

Computer Flies #1

Name: _____

Learning Objectives:

Understand the rules of Mendelian genetics and apply those rules to solve problems.

- Learn to generate crossing data, and make genetic hypotheses based on data
- Learn to test a hypothesis with chi-square test
- Learn to convert a verbal hypothesis such as "red eyes is recessive to wild type (wt)" into a quantitative hypothesis, that is, an "expected" number of offspring in a chi-square test
- Interpret the results of a chi-square test
- Figure out crosses needed to test the verbal hypotheses (ie red eyes is recessive)
- Test those hypotheses with additional crosses and chi square tests
- Revise hypothesis and test revised hypothesis

Introduction:

You will be using the computer program *Drosophila* at

<http://ScienceCourseware.org/vcise/drosophila/> to learn about Mendelian genetics.

This program allows you to uncover the Mendelian basis of real *Drosophila* mutations using the methods that geneticists must use. We use these methods even when the organism's genome has been sequenced. The benefit of using a computer program is that you get the results much more quickly than in real life, so you can plan a lot more crosses, and your flies never die. If you are able to successfully figure out the genetic basis of these traits, you have mastered Mendelian genetics. If not, keep trying. You will need to have a strong grasp of Mendelian genetics or you will be lost as we progress to more difficult applications, like gene mapping.

You will first choose a mutation to learn about, and order flies from the simulated store. Then you will cross the mutants (the P generation) and examine the offspring (F₁s) resulting from this cross. If you like, you can then generate another set of crosses to produce F₂ or BC offspring. You will need to decide what crosses will be most informative. When you have some hypothesis about how the trait(s) are inherited, you should be able to carry out a chi-square test to see if your cross gave the expected ratios. Continue doing crosses with these trait(s) until you are confident about the mode of inheritance.

In lab 1, you should explore enough traits that you are confident that you can interpret data and determine (a) dominance, (b) lethality, (c) sex linkage. In lab 2, you should be able to determine if 2 loci are linked, and determine linkage distance (map distance)

Please fill in these tables before coming to lab so you can refer to them during lab.

Table 1. Complete dominance. Let's assume that allele A (red) is dominant to a (white). What genotype and phenotype frequencies do you expect from the following crosses:

Cross	Genotype frequency			Phenotype frequency	
	AA	Aa	aa	red	white
AA x AA					
AA x Aa					
AA x aa					
Aa x Aa					
Aa x aa					
aa x aa					

Table 2. Lethality. The Manx mutation (M) in cats causes short tails when heterozygous (Mm) and death when homozygous (MM). Manx is considered a dominant lethal trait, because the heterozygote does not have the wildtype phenotype. Recessive lethal traits are also possible, where the heterozygote (Bb) is indistinguishable from the homozygous wild-type genotype (BB), but individuals homozygous for the mutation (bb) die. In either case, if a mutation kills offspring early in development, you will never see the dead offspring. You must infer the presence of the lethal mutation by its effect on phenotype frequencies.

A) What genotype and phenotype frequencies do you expect from the following crosses for a **dominant lethal** mutation:

Cross	Genotype frequency			Phenotype frequency	
	MM	Mm	mm	Wild type	Short tail
Mm x Mm					
mm x mm					

B) What genotype and phenotype frequencies do you expect for a **recessive lethal** mutation:

Cross	Genotype frequency			Phenotype frequency	
	BB	Bb	bb	Wild type	Short tail
BB x BB					
BB x Bb					
Bb x Bb					

Table 3. Sex linkage. Let's assume that blue/white color is sex-linked on the X, and that white is recessive to blue (X_A). What genotype and phenotype frequencies do you expect from the following crosses? Here, since you are separating males and females, write your frequencies as a portion of all females or males (ie 100% of females were Blue)

Cross		Genotype frequency					Phenotype frequency	
		$X_A X_A$	$X_A X_a$	$X_a X_a$	$X_A Y$	$X_a Y$	Blue	White
$X_A X_A * X_A Y$	Male							
	Female							
$X_A X_A * X_a Y$	Male							
	Female							
$X_A X_a * X_A Y$	Male							
	Female							
$X_A X_a * X_a Y$	Male							
	Female							
$X_a X_a * X_A Y$	Male							
	Female							
$X_a X_a * X_a Y$	Male							
	Female							

Chi Square test:

If you have several phenotypes in your offspring, and you have some hypothesis about how the trait is inherited, you can do a chi-square test to see if your offspring ratios are close to what you would expect given your hypothesis.

