Table des matières

1. Introduction ..................................................................................................................... 4
2. Contributors .................................................................................................................... 4
3. Support ............................................................................................................................ 5
4. Setting up QTLMap .......................................................................................................... 5
   4.1. Runtime environment with GNU software component ............................................. 5
       Pre-requisites .............................................................................................................. 5
       Compilation ............................................................................................................... 5
       OpenMP support ....................................................................................................... 5
5. Input files ........................................................................................................................ 5
   5.1. Dataset format .......................................................................................................... 6
       Pedigree file .............................................................................................................. 6
       Marker map file ....................................................................................................... 6
       The marker genotypes file ....................................................................................... 7
       Quantitative trait values file .................................................................................... 7
       Expression quantitative trait values file ................................................................... 8
6. Description of the dataset ................................................................................................ 9
   6.1. The model file ......................................................................................................... 9
   6.2. The parameter file .................................................................................................. 11
   6.3. Principles ............................................................................................................... 14
       Mixture of half-sib and full sib families .................................................................... 14
       Minimal paternal and maternal phases probability .................................................. 15
7. Analyses .......................................................................................................................... 15
   7.1. Available analysis ................................................................................................... 15
   7.2. Single real trait with pre corrected data .................................................................. 16
   7.3. Single real or discrete trait with a model description ............................................. 16
   7.4. Single real trait with a model description and a complete linearised likelihood ...... 16
   7.5. Set of real traits with a multivariate analysis (based on a multi-normal penetrance function) 16
   7.6. Set of traits with a discriminante analysis ............................................................. 17
   7.7. Single survey trait with the cox model with a model description ......................... 17
   7.8. Runtime options .................................................................................................... 17
       Analyse ..................................................................................................................... 17
       Haplotype .................................................................................................................. 18
       Optimisation .............................................................................................................. 18
       Console output mode ............................................................................................... 19
       Report output mode ............................................................................................... 19
       Number of qtl detection available ............................................................................ 19
       EQTL analysis .......................................................................................................... 20
8. Estimation of the test statistic rejection thresholds ........................................................ 20
   8.1. Estimation of the test statistic rejection thresholds with missing data ................... 20
       Format of the simulation parameter file ................................................................... 21
       Addition keys in the parameter file ........................................................................... 23
   8.2. Permutations .......................................................................................................... 24
       Information about the permutation process ............................................................. 24
   8.3. Estimate of the test statistic rejection thresholds without missing data ................ 24
<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>9. Simulate and design a new protocol</td>
<td>27</td>
</tr>
<tr>
<td>10. Output files</td>
<td>29</td>
</tr>
<tr>
<td>10.1. Analysis report</td>
<td>29</td>
</tr>
<tr>
<td>Configuration defined by the user</td>
<td>29</td>
</tr>
<tr>
<td>Description of the genealogy</td>
<td>29</td>
</tr>
<tr>
<td>Description of the markers</td>
<td>29</td>
</tr>
<tr>
<td>Description of the traits</td>
<td>30</td>
</tr>
<tr>
<td>Parental phases</td>
<td>30</td>
</tr>
<tr>
<td>Genome scan</td>
<td>30</td>
</tr>
<tr>
<td>10.2. EQTL analysis report</td>
<td>33</td>
</tr>
<tr>
<td>10.3. Analyse summary</td>
<td>34</td>
</tr>
<tr>
<td>10.4. The family likelihood</td>
<td>35</td>
</tr>
<tr>
<td>LRT Sires files</td>
<td>35</td>
</tr>
<tr>
<td>LRT Dams file</td>
<td>35</td>
</tr>
<tr>
<td>LRT grid 2 QTL</td>
<td>36</td>
</tr>
<tr>
<td>10.5. QTL effects estimations files</td>
<td>36</td>
</tr>
<tr>
<td>QTL Paternal effects</td>
<td>36</td>
</tr>
<tr>
<td>QTL Maternal effect</td>
<td>37</td>
</tr>
<tr>
<td>10.6. Parents phase report</td>
<td>37</td>
</tr>
<tr>
<td>10.7. Haplotypes assigned from parents</td>
<td>37</td>
</tr>
<tr>
<td>10.8. Grand parental segment transmission marginal probabilities</td>
<td>38</td>
</tr>
<tr>
<td>10.9. Grand parental segment transmission joint probabilities</td>
<td>38</td>
</tr>
<tr>
<td>10.10. Simulation report</td>
<td>39</td>
</tr>
<tr>
<td>10.11. Report simulations result</td>
<td>39</td>
</tr>
<tr>
<td>11. Reference</td>
<td>40</td>
</tr>
<tr>
<td>12. Appendix</td>
<td>40</td>
</tr>
<tr>
<td>12.1. Parameter file Option Keys</td>
<td>40</td>
</tr>
</tbody>
</table>
1. Introduction

QTLMap is a software dedicated to the detection of QTL from experimental designs in outbred population. QTLMap software is developed at INRA (French National Institute for Agronomical Research). The statistical techniques used are linkage analysis (LA) and linkage disequilibrium linkage analysis (LDLA) using interval mapping. Different versions of the LA are proposed from a quasi Maximum Likelihood approach to a fully linear (regression) model. The LDLA is a regression approach (Legarra and Fernando, 2009). The population may be sets of half-sib families or mixture of full- and half- sib families. The computations of Phase and Transmission probabilities are optimized to be rapid and as exact as possible. QTLMap is able to deal with large numbers of markers (SNP) and traits (eQTL).

The aim of QTLMap developers is to propose various genetic models depending on 1) the number of QTL alleles segregating (biallelic in crosses between monomorphic breeds, biallelic without hypothesis on the origin, multiallelic, haplotype identity), 2) the number of QTL segregating (one, two linked, several unlinked), 3) the number of traits under the QTL influence. The trait determinism may vary depending on 1) the trait distribution (gaussian trait, survival trait or threshold distribution), 2) the interactions between the QTL and fixed effects or other loci, 3) the residual variance structure (homo- or heteroskedasticity for half-sib families). Due to differences with the asymptotical conditions from the chi2 theory, the test statistic significance are evaluated either through numerical approximations, or through empirical calculations obtained from permutations or simulations under the null hypothesis.

QTLMap is written in fortran and either uses the NAG or SLATEC libraries.

Up to now, the following functionnalities have been implemented :

- QTL detection in half-sib families or mixture of full- and half-sib families
- One or two linked QTL segregating in the population
- Single trait or multiple trait analyses
- Nuisance parameters (e.g. sex, batch, weight...) and their interactions with QTL can be included in the analysis
- Gaussian, discrete or survival (Cox model) data
- Familial heterogeneity of variances (heteroscedasticity)
- Can handle eQTL analyses
- Computation of transmission and phase probabilities adapted to high throughput genotyping (SNP)
- Empirical thresholds are estimated using simulations under the null hypothesis or permutations of trait values
- Computation of power and accuracy of your design or any simulated design

2. Contributors

Pascale Le Roy, UMR GARen, Rennes, France
3. Support

Subscribe and post any message/question to the qtlmap-users list:

mailto:qtlmap-users@listes.inra.fr

4. Setting up QTLMap

4.1. Runtime environment with GNU software component

Pre-requisites

➢ The GNU compiler collection: gfortran 4.4, gcc
➢ Cmake 2.6.4, cross-platform, open-source build system.

Compilation

> cd ${QTLMAP_DIR}
> mkdir build
> cd build
> cmake -DCMAKE_BUILD_TYPE=Release ..
> cmake -DCMAKE_Fortran_COMPILER=gfortran ..
> make

The binary qtlmap is created in the ${QTLMAP_DIR}/build/src directory.

To install the qtlmap binary in the bin directory ${QTLMAP_DIR}/bin:
> make install

OpenMP support

supports multi-platform shared-memory parallel programming

To define the number of threads:
> export OMP_NUM_THREADS=8

5. Input files

To carry on an analysis, you need

4 data files:

Marker map
5.1. Dataset format

Pedigree file

The file contains pedigree information for the 2 last generations of a design which comprises 3 generations, i.e. parents and progeny. It must not contain the grand parental pedigree information. Each line is made of an alphanumeric ID triplet (individual, sire, dam). A fourth information gives the generation number: « 1 » for the parental generation; « 2 » for the progeny generation. An animal missing one or both parents ID has not to be included in the file. The missing value code (given in the parameterization of the analyses, see 6.2) cannot be used in the pedigree file. The file must be sorted by generation, sire ID and dam ID.

