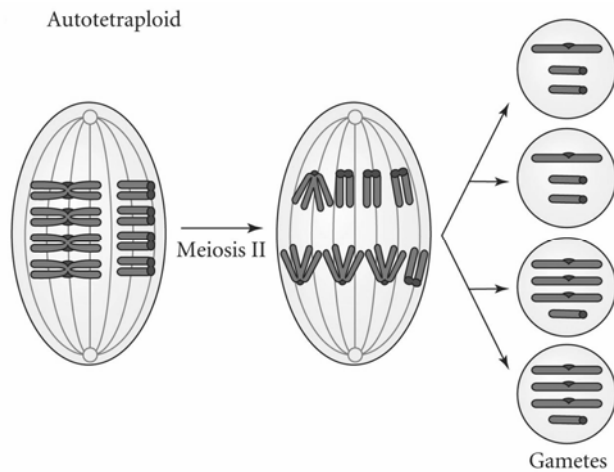
An odd number of each set of chromosomes results in problems with synapsis and segregation.

Many of the resulting cells receive an unbalanced (aneuploid) set of chromosomes.

Aneuploid gametes produce aneuploid zygotes that usually have problems because of genic imbalance.

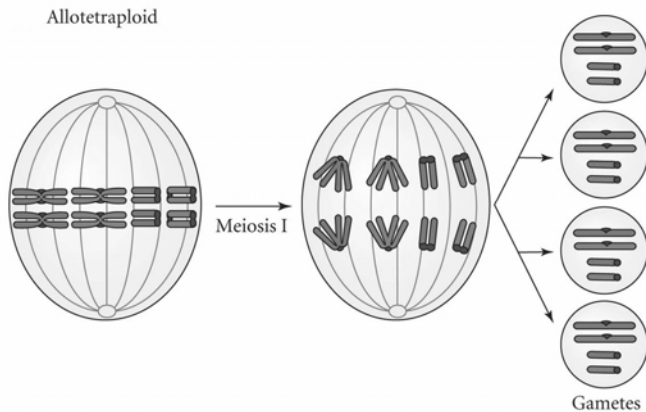


Autopolyploids with even numbers of chromosomes can also produce aneuploid gametes.



Hybrid organisms receive two different sets of chromosomes, one from each parent species. They are usually sterile because differences in gene arrangements among chromosomes results in improper synapsis and aneuploid gametes.

Duplication of whole sets of chromosomes (allopolyploidy) may result in gametes that can produce balanced sets of chromosomes.



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Allopolyploids with a diploid number of sets of chromosomes from each parent ($2N_A + 2N_B$) produce gametes that are euploid with one set of chromosomes from each parent ($N_A + N_B$).

Such organisms are potentially interfertile or self-fertile but they can't produce fertile offspring in backcrosses with either parent species.

Gamete ($N_A + N_B$) combined with gamete (N_A) produces an allotriploid ($2N_A + N_B$) that produces unbalanced sets of genes in gametes.

Thus, allopolyploids are reproductively isolated from each of their parent species. They can only reproduce with other allopolyploids or through self-fertilization. They are new species as soon as they are formed.

Many species of plants and some animals are polyploid. At least 50% of all flowering plants are polyploid.

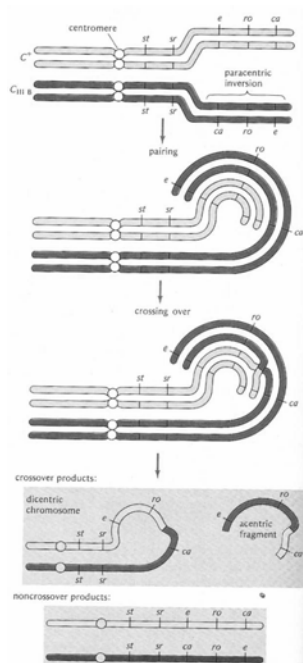
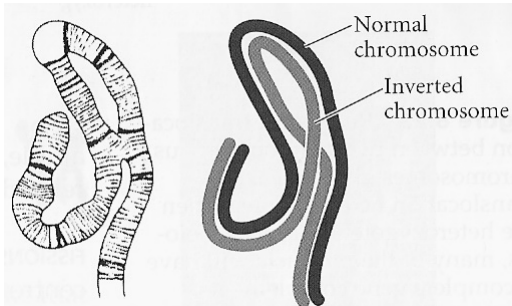
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Chromosome rearrangements

