

The MENDELSIM program - Teacher's reference manual

What you need to read

This manual is provided to teachers to help run the Mendelsim program. It is intended mainly as a reference manual for matters of detail, rather than as a manual which needs to be read before running the program.

If you wish students to use only the standard exercises and questions, it may be possible to run the program without referring to this manual. However you will need to look at least briefly through the first two chapters if you want to change the program.

Structure of this manual

The material associated with the Mendelsim program is in two parts:

- A. Instructions for setting up the program - this manual for teachers
- B. Instructions for use of the program - Student Instructions
(included as an appendix to this manual)

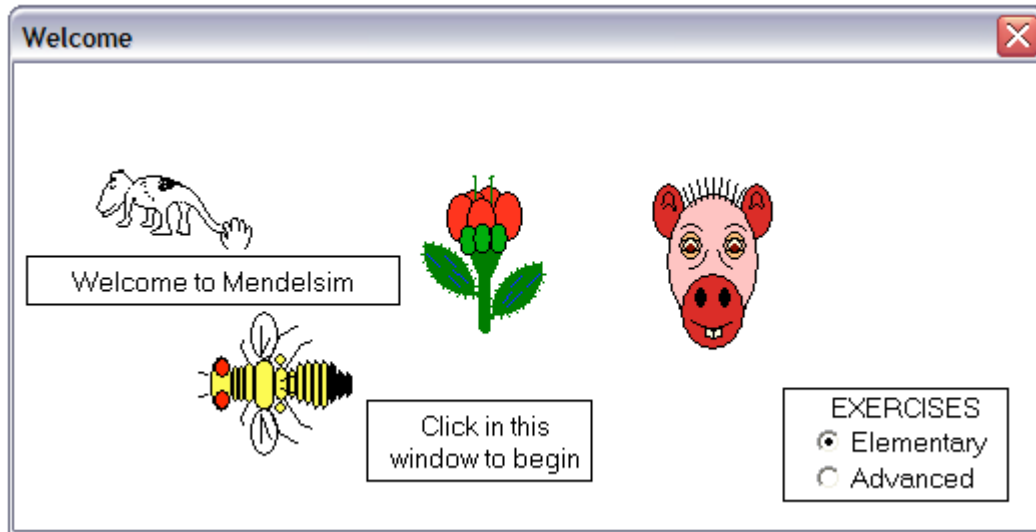
Chapter

1. **Default and Setup versions of Mendelsim**
2. **The Setup run**
3. **The standard exercises**
4. **The bank of questions**
5. **Entering parameters of the exercises**
6. **The marking of exercises**

Appendix A. Student Instructions

Chapter 1. Default and Setup versions of Mendelsim

When the Mendelsim program starts, it will show something like the following screen:



In this **default** mode, a student may choose, or be instructed to choose, the 20 elementary exercises or the 20 advanced exercises. These exercises are outlined in the following chapters.

When run in this way, the teacher has no control over what exercises the student chooses. There is also no opportunity to assess whether the exercises have been satisfactorily completed.

The Mendelsim program can, however, be tailored so that the teacher can control the exercise(s) set for the student, and be able to look up the correct answer for a particular exercise. This requires three steps:

- (i) Register on the internet at the Hands On Genetics web site
- (ii) Enter the registration information into the Mendelsim program,
- (iii) Nominate exercises.

(i) Register at the www.handsongenetics.com web site.

You may have already gone to the web site in order to read these instructions. Click the 'Register' button in the left-hand menu, which brings up a screen requesting entry of a Departmental name and address (see below). Names between 6 and 36 characters should be entered in both lines. These names will be shown on the opening screen of Mendelsim and other Hands On Genetics programs. There is no charge involved nor record kept of registrants.

To proceed, you need to enter two lines of identification. Not more than 36 characters in each please. These will be shown on the startup screen of each program. You may enter either a department name followed by an institution name, or alternatively an institution name followed by an address.

Name:

Address:

We ask you to please use a realistic name that identifies the school or college department in order to preserve the integrity of distribution of the programs.

[Next](#)

Following entry of the two lines of information (see below for an imaginary departmental name), a registration number will be shown. A record needs to be kept of this number, or alternatively a 5-line text file made of the information, including the two lines of asterisks.



Thank you for registering for the Hands On Genetics programs. The following input will enable any program from the set:

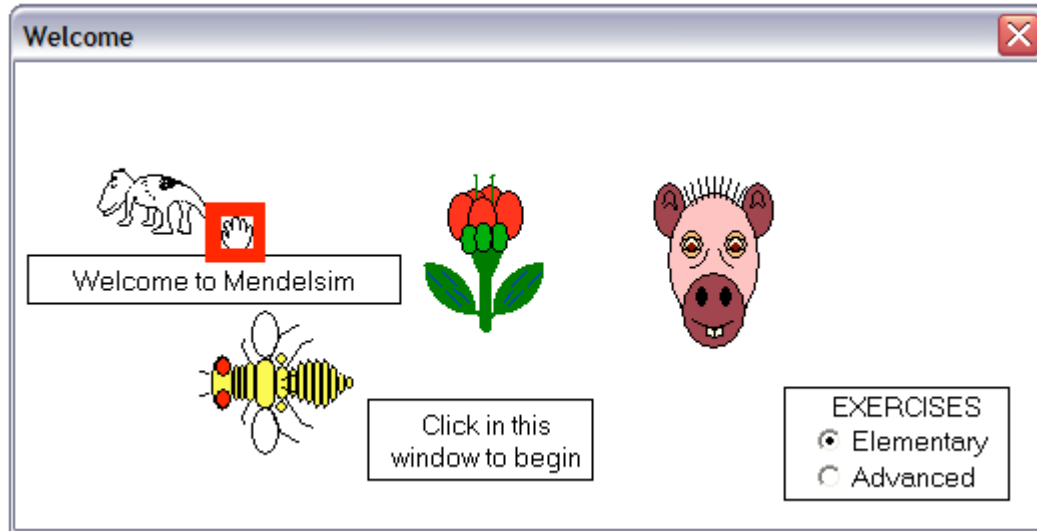
```
*****  
Line 1: Genetics Department  
Line 2: University of Sydney  
Number: 9349 1502 5390 0573  
*****
```

To use these numbers, you will first need to download one or more programs. When you start up the program, the opening screen will show a 'Register' button. Clicking this will allow you to input the three lines of information

NB. If you put these five lines into a text file, you can use this file to register without typing in anything. Alternatively type in the names and numbers into the program exactly in this form. You only need do this once.

(ii) Enter registration information into the Mendelsim program

The Welcome screen for the Mendelsim program contains a hidden entry mode. When this screen appears, hold down the Alt key (Command/Apple key on the Macintosh) and click on the Hand (highlighted in red in the picture below).



This will result in the appearance of a screen indicating that a file called 'HoG.key', the file containing registration information, has not been found. If you have already been through the web registration process, click on the 'Register now' button. If not, you will need to do this before proceeding to the next screen .

Please enter the registration name. Both lines should match exactly the lines entered to receive your registration number

Read from file

Line 1

Line 2

Please enter your 16-digit registration number

- - -

X Cancel **✓ Register**

Fill in the information provided from the web. The name and number need to agree exactly with the information provided previously. It is easier to do this by reading the 5-line text file if you have made one from the web browser screen. Successful acceptance of the registration information is indicated by a message such as the following:

Please enter the registration name. Both lines should match exactly the lines entered to receive your registration number

Line 1

Line 2

Please enter your 16-digit registration number

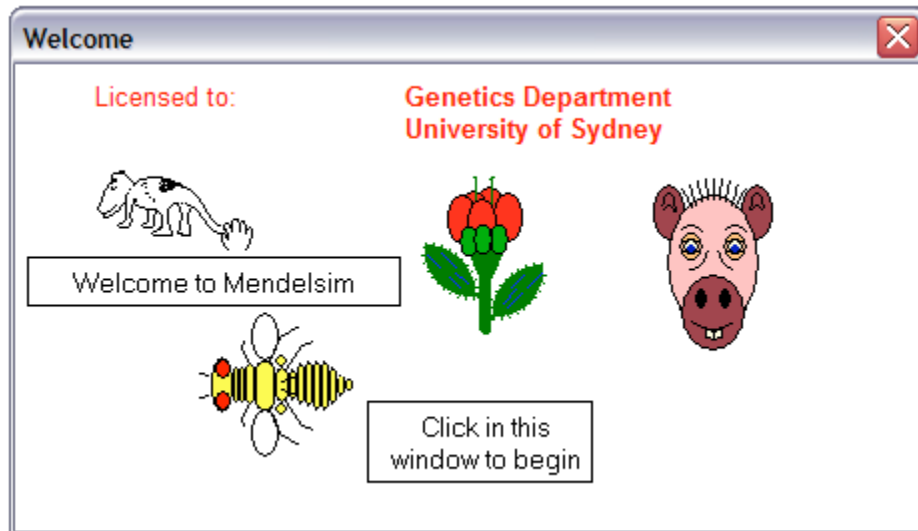
- - -

The name and number have been recorded in the 'HOG.key' file. The programs are registered for a one year period. Please ensure that the HOG.key file remains in the same folder as the programs.

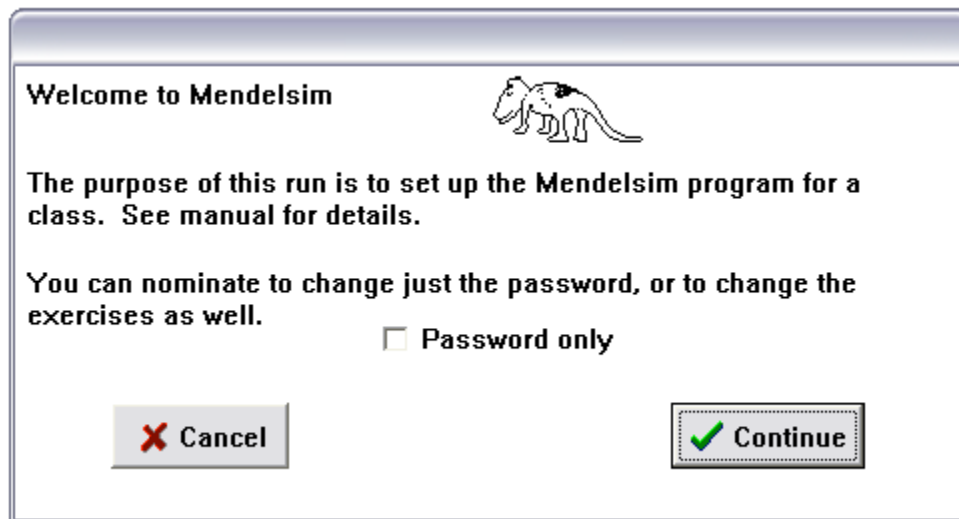
This is followed by a screen in which you agree not to sue Hands On Genetics for loss of income or livelihood if the programs do not work as indicated.

(iii) Nominating exercises (the Setup run)

When the program is next started up, and the HoG.key file is found, the startup screen changes to something like the following screen. At this stage, however, the program works essentially as previously, with access to only the elementary exercises. In order to see any benefits from the registration process, it is necessary to go through the third stage in which exercises are chosen.



This stage is again accessed by clicking on the hand with the Alt key held down. This time, the following screen is shown:



Full details for this and following screens are given in the next chapter.

(iv) Getting answers to the exercises

Once again, the entry point is the Hand click plus Alt key. If specific exercises have been set, the next screen will ask for the password. Following entry of the correct password, the following screens will allow the teacher to obtain answers to the questions. Full instructions for these screens are given in Chapter 5.

The HoG.key file

This file contains the registration information and also the information on choice of parameters for the exercises. It needs to be in the same directory as the Mendelsim program to have any effect.

The Macintosh version of the program works in a slightly different way. The Hog.key file contains only the registration information here. Parameters for the exercises are held in resource files within the program. Therefore for students to work on particular exercises, it is necessary to supply a copy of the setup program rather than requiring them to download it from the web.

The standard exercises

The 20 elementary exercises are as follows:

(1) Getting started	(11) Notation - sex-linked
(2) Make a heterozygote	(12) Sex-linked gene (1)
(3) Make homozygotes	(13) Sex-linked gene (2)
(4) Identify heterozygote	(14) Two locus cross
(5) Identify homozygotes	(15) Notation - unlinked loci
(6) No dominance	(16) Two locus ratios (1)
(7) Notation - single locus	(17) Two locus ratios (2)
(8) Single locus ratio (1)	(18) Notation - linked loci
(9) Single locus ratio (2)	(19) Linked or unlinked?
(10) Autosomal gene / sexes	(20) Estimating recombination

The 20 advanced exercises are as follows:

<input type="checkbox"/> (1) Getting started	<input type="checkbox"/> (11) Two locus intercross
<input type="checkbox"/> (2) Single locus intercross	<input type="checkbox"/> (12) Two locus testcross
<input type="checkbox"/> (3) Single locus testcross	<input type="checkbox"/> (13) Two locus unknown
<input type="checkbox"/> (4) Enumerate all crosses	<input type="checkbox"/> (14) Linked or unlinked?
<input type="checkbox"/> (5) Sex-linked crosses	<input type="checkbox"/> (15) Estimating recombination
<input type="checkbox"/> (6) Single locus unknown 1	<input type="checkbox"/> (16) Two locus mapping
<input type="checkbox"/> (7) Single locus unknown 2	<input type="checkbox"/> (17) Three locus cross
<input type="checkbox"/> (8) Rare recessive	<input type="checkbox"/> (18) Order of loci
<input type="checkbox"/> (9) Hidden sexes	<input type="checkbox"/> (19) Number of genotypes
<input type="checkbox"/> (10) Notation exercise	<input type="checkbox"/> (20) Three locus mapping

Chapter 2. The Setup run

As mentioned above, (iii), the Setup run is accessed by clicking on the Hand in the Welcome screen. This action only works after the program has been registered.

The first action is to put in a password. This prevents students from accessing setup and answer information. It also serves as part of the seed for generating student exercises. Unfortunately there is no retrieval possibility except by re-building the HoG.key file if this password is forgotten.

Nominating the exercises

The following screen is shown after the password is entered. Note that the default values have been chosen as appropriate for the majority of exercises, and you may not need to change any of the checkboxes.

The screenshot shows a dialog box with the following elements:

- Unavailable organisms:** A section with four icons and checkboxes:
 - Dinosaur dog (Tyranosaurus canis)
 - Monkbear (unknown sp.)
 - Fly (Drosophila primitiva)
 - Plant (Arabidopsis imagineria)
- EXERCISES:** A box containing:
 - Elementary
 - All
 - Advanced
 - Selected
 - No organism choice
 - Random in exercise
 - Sex in monkbears
 - Censor male dogs
 - Random start
 - Random characters
 - No 'Repeat' button
- Auto cage:** A table with columns: None, Default, All.

	None	Default	All
Fill	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>
Name	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>
- Show name
- Show 4-digit number
- No marks
- No timing
- No selftest Exs
- No selftest trials
- No answers
- Y symbol:** (1) (2)
- OK** button with a green checkmark.