<table>
<thead>
<tr>
<th>922961</th>
<th>911287</th>
<th>902206</th>
<th>1</th>
</tr>
</thead>
<tbody>
<tr>
<td>944547</td>
<td>924758</td>
<td>911714</td>
<td>1</td>
</tr>
<tr>
<td>944985</td>
<td>924758</td>
<td>912892</td>
<td>1</td>
</tr>
<tr>
<td>961924</td>
<td>922961</td>
<td>944547</td>
<td>2</td>
</tr>
<tr>
<td>961925</td>
<td>922961</td>
<td>944547</td>
<td>2</td>
</tr>
<tr>
<td>961926</td>
<td>922961</td>
<td>944547</td>
<td>2</td>
</tr>
<tr>
<td>963187</td>
<td>922961</td>
<td>944985</td>
<td>2</td>
</tr>
<tr>
<td>963188</td>
<td>922961</td>
<td>944985</td>
<td>2</td>
</tr>
<tr>
<td>963189</td>
<td>922961</td>
<td>944985</td>
<td>2</td>
</tr>
<tr>
<td>963190</td>
<td>922961</td>
<td>944985</td>
<td>2</td>
</tr>
</tbody>
</table>

*Texte 1: Example of a pedigree file*

means that the pedigree includes 7 progeny born from 1 sire and 2 dams. Sire 922961 is the son of sire 911287 and dam 902206 etc...

constraint

The file must be sorted by generation, sire ID and dam ID.

Marker map file

This file gives the locations of the markers on the chromosome(s). Each line corresponds to a single marker, and gives (order to be followed):

- marker name (alphanumerique);
- name of the chromosome carrying the marker (alphanumerique);
- marker position of the marker on the average map (in Morgan);
- marker position of the marker on the male map (in Morgan);
➢ marker position of the marker on the female map (in Morgan) ;
➢ inclusion key (=1 if the marker has to be included in the analysis, 0 if not)

<table>
<thead>
<tr>
<th>Marker</th>
<th>Position (Average)</th>
<th>Position (Male)</th>
<th>Position (Female)</th>
<th>Included</th>
</tr>
</thead>
<tbody>
<tr>
<td>SW552</td>
<td>0.08</td>
<td>0.05</td>
<td>0.09</td>
<td>1</td>
</tr>
<tr>
<td>SW64</td>
<td>0.24</td>
<td>0.24</td>
<td>0.25</td>
<td>0</td>
</tr>
<tr>
<td>CGA</td>
<td>0.49</td>
<td>0.45</td>
<td>0.55</td>
<td>1</td>
</tr>
<tr>
<td>S0088</td>
<td>0.50</td>
<td>0.37</td>
<td>0.59</td>
<td>1</td>
</tr>
<tr>
<td>SWR1002</td>
<td>0.58</td>
<td>0.49</td>
<td>0.63</td>
<td>1</td>
</tr>
</tbody>
</table>

**Texte 2: Example of a marker map file**

means that marker SW552 is on chromosome 1, at position 0.08 on the average map, 0.05 on male map and 0.09 on the female map, and will be included in the analysis of chromosome 1, etc...

**The marker genotypes file**

This file contains the animals phenotypes at the markers. The first line gives the marker names, the markers must belong to the marker map file. For each animal, a line gives its ID (as described in the pedigree file) followed by the markers phenotypes, ranked following in the first line order. Each phenotype is made of 2 alleles, unordered. When an animal has no phenotype for a marker, both alleles must be given the missing value code as given in the parametrisation of the analysis (see 6.2).

<table>
<thead>
<tr>
<th>Mark1</th>
<th>Mark2</th>
<th>Mark3</th>
</tr>
</thead>
<tbody>
<tr>
<td>911714</td>
<td>2 5 3 1 4 13</td>
<td></td>
</tr>
<tr>
<td>912892</td>
<td>8 2 6 5 4 13</td>
<td></td>
</tr>
<tr>
<td>924758</td>
<td>2 5 6 1 12 5</td>
<td></td>
</tr>
<tr>
<td>922961</td>
<td>2 2 3 1 12 13</td>
<td></td>
</tr>
<tr>
<td>944547</td>
<td>2 5 1 3 12 4</td>
<td></td>
</tr>
<tr>
<td>944985</td>
<td>2 8 1 5 12 4</td>
<td></td>
</tr>
<tr>
<td>961924</td>
<td>2 5 0 0 13 4</td>
<td></td>
</tr>
<tr>
<td>961925</td>
<td>* * 0 0 13 4</td>
<td></td>
</tr>
<tr>
<td>961926</td>
<td>2 5 0 0 0 0</td>
<td></td>
</tr>
<tr>
<td>963187</td>
<td>2 8 0 0 12 4</td>
<td></td>
</tr>
<tr>
<td>963188</td>
<td>2 2 3 1 13 4</td>
<td></td>
</tr>
<tr>
<td>963189</td>
<td>2 2 1 1 12 4</td>
<td></td>
</tr>
<tr>
<td>963190</td>
<td>2 8 1 5 12 4</td>
<td></td>
</tr>
</tbody>
</table>

**Texte 3: Example of a marker genotypes file**

means that, amongst the 5 grand parents, 3 were genotyped (911714, 912892 et 924758). For instance, grand dam 911714 is heterozygous « 2 5 » at marker SW552, the individual 961925 has no genotype at marker mark1 …etc.
**Quantitative trait values file**

This file gives the phenotypes of the traits to be analysed. The progeny performances only are considered in the analysis and must be given in the file.

For each animal, its ID (identical to the ID given in the pedigree file) is followed by information about nuisance effects (fixed effect levels, covariable value) and then by three information for each trait: the performance, a 0/1 variable IP which indicates if (IP=1) or not (IP=0) the trait was measured for this animal and must be included in the analysis, and 0/1 variable (IC) which indicates if (IC=0) it was censored or not (IC=1), this IC information being needed for survival analysis (by default IC=1).

<table>
<thead>
<tr>
<th>ID</th>
<th>SEX</th>
<th>VALUE1</th>
<th>VALUE2</th>
<th>VALUE3</th>
<th>VALUE4</th>
<th>VALUE5</th>
<th>VALUE6</th>
</tr>
</thead>
<tbody>
<tr>
<td>961924</td>
<td>1</td>
<td>10.43</td>
<td>7.8</td>
<td>1</td>
<td>1</td>
<td>77.6</td>
<td>1</td>
</tr>
<tr>
<td>961925</td>
<td>2</td>
<td>5.34</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>90.3</td>
<td>1</td>
</tr>
<tr>
<td>961926</td>
<td>1</td>
<td>12.34</td>
<td>11.3</td>
<td>1</td>
<td>1</td>
<td>103.</td>
<td>1</td>
</tr>
<tr>
<td>963187</td>
<td>2</td>
<td>9.45</td>
<td>12.7</td>
<td>1</td>
<td>1</td>
<td>98.3</td>
<td>1</td>
</tr>
<tr>
<td>963188</td>
<td>1</td>
<td>11.10</td>
<td>13.5</td>
<td>1</td>
<td>1</td>
<td>0.0</td>
<td>0</td>
</tr>
<tr>
<td>963189</td>
<td>2</td>
<td>10.11</td>
<td>10.</td>
<td>1</td>
<td>1</td>
<td>94.8</td>
<td>1</td>
</tr>
<tr>
<td>963190</td>
<td>1</td>
<td>9.98</td>
<td>14.2</td>
<td>1</td>
<td>1</td>
<td>98.3</td>
<td>1</td>
</tr>
</tbody>
</table>

Texte 4: Example of a quantitative trait values file

This file describes 2 traits. For progeny 961924, the recorded information are: sexe 1 (fixed effect), body weight 10.43 (covariable), backfat thickness 7.8mm (trait 1) and fatening period of 77.6 days (trait 2) etc...

**Expression quantitative trait values file**

This file gives the phenotypes expression traits to be analysed.

The header line is the list of animals phenotyped. The following line are the fixed effects, covariates and finally the phenotype.

The format of the nuisances effects and phenotype line is:

```
<IDANIMAL> <VALUE_ANIMAL1><VALUE_ANIMAL2>... 
```

For missing data, insert a character string which is not interpretable as a numeric (e.g. n/a).
In this previous example, the animal 6380 have a missing data for the gene 3.

6. Description of the dataset

Illustration 1: set of needed files for the analysis
6.1. The model file

In this file the model analysis of each trait is described

➢ Number of traits
➢ Number of fixed effects (nf), Number of covariables (nc)
➢ Names of the fixed effects and covariables
➢ Name of the 1st trait, nature of trait (‘r’ for real value, ‘i’ discrete ordered data and ‘c’ categorial data) model for this trait symbolized by 0/1 indicators for each fixed effects (nf first indicators), each covariables (nc following) and each interactions between the QTL and the fixed effects (nf last indicators). A fixed effect, covariable or interaction will be included in the analysis if its indicator is 1, will not be if it is 0.
➢ Name of the 2nd trait,...
➢ ..... 
➢ (Optional) The heritability h2, phenotypics and genotype correlation between traits (classical traits)
➢ A filter list of traits be kept in the analysis. This line is optional. If absent all traits described above will be analysed.

```
3 ! Number of traits
1 1 ! Number of fixed effects and covariables
sexe poids ! Names of the fixed effects and covariables
malade r 1 1 0 ! 1st trait, (nature : real value) model
malcor r 0 0 1 ! 2nd trait, (nature : real value) model
third r 0 0 0 ! 3nd trait, (nature : real value) model

correlation_matrix
0.35 0.28 0.29
0.20 0.32 0.28
0.20 0.20 0.33
```

Texte 6: Example 1 of a model file

This model file describes the performance file where one fixed effect, one covariate and three performances are referenced for each animals.

