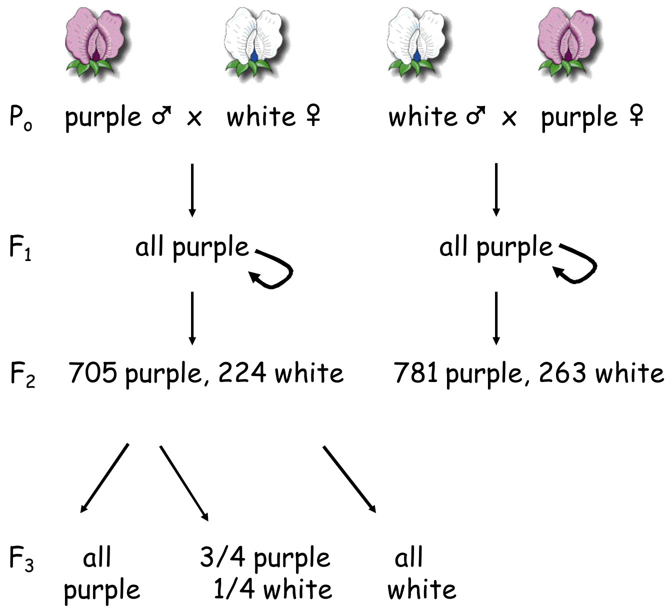
Outline

- segregation of alleles in single trait crosses
- independent assortment of alleles
- using probability to predict outcomes
- statistical analysis of hypotheses
- conditional probability in multi-generation data
- mitosis
- meiosis



P_o purple ♂ x white ♀ white ♂ x purple ♀

F_1 all purple all purple

F_2 705 purple, 224 white 781 purple, 263 white

F_3 all purple 3/4 purple 1/4 white all white

P_o purple ♂ x white ♀

PP pp

F_1 all purple

Pp

F_2 705 purple, 224 white

PP Pp pp

F_3 all purple | 3/4 purple 1/4 white | all white

P_0 is homozygous

F_1 is heterozygous

phenotype of F_1 is dominant, rare phenotype in F_2 is recessive

↓

the allele for purple is dominant to the allele for white

Pp x Pp

	P	p
P	PP	Pp
p	Pp	pp

1 PP: 2 Pp: 1 pp

3 purple :1 white

P_o purple ♂ x white ♀
PP **pp**

↓

F_1 all purple ↻
Pp

↓

F_2 705 purple, 224 white
PP **Pp** **pp**

↙ ↘ ↘

F_3 all purple | 3/4 purple 1/4 white | all white

test cross:

F_1 x recessive parent

↓

½ purple, ½ white

---

single-gene phenotypic ratios

phenotype dist^n	parent genotypes
1 "A" :0 "a"	AA x aa AA x AA AA x Aa
3 "A" :1 "a"	Aa x Aa
1 "A" :1 "a"	Aa x aa

Mendel's law of independent assortment:

two independent traits (dihybrid cross):

P_0 purple tall x white short
P/P T/T p/p t/t

F_1 purple tall
P/p T/t

F_2	purple tall	purple short	white tall	white short
	315	108	101	32
	P/- T/-	P/- t/t	p/p T/-	p/p t/t

---

two independent traits (dihybrid cross):

P_0 purple tall x white short
P/P T/T p/p t/t

F_1 purple tall
P/p T/t

F_2	purple tall	purple short	white tall	white short
	315	108	101	32
	P/- T/-	P/- t/t	p/p T/-	p/p t/t

*look at traits individually in the F_2:

purple: white	423:133	3:1
tall: short	416:140	3:1

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Using probability to predict genetic transmission ratios

when outcomes are independent, multiply the individual probabilities

$$\boxed{\text{pr(a and b)} = \text{pr(a)} \times \text{pr(b)}}$$

when outcomes are equivalent, add the individual probabilities

$$\boxed{\text{pr(a or b)} = \text{pr(a)} + \text{pr(b)}}$$

conditional probability: only a subset of outcomes are relevant

$$\text{if } \boxed{\text{pr(a)} + \text{pr(b)} + \text{pr(c)}} + \text{pr(d)} = 1$$

$$\text{then pr(a or b)} = [\text{pr(a)} + \text{pr(b)}]/[1 - \text{pr(d)}]$$

F_2	purple tall	purple short	white tall	white short
	315	108	101	32
	P/- T/-	**P/- t/t**	**p/p T/-**	**p/p t/t**

*look at traits individually in the F_2:

purple: white	423:133	3:1
tall: short	416:140	3:1

two separate traits = independent outcomes

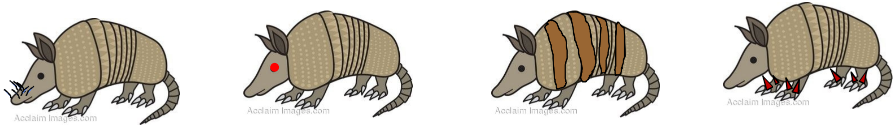
ex: $\text{pr (PP, TT)} = \text{pr (PP)} \times \text{pr (TT)} = \frac{1}{4} \times \frac{1}{4} = 1/16$