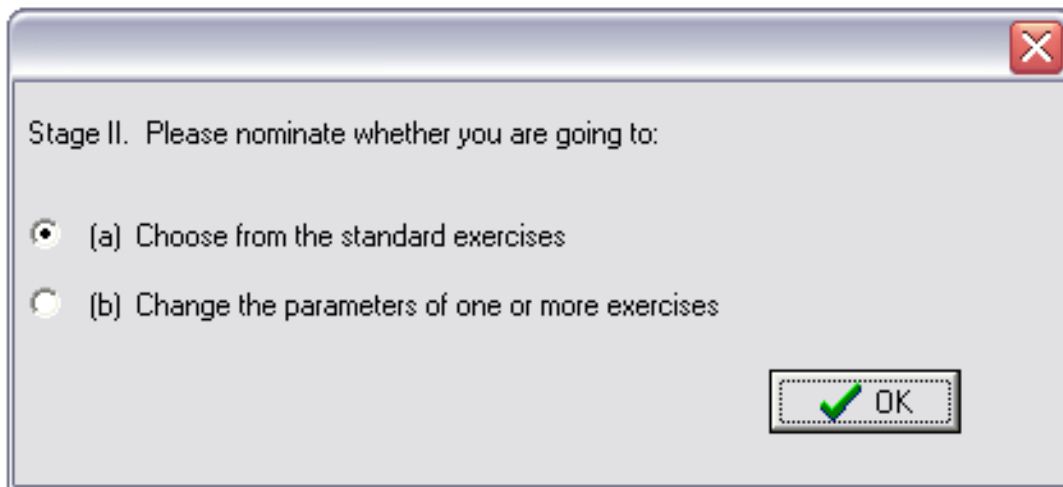
Two major choices to be made are contained in the box in the upper right corner:

(1) Elementary and Advanced exercises

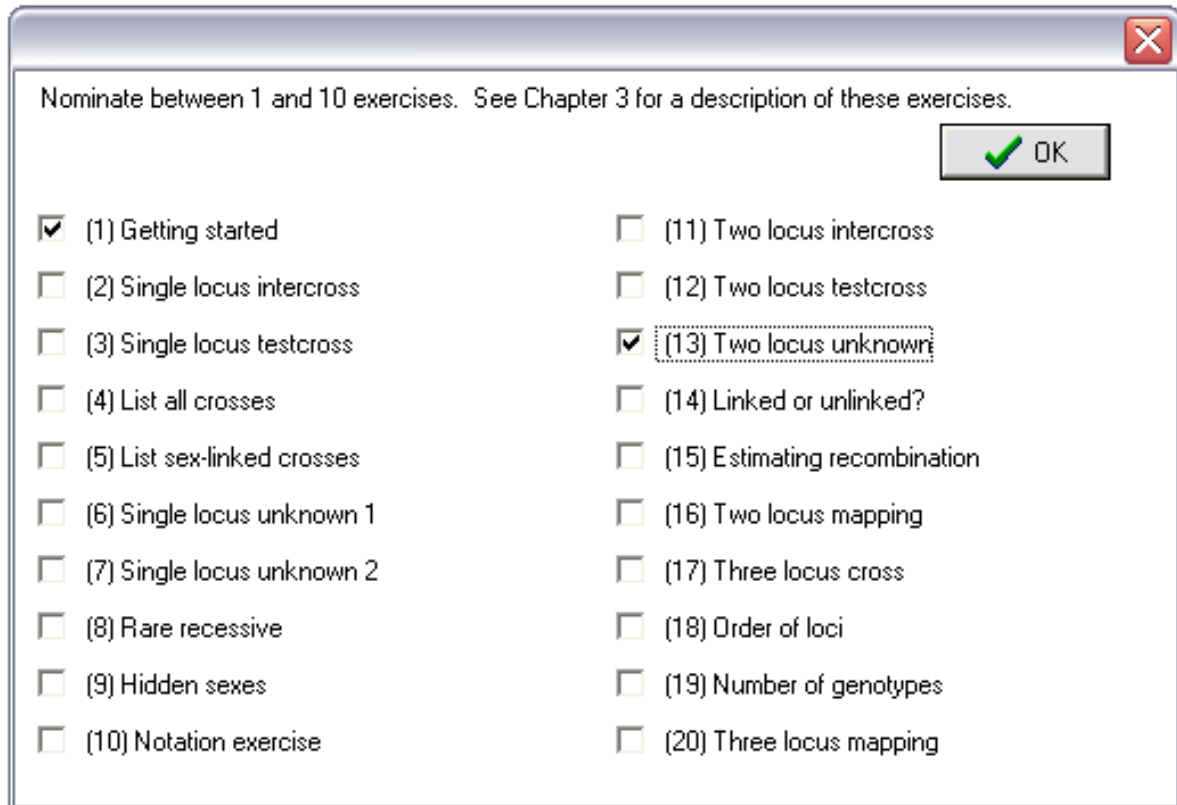
As mentioned previously, you need to choose between the two sets.

(2) All Exercises versus Selected Exercises

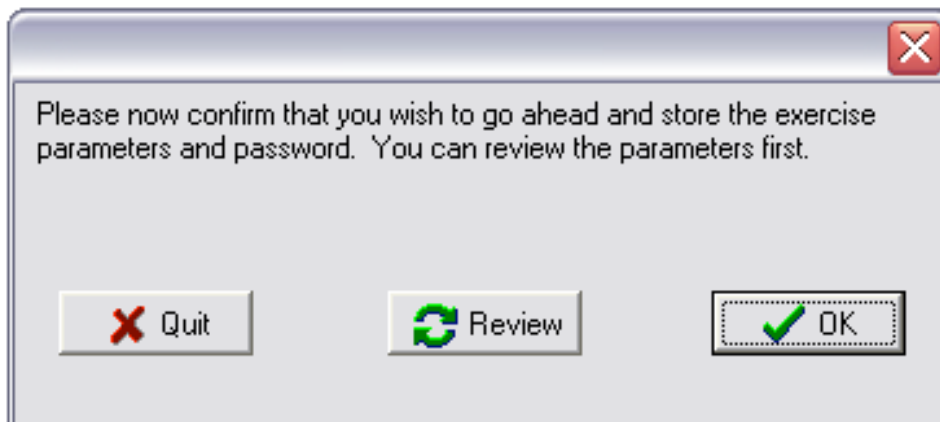
The point of registering and going through the setup run is to be able use the exercises in a structured way, rather than in the default way in which all exercises are presented at once to the student. This is initiated by checking the **Selected** box, which is the default when this screen first appears. Should you check this box, you will be presented with the next screen.



The program contains the facility to change the form of any exercise. See Chapter 5 for a discussion of this process. The current chapter and chapter 3 assume that you nominate to use just the standard exercises. Leaving button (a) selected then leads to the following screen:



The final screen allows you to cancel or confirm the choices of program parameters.



Further program parameters

(i) Choice of organism

The checkboxes above the line refer to the choice of organisms for the exercises. Although this choice may be important in the appearance of the program for students, it is relatively unimportant from a pedagogical point of view. All organisms are identical as regards the type of inheritance, the only difference being that sexes, or more specifically sex linkage, do not occur in the plant, and recombination is absent in male flies.

No organism choice

The default setting of the program, if this box is left unchecked, allows students to choose their organism. However individual organisms can be excluded from the simulation by checking the four boxes below the organisms. In some cases, as mentioned later, the student's choice will be over-ridden by the program.

Random in exercise

This button determines whether the organism will change between different runs of the same exercise, assuming that the student has not assumed complete control over the choice. Alternative possibilities are that organisms are chosen at random for each simulation, or that the same organism is used for all attempts at an exercise. The former choice is perhaps academically more desirable, but it may be easier for students if the organism does not change between different runs of the same exercise.

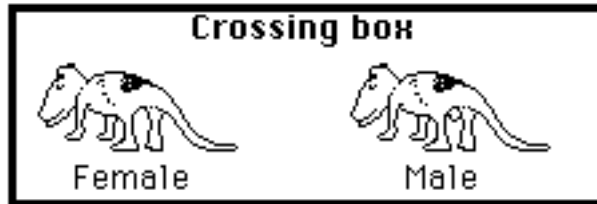
Sex in monkbeards

A problem which may arise in moving between different exercises is that some exercises involve the use of different sexes, while others, for simplicity, hide the sex of the organism. It may not be easy for a student to switch thinking between exercises in which there are no sexes and exercises where there are sexes, especially when the same organism is involved in each case. Therefore the default mode of the program ensures that all exercises in which there are no sexes are based on the monkbear, in which sex is denoted somewhat artificially by use of a ribbon or bow tie, and the plant in which there are no sexes. Exercises in which sex is used will be based on the other two organisms. This approach may be inappropriate if most of the exercises involve simulations either with or without sex as it reduces the variety of the exercises. Also the ribbon and bow tie of the bear add colour to the simulation, which will not be seen unless this box is checked.

If the Sex in monkbeards box is checked, any animal may be chosen for any exercise, although the plant is only chosen if there are no sexes. If crosses involving dogs or flies are set up in exercises in which there are no sexes, all individuals will have female phenotypes.

Censor male dogs

The second box has the effect of prohibiting the use of the 'Dog' when sexes are included. Sex in male dogs is shown using external genitalia, and some students seem to be offended by this.



(ii) Automation

	Auto cage		
	None	Default	All
Fill	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>
Name	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>

There are two aspects to automation, the more significant being governed by the **Auto cage - fill** choices. In the absence of automation, offspring have to be generated by hand, each offspring coming when the previous one has been dragged from the Offspring box. On the other hand, if automation is turned on, then the student can initiate a process in which each offspring with a phenotype which already occurs in a cage associated with the cross, is automatically added to the cage. This makes it easy to generate hundreds of offspring.

The second line of choices refers to the automatic naming of cages, depending on what genotypes are stored in the cage. If this is turned on, the student spends little time looking at phenotypes to check that an individual goes into the correct cage. It is usually appropriate for the two aspects of automation to be turned on or off together.

Whether automation is to be used depends to some extent on the purpose of using computer simulation. In one view, computer simulation is a substitute for real experimentation, so that the student carries out manipulations which are similar to those of real life. This allows students to get a feel for the enormous fluctuations which can occur by chance. Automation is unrealistic for such a use. However the program contains a variety of simulations that illustrate different genetic principles, but which involve very similar manipulations of organisms on the screen. Therefore it becomes very limiting if students are asked to do all the exercises manually. In earlier versions of the Mendelsim program which did not contain the automation feature, students often complained about the amount of time taken to generate adequate offspring numbers.

The default setting for automation has been chosen as a compromise between the above considerations. For the elementary exercises, the first 15 exercises of the elementary set are judged to be suitable without automation, while automation is suitable for the final 5 exercises. For the advanced exercises, automation is turned off for the first 10 and on for the remaining 10. Furthermore when automation is used for the first time, the program suggests the running of the Getting started exercise to explain automation.

(iii) Student name and number

Show name

Show 4-digit number

When names are used, the name becomes the basis for starting the simulation. A second student putting in the same name would therefore get exactly the same simulation, although with different numbers in the different classes. This allows students who are doing a lengthy simulation to leave the computer, and then come back to complete the exercise at some later time by putting in the same name.

You may note that checking and unchecking the **Elementary/Advanced box** affects the checking of the **Show name** box. In the simple version of the program, students are not asked to identify themselves when the program starts. This means that the program starts at random each time, and will usually give a different choice of characters if an exercise is run twice. This is appropriate for simple exercises which are done at one sitting at the computer. For more complex exercises, it is sometimes important for students to try an exercise, and later to come back to the same exercise to confirm the answers. If you are using the program to produce exercises which will afterwards be graded, it is also necessary to use names. The program, by default, suggests no name for the elementary exercises, and a name for advanced exercises, although this choice can be over-ridden.

Because student names can be put in a variety of different ways: eg. using full names, initials, capitals, etc, it has been found convenient for the program to generate a four-digit number which, after the first use, can substitute for the name. The student therefore has the choice of putting in the name in exactly the same format as previously, or of using the four-digit number to recover the simulation. When generating answers for marking of exercises, it is usually convenient for the teacher to be able to put in the four digit number rather than to type in the name in exactly the format used by the student. However the program will not show the four-digit number unless this box is checked.

Many classes will already have assigned numbers to students for other purposes, and these numbers can then be substituted for the name in the entry screen. Provided that no two students have the same number, all will get different simulations. Under this circumstance, the four-digit number is redundant, and the box should not be checked.

(iv) The marking of exercises (see also Chapter 6)

- No marks**
- No timing**

The default version of the program has marks for the questions and includes timing of the exercises. The program gives a mark to each question answered. The marks are shown in Section 4 with the questions. The marks for different questions range between 1 for the simpler questions and 8 for some of the longer ones. In general, each component of a question is worth 1 or 2 marks. At the end of each exercise, the program prints out the mark for the exercise on the screen. It also maintains running totals of the exercise and overall marks in the 'Get info' information box.

Timing may be useful in particular exercises which are being repeated. There are some exercises where the principles are only properly absorbed if the student does a number of examples, and many students seem to be stimulated by the attempts to improve their time for a particular exercise.

- No selftest Exs**
- No selftest trials**
- No answers**

The third box refer to the use of the self-test questions and answers supplied by the program. These are all suppressed if the box is checked.

As detailed in the following section and in the Student Instructions, exercises which are being carried out with genotypes hidden can be preceded by 'trials' of the same simulation with genotypes showing. Depending on whether and how students are being marked, it may be advantageous to turn off the questions for the trials.

Checking the final button allows the questions to be seen, and it also tells the student whether their answer is correct or not. However it does not supply answers in the case that the student gets the example wrong. Checking this button forces the student to work out the answer for himself/herself, even if this takes a number of tries.

(v) Miscellaneous

- Random start**
- Random characters**
- No 'Repeat' button**

The first of these boxes has an identical effect to the 'No name/number' box, in that the name which is entered is not used in the simulation. The use of this box is further described in

Section 6 when different marking strategies are discussed. The box would normally be left unchecked.

The use of random characters refers to the non-segregating characters in each simulation. Each organism in the simulation has between 6 and 8 variable characters. But only a maximum of three of these are used at any one time. What happens to the remaining non-segregating characters is irrelevant to the genetics of any particular exercise. The program normally adopts the strategy of assigning the 'wild type' character to any non-segregating character, which is the most realistic in terms of a simulation of real life organisms. This check box controls the facility to randomly assign the non-segregating characters. From a problem-solving point of view, this approach is the more rigorous one. However it leads to animals and plants with even stranger combinations of characters than seen in the normal simulations where this facility is turned off.

In the standard form of the program, as a student completes each exercise, the program puts up a **Next exercise** button and a **Repeat** button. Clicking the third box eliminates the latter button, simplifying the choice for students. They can still repeat exercises from the **Choose exercise** menu item.

