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## Specifications

Maximum number	
Individuals per family	1000
Spouses per person	No limit
Sibs per pregnancy	6
Markers per chromosome	250
Markers per family	50
Number of alleles	16, 40, or 150
Phenotypes	820
Diseases	No limit
Affection classes	15
Quantitative traits per locus	3
Quantitative loci per family	1


The Index contains a list of all Help topics available from CYRILLIC Help. For information on how to use Help, press F1 or choose *Using Windows Help* from the Help menu.

Dates are stored internally as Julian dates, with modifications that allow for all these formats (here given in day-month-year format) - 1984; 12-1984; 21-12-1984; ?1984; ?12-1984; 12-?1984; ?21-12-1984; 21-?12-1984; 21-12-?1984. The "?" signifies uncertainty in a component of a date.

Date formats are determined by the country information stored in WIN.INI. For example, the date format for Austria is yr-mth-dy, for the United States it is mth-dy-yr, and for New Zealand it is dy-mth-yr. The country information can be changed in the Control Panel application in the "MAIN" program Manager group. Double click on the "International" icon and select the appropriate item from the list in the Country: field.

## Manipulating symbols with the Mouse

### Moving individual symbols

The mouse may be used to move a pedigree symbol around the screen. Simply click on the symbol with the left button and hold the left button down while moving the mouse to the new position for the symbol. While the left button of the mouse is being held down, the cursor will change its appearance to 

### Moving a group of symbols

A group of symbols can also be moved together.

Select the group by clicking with the left mouse button on the screen beyond the upper left most symbol, and drag the cursor with the button held down until the rectangle encloses all the symbols you wish to move.

Release the mouse button.

Click the left mouse button somewhere within the rectangle and hold the button down. The cursor becomes a cross at the top left of the rectangle.

Move the mouse until the rectangle is in the correct position and release the mouse button.

The drawing will be refreshed to reflect the new positions.

### Undoing a move

The latest move, whether of one symbol or many, can always be undone by selecting the Edit|Undo move menu item, or by pressing the <Alt> and <BkSpace> keys together..

### Bringing up the individual dialogue form

*Double* click with the *left* mouse button on the symbol.

### Other mouse actions

The mouse can be used with the keyboard and the tool-bar to carry out a number of actions:

Delete an individual

Access the additional data form for an individual

(The user must provide a suitable DLL for this to work)

Define patterned bars representing chromosome regions

Set or reset pedigree loop breakpoints

Edit individual marker data

Provide information about relationships with partners

Enter quantitative values

Space the drawing out or

remove space from the drawing

## **Manipulating marriage lines**

If a couple has children, then it may be necessary to carry out either of two actions - move the line dropping down to the children relative to the parents (the default position is halfway between the parents); and allow for two or more sibships to interlock with the line joining individuals in one sibship appearing a little below that joining individuals in the other sibship, and with a loop around the point where the lines intersect.

### **Moving the drop-line**

Click with the *left* mouse button on the junction between the line joining the parents and the line dropping down to the children and hold down the button down while moving the cursor to the new position. The cursor changes to a 'cross hair' configuration during this operation. When the button is released, the line will be redrawn in the new position.

### **Returning a line to the default position**

To return the line to the default position, click on the junction with the *left* mouse button. A box appears asking you to confirm that you wish the line to be returned to the default position.

### **Lowering the line joining sibs and adding a loop over an intersecting line**

Click with the *right* mouse button on the junction of the line joining the parents and the line dropping down to the sibship. A dialogue box appears asking you how many 'steps' to lower the line and whether or not you want a loop around the point of intersection. Select the number of steps (1, 2, or 3) and choose whether or not there should be a loop over an intersecting line. Select 'OK' and the line joining the sibs will be lowered a little, and if you have so chosen, a half circle will be placed above it to show where the lines joining the sibs in the two sibships cross.



## Using the tool-bar with symbols

The tool-bar gives immediate access to a number of functions that control how the program reacts when you click on a symbol. First select one or more individuals in the drawing and then select the button on the tool-bar. The functions are as follows:-

**'Bars'**. This allows you to define or change the pattern used in the bars that can represent chromosome regions.

**'Loops'**. Set or reset pedigree loop breakpoints. This is only of use in consanguineous pedigrees for whom a linkage analysis is to be performed.


**'Quan'**. Enter quantitative values. This only works if a quantitative locus is defined in the Edit|Family information dialogue.


**'Delete'**. Delete an individual.

**'Marker'**. Edit or enter genetic marker data for an individual.

**'Spouse'**. Set the characteristics of a marriage or partnership.

**'Ind dat'**. Bring up the individual dialogue form.

**'Space'**. Add space within a drawing. The cursor changes to  Note that there should not be any individuals selected prior to selecting this button.

**'Reduce'**. Remove spaces from a drawing. The cursor changes to  Note that there should not be any individuals selected prior to selecting this button.

**'Desc'**. Draw only the descendants of a selected individual.

**'Add inf'**. Bring up the additional information dialogue form, if a DLL has been assigned.

## Scrolling with the keyboard

As well as using the scroll-bars to move around the family drawing, you can use several keys rather obvious keys to achieve the same ends.

Page Up	Move up the drawing by 2/3 screen height
Page Down	Move down the drawing by 2/3 screen height
Up Arrow	Move up the drawing by 1/3 screen height
Down Arrow	Move down the drawing by 1/3 screen height
Left Arrow	Move left in the drawing by 1/3 screen width
Right Arrow	Move right in the drawing by 1/3 screen width
Ctrl Left Arrow	Move left in the drawing by 2/3 screen width
Ctrl Right Arrow	Move right in the drawing by 2/3 screen width

## Using the keyboard with the mouse

If certain keys are pressed after one or more individuals have been selected, certain functions are performed - exactly as when you have selected an item from the tool-bar or from the floating menu.

<b>&lt;Escape&gt;</b>	Cancels mouse functions and clears any selected symbols.
<b>'B'</b>	<b>'Bars'</b> . This allows you to define or change the pattern used in the bars that can represent chromosome regions.
<b>'L'</b>	<b>'Loops'</b> . Set or reset pedigree loop breakpoints.
<b>'Q'</b>	<b>'Quan'</b> . Enter quantitative values.
<b>'Delete'</b>	<b>'Delete'</b> . Delete an individual.
<b>'M'</b>	<b>'Marker'</b> . Edit or enter genetic marker data for an individual.
<b>'P','S'</b>	<b>'Spouse'</b> . Set the characteristics of a marriage or partnership.
<b>'D'</b>	<b>'Ind dat'</b> . Bring up the individual dialogue form.
<b>'R'</b>	<b>'Desc'</b> . Draw only the descendants of an individual.
<b>'A', 'I'</b>	<b>'Add inf'</b> . Bring up the additional information dialogue form, if a DLL has been provided.

## File Menu

The File menu includes commands that enable you to open and save files, set up a new drawing, and to print the drawing.

- New...** opens the set-up dialogue for a new drawing.
- Open...** brings up the standard Windows 3.1 open file dialogue for selection of a drawing to open
- Save** Saves the drawing to the file whose full DOS name is shown in the window title. This item is greyed and unavailable if this is a new drawing.
- Save as...** Opens the standard Windows 3.1 save file dialogue so that the drawing can be saved to a new file.
- Close** Closes the drawing after presenting a message box to check that you really wish to do so and gives an opportunity to save the drawing.
- Print...** Presents the printing options dialogue, from which the drawing and documentation can be printed.
- Printing options...** Presents the dialogue that controls the choice of items to be printed as headings to drawings and lists.
- Printer set-up** Dialogues let you choose options for the selected printer, such as portrait/landscape output. There is currently no facility for choosing the printer, which has to be done in the Program Manager control panel. The printer options selected only temporarily override the Windows default options.
- Exit** Closes the program. If a drawing is being displayed, a message box is presented to check that you really want to close, or if you wish to save the drawing first.

