

Notes on QTL Cartographer

Introduction

QTL Cartographer is a suite of programs for mapping quantitative trait loci (QTLs) onto a genetic linkage map. The programs use linear regression, interval mapping ([Lander and Botstein 1989](#)), composite interval mapping ([Zeng 1993](#), [Zeng 1994](#)) and multiple interval mapping ([Kao & Zeng 1997](#), [Kao et al. 1999](#), [Zeng et al. 1999](#)) methods to dissect the underlying genetics of the quantitative traits.

Mapping is done onto a set of linked genetic markers with known recombination frequencies. Genetic linkage maps and data files can be imported from **Mapmaker**. The mapping program uses a dynamic algorithm that allows a host of statistical models to be fitted and compared, including various gene actions (additive and dominance), QTL-environment interactions, and close linkage. Presently, the mapping programs can handle data from backcrosses, intercrosses and recombinant inbred lines, as well as a few other experimental designs.

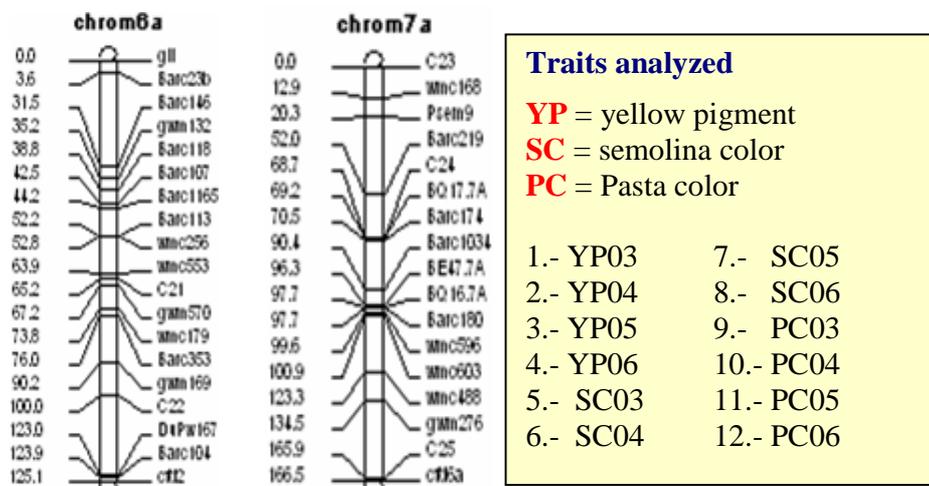
Description of the example

We are going to use a file including chromosomes 6A and 7A of our durum cross UC1113 x Kofa. The first 19 markers (*gli* to *cfb2*) correspond to chromosome 6A, and the last 17 (*C23* to *cfb6*) to chromosome 7A. The C# markers represent groups of completely markers that we have fused in a single haplotype to facilitate mapping.

The file **durum.txt** includes the raw mapping data and **DurQTL.txt** the raw mapping data plus the QTL data.

durum text: http://maswheat.ucdavis.edu/education/PDF/Mapping_course/data/durum.txt

Durabch.txt: http://maswheat.ucdavis.edu/education/PDF/Mapping_course/data/Durbatch.txt



Generating Mapmaker files for multiple chromosomes

We have prepared a file named **Durbatch.txt**
(http://maswheat.ucdavis.edu/education/PDF/Mapping_course/data/Durbatch.txt)
which includes a series of commands for Mapmaker:

```
Prepare data durum.txt
Cent Kosambi
Print names on
make chromosome chrom6a chrom7a

sequence 1 2 3 4 5 6 7 8 9 10 11 12 13 14 16 17 18 19
anchor chrom6a
frame chrom6a

sequence 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36
anchor chrom7a
frame chrom7a

sequence all
```

Start Mapmaker -> System -> cd **C:\MAP\QTL** -> exit

Once you are back in Mapmaker and you are in the correct **C:\MAP\QTL** directory type

Run Durbatch.txt

Mapmaker will run all the commands and generate the two maps

Quit and answer yes to the question of saving the data

Mapmaker has now created a series of files including **DURUM.MAP**, which will be our input with **DurQTL.txt** for QTL Cartographer