(vi) Y symbol

There does not appear to be any single standard notation for the assignment of genotypes at a sex-linked locus. The default suggested in this program is to use the 'dash' or 'minus' symbol to indicate the absence of a sex-linked gene on the Y chromosome. Thus the female and male genotypes are of the form: AA and A- respectively. While this use seems adequate, it conflicts with the use in some books in which the same symbol is used to denote alternative possibilities, so that A- can represent either AA or Aa. The symbol '*', the wild-card symbol in computer usage, would appear to be a more appropriate choice for such a symbol.

A second symbol may be useful to denote genotypes with more than one sex-linked locus. The suggested symbol in this case is 'Y', such that the genotype is denoted:

$$\frac{A \ B}{Y}$$

Chapter 3. Details of the standard exercises

Each exercise consists of a short title and a description. These are shown in bold text, and are presented to the student at the start of each exercise. Some additional comments for the benefit of teachers are given in plain text. For the advanced exercises, these comments include variants of the exercises which may be set up by changing exercise parameters (see Section 6).

Each exercise is tested by one or more questions. A list of questions associated with each exercise is given at the end of this section, and the questions themselves are outlined in the following section.

SET A - ELEMENTARY EXERCISES

(1) Getting started	(11) Notation - sex-linked
(2) Make a heterozygote	(12) Sex-linked gene (1)
(3) Make homozygotes	(13) Sex-linked gene (2)
(4) Identify heterozygote	(14) Two locus cross
(5) Identify homozygotes	(15) Notation - unlinked loci
(6) No dominance	(16) Two locus ratios (1)
(7) Notation - single locus	(17) Two locus ratios (2)
(8) Single locus ratio (1)	(18) Notation - linked loci
(9) Single locus ratio (2)	(19) Linked or unlinked?
(10) Autosomal gene / sexes	(20) Estimating recombination

A1. Getting started

This is an exercise to help get you started on the Mendelsim program. You will be given instructions on what to do from a special window, which takes you through a series of commands to show how the program works.

This is a much easier way for students to learn to use the program than using the written notes or Help menu. There are more than 50 screens of instructions, so that it may take some time for students who wish to go through all of them. In the long run, this will be helpful. Students can pull out at any time and go on to the exercises.

A2. Make a heterozygote

The aim of this exercise is to generate a heterozygote. You can use any individual on the screen to set up a cross. When you have done this, go to the 'Exercises and Questions' menu and pull down Q1.

The student is presented with four animals (or plants), with genotypes showing. The four are AA, Aa, Aa, and aa, so that it is possible to set up any cross. To do this exercise, the student simply has to set up the cross AA x aa. Then it is necessary to go to the **Exercises and Questions** menu and pull down Q1. This asks the student to click on a heterozygote.

A3. Make homozygotes

You are given a cross between two heterozygotes. The aim of this exercise is to produce both kinds of homozygotes.

This time, two parents are chosen. Genotypes are again shown, so that identification of the two homozygotes is possible. Students may or may not even notice the phenotypes at this stage.

A4. Identify heterozygote

Produce and click on a heterozygote. This time you will not be able to see the genotypes, except after you have answered the question.

This is the first exercise with genotypes hidden. However the question is a very simple one, involving just a cross between two individual of opposite phenotype and clicking on their offspring.

A5. Identify homozygotes

You are given a cross between two heterozygotes. Genotypes are hidden, but you can show them by going to the 'Genotypes' item in the 'File' menu. If you can, try to answer the questions without showing the genotypes, but show the genotypes if this is necessary.

This is potentially a much more complicated exercise. Students should have no problem in finding one homozygote, the recessive, which looks different. However locating the other homozygote is much more difficult. In this exercise, genotypes may be brought into view from the File menu, which solves this problem. However it would be worth encouraging students to return to this question later on to see if they can solve it without

revealing genotypes. Dominant homozygotes can only be identified in this case by setting up crosses to a recessive genotype, and finding individuals which fail to produce recessive offspring.

A6. No dominance

In this example there is no dominance. In the cross between two heterozygotes you should be able to identify all three genotypes.

This question asks for each of the three genotypes to be identified. It shows that, in the case of no dominance, it is easy to do this even if genotypes are not shown.

A7. Notation - single locus

This is a cross between two 'pure-breeding' parents. One offspring is shown, and you can produce more but all will be the same genotype.

The aim of the exercise is to fill in the genotypes of the parents.

This is the first example in which students need to infer an unknown genotype, basically by noting which gene is dominant. In this, as in the other 'Notation' questions, the parents are fixed, and the aim is to infer the parent genotypes and fill them in by dragging gene symbols into the appropriate boxes. Students need to understand that 'pure-breeding' implies that the individuals are homozygous.

A8. Single locus ratio (1)

This is a cross between a heterozygote and a recessive homozygote. The aim of the exercise is to produce a number of offspring and show that these offspring are approximately in the expected ratio.

This example introduces counting and ratios for the first time, for a cross with a 1 : 1 expectation.

None of the examples in the elementary exercise set considers a statistical test. For examples with the chi square test, see the equivalent exercises in the advanced exercise set.

A9. Single locus ratio (2)

This is a cross between two heterozygotes. The aim of the exercise is to produce a number of offspring and show that these offspring are approximately in the expected ratio.

Observed numbers and expected ratio for an intercross between heterozygotes.

A10. Autosomal gene with sexes

This exercise introduces the complication of separate sexes. The character involved in the exercise is NOT sex-linked (ie. it is autosomal). You should be able to identify the type of cross and calculate the expected ratio. The exercise requires you to generate offspring to see if they are in agreement with expectation.

Sexes are introduced, but not, in this example, sex linkage. It is simply an exercise in combining counts from the two sexes, or, equivalently, ignoring sex.

A11. Notation - sex-linked gene

This is a cross between two pure-breeding individuals for a sex-linked gene. You should be able to fill in the genotypes of the two parents.

A single locus example in which the exercise is to infer the sex-linked genotypes of the two parents.

A12. Sex-linked gene (1)

This is a cross between two pure-breeding individuals which differ at a sex-linked locus. Note that the male and female offspring will be of different phenotypes for this locus. The aim of the exercise is to identify individuals of particular genotypes.

Students are asked to identify three genotypes in this example, a heterozygote and two homozygotes. Because this is a sex-linked locus, only females can have the correct genotype. Genotypes are shown, which makes the exercise a reasonably easy one, although students must make up new crosses to get all the genotypes.

A13. Sex-linked gene (2)

This is a cross between two pure-breeding individuals which differ at a sex-linked locus. This time, genotypes of the offspring are not shown. If you can't see how to

answer the questions without seeing the genotypes, then run a trial or two until you see how to do it.

A somewhat more difficult example, since genotypes are not shown. However students are essentially told that one of the parents is the dominant homozygote, which is the difficult genotype to identify. In this example, a trial with genotypes showing is very useful.

A14. Two locus cross

This cross involves two segregating loci. The aim of the exercise is to identify genotypes at each of the two loci.

This example introduces one concept very simply, which is the notion of identifying genes at one locus when a second locus is segregating. As for the example with sexes, it is simply a matter of ignoring the genes at whichever locus is not being considered.

A15. Notation - unlinked loci

This is a cross between two pure-breeding individuals which differ at two loci which are unlinked. You should be able to fill in the genotypes of the two parents.

Students need to understand how to write a genotype for two unlinked loci to answer this question. Genotypes at each locus are easily inferred one at a time.

A16. Two locus ratios (1)

This is a cross involving two independent (unlinked) loci. You should produce a number of offspring and test whether they fall into the expected phenotype classes.

The two locus ratio for a testcross involving two independent loci, equivalent to Exercise 8. This example, and most of the remaining ones, are more easily answered if automation is turned on.

A17. Two locus ratios (2)

This is a second cross involving two unlinked loci. You should produce a number of offspring and test whether they fall into the expected phenotype classes.

The two locus ratio for an intercross, equivalent to Exercise 9.

A18. Notation - linked loci

This is a cross between two pure-breeding individuals which differ at two linked loci. You should be able to fill in the genotypes of the two parents.

The equivalent to Exercise 15, except that the loci are linked rather than unlinked.

A19. Linked or unlinked?

These parents differ in loci which affect two characters. The loci may be linked (on the same chromosome) or unlinked (different chromosomes). You should generate enough offspring to be able to work out which is true.

This exercise needs a reasonable number of offspring to be able to see whether the loci are unlinked (1 : 1 : 1 : 1 ratio) or linked (two of the four classes higher than the other two). It is made more difficult by the fact that there are two possibilities for linked loci, AB / ab and Ab / aB . To simplify the exercise, the single locus genotypes are shown, in black to indicate that their linkage relationship is unknown. Trials can help a lot in understanding this exercise.

A20. Estimating recombination

The aim of this exercise is to estimate the frequency of recombination between two loci.

The genotypes required to estimate the recombination frequency are provided for this exercise. Furthermore, genotypes are shown. So the student simply needs to generate enough offspring to be able to estimate the frequency of recombinant offspring, from which the estimate of map distance between the two loci is obtained.

SET B - ADVANCED EXERCISES

<input type="checkbox"/> (1) Getting started	<input type="checkbox"/> (11) Two locus intercross
<input type="checkbox"/> (2) Single locus intercross	<input type="checkbox"/> (12) Two locus testcross
<input type="checkbox"/> (3) Single locus testcross	<input type="checkbox"/> (13) Two locus unknown
<input type="checkbox"/> (4) Enumerate all crosses	<input type="checkbox"/> (14) Linked or unlinked?
<input type="checkbox"/> (5) Sex-linked crosses	<input type="checkbox"/> (15) Estimating recombination
<input type="checkbox"/> (6) Single locus unknown 1	<input type="checkbox"/> (16) Two locus mapping
<input type="checkbox"/> (7) Single locus unknown 2	<input type="checkbox"/> (17) Three locus cross
<input type="checkbox"/> (8) Rare recessive	<input type="checkbox"/> (18) Order of loci
<input type="checkbox"/> (9) Hidden sexes	<input type="checkbox"/> (19) Number of genotypes
<input type="checkbox"/> (10) Notation exercise	<input type="checkbox"/> (20) Three locus mapping

B1. Getting started

Exercise 1 is really an introduction to the Mendelsim program rather than a genetics exercise. You will be given instructions on what to do from a special window, which takes you through a series of commands to show how the program works.

This is an optional exercise which has been included to allow a student to become familiar with the program before trying out the real genetics exercises. There are about 50 small screens, which take the student through the process of generating offspring, using cages, and using most of the menu items.

All of the topics covered by this exercise can be found out by experimentation, by reading the Student Instructions or using the Help menus. Many students are reluctant to do any of these things, and need an introduction of the kind included here. The exercise has been set up to allow the student to leave it at any stage, so that it can be included as an option without forcing the student to follow it all the way through.

There are, in fact, two variants of this tutorial, depending on whether automation is nominated for this exercise. The default is for automation to be turned off in the Set A exercise introduction and turned on for Set B.

B2. Single locus intercross

You are provided with two parents from pure-breeding lines that differ in a single characteristic. Genotypes are shown.

The aim of the exercise is to set up an F1 intercross, and to test whether the observed offspring from this cross are in agreement with expectations.

For this exercise, the student is given a pair of pure breeding (homozygous) parents, and is asked to generate an intercross. This is the exercise given as an example in the previous section.

All that is involved in this exercise is to generate two progeny, replace the parents by the progeny, and produce a new progeny group. The standard form of this exercise has genotypes showing. Therefore the student can see exactly what is going on at the genotype level. The questions, however, focus on what is happening at the phenotype level.

Two questions are associated with this exercise. The first of these simply asks the student to confirm that the correct cross has been set up. The second asks for expected and observed values and then goes through a statistical test using chi-square. A simpler version of this question, which omits the statistical test, is used in Set A exercises 8, 9 for a single locus and 16, 17 for two loci.

Variants: This question can also be done for a sex-linked locus. The standard form of the question assumes dominance, so that there are two phenotype classes, but the exercise can also be done with absence of dominance, with three phenotype classes.

B3. Single locus testcross

You are provided with two parents from pure-breeding lines that differ in a single characteristic. Genotypes are not shown in this exercise. However you can, if you wish, run a 'Trial' with genotypes showing.

The aim of the exercise is to set up an F1 testcross, and to test whether the observed offspring from this cross are in agreement with expectations.

This exercise complements the previous one in asking for equivalent information for a testcross. The major difference between the two exercises, in the forms presented here, is that the second is run with genotypes hidden, but with the possibility of running a trial with genotypes showing. A slightly easier form of this exercise involves running it with genotypes hidden initially, so that they can be revealed at any stage from the 'Genotypes' menu item.

Variants: This exercise can also be run with sex-linked loci and with absence of dominance. The concepts of intercross and testcross become a little ill-defined in the case of sex-linked loci, since a cross which is equivalent to a testcross can be set up using an F1 intercross, provided that original cross is set up in the correct direction. For a sex-linked gene for this exercise, however, the cross is always set up using the dominant parent as the female.

B4. List all single locus crosses

In this exercise you are asked to list all crosses possible for a two-allele single locus character. You are provided initially with two parents which are homozygous for the two different alleles. Genotypes are showing.

You need to build up the crosses one by one, each time checking with Question 1 after you have set up the cross. You should check the 'Explain question' button to make sure that you have understood the question.

Having set up all the crosses, you are then asked to put in the expected genotypes, and then the expected phenotypes.

This exercise requires some stamina on the part of the student. However it is a useful exercise in showing the range of possible crosses and outcomes. The aim is to end up with a complete description of all six possible single locus crosses, showing their expected genotype and phenotype outputs. A screen shot of the expected phenotypes is shown in the following section in association with Question 7.

B5. List all sex-linked crosses

The aim of this exercise is to list all crosses possible for a two-allele single locus sex-linked character. You are provided initially with two animals as parents which contain the two different alleles, and genotypes are shown.

You need to build up the crosses one by one, each time checking with Question 1 after you have set up the cross. You should check the 'Explain question' button to make sure that you have understood the question.

Having set up all the crosses, you are then asked to put in the expected genotypes, and then the expected phenotypes.

This is the equivalent enumeration of crosses for a sex-linked locus. Females and males are treated separately in the offspring in this case. The last two of the associated questions try to bring out some of the particular properties of sex-linked crosses.

B6. Single locus unknown 1

The aim of this exercise is to work out the inheritance of an unknown mutation. You are given two individuals, one of which contains a mutation. You must take into account the possibility that the mutation may be lethal in homozygous condition.

This is the first of two unknown exercises for a single locus. There is also an equivalent exercises for two loci (No. 13) which is conceptually similar. The current exercise is based on a cross of the form $Aa \times aa$, where there is dominance of A over a , although it is not necessary to tell this to students. As discussed in Section 5, this cross has the property that it is not possible to infer the mode of inheritance just from the parents and offspring. The standard question includes a 50% probability that the AA genotype is lethal.

The exercise is currently presented in a form in which either character may be the mutant character. Therefore it is possible that a genotype which has been the normal genotype in questions before this one may now be lethal.

Variant: An easier variant of this question would omit the possibility of lethality. It is still a testing exercise to work out which gene is the dominant.

