

Package ‘HIBAG’

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Type Package

Title HLA Genotype Imputation with Attribute Bagging

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Description It is a software package for imputing HLA types using SNP data, and relies on a training set of HLA and SNP genotypes. HIBAG can be used by researchers with published parameter estimates instead of requiring access to large training sample datasets. It combines the concepts of attribute bagging, an ensemble classifier method, with haplotype inference for SNPs and HLA types. Attribute bagging is a technique which improves the accuracy and stability of classifier ensembles using bootstrap aggregating and random variable selection.

License GPL-3

LazyData yes

VignetteBuilder knitr

biocViews Genetics, StatisticalMethod

URL <http://www.biostat.washington.edu/~bsweir/HIBAG/>,
<http://github.com/zhengxwen/HIBAG>

NeedsCompilation yes

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R topics documented:

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| | |
|---------------|---|
| HIBAG-package | <i>HLA Genotype Imputation with Attribute Bagging</i> |
|---------------|---|

Description

To impute HLA types from unphased SNP data using an attribute bagging method.

Details

| | |
|-----------------|------------------------|
| Package: | HIBAG |
| Type: | R/Bioconductor Package |
| License: | GPL version 3 |
| Kernel Version: | v1.3 |

HIBAG is a state of the art software package for imputing HLA types using SNP data, and it uses the R statistical programming language. HIBAG is highly accurate, computationally tractable, and can be used by researchers with published parameter estimates instead of requiring access to large training sample datasets. It combines the concepts of attribute bagging, an ensemble classifier method, with haplotype inference for SNPs and HLA types. Attribute bagging is a technique which improves the accuracy and stability of classifier ensembles using bootstrap aggregating and random variable selection.

Features:

- 1) HIBAG can be used by researchers with published parameter estimates (<http://www.biostat.washington.edu/~bsweir/HIBAG/>) instead of requiring access to large training sample datasets.
- 2) A typical HIBAG parameter file contains only haplotype frequencies at different SNP subsets rather than individual training genotypes.
- 3) SNPs within the xMHC region (chromosome 6) are used for imputation.
- 4) HIBAG employs unphased genotypes of unrelated individuals as a training set.
- 5) HIBAG supports parallel computing with R.

Author(s)

Xiuwen Zheng [aut, cre, cph] <zhengx@u.washington.edu>, Bruce S. Weir [ctb, ths] <bsweir@u.washington.edu>

References

Zheng X, Shen J, Cox C, Wakefield J, Ehm M, Nelson M, Weir BS; HIBAG – HLA Genotype Imputation with Attribute Bagging. *The Pharmacogenomics Journal*. doi: 10.1038/tpj.2013.18. <http://www.nature.com/tpj/journal/v14/n2/full/tpj201318a.html>

Examples

```

# HLA_Type_Table data
head(HLA_Type_Table)
dim(HLA_Type_Table) # 60 13

# HapMap_CEU_Geno data
summary(HapMap_CEU_Geno)

#####

# make a "hlaAlleleClass" object
hla.id <- "A"
hla <- hlaAllele(HLA_Type_Table$sample.id,
  H1 = HLA_Type_Table[, paste(hla.id, ".1", sep="")],
  H2 = HLA_Type_Table[, paste(hla.id, ".2", sep="")],
  locus=hla.id, assembly="hg19")

# divide HLA types randomly
set.seed(100)
hlatab <- hlaSplitAllele(hla, train.prop=0.5)
names(hlatab)
# "training" "validation"
summary(hlatab$training)
summary(hlatab$validation)

# SNP predictors within the flanking region on each side
region <- 500 # kb
snpid <- hlaFlankingSNP(HapMap_CEU_Geno$snp.id, HapMap_CEU_Geno$snp.position,
  hla.id, region*1000, assembly="hg19")
length(snpid) # 275

# training and validation genotypes
train.geno <- hlaGenoSubset(HapMap_CEU_Geno,
  snp.sel=match(snpid, HapMap_CEU_Geno$snp.id),
  samp.sel=match(hlatab$training$value$sample.id,
  HapMap_CEU_Geno$sample.id))
test.geno <- hlaGenoSubset(HapMap_CEU_Geno,
  samp.sel=match(hlatab$validation$value$sample.id,
  HapMap_CEU_Geno$sample.id))

# train a HIBAG model
set.seed(100)
# please use "nclassifier=100" when you use HIBAG for real data
model <- hlaAttrBagging(hlatab$training, train.geno, nclassifier=4,
  verbose.detail=TRUE)
summary(model)

# validation
pred <- predict(model, test.geno)
summary(pred)

```

```

# compare
(comp <- hlaCompareAllele(hlatab$validation, pred, allele.limit=model,
  call.threshold=0))
(comp <- hlaCompareAllele(hlatab$validation, pred, allele.limit=model,
  call.threshold=0.5))

# save the parameter file
mobj <- hlaModelToObj(model)
save(mobj, file="HIBAG_model.RData")
save(test.geno, file="testgeno.RData")
save(hlatab, file="HLASplit.RData")

# Clear Workspace
hlaClose(model) # release all resources of model
rm(list = ls())

#####

# NOW, load a HIBAG model from the parameter file
mobj <- get(load("HIBAG_model.RData"))
model <- hlaModelFromObj(mobj)

# validation
test.geno <- get(load("testgeno.RData"))
hlatab <- get(load("HLASplit.RData"))

pred <- predict(model, test.geno)
# compare
(comp <- hlaCompareAllele(hlatab$validation, pred, allele.limit=model,
  call.threshold=0.5))

#####

# import a PLINK BED file
#
bed.fn <- system.file("extdata", "HapMap_CEU.bed", package="HIBAG")
fam.fn <- system.file("extdata", "HapMap_CEU.fam", package="HIBAG")
bim.fn <- system.file("extdata", "HapMap_CEU.bim", package="HIBAG")
hapmap.ceu <- hlaBED2Geno(bed.fn, fam.fn, bim.fn, assembly="hg19")

#####

# predict
#
pred <- predict(model, hapmap.ceu, type="response")
head(pred$value)
#  sample.id allele1 allele2  prob
#  1  NA10859  01:01  03:01 0.9999992
#  2  NA11882  01:01  29:02 1.0000000
#  ...

