

# Package: MHCtools (via r-universe)

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**Type** Package

**Title** Analysis of MHC Data in Non-Model Species

**Version** 1.5.3

**Description** Fifteen tools for bioinformatics processing and analysis of major histocompatibility complex (MHC) data. The functions are tailored for amplicon data sets that have been filtered using the dada2 method (for more information on dada2, visit <https://benjjneb.github.io/dada2/>), but even other types of data sets can be analyzed. The ReplMatch() function matches replicates in data sets in order to evaluate genotyping success. The GetReplTable() and GetReplStats() functions perform such an evaluation. The CreateFas() function creates a fasta file with all the sequences in the data set. The CreateSamplesFas() function creates individual fasta files for each sample in the data set. The DistCalc() function calculates Grantham, Sandberg, or p-distances from pairwise comparisons of all sequences in a data set, and mean distances of all pairwise comparisons within each sample in a data set. The function additionally outputs five tables with physico-chemical z-descriptor values (based on Sandberg et al. 1998) for each amino acid position in all sequences in the data set. These tables may be useful for further downstream analyses, such as estimation of MHC supertypes. The BootKmeans() function is a wrapper for the kmeans() function of the 'stats' package, which allows for bootstrapping. Bootstrapping k-estimates may be desirable in data sets, where e.g. BIC- vs. k-values do not produce clear inflection points ("elbows"). BootKmeans() performs multiple runs of kmeans() and estimates optimal k-values based on a user-defined threshold of BIC reduction. The method is an automated and bootstrapped version of visually inspecting elbow plots of BIC- vs. k-values. The ClusterMatch() function is a tool for evaluating whether different k-means() clustering models identify similar clusters, and summarize bootstrap model stats as means for different estimated values of k. It is designed to take files produced by the BootKmeans()

function as input, but other data can be analysed if the descriptions of the required data formats are observed carefully. The `PapaDiv()` function compares parent pairs in the data set and calculate their joint MHC diversity, taking into account sequence variants that occur in both parents. The `HpltFind()` function infers putative haplotypes from families in the data set. The `GetHpltTable()` and `GetHpltStats()` functions evaluate the accuracy of the haplotype inference. The `CreateHpltOccTable()` function creates a binary (logical) haplotype-sequence occurrence matrix from the output of `HpltFind()`, for easy overview of which sequences are present in which haplotypes. The `HpltMatch()` function compares haplotypes to help identify overlapping and potentially identical types. The `NestTablesXL()` function translates the output from `HpltFind()` to an Excel workbook, that provides a convenient overview for evaluation and curating of the inferred putative haplotypes.

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## Contents

BootKmeans . . . . .	3
ClusterMatch . . . . .	5
CreateFas . . . . .	7
CreateHpltOccTable . . . . .	8
CreateSamplesFas . . . . .	9
DistCalc . . . . .	10
GetHpltStats . . . . .	12
GetHpltTable . . . . .	13
GetReplStats . . . . .	14

GetReplTable . . . . .	15
HpltFind . . . . .	16
HpltMatch . . . . .	17
hplt_occurrence_matrix . . . . .	18
k_summary_table . . . . .	19
NestTablesXL . . . . .	19
nest_table . . . . .	21
PapaDiv . . . . .	21
parents_table . . . . .	22
replicates_table . . . . .	23
ReplMatch . . . . .	24
sequence_table . . . . .	25
sequence_table_fas . . . . .	26
sequence_table_hplt . . . . .	26
sequence_table_repl . . . . .	27
z1_matrix . . . . .	27
z2_matrix . . . . .	28
z3_matrix . . . . .	28
z4_matrix . . . . .	29
z5_matrix . . . . .	29

<b>Index</b>	<b>30</b>
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BootKmeans	<i>BootKmeans()</i> function
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## Description

[BootKmeans](#) is a wrapper for the `kmeans()` function of the 'stats' package, which allows for bootstrapping. Bootstrapping k-estimates may be desirable in data sets, where the BIC- vs. k-values do not produce clear inflection points ("elbows").

## Usage

```

BootKmeans(
  z1_matrix,
  z2_matrix,
  z3_matrix,
  z4_matrix,
  z5_matrix,
  threshold = 0.01,
  no_scans = 1000,
  max_k = 40,
  iter.max = 1e+06,
  nstart = 200,
  algorithm = "Hartigan-Wong",
  path_out = path_out
)

```

**Arguments**

<code>z1_matrix</code>	a matrix with numerical values of the first z-descriptor for each amino acid position in all sequences in the data set.
<code>z2_matrix</code>	a matrix with numerical values of the second z-descriptor for each amino acid position in all sequences in the data set.
<code>z3_matrix</code>	a matrix with numerical values of the third z-descriptor for each amino acid position in all sequences in the data set.
<code>z4_matrix</code>	a matrix with numerical values of the fourth z-descriptor for each amino acid position in all sequences in the data set.
<code>z5_matrix</code>	a matrix with numerical values of the fifth z-descriptor for each amino acid position in all sequences in the data set.
<code>threshold</code>	a numerical value between 0 and 1 specifying the threshold of reduction in BIC for selecting a k estimate for each kmeans clustering model. The value specifies a proportion of the max observed reduction in BIC when increasing k by 1 (default 0.01).
<code>no_scans</code>	an integer specifying the number of k estimation scans to run (default 1,000).
<code>max_k</code>	an integer specifying the hypothetical maximum number of clusters to detect (default 40). In each k estimation scan, the algorithm runs a kmeans() clustering model for each value of k between 1 and max_k.
<code>iter.max</code>	an integer specifying the maximum number of iterations allowed in each kmeans() clustering model (default 1,000,000).
<code>nstart</code>	an integer specifying the number of rows in the set of input matrices that will be chosen as initial centers in the kmeans() clustering models (default 200).
<code>algorithm</code>	character vector, specifying the method for the kmeans() clustering function, one of c("Hartigan-Wong", "Lloyd", "Forgy", "MacQueen"), default is "Hartigan-Wong".
<code>path_out</code>	a user defined path to the folder where the output files will be saved.

**Details**

BootKmeans() performs multiple runs of kmeans() scanning k-values from 1 to a maximum value defined by the user. In each scan, an optimal k-value is estimated using a user-defined threshold of BIC reduction. The method is an automated version of visually inspecting elbow plots of BIC- vs. k-values. The number of scans to be performed is defined by the user.

