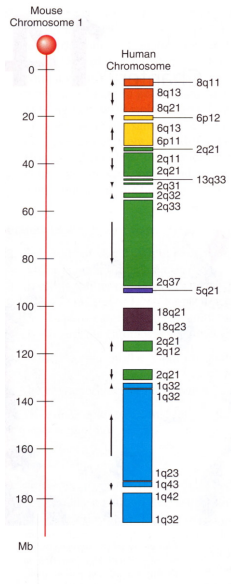
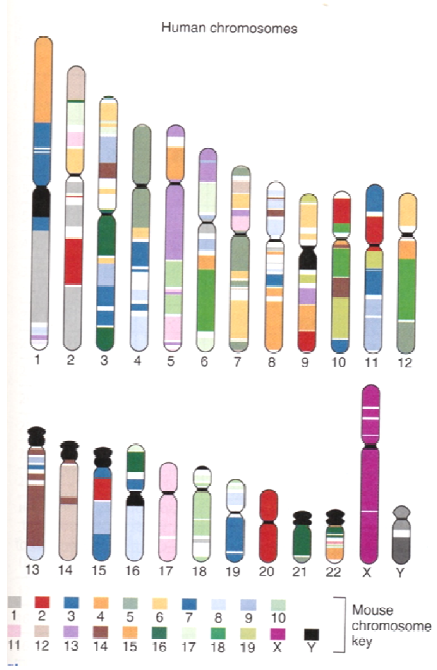
Changes in Chromosome Structure





structural rearrangements of chromosomes

changes in gene number

deletions abcedfghi ⟶ abcghi

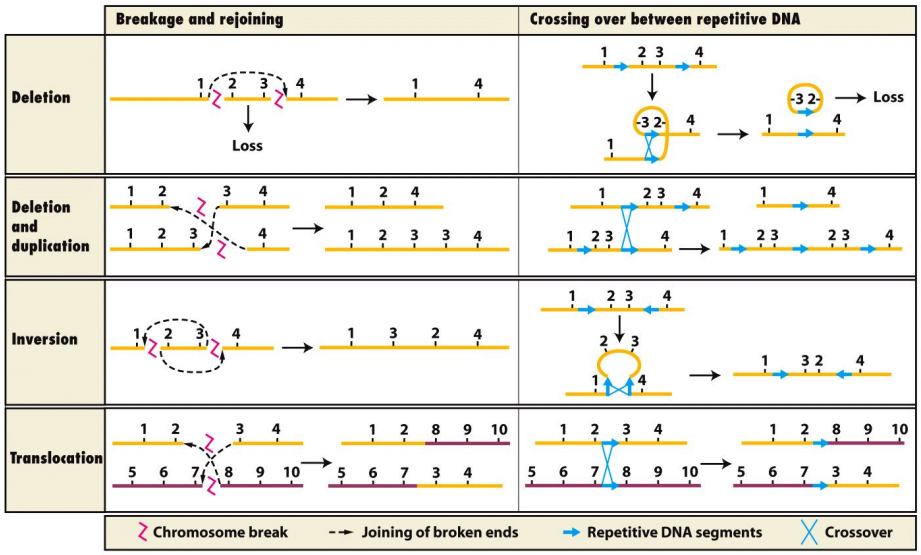
duplications abcdefghi ⟶ abcdefdefghi

changes in gene order

inversions abcdefghi ⟶ abcgfedhi

translocations abcde ⟶ abcihg

ghijkl ⟶ edjkl



Deletions

genetic effects

1) unique phenotypes
   ex. Notch
   deletion on X-chromosome in *Drosophila*

2) lethality

genotype	phenotype
$\frac{N+}{N}$	*Notch* female
$\frac{N}{N}$	lethal
$\frac{N}{\diagup}$	lethal

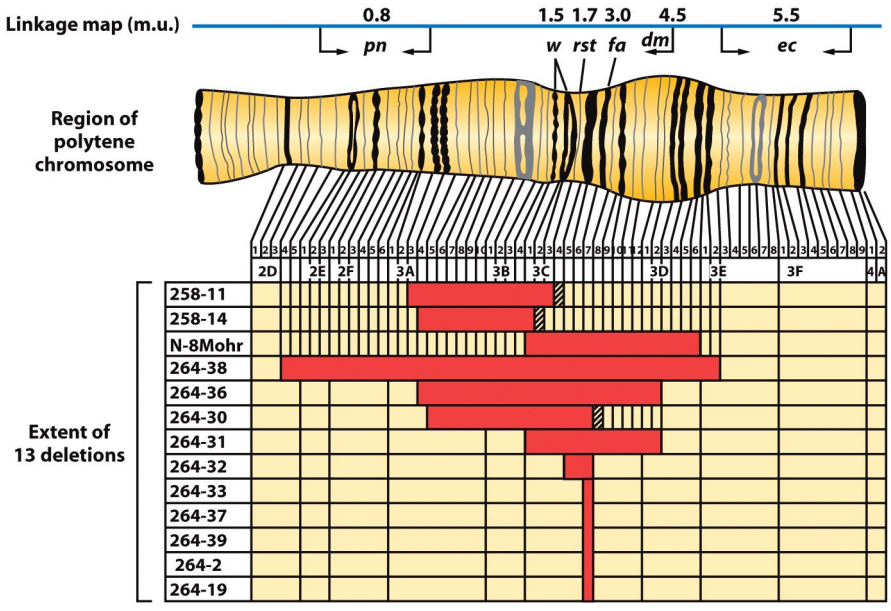
genetic effects of deletions

3) pseudodominance - expression of a recessive trait in an individual heterozygous at that locus