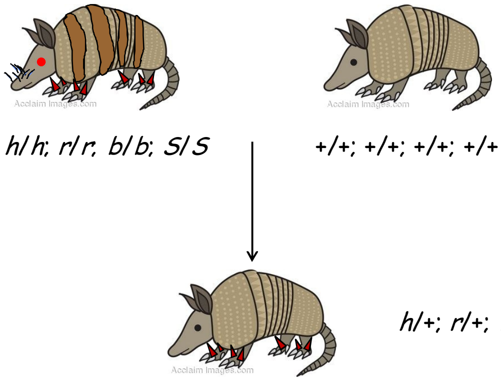
$$
\begin{aligned}
\text{pr (PP, T/t)} &= \text{pr (PP)} \times \text{pr (tT } \underline{\text{or}} \text{ Tt)} \\
&= \text{pr (PP)} \times [\text{pr (tT)} + \text{pr (Tt)}] \\
&= \tfrac{1}{4} \times [\tfrac{1}{4} + \tfrac{1}{4}] = \tfrac{1}{4} \times \tfrac{1}{2} = 1/8
\end{aligned}
$$

$$
\begin{aligned}
\text{pr (purple, tall)} &= \text{pr (purple)} \times \text{pr (tall)} \\
&= \text{pr (P/-)} \times \text{pr (T/-)} \\
&= \tfrac{3}{4} \times \tfrac{3}{4} = 9/16
\end{aligned}
$$

---

hairy snout (*h*) red eyes (*r*) banded body (*b*) spiny paws (*S*)

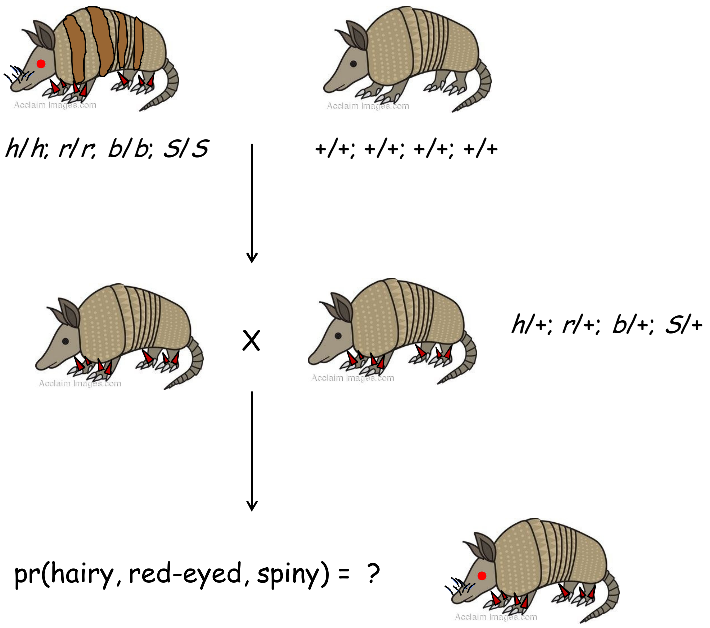




h/*h*; *r*/*r*; *b*/*b*; *S*/*S*

+/+; +/+; +/+; +/+

h/+; *r*/+; *b*/+; *S*/+



h/h; r/r; b/b; S/S

+/+; +/+; +/+; +/+

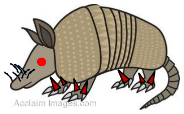
X

h/+; r/+; b/+; S/+

pr(hairy, red-eyed, spiny) = ?

---

pr(hairy, red-eyed, spiny) = ?



= pr(h/h; r/r; S/-)

= pr(h/h) x pr(r/r) x pr(S/-)

= $\frac{1}{4} \times \frac{1}{4} \times \frac{3}{4}$

= 3/64

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---

when do the data meet mendelian expectations?

if cross two heterozygotes,
expect 3:1 phenotypic ratio in offspring

-how closely do the numbers need to match???

-importance of statistical analysis

Chi-square tests: goodness-of-fit to mendelian ratios

See also pp. 47 - 50 in text

Some examples:

observed		expected	
short	long	short	long
118	42	120	40
28	9	27.75	9.25
46	16	45.75	15.25

all are approximately 3:1, but none is <u>exact</u>

for the sample size, how unlikely is result?

Compare observed and expected numbers with a goodness of fit chi-square test with n-1 degrees of freedom

$$\chi^2_{dof} = \sum \frac{(\text{observed number} - \text{expected number})^2}{(\text{expected number})}$$

dof = degrees of freedom
= number of independent classes
= number of classes - 1

observed		expected	
short	long	short	long
118	42	120	40
28	9	27.75	9.25
46	16	45.75	15.25

$$\chi^2_1 = \frac{(118 - 120)^2}{120} + \frac{(42 - 40)^2}{40}$$

$$= 0.033 + 0.1$$

$$= 0.133$$

---

scientific method -- reject null hypothesis

H_0: data fit a 3:1 ratio consistent with heterozygous parents

statistics: test how well data fit hypothesis

two possible outcomes:

- correct inference
- incorrect inference
  - --reject H_0 that is true
  - --accept H_0 that is false