For each k-estimate scan, the algorithm produces a summary of the stats incl. total within SS, AIC, and BIC, an elbow plot (BIC vs. k), and a set of cluster files corresponding to the estimated optimal k-value. It also produces a table summarizing the stats of the final selected kmeans() models corresponding to the estimated optimal k-values of each scan.

After running BootKmeans() on a data set, it is recommended to subsequently evaluate the repeatability of the bootstrapped k-estimation scans with the ClusterMatch() function also included in MHCtools.

Input data format: A set of five z-matrices containing numerical values of the z-descriptors (z1-z5) for each amino acid position in a sequence alignment. Each column should represent an amino acid position and each row one sequence in the alignment.

If you publish data or results produced with MHCtools, please cite both of the following references: Roved, J. 2022. MHCtools: Analysis of MHC data in non-model species. Cran. Roved, J., Hansson, B., Stervander, M., Hasselquist, D., & Westerdahl, H. 2022. MHCtools - an R package for MHC high-throughput sequencing data: genotyping, haplotype and supertype inference, and downstream genetic analyses in non-model organisms. Molecular Ecology Resources. <https://doi.org/10.1111/1755-0998.13645>

### Value

The function produces three folders in `path_out`, which contain for each scan the estimated k-clusters saved as .Rdata files, an elbow plot saved as .pdf, and a stats summary table saved as a .csv file. In `path_out` a summary of all scans performed in the bootstrap run is also saved as .csv. This table is also shown in the console. Should alternative elbow plots be desired, they may be produced manually with the stats presented in the summary tables for each scan.

### Note

AIC and BIC are calculated from the kmeans model objects by the following formulae: -  $AIC = D + 2 * m * k$  -  $BIC = D + \log(n) * m * k$  in which: -  $m = ncol(fit\$centers)$  -  $n = length(fit\$cluster)$  -  $k = nrow(fit\$centers)$  -  $D = fit\$tot.withinss$

### See Also

[ClusterMatch](#); [DistCalc](#)

### Examples

```
z1_matrix <- z1_matrix
z2_matrix <- z2_matrix
z3_matrix <- z3_matrix
z4_matrix <- z4_matrix
z5_matrix <- z5_matrix
path_out <- tempdir()
BootKmeans(z1_matrix, z2_matrix, z3_matrix, z4_matrix, z5_matrix, threshold=0.01,
no_scans=10, max_k=20, iter.max=10, nstart=10, algorithm="Hartigan-Wong",
path_out=path_out)
```

---

ClusterMatch

*ClusterMatch() function*


---

### Description

[ClusterMatch](#) is a tool for evaluating whether k-means() clustering models with similar estimated values of k identify similar clusters. `ClusterMatch()` also summarizes model stats as means for different estimated values of k. It is designed to take files produced by the `BootKmeans()` function as input, but other data can be analyzed if the descriptions of the data formats given below are observed carefully.

**Usage**

```
ClusterMatch(filepath, path_out, k_summary_table)
```

**Arguments**

filepath	a user defined path to a folder that contains the set of K-cluster files to be matched against each other. The algorithm will attempt to load all files in the folder, so it should contain only the relevant K-cluster files. If the clusters were generated using the <code>BootKmeans()</code> function, such a folder (named <code>Clusters</code> ) was created by the algorithm in the output path given by the user. Each K-cluster file should correspond to the <code>model\$cluster</code> object in <code>kmeans()</code> saved as a <code>.Rdata</code> file. Such files are generated as part of the output from <code>BootKmeans()</code> . <code>ClusterMatch()</code> assumes that the file names contain the string "model_" followed by a model number, which must match the corresponding row numbers in <code>k_summary_table</code> . If the data used was generated with the <code>BootKmeans()</code> function, the formats and numbers will match by default.
path_out	a user defined path to the folder where the output files will be saved.
k_summary_table	a data frame summarizing the stats of the <code>kmeans()</code> models that produced the clusters in the K-cluster files. If the data used was generated with the <code>BootKmeans()</code> function, a compatible <code>k_summary_table</code> was produced in the output path with the file name "k_means_bootstrap_summary_stats_<date>.csv". If other data is analyzed, please observe these formatting requirements: The <code>k_summary_table</code> must contain the data for each <code>kmeans()</code> model in rows and as minimum the following columns: - k-value (colname: <code>k.est</code> ) - residual total within sums-of-squares (colname: <code>Tot.withinss.resid</code> ) - residual AIC (colname: <code>AIC.resid</code> ) - residual BIC (colname: <code>BIC.resid</code> ) - delta BIC/max BIC (colname: <code>prop.delta.BIC</code> ) - delta BIC/k (colname: <code>delta.BIC.over.k</code> ) It is crucial that the models have the same numbers in the K-cluster file names and in the <code>k_summary_table</code> , and that the rows of the table are ordered by the model number.

**Details**

If you publish data or results produced with `MHCtools`, please cite both of the following references: Roved, J. 2022. `MHCtools`: Analysis of MHC data in non-model species. *Cran.* Roved, J., Hansson, B., Stervander, M., Hasselquist, D., & Westerdahl, H. 2022. `MHCtools` - an R package for MHC high-throughput sequencing data: genotyping, haplotype and supertype inference, and downstream genetic analyses in non-model organisms. *Molecular Ecology Resources*. <https://doi.org/10.1111/1755-0998.13645>

**Value**

The function returns a summary table, which for each estimated number of clusters (i.e. the k-values of the models) lists: - number of models that found *i* clusters - mean residual total within sums-of-squares - mean residual AIC - mean residual BIC - mean delta BIC/max BIC - mean delta BIC/k - mean number of allele assignments that fall outside of the *i* most abundant clusters across all pairwise comparisons between the models that found *i* clusters - mean proportion of allele assignments that fall outside of the *i* most abundant clusters across all pairwise comparisons

between the models that found *i* clusters. The summary table is also saved as a .csv file in the output path.

### See Also

[BootKmeans](#)

### Examples

```
filepath <- system.file("extdata/ClusterMatch", package="MHCtools")
path_out <- tempdir()
k_summary_table <- k_summary_table
ClusterMatch(filepath, path_out, k_summary_table)
```

---

CreateFas

*CreateFas() function*

---

### Description

[CreateFas](#) creates a FASTA file with all the sequences in a 'dada2' sequence table.

### Usage

```
CreateFas(seq_table, path_out)
```

### Arguments

seq_table	seq_table is a sequence table as output by the 'dada2' pipeline, which has samples in rows and nucleotide sequence variants in columns.
path_out	is a user defined path to the folder where the output files will be saved.

