Reminder

Exam #1 on Friday Jan 29

Lectures 1-6, QS 1-3

Office Hours:

Course web-site

Josh : Thur, Hitchcock 3:00 - 4:00 (?)

Bring a calculator

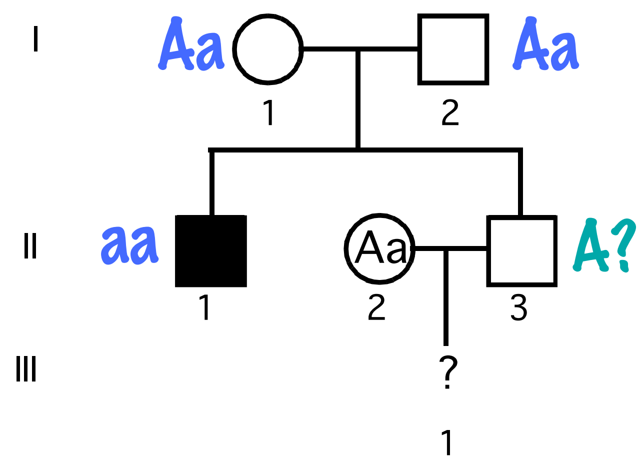
Questions/Comments/Concerns/Complaints...

Practice Question: Product Rule in Pedigrees

Example: Albinism…

a = no pigment

What is the probability that III-1 will show the trait?



P(II-3 is Aa) = 2/3

	A	a
A	AA	Aa
a	Aa	

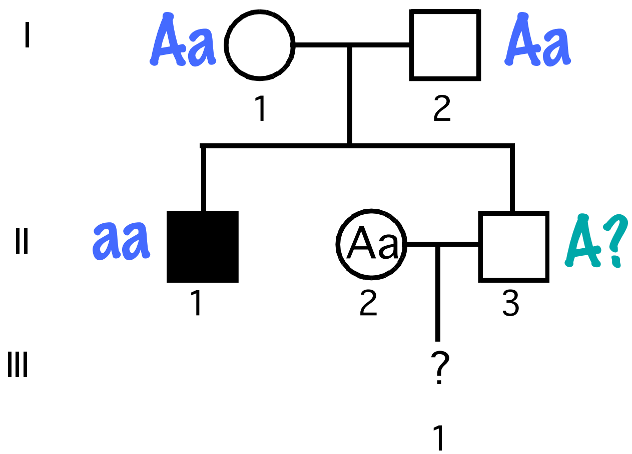
P(Aa x Aa giving aa) = 1/4

P(III-1 is aa) = 2/3 x 1/4 = 1/6

Practice question: Sum Rule in Pedigrees

The same pedigree…

What is the probability that III-1 will be **homozygous**?



Need III-1 = AA or aa. Possibilities:

AA father has AA child: 1/3 x 1/2 = 1/6

Aa father has AA child: 2/3 x 1/4 = 1/6

Aa father has aa child: 2/3 x 1/4 = 1/6

Therefore, probability of homozygous child = 1/6 + 1/6 + 1/6 = 1/2

Mendel’s Second Experiment

I have two laws!

Mendel's Second Experiment

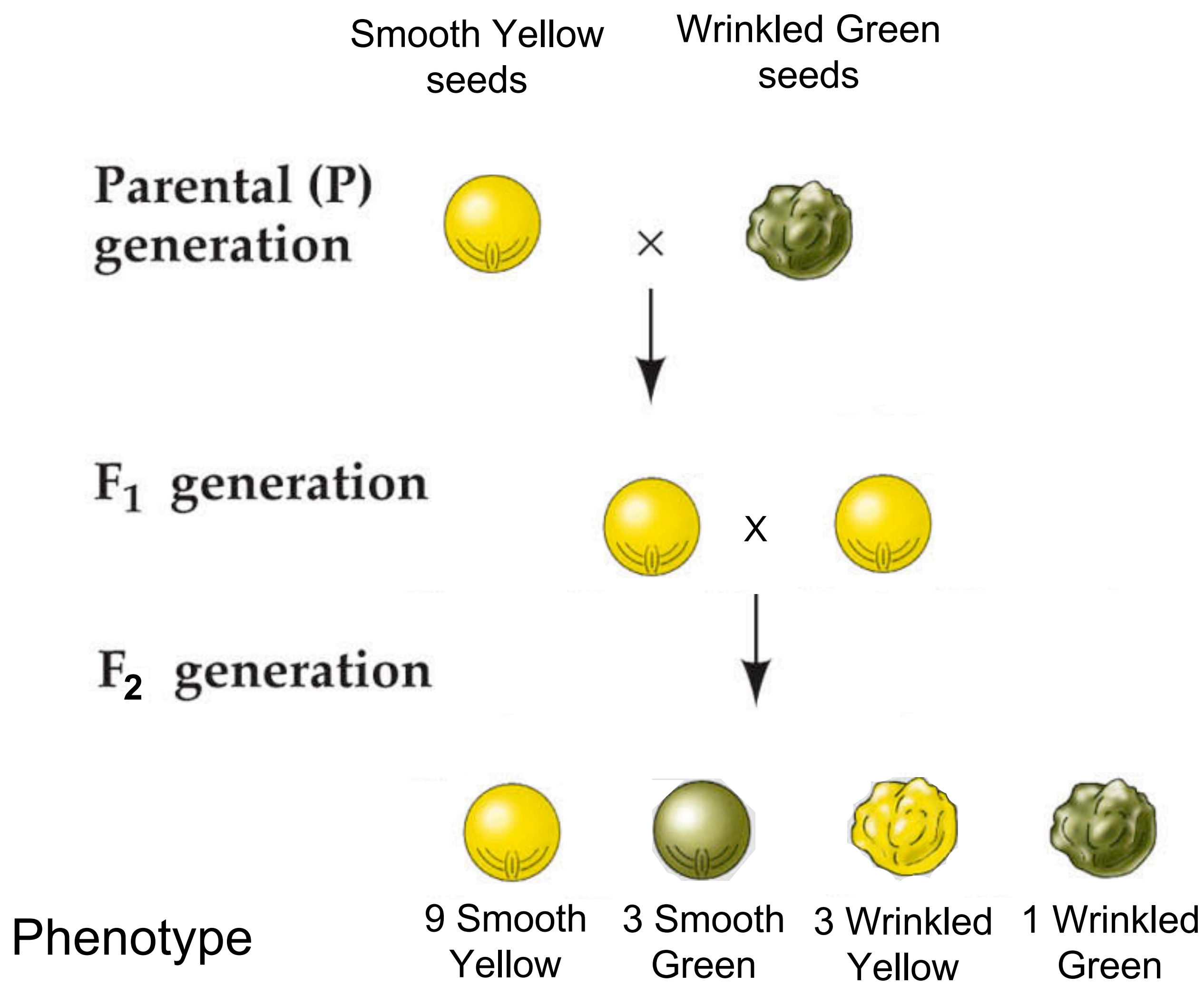
Cross two pure breeding pea plants that differ in ***two*** traits