B7. Single locus unknown 2

The aim of this exercise is to work out the genetics of a single character, which could be either sex-linked or autosomal. You are provided with just two individuals to start the exercise, and these two may or may not differ in the character.

This exercise is easier than the previous one since lethality is not included, but it involves the extra complication of sex linkage. The types of cross in this question are taken from a wider range, so different students will get more or less difficult problems here.

Both this and the previous exercise are ones in which repetition of the exercise would be beneficial. Note that a considerable amount of the tutorial is directed at helping students with these exercises.

B8. Rare recessive

When a recessive gene is rare, the trait it defines may be difficult to find. In this exercise, you are given two parents which contain, between them, just one recessive gene. The aim of the exercise is to identify the trait which is determined by the gene, and to confirm the recessive mode of inheritance.

This is a useful exercise to give students a feel for the way in which recessive genes are hidden in a population. As the exercise is presented, it will not be possible to know which character is affected until a homozygous recessive individual turns up. An instruction has been built into the program which suppresses automatic cage naming for this exercise.

Luck plays a considerable role in this exercise, as the character may turn up quickly for some students and slowly for others, and some characters will be more easily seen than others. It is not clear that there is an optimal strategy for this exercise, although since one parent must be heterozygous it is probably best to first screen parent-offspring matings using one parent, and then the other if no segregation is seen.

B9. Hidden sexes

This exercise involves individuals in which there are separate sexes. However from what is shown on the screen, you cannot tell the sexes apart.

There is also a single segregating character, which is determined by genes at a single locus. This locus may be either sex-linked or autosomal, and the exercise is to determine this without the benefit of knowing which sex is which.

You are provided with two individuals initially, one of which is female and one male, although you cannot tell which is which. These individuals may be either homozygous or heterozygous for the locus in question, or hemizygous in the case of a male if the locus is sex-linked.

A slightly 'quirky' exercise, but if students can solve this one then they really understand sex-linked inheritance.

This exercise can be tested by requiring students to fill in all genotypes, or alternatively by just asking whether the loci are autosomal or sex-linked. In the latter case, there is a 50% chance of guessing correctly, so the automatic marking is not really precise enough unless the question is repeated a number of times.

B10. Wild type notation.

The purpose of this exercise is to test genetical notation.

You are given two parents which are pure-breeding and which differ in either a single character or in two characters. The parents cannot be replaced. A single offspring is shown. Since the parents are pure-breeding, it is expected that any further offspring will be the same as the one shown, although the phenotypes of different sexes may be different.

The aim of the exercise is to fill in the genotype slots shown in the accompanying question. The exercise should be repeated a number of times.

Note on Notation exercises: A number of exercises in both Set A and Set B have 'Notation' in the title. Each of these exercises starts with a cross between two pure-breeding individuals. Although extra offspring can be generated, the parents cannot be changed. The idea behind these limited simulations is that they give sufficient information to show which character is dominant, and since the student is told that the parents are homozygous, no additional information is required. The question asks the student to fill in the genotype of each of the two parents. This example in the simpler Set A questions is useful in introducing the student to the idea of inferring genotypes from phenotypes and in introducing various notations. The exercise is used for a single autosomal locus (A7), a sex-linked locus (A11), unlinked loci (A15) and linked loci (A18). The one Set B exercise of this type combines various aspects by using two loci and testing both the Mendelian notation and the wild type notation.

There is a divergence of views on the value of introducing the wild type notation. Elementary classes can get by without introducing it at all. However students who go beyond elementary genetics will undoubtedly be exposed to it. Several screens of the tutorial are devoted to introducing this topic.

Variants: Either Mendelian or wild type notation can be specified, in which case the question becomes directed at that notation. If the question is posed twice, it is assumed that the first use is for the Mendelian notation and the second for the wild type notation.

Either one locus or two loci can be specified. For a single locus, any setting is possible, so that the default setting specifies sexes, a mixture of sex linkage and autosomal inheritance, and a mixture of dominance and absence of dominance. For two loci, although different sexes can be assumed, the inheritance should be autosomal, and the case of no dominance cannot be used. The number of possibilities would, otherwise, be much larger than the program can cope with.

B11. Two locus intercross

You are provided with two parents from pure-breeding lines that differ in two characteristics. Genotypes are not shown, and you should try to work without viewing them, but you can reveal them by using the Genotypes item from the File menu.

The aim of the exercise is to set up an F1 intercross, and to test whether the observed offspring from this cross are in agreement with expectations. The questions will ask this first for one character at a time and then for both characters together.

Exercises B11 and B12 are the two-locus equivalents of exercises B2 and B3. Both single-locus and two-locus questions can be used here. If two single locus questions are used, the program interprets these as referring to the first and second loci respectively.

Variants: Genotypes can be hidden, or they can be hidden initially.

The questions may include a component on the chi-square test (6 and 17 for one locus and two loci respectively) or these may be omitted (5 and 16). The former are used in Set B exercises and the latter in Set A.

Note that the program may not cope with all the various possible combinations of sexes and sex linkage.

B12. Two locus testcross

You are provided with two parents from pure-breeding lines that differ in two characteristics. Genotypes are not shown, but you can run trials if you wish.

The aim of the exercise is to set up an F1 testcross, and to test whether the observed offspring from this cross are in agreement with expectations. The questions will ask this first for one character at a time and then for both characters together.

B13. Two locus unknown

You are provided with parents which have two segregating characters, each of which has an unknown mode of inheritance. The aim of the exercise is to work out the mode of inheritance of each of the characters individually.

This exercise is similar to the single locus exercises. The student will be quizzed separately about the inheritance of the first and second characters. The two characters are not treated together. However as an unknown exercise it is a useful one in that it helps students to understand the idea of analysing one character at a time in the background of a second segregating character.

B14. Linked or unlinked?

In this exercise you are given a single pair of parents. These parents differ in loci which affect two characters. The loci may be linked (on the same chromosome) or unlinked (different chromosomes), and the aim of the exercise is to work out which is true. You will notice that the parents cannot be replaced in this exercise.

You should generate a number of progeny, to be able to tell from the progeny whether the loci are linked or unlinked. However before you do this, you may find that it is worth running one or more trials in which the genotypes are shown, which

will help you to see the problem more clearly. This exercise can also be run more than once with the full genotypes hidden, and it may be worth repeating the exercise to be sure that you understand the principles involved.

This exercise helps students to understand how to analyse data to test for linkage. There are two possible ways in which this exercise can be introduced, and the difference between these two needs some explanation.

The exercise is currently set up as follows. Genotypes of the parents are not shown. The offspring which come out are either in the ratio, 1 : 1 : 1 : 1, which the student is supposed to interpret as showing that the loci are unlinked, or there is an excess of two classes and a deficiency of the others, which is to be interpreted as showing linkage. The question asks simply whether the loci are linked or unlinked. Genotypes can be displayed at the end of the exercise.

While this approach seems not to worry most students, it is, in reality, not possible to interpret a 1 : 1 : 1 : 1 ratio as necessarily showing independence. This ratio could come from two different crosses:

- (a) Aa Bb x aa bb
(b) Aa bb x aa Bb

The first of these crosses is correctly interpreted as showing independence, but the second shows nothing about the linkage relationships.

This question can therefore be set in a second, more intellectually satisfactory format. Genotypes of the parents are shown. However since the aim of the exercise is to find out whether the two loci are linked or not, the complete genotypes cannot be shown. Instead, partial genotypes are shown. These are shown in black, rather than their usual red, and they are written in the form Aa Bb, which, it is explained to the students, tells them nothing about linkage.

When the exercise is posed in this form, the parent cross can be set up in either form, and the question associated with the exercise has a third option 'Can't tell', which students are expected to check if the cross is of the uninformative type. When the exercise is set up in the form with no genotypes showing, the program ensures that the cross is always of type (a) rather than type (b) (see the discussion of 'Phase' in Section 5).

B15. Estimating recombination

In this exercise, you are required to estimate the map distance between two linked loci. Initially you will not see any parents. However if you look in the Storage cage, you will find all possible genotypes. Open this cage, decide on what cross you will need to measure recombination, and remove individuals with these genotypes from the cage.

The exercise is in two parts. In the first part, you are asked to set up a cross to estimate the map distance. You will then be requested to set up a different cross to get a second estimate of the map distance.

In this exercise, students are first asked to set up a cross, and then to nominate which parent is being used to study recombination. They are expected to set up a testcross, of the form

$A B / a b \times a b / a b$. They will then be asked to estimate the recombination frequency. If the Question 19 is only asked once, that is the end of the exercise. However if it is asked twice, as in the default form, they are asked to set up a second cross to estimate recombination: $A b / a B \times a b / a b$.

Variants: This exercise can be run with or without sexes, and sex-linkage can also be used. There is a special case for this exercise where the 'Fly' organism is chosen. In this case, the program puts up a third question, which is to show that there is no recombination in the male.

B16. Two-locus mapping

The aim of this exercise is to estimate the map distance between two loci. The genotypes provided for the exercise are just the single locus mutations. Two individuals are provided for each, allowing the cross of any genotypes. Wild type individuals, lacking either mutation, are also provided.

The first, and more difficult step, in this exercise is to synthesise the genotypes for a two locus testcross. The second step is the estimation of the recombination frequency.

This, and the equivalent three-locus Exercise B20, are difficult exercises. The default form of the exercise assumes recessive mutations, so that the student must first build up the double recessive genotype. An easier form of this exercise can be set up using dominant mutations.

Variants: If the fly is specified for this exercise, it becomes an even more demanding one, since the initial recombinant gametes used in building up the stock must come from the female.

B17. Three locus cross

In this exercise you need to build up and analyse 3-point testcross data, and to draw a genetic map for the three loci.

You are provided with two pure-breeding parents which are homozygous for the three loci. No genotypes are shown.

You first need to generate the testcross, and then produce enough offspring to build up the map.

To set up the correct cross, the student has to recognise which is the recessive genotype and set up a testcross, as in Exercise B3. There is one circumstance in which this exercise may be more difficult, which is the case where the fly is chosen and the male parent is the triple dominant. In this case it is necessary to go for an extra generation to set up a cross in which the female is heterozygous and the male parent recessive at all three loci. The male backcross will provide some information in this case, but the program does not accept this cross.

B18. Order of loci

For this exercise, the computer will generate a fixed 3-point testcross. Genotypes of the parents are shown in a limited form which does not indicate the linkage relationships. No genotypes are shown for the offspring.

You should generate enough offspring to be able to infer the linkage relationships of the three loci, and then choose from a menu of 7 possibilities.

You are encouraged to repeat this exercise a number of times to master the principles involved.

This is the 3-locus equivalent of Exercise B14, except that the cross is always set up to be informative. The exercise can be done rapidly and repeated a number of times, until the principles of assigning linkage relationships for three loci become clear.

B19. Number of genotypes

This exercise involves no simulation. It is an exercise in enumeration of all possible 3-locus genotypes.

The question associated with exercise will ask you to calculate the number of possible genotypes for seven different types of linkage relationships, including sex-linked and autosomal. Having tried the question, you can, if you wish, see any or all of these genotypes and their associated phenotypes.

B20. Three-locus mapping

The aim of this exercise is to estimate the map distance between three linked loci. The genotypes provided for the exercise are just the single locus mutations. Two

individuals are provided for each, allowing the cross of any genotypes. Wild type individuals, lacking either mutation, are also provided.

The first, and more difficult step, in this exercise is to synthesise the genotypes for a three-locus testcross. The second step is the estimation of the map of the three loci.

The three locus equivalent of exercise B16.

Questions associated with Standard Exercises (see Section 4)

A1. Getting started	1			
A2. Make a heterozygote	14			
A3. Make homozygotes	13	13		
A4. Identify heterozygote	14			
A5. Identify homozygotes	13	13		
A6. No dominance	13	13	14	
A7. Notation - single locus	12			
A8. Single locus ratio (1)	4			
A9. Single locus ratio (2)	4			
A10. Autosomal gene with sexes	4			
A11. Notation - sex-linked gene	12			
A12. Sex-linked gene (1)	14	13	13	
A13. Sex-linked gene (2)	14	13	13	
A14. Two locus cross	13	14	14	
A15. Notation - unlinked loci	12			
A16. Two locus ratios (1)	16			
A17. Two locus ratios (2)	16			
A18. Notation - linked loci	12			
A19. Linked or unlinked?	18			
A20. Estimating recombination	19			
B1. Getting started	1			
B2. Single locus intercross	2	5		
B3. Single locus testcross	3	5		
B4. List all single locus crosses	6	7	8	9
B5. List all sex-linked crosses	6	7	8	10 11
B6. Single locus unknown 1	12	13		
B7. Single locus unknown 2	12	13		
B8. Rare recessive	13	13		
B9. Hidden sexes	12			
B10. Wild type notation.	12	12		
B11. Two locus intercross	14	6	6	17
B12. Two locus testcross	15	6	6	17
B13. Two locus unknown	12	12		
B14. Linked or unlinked?	18			
B15. Estimating recombination	19	19		
B16. Two-locus mapping	19			

B17. Three locus cross	20	22
B18. Order of loci	21	
B19. Number of genotypes	23	
B20. Three-locus mapping	20	22

Chapter 4. The bank of questions

This section describes the questions which guide students through the exercises. Some of these questions are intimately tied to the exercise in which they are used, eg. Questions 6,7,8 which deal with the listing of all crosses in Exercises B4, B5. In other cases, eg. Question 13 which asks the student to click on an animal of particular genotype, the question is relevant to a range of different exercises. The numbering of questions corresponds roughly to the order in which they are used in the standard exercises.

A short summary of the questions is as follows:

Single locus

1. Getting started
2. Intercross has been set up
3. Testcross has been set up
4. Observed and Expected values
5. Chi-square test
6. List all crosses
7. Expected genotype frequencies
8. Expected phenotype frequencies
9. Number of segregating crosses
10. Pseudo 3:1 ratio for a sex-linked cross
11. Opposite phenotype parents and offspring
12. Fill in the genotypes
13. Click on a homozygous individual
14. Click on a heterozygous individual
15. Autosomal versus sex-linked

Two loci

16. Expected and observed values
17. Chi-square test
18. Linked versus unlinked
19. Estimate the recombination frequency

Three loci

20. Draw the genetic map
21. Coefficient of interference
22. Order of loci
23. Number of genotypes

The program contains the facility to associate any question with any exercise (see the following section on how to do this). It should be clearer from the information presented in this section whether the combinations are meaningful ones.

As shown in the table of Section 3, some of the questions are repeated in a particular exercise, eg. Question 13 in Exercise A3. This is done to maximise the use of the questions for a variety of situations. Repetition is discussed specifically below for those questions for which this is relevant.

Question 1. Getting started

This question is an artificial one which is posed in the introductory exercise to show how to answer a question from the Questions and Answers menu

Question 2. Intercross set up

This question starts off Exercise B2, where the student is first required to set up an F1 intercross and then to fill in observed and expected values. This is a question which has to be answered correctly before the program will move on to the next question. Once the question has been correctly answered, the program will not allow the cross to be changed until the remaining questions about the cross have been answered.