The model for each performance is :

malade = \mu + sexe + \beta . poids + \varepsilon 
malcor = \mu + \text{QTL} \times \text{sexe} + \varepsilon 
third = \mu + \varepsilon 

The correlation matrix are given according the following rules :

➢ The heritability (h2) are defined in the diagonal
➢ Phenotype correlations : the upper triangle matrix
➢ Genotype correlations : the lower triangle matrix

The following example gives a model file with a filter on the trait names third and malcor
The key word « all » allows the use of the same model for all the traits (useful for eQTL detection).

To apply a filter with the key word « all » the user have to give an index trait list (referenced in the phenotype file. Trait one → index 1, Trait two → 2).

6.2. The parameter file

All information needed by an analysis is the parameter file p_analyse:

➢ name of the dataset files : genealogy, map, genotypes and performances
➢ name of the model file describing the performances
➢ paths and names of the output files :
➢ full information analysis result file
➢ summary of the analysis
➢ sire and dam family **likelihood ratio test (LRT)** along the linkage group
➢ sire and dam **QTL effect estimations** along the linkage group (under hypothesis H1 = 1 QTL and H2 = 2 QTL)
➢ grand parental **segment transmission** marginal and joint probabilities

➢ fixed options:
  ➢ chromosomes explored
  ➢ step length of the scan
  ➢ minimum size of a full sib above which the dam effects (QTL and polygenic) are estimated
  ➢ minimal paternal and maternal phase probability
  ➢ missing genotype value

The parameter file use the format `<key>=<value>`. None of the characters after the character ‘#’ are interpreted (useful to add comments).

several key may be defined:

*input file keys* :

*in_map* = `<path file>` the map file

*in_genealogy* = `<path file>` the genalogy file

*in_genotype* = `<path file>` the genotype file

*in_traits* = `<path file>` the traits file

*in_model* = `<path file>` the model files describing the performances

*optionals keys*

*opt_step* = `<real> ` step length of the scan (Morgan)

*opt_ndmin* = `<real>` Minimal number of progeny by dam : offspring size above which the polygenic and QTL effects of the dam are estimated

*opt_mindamphaseproba* = `<real>` Minimal maternal phase probability : threshold above which the probable maternal phases will be considered in the analysis

*opt_minsirephaseproba* = `<real>` Minimal paternal phase probability : the analysis is interrupted if for a sire, none of its phases reach this threshold

*opt_chromosome* = `<string,string,...>` chromosomes to be analysed, as denoted in the marker map file

*opt_unknown_char* = `<string>` string code for missing value
main output file

out_output=<path file> : Full information about the results

output analysis files keys

out_summary=<path file> : Short information about the results
out_lrt_sires=<path file> : Sire family likelihood ratio test file
out_lrt_dams=<path file> : Dam family likelihood ratio test file
out_pateff=<path file> : Sire QTL effect estimations file under Hypothesis H1
out_mateff=<path file> : Dam QTL effect estimations file
out_phases=<path file> : Parental phases informations
out_freqall=<path file> : Alleles frequencies informations
out_grid2qtl=<path file> : Sire QTL effect estimations file under Hypothesis H2
out_pded=<path file> : Grand parental segment transmission marginal probabilities
out_pded_join=<path file> : Grand parental segment transmission joint probabilities
out_haplotypes=<path file> :
out_coeffda=<path file> :

input simulation file

in_paramsimul=<path file>

output simulation file

out_maxlrt=<path file>
6.3. Principes

Mixture of half-sib and full sib families

The maximul likelihood methods implemented in QTLMap considers the population as being a mixture of half sib and full sib families. The sires and the dams are supposed unrelated. A sire (resp. a dam) may be mated to more than one dam (resp. sire). Thus, two animals of the second generation may be unrelated, half sibs or full sibs. A polygenic and a QTL effect are estimated for each parent having a large enough family. To avoid numerical difficulties, these effects are not estimated for dams having too small offspring. In this case, the dam progeny are considered as sire half sibs only. A control of the structure is allowed through the option number of progeny opt_ndmin which is given in the parameter file.
You may overload the option `opt_ndmin` and consider all families as half-sib using the runtime option `--family=1`.

**Minimal paternal and maternal phases probability**

In the current release QTLMap considers only one phase for the sire. When the runtime option – `haplotype=1,2,3` is used, the probabilities of all possible sire and dam phases are computed. If none of those probabilities for the sire exceed a given threshold (`opt_minsirephaseproba` in the parameter file) the process is aborted.

As the dams generally have a lower offspring size, all phases the probability of which exceeds a given threshold (`opt_mindamphaseproba` in the parameter file) are considered in the analysis.

### 7. Analyses

#### 7.1. Available analysis

<table>
<thead>
<tr>
<th>Calcul</th>
<th>Description</th>
<th>QTL</th>
<th>Type data</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>LA for a single trait with pre-corrected data</td>
<td>1,2</td>
<td>Real</td>
</tr>
<tr>
<td>2</td>
<td>LA for a single data with a model description</td>
<td>1</td>
<td>Real,Discrete</td>
</tr>
<tr>
<td>3</td>
<td>LA for a single data with a model description (likelihood linearised - homoscedatic)</td>
<td>1,n</td>
<td>Real</td>
</tr>
<tr>
<td>4</td>
<td>LA for a single data with a model description (likelihood linearised - heteroscedastic)</td>
<td>1,n</td>
<td>Real</td>
</tr>
<tr>
<td>5</td>
<td>LA for a set of traits with a multivariate analysis (based on a multi-normal penetrance function)</td>
<td>1</td>
<td>Real</td>
</tr>
<tr>
<td>----</td>
<td>-------------------------------------------------------------------------------------------</td>
<td>---</td>
<td>------</td>
</tr>
<tr>
<td>6</td>
<td>LA for a set of traits (without missing data) with a discriminante analysis</td>
<td>1</td>
<td>Real</td>
</tr>
<tr>
<td>7</td>
<td>LA for a single survey trait with the cox model</td>
<td>1</td>
<td>Real with censored data</td>
</tr>
<tr>
<td>8</td>
<td>LD for a single data with a model description</td>
<td>1</td>
<td>Real</td>
</tr>
<tr>
<td>9</td>
<td>LDLA for a single data with a model description</td>
<td>1</td>
<td>Real</td>
</tr>
<tr>
<td>25</td>
<td>LD for a single data with a model description (likelihood linearised - homoscedastic)</td>
<td>1,n</td>
<td>Real</td>
</tr>
<tr>
<td>26</td>
<td>LD for a single data with a model description (likelihood linearised - heteroscedastic)</td>
<td>1,n</td>
<td>Real</td>
</tr>
<tr>
<td>27</td>
<td>LDLA for a single data with a model description (likelihood linearised - homoscedastic)</td>
<td>1,n</td>
<td>Real</td>
</tr>
<tr>
<td>28</td>
<td>LDLA for a single data with a model description (likelihood linearised - heteroscedastic)</td>
<td>1,n</td>
<td>Real</td>
</tr>
<tr>
<td>23</td>
<td>LA for a set of traits with a model description</td>
<td>1,n</td>
<td>Real</td>
</tr>
</tbody>
</table>

7.2. **Single real trait with pre corrected data**

A remplir

7.3. **Single real or discrete trait with a model description**

A remplir

7.4. **Single real trait with a model description and a complete linearised likelihood**

A remplir

7.5. **Set of real traits with a multivariate analysis (based on a multi-normal penetrance function)**

A remplir
7.6. Set of traits with a discrimante analysis

A remplir

7.7. Single survey trait with the cox model with a model description

A remplir

7.8. Runtime options

Analyse
The calcul runtime option allows the choice between different types of modelling.