**Below this is a list** of the five most recently accessed family files, which can be chosen for editing.

## Edit Menu

The Edit menu includes commands that enable you to move text to and from the clipboard, to edit disease and marker information, and to re-sequence and haplotype the family.

- Undo move** If symbols have been moved, the effect of that move is reversed by selecting this menu item.
- Copy** If no individuals are selected, the window area is copied to the clipboard. If one or more individuals are selected, then a dialog is presented which gives a selection of text items that can be copied to the clipboard, including information about each individual and information on the markers.
- Zoom In** Selection leads to a doubling in size of the scale of the drawing.
- Zoom Out** Selection leads to a halving in size of the drawing.
- Re-sequence** If one of the numeric numbering systems has been chosen, then this will reorder the family so that numbers are sequential across each generation.
- Balance parents** If an individual is selected and is an only child, then selecting this menu item will balance the parents over the child.
- Form Haplotypes** Children whose parents have been phenotyped will have their phenotypes ordered according to which parent supplied each allele. Incompatible alleles are notified, so this can be used as a simple check on genotype consistency.
- Edit phenotypes...** A dialogue is presented with a list of .markers defined for the family and several options. For markers selected from the list (all can be selected), the phenotype dialogue is presented in turn for either all individuals in the family, or for any individuals whose symbols are selected.
- Family information...** A dialogue that specifies the family name, number, disease, markers, etc.
- Family markers...** Brings up the marker list for the current family.
- Edit diseases...** Brings up a list of currently defined disease and quantitative loci. These can be altered, added to, or deleted.
- Edit markers...** Brings up a list of chromosomes from which a choice of marker set to edit can be made. Markers are stored in one file per chromosome.

## Options Menu

The Options menu contains commands for altering the program's default settings - directories, graphic features, etc.

- Set-up options...** Produces a dialogue that controls the default place where blood or DNA is stored; automatic backup of edited drawings; the form of display for maiden names; the default format for homozygous phenotypes; automatic re-sequencing of families when they are saved, whether or not maiden names are always displayed, the positions of proband arrows, and the minimum distance between symbols.
- Symbol definitions...** Presents a list of the pedigree symbols available so that their meanings for a family can be specified.
- Auto redraw** Forces the program to refresh the screen whenever anything is done that might have altered the screen contents. It is useful on occasion to turn this off, particularly if you are editing a large family for which screen redrawing is slow. Note that family redrawing is **much** quicker if no only minimal identifying information is displayed.
- Redraw** This is used to ensure that the display reflects the information on the family when auto-redraw has been turned off.
- Individual dialog displayed** If this menu item is ticked, then the individual dialog is displayed for every new individual added to the family drawing. If it is not ticked, then the dialog is not displayed.
- Set distance apart** If checked, new symbols will be placed the minimum distance (as defined in the setup dialog) from their nearest neighbours, and the drawing adjusted to allow this.
- Draw all relationships** Normally this item is selected, as shown by the tick beside it. Clicking on this item turns it off. This also is a means of speeding up the drawing of large families. The program attempts to draw all individuals and relationships in a family to ensure that all the lines that should appear in the window in fact do so. If turned off, a few lines may be missing. It is turned on by selecting it again.
- Clear symbols displayed** This is useful if you are providing members of a family, or other persons, with a copy of a pedigree and wish to ensure that no phenotypic information is provided.

**Hide partners from display** This option ensures that people marrying into a pedigree are hidden from the display. Editing of the drawing is not possible in this mode, as it is intended for print-outs only.

## **Format Menu**

**Display format...** Brings up a dialogue that offers a choice of information to be displayed under symbols, the form of the line joining mates, and the numbering system. In addition, the lines to be displayed from the Additional Information field can be set - up to a maximum of five.

**Other formats...** Brings up a dialogue that gives control over four sets of items. At the top is a set of edit boxes and controls to set up the dimensions of the drawing. Horizontal scaling determines the width of the drawing and the dimensions of the symbols. The range is 10%-200% of the default setting. Vertical scaling controls the spacing between generations. The default symbol width provides finer control over just the symbols size. The "Restore default settings" button returns these controls to their original values.

The next edit box controls the length of the line immediately above symbols that connects them to their parents and siblings. The actual size in drawings is also affected proportionately by the vertical scaling percentage.

The default manner in which phenotypes are created from allele names is by combining the allele names with a separator as chosen from the radio buttons in the next box. The choice is from "/", "- ", " ", or nothing.

The next box defines the default naming system for alleles. The choice is from among "A,B,C,...", "a,b,c,...", or "1,2,3,...".

The lowermost portion of the dialogue defines the width of the various lines used in drawing the family tree and documenting it. These are the lines around symbols, the lines joining members of the family, the lines around the bars which can be used to show haplotypes, and the lines around the boxes containing the details of alleles, etc.

**Fonts...** Brings up a dialogue from which the fonts of text in drawings is controlled. Clicking on the buttons brings up the standard Windows 3.1 font dialogue box. The items are the first and second lines of the headings of printed drawings (not seen on screen); descriptive text drawn below symbols; apart from the additional information line and the DNA sample number which are selected from the lowermost button; and the text in side boxes in printed drawings which may contain allele descriptions, disease descriptions, and quantitative locus definitions.

**Screen Colours...** Brings up a dialogue from which the standard colour selection dialogue can be used to choose a colour for the window background and for text. At present, the options for printed drawings do not run to colour. The Windows program manager defaults can also be selected.





## Input/output Menu

**Input family...** Selecting this brings up the list of input formats from which to choose. The options are :- MLINK format (before or after processing by MAKEPED.EXE); the CYRILLIC format; LINKSYS.EXE data exchange format; the Oxford of John Edwards; input from a DLL.

**Input marker info...** After choosing a file from the Open file dialog, the program takes information from the file to create new markers. The format is described in the marker file format.

**Output to LIPED...** If sufficient loci are defined for the family, this item sets up the output files for analysis by LIPED.EXE, and optionally will run LIPED using a batch file.

**Output to MLINK...** If sufficient loci are defined for the family, this item sets up the output files for analysis of the family by MLINK, and optionally will run MLINK.EXE using a batch file created by the program.

## **Windows Menu**

### **Display marker window**

If a family is being displayed and it has markers defined, then selecting this item brings up a window that contains the names of the markers, in the order they are drawn below the symbols. Only the markers checked for display are listed.

### **Display/Remove tools window**

The buttons are contained in a notional window which can be displayed or by selecting this menu item.

### **Buttons across window**

The buttons can be presented as a bar across the window, or as a group two buttons wide by about 5 down. This group can be moved around the main window and this may on occasion be useful as an alternative to having the buttons across the top of the window. If this menu item is checked, the buttons will be across the window, otherwise they are in a group.

## Help Menu

- Index** select this item to get to the main index of *this* help document
- Using Windows Help** selecting this item starts the Windows Help program's "help on help"
- Creating a new family** selecting this takes you directly to the "create new family" topic in this help document
- About CYRILLIC** this brings up the standard dialogue that informs the user about the provenance of this program together with some simple system statistics - the amount of memory free, the percentage of system resources free, the mode Windows is running in, and the processor.

## **Creating a new family**

There are five steps involved in creating a family drawing.