Question 3. Testcross set up


This is the equivalent question required to start Exercise B3.


Question 4. Expected and observed values

The figure below shows a screen dump of the question which the student sees. The 'Explain question' button is present in most questions and provides information to supplement the exercise description. In this case it explains how to enter data for the expected and observed values.

Ex2 Q2

Fill in the expected ratios and the observed numbers of the following phenotypes:





Total

Expected	<input type="text"/>	:	<input type="text"/>	
Observed	<input type="text" value="0"/>		<input type="text" value="0"/>	<input type="text" value="0"/>

Mark me

Explain question

Hide question

Repetition: If referring to a single locus simulation, the question should only be used once. However if the question refers to a two-locus simulation (eg. Exercise B11), and the question is used twice, then the program takes the first use to refer to one locus and the second use to refer to the other locus.

Question 5. Chi-square test.

This supplements the previous question, by going on to ask the student to calculate the chi-square value for agreement of observed and expected values. Once the question has been answered, the student can request an additional screen showing details of the calculation. Question 5 is an alternative to Question 4. It asks for the same information as Question 4, plus the additional chi-square calculations. Exercises should use either Question 4 or 5, but not both. Note also that the same questions are used for both intercross and backcross. The computer calculates the expected ratios depending on whether they follow Question 2 or Question 3. As mentioned in conjunction with the exercises, the questions also cope with the expectation for a sex-linked locus.

Repetition: The same rules as apply to Question 4.

Question 6. List all crosses

This question asks the student to add crosses to a list until all crosses have been enumerated. The figure below shows the situation when the student is about to add the final cross to the list. This question requires the exercise to be run with genotypes showing. It copes with both autosomal and sex-linked crosses for a single locus.

Ex4 Q1

Is the current cross on the list? If not, click on 'Add to list'.
Click 'List complete' when you think all crosses have been listed.

1.	aa	x	AA	Explain question
2.	AA	x	Aa	Hide question
3.	Aa	x	Aa	
4.	Aa	x	aa	Add to list
5.	aa	x	aa	List complete

Question 7. Expected genotype frequencies

The student is asked to fill in the expected genotype ratios for all crosses. The concept is similar to the expectation of phenotypes which is discussed next.

Ex5 Q3

Fill in the expected ratios for the indicated phenotypes.

	Parent genotype			Offspring Eye shape			
				Female		Male	
				<u>Small</u>	<u>Large</u>	<u>Small</u>	<u>Large</u>
1.	ss	x	s-	all		all	
2.	ss	x	S-		all	all	
3.	Ss	x	s-	1	1	1	1
4.	Ss	x	S-		all	1	1
5.	SS	x	s-		all		all
6.	SS	x	S-		all		all

Mark me
Explain question
Hide question

Question 8. Expected phenotype frequencies

The student is asked to fill in all phenotype ratios. A screen dump of the answer to this question for a sex-linked locus is shown above, where the alleles are S and s , and the dash indicates the absence of the locus on a Y chromosome of the male:

Note that the question considers females and males separately, and expects the student to use 'all' to describe the phenotypic output for both females and males. The student has taken advantage of a facility which allows the computer to sort the crosses into a more logical order than the original order which they were produced.

Question 9. Number of segregating crosses

This question is posed in connection with the phenotype outputs for an autosomal locus (not shown here). It is a way of drawing attention to the fact that although there are six possible crosses, only two are segregating crosses, leading to 1 : 1 and 3 : 1 ratios respectively.

Question 10. Pseudo 3:1 ratio for a sex-linked cross

The student is asked to identify a cross for a sex-linked gene which gives a ratio analogous to the 3:1 ratio for an autosomal gene (No. 4 in the above list).

Question 11. Opposite parents and offspring


The student is asked to identify a cross for a sex-linked gene in which the phenotypes of the two sexes are the opposite in parents and offspring (No. 2 in the above list).

Question 12. Fill in the genotypes


This is the principal question used in testing the assignment of genotypes in unknown inheritance exercises and in 'notation' exercises. As shown in the diagram below, the student is given a 'template' of gene symbols which can be dragged into the boxes below individuals of unknown phenotype. In the example shown, the student needs to work out whether one or two genotypes can correspond to a phenotype.

Ex3 Q1

Fill in the genotypes of the individuals shown below. Click 'Explain question' for more details. Click 'Mark me' only if finished.



or



or

Explain question

Hide question

Available gene symbols
C c -

Mark me

When used in this way, the question can only deal with single locus genotypes.


Repetition: The question can be repeated with a two-locus simulation (see Exercise 13, Section 3), in which case the first use refers to one locus and the second use to the other. The question can also be repeated with a single-locus simulation, in which case the program interprets the first use as applying to the Mendelian notation, and the second use as applying to the wild type notation.

A second use for this question comes in Exercises A7, A11, A15, A18, and B10, the exercises on notation (see figure below). The question is interpreted in a slightly different way in this case, since the animals shown in the question are specifically the parents of the cross used in the exercise rather than random individuals of the same phenotype. The parents are known to be homozygous, eliminating the possibility of more than one genotype corresponding to a phenotype.


For this exercise, the question can also be used with two-locus genotypes. The example below shows how students are intended to fill in genotypes for linked loci. This example also illustrates the use of the wild type notation. The student is provided with both the recessive and dominant gene symbols, as well as the wild type symbol, +, and has to deduce which symbol is relevant to the inheritance patterns of the particular simulation.

Ex1 Q2

These parents differ in two characters which are determined by LINKED autosomal loci. The two parents are shown below. Fill in their genotypes, using the WILD TYPE notation.



+	+
+	+



p	e
p	e

Explain question

Hide question

Mark me

Available gene symbols

P p + - E e

Repetition: For either a single-locus or two-locus simulation, the program interprets the first use as applying to the Mendelian notation, and the second use as applying to the wild type notation.

Question 13. Click on an individual which is homozygous for:

This question, and the following one, complement Question 12 in asking more specifically for information about particular individuals. Questions 13 and 14 have the special property that clicking on animals on the main screen in the background of the questions does not manipulate the animals. Instead, any individual clicked on is surrounded by a rectangle to show that it has been 'selected'.

Repetition: This question focuses on the genotype at a single locus. However it can be used with two-locus genotypes. If it is repeated, the first use refers to the first locus and the second use to the second locus.

The question can also be repeated for use with single-locus genotypes. If used once, it will ask for the genotype corresponding to the dominant allele. If used twice, it will ask first for the recessive and then for the dominant. The main use for this is in connection with Exercise 8, detecting the rare recessive. The question is actually posed in a slightly different way when used in this exercise to avoid using the name of the unknown character.

Question 14. Click on an individual which is heterozygous.

This question is closely analogous to the previous one. It should only be used once for a single locus, but can be repeated for two loci, eg. Exercise A14.

Question 15. Autosomal versus sex-linked

This question simply asks students to click one or the other alternative. It is intended for use in Exercise B9 on hidden sexes, but can also be used for a simpler test of inheritance in any single-locus unknown exercise.

This question cannot be repeated for a two-locus exercise.

Two-locus questions

Question 16. Expected and observed values

Question 17. Chi square test

These are the two-locus equivalents of Questions 4 and 5. They can be used in conjunction with the single-locus questions to test for both single and joint segregations. As with the single locus questions, the chi-square question incorporates the expected and observed components, so the two questions should not be used together. Nor is repetition of these, or any other of the two or three locus questions, meaningful.

Question 18. Linked versus unlinked

This question is intended specifically for use with Exercises A18 and B14. It could, however, be used as a simple test for any two-locus unknown question.

Question 19. Estimate the recombination frequency

The student is asked to type in an estimate of the recombination frequency expressed as a percentage.

Three-locus questions

Question 20. Draw the genetic map

The student is given a template, as shown in the figure below, and asked to drag the three locus symbols to their correct designations and fill in the map distances. In the three-

locus examples, the two recombination frequencies always differ by at least 10%, and since the map is drawn approximately to scale, there should be no ambiguity in knowing which map distance to assign to which region.

Ex1 Q2

Put the appropriate locus symbols into place and fill in the map distances.

a h s

----- cM's ----- cM's -----

----- cM's -----

Question 21. Coefficient of interference

The student is asked to type in an estimate of this coefficient, which measures the reduction in the amount of double crossovers compared to expectation based on no interference. This question should only be used after Question 20, because the program does the calculations when working out the map.

Question 22. Order of loci

This question is intended for use with Exercise 17, in which the student is expected to infer the linkage relationships without necessarily calculating recombination frequencies. The form of the question is indicated below:

Ex2 Q1

Which of the following describes the linkage relationships of the three loci?

- h, p and r loci unlinked**
- h and p loci linked, r unlinked**
- h and r loci linked, p unlinked**
- p and r loci linked, h unlinked**
- Loci are linked in order h - p - r**
- Loci are linked in order h - r - p**
- Loci are linked in order p - h - r**


Hide question

h Leaf hairs

p Petal colour

r Leaf

Mark me



This question is intended to give students practice at inferring linkage relationships without going into detailed calculations. It needs to be repeated a number of times for the principles to be assimilated.

Question 23

The student is asked to type in numbers for seven different forms of genotype. This question goes with Exercise 19. The exercise/question can only be done once since there is only a single answer.

Chapter 5. Parameters of individual exercises

This chapter deals with the details of selecting individual exercises, rather than selecting all 20 of either the elementary or advanced exercises. Should you click on **Selected** in the overall parameter selection box (Page 10), the next screen is as follows. You need to select (b) rather than the default (a).

Please nominate whether you are going to:

(a) Choose from the standard exercises

(b) Change the parameters of one or more exercises

Changing individual exercises

There are two principal reasons why you may need to do this:

- (i) To change some aspect of the exercise which is not appropriate
- (ii) To present the exercise in a format for marking.

Should you nominate (b) in the above box, you will be presented with the following blank template:

EXERCISE NUMBER: 1 <input type="text"/>			Set A	
Questions	Number of loci: <input type="radio"/> 1 <input type="radio"/> 2 <input type="radio"/> 3		Exercise	
<hr/> <hr/> <hr/> <hr/> <hr/> <hr/> <hr/> <hr/> <hr/> <hr/>			None ▼	
			Exercise description	Clear
			Back	Next
			Done	

The simplest way of proceeding is to use the pull down menu of Standard exercises in the top right-hand corner to nominate the number of one of the exercises. If, for example, you nominate Exercise 1, the screen will change to the appearance shown below:

EXERCISE NUMBER: <input type="text" value="1"/>		<input type="text" value="Getting started"/>		Set A	
<input type="button" value="Questions"/>		Number of loci: <input checked="" type="radio"/> 1 <input type="radio"/> 2 <input type="radio"/> 3		Exercise	
Sexes: <input type="checkbox"/>				<input type="text" value="1"/>	
Mutations: <input type="radio"/> Rec. <input type="radio"/> Dom. <input checked="" type="radio"/> Either <input type="radio"/> Intermed. <input type="radio"/> Mixture					
Parent cross: <input checked="" type="radio"/> Aa x aa <input type="radio"/> Aa x Aa <input type="radio"/> AA x aa <input type="radio"/> Mix. <input type="radio"/> AA x Aa					
Extra parents: <input checked="" type="radio"/> No <input type="radio"/> Locked <input type="radio"/> Single locus <input type="radio"/> All					
Show genotypes: <input type="radio"/> No <input type="radio"/> Part <input checked="" type="radio"/> Yes <input type="checkbox"/> Hide offspr. <input type="checkbox"/> Hide init.					
Notation: <input checked="" type="radio"/> Mendel <input type="radio"/> Wild <input type="checkbox"/> Switch					
Exercise: <input type="checkbox"/> Single <input type="checkbox"/> No trial				<input type="text" value="No lethality"/>	
Organism: <input checked="" type="radio"/> Any <input type="radio"/> 'Dog' <input type="radio"/> 'Bear' <input type="radio"/> 'Fly' <input type="radio"/> 'Plant'					
<input type="button" value="Exercise description"/>		<input type="button" value="Clear"/>		<input type="button" value="Back"/>	
				<input type="button" value="Next"/>	
				<input type="button" value="Done"/>	

Looking at the buttons checked, you will see the form of the exercise. The organism is unisexual, since the Sexes box is not checked. Different student will be given different characters, but in each case the simulation will involve dominance (see later for the difference between checking the Recessive, Dominant or Either box). Two parents are chosen, one of which is homozygous recessive and one heterozygous. Genotypes are shown using the Mendelian notation. Question 1 is associated with the exercise as seen in the top left corner. The short exercise description 'Getting started' which appears in the editable box at the top of the parameter entry screen, is used to describe the exercise in the 'List exercises' and 'Choose exercise' menus.

If none of the settings are altered, then nominating a standard exercise in this way is equivalent to the short method covered at the start of this chapter. You are not, however, restricted to accepting the pre-set values for the exercise. Any values can be changed by checking the appropriate boxes. Similarly the short description of the exercise can be edited.

Moving through the exercises

Clear

Back

Next

Done

The **Next** and **Back** buttons allow movement through the exercises. If you click on the **Next** button, you will see that the exercise number changes to 2. If you have previously set any buttons, these will be shown, otherwise the screen will be blank as shown in the first figure, but with the appropriate exercise number showing. Note that the exercise number cannot be edited directly.

If you wish to change the form of an exercise, it is easiest to use the **Clear** button. This clears all settings, returning the box to the state shown in the top figure.

Clicking the **Done** button indicates that all exercises have been nominated, and dismisses the dialog box. This is the only means of exiting from the nomination process. You will get another chance to return to the box in case of doubt.

A maximum of 10 exercises can be set. After this, the **Next** button will return to Exercise 1.

Exercise description

As seen from the diagrams above, the exercise description, which will be displayed at the start of an exercise, can be viewed from the button at the left of the bottom row. This description can also be edited.

Standard exercises with altered parameters

As is clear from the above description, it is possible to base an exercise on one of the standard exercises, but to make changes to the parameters. Any parameters not altered, in particular the choice of questions and exercise description, will remain as in the original exercise. Also the Standard exercise number will be retained even though some of the parameters have been changed.

Care must be taken, however, that the parameters are not inadvertently returned to the original exercise parameters. For example, clicking on the menu of standard exercises will replace any parameters which have been set. Similarly, by going through the simple method for nominating exercises (see above), any parameters will automatically be re-set as the standard ones.

Note that there are two types of buttons: radio buttons which are round, and check buttons which are square. In each group of radio buttons, one should be checked. This is done for you if you nominate a standard exercise. If you do not actively choose any button in a group, then the first one will be chosen by default when the exercise is set. Check boxes are all independent of each other, and may be either checked or not.

Parameters of the exercise

This section deals in detail with the meanings of the various button settings. The following section deals with the choice of questions and the exercise description.

(1)

EXERCISE NUMBER:

The Exercise title can be edited directly, and/or can be put in by nominating a standard exercise. The Exercise number changes only in response to the **Next** and **Back** keys.