Purpose was to determine how the inheritance of one trait influenced the transmission of the other

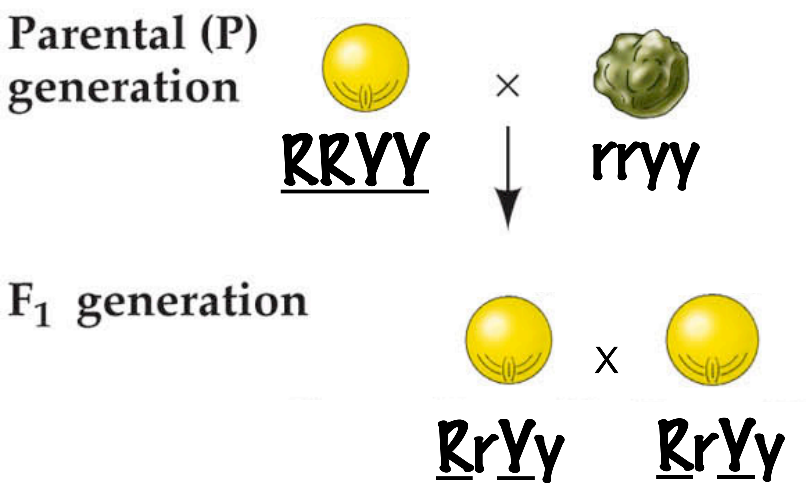
Offspring of these crosses are referred to as ***dihybrids***

hybrid for two different pairs of contrasting traits

Dihybrid Cross



Dihybrid Cross

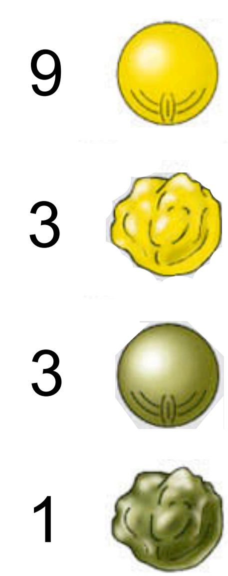


Each trait determined by a gene with two alleles

How many different types of gametes are produced?

F_2

	1/4 RY	1/4 rY	1/4 Ry	1/4 ry
1/4 RY	RRYY	RrYY	RRYy	RrYY
1/4 rY	RrYY	rrYY	RrYy	rrYy
1/4 Ry	RRYy	RrYy	RRyy	Rryy
1/4 ry	RrYy	rrYy	Rryy	rryy

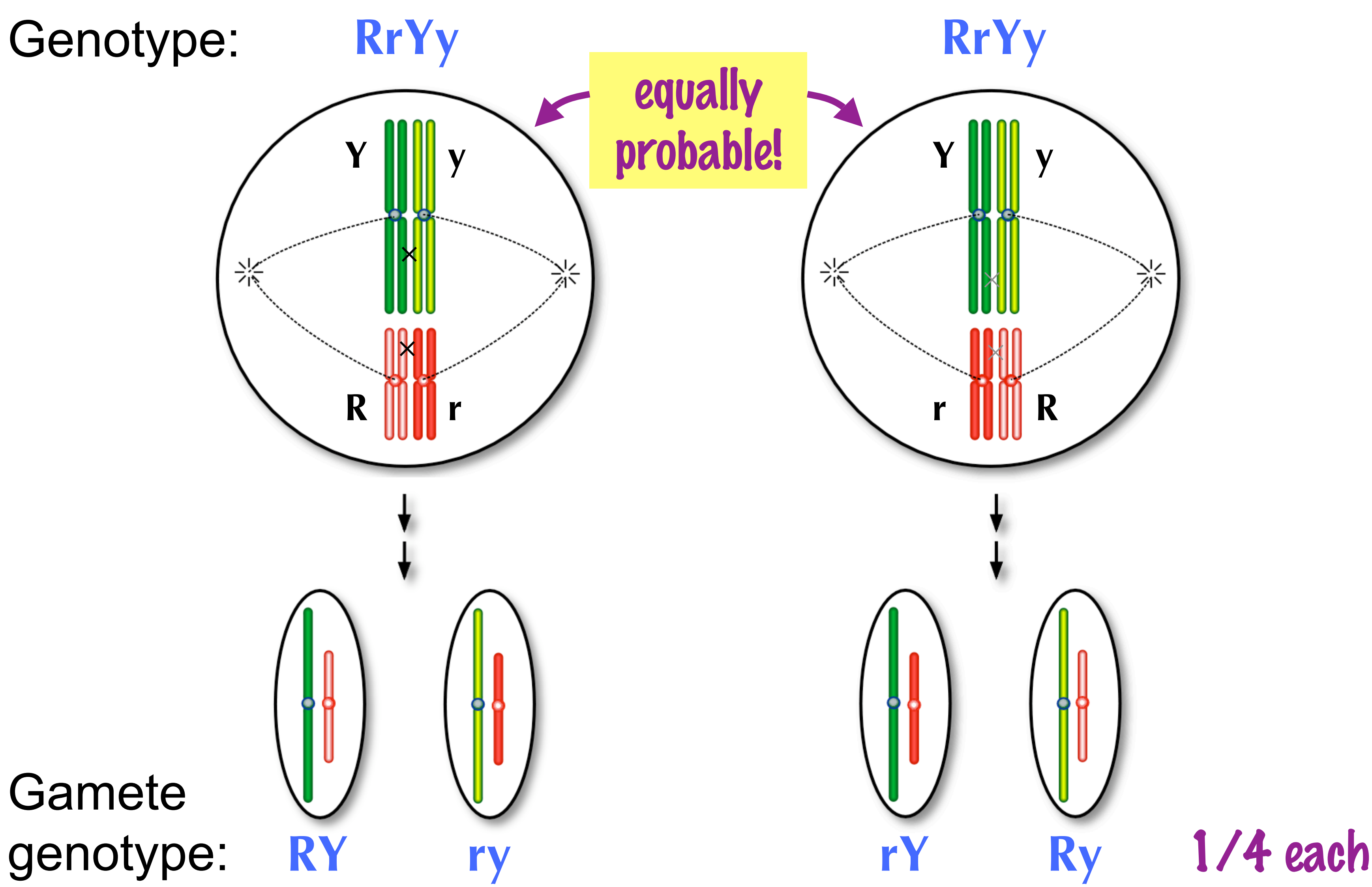


Forked line trick…

Calculating probabilities without punnett squares for IA traits:

Shape	Color		
3/4 round	3/4 yellow →	9/16	
	1/4 green →	3/16	
1/4 wrinkled	3/4 yellow →	3/16	
	1/4 green →	1/16	

Chance, Meiosis, and Independent Assortment



Mendelian Genetics

Law of Random Segregation: alleles segregate randomly in the formation of gametes

Law of Independent Assortment: unlinked traits are transmitted to offspring independently of one another

Gregor Mendel (1822–1884)

Evaluating the Goodness of Fit— χ^2 Analysis

Example: Coin flipping

Coin #1: 505 heads, 495 tails

Coin #2: 460 heads, 540 tails

Is there something wrong with either coin? How to decide? How much deviation from the expected values do we tolerate?

Statistical question to ask: What are the chances that even a normal coin would give a result this far off from the expected result?

Evaluating the Goodness of Fit— χ^2 Analysis

A measure of how well observed data conform to a specified, expected, or theoretical probability distribution.

315 yellow, round seed
108 green, round seed
101 yellow, wrinkled seed
32 green, wrinkled seed

---

556   9.84 : 3.15 : 3.375 : 1

Is this really a 9:3:3:1 ratio? Is the deviation due to chance or is there something wrong with Mendel's hypotheses?

χ^2 analysis: Test the "null" hypothesis—that the ratio of observed offspring is no different from a 9:3:3:1 ratio.

χ^2 Analysis of Mendel's Dihybrid F2 Results

- $$\chi^2 = \sum \frac{(\text{Observed-Expected})^2}{\text{Expected}}$$

(9/16 X 556)

	o	e	$(o-e)^2$	$\frac{(o-e)^2}{e}$
round, yellow	315	313	2^2	4/313 = 0.013
round, green	108	104	4^2	16/104 = 0.154
wrinkled, yellow	101	104	3^2	9/104 = 0.087
wrinkled, green	32	35	3^2	9/35 = 0.257
	556			$\Sigma = 0.511$

Degrees of freedom (df)

The number of **independently** varying parameters in the experiment (number of offspring classes-1)

Why does df matter?

More independent categories, the more opportunities for chance deviation; therefore need to make greater allowance for chance deviation

Look up the P value in a χ^2 table

P is the probability that the null hypothesis is true, and a deviation this large is due to chance

If $P > 0.05$ then we do not reject the null hypothesis

χ^2 Analysis of Mendel's Dihybrid F2 Results

- $\chi^2 = \Sigma \frac{(\text{Observed-Expected})^2}{\text{Expected}}$

(9/16 X 556)

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	556			$\Sigma = 0.511$

How many degrees of freedom? 3 (number of offspring classes - 1)

χ^2 table

P	0.995	0.975	0.900	0.500	0.100	0.050	0.025	0.010	0.005
df									
1	0.000	0.000	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	16.912	18.548

Find closest χ^2 value

P value

Find appropriate df row

What does this P value mean?

Would expect a deviation from the hypothesis of this magnitude (from chance alone) more than >90%

Therefore, do not reject the null hypothesis.

