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# HBIMPUTE

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**Increasing calling accuracy, coverage and read depth in sequence data by the  
use of haplotype blocks**



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# 1 General

HBimpute is an R-package to impute genomic data based on haplotype blocks derived by the R-package HaploBlocker (Pook et al. 2019). Methods are explained in the associated “Increasing calling accuracy, coverage and read depth in sequence data by the use of haplotype blocks” by Torsten Pook, Adnane Nemri, Eric Gerardo Gonzalez Segovia, Henner Simianer and Chris-Carolin Schön.

The developed approach and in particular the HBimpute step is patent pending by KWS SAAT SE & Co. KGaA and University of Goettingen (inventors: Torsten Pook & Adnane Nemri; application number EP20201121.9). This software is free for non-commercial use. If you are interested in using our software (and/or HBimpute in general), please contact Torsten Pook ([Torsten.pook@uni-goettingen.de](mailto:Torsten.pook@uni-goettingen.de)).

## 2 Installation

The current version of HBimpute requires HaploBlocker v.1.5.0+ (available on github) and vcfR (available on CRAN). HaploBlocker additionally requires a working version of RandomFieldsUtils (available on CRAN & github).

```
devtools::install_github("tpook92/HaploBlocker", subdir="pkg")
install.packages("vcfR")
devtools::install_github("tpook92/HBimpute", subdir="pkg")
```

Furthermore the software BEAGLE (preferably version 5.0). This can be done by downloading a beagle.jar at [https://faculty.washington.edu/browning/beagle/b5\\_0.html](https://faculty.washington.edu/browning/beagle/b5_0.html). On default we expect the beagle.jar to be placed in your R working directory and to be named “beagle5.jar”. In case your .jar is placed in a different path you can specify this via the parameter **path\_beaglejar**.

To check if you are correctly set up use the vcf-file “test.vcf” containing 2.209 SNPs for 340 DH-lines in maize via following lines code:

```
library(HBimpute)
impute(vcf = "test.vcf", out = "test_file", target_coverage = 0.9)
```

As this file contains mostly telemetric markers and default quality filters are quite conservative the resulting output VCF file will only contain 145 SNPs.

## 3 In-depth parameter explanations

### 3.1 General Parameters:

#### **hetero**

Default: FALSE; Alt: TRUE

Set this to TRUE in case you are working with non-homozygous material. In this case initial data will be phased and the two resulting haplotypes are using separately in the imputing procedure

#### **chromo**

Default: NULL; Alt: vector containing chromosome identifiers (e.g. 1:10)

On default all chromosomes in the vcf-file will be processed. To select a subset of chromosomes to consider use this parameter

#### **out**

Default: "out", Alt: any character string

Choose the name of the output file

#### **path\_beaglejar**

Default: „beagle5.jar“ Alt: provide the path to your BEAGLE Jar used to perform all beagle imputation sets.

Further parameter in BEAGLE that can directly be controlled in HBimpute the following will defaults chosen according to (Pook et al. 2020) :

**beagle\_core** (default: 10). This corresponds to the nthreads parameter in BEAGLE

**beagle\_ne** (default: 10.000). This corresponds to the ne parameter in BEAGLE

#### **estimate\_sv**

Default: FALSE alt: TRUE

Set this to TRUE to active the detection of structural variation. All regions with average read-depth above **sv\_cut1** (default: 1.3) will be called as duplications, everthing below **sv\_cut2** (default: 0.7) as a deletion. Read-depth are smoothed via a kernel density function with bandwidth **sv\_window** (default: 250.000bp). Reduce **sv\_window** if the interest is in smaller structural variation events.

#### **use\_del / use\_cnv**

Default: FALSE, Alt: TRUE

Active this to add deletion / duplication being called in the output vcf-file. Marker positions will be 1bp after the SNP-position

## 3.2 Quality Filters:

#### **max\_hetero**

Default: 0.01; Alt: numeric value between 0-1

All markers with higher share of heterozygous calls than this threshold will be removed. This parameter is only active for homozygous material.

#### **maf**

Default: 0, Alt: numeric value between {-1, 0-0.5}

All markers with lower minor allele frequency that this will be removed from the set. The default value of 0 will remove all fixated markers. Any negative value will preserve fixated markers.