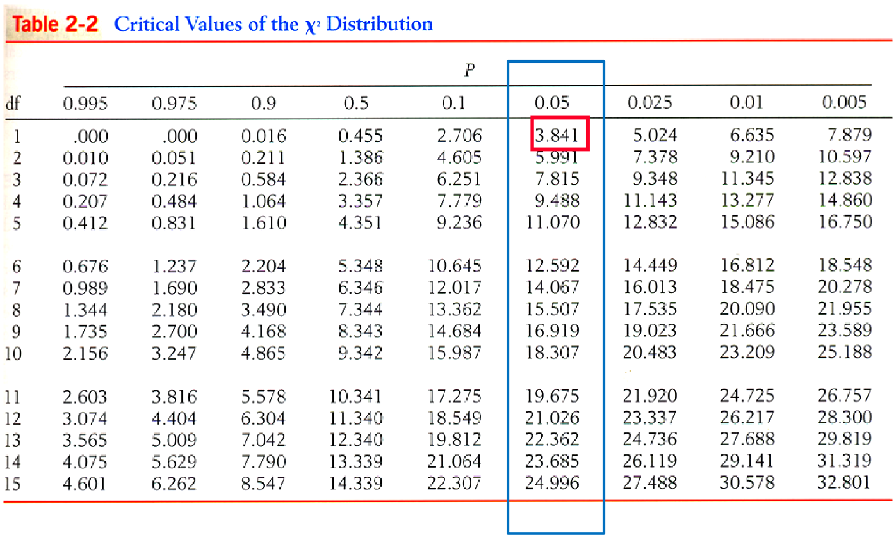


Table 2-2 Critical Values of the χ^2 Distribution

	P								
df	0.995	0.975	0.9	0.5	0.1	0.05	0.025	0.01	0.005
1	.000	.000	0.016	0.455	2.706	3.841	5.024	6.635	7.879
2	0.010	0.051	0.211	1.386	4.605	5.991	7.378	9.210	10.597
3	0.072	0.216	0.584	2.366	6.251	7.815	9.348	11.345	12.838
4	0.207	0.484	1.064	3.357	7.779	9.488	11.143	13.277	14.860
5	0.412	0.831	1.610	4.351	9.236	11.070	12.832	15.086	16.750
6	0.676	1.237	2.204	5.348	10.645	12.592	14.449	16.812	18.548
7	0.989	1.690	2.833	6.346	12.017	14.067	16.013	18.475	20.278
8	1.344	2.180	3.490	7.344	13.362	15.507	17.535	20.090	21.955
9	1.735	2.700	4.168	8.343	14.684	16.919	19.023	21.666	23.589
10	2.156	3.247	4.865	9.342	15.987	18.307	20.483	23.209	25.188
11	2.603	3.816	5.578	10.341	17.275	19.675	21.920	24.725	26.757
12	3.074	4.404	6.304	11.340	18.549	21.026	23.337	26.217	28.300
13	3.565	5.009	7.042	12.340	19.812	22.362	24.736	27.688	29.819
14	4.075	5.629	7.790	13.339	21.064	23.685	26.119	29.141	31.319
15	4.601	6.262	8.547	14.339	22.307	24.996	27.488	30.578	32.801

---

observed		expected	
short	long	short	long
118	42	120	40
28	9	27.75	9.25
46	16	45.75	15.25

$$\chi^2_1 = \frac{(118 - 120)^2}{120} + \frac{(42 - 40)^2}{40}$$

$$= 0.033 + 0.1$$

$$= 0.133 \qquad p > 0.5$$

reject only if $p < 0.05$

Forward genetics

choose a phenotype of interest

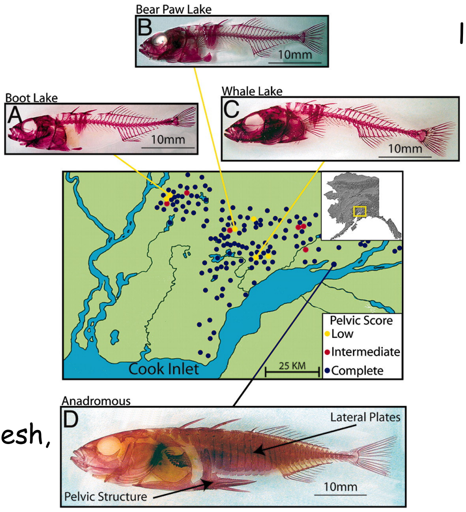
↓

find variants of that phenotype

↓

check variants for single gene inheritance

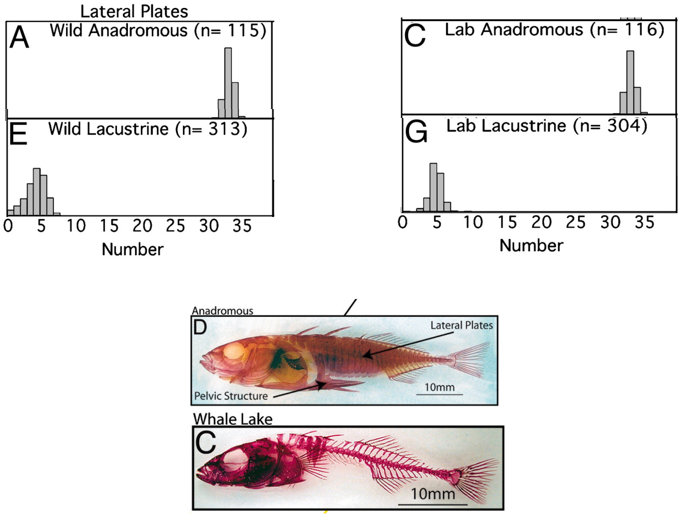
Inheritance of lateral plate armour in sticklebacks