Linkage and Genetic Maps

- Genetic linkage
- Molecular markers
    - SNPs
    - VNTRs
    - RFLPs

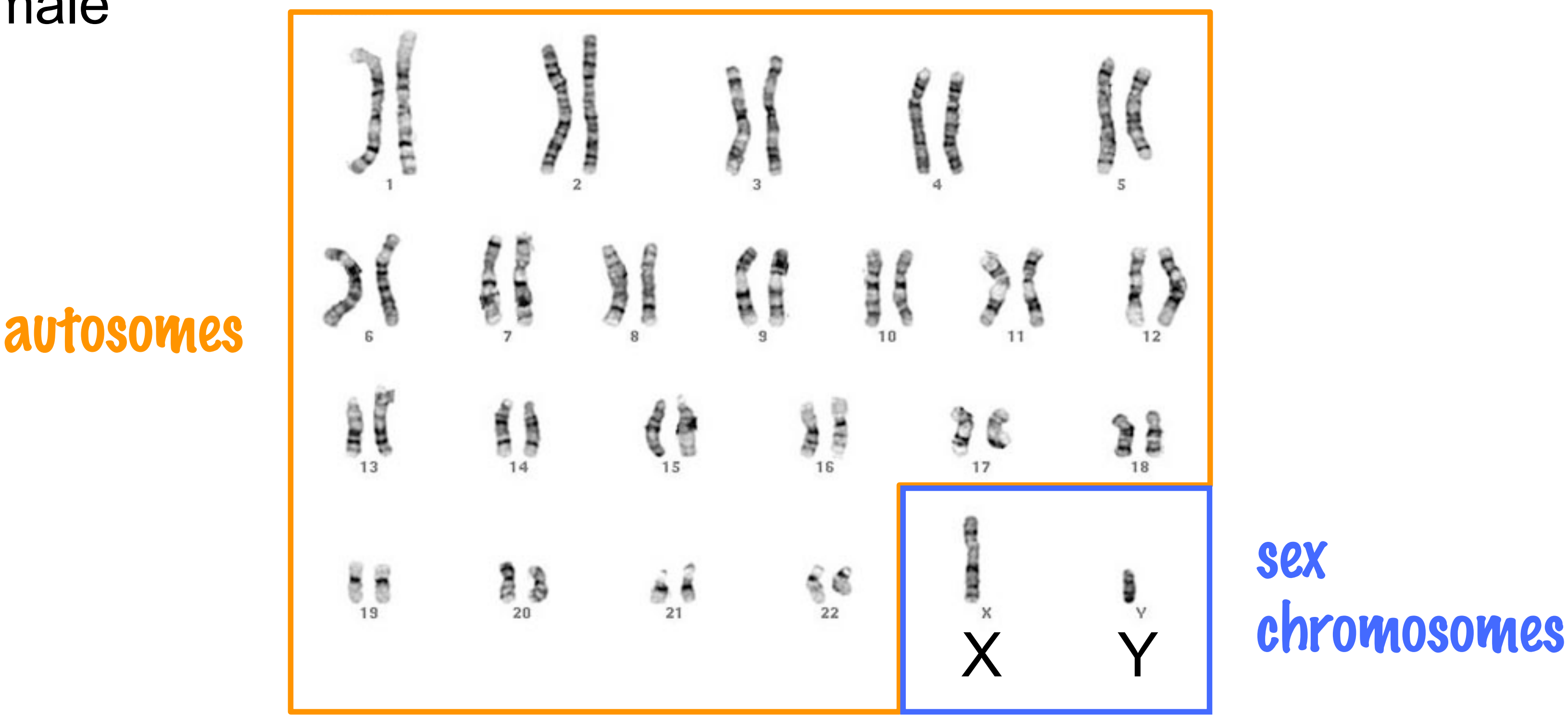
A Quiz Section Digression…

Sex Determination

In lots of animals (fruit flies, mammals…)

XX = female

XY = male

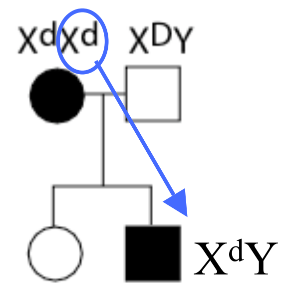


A Quiz Section Digression…

X-linked recessive traits…

- more affected men than women (rare traits… almost exclusively affect men)

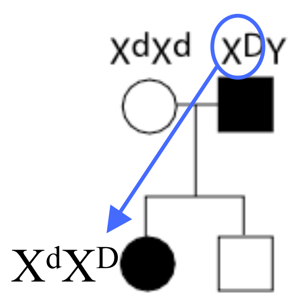
- sons of affected women will be affected



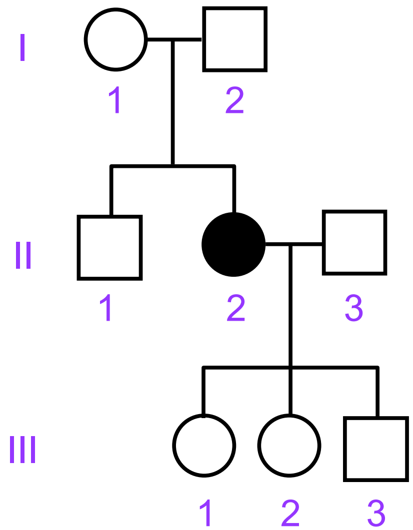
X-linked dominant traits…

- affected women: each child has 50% chance of being affected

- affected man: will transmit trait to all his daughters and none of his sons



A Quiz Section Digression…



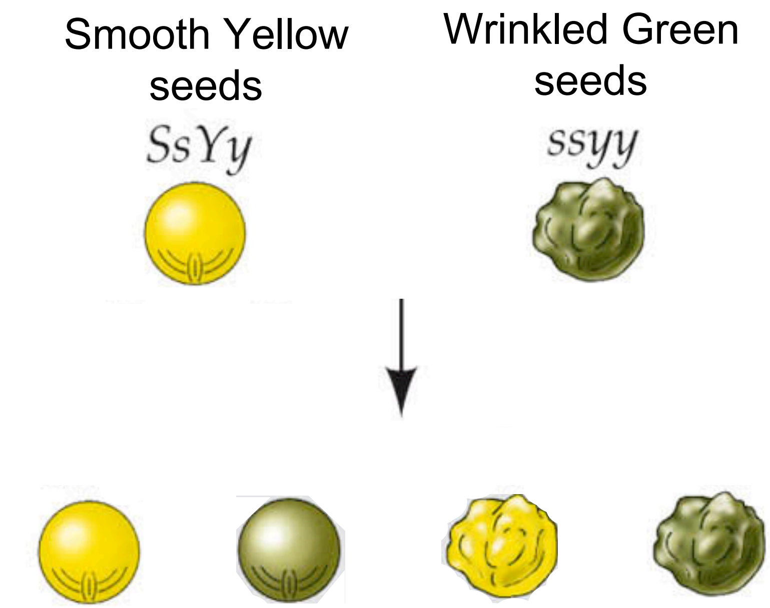
Is this pedigree consistent with X-linked inheritance?

i.e.,

Can you rule out X-linked recessive inheritance? If so, why?

Can you rule out X-linked dominant inheritance? If so, why?

