

crimaptools: a tutorial

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This **crimaptools** package creates input files, runs CRI-MAP and parses output files for analyses of linkage mapping and recombination rate estimation in CRI-MAP v2.504 (Windows) and CRI-MAP v2.507 (Linux). CRI-MAP is tirelessly maintained by [Jill Maddox](#) - **crimaptools** is merely a wrapper for carrying out commonly run CRI-MAP functions.

The **crimaptools** package is still in progress in terms of optimisation , but should run if instructions are followed carefully. Compiled CRI-MAP is bundled with this library. For more information on how it is used from the command line, check out Paris Veltsos's tutorial [here](#).

The package can be installed using devtools:

```
library(devtools)
install_github("susjoh/crimaptools")
```

1. Example dataset.

crimaptools requires two inputs to create, run and parse files:

1. A GenABEL **gwa**.data object containing genotype information for IDs
2. A pedigree object that specifies the individual families used in CRI-MAP, with columns for the ANIMAL, FATHER, MOTHER and FAMILY.

An example dataset from Red deer is included, and can be called using **data(deer)**

```
data(deer)

ls()
```

```
## [1] "deer.abel" "deer.famped" "deer.ped"
```

```
deer.famped
```

##	ANIMAL	FATHER	MOTHER	Family
## 1	4440	0	0	Offspring_Mum_108
## 2	3018	0	0	Offspring_Mum_108
## 3	1169	0	0	Offspring_Mum_108
## 4	1806	1169	3018	Offspring_Mum_108
## 5	108	4440	1806	Offspring_Mum_108
## 6	3049	0	0	Offspring_Mum_109
## 7	1289	0	0	Offspring_Mum_109
## 8	329	0	0	Offspring_Mum_109
## 9	1911	329	1289	Offspring_Mum_109
## 10	109	3049	1911	Offspring_Mum_109
## 11	1303	0	0	Offspring_Mum_110
## 12	1289	0	0	Offspring_Mum_110

```
## 13      329      0      0 Offspring_Mum_110
## 14     1911     329    1289 Offspring_Mum_110
## 15      110    1303    1911 Offspring_Mum_110
## 16     1920      0      0 Offspring_Mum_111
## 17     1289      0      0 Offspring_Mum_111
## 18      329      0      0 Offspring_Mum_111
## 19     1911     329    1289 Offspring_Mum_111
## 20      111     1920    1911 Offspring_Mum_111
```

2. Creating a CRI-MAP input file.

This is done using the function `create_crimap_input`. This requires the `deer.abel` and `deer.famped` objects, but also requires additional inputs such as `analysisID`, used as a flag for running CRI-MAP. An ordered list of SNP loci (`snplist =`) *or* a chromosome number (`chr =`) must be specified. It is also possible to specify the directory to which the output should be written, and `clear.existing.analysisID` will get rid of any previous builds carried out with the same `analysisID`. Let's run the analysis for chromosome 3, and give it the `analysisID` 3a.

```
library(crimaptools)

create_crimap_input(gwaa.data = deer.abel,
                    familyPedigree = deer.famped,
                    analysisID = "3a",
                    chr = 3,
                    outdir = "crimap",
                    clear.existing.analysisID = TRUE)
```

```
## Recoding alleles to numeric values...

## ...done

## Merging pedigree and genotype information...

## ...done.

## Parsing and writing to crimap/chr3a.gen...

## ...done
```

In the directory `crimap`, an input file `chr3a.gen` will have been created.

3. Run *prepare* and extract and deal with mendelian errors.

The `.gen` file must now be run through *prepare* to produce the field used for linkage mapping and crossover estimation. This can be done using the function `run_crimap_prepare`.

```
run_crimap_prepare(genfile = "crimap/chr3a.gen")
dir("crimap")

## [1] "chr3a.dat"      "chr3a.gen"      "chr3a.loc"      "chr3a.par"
## [5] "chr3a.pre"      "crimapinput1"
```

The function has produced the .pre, .loc, .par and .dat files. The .pre file will contain information on mendelian errors between parents and offspring, which can be extracted using the `parse_mend_err` function. This creates a further file with the extension .mnd, which has a column for each ID and the problematic locus:

```
parse_mend_err(prefile = "crimap/chr3a.pre",
               genfile = "crimap/chr3a.gen",
               familyPedigree = deer.famped)
```

```
## Writing new file crimap/chr3a.mnd
```

```
read.table("crimap/chr3a.mnd", header = T)
```

```
##   ANIMAL      SNP.Name
## 1    111 cela1_red_3_74862326
## 2    1920 cela1_red_3_74862326
```

Information from this file can be used to mask mendelian errors in the .gen file, by rerunning the `create_crimap_input` with `use.mnd = TRUE`:

```
create_crimap_input (gwaa.data = deer.abel,
                    familyPedigree = deer.famped,
                    analysisID = "3a",
                    chr = 3,
                    outdir = "crimap",
                    clear.existing.analysisID = TRUE,
                    use.mnd = TRUE)
```

```
## Recoding alleles to numeric values...
```

```
## ...done
```

```
## Merging pedigree and genotype information...
```

```
## ...done.
```

```
## Masking Mendelian errors...
```

```
## ...done.
```

```
## Parsing and writing to crimap/chr3a.gen...
```

```
## ...done
```

```
run_crimap_prepare(genfile = "crimap/chr3a.gen")
```

```
parse_mend_err(prefile = "crimap/chr3a.pre", genfile = "crimap/chr3a.gen", familyPedigree = deer.famped)
```

```
## No Mendelian errors detected. No changes made to .mnd file.
```

4. Build a linkage map.

Now the dataset is ready for linkage mapping and characterisation of crossovers. This assumes the order of the deer.abel dataset when chromosome is specified; if snplist was specified in `create_crimap_input` then it assumes the order of the snplist itself. The linkage map can be obtained by running `run_crimap_map`, which may be slow for large numbers of markers/families, and then parsed with `parse_map`, which provides sex specific maps:

```
run_crimap_map(genfile = "crimap/chr3a.gen")
dir("crimap")
```

```
## [1] "chr3a.dat"      "chr3a.gen"      "chr3a.loc"
## [4] "chr3a.map"      "chr3a.mnd"      "chr3a.mndverbose"
## [7] "chr3a.ord"      "chr3a.par"      "chr3a.pre"
## [10] "crimapinput1"
```

```
deer.map <- parse_map(mapfile = "crimap/chr3a.map")
head(deer.map)
```

```
##      Order      SNP.Name cMPosition.Female cMPosition.Male Female.r
## 1      0  cela1_sika_3_247473      0.000      0      0.000
## 3      1  cela1_sika_3_1709255      0.000      0      0.211
## 5      2  cela1_sika_3_1763550     22.546      0      0.211
## 7      3  cela1_sika_3_2122831     45.091      0      0.000
## 9      4  cela1_red_3_3089490     45.091      0      0.000
## 11     5  cela1_red_3_3118111     45.091      0      0.000
##      cMdiff.Female Male.r cMdiff.Male analysisID
## 1      0.000      0      0      3a
## 3     22.546      0      0      3a
## 5     22.546      0      0      3a
## 7      0.000      0      0      3a
## 9      0.000      0      0      3a
## 11     0.000      0      0      3a
```

5. Characterising recombination events.

The recombination events can be obtained by running `run_crimap_chrompic`, which again may be slow for larger numbers of markers/families. A sex averaged linkage map can be parsed with `parse_map_chrompic` and crossovers can be extracted with `parse_crossovers`, which also requires the family pedigree:

```
run_crimap_chrompic(genfile = "crimap/chr3a.gen")
```

```
deer.cmpmap <- parse_map_chrompic(chrompicfile = "crimap/chr3a.cmp")
head(deer.cmpmap)
```

```
##      Order      SNP.Name cMPosition      r cMdiff analysisID
## 1      1  cela1_sika_3_247473      0.000 0.000 0.000      3a
## 3      2  cela1_sika_3_1709255      0.000 0.211 22.546      3a
## 5      3  cela1_sika_3_1763550     22.546 0.211 22.546      3a
## 7      4  cela1_sika_3_2122831     45.091 0.000 0.000      3a
## 9      5  cela1_red_3_3089490     45.091 0.000 0.000      3a
## 11     6  cela1_red_3_3118111     45.091 0.000 0.000      3a
```

```
deer.xovers <- parse_crossovers(chrompicfile = "crimap/chr3a.cmp", familyPedigree = deer.famped)
deer.xovers[1:2,]
```

```
##
## 1 ---1-----1-----1--1---1---1-1--1-----11-1-1111--111-----1-----
## 2 -0-----111-----1---1---1-11--1---1-1-1---1--1-----1--1-----1--1-----11--1-----
##   ANIMAL RecombCount parent          Family No.Inf.Loci First.Inf.Order
## 1    108           1 MOTHER Offspring_Mum_108          480           4
## 2    109           3 MOTHER Offspring_Mum_109          421           2
##   Last.Inf.Order FATHER MOTHER RRID analysisID
## 1           1845   4440   1806 1806           3a
## 2           1786   3049   1911 1911           3a
##               UniqueID
## 1 3a_Offspring_Mum_108_1806_MOTHER
## 2 3a_Offspring_Mum_109_1911_MOTHER
```

Column `data` is the inheritance pattern from grandparents, with each character representing an ordered SNP. 0 is grandmaternal, 1 is grandpaternal. `RRID` is the parent in which the meiosis took place.

6. Investigating doubles crossovers.

Genotyping and/or phasing errors can lead to erroneous calls of double crossovers. These can be investigated by running `check_double_crossovers` on the parsed crossovers:

```
deer.doubles <- check_double_crossovers(parsed.xovers = deer.xovers)
```

```
## Splitting chromosome into segments of shared grandparental origin
```

```
head(deer.doubles)
```

```
##   Phase StartPos StopPos StartSpan StopSpan InfCount Segment Segment.Count
## 1     1         4      62         1     117        19         1           2
## 2     0       117    1845         62    1845       461         2           2
## 3     0         2        2         1         8         1         1           4
## 4     1         8     395         2     402        96         2           4
## 5     0       402     402       395     403         1         3           4
## 6     1       403    1786       402    1786       323         4           4
##   Type                UniqueID                Family RRID parent
## 1 First 3a_Offspring_Mum_108_1806_MOTHER Offspring_Mum_108 1806 MOTHER
## 2 Last 3a_Offspring_Mum_108_1806_MOTHER Offspring_Mum_108 1806 MOTHER
## 3 First 3a_Offspring_Mum_109_1911_MOTHER Offspring_Mum_109 1911 MOTHER
## 4 Mid 3a_Offspring_Mum_109_1911_MOTHER Offspring_Mum_109 1911 MOTHER
## 5 Mid 3a_Offspring_Mum_109_1911_MOTHER Offspring_Mum_109 1911 MOTHER
## 6 Last 3a_Offspring_Mum_109_1911_MOTHER Offspring_Mum_109 1911 MOTHER
##   analysisID Singleton
## 1          3a         no
## 2          3a         no
## 3          3a         yes
## 4          3a         no
## 5          3a         yes
## 6          3a         no
```

This takes the phasing information and returns information on the Phase fragments per chromosome (i.e. runs from a single grandparent. Phase: 0 = grandmaternal, 1 = grandpaternal; StartPos and StopPos are the first and last informative positions of the fragment, StartSpan and StopSpan are the closest informative SNPs on either side of the fragment (if first or last, then is first or last SNP); InfCount is the number of informative SNPs in the fragment; Segment is the order of the fragment, numbered 1:N; Type is whether the fragment was the first, last or occurred in the middle of the chromosome; RRID is the individual in which the meiosis occurred.

Physical map information for the markers can also be added by specifying map positions in a data frame with headers SNP.Name, Position, Order and analysisID:

```
library(GenABEL)
```

```
## Loading required package: MASS
```

```
## Loading required package: GenABEL.data
```

```
physmap <- data.frame(SNP.Name = snpnames(deer.abel)[chromosome(deer.abel) == 3],
  Position = map(deer.abel)[chromosome(deer.abel) == 3],
  Order = 1:length(which(chromosome(deer.abel) == 3)),
  analysisID = "3a")
```

```
deer.doubles <- check_double_crossovers(parsed.xovers = deer.xovers, physical.map = physmap)
```

```
## Splitting chromosome into segments of shared grandparental origin
```

```
head(deer.doubles)
```

```
##   Phase StartPos StopPos StartSpan StopSpan InfCount Segment Segment.Count
## 1     1         4      62         1     117        19         1           2
## 2     0     117    1845         62    1845       461         2           2
## 3     0         2        2         1         8         1         1           4
## 4     1         8     395         2     402        96         2           4
## 5     0     402     402     395     403         1         3           4
## 6     1     403    1786     402    1786       323         4           4
##   Type                               UniqueID           Family RRID parent
## 1 First 3a_Offspring_Mum_108_1806_MOTHER Offspring_Mum_108 1806 MOTHER
## 2 Last 3a_Offspring_Mum_108_1806_MOTHER Offspring_Mum_108 1806 MOTHER
## 3 First 3a_Offspring_Mum_109_1911_MOTHER Offspring_Mum_109 1911 MOTHER
## 4 Mid 3a_Offspring_Mum_109_1911_MOTHER Offspring_Mum_109 1911 MOTHER
## 5 Mid 3a_Offspring_Mum_109_1911_MOTHER Offspring_Mum_109 1911 MOTHER
## 6 Last 3a_Offspring_Mum_109_1911_MOTHER Offspring_Mum_109 1911 MOTHER
##   analysisID StartPos.GenomePos StopPos.GenomePos StartSpan.GenomePos
## 1          3a          2122831          7067364          247473
## 2          3a          10792068          121375733          7067364
## 3          3a          1709255          1709255          247473
## 4          3a          3155501          29013193          1709255
## 5          3a          29656063          29656063          29013193
## 6          3a          29689850          117062248          29656063
##   StopSpan.GenomePos PosLength SpanLength Singleton
## 1          10792068    4944533    10544595         no
```

```
## 2      121375733 110583665 114308369      no
## 3      3155501    0      2908028      yes
## 4      29656063 25857692 27946808      no
## 5      29689850    0      676657      yes
## 6      117062248 87372398 87406185      no
```

This outputs additional columns with the genome positions for Pos and Span values, and also PosLength and SpanLength, which is the difference between the start and stop positions.

The user then has some choice of which lines may be erroneous. For example, singletons may be removed.

```
deer.remove <- subset(deer.doubles, Singleton == "yes")

deer.xovers.clean <- revise_double_crossovers(parsed.xovers = deer.xovers, removeSections = deer.remove)
```

```
## [1] "Fixing Problem 1 of 3"
```

```
deer.xovers.clean
```

```
##
## 1 ---1-----1-----1--1---1---1-1--1-----11-1-1111--111-----1-----
## 2 -----111-----1---1---1-11--1---1-1-1---1--1-----1--1-----1-1-----11--1-----
## 3 -1-----111-----1-10--0--0-0--0--0-0--0--00--0-0-----0-----0--00--0-----
## 4 -0-----000-----1---1-----1-----1---1---1--11--1--1-----1--1-----1--11--1-----
##   ANIMAL RecombCount parent          Family No.Inf.Loci First.Inf.Order
## 1    108             1 MOTHER Offspring_Mum_108          480             4
## 2    109             0 MOTHER Offspring_Mum_109          421             2
## 3    110             2 MOTHER Offspring_Mum_110          421             2
## 4    111             1 MOTHER Offspring_Mum_111          417             2
##   Last.Inf.Order FATHER MOTHER RRID analysisID
## 1          1845   4440   1806 1806          3a
## 2          1786   3049   1911 1911          3a
## 3          1786   1303   1911 1911          3a
## 4          1778   1920   1911 1911          3a
##               UniqueID
## 1 3a_Offspring_Mum_108_1806_MOTHER
## 2 3a_Offspring_Mum_109_1911_MOTHER
## 3 3a_Offspring_Mum_110_1911_MOTHER
## 4 3a_Offspring_Mum_111_1911_MOTHER
```