genotype	phenotype
$\frac{N^+}{N}$	*Notch* female
$\frac{N}{N}$	lethal
$\frac{N}{}$	lethal
$\frac{N^+w}{N(w^+)^*}$	*Notch*, *white* female
$\frac{N^+fa\ spl}{N(fa^+\ spl^+)^*}$	*Notch*, *facet*, *split* female

*deleted region

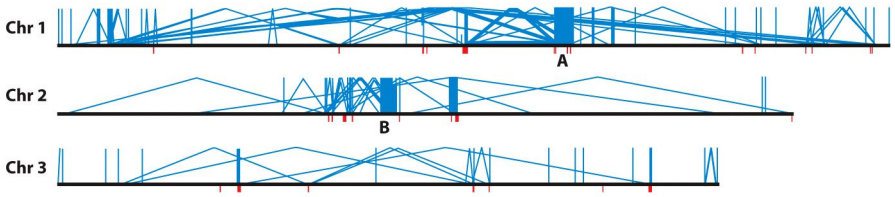
deletion mapping



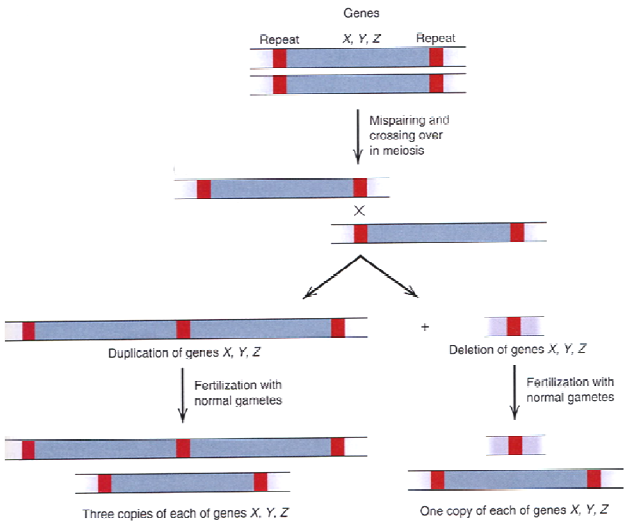
Gene Duplications

non-reciprocal recombination (one duplication, one deletion)

tandem (a bc bc bc bc def)
or insertional



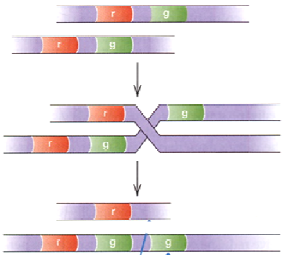
nonreciprocal recombination leads to copy number variants



red-green colorblindness is produced by unequal crossing-over

red, green opsin genes on X-chromosome

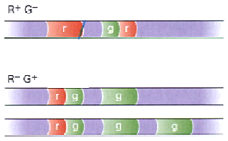
unequal crossing over produces deletions and duplications



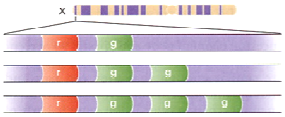
del_{green}

dpl_{green}

crossing-over within the genes produces defects in red-green perception



copy number variants (CNVs)



Underdeveloped		Normal development		Overdeveloped
Absent or delayed speech	←	Language	→	Auditory hallucinations
Reduced sense of self	←	Sense of self	→	Delusions of grandeur: Megalomania
Impaired mentalistic skill	←	Mentalistic skill	→	Delusions of conspiracy: Paranoia
Basic emotions	←	Social emotionality	→	Depression, elation
Challenged in verbal logic	←	Logical, analytic skill	→	Twisted logic
Limited goal pursuit	←	Complex, regulated goal pursuit	→	Obsessive goal pursuit: Mania
Symptoms associated with autism spectrum disorder				Symptoms associated with schizophrenia

	autism spectrum		schizophrenia		
CNV region	deletion	duplication	deletion	duplication	p value
1q21.1	2	10	15	4	0.001
16p11.2	14	5	5	24	0.0001
22q11.21	1	8	16	1	0.00005
22q13.3	5	0	0	4	0.008