Importing data from Mapmaker into QTL Cartographer

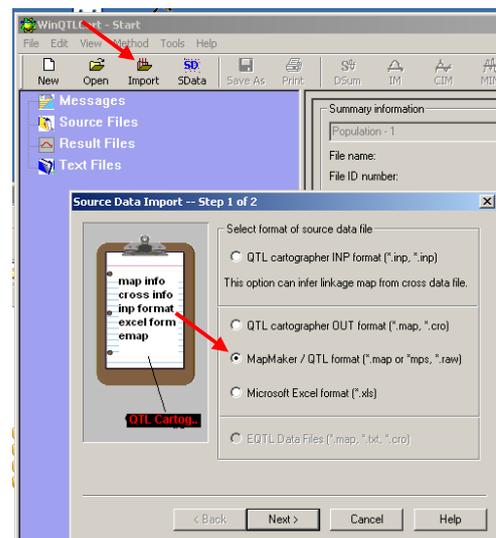
1. Start QTL Cartographer

Start -> Programs -> Bioinformatics -> QTL Cartographer

2. Right Click on the QTL Cartographer icon and send it to the Front Desk for future use

3. Select -> **Import** on the top panel

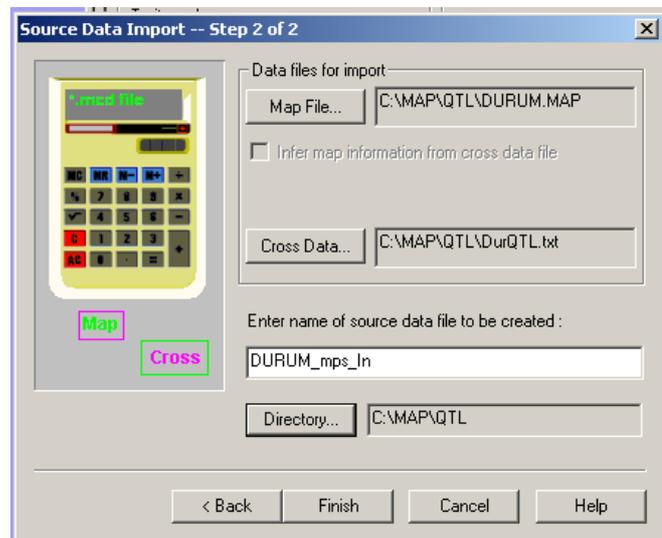
4. Select **MapMaker/QTL** format



5. Click **Map File** and browse for the **DURUM.MAP** in your C:\MAP\QTL directory

6. Click **Cross Data** browse for the Durum.txt in your C:\MAP\QTL directory

7. Enter Name of source data file to be created **DURUM_mps_In**: it creates a file with the extension **DURUM_mps_In.mcd**



This file can be directly opened by QTL cartographer without the need to import from Mapmaker again

8. Click **Directory**: to establish the directory where to file will be stored. Click **Modify...** and select your C:\MAP\QTL directory. Click **SET** to finish selecting the target directory.

QTL cartographer assumes Haldane distances. TO convert to Kosambi click Basic Information and select Map function (in the bottom) = Kosambi

Analysis of data with QTL Cartographer

1. **Mapping function**: QTL cartographer assumes Haldane distances. To convert to Kosambi click **Basic Info...** and select Map function (in the bottom) = **Kosambi** ->OK

2. **Analysis**: Select **Composite Interval Mapping**

Click **GO**

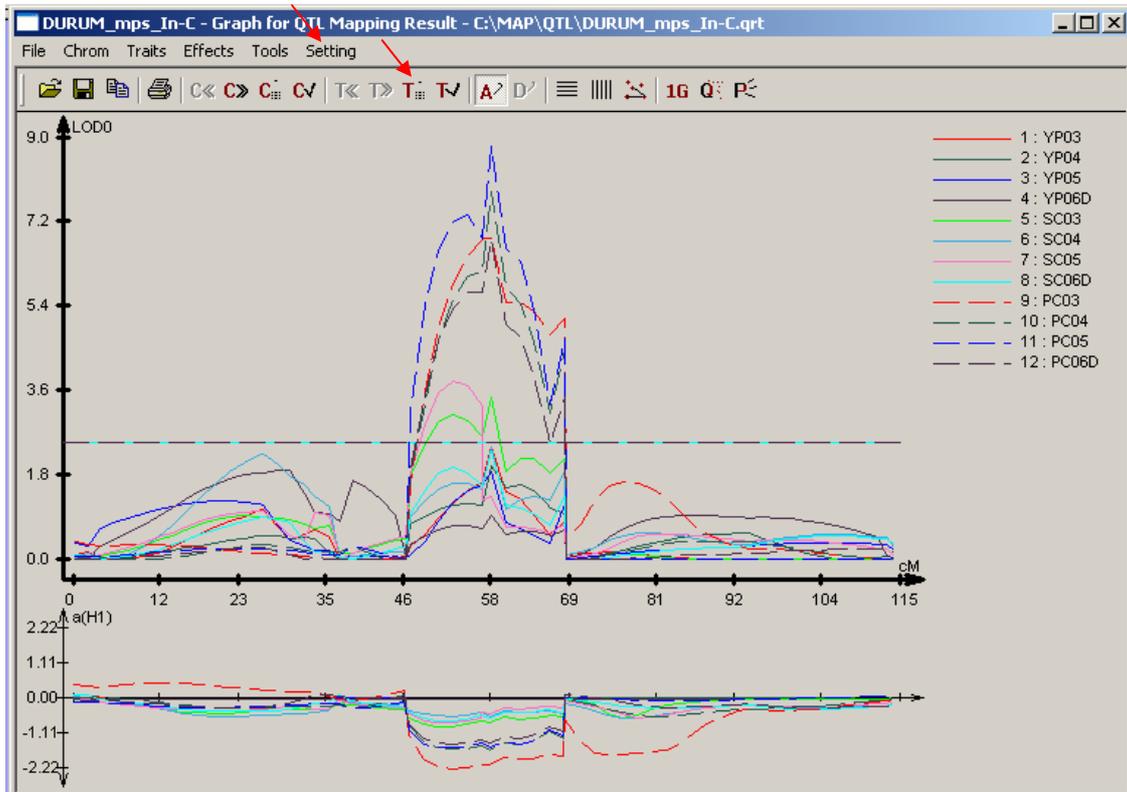
Click **Control** and in Regression Method select: **Forward and Backward Method**

Press START to create a file with the extension “.qrt” (takes \cong 2 minutes)

Once the QTL image appears select **Setting** on top panel and select **“Show trait names or Legend”**

To see all traits Click on the **T symbol** indicated by the arrow

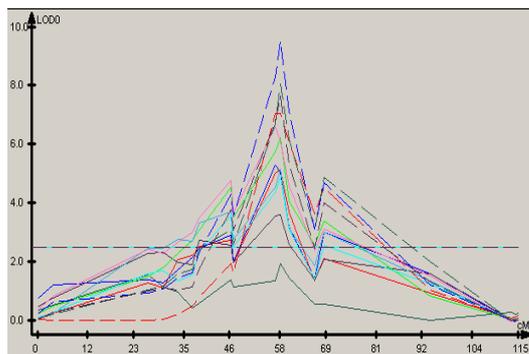
To change chromosome click on **C>**



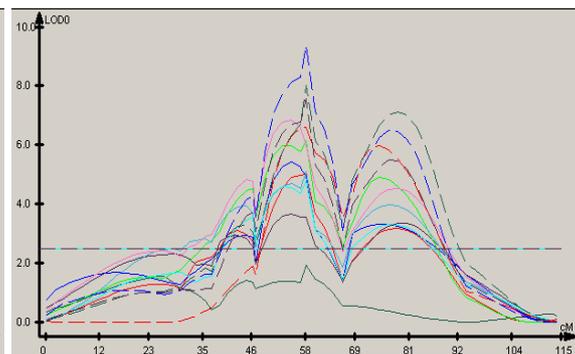
The lower curve indicates which allele contributes the positive effect.

Compare the results on 6A from the CIM analysis with

Single Marker analysis



Interval Mapping Analysis



Summary from QTL Cartographer Manual (Included in your files)

Single-marker analysis

When to use: For quick scanning of the entire genome (all chromosomes) to find best possible QTLs. Use single-marker analysis first to ensure your data file is clean; then move on more sophisticated analysis methods, such as [Interval Mapping](#) and [Composite Interval Mapping](#).

How it works: Single-marker analysis is based on the idea that if there is an association between a marker genotype and trait value, it is likely that a QTL is close to that marker locus.

Comments: Single-marker analysis can be somewhat useful for a quick look at data, but it has been superseded by Interval Mapping and Composite Interval Mapping. IM and CIM are more thorough and accurate indicators of QTL. The prime value of WinQTLCart's single-marker analysis is its identification of missing data that could affect later analysis.

Running a single-marker analysis

1. Open a mapping source data file (an .MCD file) into the WinQTLCart main window.
2. Select Method>Single-Marker Analysis. WinQTLCart analyzes the data and displays the single marker analysis controls in the form pane. The information pane on the right includes the analysis results.
3. Select a trait for display from the Trait Selection pull-down list. All the traits present in the file will be on the list.
4. For each trait, the information pane on the right displays WinQTLCart's statistical summary of the file. (You can view this summary in a larger window by clicking the Result button in the Statistical Summary group box, just to the left of the information pane.)
5. In the Single Marker Analysis group box, click Result to view the analysis result for the selected trait. You can change the font used by the display window to make the results easier to read.