1. Providing basic facts about the family - select the menu item "File, New family..".
2. Placing symbols on the screen
3. Entering information about each individual - names, markers status, disease status, etc.
4. Defining relationships
5. Saving the drawing

## Family information dialogue

This dialogue box (brought up from the File, New family... or File, Family Info... menu items) contains the following items :-

**Family ID number** - this can be any text up to 20 characters in length.

**Family name** - up to 30 characters in length.

**Num individuals in family** - this keeps track of the size of the family.

**Max num individuals** - CYRILLIC has a preset maximum family size which is presently 1000 persons, for no particularly good reason.

**Family condition** - this can be selected from the drop-down list box of disease names that you have entered (from the Edit|Edit diseases menu item), or any other name can be typed in. It can be up to 40 characters in length.

**Quantitative value** - this *must* be selected from the drop-down list, and thus any quantitative loci must be entered into the disease list beforehand using the Edit|Edit diseases... menu item. They are treated as diseases by the program and handled by the same menu items and dialogues.

**Comments** - up to 120 characters in length. Note that Windows 3.1 allows you to force a new line in the edit box by pressing <Ctrl>J.

**Date of original information** - this must be entered in the date display format defined as your Windows default. Any separator can be used between the day, month, and year. This date is printed on print-outs for documentation.

**Date of last update** - the format is as for the date of original information. This also is used in print-outs for documentation purposes, and is **not** updated whenever the family drawing is edited.

**Select family markers** - This button gives access to the family marker selection dialogues. The markers must be defined before selecting this button.

## **Family markers**

Each family can have data on up to 50 markers on any one chromosome. The list of markers can be updated by selecting the 'Select family markers' button in the dialogue brought up by the "File|Family Info..." menu item. When the "Select family markers" button is selected for the first time, the chromosome selection dialogue appears and when a chromosome is chosen, the list of markers is given for a selection to be made. Only then does the family marker dialogue appear. The only way of storing markers from more than one chromosome for a family is to duplicate the family and edit the marker data.

## **Initialise Markers**

Selecting this button resets the number of markers to zero and the chromosome to none. A message box checks that you really wish to do this.

## **Reorder**

Selecting this button checks the order of the markers against the chromosome marker file, and ensures that they are the same. This is useful if you change the order in the marker file for some reason and wish to ensure that the order in the family reflects this. If the orders are the same, the button is greyed out.

## **Add New Marker**

If you select this button, a list-box with all the markers for the currently chosen chromosome appears. This is a multi-select list-box so that any combination of markers can be chosen. Markers already chosen for the family are not displayed.

## **Deleting a marker from the list**

If you select a marker in the list, a dialogue appears with several buttons. One states "**Delete marker**". If this is selected, you are asked to confirm that you wish to delete the marker from the list. If you subsequently reinstate the marker, the phenotypes of individuals in the family are lost.

## **Hiding/displaying a marker on the screen**

If you select a marker in the list, one of the options you can choose from the dialogue that is presented, is "**Hide marker**" if the marker is currently displayed on screen, or "**Display marker**" otherwise. If you choose the button, then display is turned off/on. Note that in order to have markers displayed on the screen, the selection must be made in the dialogue brought up selecting by the 'Options, Screen defaults...' menu item. If a disease class and/or quantitative value are defined, the display of their values is also controlled in the same way.

## **Marker ordering in list box**

This allows for either the order in which the markers are stored in the file, or alphabetic order.

## **Placing symbols on the screen**

The first symbol is placed by simply clicking anywhere in the window with either the left or right mouse button. Using the *left* mouse button produces the symbol for a female, the *right* mouse button produces the symbol for a male.

The individual dialogue form will appear for any identifying information to be entered.

Once the first symbol is drawn, click on that symbol with the *right* mouse button. A dialogue with buttons for relationships comes up. Selecting a button causes the dialogue to disappear and the mouse cursor to change to a circle inside a square. Clicking with the left mouse button anywhere on the screen causes the new symbol to be drawn on that place and the connecting lines to the first symbol also drawn.

Symbols may be moved around the screen after drawing.

## **Adding parents**

Adding parents for a symbol is slightly tricky. Click on the symbol with the right mouse button and select the "Father" button. Place this person on the screen. Then click on the child's symbol with the right mouse button and select "Mother". Place this symbol and the lines will be connected correctly. The sequence "child -> father -> wife" is logically incorrect and will not work.



## **Individual dialogue**

This is a large and complex dialogue that gives all the identifying information about an individual and their genetic status for any disease locus defined for the family.

### **Surnames**

This can be up to 20 characters in length. The name can be typed in or selected from the drop down list box. To drop the list down using the keyboard, press <Alt> plus the Down Arrow key.

### **Other surnames**

Up to 30 characters. In print-outs will appear in the form "Surnames (Other surnames)"

### **Forenames**

Up to 30 characters.

### **Known as**

Up to 20 characters. In print-outs will appear as "Known as (Forenames)"

### **Maiden name**

Up to 20 characters. This is only displayed for women who do not have a father in the drawing.

### **Address**

Up to 255 characters.

### **Additional info**

Up to 255 characters. This information can be displayed on drawings in a font different from the rest of the information about the individual. Up to five lines of text can be displayed individually as they appear in the edit box. The 'Format|Display format...' menu item produces a dialogue that has a set of buttons that can turn the display of particular lines on or off.

### **Comment**

Maximum of 255 characters.

### **Date of birth**

Enter in the format chosen as the Windows default. It is stored as a Julian date. The date can include day, month, and year, month and year, or just the year. The year should be 4 digits.

### **Date of death**

Enter as for date of birth. If the date of death is unknown, a "?" will ensure that the symbol is drawn correctly.

### **Proband**

If this is checked, an arrow is drawn pointing to the symbol. When families are output to MLINK, if there is a proband, the program will ask if you want the genetic risk for the person calculated.

### **All markers unknown**

This can be used to reset the marker phenotypes to unknown.

### **Pregnancy outcomes**

This drop down list box contains options for various states and conclusions to a pregnancy.

### **Genetic symbols**

This drop down list contains the symbol patterns and their definitions, if the user has supplied any.

### **Additional symbols**

This drop down list box holds the set of addition symbols that can be added to the genetic symbol.

**Multiple pregnancies**

This item is largely for information but if a child is a member of a multiple pregnancy, they can be removed from the multiple pregnancy by choosing "Singleton" from the drop down list box.

**Liability class**

Below the title is the liability class number assigned to the symbol. The drop down list box contains the titles of the classes defined for the family disease locus, if any.

**Male, female, Sex unknown**

The sex can be altered by the user. Note that the program does not check that it makes sense in terms of marriage partners.

**Disconnect from parents**

A symbol can be disconnected from the relationship with parents so that it can be assigned to a different sibship.

**Additional data**

If the user has supplied a DLL that keeps track of information about individuals in the families, additional to that kept by CYRILLIC, selecting this button gives access to the DLL and the additional record.

**Identifier**

It is possible to identify the individuals using any set of characters. Such identifiers are only displayed if the "Number entered" button is checked in the "Format|Display format..." dialogue.

**Markers**

If this button is selected, the marker phenotype dialogue appears.

**Adopted**

If this is checked, the symbol is surrounded by part of a square.

**Possibly adopted**

If this is checked, the symbol is surrounded by part of a square, with a question mark beside it.

## **Saving family**

When a family is drawn for the first time, the "File|Save" menu item is greyed out and only the "File|Save as..." item is available. When this is selected, the standard Windows 3.1 file save dialogue appears. Unless this is cancelled, the drawing is then saved to the disk file selected. If the file already exists, the program checks that you wish to overwrite it. Once a file has been saved, selecting "File|Save" saves it without other intervention.