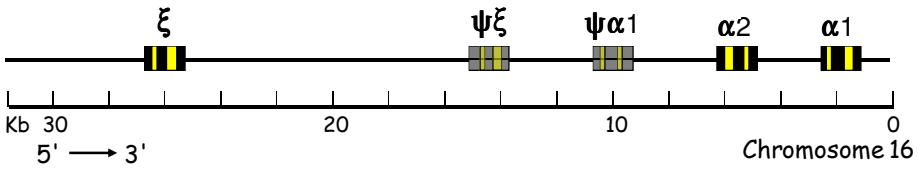
Crespi et al 2010 PNAS 107:1736

Outcome of duplication events

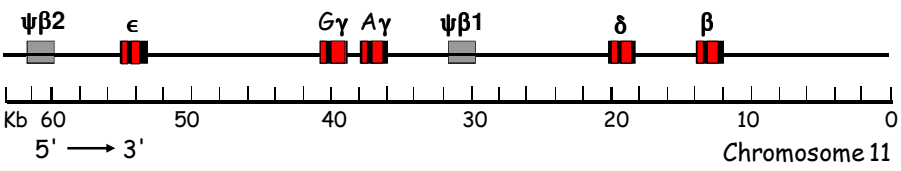
1) pseudogene

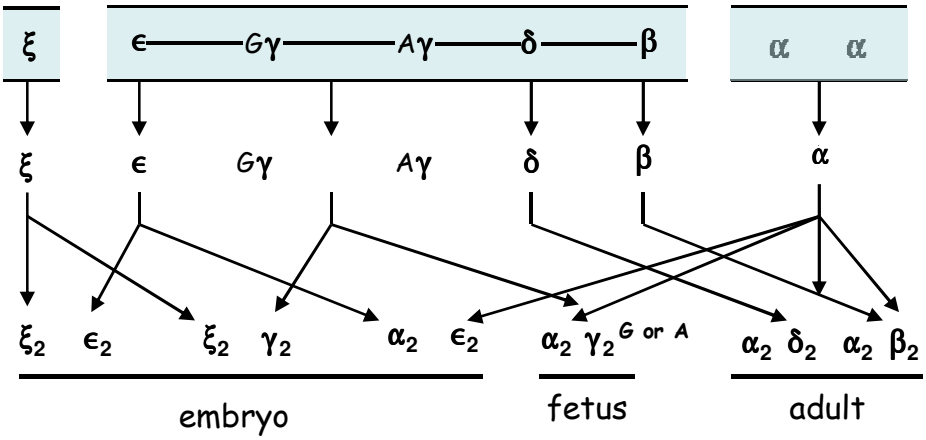
2) gene families ⟶ specialization
(e.g., globin genes)

α-like globin gene cluster



β-like globin gene cluster





Family	number of duplicate genes
Common proteins	
Actins	5 - 30
tubulins (α and β)	5 - 15
myosin, heavy chain	5 - 10
histones	100 - 1000
keratins	>20
heat shock proteins	3
Insects	
eggshell proteins	>50
Vertebrates	
globins - α	1 - 3
- β-like	≥50
ovalbumin	3
vitellogenin	5
immunoglobulins	>500
transplantation antigens	50 - 100

Outcome of duplication events

1) pseudogene

2) gene families ⟶ specialization
(e.g., globin genes)

3) novel function

Phopholipase A_2 Genes: Snake Venom


Group I pancreatic enzyme ⟶ antiplatelet ⟶ neurotoxin


Group II inflammatory response ⟶ myotoxins




deletions and duplications

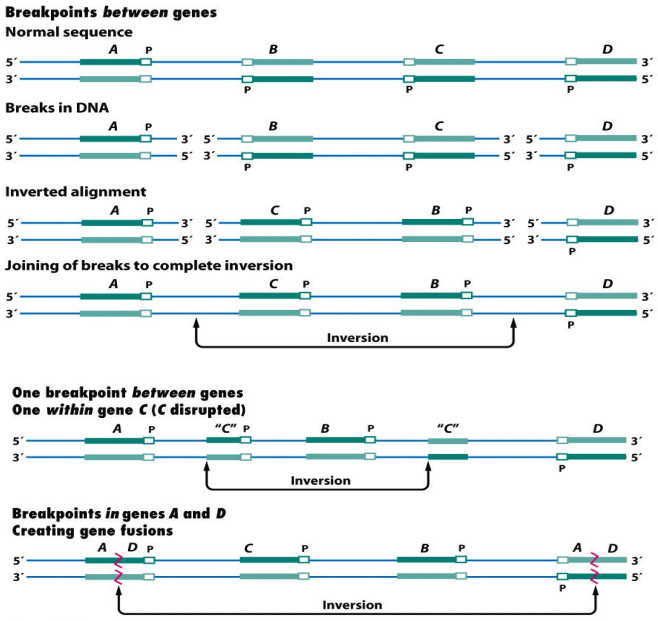
alter number of genes present on chromosome

may change the phenotype of a heterozygote
--changes in amount of product

phenotypic effects are usually additive

alteration of gene location may modify expression

Inversions



Inversions

pericentric – inverted region includes centromere

abc•def ⟶ aed•cbf

paracentric – inversion outside of centromere

ab• cdefg ⟶ ab • cfedg

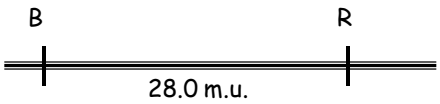
detect genetically (heterozygotes)

somewhat lower fertility

reduced levels of recombinant progeny

Mediterranean fruit fly
body color: black (B-), gray (bb)
eye shape: round (R-), star (rr)