To do a chi square test, figure out what offspring ratios you expect, based on whether you think the mutation is dominant or recessive (or sex linked or lethal, etc). This is your null hypothesis.

Example:

Null hypothesis (in words): Red is dominant to white.

Crosses: You make an F_1 cross between true-breeding red and white, and get all red offspring, so it is likely that the red is dominant to white, and that all F_1 s are heterozygous. You cannot do a chi square test on this generation, however, because all of your offspring have the same phenotype. You need more than one phenotype.

If your null hypothesis is true, in the F_2 generation, you expect 3 red to 1 white offspring (If you aren't sure why, use Punnett squares to go through both F_1 and F_2 crosses).

Therefore, your "null hypothesis" in numerical terms is 3:1. In the lab, the computer will do the chi square test for you, if you type in your numerical hypothesis. When doing a chi square test by hand, you will need to calculate an "Expected value" (number) off

offspring of each phenotype. Here's how expected numbers are calculated: A 3:1 ratio equals $\frac{3}{4} : \frac{1}{4}$. If you sampled 1000 offspring, you expect $1000 \times \frac{3}{4} = 750$ red offspring, and $1000 \times \frac{1}{4} = 250$ white offspring.

Getting Started:

You can try the rest at home, or wait and do it in lab so your TA can give you tips. I recommend reading through this handout before lab.

- 1) Open Firefox or Safari and go to <http://ScienceCourseware.org/vcise/drosophila/>
The program does not work correctly on Explorer
- 2) Log in as Guest.
- 3) Now you can follow the onscreen directions and start making crosses.

When you get to the first picture of flies, notice the difference between males and females in the shape and color of the anterior (butt). This is how you will distinguish males and females when you work with real *Drosophila*.

To make your cross, choose a female with one mutation and cross it with a wild type male.

Observe the F1 offspring.

Take notes.

Cross the F1s to make F2s.

Tips:

Once you have made a few sets of crosses and you know how to use the program, you may want to click on the "options" tab and uncheck "Transitions" to speed up the crossing process.

Take notes on the crosses you make and their results, .

All flies from the store are true breeding except the flies with lethal mutations – those are heterozygous.

All of the mutations in this computer program are real *Drosophila* mutations. The names of the mutations are real. However the abbreviations are not standard. They are capitalized to avoid telling you dominance of the mutation. Also, in a few cases, the mutation characteristics are a bit different from real life. "+" is always used as the abbreviation for the wild-type allele. This is standard in *Drosophila* notation.

If the program starts to act weird, log out and log back in. To log out, push the back button on your browser until you get to the login screen.

Log out and log back in when switching from one set of crosses to the next. Otherwise, you get too many files in your incubator, and the program gets weird.

Let's make crosses:

Dominant vs Recessive:

Let's start with the *apterous* mutation (under wing size). Make some crosses to figure out if *apterous* is dominant or recessive. You'll need to figure out a strategy on your own for figuring out the inheritance of a trait. All of the flies from "Fly's supplies" fly store are true breeding except those with lethal mutations.

1) *How can you figure out whether the mutation is dominant or recessive?* You should be able to answer this with a single cross, and confirm it in the second generation. Although to be certain, I would probably do a few more crosses. **Describe what cross(es) you can make to figure this out and how you reach your conclusions. It may be helpful to look at Table 1. Punnet squares may be useful in your description. If you're not certain, make a few crosses to see which are informative.**

2) After you think you know whether the trait is dominant or recessive, test your hypothesis with a chi square test.

Describe your chi square test and how you interpret the results of the test:

a) What is your null hypothesis (circle one)?

