

## The GELSIM program - Instructor's guide

The Hands On Genetics series of programs aims to provide students with the opportunity to try out genetics exercises for themselves. The student is confronted with a real-life situation, in this case the restriction enzyme mapping of a piece of DNA. The aim of the exercise is to allow students to understand the process whereby DNA is cut with a variety of enzymes and a map produced from the resulting gel patterns.

This program will be run by a number of students in a class. Each student will have a unique problem. Thus the exercise needs to be structured in a way which allows the person in charge of the class to assess the answers individually for each student.

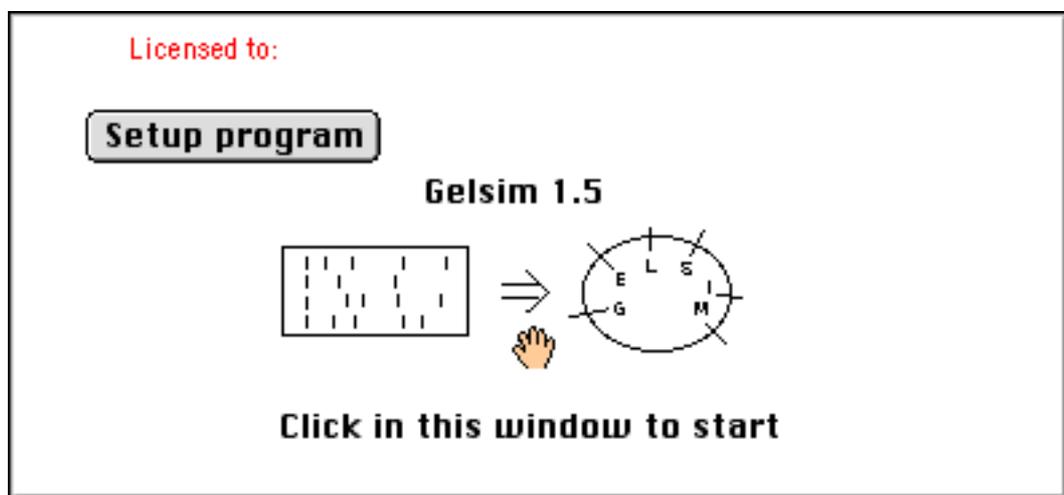
### Why a 'set up' run of the program is needed

A basic problem which needs to be overcome is that you, the instructor, need to know the way of getting the correct answers from the program, while the student should not be able to get this information. Unless some complex form of copy protection is used, which usually defeats the purpose of providing easy access to the program for both instructor and student, it will often be possible for the student to secure from somewhere a copy of the same program which you have.

The Hands On Genetics series provides the following solution to this problem. Students in a class must use a version of the program which has been set up by the instructor. In the first run of the program, a password (or number) is put in by the instructor, and is concealed within the program. This password changes the exercise which is given to each student, and is also required to get the solutions to the exercise. Provided that the password is kept secure, only the instructor should be able to read off the correct answers at the end of the exercise.

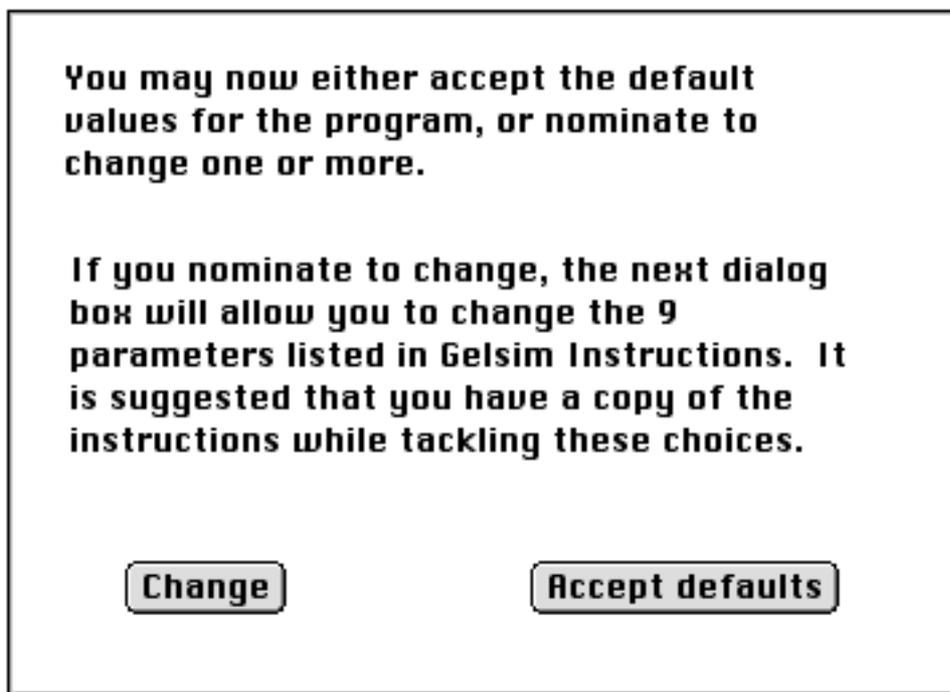
### The 'set up' run

Double click on the program icon to start the program. The introductory screen should show something like the following, where the name under which you have licensed the program will be shown:



Click on the **Setup program** key. You will then be see a screen which introduces you to the program, followed by a screen for putting in the password. The password can have any combination of letters, numbers or special symbols. As you type, you will not see the password. The program will then ask you to repeat the password.

You will then be asked to confirm whether the program is ready for distribution to the class, or whether you wish to change some of the default values, as shown below. Before nominating to change the default settings of the program, you should read the next section.



### **Tailoring the exercise**

The diagram below shows the parameters which can be changed:

- (1) The length of the sequence is currently in the range 12 - 13 Kb. All of the restriction enzymes are 6 base cutters, and the program assumes a totally random DNA sequence with A+T frequency equal to 50%. Thus each enzyme cuts every 4096 bases on average, giving an expectation for a 12kb sequence that each enzyme will cut the sequence approximately 3 times on average. The range of possible sequence lengths can be reset to any desired value between 4kb and 30kb. Chance is built into the choice of sequence length, so that the value here is actually the bottom of a range of width 1kb. For example, if a length of 20kb is nominated, then the program will randomly assign a length for each student in the range 20 - 21kb.
- (2) Mapping in real life is sometimes made difficult by the fact that two enzymes cut very close to each other, making it impossible to see the fragment between the two. Since it would be unfair for some students in the class to be confronted with this situation and others not to, the easiest course is to nominate a minimum fragment size, currently 50 bases. Fragments of size 20 or less can in fact be visualised if the running time and/or voltage of the gel are reduced to their minimum values.

<b>(1) Sequence length (bottom of range)</b>		<b>(5)</b>	<input checked="" type="radio"/> <b>Can use fragments</b>
	<b>12 kb</b>		<input type="radio"/> <b>No fragments</b>
<b>(2) Minimum bases between sites</b>		<b>(6)</b>	<input checked="" type="radio"/> <b>Run one or more tracks</b>
	<b>50 bases</b>		<input type="radio"/> <b>Run full gels only</b>
<b>(3) Probability of circular sequence</b>		<b>(7)</b>	<input checked="" type="radio"/> <b>Hide answers</b>
	<b>50 %</b>		<input type="radio"/> <b>Show answers</b>
<b>(4) Variability between gel runs</b>		<b>(8)</b>	<input checked="" type="radio"/> <b>Tutorial</b>
	<b>0 %</b>		<input type="radio"/> <b>No tutorial</b>
		<b>(9)</b>	<input checked="" type="radio"/> <b>Trial</b>
			<input type="radio"/> <b>No trial</b>
			<b>Cancel</b>
			<b>OK</b>

(3) The program currently, by default, assigns a circular sequence or a linear one with probability 50%. This may not be a normal situation, since usually one would know whether the sequence was circular or linear. However it is a useful exercise for students to be able to work this out, and it does not make the exercise much easier or harder either way. This probability may be set to any value between 0 (always linear) and 1 (always circular).

(4) The default mode of the program ensures that all gels run at the same rate. Two gels run with the same sized fragments with the same voltage and running time will produce identical results. This eases the pain for students, in that they only need to calibrate the sizes once for a standard gel. (Different students will, however, get slightly different rates). This somewhat artificial restriction can be lifted by specifying a variability factor. Although practice in the calculation of sizes may be important, it should be emphasised that the exercise of mapping a sequence can be a substantial one even if the gels are set to constant running rates.

(5) The program contains the facility for students to cut fragments out of the gel, and then to restrict them with another enzyme. This makes it much easier to assign new enzyme sites once a preliminary map has been built up. At the cost of running lots of reactions and gels, which is not a problem on the computer, a very complete map can be built up. If you want to make the exercise a more challenging one (as it was in the days before low melting point agarose), you can nominate to hide this facility.

(6) For convenience, the exercise is currently set up so that DNA samples are cut and loaded sequentially, rather than, as in reality, putting a number of samples on to digest and then loading them onto a gel sequentially. In real life, one usually makes a decision on how many samples are going to be digested, then puts them all on to digest at the same time. It would be

somewhat artificial to make the computer program run this way. However if you want the students to have to think ahead to make such a decision, then you can achieve the same effect by specifying that a gel can only be run when all the slots have been filled. By current default, the gel can be run at any stage when one or more samples has been loaded. Under this regime, there is no value for the student in nominating anything other than the maximum number of tracks (7) per gel.