Cross	F_1	Testcross Offspring	
BR/BR (California) x br/br (California)	BR/br	BR/br	36%
		br/br	36
		Br/br	14
		bR/br	14
BR/BR (Chile) x br/br (Chile)	BR/br	BR/br	36%
		br/br	36
		Br/br	14
		bR/br	14

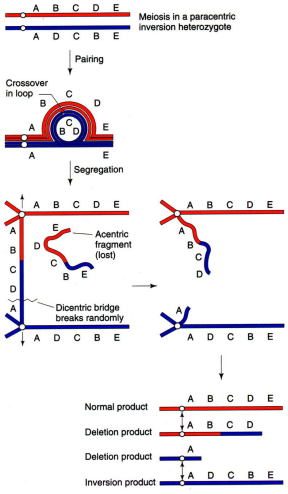


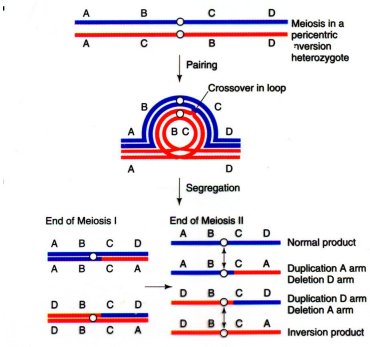
Mediterranean fruit fly
body color: black (B-), gray (bb)
eye shape: round (R-), star (rr)

Cross	F1	Testcross Offspring	
BR/BR (California) x br/br (California)	BR/br	BR/br br/br Br/br bR/br	36% 36 14 14
BR/BR (Chile) x br/br (Chile)	BR/br	BR/br br/br Br/br bR/br	36% 36 14 14
BR/BR (California) x br/br (Chile)	BR/br	BR/br br/br Br/br bR/br	48% 48 2 2
or reciprocal			

detection of inversions in heterozygotes

reduced levels of recombinant progeny
- reduced precision of pairing
- recombinant chromosomes are fragments
and/or carry large deletions/duplications





Inversions, con't

detect genetically (heterozygotes)

somewhat lower fertility

reduced levels of recombinant progeny*

- reduced precision of pairing

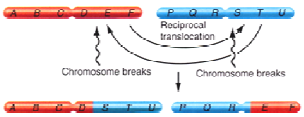
- recombinant chromosomes are fragments and/or carry large deletions/duplications

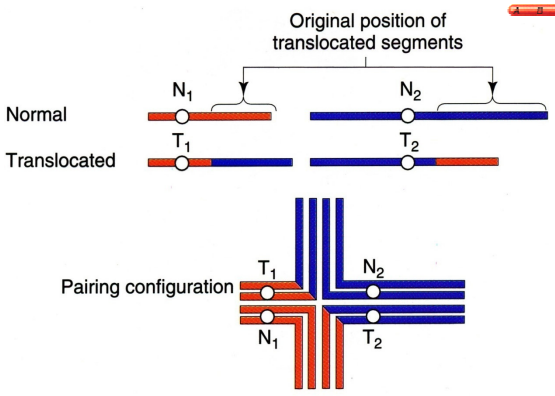
maintenance of particular combinations of alleles at different loci

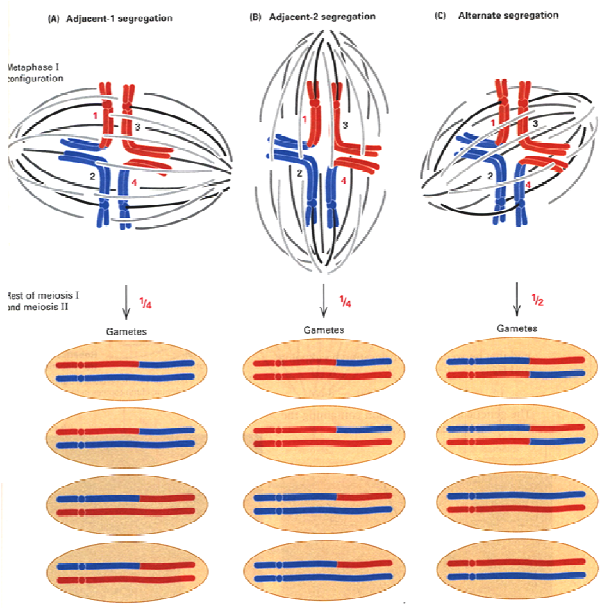
Translocations

breakage and exchange of sections between non-homologous chromosome

reciprocal*, non-reciprocal







Translocations, con't

detect genetically

severely reduced fertility

cosegregation of genes
known to be on different chromosomes

reduced recombination

changes in phenotype

inversions and translocations

change the spatial arrangement of genes

often, no change in gene expression, phenotype

affect gene function, phenotype
if rearrangement breakpoint lies within a gene

rearrangement may modify gene expression

suppress recombination,
maintain combinations of alleles across loci

Take-home points

chromosome structure may vary in a manner analogous to allelic variation within a gene; they can be studied by cytogenetic, genetic, and molecular methods