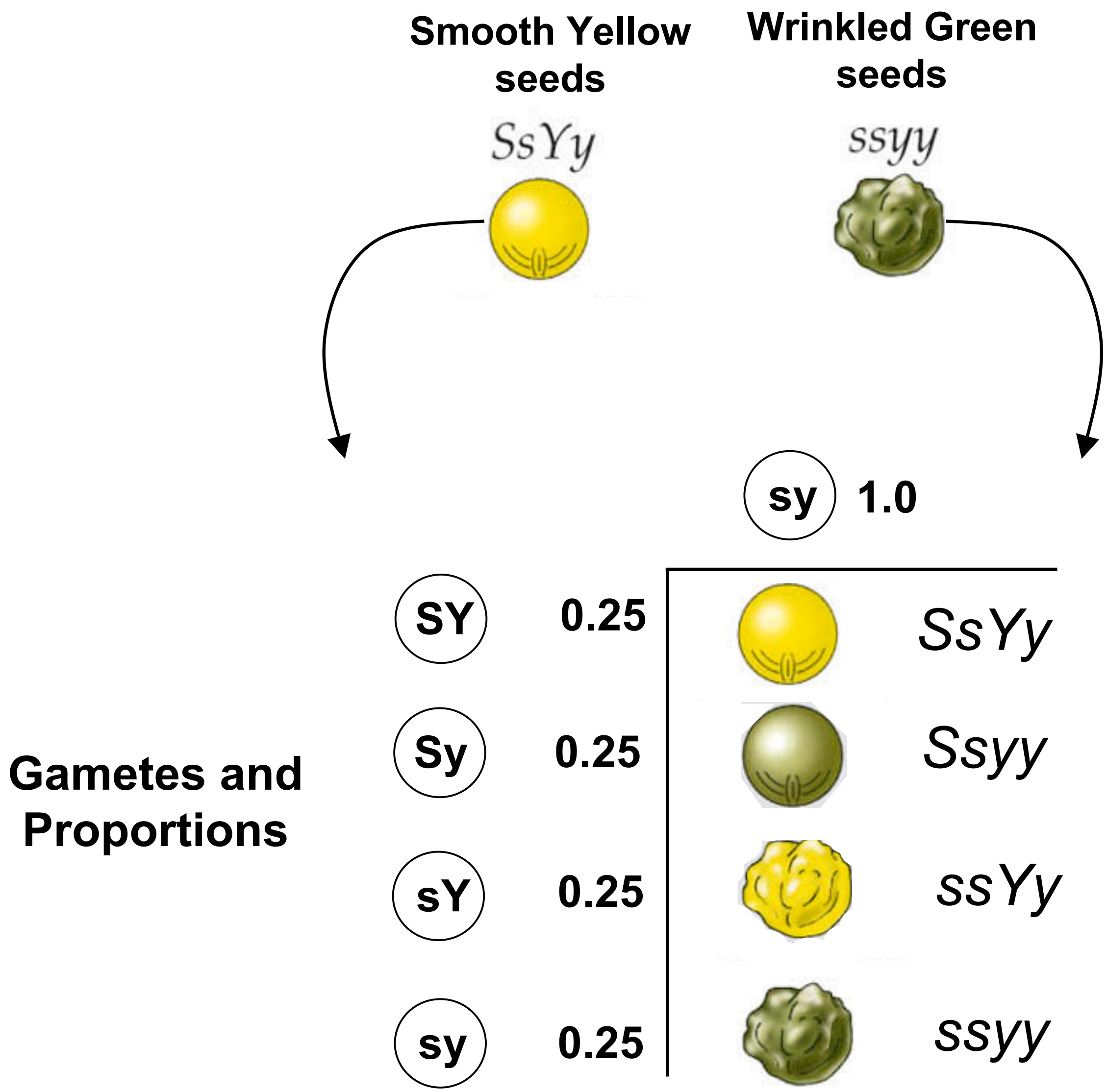
What Phenotypic Ratio Do We See in a Test Cross?



Phenotype	Smooth Yellow	Smooth Green	Wrinkled Yellow	Wrinkled Green
Ratio	1	1	1	1

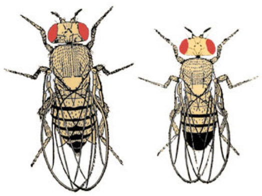
Why?

Because…



Smooth Yellow seeds
SsYy
Wrinkled Green seeds
ssyy
sy 1.0
SY 0.25
Sy 0.25
sY 0.25
sy 0.25
Gametes and Proportions
SsYy
Ssyy
ssYy
ssyy

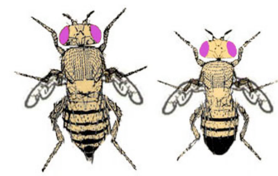
Testing the Hypothesis of Independent Assortment



wild type
$pr^+ pr^+ vg^+ vg^+$

x

purple eyes
vestigial wings
$pr\ pr\ vg\ vg$



gamete? → wild type pheno $pr^+ pr\ vg^+ vg$ ← gamete?

testcross

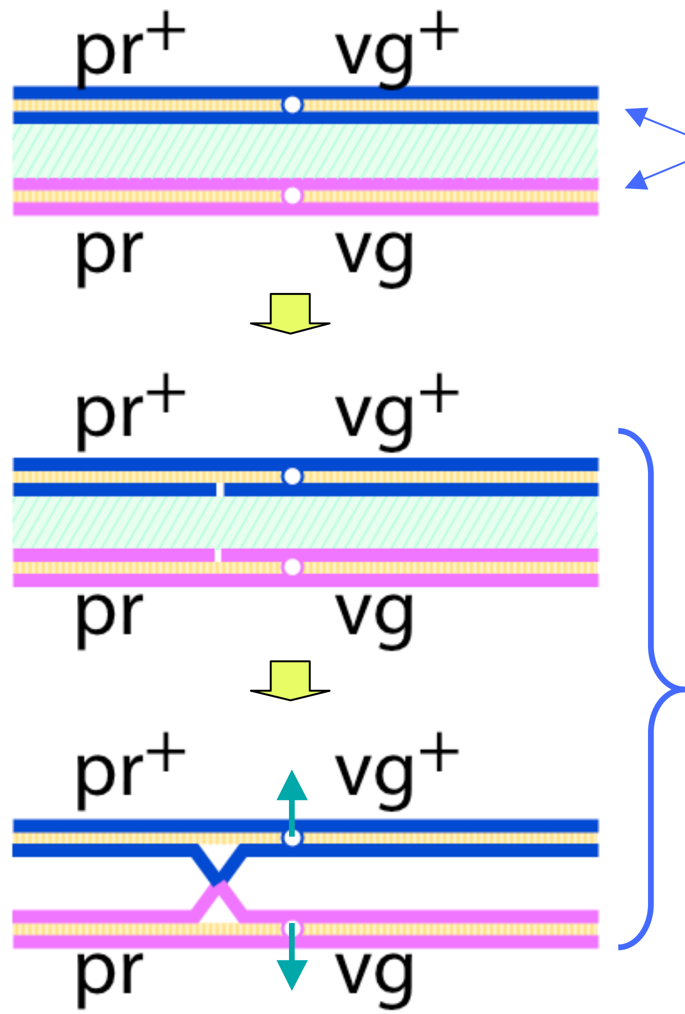
[ ]

testcross parent genotype?