lacustrine =
lake-dwelling

anadromous =
born/breed in fresh,
marine juveniles

Cresko, William A. et al. (2004) Proc. Natl. Acad. Sci. USA 101, 6050-6055



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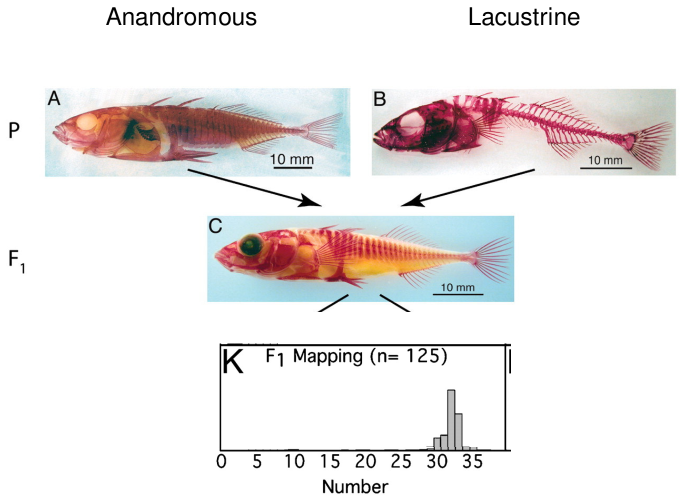
PNAS



Cresko, William A. et al. (2004) Proc. Natl. Acad. Sci. USA 101, 6050-6055

PNAS

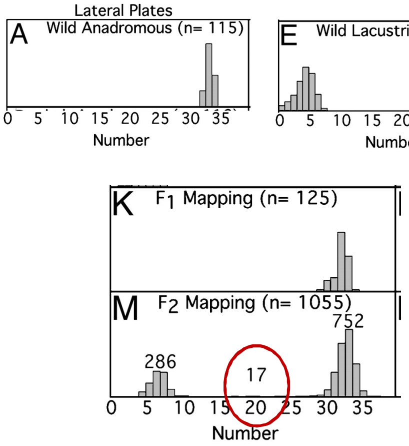
anadromous × lacustrine

↓

anandromous

↓

752 anandromous
286 lacustrine



Cresko, William A. et al. (2004) Proc. Natl. Acad. Sci. USA 101, 6050-6055

PNAS

---

observed		expected	
anandromous	lacustrine	anandromous	lacustrine
752	303	791.25	263.75

$$\chi^2_1 = \frac{(752 - 791.25)^2}{1055} + \frac{(303 - 263.75)^2}{1055}$$

$$= 1.4602 + 1.4602$$

$$= 2.92, \quad 0.1 > p > 0.05$$

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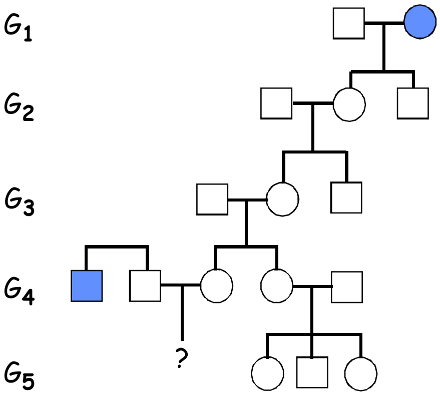
---

tranmission probabilities with multiple generations

galactosemia is an autosomal recessive disease (gg)

expectant couple: husband’s brother had galactosemia; wife’s great-grandmother had galatosemia; wife’s sister has 3 children, none have disease



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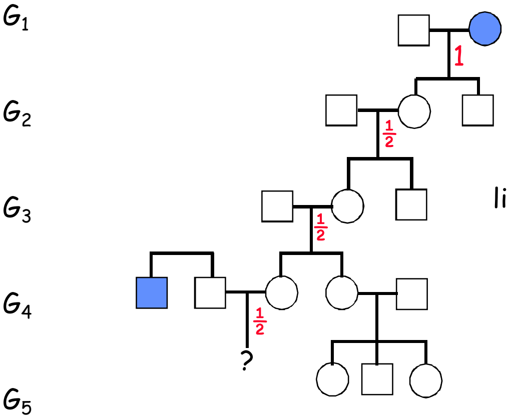


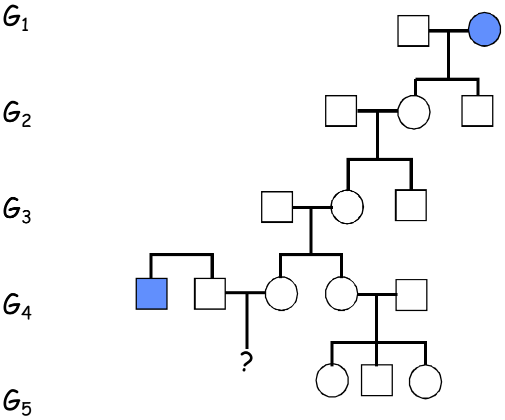
likelihood from maternal side:
$(\frac{1}{2})^3 = 1/8$

---

tranmission probabilities with multiple generations

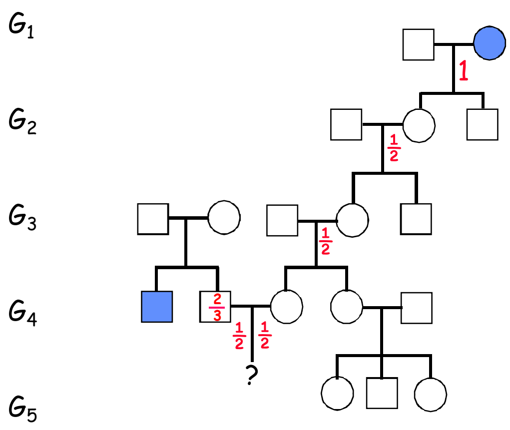
galactosemia is an autosomal recessive disease (gg)

expectant couple: husband's brother had galactosemia; wife's great-grandmother had galatosemia; wife's sister has 3 children, none have disease



pr(maternal transmission)
= 1/8

pr(father is Gg) = ??