there is no "best" arrangement of genes: standard, like wild type, refers to the most common arrangement, particularly in a well-studied lab strain

deletions and duplications change the number of genes present but not the order; all rearrangements change the spatial arrangement of genes; changing the location of a gene can affect phenotypic expression

duplications can lead to diversification of gene function; they are important for genome evolution

inversions maintain specific combinations of alleles across loci

Changes in chromosome number

aneuploidy - single chromosome/single homologous pair

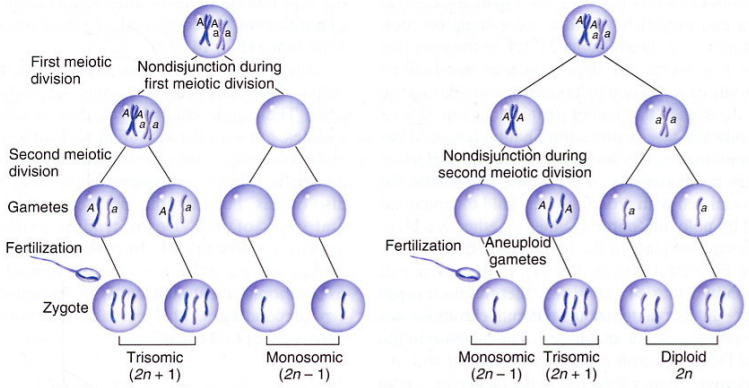
polyploidy - entire haploid complement

both associated with large changes in phenotype
because a large number of genes is involved

Aneuploidy

duplication/loss of one/both members
of a homologous pair of chromosomes

non-disjunction in meiosis



Aneuploidy

duplication/loss of one/both members of a homologous pair

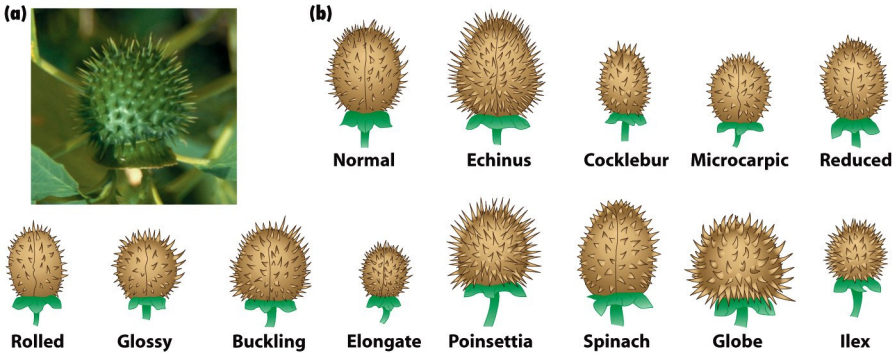
non-disjunction in meiosis

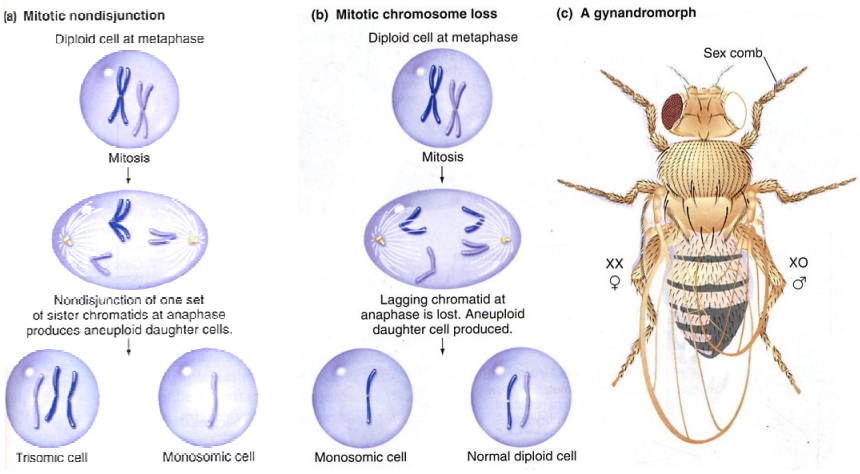
loss of both members of a homologous pair is always lethal