For I.A., expect:	1 :	1 :	1 :	1 ratio
phenotypes:	$pr^+ vg^+$	$pr^+ vg$	$pr\ vg^+$	$pr\ vg$
actual result:	1339 :	151 :	154 :	1195

Recombination… a brief review

sister chromatids
(each is a double helix)



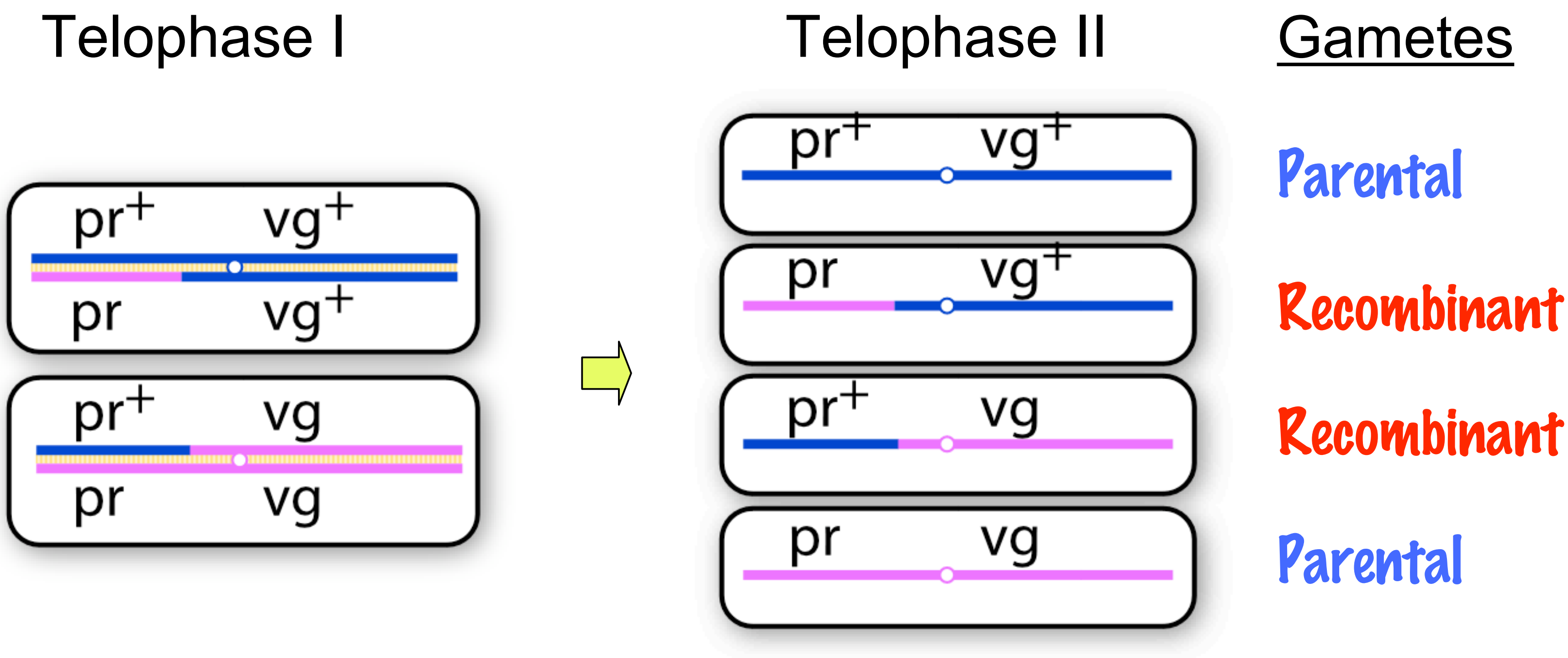
homologues

enzymatic nicking

strand exchange

resealing

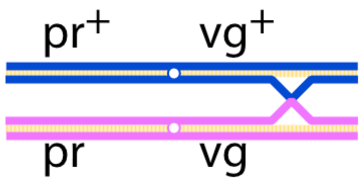
Crossovers… a brief review (cont'd)



One recombination event: 2 recombinant and 2 non-recombinant products

Other types of crossovers (between the loci of interest)

 # xovers — **resulting gametes**



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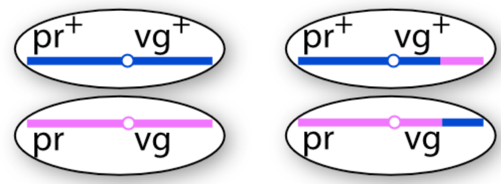
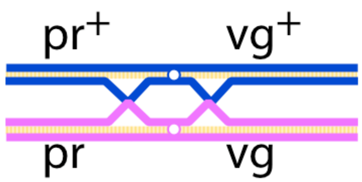
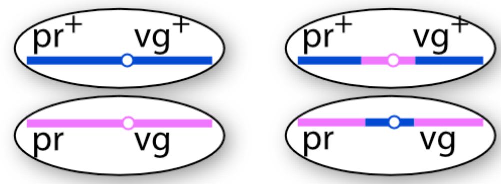


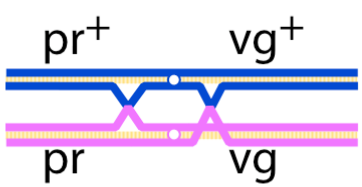
parental



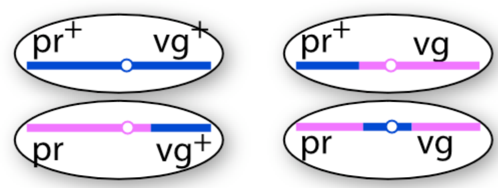
2
(2 chromatids)



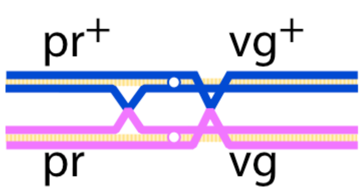
parental!



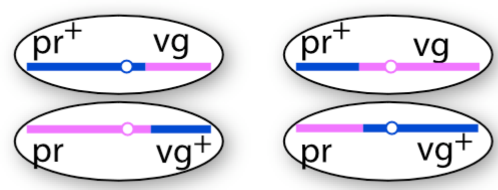
2
(3 chromatids)



2 parental
2 non-par.



2
(4 chromatids)



4 non-par.