(2)

Number of segregating loci: 1 2 3

Checking a standard exercise automatically sets these and other buttons.

(3)

Sexes: **Sex linkage:**

or

Sexes: **Sex linkage:** **No** **Yes** **Mixture**

If the **Sexes** box is unchecked, as shown in the first line, a unisex organism is provided, and there is no possibility for sex-linked inheritance.

Checking the **Sexes** box brings up the possibility of sex linkage. The default for this is the first button, **No**, so that autosomal inheritance will be assumed even if there are different sexes.

Checking the **Mixture** box gives a result which is interpreted by the program in somewhat different ways depending on what other boxes are checked. If a single locus is checked, then there will be a 50% probability that the locus will be sex-linked and 50% probability of autosomal. If two loci are nominated, then the choice depends on the **Linkage** buttons (see below). For example, if the **Independent** loci button is nominated, then there will be a 50% probability that one of the two loci is sex-linked and one autosomal, and a 50% probability that both loci are autosomal (but unlinked). If the **Linked** loci button is checked, then there is a 50% probability that both loci are sex-linked and a 50% probability that both loci are autosomal. These rules may seem rather complex, but they are chosen to produce the most appropriate forms of the standard exercises.

(4)

Mutations: **Rec.** **Dom.** **Either** **Intermed.** **Mixture**

The range of choices for this line is to take account of the various possibilities under the 'wild type' notation. The Mendelsim program generally accepts the idea that there is a 'wild type' or 'normal' appearance for each organism. A wild type dog, for example, has a long tail. One with a short tail is a mutant.



A 'normal' dog



A 'mutant' dog

When the wild type notation is used, the genotypes and phenotypes corresponding to recessive and dominant mutations are as follows:

Recessive mutation:	Genotype	aa	a+	++
	Phenotype	short tail	long tail	

Dominant mutation:	Genotype	AA	A+	++
	Phenotype	short tail		long tail

There is a clear difference between these two situations. Under the Mendelian notation, on the other hand, where no distinction is made between wild type and mutant, there is no distinction between 'dominance' and 'recessiveness'. Long tail and short tail are just two characters, and there is no reason why one should be systematically dominant over the other. **If the Mendelian notation is being used, then it is usually appropriate to check the box labelled 'either'**. In this case, either character can be dominant with 50% probability. Ticking the recessive box would mean that long tail is always dominant to short tail, presence of the black patch is always dominant to absence, etc, despite the fact that these are supposed to be random characters. In exercises where unknown mutations are involved, it would be particularly inappropriate to make this choice.

The choice of the 'Random characters' program parameter has been mentioned previously in Section 2. If this box is checked, every character other than those involved in the exercise will be chosen at random rather than being wild type. Under the Mendelian notation, it would be academically desirable to do this. However the appearance of animals carrying many mutations can become quite grotesque.

Checking the intermediate box ensures that there are three phenotype classes in the exercise. Checking the mixtures box gives a one-third chance that the mutant will be dominant, one-third recessive, and one-third intermediate.

(5)

Linkage: Indep. Linked Mix.

This line is shown only when two or more loci are chosen. For two loci, the first three buttons give respectively 0, 100% and 50% probability that the genes are linked. For three loci, checking the **Mixed** button gives a mixture of cases in which all three loci are linked, two are linked and one independent, and all three independent, each with equal probability.

Recombination frequencies between linked loci are chosen randomly in the range 10 - 30% in units of 5%, ie. the expected recombination frequency will be either 10%, 15%, 20%, 25% or 30%. There is also an additional criterion for exercises involving 3 linked loci. The program ensures that the two adjacent recombination frequencies will always differ by at least 10%. This is done to ensure that the linkage map can be correctly oriented.

Crossover interference is put into the program using a formula due to Kosambi. However empirical calculation has shown that in small progeny groups with this formula there are frequently more double recombinants than expected with no interference. Therefore the program arbitrarily generates only half as many double crossovers as expected under the formula.

(6)

Mixed phase ▼

Parent cross: Aa x aa Aa x Aa AA x aa Mix. AA x Aa

(7)

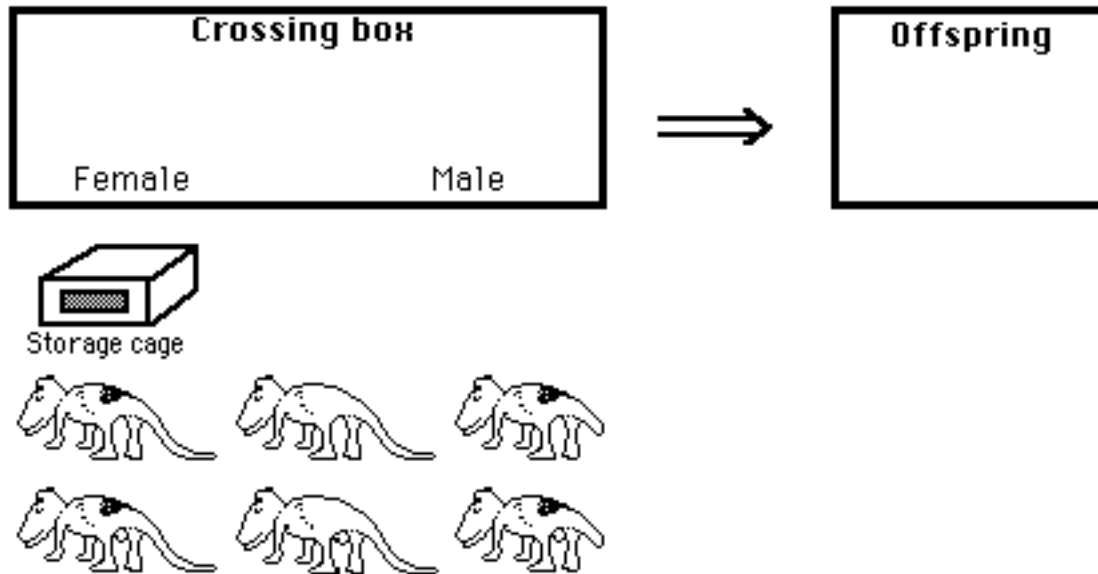
Extra parents: No Locked Single locus All

There are three ways in which animals can be presented to students. The three choices are specified in Line 7. The first way is if the No or Locked buttons are checked in line 7. In this case, two parents are nominated and appear initially in the Crossing Box as shown in the figure of Chapter 2. In this case line 6 is activated, and the parent cross must be specified. Note that 'Locked' actually refers to the case where there are *no* extra parents, and the two parents provided in the crossing box cannot be changed, eg. Exercises 14, 17.

If either of the other buttons is specified, then the Parent cross becomes irrelevant and is not shown. Neither is the Phase box, which describes the choice of markers in crosses where there are two or more loci.

If the Single locus box is checked, pure breeding parents for each individual nominated locus are provided to the student, as well as a wild type which contains no mutations. For

a two locus exercise, there will therefore be two single locus genotypes and a wild type. However in order to allow crosses between all genotypes, two individuals of each type are provided, of opposite sex if sexes have been nominated. The figure below shows the starting situation for an exercise in which the student is provided with two loci and asked to find the linkage relationships between the two. Note that the two slots in the Crossing Box are now labelled as Female and Male rather than Parent 1 and Parent 2. In this case the animals appear on the main screen rather than in the Crossing Box, and the student must select two and move them to the Crossing Box to start the exercise.



The last type of initial condition occurs if all possible genotypes/phenotypes are presented to the student. Because of the number of animals which need to be generated, they appear initially in the Storage Cage to avoid cluttering up the screen. In cases of 3-locus simulations where many genotypes need to be generated, their initial production may take a significant amount of time.

Nominating parent crosses

In the case where a single original cross is presented to the student, as is the case for many of the exercises, considerable care must be taken over the form of the initial two parents. All animals which are to be involved in the simulation must be descendants of the original two in this case.

In unknown exercises, part of the dilemma concerns the question of whether all students should be given the same cross or whether different students should get different crosses. In exercises involving unknown genotypes, communication between students means that it may be unsatisfactory to give all students in the class exactly the same simulation, even if different characters are involved. On the other hand if different students get different simulations there is the concern that the exercises may be of unequal difficulty.

For example, considering genotypes at a single autosomal locus with dominant and recessive alleles A and a , the obvious crosses which can be set up are:

- (a) $AA \times aa$
- (b) $Aa \times Aa$
- (c) $Aa \times aa$

The other three possible crosses result in all parents and offspring with the same phenotypes. Only the cross $AA \times Aa$, which is used in Exercise 8, has the possibility of providing any segregation, and considerable effort may be required to see this.

In the above, cross (c) poses a difficulty which is not present in crosses (a) and (b). The latter allow the student, or at least a good student, to infer immediately which is the dominant and which is the recessive allele. Cross (c), on the other hand, is ambiguous, and it is necessary to set up a further cross to determine which genotype is which. Therefore it may seem somewhat unfair for some students to be confronted with cross (c) and some with cross (a) or (b). On the other hand, as mentioned above, it reduces the scope of the exercise if all students are given either cross (c) or alternatively cross (a) or (b).

The unknown exercises (B6 and B7 for a single locus, B13 for two loci, have been described in Chapter 4. In exercise B6, all students are given a single locus cross of type (c). In Exercise B7, students are given a mixture of the three crosses, with the added complication of sex-linkage. In the two-locus example, a mixture of crosses has also been nominated. In this case, in order to make exercises of approximately equal difficulty, the program interprets the Mixture as meaning that one locus should involve cross (c) while the other should be of type (a) or (b). The addition of the possibility of sex linkage and/or lethality means that there is a large number of overall possibilities in this case.

Phase

This box specifies the relationship between markers in a parental cross involving more than one locus. It does not necessarily refer directly to linkage relationships. If there are two parents, each pure-breeding for two unlinked loci, the cross could be either:

- (i) $AA BB \times aa bb$
- or
- (ii) $AA bb \times aa BB$

The term 'phase' applies to dominance relationships. Thus cross (i) is said to be 'In phase' and cross (ii) 'Out of phase'. The default state of this selection is 'Mixed phase', in which case there will be a mixture of the two types of cross.

This choice is important where tests for linkage are being carried out. A testcross is easily set up in case (i) but not in case (ii). Therefore the settings for Exercise 12 specify that the markers are In phase. On the other hand, for an intercross the specification of phase is not important, and the setting for Exercise 11 specified 'Mixed phase'.

The same rules apply if one parent is specified as being heterozygous, and one as homozygous, or if there is a mixture of loci. An 'In phase' cross in this case is:

$Aa Bb \quad \times \quad aa bb$

from which linkage relationships may be inferred immediately, while an 'Out of phase' cross is:

$Aa bb \quad \times \quad aa Bb$

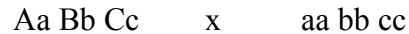
from which nothing about the linkage relationships can be inferred.

Checking the Phase box has no effect if the parental cross is $Aa \times Aa$.

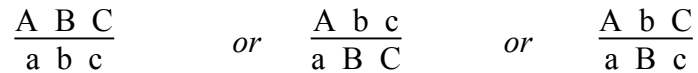
When there are three loci, checking 'In phase' will again result in the three loci being heterozygous or homozygous in the same individual. The 'In phase' setting is employed in Exercises B16 and B17, where students set up or are presented with a 3-point test-crosses. In Exercise B16, all crosses must initially be of the form:



In Exercise B17, the cross will be:

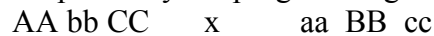


If there is linkage in this case, there are three possible genotypes or 'linkage phases':

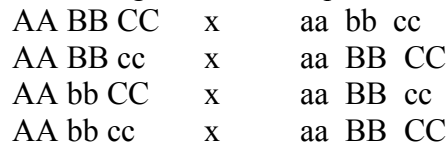


Note that the choice of an 'In phase' cross does not affect the choice of such genotypes. Each of the above is equally likely if a triple heterozygote cross is nominated.

It is not possible for three loci to be simultaneously 'Out of Phase'. This setting in a three locus cross is interpreted by the program as giving (for a homozygous cross):



The 'Mixed phase' setting leads to an equal mixture of the four possible types of cross:



(8)

Show genotypes: No Part Yes Hide offspr. Hide init.

The decision on whether to show genotypes is obviously critical in the form of the exercise. If the **No** button is checked, genotypes will be suppressed. This is the default state. If the **No** button is checked, the **Genotypes** item in the **File** menu will also be hidden.

Note that even if genotypes are hidden, students can elect to see them after they have finished all questions in an exercise by clicking the **See genotypes** button, which appears when the last question is answered. Clicking this button also brings back the genotypes menu item, allowing genotypes to be edited.

The **Partial** button refers to the case where individual locus genotypes are shown, but not their linkage relationships. The notation in this case is the same as for unlinked genes, although it is distinguishable by the fact that complete genotypes are shown in red whereas partial ones are shown in black. Complete and incomplete two-locus genotypes are shown below:



Complete genotype



partial (black) or unlinked (red)

It is possible to show genotypes in the parents but not in the offspring, eg. Exercise 14, by checking the **Yes** button and also the **Hide offspring** button. For reasons of storage space in the Mendelsim program, this facility is not available with three-locus genotypes, so that the **Hide offspring** button is hidden when the 3-locus button is checked.

The **Hide initial** determines whether genotypes will be shown when the animals first appear. If this box is not checked, but one of the genotype buttons is checked, then genotypes are available from the **Genotypes** item in the **File** menu, but not shown initially. This may be useful in the case where a student wishes to try to infer genotypes before looking at the answer.

Genotypes are standardly shown on the screen in red. If the **Colours** button is checked, independent loci will be shown in different colours, including green for sex-linked loci. Since the notation already makes it clear which loci are independent or sex-linked, the added colour is not strictly needed.

(9)

Notation:

Mendel

Wild

Switch

These buttons can be used to switch between the two different notations. The Mendelian notation is suggested as the default in early exercises, and the wild type notation in later exercises. If the Switch button is checked, then the student can switch between the two notations in the Show genotypes dialog box. Note that any change of notation made by the student over-rides the notation provided by default in later exercises. Thus if, for example, the student changes to Mendelian notation, then if a new exercise is nominated with genotypes shown, the Mendelian notation will be continued even if the wild type notation has been set by the program.

(10)

Exercise:

Single

No trial

Hidden sex

No lethality ▼

If the **Single** box is unchecked, students can have multiple tries at a particular exercise. It is appropriate to check this box when students are being marked on their answer to a question.

Students can move between exercises using the **Choose exercise** item from the **File** menu. If they are currently engaged in an exercise in which the Single button is checked,

the item will be dimmed to indicate that it is inappropriate to ask for a different exercise. An example of this is shown below:

Nominate exercise number:

1. Single locus backcross and intercross

2. Two locus backcross and intercross

3. Single locus unknown

4. Two locus linkage test

5. Three point linkage

A trial of an exercise is allowed if genotypes are suppressed in the exercise, provided the **No Trial** button is unchecked. A trial consists of the same exercise, with genotypes shown instead of hidden. Questions may or may not be suppressed in trials depending on the state of buttons in the program parameters menu (see Chapter 3).