loss or gain of one chromosome may be lethal

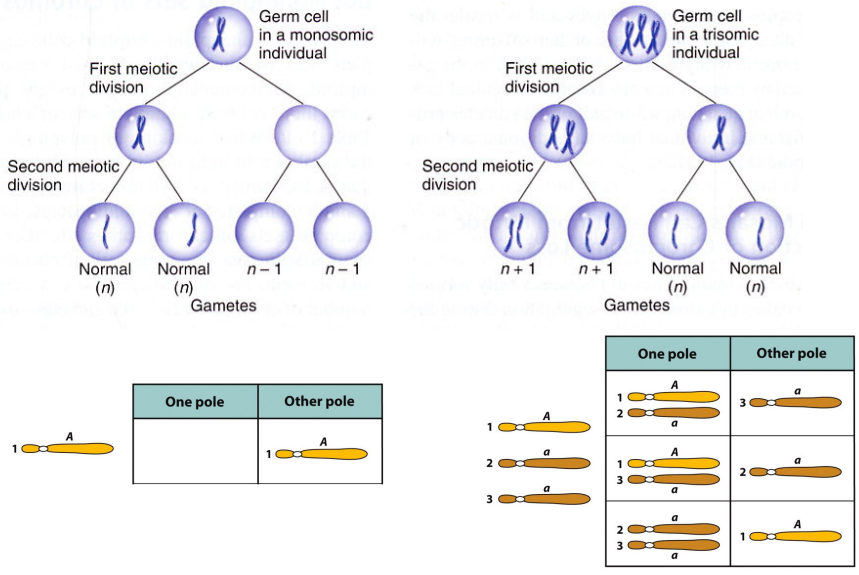
- deleterious balance of gene products
  (duplication/deletion of many genes)
- pseudodominance of an entire chromosome

trisomics of *Datura*





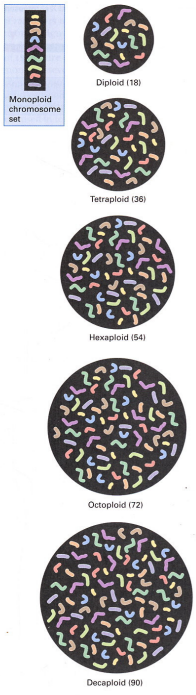
aneuploid individuals produce aneuploid gametes

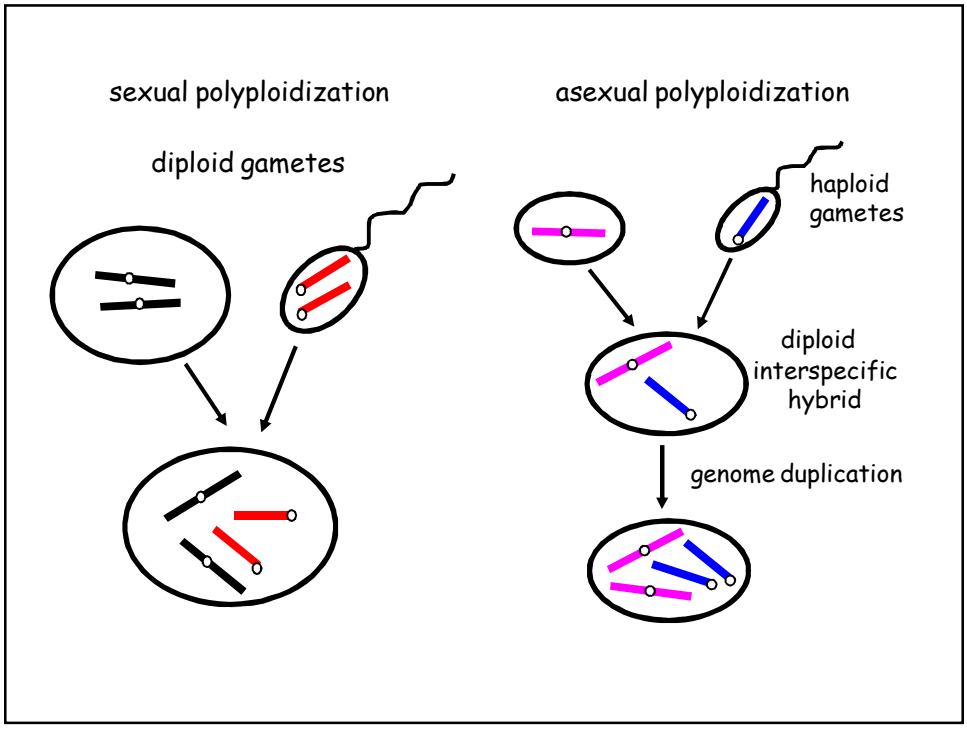


	100,000 PREGNANCIES	
	15,000 spontaneous abortions 7,500 chromosomally abnormal	85,000 live births 550 chromosomally abnormal
Trisomy		
1	0	0
2	159	0
3	53	0
4	95	0
5	0	0
6–12	561	0
13	128	17
14	275	0
15	318	0
16	1229	0
17	10	0
18	223	13
19–20	52	0
21	350	113
22	424	0
Sex chromosomes		
XYY	4	46
XXY	4	44
XO	1350	8
XXX	21	44