<Ctrl>+<F2> -> Save as  
<F2> -> Save

Along with the details of the family, some information about default settings is also stored - the numbering system used, the display settings, clipboard settings, and the symbol descriptions.

## **Abandon family drawing - close family**

Changes to a family can be abandoned in several ways.

File|Close: selecting this menu item brings up a message box to check if you wish to save the family first, or to cancel. The screen is then cleared.

File|New...: selecting this menu item brings up a message box to check whether or not the file should be saved, and then presents the new family information dialogue.

File|Open...: selecting this brings up the same message box before presenting the standard file open dialogue.

File|1..5: Selecting one of the previously edited file names brings up the checking message before opening the previous file.

File|EXIT: brings up a message box from which the action can be cancelled, or the file saved or abandoned before exiting the program.

## **Open a family file**

A new family can be brought up, even if the screen is already displaying a family, in two ways. A family can also be imported from other types of file, such as MLINK pedigree files.

File|Open...: selecting this brings up the same message box before presenting the standard file open dialogue.

File|1..5: Selecting one of the previously edited file names brings up the checking message before opening the previous file.

## **Allele details dialogue**

### **Marker name**

The name of a marker can be up to 20 characters in length. You can use any text characters.

### **Numbered alleles**

This system has the alleles numbered in order. The edit box for the number of alleles must be filled in, but a default of 2 is supplied. The maximum number of alleles is 40, but be warned that input files for various versions of MLINK are limited to different numbers of alleles. The standard PC version has a limit of 5! Alleles will be given default names, but you can set the frequencies by clicking on the allele names in the list box.

### **Allele names alterable**

If this is selected, then the phenotypes are always derived from the allele names and phenotypes cannot be changed. Allele names and frequencies can be altered by selecting the allele names from the list box. The maximum number of alleles is 150.

### **Allele and phenotype names alterable**

If this is selected, then as the default, the phenotypes are derived by the program from the allele names. However, the phenotype names can be altered in a dialog that appears when the OK button is selected. Allele names and frequencies can be altered by selecting alleles from the list box. The maximum number of alleles is 40.

### **VNTR - entered as allele length**

Markers of this type usually have too many alleles to list. The individual phenotype record can contain an arbitrary number or a DNA fragment length such as 1200, 1.2, etc. The upper limit is 65000, which is translated by the program into kb as 65.0. On output for linkage analysis, the number of VNTR marker phenotypes can be reduced for a family, on the understanding that certain conditions are met by the phenotypic information for the family.

### **System shows dominance**

This signals to the program that the number of phenotypes is not necessarily directly related to the number of alleles, and that alleles will have non-standard factor definitions. The phenotype names and the factor definitions can be altered in the dialog that appears when the OK button is selected. The maximum number of alleles is 40.

### **Oxford allele description**

This system has the alleles numbered in order, but the first two alleles are an upper-case letter and a lower-case letter. The edit box for the number of alleles must be filled in, but a default of 2 is supplied. The adjacent edit box must also contain a suitable letter, although a default of "A,a" is assumed. On output to MLINK or LIPED, this system is treated as for Numbered alleles. The maximum number of alleles is 40.

### **Comments/references etc**

This can be used to document the allele with a literature reference or any other information, up to a maximum of 255 characters.

### **Chromosome band**

In the usual notation, eg. p13.112

**Relative % chromosome position**

This is the position of the marker on the chromosome, with the telomere of the short arm set at 0% and the telomere of the long arm at 100%.

**McKusick number**

In the usual form.

**Enzyme**

The name of the enzyme used. In lists, etc, the marker name will usually be presented in the form "DXS84(PstI)".

**Probe**

The name of the probe. In lists, etc, the marker name will usually have this appended in the form 'DXS84-p4'.

**OK**

On selecting this button, a dialogue for editing phenotypes is presented if the marker is dominant or codominant.

**Cancel**

All changes are cancelled.

**Delete marker**

The marker is removed from the list after you have an opportunity to change your mind.

**Reposition marker**

Markers are stored in the order set by the user. If this button is selected, the marker is removed from the list and a new position can be assigned to it by making a selection from a list-box containing all the other markers in their chromosomal order.

**Allele names and frequencies**

This box lists the names of the alleles and their frequencies. Selecting one of them gives an opportunity to change the frequency of the allele. If the system is codominant or shows dominance, then the name also can be changed.

## Input from MLINK pedigree files

Standard MLINK pedigree files can be input into CYRILLIC without alteration, but they require a small ASCII file to provide information about the loci as the standard LINKAGE file describing loci cannot be used to match loci stored by the program. This file should be stored with a ".MDF" extension, preferably in the same directory as the data files.. The pedigree file can contain more than one family.

Note that complex families will not necessarily be drawn as well as they could be drawn by hand. If individuals have two or three partners, the lines dropping down to the children may need moving a little and there may be rather more space within the drawing than is elegant. The .MDF file format is as follows:

Test MLINK families.	{This is a line for documentation only & is otherwise ignored}
3	{Chromosome number - 1..22, X, Y, U =unknown }
n	{Number of loci, including disease and quantitative loci}
Locus name 1	{Name of first locus}
Numbered alleles	{Describes the type of locus in terms used by the LINKAGE package - 'Affection locus', 'Factor Union system', 'Numbered alleles', or 'Quantitative locus'; if the locus is an Affection locus, this line must be followed by another giving the number of affection classes; if the locus is quantitative, the next line must contain the number of quantitative values to be read. Only the first letter is actually read.}
.	
.	
Locus name n	{The description for the last locus}
Clear all symbols	{The program will ignore disease status if there is a field for this - the alternative is 'Keep symbols'}
Pedigree number first	{Implies that each record contains a pedigree number - alternative is 'No pedigree number'}
DNA sample number present	{An optional DNA sample number - or any other number - can precede the marker data. The alternative is 'No DNA sample number.'}

An example is as follows:

```
Test family
1
4
Test disease
Affection locus
5
Marker
Numbered alleles
Marker2
Numbered alleles
Marker3
```



Numbered alleles  
Keep symbols  
Pedigree number first  
No DNA sample number

## Open file dialog for the .MDF file

The open file dialog box for the .MDF file is a modified version of the standard Windows 3.1 Open file dialog. The extensions are three buttons labelled as follows:

**Use chosen file** - if this radio button is selected when the dialog is closed, then the file will be used without modification.

**Edit chosen file** - if this radio button is selected when the dialog is closed, then the file will be read and then presented in a dialog box for editing.

**Create new file** - if this button is selected, then a new .MDF file will be created after you have edited the contents of a dialog box. If you do not enter a name for the .MDF file in the edit control at the top of the dialog, the name of the pedigree file will be used with the .MDF extension.

## **Edit .MDF file dialog**

This dialog presents all the information held in the .MDF file. The fields are as follows

**List of loci in order** - this list box contains all the loci in the order in which they are located in the individual records of the pedigree file.

**Description of file** - This is text up to 80 characters long that is used to identify the file. If it is left blank, then it will have the file name and current date placed in it.

**Pedigree number present in file** - The first item in the individual record in the pedigree file may contain a pedigree number (if it has been processed by MAKEPED.EXE, it will contain a pedigree number). Usually checked.

**Sample number placed before loci** - some people document their files with a sample number placed before the locus information. Usually unchecked.

**Ignore disease information** - on occasion the disease information in the pedigree file may be confusing. Checking this option makes the program ignore it. Usually unchecked.

**Rewrite original file after closing** - if this is a new file being created, this check button will be greyed out. Otherwise if you have chosen to edit a .MDF file, then checking this button will ensure that changes are made to the original file. Usually checked.

**Add new locus to list box** - Adding a locus to the list shown in the list box entails two steps. Firstly, ensure that the item in the list box that you wish the new locus to follow is selected by clicking on it once. Secondly, select the 'Add new locus to list box' button. A dialog appears with listboxes containing the names of all the available loci. Select one of them and the dialog is closed and the name added to the list box. Instructions on how to enter locus names is included in the dialog. For marker loci, a message box also asks if the locus is formatted as numbered alleles or as a factor union system in the pedigree file.

**Removing an item from the list box** - double click on the item and select the button labelled 'Yes' in the message box that appears.

There is no provision for reordering the items in the list box.

## **Viewing a complete family**

The present version of the program does not have a facility for viewing a complete family drawing, but this can be accomplished for all but the largest families by using the scaling features.

Choose the Format|Other formats... menu item. The other formats dialogue appears. The uppermost portion controls the scaling of the drawing. The edit box titled "Default symbol width in tenths of a mm" sets the standard symbol size and the normal horizontal scaling. The two spin controls determine the horizontal and vertical scaling as a percentage of the default value. The range is from 10% of the default to 200%. Although the horizontal scaling (and not the vertical scaling) controls the symbol size, it does not affect the font size.

## **Re-sequencing a family**

In the Roman numerals numbering system, the sequence of numbers of individuals within a generation may not necessarily be in order from left to right. This can be corrected by choosing the Edit|Resequence... menu item. The family is then reordered with the numbers within generations increasing from left to right.

In general, if the Roman numbering system is the default (as set in the dialogue brought up by selecting the Format|Display formats... menu item), when new individuals are entered they are assigned the next sequential number for their generation. For many families this is adequate and there is no need to have the numbers in order within generations.

There is a further option of having a family re-sequenced automatically or by choice every time the file is saved. This is set in the dialogue brought up by selecting the Options|Setup options... menu item. The default is "never".

## **Correcting the spacing of a family**

To effect changes in the spacing of rows and columns of the drawing, the tool-bar must be displayed. If it is not shown, select the Window|Display Tools Window menu item.

### **The "Space" button**

This button adds space between rows or columns of the pedigree. To use it, proceed as follows:

Select the button. The cursor will change to a double headed arrow.

Place the cursor over the spot you wish to add space - either between individuals or between generations.

Press and release the left mouse button. A dialog appears.

Select the number of spaces using the 'spin' control or the edit box beside it.

Select the direction.

Select OK.

The screen will be redrawn with the spaces added.

### **The "Reduce" button**

This button behaves exactly as does the "Space" button with the same dialogue, but the effect is to remove space from the drawing.

## **Printing a family drawing**

Three menu items provide control over the printer. There is no option to change the Windows default printer as defined in the Printers utility of the Control Panel supplied by the Program Manager.

### **File|Printer set-up**

This gives access to the printer set-up dialogue provided by the printer driver. The facilities vary according to the type of printer, but almost always will include an option of printing in Portrait mode or Landscape mode. Most usually for pedigrees it is best to use Landscape mode, with the width of the page being greater than the length. Whatever setting you use in CYRILLIC is stored in the initialisation file and used whenever you access any printer functions. This way, if Landscape is your standard preference, it will not reset the Windows default as used by other programs such as word processors.

### **File|Printing options...**

This brings up a dialogue box which is divided into three parts. The upper part is greyed out. The middle part contains check boxes that control the items included in the page headings for drawings or for lists of individuals. The lower part controls the options that appear in side boxes in drawings only - these include details of disease loci, marker alleles, quantitative loci, and symbol descriptions. Any changes made here are used as the defaults for the next print-out.

### **File|Print...**

This brings up the printing options dialogue box with the upper part greyed. In the lower two parts, any components that the family does not contain are greyed out. The upper part contains three check boxes that need to be checked to print either the drawing, and or lists of individuals in the family. Some printers allow for multiple copies. If this item is not greyed, then the number of copies can be set. The number of pages that the drawing will occupy is also given.

## **Printing keys to a family, or lists of individuals**

In addition to printing the drawing of a pedigree, the program can also produce a list of the individuals in the pedigree, sorted either by name or by pedigree number.

This is achieved from the File|Print... menu item, just as for printing the drawings of pedigree. In the upper part of the program, simply select the type of sorting method to be used, or both. The options in the box below this also control the page headings for these lists.



## Using the clipboard to transfer information about a family

Two types of information can be sent to the clipboard - a drawing, or part of a drawing, or lists of information about individuals in the family.

### Parts of the drawing

If the Edit|Copy... menu item is selected *without* any individuals selected, then the drawing will be copied to the clipboard as a Windows metafile. The portion of the drawing copied is always the size of the full screen and thus is a little larger than the client area of the program's main window.

This drawing can be pasted into word processor documents and edited in whatever way the word processor allows. Most painting or drawing programs will also allow it to be pasted into a document. Metafiles are lists of instructions for the drawing rather than the drawing itself and allow much better precision than the alternative bitmap format.

### Lists of individual data or marker data

If at least one individual is selected, and the Edit|Copy... menu item is selected, a dialogue appears that is used to define the information to be passed to the clipboard. The information is sent in table format - records for an individual or marker are on separate lines, with columns separated by tabs. The components of the dialogue are as follows:-

#### List details of individuals / List details of markers

These two items control the type of information included. If the former is selected, the items in the left panel control the output and information about individuals in the family are sent to the clipboard. If the marker list is selected, the right panel controls the output and information about the family markers is sent to the clipboard. Both options can be selected at the same time.

#### Include column headings

This determines whether headings are placed above each column.

#### Include heading

This controls whether or not the text in the edit box labelled "Heading" is sent first on a separate line.

#### All individuals / Selected individuals

These radio buttons determine whether information is sent about all individuals in the family, or only for those who have been selected.

#### Individual details

Only items that are checked in this panel will be sent to the clipboard for each person. If the box "Place marker details in the heading" is checked, and the "Include column headings" box is checked, the heading will be amplified to include the marker details. If the check box "Separate columns" is checked, the marker data is sent in separate fields, otherwise it is sent in one field, with a comma separating the phenotypes.

#### Marker details

Only items checked in this panel will be included in the output.

**Chromosome dialog**

This dialog only contains buttons, one for each chromosome (1 to 22, X, Y, & unknown). Marker information is stored in one file per chromosome, with a limit of 250 markers per chromosome. Selecting a button selects that chromosome.

## **Adding new markers or editing marker information**

This can be done at any time, but marker names cannot be altered if they are already in use by the family being displayed.

### **The chromosome dialogue**

Select the Edit|Edit markers... menu item or press ^M (this is the same as the <Enter> key, so that pressing this key has the same effect). A dialogue that comprises buttons with chromosome numbers on them appears. When one is selected, the file is opened, or you are asked if you wish to create a new marker file for that chromosome. If you do so the next dialogue appears.

### **The marker name list dialogue**

This comprises a list box with the names of all the markers for that chromosome, a button for creating new markers, and two radio buttons to alter the order of the names in the list box.

Clicking on an item in the list box brings up the **marker allele edit dialogue**.

Selecting one of the two radio buttons ("Alphabetic order" or "Chromosome order") orders the marker names accordingly.

Selecting the "Create new marker" button brings up the **marker allele edit dialogue** ready for a new marker to be entered.

When the allele dialogue is closed, the action taken depends on the type of marker and whether or not it is a new one.

### **Phenotypes dialogue**

If the marker is dominant or co-dominant, the phenotypes dialogue appears. This contains three list boxes. If the marker is co-dominant, then the two at the right are greyed out as they are for information only, with the MLINK factor definitions displayed. Clicking on a phenotype name in the list box at the left brings up a dialogue that allows the name of the phenotype to be altered. If you wish to alter all the phenotypes, selecting the button labelled "Edit phenotypes" causes all the phenotypes to be presented in turn.

### **Chromosome order dialogue**

If this is a new marker, a list box with the names of the markers in chromosome order appears. There are three possible actions. If you click on the button labelled "At front of file", the marker will head the list. If you select the "At end of file" button, the marker will be placed last. Otherwise, if you select one of the names in the list box, the marker will be placed *after* that marker in the chromosome order.

### **The marker name list dialogue**

This comprises a list box with the names of all the markers for that chromosome, a button for creating new markers, and two radio buttons to alter the order of the names in the list box.

**List box** - selecting an item from the list box opens the marker definition dialog box

**Marker ordering in list box** - the two options are chromosome order, which is the order in which the markers are stored in the file; and alphabetic ordering on the marker name. The case of the marker name affects the order.

**Create new marker** - this button opens the marker dialog box with empty fields.

**Close** - on closing the dialog, the marker file is rewritten if any marker has been altered or added to the list.

## **Adding a new disease locus or editing disease locus information**

This can be carried out at any time.

### **Disease locus list**

This is brought up by selecting the Edit|Edit diseases... menu item or pressing ^D. It comprises a list box and five buttons. The list box contains the names of the loci in alphabetic order. Double clicking on a name with the *left* button has the same effect as selecting the "Edit..." button.

"Close". This button removes the dialogue and rewrites the file of disease locus information.

"Rename". This brings a dialogue that allows the name of the selected (highlighted) disease from the list box to be altered.

"Delete". This button brings up a message box to check that you really wish to remove the disease from the list and the file.

"New disease". An edit box appears for the name of the new disease to be entered, then the **locus information** dialogue appears.

"Edit...". This brings up the **locus information** dialogue for changes to the information to be made.

## Disease locus information dialogue

This dialogue contains the following items:

"Affection" & "Quantitative". These two radio buttons determine the type of the locus. Affection loci have penetrances defined, whereas quantitative loci have only quantitative values.

"Frequency of disease allele". Enter the frequency of the disease allele as a decimal. For instance 0.0001.

"Chromosome". Enter the chromosome number in the usual way.

"Male mutation rate" & "Female mutation rate". These are entered in the usual way as decimals. They can be set to 0.0.

"Cancel". This has the expected action.

"Set default markers for disease".. A set of markers can be defined that are always presented as an option when the disease is selected in the **family information** dialogue. In fact the process is identical to the process of selecting markers for a family.

"OK"..This brings up one of two dialogues - the penetrance dialogue or the quantitative variable dialogue.

### **Penetrances**

The simplest way to enter the penetrances is to select the "Enter values" button. The program asks how many classes there are and then cycles through the penetrances for each genotype and the descriptions of the classes. The descriptions are used to annotate lists and are presented in the individual data dialogue. Selecting an item in one of the list boxes brings up an edit box for the information to be changed.

### **Quantitative loci**

To fill this in, determine how many traits are measured for this locus (most usually one) and enter the number in the upper edit box. Then fill in the means for the three genotypes. The rows of means are labelled 1, 2, and 3 - only fill in as many rows as there are traits.

The variance-covariance matrix also needs to be entered. MLINK assumes that the two homozygous genotypes have equal variances, so that only one variance is needed if there is only one trait. For two traits, the variances-covariances are entered in the order V11; V12; V22 down the column. For three traits the order is V11; V12; V13; V22; V23; V33. The value of the "Heterozygote multiplier" is used to correct the heterozygote variances. For instance, with one trait and a variance of 2 and heterozygote multiplier of 1.5, the variances will be as follows for the three genotypes:-  $V_{11NN} = 2.0$ ;  $V_{11ND} = 3.0$  ;  $V_{11DD} = 2.0$ .

The phenotypic values are displayed using the number of decimal places in the 'Decimal places:' column.

If the values in the 95% range edit boxes are not equal to zero, then *for trait one only*, the values on output will be trimmed to these values. If the "Log transform" radio button is selected, then all values for the first trait will be transformed on output. It is assumed that the variances and means will have been transformed and do not need transformation on output.



## Input from databases of pedigree information

CYRILLIC will draw a pedigree diagram from files in a standard format that most databases should be able to produce with a little macro programming. Each file can contain only one family.

Note that complex families will not necessarily be drawn as well as they could be drawn by hand. If individuals have two or three partners, the lines dropping down to the children may need moving a little and there may be rather more space within the drawing than is elegant.

The file is a standard DOS text file, containing lines made up as follows with optional items shown between '#' and comments in brackets:-

Family name {This can be any text}

Family number {This can be any text and does not have to be a number}

Genetic condition {Note that it does not have to match a name known to CYRILLIC}

Chromosome {1..22,X,Y, or U Unknown}

Number of markers

Name of marker 1 {Marker names must be defined in CYRILLIC before entering a family as there is no way of entering a name as the family is input, although CYRILLIC does allow you to choose another marker from the list known to it if the marker name is not recognised}

Name of marker 2

... and so on for as many markers as are supplied for each individual

ID DadID MumID Sex DiseaseStatus #Quantitative value#

{each item separated by 1 or more spaces; disease status must either be one of 'A'=affected or 'N'=unaffected, or confirm to the Pedigree/Draw "attribute symbol codes" described below; sex is 'F'=female, 'M'=Male, or 'U'=unknown; the IDs must be numbers but do not have to be sequential}

Marker 1 Phenotype {Phenotypes can be of four different types depending on how the marker is defined within CYRILLIC. The types are as follows:

VNTR Supply the two fragment sizes separated by spaces. e.g. '4000 4200'; these must be whole numbers; decimals are not allowed;

Numbered alleles or extended alleles - supply the two allele numbers. e.g. '3 5';

Oxford alleles follow the Oxford system, i.e. alleles are numbered in order Capital letter, the same lowercase letter, number, that is Q, q, 3, ....; e.g. 'Q q'; Other systems which have allele names combined in a logical way. e.g. 'C/D', or '2/3', or '3.1/3.8', etc. " can be used to represent unknown phenotypes.}

Marker 2 Phenotype

... 'and so on for as many markers as given'

Individual name {This should be in the form 'Surname(Other surnames), Forenames (Known As)'} }

Date of birth {The format required is the Windows default or it can be left blank}  
Date of death {The format required is the Windows default or it can be left  
blank}  
DNA sample number {Up to 15 characters or a blank line}  
... 'This sequence of lines is then repeated for each individual in the family'  
END {This is an obligatory end of file marker}.

## **Pedigree/Draw "Attribute symbol codes"**

This is a six character code of the format "TSSSSC" where T=trait symbol, SSSS are status symbols, and C is a code symbol. The code symbol is ignored by CYRILLIC, but the other five columns can all be used. If the disease status field in the file is only one character long, then it is assumed to use the previous style. If it is two or more characters long, then Pedigree/Draw format is assumed. This implies that only the "@" character can be used as a blank filler character.

Using the CYRILLIC conventions for symbols, the trait codes are :- A »q4; B »q1; C »q1+q4; D »q2; E »q2+q4; F »q1+q2; G »q1+q2+q4; H »q3; I »q3+q4; J »q1+q3; K »q1+q3+q4; L »q2+q3; M »q2+q3+q4; N »q1+q2+q3; O"»q1+q2+q3+q4; P»Unknown.