Hidden sex is a special feature which only appears when the 'Bears' button is clicked. It is used in Exercise B9.

Lethality belongs, strictly speaking, to the 'Mutations' choices of Line (4). The choice of lethality over-rides the other options of this line. An example is shown below for the 'Patch' character. A single dose of the *P* gene produces a change in phenotype, and two doses is lethal.

Genotype	<i>pp</i>	<i>Pp</i>	<i>PP</i>
Phenotype			

The main use for lethality in the program is in the unknown exercises. In order to maintain generality, the program makes it equally likely that either character could be the lethal one. In the example of the patch character, therefore, there is an equal chance that the genotypes and phenotypes could be:

Genotype	<i>pp</i>	<i>Pp</i>	<i>PP</i>
----------	-----------	-----------	-----------

Phenotype



This leads to the somewhat anomalous situation that a character which is generally the 'wild type' character is now lethal in homozygous condition. Students are warned in the instructions for the program not to expect the same meaning for a character in two different exercises, so that this may not seem a problem. However to maintain consistency with the wild type notation, in exercises where the wild type notation is specified, any occurrence of a mutation will be taken to be of the first kind and not of the second kind.

There are four levels of lethality, 0 (default), 25%, 50% and 100%. These numbers apply as follows to the cases of single and multiple loci. For a single locus, the probabilities of lethality are equal to the indicated level. For two or three loci, the probabilities apply to only one locus chosen from the set. For a two-locus unknown exercise, for example, if 50% lethality is specified, there is a 50% probability that one locus will contain a lethal and the other will be normal, and a 50% probability that both loci will be normal. There are no cases where both loci contain lethals.

The option of lethality is only available when the parent crosses (Line 6) are of a suitable kind. Clearly if the cross $AA \times aa$ is specified, lethality is not possible. The program also disallows the possibility of lethality when there are more than two founding individuals, owing to the possibility of presenting lethal genotypes.

(11)

Organism: Any 'Dog' 'Bear' 'Fly' 'Plant'

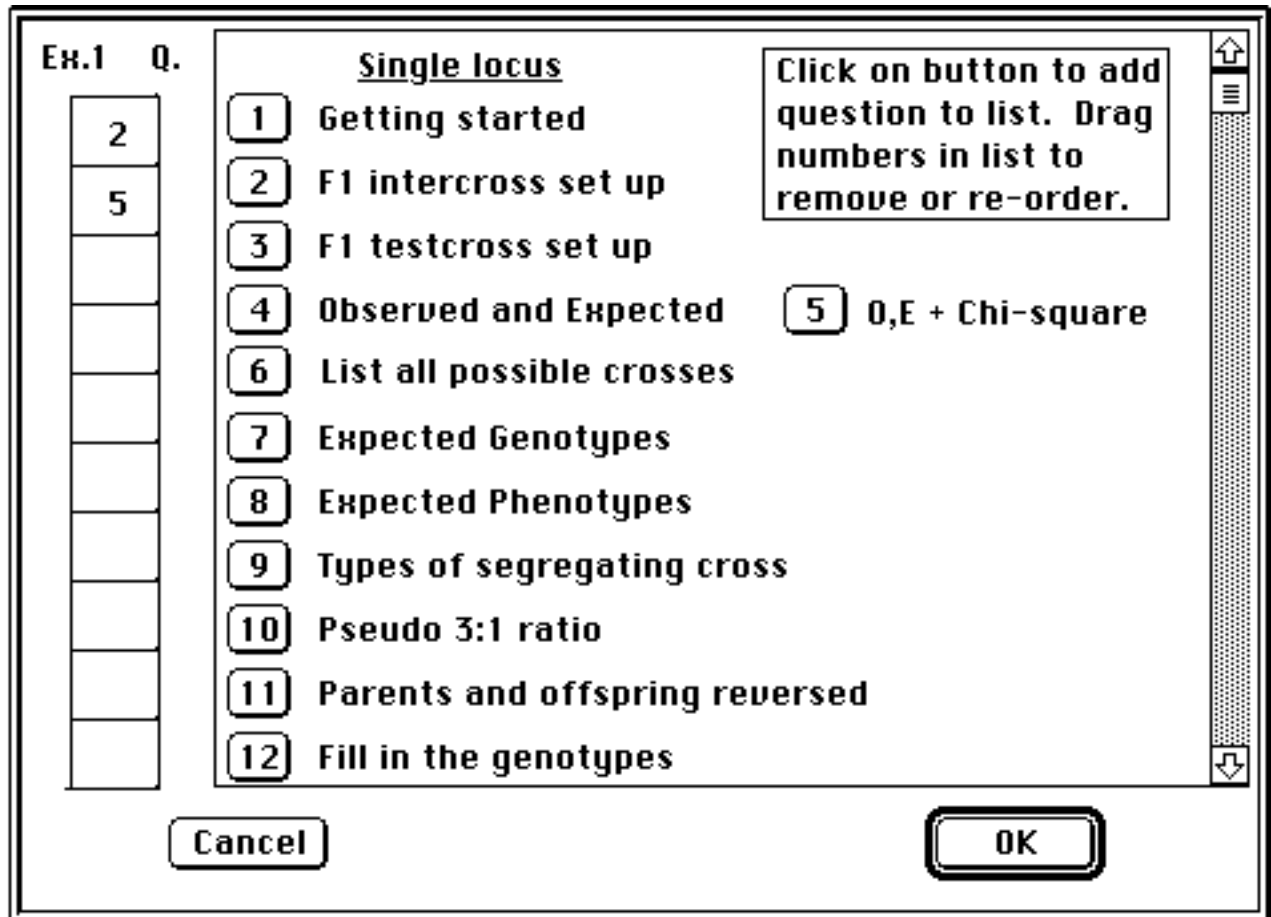
The default choice of 'Any' is over-riden by the options presented in the parameter menu, which in turn may be over-riden by student choice. However the choice of a particular organism for a particular exercise over-rides any choice the student may have made. There are, in practice, only two cases where the choice of organism is of importance. One is the choice of the Monkbear in the hidden sexes exercise. The second is the choice of the fly in exercises where there is some reason to look at the difference between female and male recombination.

Sex linkage does not occur in the plant. When sexes are nominated, the Plant choice is hidden.

Selecting Questions

Questions

Clicking the Questions button brings up a screen for question selection. The diagram below shows the single locus questions, and the others may be scrolled into view.



To add a question to the list, click on the number of the question. The number is added at the bottom of the list.

Questions on the list are removed or re-ordered by dragging rather than clicking. To remove a question from the list, click on it, drag it out of the list and drop it just to the right of the list. To re-order questions, drag them either up or down in the list.

There is no scope for making any changes in the actual questions. The only choice is whether to use a question or not for a particular exercise.

Chapter 6. Marking of exercises

Broadly speaking, there are two ways to assess students' progress. The first is to present an exercise and to allow the computer to mark it. The second is to require the student to hand in a written report for the teacher to mark.

As mentioned throughout this manual, the Mendelsim program comes with a series of self-test questions which can provide a mark. The main purpose of these questions is, however, to guide the students through the exercises, and provide instant feedback on what has been learned. Their use for marking is a secondary consideration.

The most serious limitation to the use of computer marking comes from the fact that a program which provides feedback to the student can only be used with considerable difficulty to provide a mark as well. Basically, a student can use the program twice, the first time to find out the correct answer and the second time to feed back the correct answer and get a mark.

The only possibility for a marking system for a non-networked computer which overcomes this problem is to configure the program such that each use potentially sets a different problem from the previous use. This can be done with the Mendelsim program. The problem with this approach is that a student's work then has to be completed in a single session at the computer. This is only satisfactory for the simpler problems. With problems of any complexity, the student should be allowed, and indeed encouraged, to return to the computer after thinking about the problem, either to put in answers or to continue with the same simulation.

Hand marking of exercises

Some exercises provide a suitable basis for a report which the student can be asked to submit for hand marking. For an exercise of this kind, it is logical to check the Single Exercise box (Section 5). Otherwise the student may get multiple copies of the question, and it is unclear which one is being marked. The 'No self-test exercises' button should also be checked in this case, otherwise the computer will provide an answer. Note that hand marking only makes sense if names are used, ie. do *not* check the 'No name/number' box in the global parameters entry box (Section 1).

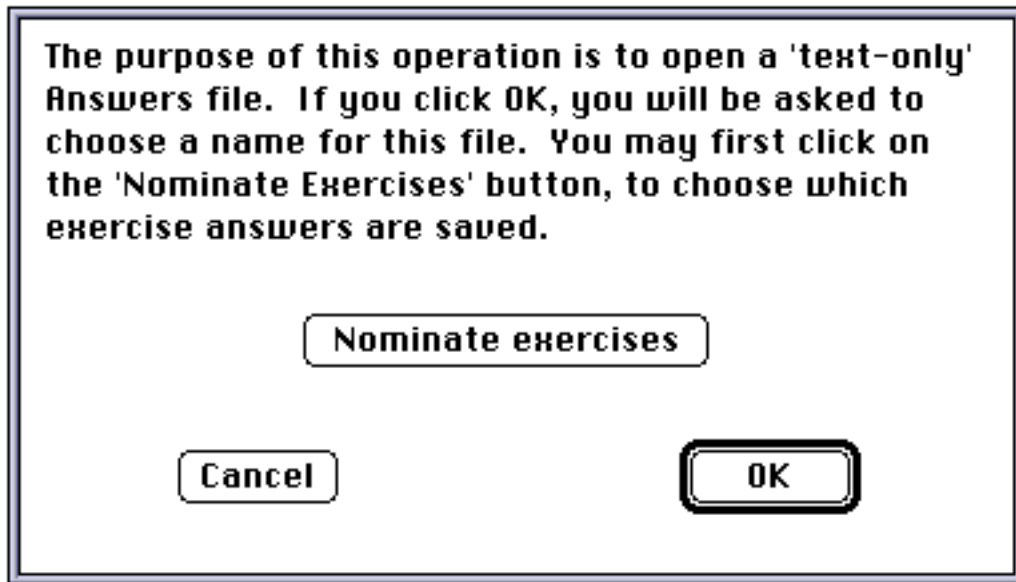
The remainder of this section explains how to use the program to obtain answers for such marking. The program is structured to expedite this process as much as possible.

Entering 'Answer mode'

The process has already been described in Section 2. The same screen which serves as an entry point for the editing of exercises also serves to introduce the marking process.

Obtaining answers to exercises

When the 'Answer mode' dialog box appears, this is accompanied by a new Answers menu, which provides the way of getting answers. The simplest way of doing this is through the printout of answers to a text file. This can be done either by clicking on the 'Save answers' button in the dialog box or by nominating the 'Save to Answers file...' item in the Answers menu. Clicking the 'save answers' button will lead to the following box:



There may be a mixture of exercises, only some of which have fixed answers. As a first attempt, the program assumes that any exercise in which the Single Exercise box is checked (see above) will be one in which there are fixed answer which the student is expected to provide.

The default condition will, therefore, assume that only genotypes for fixed exercises should be printed out. Clicking the 'Nominate exercises' button will show which exercise answers are to be saved. In the dialog box shown below, for example, only Exercise 4 has a fixed answer, and the default setting shows this. This setting may be changed by checking or unchecking any box. Checking an exercise in which multiple simulations are permitted will result in the program printing out the genotypes of the first individuals presented to the student in that exercise:

Once you have clicked on OK to indicate that you wish to save answers, you will be asked to choose a name for the file through a standard dialog box.

Nominate exercise number:

1. **Single locus backcross and intercross**

2. **Sex-linked cross**

3. **Three locus genotypes**

4. **Two locus linkage (recessive)**

Once you have finished this process, you will be asked to nominate a student name or number. Successive students may then be nominated using the 'Next student' item from the Answers menu. As each student name or number is read in, genotype information is automatically added to the Answers file if one has been nominated. It is not necessary to cycle through the exercises done by each student. Note that if a new Answers file is nominated from the 'Save to Answers file...' item while a student name is showing, it will be necessary to read in that student name or number again for the answers to be saved.

The printout of answers to a text file is necessarily limited. For example, the printout of answers for one student may be as shown below. Only verbal descriptions of the characters are possible. Any genetic maps are shown using printing characters which should be shown in a fixed-length font in order for the symbols to line up properly. The advantage of this form of listing answers is its flexibility. The answers are printed to a text file which may be viewed and/or printed out in any word-processing program. Different student outputs may be joined or separated. The output for each student includes a '\$' character which may be replaced by a page break for printing.

```

$
Student Name: Fred Jones
Exercise No. 2
Single locus
Genotype:      ++          Female          cc          Male          c.
Canines:      Present    Present    Absent    Present    Absent
Exercise No. 4
Two linked loci:
  s              22 cM              t
  +-----+
Genotype:      ++          s+          ss
Stripe:      Present    Present    Absent
Genotype:      ++          t+          tt
Tail:         Long      Long      Short

```

The alternative method of getting answers is through a screen which can be accessed from the 'Show Map / genotypes' item from the Answers menu. This gives the answers for only one exercise at a time.

☐
Linkage map

Name: Fred Jones Number: 7239

Exercise No. 4

Two linked loci:

s
t

┌
└
22 cM

++

s+

ss

++

t+

tt

χ^2 test

The program contains the facility to calculate χ^2 values for standard 1-locus and 2-locus segregations. These are:

1-locus 1 : 1 3 : 1 1 : 2 : 1
 2-locus 1 : 1 : 1 : 1 3 : 3 : 1 : 1 9 : 3 : 3 : 1

The observed numbers obtained by the student must be entered into the program, which will then print the χ^2 value.

A trial run

It is **strongly recommended** that, following the setup run of the program, you run through the exercises and try to recover the answers for at least one student name or number in any of the ways described above. Possible difficulties should thus be uncovered before the program has been used by large numbers of students.

Appendix A. Student Mendelsim instructions

On-line Help

You can get on-line information about the Mendelsim program in several ways:

(1) The **Getting started** exercise.

You will very likely find that the program opens up into this exercise. It contains about 50 small screens which will give you a hands-on introduction to the various aspects of the program. This is the easiest way of learning about the program.

(2) The **Help** menu

The information under this menu largely overlaps with these notes.

(3) **Explain question**

Much of the Mendelsim program is based on answering questions which the program poses. Each question has an 'Explain question' button, which you will need to consult to find exactly what is expected in answering the question.

(4) **Exercise description**

The program is based on exercises. Each is explained briefly by a window which comes up when the exercise is first introduced. You can look at this information again at any time by accessing the **Current exercise description** item in the **Exercises and questions** menu.

You should note that the Mendelsim program can be set up in a number of different ways. The version that you are working with may not be exactly as described in these notes.

General program instructions

Animals (or plants)

The essence of what the Mendelsim program does is to take two parents, and make an offspring from them. The parents must be in the 'crossing box'. The offspring appears in the 'offspring box'.