1) Analysis of a single real trait with pre corrected data
   >>${QTLMAP_PATH}/qtlmap p_analyse --calcul=1
2) Analysis a single real or discrete trait with a model description
   >>${QTLMAP_PATH}/qtlmap p_analyse --calcul=2
3) Analysis a single real trait with a model description and a complete linearised likelihood (homoscedastic and heteroscedastic)
   >>${QTLMAP_PATH}/qtlmap p_analyse --calcul=3
   >>${QTLMAP_PATH}/qtlmap p_analyse --calcul=4
4) Analysis a set of real traits (without missing data) with a multivariate analysis (based on a multi-normal penetrance function)
   >>${QTLMAP_PATH}/qtlmap p_analyse --calcul=5
5) Analysis a set of traits (without missing data) with a discriminant analysis
   >>${QTLMAP_PATH}/qtlmap p_analyse --calcul=6
6) Analyse a single survey trait with the cox model
   >>${QTLMAP_PATH}/qtlmap p_analyse --calcul=7
7) Analyse a single survey trait with the LD
   >>${QTLMAP_PATH}/qtlmap p_analyse --calcul=8
8) Analyse a single survey trait with the LDLA
   >>${QTLMAP_PATH}/qtlmap p_analyse --calcul=9
9) Analysis a single real trait with a model description and a complete linearised likelihood (homoscedastic and heteroscedastic) with the LD
   >>${QTLMAP_PATH}/qtlmap p_analyse --calcul=25
   >>${QTLMAP_PATH}/qtlmap p_analyse --calcul=26
10) Analysis a single real trait with a model description and a complete linearised likelihood (homoscedastic and heteroscedastic) with the LDLA
Haplotype

Changing the calculus of the parental phases and for all progeny, the grand parental segment transmission adapted for SNP.

```bash
> ${QTLMAP_PATH}/qtlmap p_analyse –calcul=1 –snp
```

<table>
<thead>
<tr>
<th><strong>--haplotype</strong></th>
<th><strong>Description</strong></th>
</tr>
</thead>
</table>
| 1 | “Classical” approach by enumeration  
All possible phases are considered in turn and their probability computed  
Transmission probabilities are computed using all available information  
Recommended for small number of markers |
| 2 | Optimised approach for sparse maps  
All possible phases are considered in turn and their probability computed  
Transmission probabilities are computed using local information |
| 3 | Approximate phasing based on closest marker information  
Exact transmission probability minimising the computation  
Recommended for dense maps |
| 4 | |

Optimisation

The `--optim` runtime option allows a control of the optimisation procedure. The following table describes the available methods.

<table>
<thead>
<tr>
<th><strong>--optim</strong></th>
<th><strong>Description</strong></th>
<th><strong>DEPENDANCES</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>E04JYF NAG routine - quasi-Newton</td>
<td>NAGG</td>
</tr>
<tr>
<td>2</td>
<td>L-BFGS routine - the Broyden-Fletcher-Goldfarb-Shanno quasi-Newton</td>
<td>no</td>
</tr>
<tr>
<td>5,...,11</td>
<td>LUKSAN optimisation</td>
<td>no</td>
</tr>
</tbody>
</table>
methods may be parametrized with the following options:

- \texttt{opt_optim_maxeval} : maximum number of objective function
- \texttt{opt_optim_maxtime} : maximum time to find the solution of the objective function
- \texttt{opt_optim_tolx} : tolerance lower bound of a step
- \texttt{opt_optim_tolf} : stopping criteria lower bound of the objective function
- \texttt{opt_optim_tolg} : stopping criteria lower bound of the gradient
- \texttt{opt_optim_h_precision} : precision to obtain the gradient


\textbf{Console output mode}

- To get the maximum information during the process, add \texttt{--v} (or \--verbose) to the command
  \begin{verbatim}
  >${QTLMAP_PATH}/qtlmap p_analyse --calcul=1 -v
  \end{verbatim}
- When debugging the software, add \texttt{--d} (or \--debug) to the command
  \begin{verbatim}
  >${QTLMAP_PATH}/qtlmap p_analyse --calcul=1 -d
  \end{verbatim}
- To avoid output, add \texttt{--q} (or \--quiet) to the command
  \begin{verbatim}
  >${QTLMAP_PATH}/qtlmap p_analyse --calcul=1 -q
  \end{verbatim}

\textbf{Report output mode}

When performing eQTL analysis (using \texttt{--data-transcriptomic} command) or simulation the output is minimised. To force the classical reporting format, use the runtime option \texttt{--print-all}.

Example:

\begin{verbatim}
 >${QTLMAP_PATH}/qtlmap p_analyse --calcul=1 --data-transcriptomic --print-all
\end{verbatim}

\textbf{Number of qtl detection available}

For most of the analyses (controlled by the runtime option \texttt{--calcul}), only 1 QTL is considered in the model. However, this number may be increased to 2 if \texttt{calcul=1} to 2 or more if \texttt{calcul = 3} or 4. The number of QTL is given by the \texttt{--qtl} runtime option.

<table>
<thead>
<tr>
<th>Analysis --calcul</th>
<th>QTL test detection --qtl</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1,2</td>
</tr>
<tr>
<td>2,7,8,9,10</td>
<td>1</td>
</tr>
<tr>
<td>3,4,25,26,27,28</td>
<td>&gt;=1</td>
</tr>
<tr>
<td>5,6</td>
<td>1</td>
</tr>
</tbody>
</table>

QTLMap 0.7
Example:

>`${QTLMAP_PATH}/qtlmap p_analyse --calcul=1 --qtl=1`

**EQTL analysis**

When looking for eQTL the number of traits to be analysed becomes very large. In this case, specific routines are needed, and ad hoc output are produced. To get this situation, the runtime option data-transcriptomic must be indicated

>`${QTLMAP_PATH}/qtlmap p_analyse --calcul=1 --qtl=1 --data-transcriptomic`

8. Estimation of the test statistic rejection thresholds

8.1. **Estimation of the test statistic rejection thresholds with missing data**

A specific file, `opt_paramsimul (param_sim)` must be provided by the user. This file contains the needed information about the simulation:

- QTLs informations
- Number of QTLs (N)
- N QTL positions in Morgan
- N chromosomes where are localised QTLs
➢ N QTL allele frequencies in the grand sire population

➢ Traits informations
  ➢ Number of traits (M)
  ➢ List of traits (M lines) corresponding to the model file
  ➢ N QTLs effects for each M traits

If the simulations are made under the null hypothesis (No QTL on the linkage group) the user has only to give the second part (Trait) of the simulation parameter file.

In the case of simulations made under the hypothesis of N QTL, N≠0, (this case occurs when the aim is to get rejection thresholds for the test of H1 “only 1 QTL” vs. H2 “2 QTLs” segregating), the QTL is supposed to be biallelic Q1,Q2 and the genotypes frequencies in the parental population are Q1Q1 : f1.(1-f1), Q1Q2 : f1.f1+(1-f1).(1-f1), Q2Q2 : (1-f1).f1, where f1 is the frequency of the first allele if the grand sire population, the second allele in the grand dam population. To get for instance all parents heterozygous, the frequency f1 must be given the value 1. or 0.

**Format of the simulation parameter file**

```
QTL
<integer>
```

The specific “QTL” Label on the first line, followed by and the number of QTLs to be simulated.

```
Position  <real> <real> ...
chromosome <integer> <integer> ...
frequency  <real> <real> ...
```

The user defined for each QTL:
- its position
- the chromosome where it is located
- the frequency in grand sire population P1

```
TRAITS
<integer>
```

The specific TRAITS Label on a first line, then the number of traits to be simulated.

```
<IDNAME>
```

For continuously distributed traits: the name of one of the traits as referenced in the model file.

```
<IDNAME_DISCR_DATA> <int> <real> <real>
```

For discrete traits: the name of one of the discrete traits as referenced in the model file, with:
➢ its heritability
➢ the number of modalities
➢ the frequency of each modality

```
qtleffect <real> <real>...
```

Only if one or more QTL is defined:
➢ QTL 1 Effect on trait 1, QTL 1 Effect on trait 2,...,QTL 2 Effect on trait 1,QTL 2 Effect on trait 2,...

On the whole, the `opt_paramsimul` is the following:

The entirely format:

```
QTL
<integer>
Position <real> <real> ...
chromosome <integer> <integer> ...
frequency <real> <real> ...

TRAITS
<integer>
<IDNAME> | <IDNAME_DISCR_DATA> <int> <real> <real>
( qtleffect <real> <real>...) 0/1 (*)
```

(*) : The qtleffect line is defined if at least one QTL are simulated.

Example of a parameter file for the estimation of the rejection thresholds for the test « There are one qtl on the linkage group» against « there are no QTL »

```
TRAITS
2
imf
bardiere

Texte 11: Parameter simulation file
```

```
2
0 0
nofix nocov
imf r 0 0 0
bardiere r 0 0 0

Texte 12: Model file
```

Example of a parameter file for the estimation of the rejection thresholds for the test « There are two qtl on the linkage group» against « there are one QTL at the position 0.6 Morgan on the first chromosome on the linkage group»
In this example, the QTL simulated have an effect 0.4 on the first trait and 0.5 on the second traits. The QTL have a frequency of 100%...

```
QTL
1
position 0.6
chromosome 1
frequency 1.0

TRAITS
2
imf
bardiere
qtleffect 0.4 0.5
```

Texte 13: Parameter simulation file

**Addition keys in the parameter file**

The parameters simulation file is given in the parameter analyse file with the key `in_paramsimul`.