Linkage and recombination—summary

Genes on the same chromosome can show *linkage* instead of independent assortment

> Gametes (mostly) have the same allele combinations as the homologs in the parent

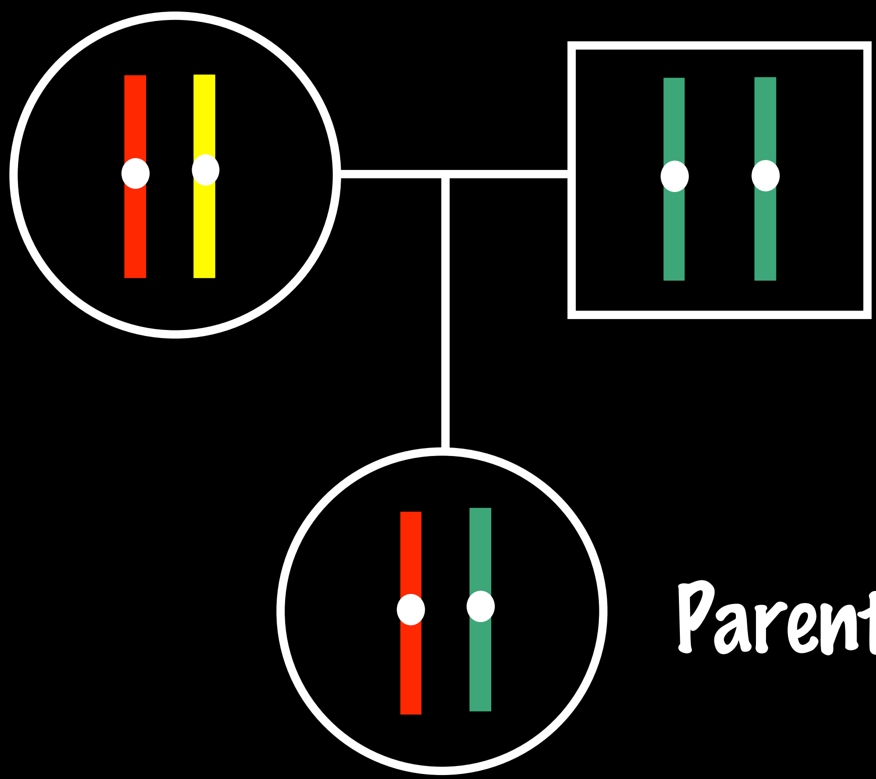
Recombination can give rise to gametes with non-parental (i.e, recombinant) allele combinations

> Two parental types are more abundant and roughly equal
>
> Non-parental types are less abundant and roughly equal to each other

Identifying the Parental Type

Time Out!

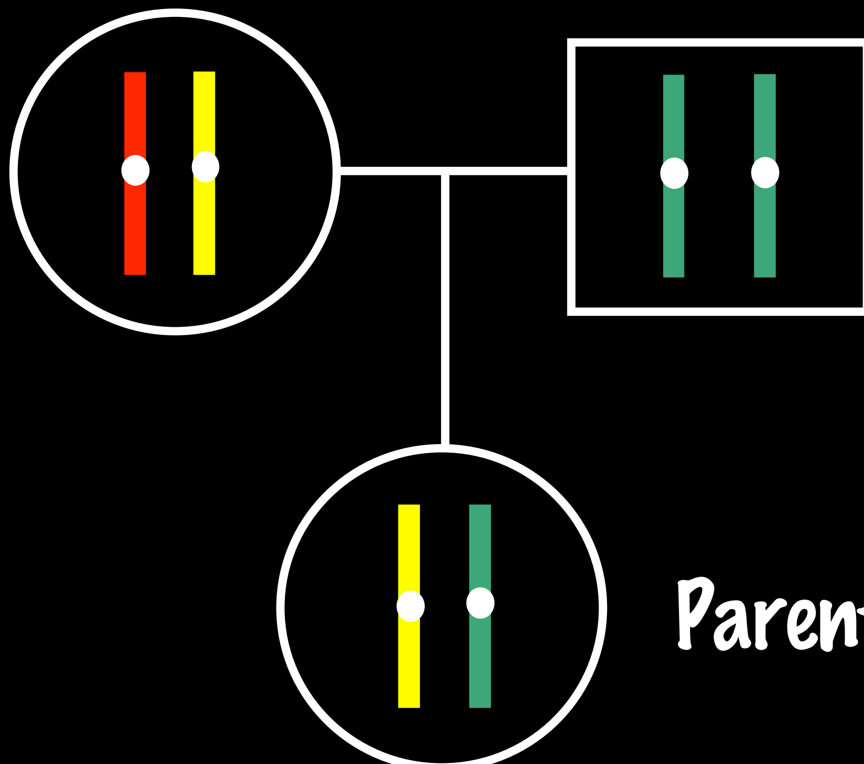
Parental type: the arrangement of alleles on the parental chromosomes



Parental type

Time Out!

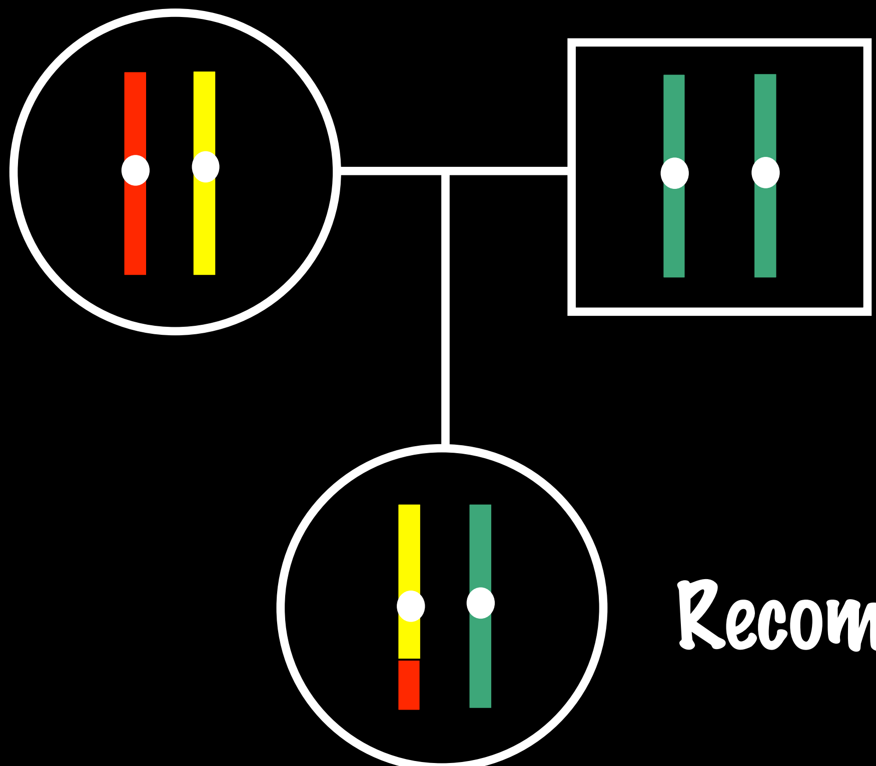
Parental type: the arrangement of alleles on the parental chromosomes



Parental type

Time Out!