### **max\_depth**

Default: 10, Alt: integer value

All allele calls with more than **max\_depth** read supporting this call will be set the **max\_depth** – reads to reduce the effect of extremely high read depth (and thereby high weighed in the imputation).

### **quali\_filter**

Default: TRUE, Alt: FALSE

Activating this will enable the filtering of the imputed dataset after the HBimpute step to remove marker with appeared low marker quality. Default are set conservative and should only remove extreme cases

### **max\_na**

Default: 0.5, Alt: numeric value between 0-1

All markers with more than **max\_na** of all variants not called after the HBimpute step are removed from the set as this indicated low marker quality.

### **min\_depth**

Default: 0.5, Alt: numeric value between 0-1

All markers with an average read depth below **min\_depth** of the average read depth are removed from the set as this indicated low marker quality.

## 3.3 Haplotype library

### **hb\_data // hb\_map**

Default: NULL alt: haplotype dataset / vector of physical positions (only one chromosome supported!)

To derive the haplotype library not based on the genetic dataset itself but another dataset (HB-array) provide input here.

The following parameter all directly correspond to parameter in HaploBlocker to shape the structure of you haplotype library. For extended documentation readers are referred to the “Guidelines to HaploBlocker”.

### **window\_size**

Default: 20, Alt: any integer value

### **target\_coverage**

Default: NULL, Alt: numeric value: 0-1 (we usually recommend 0.9 – 0.95).

### **min\_majorblock**

Default: 5000, Alt: any integer value

### 3.4 Expert parameter

Following parameter all should have reasonable input, but depending on the application changing some of those setting could make sense.

#### **min\_confi**

Default: 4, alt: numeric value 1-Inf

This parameter is to set the ratio between read for one variant and reads for all other variants to call a genetic variant.

#### **hetero\_is\_missing**

Default: TRUE Alt: FALSE

This parameter is only active when (**hetero** == FALSE) and control if heterozygous entries will be set to NA.

#### **overwrite\_call**

Default: FALSE, Alt: TRUE

Activate this to always preserve the original base call from the input vcf. Even if HBimpute is seeing clear indication for another variant. Use **overwrite\_call\_min\_depth** (default: 1) to only replace those alleles with at least a given number of reads supporting this call.

#### **overwrite\_na**

Default: TRUE, Alt: FALSE

Active this to replace HBimpute called of NA (usually due to calling threshold not exceeded) by the original call from the input vcf. Use **overwrite\_na\_min\_depth** (default: 1) to only replace those alleles with at least a given number of reads supporting this call.

### 3.5 Parameters mostly used in testing:

#### **geno, depth, allele, lines, posi, zero\_two\_coding**

Default: NULL

These inputs can substitute the use of a vcf-file. They come with no advantage besides potentially loading times than for a vcf-file.

**del\_freq / cutoff / cnv\_freq / cnv\_min (( Old structural variation module ))**

Default: 0.1, 0.9999, 0.1, 2

Only markers with at least **del\_freq /cnv\_freq** of the individuals with identified structural variation are included in the new data panel.

Deletions are called based on the number of present reads being below the cutoff-quantile of the binomial distribution.

CNVs are called if the local read-depth (standardized by the number of individuals considered) in the given marker is higher than **cnv\_min**.

### **ref\_panel**

Default: NULL Alt: path to an additional vcf-file containing a reference panel

This code is currently only written for heterozygous material and not generalized for multiple chromosomes! If you want to use this – contact me so I can update the code!

Basic idea of a reference panel is to use read from individuals not included in the dataset.

### **extended\_output**

Default: FALSE Alt: TRUE

Activating this will store an additional RData file containing information on read-depth, estimated structural variation and the haplotype library.

## References

- Pook, Torsten; Mayer, Manfred; Geibel, Johannes; Weigend, Steffen; Caverio, David; Schoen, Chris C.; Simianer, Henner (2020): {Improving imputation quality in BEAGLE for crop and livestock data}. In: *G3: Genes, Genomes, Genetics* 10 (1), S. 177–188.
- Pook, Torsten; Schlather, Martin; de los Campos, Gustavo; Mayer, Manfred; Schoen, Chris Carolin; Simianer, Henner (2019): {HaploBlocker}. {Creation of subgroup specific haplotype blocks and libraries}. In: *Genetics*, 1045-1061.

## 4 Acknowledgements

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