A second key (optional) `out_maxlrt` specifies the name of a file reporting the maximum likelihood ratio test values found in the simulations.
# qtlmap --help-panalyse : for more information

##### USER FILES

in_map=carte
in_genealogy=genea
in_genotype=typage
in_traits=perf
in_model=model
in_paramsimul=param_sim_simul

##### ANALYSIS PARAMETERS

# analysis step : in Morgan
# minimum : 0.000001
opt_step = 0.1
# minimal number of progeny by dams
opt_ndmin=20
#Minimal paternal phase probability
opt_minsirephaseproba=0.80
# overload :
opt_minsirephaseproba=0.90
#Minimal maternal phase probability
opt_mindamphaseproba=0.10
# chromosome to analyse
opt_chromosome=7
# for several chromosomes
#opt_chromosome=7,8,Y
# missing phenotype marker value
opt_unknown_char=0

##### OUTPUT

out_output=./OUTPUT/result
out_summary=./OUTPUT/summary
out_maxlrt=./OUTPUTSIM/simul

Texte 14: Example of a parameter file to estimate the rejections thresholds with missing data
8.2. Permutations

The rejection thresholds may be obtained with permutations on performances. This option is available with the runtime option --permute

> ${QTLMAP_PATH}/qtlmap p_analyse --calcul=1 --nsim=100 --permute

Information about the permutation process

The permutation option concerns the phenotypes and all nuisances effects attached to the phenotypes.

The performances are permuted within the full sib family. However, if the number of progeny for a dam is less than the minimum between opt_ndmin key value (building full sib family) and 10 (this figure was chosen by the developers of QTLMap and will be controlled by advanced users soon), the permutation is realized within half sib family.

In multi-trait analysis (multi-variate or discriminant), only phenotyped animals are permuted.

In successive uni-trait analysis, animal without any phenotype are not included in the permutation.

8.3. Estimate of the test statistic rejection thresholds without missing data
The user have the possibility to estimate thresholds rejections for dummy traits, assuming there is no missing data. In this case, the parameter file does not need the keys `in_model` nor `in_trait`.

The parameter simulation file will have a specific head section for simulation trait: `SIMULTRAITS`.

This section is identical to the TRAIT section but an additional information about the nature of the trait as described for the model file. This information is given next the IDNAME of trait:

- `r` for real data
- `i` for integer (ordered discrete data)

```plaintext
QTL
<integer>
Position <real> <real> ...
chromosome <integer> <integer> ...
frequency <real> <real> ...

SIMULTRAITS
<integer>
<IDNAME> r <real> | <IDNAME_DISCR_DATA> i <real> <int> <real> <real>
{ correlation [ [ a ] [ b c] [ d e f] ... ] } 0/1 (*)
{ qtleffect <real> <real>...} 0/1 (**)```
#qtlmap --help-panalyse : for more information

##### USER FILES
in_map=carte
in_genealogy=genea
in_genotype=typage
in_paramsimul=param_sim_simul

##### ANALYSIS PARAMETERS
# analysis step : in Morgan
#minimum : 0.000001
opt_step = 0.1
# minimal number of progeny by dams
opt_ndmin=20
#Minimal paternal phase probability
opt_minsirephaseproba=0.80
# overload :
opt_minsirephaseproba=0.90
#Minimal maternal phase probability
opt_mindamphaseproba=0.10
# chromosome to analyse
opt_chromosome=7
#for several chromosomes
#opt_chromosome=7,8,Y
#missing phenotype marker value
opt_unknown_char=0

##### OUTPUT
out_output=./OUTPUT/result
out_summary=./OUTPUT/summary
out_maxlrt=./OUTPUTSIM/simul

Texte 15: Example of a parameter file to estimate the rejections thresholds without missing data
9. Simulate and design a new protocol

QTLMap offers you the possibility of simulating all the data (markers, genealogy, traits) in order to plan a new experiment. You will get in the output file (named by the out_maxlr= ./OUTPUTSIM/simul option in the following example) the value of the LRT resulting from the simulation, allowing an estimation of designs power.

To perform those simulations, two specific section must be created in the param_sim file:
The first, with the头section MARKERS, must give on a single line
Marker density (M), number alleles/marker, map size (Morgan)

The second, with the head section GENEALOGY, followed by the key word F2, BC or OUT-BRED depending on the type of population, and a line giving the number of sires, of dam/sire and of progeny / dam

QTLMap 0.7

28/44
in_paramsimul=param_sim_optim

##### ANALYSIS PARAMETERS
# analysis step : in Morgan
#minimum : 0.000001
opt_step = 0.1
# minimal number of progeny by dams
opt_ndmin=20
# chromosome to analyse
opt_chromosome=7

##### OUTPUT
out_output=./OUTPUT/result
out_summary=./OUTPUT/summary
out_maxlrt=./OUTPUTSIM/simul

Texte 16: Example of a parameter file to design a new protocol
10. **Output files**

A set of files is proposed to the user as the result of an analysis or a simulation:

- The main output (analyse report, simulation report)
- A summary

Additional files (optional) in analysis case:

- Likelihood ratio test profile (per Sire, per Dam, global)
- QTL effect estimation at each tested position (Sire and dam)
- Parental phases report
- Alleles frequencies informations
- Haplotypes assigned from parents
- Grand parental segment transmission marginal probabilities
- Grand parental segment transmission joint probabilities

Specifics files:

- Coefficients of the discriminant analysis among the linkage group

Additional file (optional) in a simulation/permutation case:

- Maximum likelihood Ratio Test and optimal positions reached for each simulations/permutations

10.1. **Analysis report**

The **first part** describes the data as given by the user

The name of the corresponding file is given by the user with the key *out_output* in the parameter file

**Configuration defined by the user**

The list of option keys used by the application (runtime environment) is given (All keys are described at the end of this document).

**Description of the genealogy**

Number of parents, grand-parents and progenies

**Description of the markers**

Number of animal genotyped

Number and names of the genetic markers, of alleles by marker and allele frequencies
Warning about the equilibrium of marker transmission within each family

**Description of the traits**

Names of the quantitative traits, for each trait :

- number of animals measured
- number of animals measured for both performance traits and marker genotypes
- mean, variance, minimum and maximum
- Names of fixed effect, if any, with the list of levels
- Names of the covariates, if any, with their mean, variance, minimum and maximum

The **second part** describes the result of the phase building

**Parental phases**

A part of the most probable phases of the reproducers, built from available marker and pedigree information, are listed. The full information is found in the specific file.

A control is given to the user with the keys

*opt_minsirephaseproba* and *opt_mindamphaseproba* (Minimal sire and dam phase probability)

In the **third part**, results of the genome scan are given for each traits. Details depends on tests and models.

**Genome scan**
<table>
<thead>
<tr>
<th>Section</th>
<th>calcul</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Possible confusions between QTL and other effects</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Residual variances and estimation of the main effects (polygenic,QTL)</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>LRT for the nuisance effects</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risk Factor estimation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Precision of the parameter estimation</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General Mean estimation</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nuisances effects estimations</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td></td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interactions between QTL and fixed effects</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Traits residual correlations</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>x</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Tableau 1: Output availables according to the analysis**

**Confusion between QTL effects and all other effects**

As the design may be poorly balanced, leading to strong colinearity between QTL and some other effects in the model, a warning is provided if this situation occurs. The confusion is measured by the correlation between the columns of the incidence matrix in an equivalent fully linear model at the starting position of the scan (a warning is edited if this correlation exceeds `opt_eps_confusion`).

A second test of confusion between the QTL and other estimable effects finally kept in the model is edited.

**Variances and estimation of main effects**

Within sire residual variance estimations are printed under all tested hypotheses (no QTL, one QTL, two QTL,...). The maximum likelihood solutions for the parameters are given, with an indication about their precision (available only for `calcul =2, 3, 4`), estimated by the diagonal element of the incidence matrix in an equivalent fully linear model: the lower the better:

- `global mean`
- `sire QTL effects`
• dam QTL effects
• sire polygenic effects
• dam polygenic effects
• covariables
• fixed effects

The two following example give difference report according to the calcul option.

Estimation of parameters under H0

Within sire standard deviation
** Trait bardiere **
sire 910001 s.d. : 0.551
sire 910045 s.d. : 0.578
sire 910081 s.d. : 0.659
sire 910088 s.d. : 0.663

<table>
<thead>
<tr>
<th>parameter</th>
<th>estimable ?</th>
<th>value</th>
<th>precision</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Sire</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sire 910001</td>
<td>yes</td>
<td>6.902</td>
<td>0.000</td>
</tr>
<tr>
<td>Sire 910045</td>
<td>yes</td>
<td>7.091</td>
<td>0.000</td>
</tr>
<tr>
<td>Sire 910081</td>
<td>yes</td>
<td>7.220</td>
<td>0.000</td>
</tr>
<tr>
<td>Sire 910088</td>
<td>yes</td>
<td>7.441</td>
<td>0.000</td>
</tr>
<tr>
<td>Mean dam</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dam 910014 [Sire 910001]</td>
<td>yes</td>
<td>0.040</td>
<td>0.000</td>
</tr>
<tr>
<td>Dam 910002 [Sire 910081]</td>
<td>yes</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>Dam 910010 [Sire 910081]</td>
<td>yes</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>Dam 910074 [Sire 910088]</td>
<td>yes</td>
<td>0.000</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Texte 17: Estimation of variances and polygenic effect under hypothesis null with the calcul=1

Note that with calcul=1, the precision is not computed and is arbitrary given the vaue 0.0
**Estimation of parameters under H0**

Within sire standard deviation

- Trait bardiere:
  - Sire 910001: s.d. = 0.550
  - Sire 910045: s.d. = 0.579
  - Sire 910081: s.d. = 0.658
  - Sire 910088: s.d. = 0.654

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimable?</th>
<th>Value</th>
<th>Precision</th>
</tr>
</thead>
<tbody>
<tr>
<td>General Mean</td>
<td>yes</td>
<td>7.539</td>
<td>0.033</td>
</tr>
<tr>
<td>Sire polygenic effects</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sire 910001</td>
<td>yes</td>
<td>-0.666</td>
<td>0.067</td>
</tr>
<tr>
<td>Sire 910045</td>
<td>yes</td>
<td>-0.448</td>
<td>0.058</td>
</tr>
<tr>
<td>Sire 910081</td>
<td>yes</td>
<td>-0.264</td>
<td>0.065</td>
</tr>
<tr>
<td>Sire 910088</td>
<td>no</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dam polygenic effects</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dam 910014 [Sire 910001]</td>
<td>yes</td>
<td>0.061</td>
<td>0.069</td>
</tr>
<tr>
<td>Dam 910002 [Sire 910001]</td>
<td>yes</td>
<td>-0.052</td>
<td>0.073</td>
</tr>
<tr>
<td>Dam 910010 [Sire 910081]</td>
<td>yes</td>
<td>-0.129</td>
<td>0.068</td>
</tr>
<tr>
<td>Dam 910074 [Sire 910088]</td>
<td>yes</td>
<td>-0.221</td>
<td>0.075</td>
</tr>
</tbody>
</table>

NOTE: known allelic origin means QTL effect = maternal - paternal allele effects

---

**Interactions between QTL and fixed effects**

When interactions between the QTL and m fixed effects are considered in the model, the dam and sire qtl effects are estimated for each level of the composite interacting fixed effect (if n₁, n₂...nᵰ are the number of levels for effect 1, 2,...m, a total of n₁n₂...nᵰ qtl effects are estimated for each parents).

**Testing nuisances effects**

For each of the nuisance effect, a LRT is reported with the value and significance of the likelihood ratio when comparing a model with or without this effect. The significance is the probability for the LRT to be higher than the observed value under H₀ (no effect). When this probability exceeds the standard threshold corresponding to the 5, 1 or 0.1 Pent level, the effect should be removed from the model.

<table>
<thead>
<tr>
<th>Tested effect</th>
<th>df.</th>
<th>Likelihood ratio</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>f₁ (direct effect)</td>
<td>23</td>
<td>100.823</td>
<td>1.000</td>
</tr>
<tr>
<td>f₂ (direct effect)</td>
<td>10</td>
<td>121.576</td>
<td>1.000</td>
</tr>
<tr>
<td>sex (direct effect)</td>
<td>2</td>
<td>11.146</td>
<td>1.000</td>
</tr>
</tbody>
</table>

---

**Risks factor estimation**

QTLMap 0.7
 Traits residual correlations

10.2. **EQTL analysis report**

A special format presents the report analysis for each gene expression (depends the dynamic flag `{--data-transcriptomic}`). Only calculus 1,2,3,4 manage this format (single trait analysis).

For each hypothesis, the report gives:

- The header of the following array
- Array with:
  - first column: gene name
  - others column: estimation of each parameters given in the header

note:
The values 0.0 means that the parameter is not estimable.

<table>
<thead>
<tr>
<th>Hypothesis :0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Given parameters are respectively:</td>
</tr>
<tr>
<td>Gene position on the array, [ *std dev *1940][General Mean][Sire polygenic effects]</td>
</tr>
<tr>
<td>note : 0.0 mean not estimable</td>
</tr>
<tr>
<td>1 0.132 -0.106 0.000</td>
</tr>
<tr>
<td>2 0.116 -0.114 0.000</td>
</tr>
<tr>
<td>3 0.165 -0.148 0.000</td>
</tr>
<tr>
<td>4 0.097 0.174 0.000</td>
</tr>
<tr>
<td>5 0.135 -0.147 0.000</td>
</tr>
<tr>
<td>6 0.259 -0.059 0.000</td>
</tr>
</tbody>
</table>

*Texte 20: EQTL report under hypothesis 0*

<table>
<thead>
<tr>
<th>Hypothesis :1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Given parameters are respectively:</td>
</tr>
<tr>
<td>Gene position on the array, Chromosome 1, QTL Position 1,H0/H1,[ *std dev *1940][General Mean][Sire QTL effects [1]][Sire polygenic effects]</td>
</tr>
<tr>
<td>note : 0.0 mean not estimable</td>
</tr>
<tr>
<td>1 1.080 0.930 2.281 0.128 -0.106 0.033 0.000</td>
</tr>
<tr>
<td>2 1.000 0.830 6.953 0.115 -0.114 -0.017 0.000</td>
</tr>
<tr>
<td>3 1.080 1.430 4.946 0.157 -0.139 -0.055 0.000</td>
</tr>
<tr>
<td>4 1.000 1.430 2.248 0.095 0.174 -0.023 0.000</td>
</tr>
<tr>
<td>5 1.080 1.230 8.247 0.134 -0.147 -0.010 0.000</td>
</tr>
<tr>
<td>6 1.080 1.430 2.087 0.254 -0.057 -0.059 0.000</td>
</tr>
</tbody>
</table>

*Texte 21: EQTL report under hypothesis 1*
Hypothesis 2
Given parameters are respectively:
Gene position on the array, Chromosome 1, QTL Position 1, Chromosome 2, QTL Position 2, H0/H2, H1/H2, [ *std dev *1940][General Mean][Sire QTL effects [1]][Sire QTL effects [2]][Sire polygenic effects]

note : 0.0 mean not estimable

<table>
<thead>
<tr>
<th></th>
<th>1.000</th>
<th>1.130</th>
<th>1.000</th>
<th>1.430</th>
<th>4.933</th>
<th>2.632</th>
<th>0.125</th>
<th>-0.105</th>
<th>0.004</th>
<th>-0.071</th>
<th>0.000</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2.000</td>
<td>1.530</td>
<td>1.000</td>
<td>1.730</td>
<td>1.104</td>
<td>0.451</td>
<td>0.114</td>
<td>-0.113</td>
<td>-0.038</td>
<td>0.026</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td>3.000</td>
<td>0.930</td>
<td>1.000</td>
<td>1.830</td>
<td>0.842</td>
<td>5.396</td>
<td>0.148</td>
<td>-0.142</td>
<td>0.371</td>
<td>-0.365</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td>4.000</td>
<td>1.030</td>
<td>1.000</td>
<td>1.330</td>
<td>2.963</td>
<td>0.715</td>
<td>0.094</td>
<td>0.174</td>
<td>0.019</td>
<td>-0.017</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td>5.000</td>
<td>1.530</td>
<td>1.000</td>
<td>1.730</td>
<td>1.095</td>
<td>0.848</td>
<td>0.133</td>
<td>-0.146</td>
<td>-0.032</td>
<td>0.034</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td>6.000</td>
<td>0.830</td>
<td>1.000</td>
<td>1.530</td>
<td>2.245</td>
<td>0.237</td>
<td>0.253</td>
<td>-0.057</td>
<td>-0.029</td>
<td>-0.045</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Texte 22: EQTL report under hypothesis 2

10.3. Analyse summary

In the file SUMMARY (parameter file key out_summary), several chapters are given summarising the analysis under all hypothesis.
For each hypothesis (H0 : 0 qtl, H1 : 1 qtl, H2 : 2qtl, ...)
for each analysed variable (by lines)
  - Number of genotyped progeny with phenotypes for the trait
  - Maximum likelihood ratio
  - QTL most likely positions
  - for each sire
    - Estimations of the QTL effect
    - Within sire family standard deviation
    - Significance of the QTL effect (based on a Student test). ‘sign’ = significant; ‘ns’= not significant; ‘na’=not available.

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>Max Lik</th>
<th>Pos (M)</th>
<th>Sire</th>
<th>910001</th>
<th>910045</th>
<th>910081</th>
<th>910088</th>
</tr>
</thead>
<tbody>
<tr>
<td>bardiere</td>
<td>236</td>
<td>45.2</td>
<td>1</td>
<td>0.7</td>
<td>-0.089</td>
<td>0.511</td>
<td>sign</td>
<td>-0.118</td>
</tr>
<tr>
<td>imf</td>
<td>236</td>
<td>43.7</td>
<td>1</td>
<td>0.7</td>
<td>0.156</td>
<td>0.338</td>
<td>sign</td>
<td>0.187</td>
</tr>
<tr>
<td>bardiere</td>
<td>236</td>
<td>45.2</td>
<td>1</td>
<td>0.7</td>
<td>-0.089</td>
<td>0.511</td>
<td>sign</td>
<td>-0.118</td>
</tr>
<tr>
<td>imf</td>
<td>236</td>
<td>43.7</td>
<td>1</td>
<td>0.7</td>
<td>0.156</td>
<td>0.338</td>
<td>sign</td>
<td>0.187</td>
</tr>
</tbody>
</table>

Texte 23: Summary with --qtl=3 option
10.4. **The family likelihood**

The user have to define the following key to obtains the likelihood ratio test among the linkage group under hypothesis one: `out_lrsires`, `out_lrdam`, and/or the grid of the likelihood ratio test under hypothesis two: `out_grid2qtl`.

**LRT Sires files**

For each tested position, the file contains:
Chromosome, Position, global LRT, Sire 1 LRT, Sire 2 LRT …

<table>
<thead>
<tr>
<th>Chr</th>
<th>Pos</th>
<th>GlobalLRT</th>
<th>910001</th>
<th>910045</th>
<th>910081</th>
<th>910088</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.010</td>
<td>8.63</td>
<td>4.93</td>
<td>0.91</td>
<td>2.47</td>
<td>0.33</td>
</tr>
<tr>
<td>1</td>
<td>0.020</td>
<td>8.62</td>
<td>4.82</td>
<td>1.03</td>
<td>2.47</td>
<td>0.30</td>
</tr>
<tr>
<td>1</td>
<td>0.030</td>
<td>8.56</td>
<td>4.66</td>
<td>1.14</td>
<td>2.45</td>
<td>0.31</td>
</tr>
<tr>
<td>1</td>
<td>0.040</td>
<td>8.47</td>
<td>4.47</td>
<td>1.23</td>
<td>2.41</td>
<td>0.35</td>
</tr>
<tr>
<td>1</td>
<td>0.050</td>
<td>8.29</td>
<td>4.24</td>
<td>1.28</td>
<td>2.34</td>
<td>0.42</td>
</tr>
<tr>
<td>1</td>
<td>0.060</td>
<td>8.35</td>
<td>4.21</td>
<td>1.35</td>
<td>2.31</td>
<td>0.48</td>
</tr>
</tbody>
</table>

**Text 24: Sire likelihood file**

**LRT Dams file**

For each tested position, the file contains:
Chromosome, Position, Dam 1 LRT, Dam 2 LRT …
Note: when the offspring size of a dam is below the threshold for the search of the phase, the LRT is fixed at 0.000 (see `opt_ndmin` option).

**LRT grid 2 QTL**

The file presents two tables:

The first part of the output concerns the comparison between the 1 and 2 QTL hypotheses
The fist line gives possible 1\(^{st}\) QTL position
The following lines give a possible 2\(^{nd}\) QTL position, followed by the LRT (1 vs. 2 QTL) for each couple of positions

The second part of the output concerns the comparison between the 0 and 2 QTL hypotheses
The fist line gives possible 1\(^{st}\) QTL position
The following lines give a possible 2\(^{nd}\) QTL position, followed by the LRT (0 vs. 2 QTL) for each couple of positions
10.5. **QTL effects estimations files**

The user has to define the following key to obtain the QTL estimations among the linkage group under hypothesis one: `out_pateff`, `out_matteff`.

**QTL Paternal effects**

For each tested position, the file contains:
- Chromosome, Position, Sire 1 QTL effect estimation, Sire 2 QTL effect estimation …

**QTL Maternal effect**

For each position, the file contains:
- Chromosome, Position, Dam 1 QTL effect estimation, Dam 2 QTL effect estimation …

Note: the QTL effect are given only for dams the offspring size of which is over the threshold given by `opt_ndmin`
10.6. Parents phase report

10.7. Haplotypes assigned from parents

Two lines are edited for each progeny.

- The first contains:
  - Progeny ID followed by an “s” indicator (for sire origin)
  - The list of marker alleles transmitted by the sire to the progeny
  - “origin” as a separator
  - The list of sire grand parental origin of the haplotypes transmitted by the sire: 1 for grand sire, 2 for grand dam and “un” for unknown, assuming the most probable sire phase

- The second contains:
  - Progeny ID followed by an “d” indicator
  - The list of marker alleles transmitted by the dam to the progeny
  - “origin” as a separator
  - The list of dam grand parental origin of the haplotypes transmitted by the dam: 1 for grand sire, 2 for grand dam and “un” for unknown, assuming the most probable dam phase

```
91104  s  1   9   3   2   1   3   6   1   .... origin :  2   2    2   2   2   2     1   1  un
91104  d  2   9   ........1   3   ....3   .... origin :  1   1   un  un   2   2    un   1  un
91105  s  2   5   11  6   3   2   6   1   19   origin :  1   1    1   1   1   1     1   1   2
91105  d  6   9   ........2   5   ....2   19   origin :  2   1   un  un   1   1    un  2   1
```

Texte 27: haplotypes file

10.8. Grand parental segment transmission marginal probabilities

Each line gives for a tested QTL position x

- The sire ID
- The dam ID
- The dam phase number in the order of the main results file
- The progeny ID
- The probability that the progeny inherited the 2nd sire allele (in the order of the main result file) at position x given the dam phase
- The probability that the progeny inherited the 2nd dam allele (in the order of the main result file) at position x given the dam phase
### 10.9. Grand parental segment transmission joint probabilities

Each line gives for a tested QTL position x

- Position
- Sire ID
- Dam ID
- Dam phase number in the order of the main results file
- Progeny ID
- Probability that the progeny inherited the 1<sup>st</sup> sire and 1<sup>st</sup> dam alleles (in the order of the main result file) at position x given the dam phase
- The probability that the progeny inherited the 1<sup>st</sup> sire and 2<sup>nd</sup> dam alleles (in the order of the main result file) at position x given the dam phase
- Probability that the progeny inherited the 2<sup>nd</sup> sire and 1<sup>st</sup> dam alleles (in the order of the main result file) at position x given the dam phase
- Probability that the progeny inherited the 2<sup>nd</sup> sire and 2<sup>nd</sup> dam alleles (in the order of the main result file) at position x given the dam phase

---

**Texte 28: Grand parental segment transmission marginal probabilities file**

**Position** | **Sire** | **Dam** | **Dam Phase** | **Animal** | **p(2nd sire allele)** | **p(2nd dam allele)**
--- | --- | --- | --- | --- | --- | ---
1. | 910001 | 910014 | 1 | 944217 | 1.000 | 0.000
2. | 910001 | 910014 | 1 | 944217 | 0.999 | 0.001
3. | 910001 | 910014 | 1 | 944217 | 0.999 | 0.001
4. | 910001 | 910014 | 1 | 944217 | 0.999 | 0.001
5. | 910001 | 910014 | 1 | 944217 | 0.999 | 0.001
...

---

**Texte 29: Grand parental segment transmission marginal probabilities file**

**Position** | **Sire** | **Dam** | **Dam Phase** | **Animal** | **p(Hs1/Hd1)** | **p(Hs1/Hd2)** | **p(Hs2/Hd1)** | **p(Hs2/Hd2)**
--- | --- | --- | --- | --- | --- | --- | --- | ---
1. | 910001 | 910014 | 1 | 944217 | 0.000 | 0.000 | 1.000 | 0.000
2. | 910001 | 910014 | 1 | 944217 | 0.001 | 0.000 | 0.999 | 0.001
3. | 910001 | 910014 | 1 | 944217 | 0.001 | 0.000 | 0.999 | 0.001
4. | 910001 | 910014 | 1 | 944217 | 0.001 | 0.001 | 0.998 | 0.001
5. | 910001 | 910014 | 1 | 944217 | 0.000 | 0.001 | 0.999 | 0.000
6. | 910001 | 910014 | 1 | 944217 | 0.001 | 0.001 | 0.999 | 0.001
7. | 910001 | 910014 | 1 | 944217 | 0.003 | 0.001 | 0.884 | 0.112
...

---

QTLMap 0.7
10.10. Simulation report

Test statistic distribution:
Number of simulations: 100
Mean: 14.24685
Standard deviation: 4.07168
Skewness: 0.70693
Kurtosis: 1.05302
Minimum: 6.62047
Maximum: 28.64581

<table>
<thead>
<tr>
<th>chromosome</th>
<th>genome</th>
<th>Threshold</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1000</td>
<td></td>
<td>19.39</td>
</tr>
<tr>
<td>0.0500</td>
<td></td>
<td>21.39</td>
</tr>
<tr>
<td>0.0100</td>
<td>chrom_level</td>
<td>27.40</td>
</tr>
<tr>
<td>0.0050</td>
<td>*</td>
<td>28.18</td>
</tr>
<tr>
<td>0.0027</td>
<td>nb_chrom</td>
<td>28.44</td>
</tr>
<tr>
<td>0.0010</td>
<td></td>
<td>28.58</td>
</tr>
<tr>
<td>0.0005</td>
<td></td>
<td>28.61</td>
</tr>
<tr>
<td>0.0001</td>
<td></td>
<td>28.64</td>
</tr>
</tbody>
</table>

For each analysed variable, a single line gives the empirical thresholds at 5, 1 and 0.1 % at the chromosome and the genome level. The genome level corresponds to a genome scan of 18 autosomes in pigs. For any other species, the genome level is obtained easily multiplying the chromosome level by the number of chromosomes. In such cases, see the RESULT file for low chromosome wide quantile estimations.

10.11. Report simulations result

This file gives the maximum LRT reached with its associated position (and the linkage group) under the N hypothesis for each simulation/permutation.

For each analysed variable:
- a header to explain the following line to the user
- for each simulation:
  - The Maximum likelihood ratio test
  - Position and linkage group of the first QTL
  - Position and linkage group of the second QTL
  - ...

# Trait [traitsimul1] LRTMAX H0/H1 , Position CHR, Position DX
12.7928 1 0.4100
18.5180 1 0.1100
17.0331 1 1.2100

# Trait [traitsimul2] LRTMAX H0/H1 , Position CHR, Position DX
8.9628 1 0.7100
9.3228 1 1.0000
16.6090 1 0.7100

Texte 30: The simulation report file H1
# Trait \[traitsimul1\] LRTMAX H0/H1 , Position CHR, Position DX LRTMAX H1/H2 , Position1 CHR, Position1 DX

Position2 CHR, Position1 DX2

<table>
<thead>
<tr>
<th></th>
<th>Value 1</th>
<th>Value 2</th>
<th>Value 3</th>
<th>Value 4</th>
<th>Value 5</th>
<th>Value 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.7928</td>
<td>0.4100</td>
<td>9.6459</td>
<td>0.4100</td>
<td>1.2100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18.5180</td>
<td>0.1100</td>
<td>14.2922</td>
<td>0.1100</td>
<td>1.0100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>17.0331</td>
<td>1.2100</td>
<td>15.4039</td>
<td>0.3100</td>
<td>1.2100</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

# Trait \[traitsimul2\] LRTMAX H0/H1 , Position CHR, Position DX LRTMAX H1/H2 , Position1 CHR, Position1 DX

Position2 CHR, Position1 DX2

<table>
<thead>
<tr>
<th></th>
<th>Value 1</th>
<th>Value 2</th>
<th>Value 3</th>
<th>Value 4</th>
<th>Value 5</th>
<th>Value 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.9628</td>
<td>0.7100</td>
<td>12.8711</td>
<td>1.5100</td>
<td>1.6100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9.3228</td>
<td>1.0000</td>
<td>8.4281</td>
<td>0.0100</td>
<td>0.3100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>16.6090</td>
<td>0.7100</td>
<td>9.5829</td>
<td>0.3100</td>
<td>0.4100</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Reference**


**Appendix**

**12.1.Parameter file Option Keys**

<table>
<thead>
<tr>
<th>Key</th>
<th>Description</th>
<th>Default</th>
</tr>
</thead>
<tbody>
<tr>
<td><code>in_map</code></td>
<td>Input map file</td>
<td></td>
</tr>
<tr>
<td><code>in_genealogy</code></td>
<td>Input genealogy file</td>
<td></td>
</tr>
<tr>
<td><code>in_genotype</code></td>
<td>Input genotype file</td>
<td></td>
</tr>
<tr>
<td><code>in_traits</code></td>
<td>Input traits file</td>
<td></td>
</tr>
<tr>
<td><code>in_model</code></td>
<td>Input model description of traits</td>
<td></td>
</tr>
<tr>
<td><code>in_paramsimul</code></td>
<td>Input simulation parameters</td>
<td></td>
</tr>
<tr>
<td><code>opt_step</code></td>
<td>Chromosomic segment exploration steps in Morgan</td>
<td>0.05</td>
</tr>
<tr>
<td><code>opt_ndmin</code></td>
<td>Minimal number of progeny by dam</td>
<td></td>
</tr>
<tr>
<td><code>opt_minsirephaseproba</code></td>
<td>Minimal sire phase probability</td>
<td>0.90</td>
</tr>
<tr>
<td><code>opt_mindamphaseproba</code></td>
<td>Minimal dam phase probability</td>
<td>0.10</td>
</tr>
<tr>
<td><code>opt_unknown_char</code></td>
<td>Unknown genotype value</td>
<td>'0'</td>
</tr>
<tr>
<td><code>opt_eps_cholesky</code></td>
<td>coeff cholesky decomposition</td>
<td>0.5</td>
</tr>
</tbody>
</table>

**QTLMap 0.7**
<table>
<thead>
<tr>
<th>Option</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><code>opt_chromosome</code></td>
<td>Linkage group</td>
</tr>
<tr>
<td><code>out_output</code></td>
<td>Main report file</td>
</tr>
<tr>
<td><code>out_summary</code></td>
<td>Output summary file</td>
</tr>
<tr>
<td><code>out_lrt_sires</code></td>
<td>Output file paternal effects</td>
</tr>
<tr>
<td><code>out_lrt_dams</code></td>
<td>Output file maternal effects</td>
</tr>
<tr>
<td><code>out_pded</code></td>
<td>Grand parental segment transmission marginal probabilities</td>
</tr>
<tr>
<td><code>out_pded_join</code></td>
<td>Grand parental segment transmission joint probabilities</td>
</tr>
<tr>
<td><code>out_phases</code></td>
<td>Parental phases file</td>
</tr>
<tr>
<td><code>out_freqall</code></td>
<td>Allele frequency file</td>
</tr>
<tr>
<td><code>out_haplotypes</code></td>
<td>Haplotype file</td>
</tr>
<tr>
<td><code>out_pateff</code></td>
<td>Sire QTL effect estimations</td>
</tr>
<tr>
<td><code>out_mateff</code></td>
<td>Dam QTL effect estimations</td>
</tr>
<tr>
<td><code>out_maxlrt</code></td>
<td>Simulation report(Position and max LRT)</td>
</tr>
<tr>
<td><code>opt_eps_confusion</code></td>
<td>Threshold to test confusion between level inside a contingency matrix</td>
</tr>
<tr>
<td><code>opt_eps_hwe</code></td>
<td>Threshold to check the equilibrium of marker transmission within each family</td>
</tr>
<tr>
<td><code>opt_eps_linear_heteroscedastic</code></td>
<td>Threshold for convergence in the linear mode heteroscedastic</td>
</tr>
<tr>
<td><code>opt_max_iteration_linear_heteroscedastic</code></td>
<td>Maximum iteration in the linear mode heteroscedastic to avoid infinity loop</td>
</tr>
<tr>
<td><code>opt_eps_recomb</code></td>
<td></td>
</tr>
<tr>
<td><code>opt_nb_haplo_prior</code></td>
<td></td>
</tr>
<tr>
<td><code>opt_pro_haplo_min</code></td>
<td></td>
</tr>
<tr>
<td><code>opt_long_min.ibs</code></td>
<td></td>
</tr>
<tr>
<td><code>opt_longhap</code></td>
<td></td>
</tr>
<tr>
<td><code>opt_optim_maxeval</code></td>
<td></td>
</tr>
<tr>
<td><code>opt_optim_maxtime</code></td>
<td></td>
</tr>
<tr>
<td><code>opt_optim_tolx</code></td>
<td></td>
</tr>
<tr>
<td><code>opt_optim_tolf</code></td>
<td></td>
</tr>
<tr>
<td><code>opt_optim_tolg</code></td>
<td></td>
</tr>
<tr>
<td>opt Optim h_precision</td>
<td></td>
</tr>
</tbody>
</table>