The Status codes are A »deceased; B »adopted; C »proband; D »cross at upper right edge; E »untested; F »cross symbol; G »spontaneous abortion; H »therapeutic abortion; I »pregnancy; J »miscarriage; K »still birth; L »lived less than 1 day; M »no offspring; N »dizygotic twin; O »monozygotic twin; P »zygosity unknown; Q »cross over symbol; R »x-linked carrier.

## **Output to the LIPED program**

Before creating an output file for LIPED, you must decide upon a suitable directory for the output files. This usually will be the directory in which the LIPED.EXE program resides. If you want CYRILLIC to run LIPED for you using the output file as input to LIPED, then the directory containing LIPED.EXE must be used.

In order to create or add to an output file for LIPED, select the Input/output|Output to LIPED... menu item or press the <F9> function key. A dialogue appears with three components.

On the left are two list boxes that function in a similar way to the list boxes in the standard file open dialogues. Use the list box on the right to obtain the correct directory and either select a file name from the list box on the left or enter it in the edit box at the top. CYRILLIC has a default of 'liped.inp' for the file name.

On the right is a box containing the two options 'Append to pedigree file' and 'Rewrite pedigree file'. If an file of the same name is already present, then the program can add the new pedigree to the end of the file, and will assume that you will select the same markers. Otherwise it will create a new one.

Below this is a check box labelled "Run program. If this is checked, the program will create a small batch file and run LIPED, assuming that LIPED.EXE is in the chosen directory.

On exiting the dialogue, a list box is presented with the names of the loci defined for the family. Select one as the LIPED main locus. The list-box re-appears without the main locus listed so that you can select the other loci for the analysis. Then a dialogue asks for the form of the analysis. From this point on it is essential that you have the LIPED documentation or understand LIPED input files as the questions are not self explanatory.

## Output to the LINKAGE package

Before creating an output file for MLINK, you must decide upon a suitable directory for the output files. This usually will be the directory in which the LINKAGE programs reside. If you want CYRILLIC to run MLINK for you using the output files as input to MLINK, then the directory containing MLINK.EXE must be used. This directory must also hold MAKEPED.EXE and UNKNOWN.EXE from the LINKAGE package.

In order to create or add to an output file for MLINK, select the Input/output|Output to MLINK... menu item or press the <F10> function key. A list box containing the loci defined for the family now appears. Select the markers you wish to analyse. Note that if there are only two loci, the list box does not appear, as the program assumes these will be chosen.

Next a dialogue appears with three components.

On the left are two list boxes that function in a similar way to the list boxes in the standard file open dialogues. Use the list box on the right to obtain the correct directory and either select a file name from the list box on the left or enter it in the edit box at the top. CYRILLIC has a default of 'liped.inp' for the file name.

On the right is a box containing the two options 'Append to pedigree file' and 'Rewrite pedigree file'. If an file of the same name is already present, then the program can add the new pedigree to the end of the file, and will assume that you will select the same markers. Otherwise it will create a new one.

Below this box is a check box labelled 'Rewrite locus file'. If this is checked, the MLINK locus definition file will be written or created.

Below this is a check box labelled 'Run program'. If this is checked, the program will create a small batch file and run MLINK, assuming that MLINK.EXE is in the chosen directory.

At the bottom of the form is a check box that is labelled 'Use IDs rather than sequence numbers'. If the family was created with sequence numbers entered by the user, this check box can be used so that the entered numbers are used, rather than the sequential number. Otherwise the check box is greyed.

On exiting the dialogue, if there are any probands in the family, a message box asks if you want the output file set up for risk analysis.

If the locus file is to be re-written, a list of questions appears about locus positions if there are more than two (this only applies to disease loci, otherwise the marker order is assumed). This is followed by requests for recombination fractions, increments, and stop values. On completion, if requested, MLINK will then be run.

## **Defining new relatives of an individual**

New relatives are defined by clicking on the symbol with the *right* mouse button. This brings up a dialogue which contains a variety of types of relationship, only some of which will be available, depending on whether the person has a partner and has parents already defined. When a relationship is selected, the dialogue disappears and the cursor changes to a cross with 'Rel' above it and 'Pos' below it.

If the left button is pressed with the cursor over blank space on the screen, the new individual dialogue appears and the symbol will be drawn there unless the "Cancel" button is selected on exit from the dialogue. If an individual is selected, they may or may not be connected, depending on the relationship and the individual.

## Delete individuals

### Delete connections

Parents - In the **individual data** dialogue is a button labelled "Disconnect from parents". Selecting this removes the connection to the parents. To reconnect an individual to their parents, both parents will have to **connected individually**.

Partners - in the **Spouse dialogue** is button labelled "Delete relationship". If this is selected and there are no children, then the relationship is removed.

Other relationships - these have to be removed by using one of the methods above on the relative.

## **Spouse/partner information**

To change the nature of a relationship, click on the symbol of one of the partners and then select the "Spouse" button from the tool-bar. The partner definition dialogue appears. The list box on the left lists the partners for that person by name of number. The buttons listed below only apply to the relationship to the person *selected in the list-box*.

Consanguineous. If this is selected, then the line joining the partners is doubled.

No issue. If this is selected and the couple have no children, then the line joining them will have a line dropping down and ending in a bar signifying that they had no children.

Normal. If this is selected, the lines are drawn in the default manner.

Separated. If this is selected, a single slanting line is drawn midway between the two partners.

Divorced. A double slanted line is drawn midway between the two partners.

Informal. The line(s) joining the partners are drawn dotted.

Delete relationship.



## **Multiple pregnancies**

To draw a twin pregnancy proceed as follows:

Place the first member of the twin pregnancy on the screen by selecting one of the parents and adding a son or daughter. Click on the son or daughter with the right mouse button and then choose the appropriate twin type from the dialog box and place the individual on the screen. The appropriate lines will be drawn. To extend the pregnancy to triplets, select one of the twins, choose the triplet button from the dialog and place on the screen the next member of the multiple pregnancy.

To create twins from two singletons already drawn:

Ensure that the two individuals are side by side on the screen. Click on one of the singletons with the right mouse button and choose the appropriate type of twin (the program does not check that it makes sense - that is up to you). Then click on the other member of the twin pair. The lines will be redrawn to fit the new representation. The multiple pregnancy can be extended in the same way.

## Marker file input format

It is possible to input marker information from a standard DOS text file. The program will read the file and create new markers in the designated chromosome.

An example of the file is as follows:

Set of markers for chromosome 16

```
D16S1    16 <2 0.4 0.6> {,c62b3}
D16S2    16      <3> {PstI}
D16S3    16.17  ( p122 ) {,,113460.0}
D16S4    16.17  ( p122 ) <4> {PstI,,}
D16S5    16.21  ( p122 ) <3 0.5 .3 .2> {PstI,,114570.1}
D16S6    16.28  ( p12.1) <2>  {PstI,c62b3,} [This is an example of a
marker]
Z
```

DESCRIPTION of the format:-

Line 1 Description of marker file. This must be present but is for your documentation only.

Line 2 and on :

each line can have up to six items with only the first two being mandatory; if the line contains just a name followed by two numbers, then it is assumed that the it contains the marker name, the chromosome number, and that number of alleles items must be separated by one or more spaces; the first item must begin in the second or third column as the list is concluded by a line containing the character 'Z' in the first position. The order of the items is important, and must conform to the list below. However, any item may be missed out. If the number of alleles is missing then it is assumed to equal 2.