### Details

If you publish data or results produced with MHCtools, please cite both of the following references: Roved, J. 2022. MHCtools: Analysis of MHC data in non-model species. *Cran*. Roved, J., Hansson, B., Stervander, M., Hasselquist, D., & Westerdahl, H. 2022. MHCtools - an R package for MHC high-throughput sequencing data: genotyping, haplotype and supertype inference, and downstream genetic analyses in non-model organisms. *Molecular Ecology Resources*. <https://doi.org/10.1111/1755-0998.13645>

### Value

A FASTA file with all the sequences in a 'dada2' sequence table. The sequences are named in the FASTA file by an index number corresponding to their column number in the sequence table.

### See Also

[CreateSamplesFas](#); for more information about 'dada2' visit <https://benjjneb.github.io/dada2/>

**Examples**

```
seq_table <- sequence_table_fas
path_out <- tempdir()
CreateFas(seq_table, path_out)
```

---

CreateHpltOccTable      *CreateHpltOccTable() function*

---

**Description**

[CreateHpltOccTable](#) is designed to create a haplotype-sequence occurrence matrix from the set of R lists with putative haplotypes output by the `HpltFind()` function. `CreateHpltOccTable()` assumes that data originated from a diploid species.

**Usage**

```
CreateHpltOccTable(seq_table, filepath, path_out)
```

**Arguments**

<code>seq_table</code>	<code>seq_table</code> is a sequence table as output by the 'dada2' pipeline, which has samples in rows and nucleotide sequence variants in columns.
<code>filepath</code>	is a user defined path to the folder where the output files from the <code>HpltFind()</code> function have been saved.
<code>path_out</code>	is a user defined path to the folder where the output files will be saved.

**Details**

If you publish data or results produced with MHCtools, please cite both of the following references: Roved, J. 2022. MHCtools: Analysis of MHC data in non-model species. Cran. Roved, J., Hansson, B., Stervander, M., Hasselquist, D., & Westerdahl, H. 2022. MHCtools - an R package for MHC high-throughput sequencing data: genotyping, haplotype and supertype inference, and downstream genetic analyses in non-model organisms. Molecular Ecology Resources. <https://doi.org/10.1111/1755-0998.13645>

**Value**

A binary (logical) occurrence matrix with the data set sequences (inherited from `seq_table`) in columns and the putative haplotypes inferred by the `HpltFind()` function in rows.

**See Also**

[HpltFind](#); for more information about 'dada2' visit <<https://benjjneb.github.io/dada2/>>



## Examples

```
seq_table <- sequence_table
filepath <- system.file("extdata/HpltFindOut/", package="MHCtools")
path_out <- tempdir()
CreateHpltOccTable(seq_table, filepath, path_out)
```

---

CreateSamplesFas	<i>CreateSamplesFas() function</i>
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---

## Description

**CreateSamplesFas** creates a set of FASTA files with the sequences present in each sample in a 'dada2' sequence table.

## Usage

```
CreateSamplesFas(seq_table, path_out)
```

## Arguments

seq_table	seq_table is a sequence table as output by the 'dada2' pipeline, which has samples in rows and nucleotide sequence variants in columns.
path_out	is a user defined path to the folder where the output files will be saved.

## Details

If you publish data or results produced with MHCtools, please cite both of the following references: Roved, J. 2022. MHCtools: Analysis of MHC data in non-model species. *Cran.* Roved, J., Hansson, B., Stervander, M., Hasselquist, D., & Westerdahl, H. 2022. MHCtools - an R package for MHC high-throughput sequencing data: genotyping, haplotype and supertype inference, and downstream genetic analyses in non-model organisms. *Molecular Ecology Resources*. <https://doi.org/10.1111/1755-0998.13645>

## Value

A set of FASTA files with the sequences present in each sample in the sequence table. The sequences are named in the FASTA files by an index number corresponding to their column number in the sequence table, thus identical sequences will have identical sample names in all the FASTA files.

## See Also

**CreateFas**; for more information about 'dada2' visit <<https://benjjneb.github.io/dada2/>>

## Examples

```
seq_table <- sequence_table_fas
path_out <- tempdir()
CreateSamplesFas(seq_table, path_out)
```

DistCalc

*DistCalc() function***Description**

**DistCalc** calculates Grantham distances, Sandberg distances, or p-distances from pairwise comparisons of aligned sequences.

**Usage**

```
DistCalc(
  seq_file,
  path_out,
  input_fasta = NULL,
  input_seq = "aa",
  aa_dist = NULL,
  codon_pos = NULL,
  dist_type = "G"
)
```

**Arguments**

<code>seq_file</code>	is a sequence occurrence table as output by the 'dada2' pipeline, which has samples in rows and nucleotide sequence variants in columns. Optionally, a fasta file can be supplied as input in the format rendered by <code>read.fasta()</code> from the package 'seqinr'.
<code>path_out</code>	is a user defined path to the folder where the output files will be saved.
<code>input_fasta</code>	optional, a logical (TRUE/FALSE) that indicates whether the input file is a fasta file (TRUE) or a 'dada2'-style sequence table (NULL/FALSE). The default is NULL/FALSE.
<code>input_seq</code>	defines the type of sequences in <code>seq_file</code> . It may take the values 'nucl' or 'aa'.
<code>aa_dist</code>	is optional, a logical (TRUE/FALSE) that determines whether nucleotide sequences should be translated to amino acid sequences before distance calculation, default is NULL/FALSE. Note that <code>aa_dist</code> must be set to TRUE, if Grantham or Sandberg distances are calculated from an alignment of nucleotide sequences.
<code>codon_pos</code>	is optional, a vector of comma separated integers specifying which codons to include in distance calculations. If omitted, distance calculations are made using all codons. Note: When calculating nucleotide P-distances, <code>codon_pos</code> should be specified as a vector of nucleotide positions.
<code>dist_type</code>	is used to specify which kind of distances that are calculated. It takes the values 'G' for Grantham distances, 'S' for Sandberg distances, or 'P' for p-distances. The argument is optional with 'G' as default setting.