pr(father is Gg) = ??

normal phenotype:
GG or Gg

genotype:
GG
Gg
gG

pr(Gg) = 2/3

pr(child) = pr(father transmits allele) x pr(mother transmits allele)
= (1/3) x (1/8)
= 1/24

Outline

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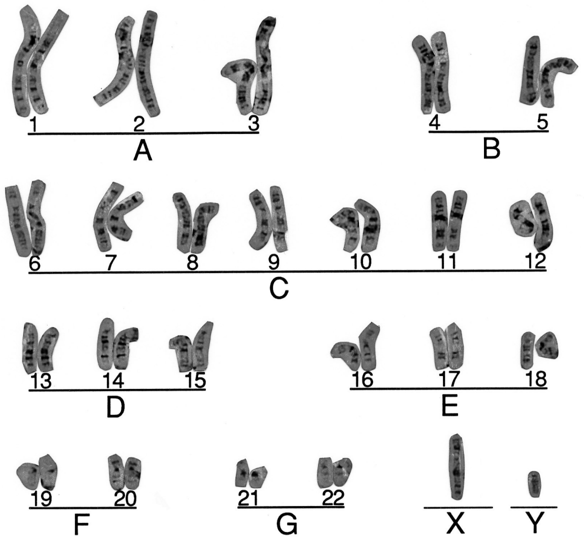
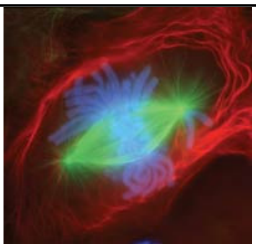
Genes are carried on chromosomes



Replication of genetic material



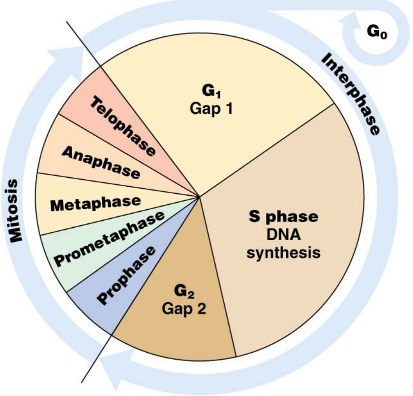
- maintenance of constant number of chromosomes within the cells of an individual

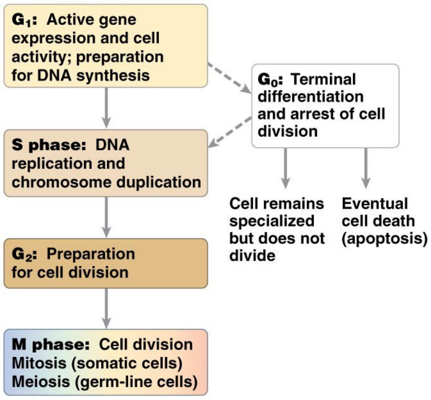
mitosis

- maintenance of constant number of chromosomes between individuals of a species

meiosis

mitosis, meiosis are part of the cell cycle





G_1: Active gene expression and cell activity; preparation for DNA synthesis

S phase: DNA replication and chromosome duplication

G_2: Preparation for cell division

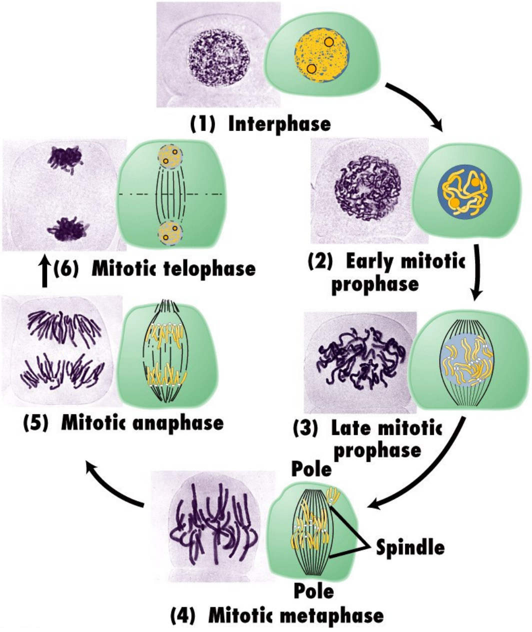
M phase: Cell division
Mitosis (somatic cells)
Meiosis (germ-line cells)

G_0: Terminal differentiation and arrest of cell division

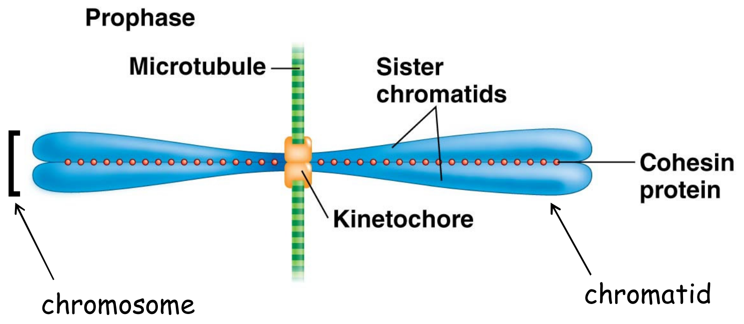
Cell remains specialized but does not divide

Eventual cell death (apoptosis)