Choices: *apterous* is dominant or *apterous* is recessive to wild type

b) What cross are you testing below? (If you are testing the F₂ generation, describe both the F₁ and F₂ crosses used to generate these offspring)

Offspring:

Phenotype	Observed Num	Expected ratio
wildtype		
apterous		

Chi square test statistic (χ^2): _____

Degrees of Freedom (d.f.): _____

Level of significance (P-value): _____

Does this result indicate that you should reject your null hypothesis? Why or why not?

Based on the results of your chi square test, do you conclude that the *apterous* mutation is dominant or recessive? Why?

Lethality:

3) How can you figure out if a mutation is lethal? Look at Table 2.

4) Let's look at the *aristopedia* mutation (under antennae). Make some crosses to figure out if this trait is dominant or recessive, and if it is lethal. Explain your crosses and how you reached your conclusions.

5) Use a chi-square test the null hypothesis that this mutation is NOT lethal:
First, state your null hypothesis, including whether the trait is dominant or recessive:

Describe the cross you are testing:

Phenotype	Observed Num	Expected ratio

Chi square test statistic (χ^2): _____

Degrees of Freedom (d.f.): _____

Level of significance (P-value): _____

Does this indicate that you should reject your null hypothesis? Why or why not?

Use a chi-square test the null hypothesis that this mutation IS lethal:

First, state your null hypothesis, including whether the trait is dominant or recessive:

Describe the cross you are testing:

Phenotype	Observed Num	Expected ratio

Chi square test statistic (χ^2): _____

Degrees of Freedom (d.f.): _____

Level of significance (P-value): _____

Does this indicate that you should reject your null hypothesis? Why or why not?

Based on the results of your chi square tests, do you conclude that the *aristapedia* mutation is lethal? Why?

Sex Linkage:

6) If a trait is sex-linked, do you ever see different phenotype ratios in males and females from the same cross (look at Table 3)? _____ Do you ever see this in a trait that is not sex linked? _____ Which crosses in Table 3 above support your answer? These are the crosses you might want to use to figure out if a trait is sex linked.

7) Make some crosses to see whether *yellow body* (under body color) is sex-linked. Explain your crosses and how you reached your conclusions.

8) Use a chi-square test the null hypothesis that this mutation IS sex-linked.
First, state your null hypothesis, including whether the trait is dominant or recessive:

Describe the cross you are testing:

Phenotype	Sex	Observed Num	Expected ratio

Chi square test statistic (χ^2): _____

Degrees of Freedom (d.f.): _____

Level of significance (P-value): _____

Does this indicate that you should reject your null hypothesis? Why or why not?

Based on the results of your chi square tests, do you conclude that the *yellow body* mutation is sex-linked? Why?

Choose any mutation:

9) Which mutation did you choose? _____

Ask yourself:

- "What would I expect from this cross if the mutant is recessive?"
- "What would I expect if the mutant is dominant?"
- "What would I expect if the mutant is sex-linked?"
- "What would I expect if the mutant is lethal"

10) Do some crosses, and ask yourself whether they are inconsistent with any of the above hypotheses. You can rule out any hypotheses that are inconsistent with your results.

Which hypotheses have you ruled out?

11) Which hypotheses are consistent with your results?

Do some more crosses to test the remaining hypotheses that you haven't ruled out. When you think you know the answer, test the ratios from some of your crosses with the chi square test.

12) Conclusion: Is the mutation dominant, recessive, lethal, and/or sex-linked?

13) Explain how you reached your conclusion: what crossing results led you to your conclusions, what chi-square tests did you carried out, and how did you interpret them:

A) Dominant: consistent or inconsistent, explain how your crosses are consistent or not

B) Recessive: consistent or inconsistent, explain how your crosses are consistent or not

C) Sex-linked: consistent or inconsistent, explain how your crosses are consistent or not

D) Lethal: consistent or inconsistent, explain how your crosses are consistent or not

Now choose a second mutation, and figure out its genetic basis:

mutation: _____

14) Is it dominant, recessive, lethal, sex-linked?

15) Explain how you reached this conclusion: