

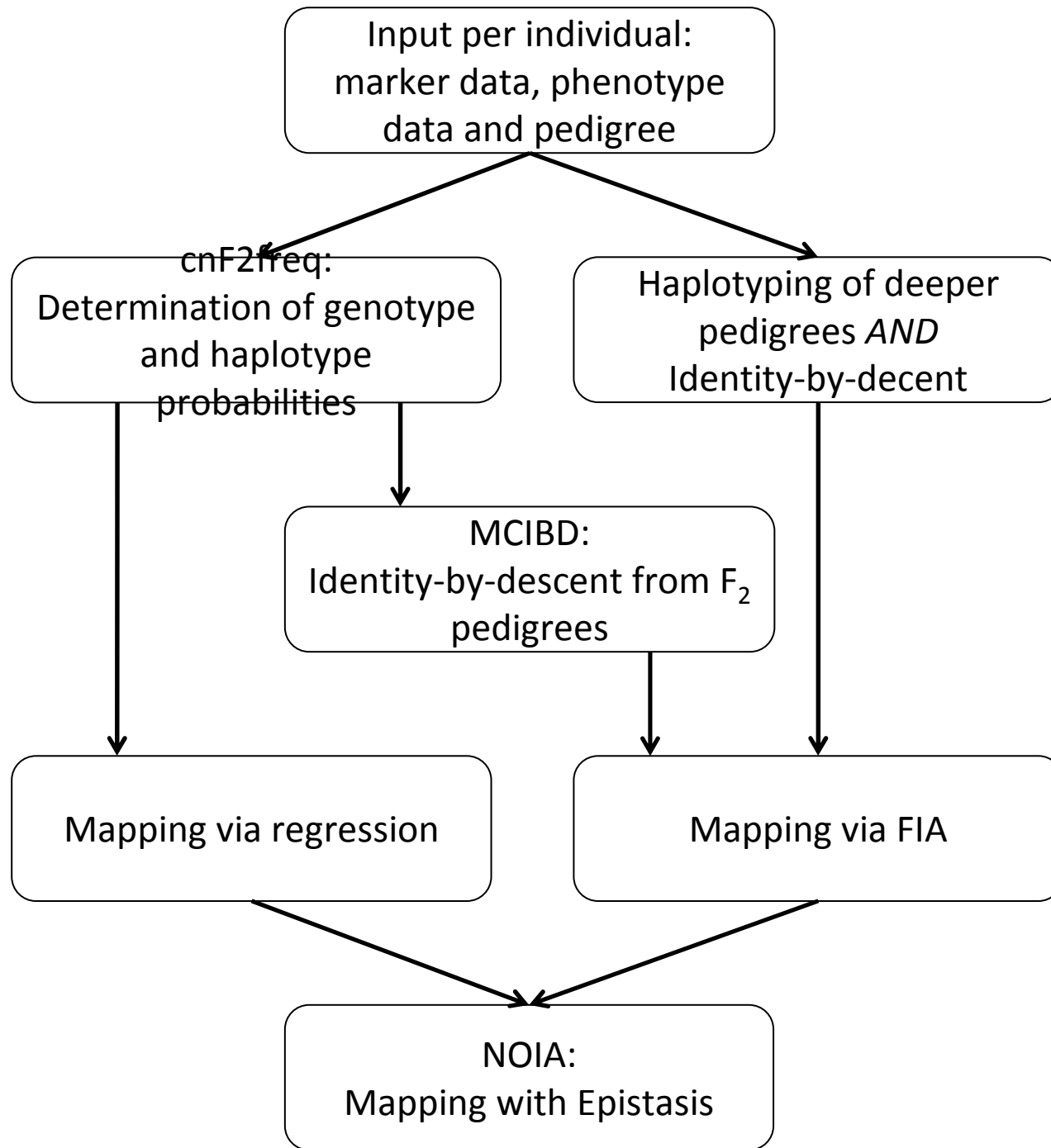
A new R package for QTL analysis

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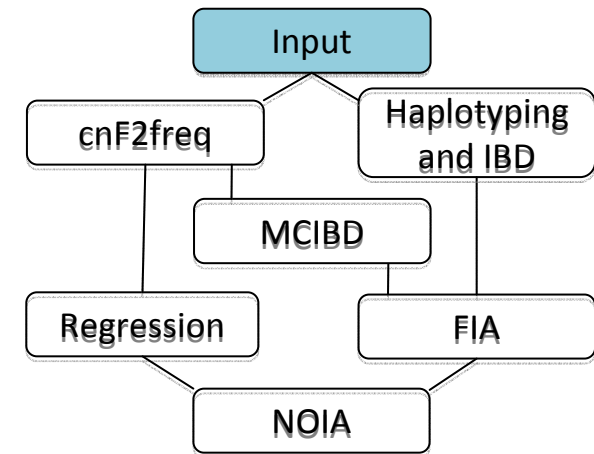
Aim of package

- Analysis of intercrosses from outbred lines
 - From F_2 crosses and back-crosses
 - From advanced intercrossed lines
- Determine QTL positions
- Determine epistatic interactions
- Fast and easy to use
- Explain genetic basis of complex traits including interactions



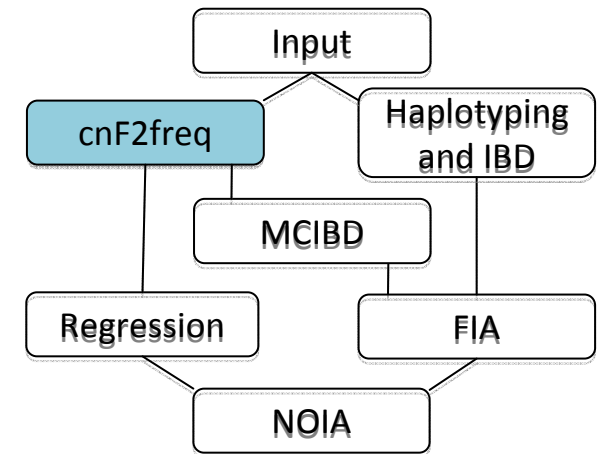
Input

- Common input files
 - Genotype
 - Individual data
 - Pedigree
- Initial checks
- Store data in single R-binary file



cnF2freq

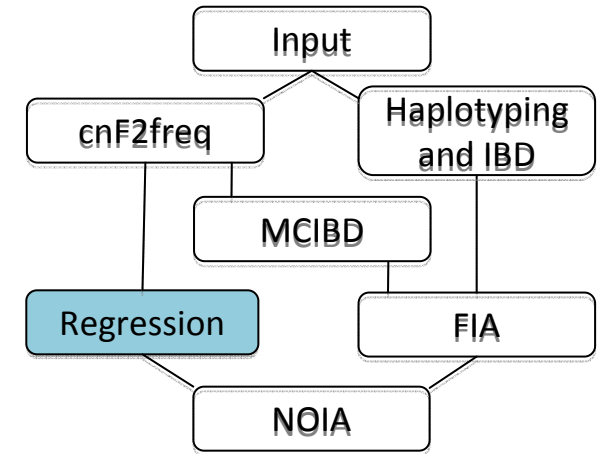
- Determine genotype probabilities from outbred lines
 - Use marker and pedigree data
 - F_2 and back-crossed
 - Hidden Markov Model
- Efficient estimation from large datasets



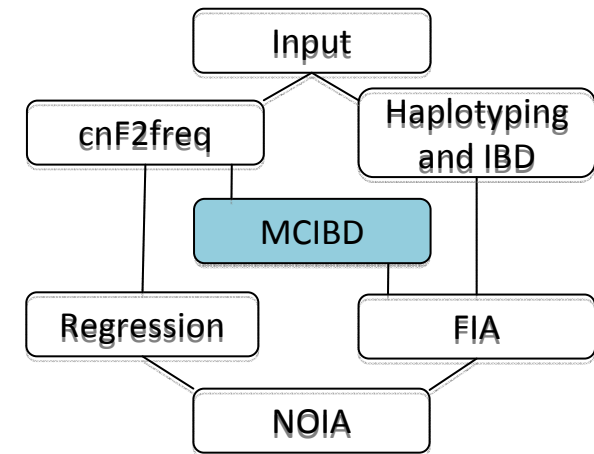
Nettelblad C., Holmgren S., Crooks L. and Carlborg Ö. 2009. *cnF2freq: Efficient Determination of Genotype and Haplotype Probabilities in Outbred Populations Using Markov Models*. *Bioinformatics and Computational Biology*, 307-319. Heidelberg: Springer Berlin.

Regression

- Haley-Knott regression to determine QTL
- Permutation testing

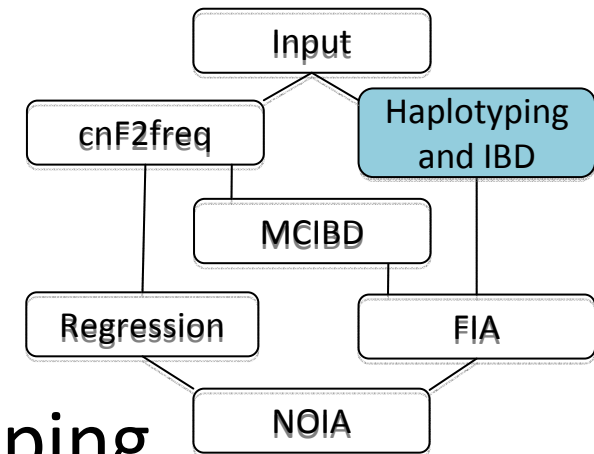


MCIBD



- Estimation of IBD matrix
- Approached by Monte Carlo sampling from marker probability matrix
- Available in combination with cnF2freq on R-forge
- Used for variance component QTL analysis

Haplotyping and IBD



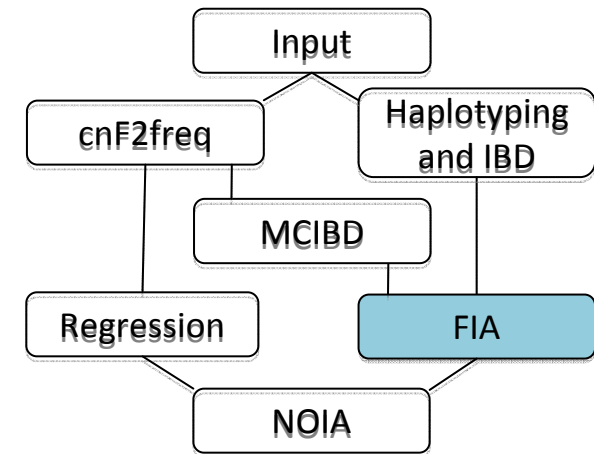
- Advanced intercross line haplotyping
 - FORTRAN based application
 - Infer marker-phase deterministically
- Estimation of IBD matrix
 - FORTRAN based application
 - Computationally efficient estimation of IBD
- Used for variance component QTL analysis

Besnier F. and Carlborg Ö. 2007. *A general and efficient method for estimating continuous IBD functions for use in genome scans for QTL*

BMC Bioinformatics **8**: 440

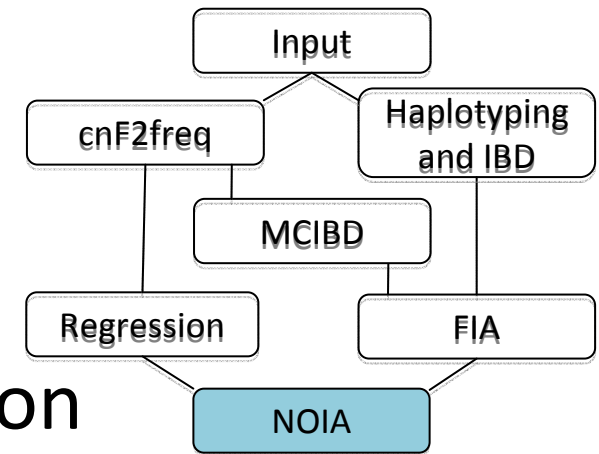
FIA

- Flexible Intercross Analysis
- Uses a general variance component model and utilizes the score statistic
- Models single and epistatic QTL
- More relaxed assumptions than fixed effect models
- Less sensitive to founder effects
- Require IBD



Rönnegård L., Besnier F. and Carlborg Ö. 2008. *An improved method for quantitative trait loci detection and identification of within-line segregation in F2 intercross designs*. Genetics **178**: 2315-2326

NOIA



- Natural and orthogonal interaction
- Include genotype frequencies from analyzed populations
 - Meaningful in population context
 - Provide proper decomposition of genetic variance
- Genotype-phenotype map
- Epistatic interactions

Álvarez-Castro J.M. and Carborg Ö. 2007. *A unified model for functional and statistical epistasis and its application in quantitative trait Loci analysis*. *Genetics* **176**: 1151-1167.

Optimized

- Front end R
- Optimized Fortran and C++ code
- Code also optimized for parallel computing
 - Clusters
 - Grids
 - Multi-core
 - or combination of above

Additional

- Well documented
- Different input formats
- Mendelian errors
- Handle sex chromosomes
- Infer parents
- Visualization

Conclusion

- Main effect and interacting QTL detection
- Outbred lines
- Large datasets
- F_2 , back-crosses and advanced intercross lines
- Different models

Acknowledgments

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 - (Mats Petterson, Xia Shen, Anna Johansson, Lucy Crooks, Xidan Li, Stefan Marklund, Weronica Ek, Marcin Kierczak and Örjan Carlborg)
- Other Co-Authors
 - (José Álvarez-Castro, Francois Besnier, Carl Nettelblad and Lars Rönnegård)