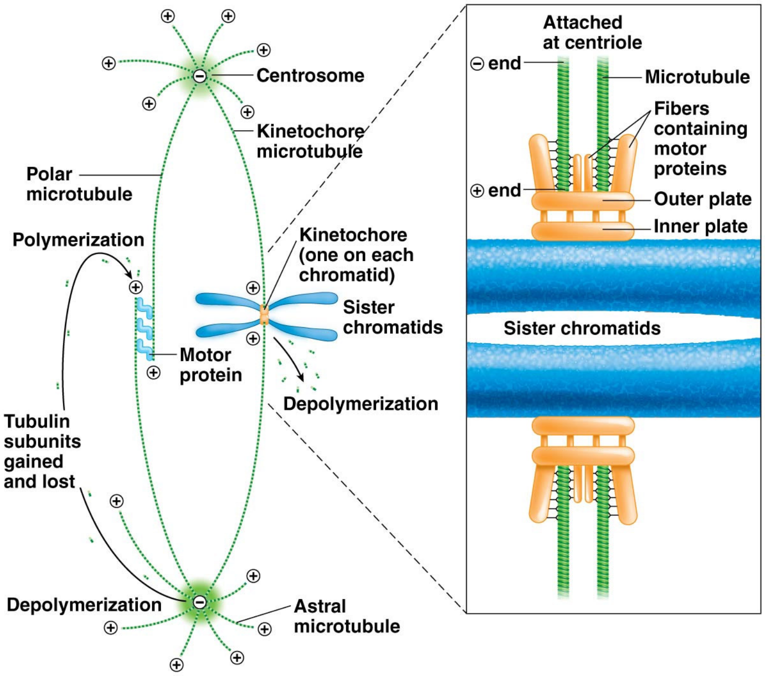
Mitosis

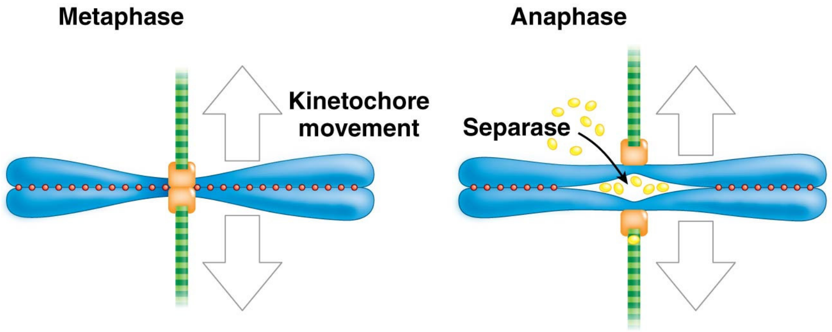


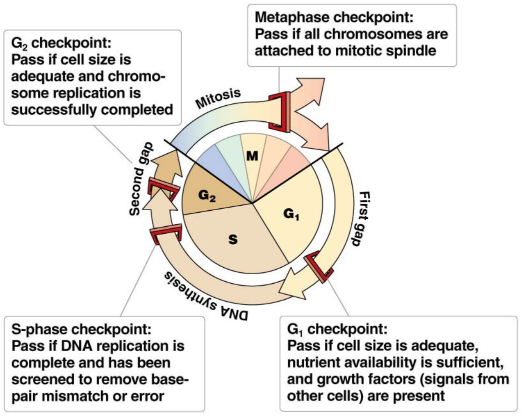
[redacted]


Prophase

Microtubule
Sister chromatids
Cohesin protein
Kinetochore
chromosome
chromatid


Centrosome
Kinetochore microtubule
Polar microtubule
Polymerization
Kinetochore (one on each chromatid)
Sister chromatids
Motor protein
Depolymerization
Tubulin subunits gained and lost
Depolymerization
Astral microtubule
Attached at centriole
⊖ end
Microtubule
Fibers containing motor proteins
⊕ end
Outer plate
Inner plate
Sister chromatids

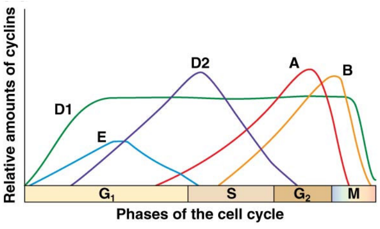



Metaphase checkpoint:
Pass if all chromosomes are attached to mitotic spindle

G_2 checkpoint:
Pass if cell size is adequate and chromosome replication is successfully completed

S-phase checkpoint:
Pass if DNA replication is complete and has been screened to remove base-pair mismatch or error

G_1 checkpoint:
Pass if cell size is adequate, nutrient availability is sufficient, and growth factors (signals from other cells) are present



meiosis occurs in gonads

process by which genome is halved to produce haploid gametes

[redacted]