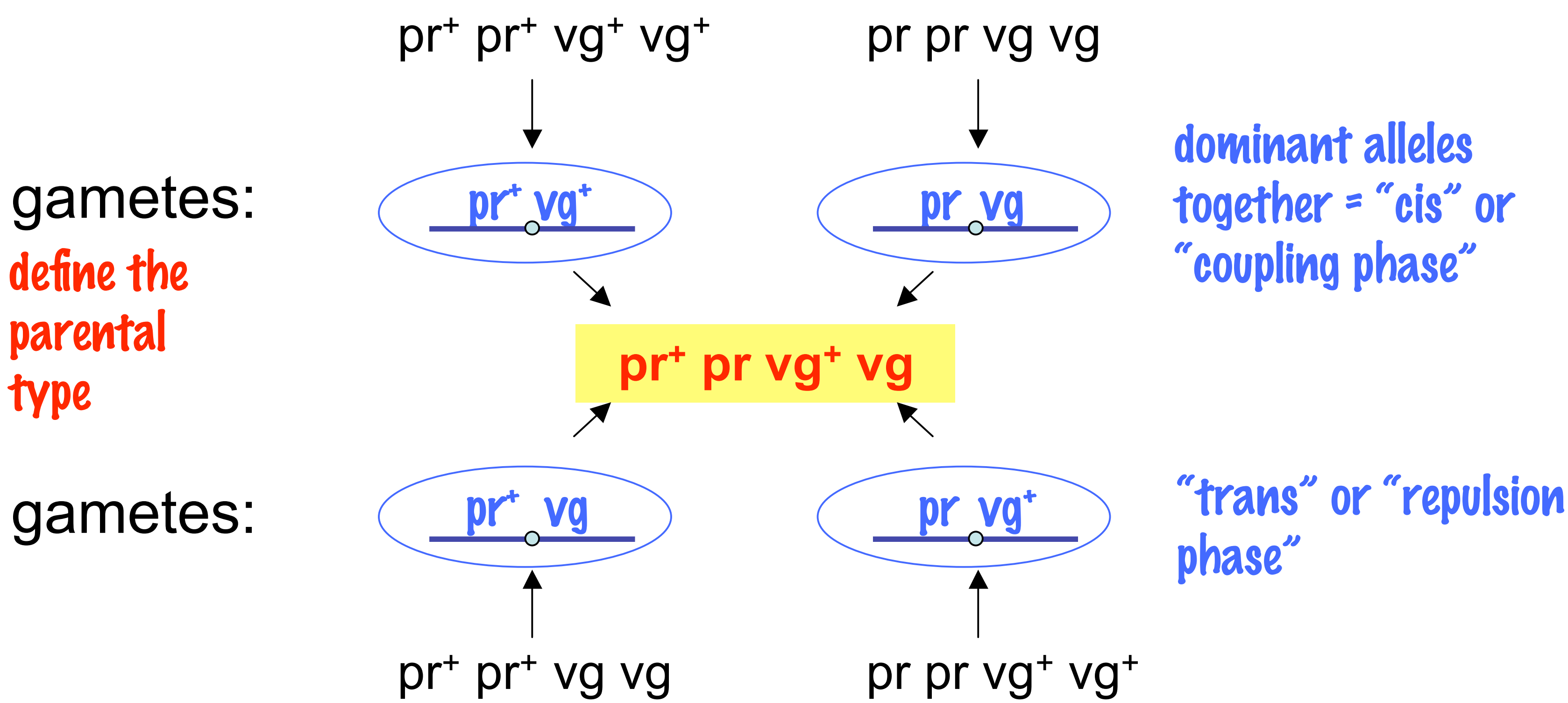
Parental type: the arrangement of alleles on the parental chromosomes



Recombinant type

Identifying the Parental Type

Option 1. Know the gametes that made the heterozygous parent



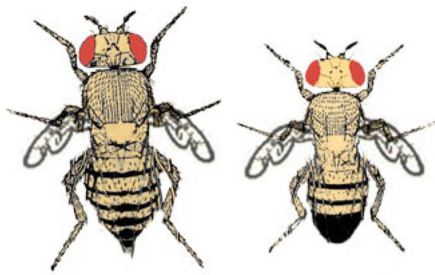
Identifying the Parental Type

Option 2. The two most abundant progeny types

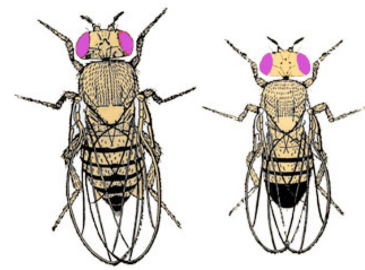
(only works if the genes show linkage)

Cross: pr$^+$ pr vg$^+$ vg x pr pr vg vg

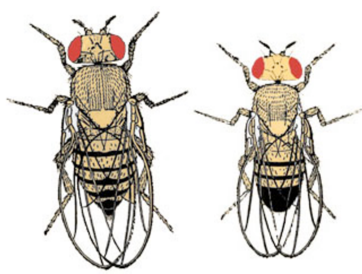
Progeny:



1287 $\frac{\text{pr vg}}{\text{pr}^+\text{ vg}}$



1204 $\frac{\text{pr vg}}{\text{pr vg}^+}$



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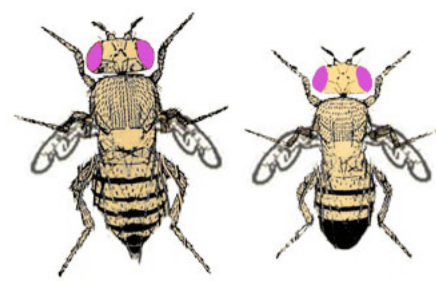

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What were the gametes that made the heterozygous parent?