Breakage and reunion of chromosomes can change gene order or change the distribution of genes among chromosomes. Such changes generally have little or no effect on the phenotype of the organism. Some rearrangements can have effects on the frequency of recombination and fertility.

An inversion of gene order: ABCDEFG \longrightarrow ABEDCFG

results in a loop arrangement in the chromosomes during synapsis

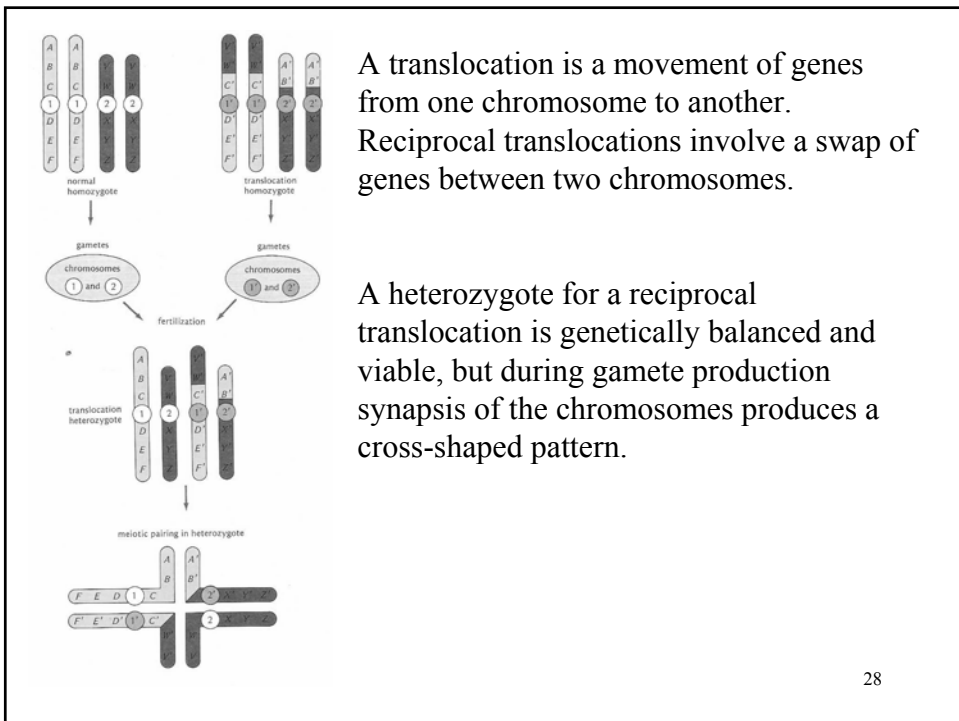
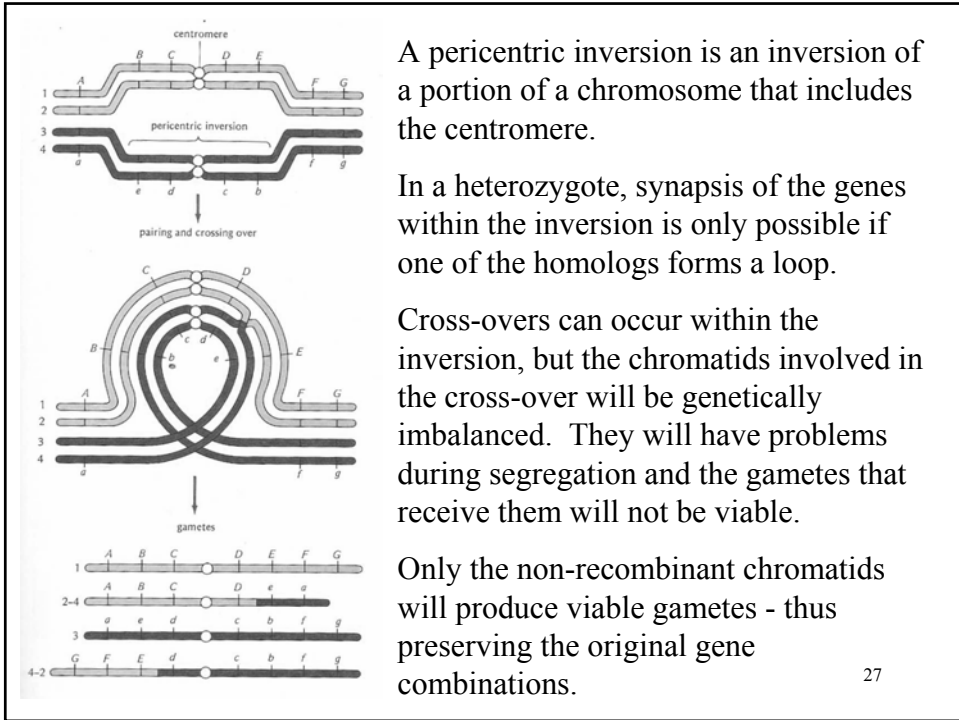