To make a new offspring, simply drag the old one out of the box. Provided both parents are present, a new offspring will automatically appear in the box once it is empty.

The program allows you to change the animals used as parents. Drag one or both parents out of the crossing box. Then replace the parent(s) with whichever individual you wish to cross. If there is still an offspring in the box from a previous cross, the program will ask you to remove this before setting up a new cross.

Cages

Cages are provided in order to keep your offspring in an orderly manner. You do not have to use them, but you will lose track of what animals you have if you don't.

There are two sorts of cages. The first is the Storage cage which appears automatically on the screen when the program starts. This cage is intended primarily for storage of individuals after they have been used in crosses, so that you can go back and re-cross them if necessary.

The second type of cage is one that you create yourself by dragging down from the shelf of extra cages. Each time you do this, a dialog box will request a name for the cage. Try to print something which is suggestive of the character or characters you are scoring. But don't worry if you choose an inappropriate name, because you can always change it. Some versions of the program will not ask for a cage name, but will assign it automatically when the cage is used.

Put an animal in the cage by dragging it over the cage and releasing the mouse button. It should automatically go in. The appearance of the cage changes to show that there is an animal inside. Avoid having two cages close together, which might lead to confusion as to which cage the animal goes into.

The number on the cage shows how many animals are inside. You may not need to look into the cage to see the animals there. However if you do, then to see into a cage you must first 'Select' it. Do this by clicking on it or moving it. You will see that the cage is surrounded by a rectangle which shows that it is selected. Now you should be able to access the **Look in cage** item of the **Cages** menu. Alternatively, you may double-click on the cage to open it, although you may find that this does not work as easily as opening it from the menu.

Each cage holds a maximum of 100 offspring. If you fill a cage, you will need to clear it out or start another. The maximum number of cages which can exist at any one time is 16, in addition to the Storage cage. It is unlikely that you will use

all of these, but if you have used all your cages then you will need to recycle one before you can start another.

If you want to remove an animal to use as a parent, drag it to the EXIT, which is on the right side of the cage box. The animal will disappear from the cage, and you should see it appear on the main screen in the background. However you can not access it until the cage has been closed.

Sometimes, in order to find the animal you want, you may have to use the 'scroll bar' and scroll down the cage. In this case the exit door will scroll out of view. However you still just need to drag the animal to the right side of the cage to remove it.

Close the cage down from the **Cages** menu. You cannot do anything else while the cage is open. As an alternative means of closing the cage, you can click on the 'go-away' box, which is the small box at the top of the cage screen.

Cages can be cleared in several ways. There are items in the **Cages** menu which allow you to empty a cage or to recycle it, and you can do this either for each cage individually or for all cages together. There are shortcut methods for individual cages in which you drag them to the trash (empty) or back onto the shelf (re-cycle). In all cases you will first have to click on a dialog box to confirm your action in order to be sure that you are not mistakenly throwing away cages or animals.

The **Cages** menu also contains the item **Clear animals not in cages**. This action does not affect animals which are in the parent or offspring boxes. You may also throw away individual animals by dragging them to the Trash.

Animals are stored in the cage in the order in which they are put in, going from left to right and then down the cage. If an animal is removed from the Storage cage, its spot is left unfilled. If you shut the cage and open it again you should see the same unfilled spots. Thus you can always go back to any animal, which will be where it was originally put. For cages other than the Storage cage, however, the remaining animals close up when the cage is opened again.

Changing exercises

As soon as you complete an exercise, a **Next exercise** button will appear. Clicking this will take you to the next exercise in sequence. Alternatively, you can go to any exercise, or repeat the current exercise, by using the **Choose exercise** command from the **Exercises and questions** menu. Simply click on the exercise you wish to try and click the OK button.

When you access the **Choose exercise** command, you may find that the exercise you are currently doing is dimmed. This indicates that you cannot attempt different examples of the same exercise (however you may still be able to run trials - see below). You can do another exercise and then come back to this exercise, but it will be exactly the same exercise as previously.

In moving between different exercises, the same organism and same character may show up more than once. A limited number of characters is available for the simulation, so that if you attempt many exercises, it is inevitable that previously seen characters will eventually show up again. However it is important to note that re-occurrence of the same character does not imply anything about its mode of inheritance. The same character may be inherited as a dominant in one exercise and as a recessive in another.

Trials

The hardest type of genetics exercises is one in which, as in real life, you do not see the underlying genotypes. You will usually find that it helps you to think about the exercise if you can run through an equivalent simulation with the genotypes showing. '**Trials**' allows you to do this. For more information about this command, see the section below on 'Menu items'.

Depending on how the exercise has been set up, genotypes may not be shown initially. However they will be available from the **Genotypes** item in the **File** menu. This enables you to try the exercise in a number of ways. You may turn them on at the start of the exercise so that they are visible at all stages. Alternatively you may start the exercise without seeing them, and turn them on only when you feel you need to.

To access the **Trial** item, you will have to cut short the simulation you are doing. Only one simulation may be in progress at a time.

Exercises and questions

Most exercises are based around a set of questions, which appear at the bottom of the menu of this name. The questions vary in length and difficulty. In some cases you will need to get the correct answer to a question before moving to the next one, but in most cases the program will just give a mark to the answer you have put in.

Most questions have no effect on the simulation in the background, so that you can continue with whatever you are doing. Some questions, however, ask you to click on an individual of a particular genotype, and in this case you cannot continue with the simulation until the question is hidden.

It may help, when beginning an exercise, to see what questions you are expected to answer. Frequently, however, you can only look at the first question. The others are suppressed until the first question is completed, although the name may give some clue as to what the question is about.

Questions must always be marked in order. However if a question is showing, you can work on it at any stage, and the work will not be lost when the question is hidden.

Auto offspring

This command may not be available for all exercises. If available, it enables you to generate large numbers of offspring automatically. However a certain amount of preparation is needed before you can use it. It works by adding offspring to cages, so you must have set up the appropriate cages before the command is activated.

Each time you have a pair of parents in the crossing box, this is known as a 'cross'. The program keeps track of how many crosses you have set up. Each time the parents are changed, the 'cross number' will be automatically incremented. The number of the 'current cross' is shown in the **Get info** command (see below). You need not be aware of this cross number, but if you want to use the Auto offspring command, then you must have cages which contain only offspring for the current cross.

Each time you add an animal to an empty cage, that cage becomes associated with the current cross. However this works only for an empty cage. Adding animals to a cage which already contains offspring from a previous cross will not associate that cage with the current cross.

You need two associated cages before the Auto offspring command becomes activated. Once this has happened, then as soon as you drag an offspring directly from the offspring box into one of the cages, extra offspring will start to be generated.

Each time an offspring is generated which exactly matches the phenotype of an animal in one of the cages, the offspring will be added to that cage. However if no offspring of matching phenotype is found, then the process stops and the offspring is shown in the offspring box. At this stage you can add the offspring to one of the cages yourself, or make a new cage and add the offspring. After either of these actions the generation of new offspring will automatically re-start.

The generation of offspring will continue until either the mouse button is pressed or the number in one of the cages reaches the maximum of 100. You can re-start the process by making a new cage for the phenotype of the filled cage.

You may mix any phenotypes you wish in a cage, eg. you might want to mix females and males which are otherwise of the same phenotype. However considerable care in putting offspring into cages must be exercised. The program searches sequentially through the cages when adding a new offspring, and if a single example of the same phenotype is found, it will add the offspring to that cage. The consequences of putting an individual into the wrong cage in the early stages of setting up a cross may thus be unpredictable.

Use of names

When you activate the program you may be confronted with a dialog box, asking you to enter your name. You will see that the blinking 'cursor' is in the **Name** box, so that anything you type comes into this box.

When you have typed in your name, and clicked on the **OK** button, or pressed Return, you may be presented with another dialog box showing a 4-digit number the program has assigned to you. You should write this number down. The reason for this number is that you will possibly need to come back to run the program again, and it is easier to remember a 4-digit number than to remember the exact format in which you typed your name, eg. did you use capitals or lower case, full name or initials etc. Now click on the OK button, and you are ready to start the simulation.

Returning to use the program

You should type in your 4-digit number rather than name. If you are repeating the same exercises, then you should get exactly the same opening screen as you got last

time. So, when they appear, check to see that the animals (or plants) are exactly the same as those you got the first time. If they are not, then something has gone wrong, either in the entering of the number or in the program. Note that the offspring will not necessarily be the same as those you got last time, since chance is built into the simulation.

MENU COMMANDS

(1) File menu

Get info

This command shows summary statistics of the current status of your current simulation. In the left-hand column are shown your name. Then follow statistics on the total number of animals which have been generated, the number still surviving, and the number currently in cages.

The right-hand column shows statistics on the current cross. It shows the cross number, which is used by the program to keep track of which cross is in progress. If either parent has been removed from the crossing box, then the screen will show that no cross is in effect. Note that if a parent is removed from the crossing box and put back straight away, the cross number will not be changed. However if a cross is repeated with the same pair of parents after another cross has been set up, the program will give the cross a new number.

The right-hand column also gives information on the names of cages associated with the current cross. Before activating the Auto offspring command, you might check this information to be sure that the correct cages are in place.

Genotypes

Some exercises will allow you to look at genotypes of the organisms on the screen. If this is the case, the Genotypes item will be present. If not, this item will be absent.

When you access this item, you will see a diagram of the offspring you are dealing with, pointers to a number of characters with single letter notations, and a list of names of characters with check boxes. Some of these letters and names

will be dimmed. Only those which are associated with variable characters in the current simulation will be activated.

The list on the right-hand side specifies which characters you wish to be shown. Initially all characters are checked, so that the complete genotype will be shown if you click OK. You may, however, wish to concentrate on just one character, in which case you should leave that character checked and uncheck the others. Note that once you click on OK, all animals shown on the screen need to be re-generated, which may take some time.

You may also change the notation used to describe each character. The space available on the screen restricts the notation to a single letter for each character. However you may nominate any letter for each of the variable characters. Each is initially shown in upper case, but can equivalently be shown in lower case. The genotype which appears on the screen will be determined by the dominance.

Colour

If you have problems with colour vision, you may find that the colours chosen for organisms are not ones which you find easy to distinguish. All colours may be edited using the Colour item in the File menu.

The screen which appears when you access this item depends on which organism is currently involved in the simulation. If the 'dogs' are being simulated, no colour editing of phenotype is possible. The other organisms allow more than one character to be edited.

To edit a colour, click on the patch showing that colour. This patch will be surrounded by a rectangle to show that it is selected, and a 'colour picker' dialog box will be shown. The form of this colour picker depends on the particular machine you are working on. While you are working with the colour picker, the colours shown in the background may not be reliable. To nominate a new colour, you need to click on the OK button in the colour picker and also the OK button in the colour dialog box.

The effect of choosing a new colour may not easily be appreciated until you see organisms on the screen showing the colour. Once a new colour has been nominated, all subsequent exercises until you quit will show the new colour.

The colour of genotypes may also be edited. Genes on different chromosome will then be shown in different colours. Sex-linked genes are shown in green, and non-sex-linked (autosomal) genes in reddish colours. The form in which the genotype is written already contains all the information to show chromosomal

information, so that the use of colours for genotype information is not strictly necessary. However in some exercises you may see that the genotype is written in black rather than in colour. The program does this to indicate that the linkage relationship of the loci is unknown, ie. they may be linked or unlinked.

(2) Auto menu

Auto offspring

Auto cage names

These menu items are used to turn on or turn off the relevant item. If auto-offspring is checked, for example, then the auto offspring generation process is started by dragging offspring from the offspring box into a cage. See the program Help item or run the introductory exercise for a more detailed account. Note that these items may not be available for all exercises

(3) Cages menu

Name/rename cage

This item allows you to change the name of a cage at any time. The item will be dimmed unless a particular cage is selected by clicking on it. To rename a cage, click on the cage, which causes a red selection rectangle to appear around it, go to the menu item, and edit or type the new cage name, followed by 'return' or clicking OK.

Empty cage

Recycle cage

These two items are also dimmed unless a cage is selected. The effect of the first is to clear out the cage but to leave it on the screen at its current position with the name unchanged. The effect of the second is to dispose of the contents and return the cage to the spare cages shelf. Each of these actions must first be confirmed in a dialog box.

Short cuts are available for both of these actions. In the first case, drag the cage to the trash. In the second, drag the cage back up to the spare cages shelf.

Empty all cages

Recycle all cages

These commands refer to all cages rather than to a single cage. They are available at all times after cages have been created and used. The commands do not refer to the Storage cage. This cage can be individually emptied, but not recycled.

Clear animals not in cages

This command disposes of all uncaged animals from the screen except those in the crossing and offspring boxes. Individual animals may also be cleared by dragging to the trash.

Look in cage Shut cage

These items are needed to see the detailed contents of a cage. See the program Help for more detailed descriptions. The first item is dimmed until a cage is selected. The second is dimmed at all times, except when a cage is open in which case it is the only item which is activated.

(4) Exercises and Questions menu

Choose exercise

As indicated in Program help, to start a new exercise, either a repeat of the one you are doing or a different exercise, use this item. It will bring up a dialog box in which you may nominate a different exercise, click OK without nominating a new exercise to start a new version of the same one, or press Cancel to go back to where you were. Some versions of the program may also have a button which allows you to nominate the organism at this stage.

List of exercises

This item lists details of all the exercises in the current set. The different columns are as follows:

G: Genotypes are shown, either initially or through the Genotypes menu item.

T: You may run trials of this exercise, using the Trials menu item.

M: You may have multiple tries of this exercise.

1: Number of marks for the exercise.

2: Marks you have obtained. Accumulates if you try the exercise more than once.

3: Total marks for the exercise, = Number of marks (1) x Number of tries.

Current exercise description

Each exercise has a description which appears automatically when the exercise starts up. You may see this description at any time using this item.

Rules for questions

Some rules which apply to the answering of all questions. You should read through these the first time you answer questions.

Questions associated with the exercise

These are given at the bottom of the menu following a line separator. They are always given in the form such as:

Ex1 Q1 - Do something

This would be the first question of Exercise 1. Most questions will have an associated Explain question button which gives further details about what is expected, and which you should read before attempting the question.

A **Mark me** button is present in most questions. In some cases, this button will not show up until it is appropriate to have the question marked. You should always be careful that you have completed all that you intend to do on a question before pressing this button.

(5) Trial menu

When you access this item, the simulation you are doing will be stopped, and you will be given a new simulation, probably involving different characters. A label will appear on the screen under the spare cages to indicate that a trial is in progress. The **Genotypes** item will appear in the **File** menu.

When a trial is in progress, there are two other menu changes:

(a) The items in the **Trial** menu change. Whereas previously there was one item, **Trial**, now you will see

New trial

End trial

Use the first of these items to start another trial, and the second item when you have finished with trials and want to go back to the original exercise.

(b) The first item in the **Exercises and Questions** menu, **Choose exercise**, will be dimmed. It only becomes accessible again after you access the **End trial** item.

(6) Help menu

The information under this menu is essentially the information contained within these notes.