(7) The default version of the program will not show the answers to students. If you have put in a password, the program makes it easy for you to check any combination of enzymes for any student. From one point of view, there is little point in allowing students to see the answers. The program contains the facility to run trials [see (9) below], which already allows the student to run exercises for which they can see the underlying map.

(8) The program contains a tutorial, which runs briefly through some principles of mapping. You can choose to show or hide this tutorial.

(9) The program contains the facility to allow students to run trial examples, and to view the true maps of these sequences. In this mode, the student has the same view of the answers as does the instructor in the case of unknown samples. However the answers are available only for trial examples. The student may run as many trial examples as desired, but must eventually return to the unknown exercise, for which the true map can only be shown by using the password.

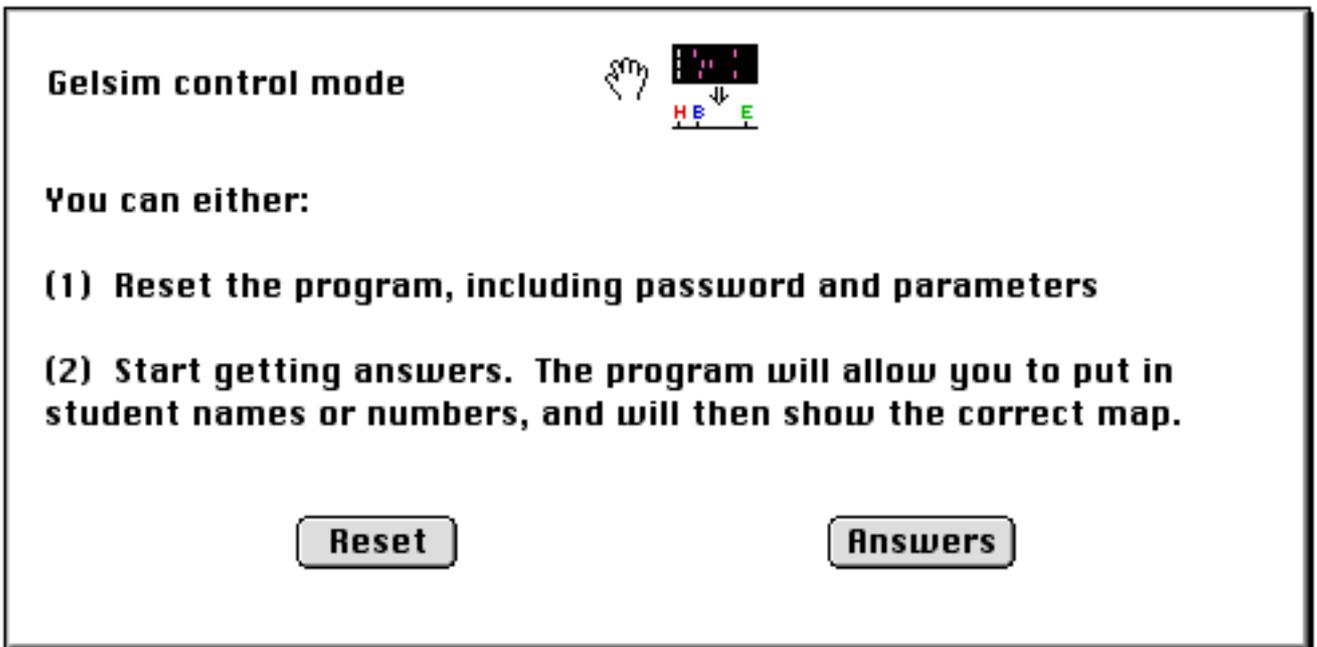
### **Instructions for students**

The instructions which you are reading at present are not appropriate for showing to students. A different set of specific instructions on how to run the program is needed. Included with the program you should find a printed set of instructions, labelled Default Instructions, which can be copied for distribution to students. Some of the information which is printed on these sheets is also shown on the Help screens, although some details are not shown on these screens. The more adventurous students will probably not need to look at the printed material or the Help screens.

If you alter some of the default values of the program, you may want to consider altering the student instructions.