## Details

The DistCalc() function takes a fasta file or a 'dada2'-style sequence occurrence table (with aligned sequences as column names and samples in rows) as input and produces a matrix with pairwise distances for all sequences in the data set. If calculation of Sandberg distances is specified, the function additionally outputs five tables with physico-chemical z-descriptor values (based on Sandberg et al. 1998) for each amino acid position in all sequences in the data set. These tables may be useful for further downstream analyses, such as estimation of MHC supertypes. If a sequence occurrence table is provided as input, the DistCalc() function furthermore produces a table with the mean distances from all pairwise comparisons of the sequences in each sample in the data set. (Note: The mean distance will be NA for samples that have 0 or 1 sequence(s).)

Grantham distances and Sandberg distances are calculated as described in Pierini & Lenz 2018. The Grantham distances produced by DistCalc() are simply the mean Grantham distances (Grantham 1974) between all amino acid codons in sequence pairs. When calculating Sandberg distances, DistCalc() first computes Euclidian distances between all amino acid pairs based on the five physico-chemical z-descriptors defined in Sandberg et al. 1998. Sandberg distances are then calculated as the mean Euclidian distances between all amino acid codons in sequence pairs. P-distances calculated by DistCalc() are simply the proportion of varying codons between pairs of sequences.

The DistCalc() function includes an option for the user to specify which codons to compare, which is useful e.g. if conducting the analysis only on codons involved in specific functions, such as peptide binding of an MHC molecule. Note: When calculating nucleotide P-distances, codon\_pos is applied directly on the nucleotide sequences. This allows the user to calculate divergence in e.g. first, second, or third codon positions. Hence, codon\_pos should be specified as a vector of nucleotide positions when calculating nucleotide P-distances.

DistCalc() also accepts calculating amino acid distances directly from protein-coding DNA sequences using the standard genetic code.

The DistCalc() function accepts the following characters in the sequences: Nucleotide sequences: A,T,G,C Amino acid sequences: A,R,N,D,C,Q,E,G,H,I,L,K,M,F,P,S,T,W,Y,V

It accepts gaps defined by '-'. Nucleotide triplets containing gaps are translated to 'X', if amino acid distances are calculated directly from DNA nucleotide sequences. Please note that '-' or 'X' are treated as unique characters in p-distance calculations. The function will not accept 'X' or gaps in Grantham or Sandberg distance calculations. If you wish to exclude codons with 'X' or gaps from distance calculations, please use the codon\_pos option to specify which codons to compare.

If you publish data or results produced with MHCtools, please cite both of the following references: Roved, J. 2022. MHCtools: Analysis of MHC data in non-model species. *Cran.* Roved, J., Hansson, B., Stervander, M., Hasselquist, D., & Westerdahl, H. 2022. MHCtools - an R package for MHC high-throughput sequencing data: genotyping, haplotype and supertype inference, and downstream genetic analyses in non-model organisms. *Molecular Ecology Resources*. <https://doi.org/10.1111/1755-0998.13645>

If you calculated Grantham or Sandberg distances, please additionally cite: Pierini, F., Lenz, T.L. 2018. Divergent allele advantage at human MHC genes: Signatures of past and ongoing selection. *Mol. Biol. Evol.* 35, 2145-2158.

...and either of the following references: Grantham R. 1974. Amino acid difference formula to help explain protein evolution. *Science* 185:862-864. Sandberg M, Eriksson L, Jonsson J, Sjöström M, Wold S. 1998. New chemical descriptors relevant for the design of biologically active peptides. A multivariate characterization of 87 amino acids. *JMed Chem.* 41(14):2481-2491.

**Value**

The function returns a matrix with distances from all pairwise sequence comparisons, where *n* is the number of sequences. If a sequence occurrence table is given as input file, the function additionally returns a table with the mean distance for each sample in the data set. If a sequence occurrence table is given as input file, the sequences are named in the output matrix by an index number that corresponds to their column number in the input file. If calculation of Sandberg distances is specified, the function additionally outputs five tables with physico-chemical z-descriptor values for each amino acid position in all sequences in the data set. All output tables are saved as .csv files in the output path.

**See Also**

For more information about 'dada2', visit <<https://benjjneb.github.io/dada2/>>

**Examples**

```
seq_file <- sequence_table_fas
path_out <- tempdir()
DistCalc(seq_file, path_out, input_fasta=NULL, input_seq="nucl", aa_dist=NULL,
codon_pos=c(1,2,3,4,5,6,7,8), dist_type="P")
```

---

GetHpltStats

*GetHpltStats()* function

---

**Description**

**GetHpltStats** uses the output files produced by the **HpltFind()** function to calculate the mean of the mean proportion of incongruent sequences across all nests in the data set.

**Usage**

```
GetHpltStats(filepath)
```

**Arguments**

filepath	is a user defined path to the folder where the output files from the <b>HpltFind()</b> function have been saved.
----------	--

**Details**

If you publish data or results produced with MHCtools, please cite both of the following references: Roved, J. 2022. MHCtools: Analysis of MHC data in non-model species. Cran. Roved, J., Hansson, B., Stervander, M., Hasselquist, D., & Westerdahl, H. 2022. MHCtools - an R package for MHC high-throughput sequencing data: genotyping, haplotype and supertype inference, and downstream genetic analyses in non-model organisms. Molecular Ecology Resources. <https://doi.org/10.1111/1755-0998.13645>

**Value**

A mean of the mean proportion of incongruent sequences for each nest.

**See Also**

[HpltFind](#); [GetHpltTable](#)

**Examples**

```
filepath <- system.file("extdata/HpltFindOut/", package="MHCtools")
GetHpltStats(filepath)
```

---

GetHpltTable

*GetHpltTable() function*


---

**Description**

[GetHpltTable](#) uses the output files produced by the [HpltFind\(\)](#) function to produce a table with the mean proportion of incongruent sequences for each nest. If the mean proportion of incongruent sequences is generally low, but certain nests have many incongruent sequences, biological reasons may be causing the mismatches, e.g. extra-pair fertilizations or recombination events.

**Usage**

```
GetHpltTable(filepath)
```

**Arguments**

`filepath` is a user defined path to the folder where the output files from the [HpltFind\(\)](#) function have been saved.

**Details**

If you publish data or results produced with MHCtools, please cite both of the following references: Roved, J. 2022. MHCtools: Analysis of MHC data in non-model species. *Cran.* Roved, J., Hansson, B., Stervander, M., Hasselquist, D., & Westerdahl, H. 2022. MHCtools - an R package for MHC high-throughput sequencing data: genotyping, haplotype and supertype inference, and downstream genetic analyses in non-model organisms. *Molecular Ecology Resources*. <https://doi.org/10.1111/1755-0998.13645>

**Value**

A table with the mean proportion of incongruent sequences for each nest.