Item 1 Marker name;

Item 2 Marker chromosome and relative % position along the chromosome in the format "15" for the chromosome only, or "15.33" for the chromosome and the relative position;

Item 3 Band position enclosed in "()", e.g. "( p13.2 )".

Item 4 Number of alleles and frequencies enclosed by "<>", e.g. "<2>" for number of alleles only, or "<3 0.4 .5 0.1>" for alleles plus frequencies the numbers are separated by spaces;

Item 5 Enzyme, probe, and McKusick number enclosed by "{}" in the format "{Enzyme,probe,McKusick number}" with empty fields represented by commas, e.g. "{,326110}".

Item 6 Comment enclose by "{}". This can be any text up to 255 characters in length.

Final line contains "Z" only

**Input from Pedigree/Draw files**

There is an additional option in the input data form which allows data input from the 'pedigree' file format used by this Macintosh program. The number of displayable symbols has been increased slightly to cope with this format and the 'Additional info' field in the individual data dialog is now a multiline edit box - up to 255 characters can be stored comprising up to five lines. These lines are displayed one below the other and are intended for use by this system only, as no attempt is made to make any marker data below this start in a consistent place on screen. In the 'Format|Display format...' dialog is a small set of buttons labelled 1 to 5 which control which, if any, of the additional information lines are displayed. They are only effective if the 'Additional info' check box is selected. However, this feature may be useful for displaying a variety of text items.

When this input format is selected, a small dialog appears containing 5 buttons, one for each line of text. Selecting one of the buttons brings up a list box from which you may select an item which will hold the content of that line. The text is removed from the additional information. This feature allows you to set up correspondences between the pedigree/draw text and the individual data record in CYRILLIC.

Note that CYRILLIC was not written so as to be able to draw complex inbred pedigrees from input files. If there is real demand for these features, the drawing algorithm could be extended in a future release.

## **Distance between symbols**

The 'Options|Setup...' dialog has an edit box that contains the distance that separates new individuals in the drawing from the nearest symbols. If the 'Options|Set distance apart' menu item is checked, the distance is used as the standard distance between symbols and newly created symbols are moved to allow for this.

## **The position of proband arrows**

Proband arrows can be placed in any of six positions relative to the symbols - to the left, to the right, above left, above right, below left, and below right.

## **Windows Keys**

The keyboard topics below come from Help for Windows. You can create similar keyboard topics for your application's Help. Choose from the following list to review the keys used in Windows:

[Cursor Movement Keys](#)

[Dialog Box Keys](#)

[Editing Keys](#)

[Help Keys](#)

[Menu Keys](#)

[System Keys](#)

[Text Selection Keys](#)

[Window Keys](#)

## Cursor Movement Keys

<b>Key(s)</b>	<b>Function</b>
DIRECTION key	Moves the cursor left, right, up, or down in a field.
End or Ctrl+Right Arrow	Moves to the end of a field.
Home or CTRL+Left Arrow	Moves to the beginning of a field.
PAGE UP or PAGE DOWN	Moves up or down in a field, one screen at a time.

## Dialog Box Keys


<b>Key(s)</b>	<b>Function</b>
TAB	Moves from field to field (left to right and top to bottom).
SHIFT+TAB	Moves from field to field in reverse order.
ALT+letter	Moves to the option or group whose underlined letter matches the one you type.
DIRECTION key	Moves from option to option within a group of options.
ENTER	Executes a command button. Or, chooses the selected item in a list box and executes the command.
ESC	Closes a dialog box without completing the command. (Same as Cancel)
ALT+DOWN ARROW	Opens a drop-down list box.
ALT+UP or DOWN ARROW	Selects item in a drop-down list box.
SPACEBAR	Cancels a selection in a list box. Selects or clears a check box.
CTRL+SLASH	Selects all the items in a list box.
CTRL+BACKSLASH	Cancels all selections except the current selection.
SHIFT+ DIRECTION key	Extends selection in a text box.
SHIFT+ HOME	Extends selection to first character in a text box.
SHIFT+ END	Extends selection to last character in a text box



## Editing Keys

<b>Key(s)</b>	<b>Function</b>
Backspace	Deletes the character to the left of the cursor. Or, deletes selected text.
Delete	Deletes the character to the right of the cursor. Or, deletes selected text.

## Help Keys

<b>Key(s)</b>	<b>Function</b>
F1	<p>Gets Help and displays the Help Index for the application. If the Help window is already open, pressing F1 displays the "Using Windows Help" topics.</p> <p>In some Windows applications, pressing F1 displays a Help topic on the selected command, dialog box option, or system message.</p>
SHIFT+F1	<p>Changes the pointer to  so you can get Help on a specific command, screen region, or key. You can then choose a command, click the screen region, or press a key or key combination you want to know more about.</p> <p>(This feature is not available in all Windows applications.)</p>

## Menu Keys

<b>Key(s)</b>	<b>Function</b>
Alt	Selects the first menu on the menu bar.
Letter key	Chooses the menu, or menu item, whose underlined letter matches the one you type.
Alt+letter key	Pulls down the menu whose underlined letter matches the one you type.
LEFT or RIGHT ARROW	Moves among menus.
UP or DOWN ARROW	Moves among menu items.
Enter	Chooses the selected menu item.

## System Keys

The following keys can be used from any window, regardless of the application you are using.

<b>Key(s)</b>	<b>Function</b>
Ctrl+Esc	Switches to the Task List.
Alt+Esc	Switches to the next application window or minimized icon, including full-screen programs.
Alt+TAB	Switches to the next application window, restoring applications that are running as icons.
Alt+PrtSc	Copies the entire screen to Clipboard.
Ctrl+F4	Closes the active window.
F1	Gets Help and displays the Help Index for the application. (See <a href="#">Help Keys</a> )

## Text Selection Keys

<b>Key(s)</b>	<b>Function</b>
SHIFT+LEFT or RIGHT ARROW	Selects text one character at a time to the left or right.
SHIFT+DOWN or UP	Selects one line of text up or down.
SHIFT+END	Selects text to the end of the line.
SHIFT+HOME	Selects text to the beginning of the line.
SHIFT+PAGE DOWN	Selects text down one window. Or, cancels the selection if the next window is already selected.
SHIFT+PAGE UP	Selects text up one window. Or, cancels the selection if the previous window is already selected.
CTRL+SHIFT+LEFT or RIGHT ARROW	Selects text to the next or previous word.
CTRL+SHIFT+UP or DOWN ARROW	Selects text to the beginning (UP ARROW) or end (DOWN ARROW) of the paragraph.
CTRL+SHIFT+END	Selects text to the end of the document.
CTRL+SHIFT+HOME	Selects text to the beginning of the document.

## Window Keys

<b>Key(s)</b>	<b>Function</b>
ALT+SPACEBAR	Opens the Control menu for an application window.
ALT+Hyphen	Opens the Control menu for a document window.
Alt+F4	Closes a window.
Alt+Esc	Switches to the next application window or minimized icon, including full-screen programs.
Alt+TAB	Switches to the next application window, restoring applications that are running as icons.
Alt+ENTER	Switches a non-Windows application between running in a window and running full screen.
DIRECTION key	Moves a window when you have chosen Move from the Control menu. Or, changes the size of a window when you have chosen Size from the Control menu.



## **Clipboard**

This is a topic that describes the Windows term "clipboard". If you click the "clipboard" term within the Copying Text or Glossary topic, this Help topic will be displayed in a pop-up window.

This topic is also tagged with the keyword "clipboard," for use with the WinHelp Search option.