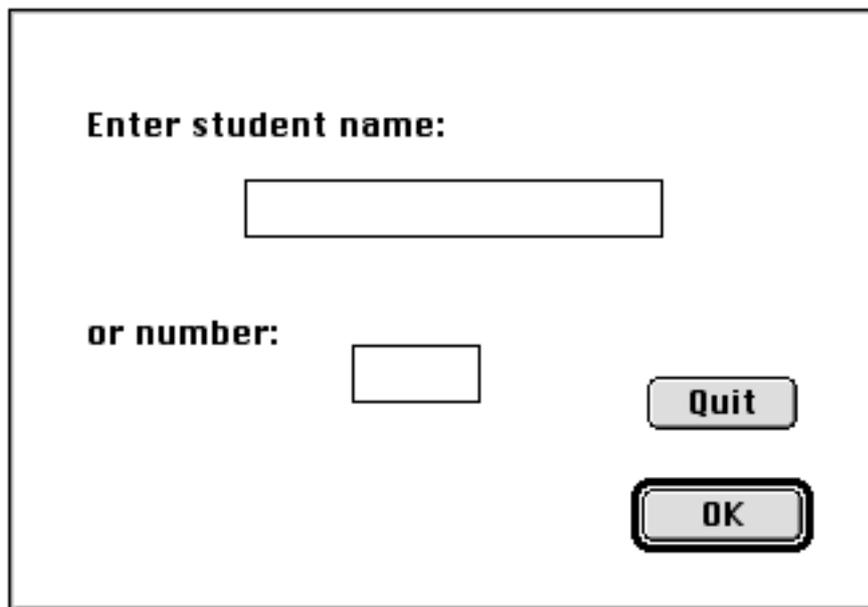
### **Getting the answers**

After the program has been set up, the **Setup program** key will no longer be seen. However as seen in the first diagram, the Introductory screen contains a 'hand'. If you hold down the Apple/command key (Macintosh) or Alt key (Windows) and click on the hand, the program will show the following screen:



Click on the **Reset** key to go through the same setup routine as previously. Click on the **Answers** key to get the program to show answers for individual students.

Once you click on the **Answers** key, the menus change, and the following screen will be shown for entry of a student name or number:



A second dialog box will now be shown. This is similar to the dialog box which students use to nominate which enzymes to cut their DNA. You should check each enzyme which has been used:

**Which enzymes should be shown in map?**

All

<input type="checkbox"/> Apal	<input type="radio"/>
<input type="checkbox"/> BamHI	<input type="radio"/>
<input type="checkbox"/> ClaI	<input type="radio"/>
<input type="checkbox"/> DraI	<input type="radio"/>
<input type="checkbox"/> EcoRI	<input type="radio"/>
<input type="checkbox"/> HindIII	<input type="radio"/>
<input type="checkbox"/> KpnI	<input type="radio"/>
<input type="checkbox"/> MluI	<input type="radio"/>
<input type="checkbox"/> NcoI	<input type="radio"/>
<input type="checkbox"/> PstI	<input type="radio"/>
<input type="checkbox"/> Sall	<input type="radio"/>
<input type="checkbox"/> XhoI	<input type="radio"/>

Click on a button to make enzyme first in list

In checking a map produced by the student, it is convenient if the output can be altered to produce a comparable map. For a linear sequence, the only ambiguity is the orientation of the map. For a circular map, the decision must also be made of which enzyme is at (or near) the apex (12 o'clock). A series of radio buttons allows any enzyme to be chosen to appear at the apex of the diagram. This button will have no effect if the map turns out to be linear.

When the **OK** button is clicked, a map will be shown on the screen. Either a linear or circular map may then be re-oriented left to right by using the **Flip** item in the **Answers** menu.. Similarly, if an enzyme has been nominated for the apex which occurs more than once in the sequence, the next occurrence of the enzyme may be placed at the apex by clicking the **Change origin** item.

Once the desired map has been shown on the screen, it may be saved to a text file. This is done by going to **Save to answers file** in the **Answers** menu. The first time you do this, you will be asked for a file name. Answers for different students are appended to the same file. After exiting from the program, this file may be accessed using any word-processing program for viewing or printing. It is best viewed using a fixed-space font such as Courier or Monaco.

### A trial run

It is strongly recommended that, following the setup run of the program, you try to recover the answers for at least one student name or number in the manner described above. It may also be reassuring to run through the program to check that the gels shown are in agreement with expectation. Any possible difficulties should thus be uncovered before the program has been used by large numbers of students.

## **Running and marking the exercise**

As well as altering the program to make the running easier or harder, the exercise can be modified simply by requiring students to map more or less enzyme sites. It may be reasonable to set a target for the student to map around a dozen sites, rather than requiring the exhaustive mapping of all sites.

It is difficult to avoid the requirement that each student must produce a report, showing at minimum the inferred sequence. Marking many such reports is necessarily time-consuming, but the ability of the program to produce printed outputs appropriate for each student should speed up this process as much as possible.