**See Also**

[HpltFind](#); [GetHpltStats](#)

**Examples**

```
filepath <- system.file("extdata/HpltFindOut/", package="MHCtools")
GetHpltTable(filepath)
```

---

GetReplStats

*GetReplStats function*


---

**Description**

[GetReplStats](#) uses the output files produced by the `ReplMatch()` function to calculate statistics on the agreement between replicated samples in the sequencing experiment.

**Usage**

```
GetReplStats(filepath)
```

**Arguments**

`filepath` is a user defined path to the folder where the output files from the `ReplMatch()` function have been saved.

**Details**

If you publish data or results produced with MHCtools, please cite both of the following references: Roved, J. 2022. MHCtools: Analysis of MHC data in non-model species. Cran. Roved, J., Hansson, B., Stervander, M., Hasselquist, D., & Westerdahl, H. 2022. MHCtools - an R package for MHC high-throughput sequencing data: genotyping, haplotype and supertype inference, and downstream genetic analyses in non-model organisms. Molecular Ecology Resources. <https://doi.org/10.1111/1755-0998.13645>

**Value**

A list containing the number of replicate sets with zero incongruent sequences, the proportion of replicate sets with zero incongruent sequences, the mean of the mean proportion of incongruent sequences across all replicate sets, and the repeatability of the sequencing experiment.

**See Also**

[ReplMatch](#); [GetReplTable](#)

**Examples**

```
filepath <- system.file("extdata/ReplMatchOut/", package="MHCtools")
GetReplStats(filepath)
```

---

GetReplTable	<i>GetReplTable function</i>
--------------	------------------------------

---

## Description

[GetReplTable](#) uses the output files produced by the `ReplMatch()` function to produce a table with the replicate sets and their respective mean proportion of incongruent sequences.

## Usage

```
GetReplTable(filepath)
```

## Arguments

filepath	is a user defined path to the folder where the output files from the <code>ReplMatch()</code> function have been saved.
----------	---

## Details

If you publish data or results produced with MHCtools, please cite both of the following references: Roved, J. 2022. MHCtools: Analysis of MHC data in non-model species. *Cran*. Roved, J., Hansson, B., Stervander, M., Hasselquist, D., & Westerdahl, H. 2022. MHCtools - an R package for MHC high-throughput sequencing data: genotyping, haplotype and supertype inference, and downstream genetic analyses in non-model organisms. *Molecular Ecology Resources*. <https://doi.org/10.1111/1755-0998.13645>

## Value

A table with the mean proportion of incongruent sequences for each replicate set.

## See Also

[ReplMatch](#); [GetReplStats](#)

## Examples

```
filepath <- system.file("extdata/ReplMatchOut/", package="MHCtools")
GetReplTable(filepath)
```

HpltFind

*HpltFind() function***Description**

**HpltFind** is designed to automatically infer major histocompatibility complex (MHC) haplotypes from the genotypes of parents and offspring in families (defined as nests) in non-model species, where MHC sequence variants cannot be identified as belonging to individual loci. **HpltFind()** assumes that data originated from a diploid species. The functions **GetHpltTable()**, **GetHpltStats()**, and **NestTablesXL()** are designed to evaluate the output files.

**Usage**

```
HpltFind(nest_table, seq_table, alpha = 0.8, path_out)
```

**Arguments**

nest_table	is a table containing the sample names of parents and offspring in each nest. This table should be organized so that the individual names are in the first column (Sample_ID), and the nest number is in the second column (Nest). For each nest, the first two rows should be the parents, followed immediately by the offspring in the subsequent rows, and then followed by the next nest, and so on. It is assumed that nests are numbered consecutively beginning at 1.
seq_table	seq_table is a sequence table as output by the 'dada2' pipeline, which has samples in rows and nucleotide sequence variants in columns.
alpha	a numerical value between 0 and 1 (default 0.8) specifying a threshold by which a set of sequences overlapping between a chick and a parent will be assigned to the putative parental A haplotype or passed to the B haplotype. Typical values are in the range 0.6-0.9. In data sets with many different MHC alleles per individual (i.e. many MHC gene copies), alpha may be set high. In data sets with fewer MHC alleles per individual, it should be set lower. A range of alpha values may be tested to find the optimal setting for a given data set, e.g. by evaluating the mean proportion of incongruent sequences across the data set using <b>GetHpltStats()</b> .
path_out	is a user defined path to the folder where the output files will be saved.

**Details**

If you publish data or results produced with MHCtools, please cite both of the following references: Roved, J. 2022. MHCtools: Analysis of MHC data in non-model species. Cran. Roved, J., Hansson, B., Stervander, M., Hasselquist, D., & Westerdahl, H. 2022. MHCtools - an R package for MHC high-throughput sequencing data: genotyping, haplotype and supertype inference, and downstream genetic analyses in non-model organisms. Molecular Ecology Resources. <https://doi.org/10.1111/1755-0998.13645>



**Value**

A set of R lists containing for each nest the putative haplotypes, the names of sequences that could not be resolved with certainty in each parent, the names of the sequences that were incongruent in the genotypes of the nest, and the mean proportion of incongruent sequences (which is a measure of the haplotype inference success and largely influenced by the exactness of the genotyping experiment). The sequences are named in the output by an index number corresponding to their column number in the sequence table, thus identical sequences will have identical sample names in all the output files. These files can be reopened in R e.g. using the `readRDS()` function in the base package. Note: `HpltFind()` will overwrite any existing files with the same output file names in `path_out`.

**See Also**

[GetHpltTable](#); [GetHpltStats](#); [NestTablesXL](#); [CreateHpltOccTable](#); for more information about 'dada2' visit <<https://benjjneb.github.io/dada2/>>

**Examples**

```
nest_table <- nest_table
seq_table <- sequence_table
path_out <- tempdir()
HpltFind(nest_table, seq_table, alpha=0.8, path_out)
```

HpltMatch

*HpltMatch() function***Description**

Putative haplotypes may be identical to each other, or they may differ only by incongruent or unresolved sequences. It is therefore useful to curate putative haplotypes by comparing them to identify potentially overlapping types as candidates for further investigation. [HpltMatch](#) calculates the proportion of matching sequences between pairs of haplotypes and produces a .csv table with values in a lower left matrix. If a threshold value is specified, a list of haplotype matches where the proportion of matching sequences exceeds the threshold will be produced.