Polyploidy

- duplication or loss of one or both entire haploid sets of chromsomes

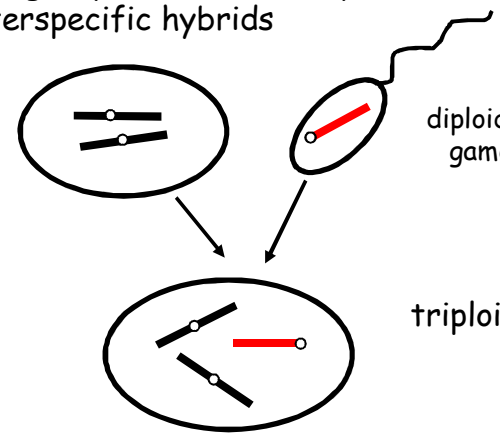




Polyploidy

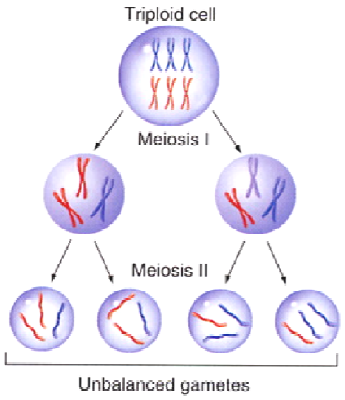
triploids (3n) ⟶ fusion of diploid and haploid gametes

common in some groups of fish and reptiles, often interspecific hybrids



Polyploidy

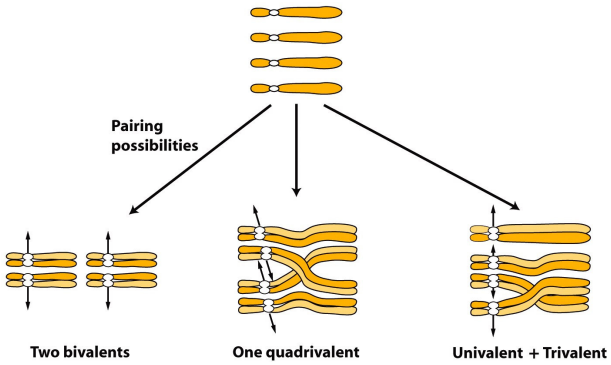
triploids (and other odd-numbered haploid sets):
- often sterile
- chromosomal pairing/segregation during meiosis
- aneuploid gametes
- asexual reproduction is common



pr(haploid gamete) = $(\frac{1}{2})^{n-1}$

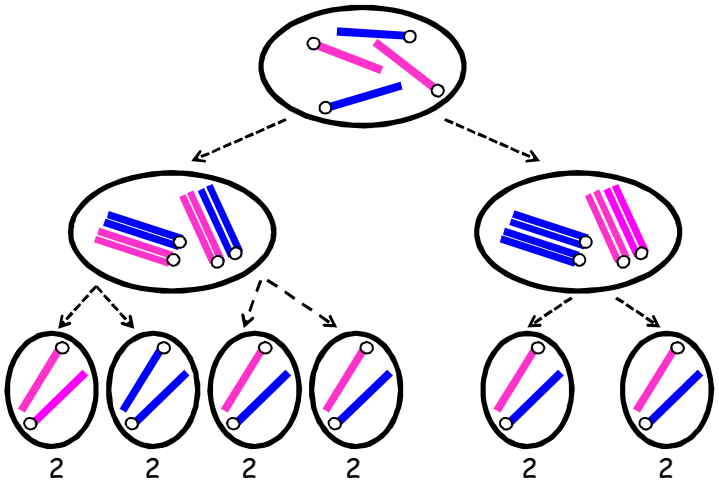
Polyploidy

tetraploids (and other even numbered sets):
- normal pairing of homologs during meiosis
- usually normal segregation
- usually fertile



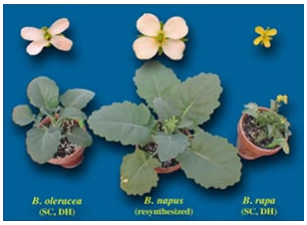
Polyploidy

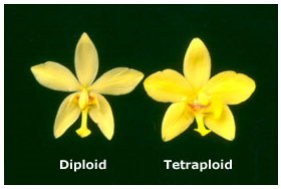
tetraploids (and other even numbered sets):
diploid gametes ⟶ tetraploid or triploid offspring