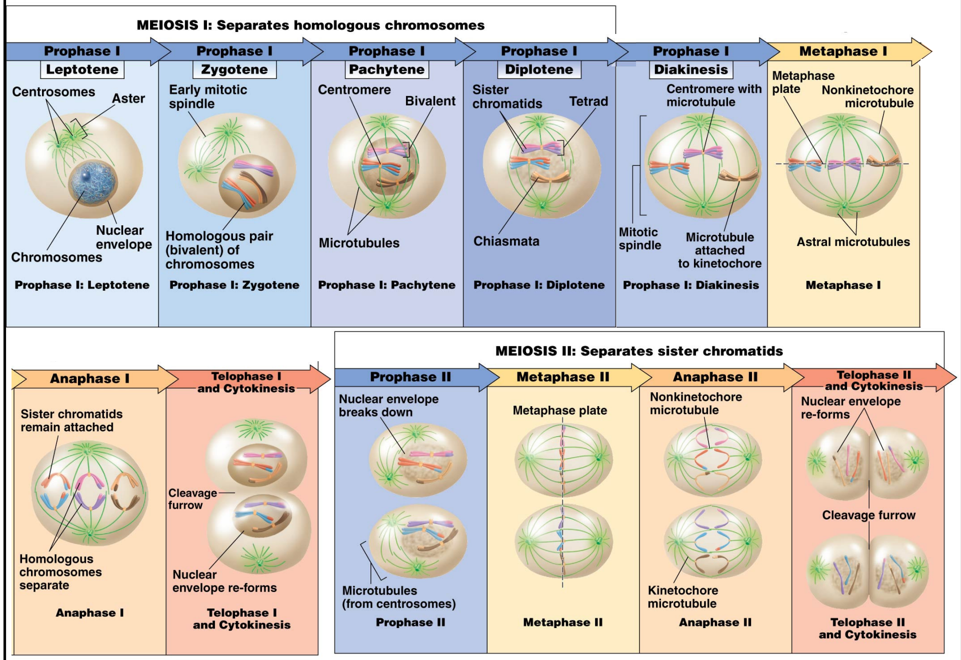
→ **1**) pairing of replicated homologous chromosomes

→ **2**) genetic crossover = exchange between homologous chromosomes

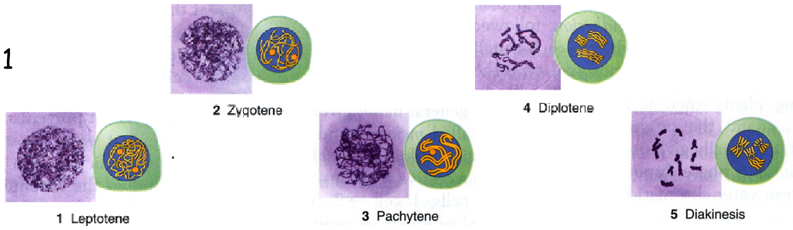
→ **3**) separation of homologous pairs during the first meiotic division (centromeres do *not* divide)