**Usage**

```
HpltMatch(hplt_occ_matrix, path_out, threshold = NULL)
```

**Arguments**

`hplt_occ_matrix`

A binary (logical) occurrence matrix with the data set sequences in columns and the putative haplotypes in rows, as produced by the `CreateHpltOccTable()` function.

`path_out`

a user defined path to the folder where the output file(s) will be saved.

`threshold`

a numerical value between 0 and 1 (default NULL) specifying a threshold for the proportion of matching sequences between haplotypes.

**Details**

Note: The `NestTablesXL()` function provides a useful format for further investigation of potentially overlapping haplotypes.

If you publish data or results produced with MHCtools, please cite both of the following references: Roved, J. 2022. MHCtools: Analysis of MHC data in non-model species. Cran. Roved, J., Hansson, B., Stervander, M., Hasselquist, D., & Westerdahl, H. 2022. MHCtools - an R package for MHC high-throughput sequencing data: genotyping, haplotype and supertype inference, and downstream genetic analyses in non-model organisms. Molecular Ecology Resources. <https://doi.org/10.1111/1755-0998.13645>

**Value**

A table specifying the proportions of matching sequences between pairs of haplotypes (in a lower left matrix). If a threshold value is specified, a list of haplotype matches where the proportion of matching sequences exceeds the threshold will be printed to the console. The list will also be saved in the output path, and can be reopened in R e.g. using the `readRDS()` function in the base package. Note: `HpltMatch()` will overwrite any existing files with the same output file names in `path_out`.

**See Also**

[HpltFind](#); [CreateHpltOccTable](#); [NestTablesXL](#)

**Examples**

```
hplt_occ_matrix <- hplt_occurrence_matrix
path_out <- tempdir()
HpltMatch(hplt_occ_matrix, path_out, threshold=NULL)
```

---

```
hplt_occurrence_matrix
```

*Data hplt\_occurrence\_matrix*

---

**Description**

`hplt_occurrence_matrix` is an example of a binary occurrence matrix derived from a randomized real major histocompatibility complex (MHC) data set. The matrix was generated using the `CreateHpltOccTable()` function.

**Usage**

```
hplt_occurrence_matrix
```

**Format**

`hplt_occurrence_matrix` is a data frame with 136 putative haplotypes in rows and 329 MHC sequence variants in columns.

**Source**

original data.

---

k_summary_table	<i>k_summary_table.rda</i>
-----------------	----------------------------

---

**Description**

k\_summary\_table contains the results from a bootstrapped kmeans clustering analysis performed on the test data in the tables z1\_matrix\_test\_data, z2\_matrix\_test\_data, z3\_matrix\_test\_data, z4\_matrix\_test\_data, and z5\_matrix\_test\_data using BootKmeans().

**Usage**

```
k_summary_table
```

**Format**

k\_summary\_table is a data frame with observations from 10 k-estimation scans in rows and their respective stats in 11 columns.

**Source**

original data.

---

NestTablesXL	<i>NestTablesXL() function</i>
--------------	--------------------------------

---

**Description**

[NestTablesXL](#) reads the R lists output by the HpltFind() function and translates them to an Excel workbook for more convenient evaluation of the inferred haplotypes and curation of unresolved and incongruent sequences. The workbook contains separate tabs for each nest in the data set and provides an overview of the genotypes of the samples in each nest and the inferred haplotypes.

**Usage**

```
NestTablesXL(nest_table, seq_table, filepath, path_out)
```

## Arguments

<code>nest_table</code>	is a table containing the sample names of parents and offspring in each nest. This table should be organized so that the individual names are in the first column ( <code>Sample_ID</code> ), and the nest number is in the second column ( <code>Nest</code> ). For each nest, the first two rows should be the parents, followed immediately by the offspring in the subsequent rows, and then followed by the next nest, and so on. It is assumed that nests are numbered consecutively beginning at 1. Please use the same table as was used to generate the haplotypes using <code>HpltFind()</code> .
<code>seq_table</code>	<code>seq_table</code> is a sequence table as output by the 'dada2' pipeline, which has samples in rows and nucleotide sequence variants in columns. Please use the same table as was used to generate the haplotypes using <code>HpltFind()</code> .
<code>filepath</code>	is a user defined path to the folder where the output files from the <code>HpltFind()</code> function have been saved.
<code>path_out</code>	is a user defined path to the folder where the output file will be saved.

## Details

If you publish data or results produced with MHCtools, please cite both of the following references: Roved, J. 2022. MHCtools: Analysis of MHC data in non-model species. *Cran*. Roved, J., Hansson, B., Stervander, M., Hasselquist, D., & Westerdahl, H. 2022. MHCtools - an R package for MHC high-throughput sequencing data: genotyping, haplotype and supertype inference, and downstream genetic analyses in non-model organisms. *Molecular Ecology Resources*. <https://doi.org/10.1111/1755-0998.13645>

## Value

An Excel workbook with individual tabs for each nest in `nest_table`. Each tab contains a binary (logical) occurrence matrix with the samples from each nest in columns and sequences (inherited from `seq_table`) in rows. The order of the samples is derived from `nest_table`, with parents in the two leftmost columns. Each tab also lists the putative haplotypes inferred by the `HpltFind()` function and provides lists of unresolved sequences in haplotypes, sequences with unidentified decent (i.e., present in parents but not in offspring), sequences not assigned to haplotypes, and sequences with unidentified origin (i.e., present in offspring but not in parents). Note: `NestTablesXL()` will overwrite any existing file with the output file name in `path_out`.

## See Also

[HpltFind](https://benjjneb.github.io/dada2/); for more information about 'dada2' visit <<https://benjjneb.github.io/dada2/>>

## Examples

```
nest_table <- nest_table
seq_table <- sequence_table_hplt
filepath <- system.file("extdata/HpltFindOut/", package="MHCtools")
path_out <- tempdir()
NestTablesXL(nest_table, seq_table, filepath, path_out)
```

---

nest_table	<i>Data nest_table</i>
------------	------------------------

---

### Description

nest\_table, parents\_table, and sequence\_table comprise a randomized dataset derived from a real major histocompatibility complex (MHC) genotyping experiment with data from parents and offspring. The nucleotide sequences have been replaced with randomly generated sequences, and sample names have been anonymized.

### Usage

```
nest_table
```

### Format

nest\_table is a data frame with 213 samples in rows and 2 columns:

**Sample\_ID** Sample ID

**Nest** Nest index number

### Source

original data.

