Thomas Hunt Morgan's Drosophila Experiments

Imagine the setting. Mendelian ideas of inheritance are being enthusiastically discussed by many researchers. The structure of chromosomes has been closely observed and the process of meiosis described for the first time.

> "The association of chromosomes in pairs and their subsequent separation during [meiosis] may constitute the physical basis of the Mendelian law of heredity."
>
> Sutton, W. S. 1902. On the morphology of the chromosome group in *Brachystola magna*. *Biological Bulletin*, 4:24-39.

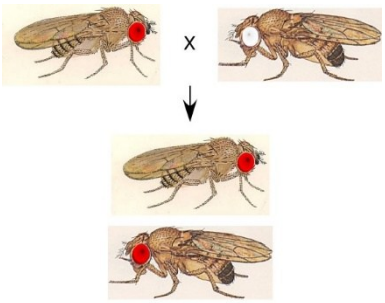
Walter Sutton, and others had also suggested that sex was determined via chromosome-based inheritance, through observations of chromosomes in males and females.

Morgan, however, had long resisted the idea of chromosome based inheritance, because he did not approve of scientific data acquired by passive observation, the experimental method of Sutton.

Thomas Hunt Morgan's famous "fly room" at Columbia University was the site of many discoveries using the fruit fly *Drosophila melanogaster* as a model to study genetics.

Morgan thought that the concept of genes carried on chromosomes was nothing but a human invention. Morgan had spent years carrying out experiments hoping to find the experimental evidence to either support or disprove these ideas. Finally, in 1910, Morgan discovered a single fly with white eyes that was about to provide just the evidence he had been looking for. (Normal fruit flies have red eyes, not white eyes.)

Morgan immediately crossed this white-eyed male fly to its red-eyed sisters (Morgan, 1910).



He assumed that white eye was recessive (w) and red eye was the dominant wild type (+)

Parent genotypes: ++ X ww

	w	w
+	+w	+w
+	+w	+w

F1 phenotypes all wild type (red eye) but now heterozygous

No surprises here, so as Mendel had done, he crossed the F1 offspring with each other.

Complete the punnet square of expected phenotype ratios after Morgan's cross between two heterozygous flies

Parent genotypes: +w X +w

	+	w
+		
w		

Expected F1 phenotypes:

_____ Red eye flies (mixed male and female) : _____ white eye flies (mixed male and female)

As there should be an equal number of males and females we can predict a ratio of each sex separately.

_____ Red eye males : _____ white eye males: _____ red eye female : _____ white eye female

Try this white eye breeding experiment yourself using the Drosophila lab
http://www.kscience.co.uk/animations/drosophila2.htm

Record your results here: Use totals from two identical crosses from the simulation. Total 50 flies.

Phenotype	**Mendel's Ratio**	**Expected**	**Observed**	**$(O\text{-}E)^2/E$** Show working out here …
Red eye males				
White eye males				
Red eye females				
White eye females				
Total		50	50	Chi squared value $\sum(O-E)^2/E$ = (Has 3 df in this table)

Chi-Square statistic look-up table

No significant difference				**Critical value**	**Significant difference**				
probability	0.995	0.20	0.10	0.05	0.025	0.02	0.01	0.005	0.001
3 df	0.0717	4.642	6.251	7.815	9.348	9.837	11.345	12.838	16.266

Morgan observed the following phenotypes in his F2 generation:

- 2,459 red-eyed females
- 1,011 red-eyed males
- 782 white-eyed males

There were no white-eyed females!

Suggest your own explanation of why the results show the pattern in the table

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Morgan wondered if the trait was sex-limited and only expressed in male flies. Is white eye fatal in females?

To test whether females can express the white eye characteristic, Morgan completed a second cross between the original white-eyed male fly and some of his F_1 daughters who were heterozygous.

Parent genotypes: ww (male) X +w (female)

	w	w
+		
w		

Expected F1 phenotypes:

_____ Red eye males : _____ white eye males: _____ red eye female : _____ white eye female

Try this breeding experiment yourself using the Drosophila lab. (un-tick the "True breeding" box)
http://www.kscience.co.uk/animations/drosophila2.htm

Calculate Expected ratios using 50 flies by adding two sets of results. Record your results here:

Phenotype	**Mendel's Ratio**	**Expected**	**Observed**	**$(O-E)^2/E$** Show working out here …
Red eye males				
White eye males				
Red eye females				
White eye females				
Total		50	50	Chi squared value $\sum(O-E)^2/E$ = (Has 3 df in this table)

Suggest your own explanation of the results

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When Morgan did this experiment he obtained these results:

- 129 red-eyed females
- 132 red-eyed males
- 88 white-eyed females
- 86 white-eyed males

White-eyed females can exist, and the groups had approximately equal numbers.

Morgan therefore hypothesized that the eye-colour trait was connected with the sex chromosome (Morgan, 1910). Female fruit flies have XX chromosomes and males have XY

Test the theory by calculating expected phenotypes using the notation for sex-linked genes

Parent genotypes: X^wY (male) x X^+X^w (female)

	X^+	X^w
X^w		
y		

Expected F1 phenotypes:

_____ Red eye males : _____ white eye males: _____ red eye female : _____ white eye female

Do the results match the model?

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Once Morgan had accepted that genes are carried on chromosomes it didn't take long for Morgan to find two genes on the same chromosome. This was more evidence of genetic linkage, (Morgan, 1911).