Click the Save... button in this group to save the marker analysis results to a text file.

6. In the Statistical Summary group box, click Result to view the summary in a larger display window. Click the Save... button to save the statistical results to a text file.

The statistical summary includes:

- Basic summary of the data
- A histogram for the quantitative trait

Interval Mapping

What it is: Interval mapping (IM) is an extension of [single-marker analysis](#). In single-marker analysis, only one marker is used in QTL mapping but effects are underestimated and the QTL position cannot be determined. Interval mapping provides a systematic way to scan the whole genome for evidence of QTL. Lander Botstein (1989) developed the Interval Mapping (IM) approach in which one marker interval at a time is analyzed to construct a putative QTL by performing a likelihood ratio test (LRT) at every position in the interval.

IM uses two observable flanking markers to construct an interval within which to search for QTL. A map function (either Haldane or Kosambi) is used to translate from recombination frequency to distance or vice versa. Then, a LOD score is calculated at each increment (walking step) in the interval.

Finally, the LOD score profile is calculated for the whole genome. When a peak has exceeded the threshold value, we declare that a QTL have been found at that location.

When to use it: IM is a good general standard to use for all datasets.

High-level process

Here's a quick overview of how to use WinQTLCart's IM implementation. The first few times you run this analysis, go with the WinQTLCart default values for the form's parameters. The defaults provide the best all-around parameter settings, especially for initial analysis sessions.

1. Select the IM analysis method.
2. Select the chromosome(s) and trait(s) you want to analyze.
3. Select a threshold level to apply to the selected trait(s). Select either [By manual input](#) (the WinQTLCart default) or [By permutations](#) (to have WinQTLCart determine an optimum threshold). Click OK to start the calculations for the threshold level.
4. Following threshold calculation, set [IM form parameters](#). Select a walk speed in cM. It's recommended you use the same walk speed for your entire dataset. Don't reset the walk speed between runs or your results will not be comparable.
5. Click Start to begin the analysis.

Running interval mapping analysis

WinQTLCart provides default values for the parameters in this form. The defaults provide the best all around parameter settings, especially for initial analysis sessions.

Interval mapping analysis uses WinQTLCart mapping source data files (.MCD files). Use WinQTLCart's import commands to move your source data files from text to .MCD format.

1. Open a source data file into the WinQTLCart main window.
2. Select Method>Interval Mapping. WinQTLCart displays the interval mapping analysis controls in the form pane.

Composite Interval Mapping

The approach of Interval Mapping (IM) considers one QTL at a time in the model for QTL mapping. Therefore, IM can bias identification and estimation of a QTL when multiple QTLs are located in the same linkage group. Jansen (1993) and Zeng (1993, 1994) independently proposed the idea of **combining IM with multiple regression analysis in mapping**. Zeng named this combination “**composite interval mapping**” (CIM). When testing for the putative QTL in an interval CIM uses other markers as covariates to control for other QTL and to reduce the residual variance such that the test can be improved. The model of CIM includes one QTL and markers.

What it is: Composite interval mapping (CIM) adds background loci to simple **interval mapping** (IM). CIM fits parameters for a target QTL in one interval while simultaneously fitting partial regression coefficients for "background markers" to account for variance caused by non-target QTL.

"In theory, CIM gives more power and precision than simple IM because the effects of other QTL are not present as residual variance. Furthermore, CIM can remove the bias that would normally be caused by QTL that are linked to the position being tested."

Background markers are usually 20-40cM apart.

High-level workflow

Here's a quick overview of how to use WinQTLCart's CIM implementation. The first few times you run this analysis, go with the WinQTLCart default values for the form's parameters. The defaults provide the best all-around parameter settings, especially for initial analysis sessions.

1. Select the CIM analysis method. Select the chromosome(s) and trait(s) you want to analyze.
2. Select a threshold level. Click OK to start the calculations for the threshold level. This may take from several minutes to several hours to run.
3. Following threshold calculation, set **CIM form parameters** . Select a walk speed in cM. It's recommended you use the same walk speed for your entire dataset. Don't reset the walk speed between runs or your results will not be comparable. Click Start to begin the analysis. The analysis may take from 20 minutes to several hours to run.

Running composite interval mapping analysis

WinQTLCart provides default values for the parameters in this form. The defaults provide the best all around parameter settings, especially for initial analysis sessions.

Composite interval mapping analysis uses WinQTLCart source data mapping files (.MCD files). Use WinQTLCart's import commands to move your source data files from text to .MCD format.

1. Open a source data file into the WinQTLCart main window.
2. Select Method>Composite Interval Mapping. WinQTLCart displays the CIM analysis controls in the form pane.