---

PapaDiv	<i>PapaDiv() function</i>
---------	---------------------------

---

### Description

**PapaDiv** calculates the joint major histocompatibility complex (MHC) diversity in parent pairs, taking into account alleles that are shared between the parents. The joint diversity in parent pairs is often of interest in studies of mate choice, fitness, and heritability.

### Usage

```
PapaDiv(parents_table, seq_table, path_out)
```

### Arguments

**parents\_table** is a table containing the sample names of the parents in each nest. This table should be organized so that each row represents one nest, with the individual names of the mothers in the first column (Mother), and the individual names of the fathers in the second column (Father).

**seq\_table** seq\_table is a sequence table as output by the 'dada2' pipeline, which has samples in rows and nucleotide sequence variants in columns.

**path\_out** is a user defined path to the folder where the output files will be saved.

## Details

The PapaDiv() function outputs a set of R lists containing for the joint diversity of each parent pair, the proportion of sequences that are shared between the parents, the diversity of each of the parents, the observed sequence variants in each parent, the matched sequence variants, and the incongruent sequence variants in each parent.

In addition, PapaDiv() produces a summary table with the names of the parents in a pair, their respective MHC diversities, and the joint parent pair diversity.

If you publish data or results produced with MHCtools, please cite both of the following references: Roved, J. 2022. MHCtools: Analysis of MHC data in non-model species. Cran. Roved, J., Hansson, B., Stervander, M., Hasselquist, D., & Westerdahl, H. 2022. MHCtools - an R package for MHC high-throughput sequencing data: genotyping, haplotype and supertype inference, and downstream genetic analyses in non-model organisms. Molecular Ecology Resources. <https://doi.org/10.1111/1755-0998.13645>

## Value

a set of R lists containing for the joint diversity of each parent pair, the proportion of sequences that are shared between the parents, the diversity of each of the parents, the observed sequence variants in each parent, the matched sequence variants, and the incongruent sequence variants in each parent. The sequences are named in the output by an index number corresponding to their column number in the sequence table, thus identical sequences will have identical sample names in all the output files. These files are saved in a sub folder in the output path called Parent\_pairs (created by PapaDiv()) and can be reopened in R e.g. using the readRDS() function in the base package. For downstream data analysis, the PapaDiv() function also produces a summary table with the names of the parents in a pair, their respective MHC diversities, and the joint parent pair diversity. This table is saved as a .csv file in the output path.

## See Also

For more information about 'dada2' visit <<https://benjjneb.github.io/dada2/>>

## Examples

```
parents_table <- parents_table
seq_table <- sequence_table
path_out <- tempdir()
PapaDiv(parents_table, seq_table, path_out)
```

---

parents\_table

*Data parents\_table*

---

## Description

nest\_table, parents\_table, and sequence\_table comprise a randomized dataset derived from a real major histocompatibility complex (MHC) genotyping experiment with data from parents and offspring. The nucleotide sequences have been replaced with randomly generated sequences, and sample names have been anonymized.

**Usage**

parents\_table

**Format**

parents\_table is a data frame with 57 parent pairs in rows and 2 columns:

**Mother** Mother ID

**Father** Father ID

**Source**

original data.

---

replicates_table	<i>Data replicates_table</i>
------------------	------------------------------

---

**Description**

replicates\_table and sequence\_table\_repl comprise a randomized dataset derived from a real major histocompatibility complex (MHC) genotyping experiment with technical replicates. The nucleotide sequences have been replaced with randomly generated sequences, and sample names have been anonymized.

**Usage**

replicates\_table

**Format**

replicates\_table is a data frame with 111 technical replicate samples in rows and 2 columns:

**Sample\_ID** Technical replicate sample ID

**Replic\_set** Index number of replicate set

**Source**

original data.

ReplMatch

*ReplMatch() function***Description**

In amplicon filtering it is sometimes valuable to compare technical replicates in order to estimate the accuracy of a genotyping experiment. This may be done both to optimize filtering settings and to estimate repeatability to report in a publication. **ReplMatch** is designed to automatically compare technical replicates in an amplicon filtering data set and report the proportion of mismatches. The functions `GetReplTable()` and `GetReplStats()` are designed to evaluate the output files.

**Usage**

```
ReplMatch(repl_table, seq_table, path_out)
```

**Arguments**

<code>repl_table</code>	is a table containing the sample names of technical replicates in the data set. This table should be organized so that the individual names are in the first column ( <code>Sample_ID</code> ), and the index number of the replicate set is in the second column ( <code>Replic_set</code> ). Replicate sets may contain more than two replicates, but sets must be numbered consecutively beginning at 1.
<code>seq_table</code>	<code>seq_table</code> is a sequence table as output by the 'dada2' pipeline, which has samples in rows and nucleotide sequence variants in columns.
<code>path_out</code>	is a user defined path to the folder where the output files will be saved.

**Details**

Note: `ReplMatch()` will throw a warning if all samples in a replicate set have 0 sequences. In that case, the `mean_props` for that replicate set and the repeatability for the data set will be `NaN`, and `ReplMatch()` will report which replicate set is problematic and suggest to remove it from the `repl_table`. If removing replicate sets, beware that the replicate sets in `repl_table` must be numbered consecutively beginning at 1.

If you publish data or results produced with MHCtools, please cite both of the following references: Roved, J. 2022. MHCtools: Analysis of MHC data in non-model species. *Cran.* Roved, J., Hansson, B., Stervander, M., Hasselquist, D., & Westerdahl, H. 2022. MHCtools - an R package for MHC high-throughput sequencing data: genotyping, haplotype and supertype inference, and downstream genetic analyses in non-model organisms. *Molecular Ecology Resources*. <https://doi.org/10.1111/1755-0998.13645>

**Value**

A set of R lists containing for each replicate set the observed sequence variants, the names of the sequences that were incongruent in the replicates, and the mean proportion of incongruent sequences (if 100 matches are expected between the replicates, this is equivalent of an error rate in the sequencing process). The sequences are named in the output by an index number corresponding to their



column number in the sequence table, thus identical sequences will have identical sample names in all the output files. These files can be reopened in R e.g. using the `readRDS()` function in the base package.