A paracentric inversion is an inversion of a portion of a chromosome that does not include the centromere.

In a heterozygote, synapsis of the genes within the inversion is only possible if one of the homologs forms a loop.

Cross-overs can occur within the inversion, but the chromatids involved in the cross-over will be genetically imbalanced and either be dicentric or acentric. They will have problems during segregation and the gametes that receive them will not be viable.

Only the non-recombinant chromatids will produce viable gametes - thus preserving the original gene combinations.



translocation heterozygote

segregation at first meiotic division

gametes: no duplications or deficiencies

(a) Alternate segregation

gametes: no duplications or deficiencies

gametes: duplications [A, B], deficiencies [Y, Z]

(b) Adjacent-1 segregation

gametes: duplications [Y, Z], deficiencies [A, B]

gametes: duplications [C, D, E, F], deficiencies [X, Y, Z]

(c) Adjacent-2 segregation

gametes: duplications [X, Y, Z], deficiencies [C, D, E, F]

At anaphase centromeres are pulled to opposite poles. There are three possible ways the centromeres can associate - alternate, adjacent-1, and adjacent-2.

Only alternate segregation will result in genetically balanced gametes.

Thus, the only viable gametes from a translocation heterozygote will have chromosomes identical in genetic constitution to the sets received from its parents.

Thus, translocation heterozygotes will not exhibit independent assortment of these pairs of chromosomes. This also preserves gene combinations.

Translocation heterozygotes are partially sterile and this may form the basis for partial post-zygotic isolation between closely related species.

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Chromosome number can change through fission or fusion of chromosomes or pieces of chromosomes.

Breaks

A B

A' + B'

Dot

2 acrocentrics

Metacentric

(a) Fusion

C D

C' + D'

Dot

Metacentric

2 acrocentrics

(b) Dissociation

Break in centromere

E F

E' + F'

Metacentric

2 telocentrics

(b) Fission

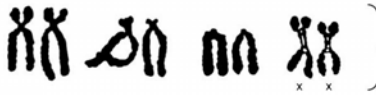
Karyotypic changes through fission and fusion can be dramatic.

Such changes can be the cause of reproductive isolation between related species.

Muntiacus reevesii (2N = 46)



Muntiacus muntiacus (2N = 8)



Indian muntjac
Muntiacus muntjak



The karyotypes of primates differ by gene rearrangements within chromosomes (as shown by banding patterns) and difference in chromosome number due to fusion or fission of chromosomes.