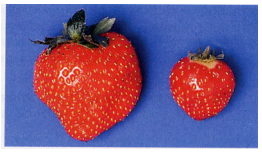


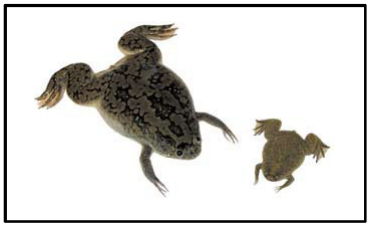
Polyploidy

tetraploids:
often more vigorous (or larger) than parental species



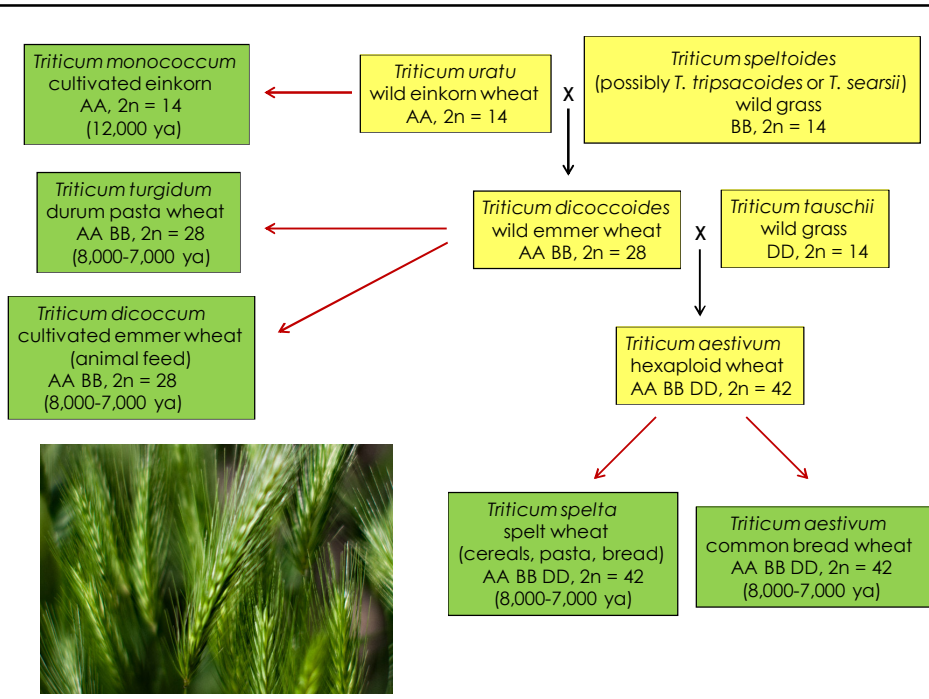






polyploidy is important in two contexts

- agricultural manipulations that generate new crops



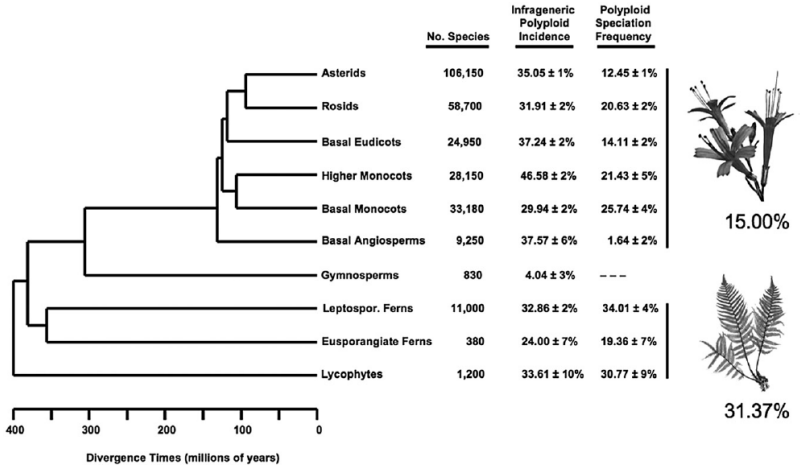
polyploidy is important in two contexts

- agricultural manipulations that generate new crops

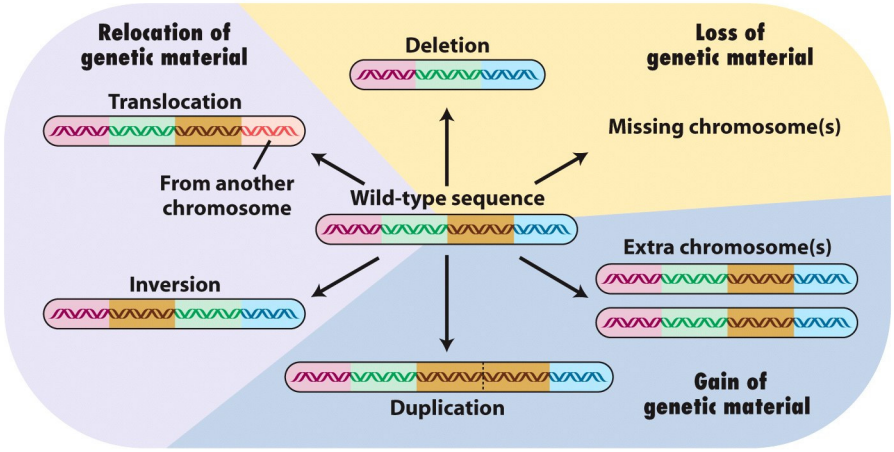
- speciation, especially of plants

Synthetic polyploids of *Tragopogon miscellus* (left) and *T. mirus* (right)
When A is the parent progeny C-F result but when B is the parent progeny G-J are produced.
From Tate *et al.* 2009. American Journal of Botany 96: 979-988.

polyploidy drives speciation in plants



Types of chromosome changes



Take-home points

number changes can involve the gain or loss of a single homolog (aneuploidy) or an entire haploid genome (polyploidy)

both types of changes arise from nondisjunction during meiosis

aneuploidy virtually always has severe, deleterious phenotypic consequences

polyploids may experience difficulty during meiosis and be sterile (e.g. triploids) or potentially be more vigorous than diploid relatives (allotetraploids)

ploidy changes have been important in crop development and in the origin of new species