### See Also

[GetReplTable](#); [GetReplStats](#); for more information about 'dada2' visit <<https://benjjneb.github.io/dada2/>>

### Examples

```
repl_table <- replicates_table
seq_table <- sequence_table_repl
path_out <- tempdir()
ReplMatch(repl_table, seq_table, path_out)
```

---

sequence_table	<i>Data sequence_table</i>
----------------	----------------------------

---

### Description

`nest_table`, `parents_table`, and `sequence_table` comprise a randomized dataset derived from a real major histocompatibility complex (MHC) genotyping experiment with data from parents and offspring. The nucleotide sequences have been replaced with randomly generated sequences, and sample names have been anonymized.

### Usage

```
sequence_table
```

### Format

`sequence_table` is a data frame with 334 samples in rows and 329 DNA sequence variants in columns.

### Source

original data.

---

sequence_table_fas	<i>Data sequence_table_fas</i>
--------------------	--------------------------------

---

**Description**

sequence\_table\_fas is a randomized dataset derived from a real major histocompatibility complex (MHC) genotyping experiment. The nucleotide sequences have been replaced with randomly generated sequences, and sample names have been anonymized.

**Usage**

sequence\_table\_fas

**Format**

sequence\_table\_fas is a data frame with 100 samples in rows and 166 DNA sequence variants in columns.

**Source**

original data.

---

sequence_table_hplt	<i>Data sequence_table_hplt</i>
---------------------	---------------------------------

---

**Description**

sequence\_table\_hplt is a randomized test data set derived from a real major histocompatibility complex (MHC) genotyping experiment. This table differs from the sequence\_table by having the nucleotide sequences replaced with sequence names. Sample names have been anonymized from the real data set.

**Usage**

sequence\_table\_hplt

**Format**

sequence\_table\_hplt is a data frame with 334 samples in rows and 329 sequence variants in columns.

**Source**

original data.

---

sequence_table_repl	<i>Data sequence_table_repl</i>
---------------------	---------------------------------

---

**Description**

replicates\_table and sequence\_table\_repl comprise a randomized dataset derived from a real major histocompatibility complex (MHC) genotyping experiment with technical replicates. The nucleotide sequences have been replaced with randomly generated sequences, and sample names have been anonymized.

**Usage**

```
sequence_table_repl
```

**Format**

sequence\_table\_repl is a data frame with 412 samples in rows and 511 DNA sequence variants in columns.

**Source**

original data.

---

z1_matrix	<i>z1_matrix.rda</i>
-----------	----------------------

---

**Description**

z1\_matrix comprise a randomized dataset derived from 70 nucleotide sequences of a real major histocompatibility complex (MHC) genotyping experiment. z1-descriptor values have been extracted from a subset of 8 amino acid codons and sequence names have been anonymized.

**Usage**

```
z1_matrix
```

**Format**

z1\_matrix is a data frame with 70 sequences in rows and z1-descriptor variables for 8 sequence codons in columns.

**Source**

original data.

---

`z2_matrix``z2_matrix.rda`

---

**Description**

`z2_matrix` comprise a randomized dataset derived from 70 nucleotide sequences of a real major histocompatibility complex (MHC) genotyping experiment. `z2`-descriptor values have been extracted from a subset of 8 amino acid codons and sequence names have been anonymized.

**Usage**

```
z2_matrix
```

**Format**

`z2_matrix` is a data frame with 70 sequences in rows and `z2`-descriptor variables for 8 sequence codons in columns.

**Source**

original data.

---

`z3_matrix``z3_matrix.rda`

---

**Description**

`z3_matrix` comprise a randomized dataset derived from 70 nucleotide sequences of a real major histocompatibility complex (MHC) genotyping experiment. `z3`-descriptor values have been extracted from a subset of 8 amino acid codons and sequence names have been anonymized.

**Usage**

```
z3_matrix
```

**Format**

`z3_matrix` is a data frame with 70 sequences in rows and `z3`-descriptor variables for 8 sequence codons in columns.

**Source**

original data.

---

z4_matrix	<i>z4_matrix.rda</i>
-----------	----------------------

---

**Description**

z4\_matrix comprise a randomized dataset derived from 70 nucleotide sequences of a real major histocompatibility complex (MHC) genotyping experiment. z4-descriptor values have been extracted from a subset of 8 amino acid codons and sequence names have been anonymized.

**Usage**

```
z4_matrix
```

**Format**

z4\_matrix is a data frame with 70 sequences in rows and z4-descriptor variables for 8 sequence codons in columns.

**Source**

original data.

---

z5_matrix	<i>z5_matrix.rda</i>
-----------	----------------------

---

**Description**

z5\_matrix comprise a randomized dataset derived from 70 nucleotide sequences of a real major histocompatibility complex (MHC) genotyping experiment. z5-descriptor values have been extracted from a subset of 8 amino acid codons and sequence names have been anonymized.

**Usage**

```
z5_matrix
```

**Format**

z5\_matrix is a data frame with 70 sequences in rows and z5-descriptor variables for 8 sequence codons in columns.

**Source**

original data.

# Index

## \* datasets

- hplt\_occurrence\_matrix, 18
- k\_summary\_table, 19
- nest\_table, 21
- parents\_table, 22
- replicates\_table, 23
- sequence\_table, 25
- sequence\_table\_fas, 26
- sequence\_table\_hplt, 26
- sequence\_table\_repl, 27
- z1\_matrix, 27
- z2\_matrix, 28
- z3\_matrix, 28
- z4\_matrix, 29
- z5\_matrix, 29

- replicates\_table, 23
- ReplMatch, 14, 15, 24, 24
- sequence\_table, 25
- sequence\_table\_fas, 26
- sequence\_table\_hplt, 26
- sequence\_table\_repl, 27
- z1\_matrix, 27
- z2\_matrix, 28
- z3\_matrix, 28
- z4\_matrix, 29
- z5\_matrix, 29

BootKmeans, 3, 3, 7

ClusterMatch, 5, 5  
CreateFas, 7, 7, 9  
CreateHpltOccTable, 8, 8, 17, 18  
CreateSamplesFas, 7, 9, 9

DistCalc, 5, 10, 10

GetHpltStats, 12, 12, 13, 17  
GetHpltTable, 13, 13, 17  
GetReplStats, 14, 14, 15, 25  
GetReplTable, 14, 15, 15, 25

hplt\_occurrence\_matrix, 18  
HpltFind, 8, 13, 16, 16, 18, 20  
HpltMatch, 17, 17

k\_summary\_table, 19

nest\_table, 21  
NestTablesXL, 17–19, 19

PapaDiv, 21, 21  
parents\_table, 22