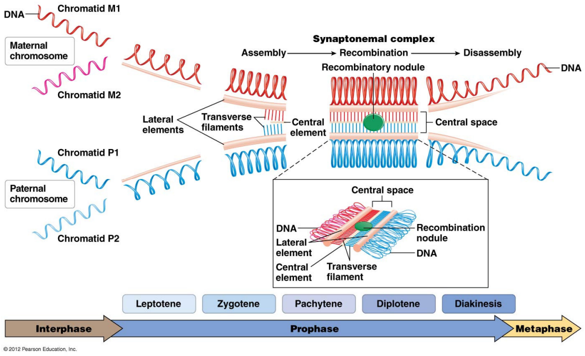
4) sorting of replicated chromosomes

5) nucleus & cell division

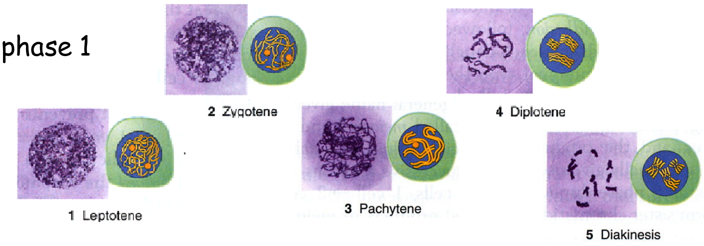


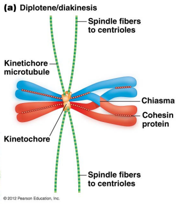
Prophase 1



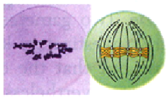


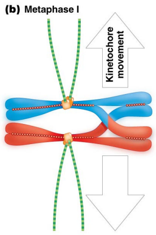
Prophase 1





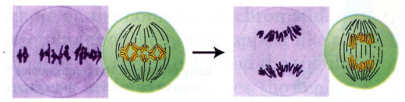
Metaphase 1

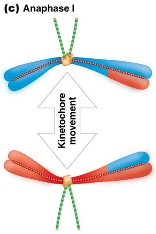


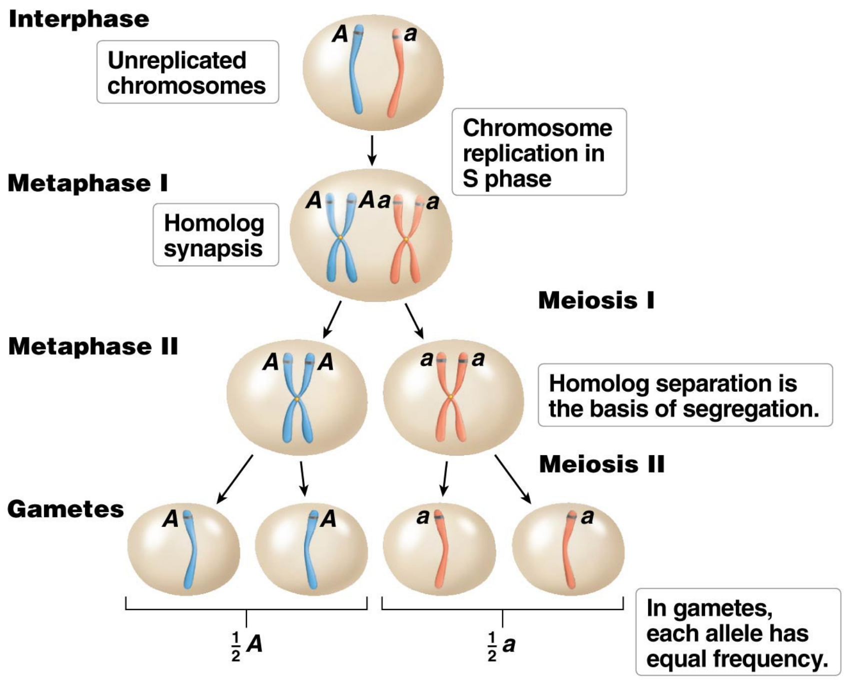


Anaphase 1

reduction division







---

independent assortment and meiosis

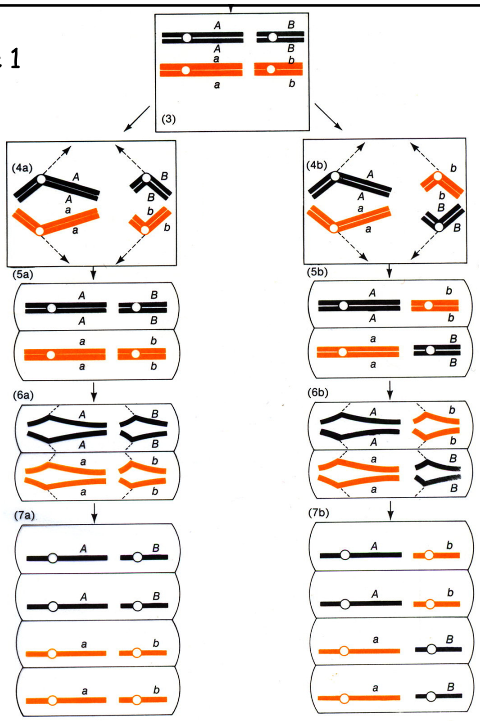
initial cross of strains homozygous at two loci:

A/A; B/B × a/a; b/b

↓

A/a; B/b

what happens when this individual undergoes meiosis?



Prophase 1

Anaphase 1
reduction division

Anaphase 2

independent
assortment
of genes on
different
chromosomes

---

independent assortment and meiosis

initial cross of strains homozygous at two loci:

A/A; B/B × a/a; b/b

↓

A/a; B/b

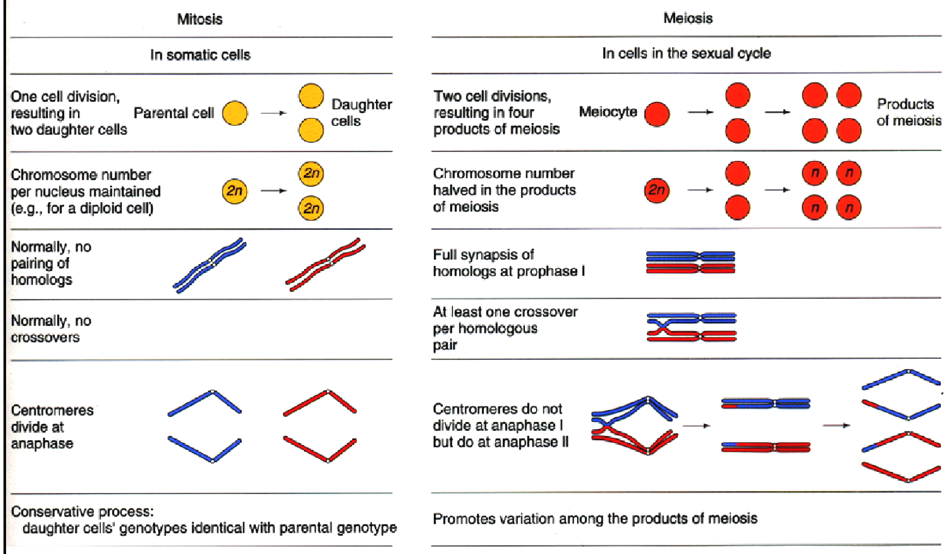
what happens when this individual undergoes meiosis?

four, equally likely, types of gametes:

A; B A; b a; B a; b

Cross two heterozygotes—four possible phenotypes:

A/-; B/- A/-; b/b a/a; B/- a/a; b/b



Mitosis	Meiosis
In somatic cells	In cells in the sexual cycle
One cell division, resulting in two daughter cells Parental cell → Daughter cells	Two cell divisions, resulting in four products of meiosis Meiocyte → → Products of meiosis
Chromosome number per nucleus maintained (e.g., for a diploid cell) 2n → 2n 2n	Chromosome number halved in the products of meiosis 2n → → n n n n
Normally, no pairing of homologs	Full synapsis of homologs at prophase I
Normally, no crossovers	At least one crossover per homologous pair
Centromeres divide at anaphase	Centromeres do not divide at anaphase I but do at anaphase II
Conservative process: daughter cells' genotypes identical with parental genotype	Promotes variation among the products of meiosis

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Take home points

haploid number (n) represents the number of different kinds of chromosomes; diploid (2n) is the total number

homologous chromosomes contain the same genes in the same order; homologs can be identified by shared features

in mitosis, a diploid cell undergoes one round of DNA replication and nuclear division, resulting in two genetically identical products

in meiosis, a diploid cell undergoes one round of DNA replication and two nuclear divisions, resulting in four genetically unique haploid cells (gametes)

meiosis differs from mitosis in that:
- homologous chromosomes pair
- homologs undergo recombination
- during the first cell division, the paired homologs separate to opposite poles of the cell