To test for linkage completed a new cross between a male fly with an ebony body (e) and scarlet eyes (st) with a wild type female. (+)

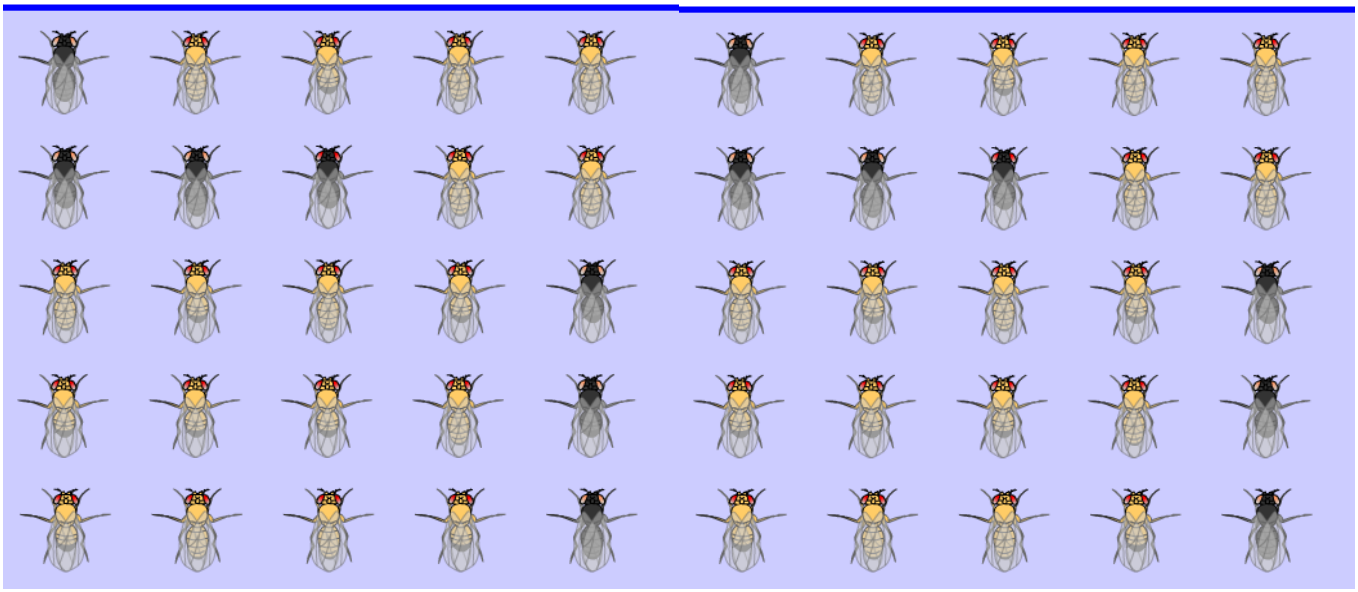
Parent genotypes: e e st st (male) X $e^+ e^+ st^+ st^+$ (female)

	$e^+ st^+$
e st	ee^++st st^+.

Expected F1 phenotypes: all will be wild type body colour, and wild type red eye.

They will all be heterozygous for each feature so a final cross between a double heterozygous male and double heterozygous female should give the mendelian 9:3:3:1 ratio.

Try this breeding experiment yourself using the Drosophila lab. We will ignore the sex of the flies in this cross. (or simply count the flies in this image) http://www.kscience.co.uk/animations/drosophila2.htm



Record your results here:

Phenotype	Mendel's Ratio	Expected	Observed	$(O\text{-}E)^2/E$ Show working out here …
normal	9	28.0		
Scarlet normal	3	9.4		
Normal ebony	3	9.4		
Scarlet ebony	1	3.2		
Total		50	50	Chi squared value $\sum(O-E)^2/E$ = (Has 3 df in this table)

Which types of flies are recombinants?

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What do you notice about the number of recombinants?

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Which types are the parental types?

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Morgan finally accepted that genes are inherited on chromosomes, this was the experimental proof he had been looking for.

Explain why these results support the idea that genes are inherited on chromosomes?

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Genetic notation for linked genes

Consider the cross between a male fly with an ebony body (e) and scarlet eyes (e e st st) with a wild type female. ($e^+e^+st^+st^+$) We know that the genes are both on chromosome 3 in Drosophila so we can use linkage notation.

The alleles for each gene are written above a little line, which represents the chromosome. Genotypes are written in two rows, see this example below.

Parent genotypes: $\underline{e\ st}$ $\underline{e^+\ st^+}$
e st (male) X $e^+\ st^+$ (female)

	$\underline{e^+\ st^+}$
$\underline{e\ st}$	$\underline{e^+\ st^+}$ e st

Expected F1 phenotypes: all will be wild type body colour, and wild type red eye.

Try to complete the punnet square for the self-cross of the F1 above. Remember: e^+ & st^+ = alleles for wild type.

F1 Parent genotypes: $\underline{e^+\ st^+}$ X $\underline{e^+\ st^+}$
e st e st

	$\underline{e^+\ st^+}$	$\underline{e\ st}$
$\underline{e^+\ st^+}$		
$\underline{e\ st}$		

F2 Offspring phenotypes: _____

This model explains linkage, but a real cross produces recombinants too. Explain how this recombination of alleles for different genes happens, referring to meiosis. (hint: think of prophase I)

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Soon after, work from Morgan's lab found further evidence that genes are located on chromosomes, and he also predicted (correctly) that recombination was caused by crossing over.