```

```
# delete the temporary files
unlink(c("HIBAG_model.RData", "testgeno.RData", "HLASplit.RData"), force=TRUE)
```

| | |
|-----------------|--|
| HapMap_CEU_Geno | <i>SNP genotypes of a study simulated from HapMap CEU genotypic data</i> |
|-----------------|--|

Description

An object of [hlaSNPGenoClass](#) of 60 samples and 1564 SNPs.

Usage

```
HapMap_CEU_Geno
```

Value

A list

References

http://hapmap.ncbi.nlm.nih.gov/downloads/genotypes/2010-08_phaseII+III/forward/

The International HapMap Consortium. A second generation human haplotype map of over 3.1 million SNPs. *Nature* 449, 851-861. 2007.

| | |
|-----------|----------------------------|
| hlaAllele | <i>A list of HLA types</i> |
|-----------|----------------------------|

Description

Return an object of [hlaAlleleClass](#), which contains HLA types.

Usage

```
hlaAllele(sample.id, H1, H2, max.resolution="", locus="any", assembly="auto",
  locus.pos.start=NA, locus.pos.end=NA, prob=NULL, na.rm=TRUE)
```

Arguments

| | |
|-----------------|---|
| sample.id | sample IDs |
| H1 | a vector of HLA alleles |
| H2 | a vector of HLA alleles |
| max.resolution | "2-digit", "4-digit", "6-digit", "8-digit", "allele", "protein", "2", "4", "6", "8", "full" or "": "allele" = "2-digit", "protein" = "4-digit", "full" and "" indicating no limit on resolution |
| locus | the name of HLA locus: "A", "B", "C", "DRB1", "DRB5", "DQA1", "DQB1", "DPB1", or "any", where "any" indicates any other multiallelic locus |
| assembly | the human genome reference: "hg18", "hg19" (default), "hg20"; "auto" refers to "hg19"; "auto-silent" refers to "hg19" without any warning |
| locus.pos.start | the starting position in basepair |
| locus.pos.end | the end position in basepair |
| prob | the probabilities assigned to the samples |
| na.rm | if TRUE, remove the samples without valid HLA types |

Details

The format of H1 and H2 is "allele group : different protein : synonymous mutations in exons : synonymous mutations in introns"L, where the suffix L is express level (N, null; L, low; S, secreted; A, aberrant; Q: questionable). For example, "44:02:01:02L". If max.resolution is specified, the HLA alleles will be trimmed with a possible maximum resolution.

Value

Return a [hlaAlleleClass](#) object, and it is a list:

| | |
|-----------|--|
| locus | HLA locus |
| pos.start | the starting position in basepair |
| pos.end | the end position in basepair |
| value | a data frame |
| assembly | the human genome reference, such like "hg19" |

The component value includes:

| | |
|-----------|---------------------------|
| sample.id | sample ID |
| allele1 | HLA allele |
| allele2 | HLA allele |
| prob | the posterior probability |

Author(s)

Xiuwen Zheng

See Also

[hlaAlleleDigit](#), [hlaAlleleSubset](#)

Examples

```
head(HLA_Type_Table)
dim(HLA_Type_Table) # 60 13

# make a "hlaAlleleClass" object
hla.id <- "A"
hla <- hlaAllele(HLA_Type_Table$sample.id,
  H1 = HLA_Type_Table[, paste(hla.id, ".1", sep="")],
  H2 = HLA_Type_Table[, paste(hla.id, ".2", sep="")],
  locus=hla.id, assembly="hg19")
summary(hla)

# encode other loci
hlaAllele("HD0010", "1", "2", locus="NewLocus")
```

| | |
|----------------|--------------------------|
| hlaAlleleClass | <i>Class of HLA Type</i> |
|----------------|--------------------------|

Description

The definition of a class for HLA types, returned from [hlaAllele](#).

Value

There are following components:

| | |
|-----------|--|
| locus | HLA locus |
| pos.start | the starting position in basepair |
| pos.end | the end position in basepair |
| value | a data frame |
| assembly | the human genome reference, such like "hg19" |
| postprob | a matrix of all posterior probabilities |

The component value includes:

| | |
|-----------|---------------------------|
| sample.id | sample ID |
| allele1 | HLA allele |
| allele2 | HLA allele |
| prob | the posterior probability |

Author(s)

Xiuwen Zheng

See Also[hlaAllele](#)

| | |
|----------------|-------------------------|
| hlaAlleleDigit | <i>Trim HLA alleles</i> |
|----------------|-------------------------|

Description

Trim HLA alleles to specified width.

Usage

```
hlaAlleleDigit(obj, max.resolution="4-digit", rm.suffix=FALSE)
```

Arguments

| | |
|----------------|---|
| obj | should be a hlaAlleleClass object or characters |
| max.resolution | "2-digit", "4-digit", "6-digit", "8-digit", "allele", "protein", "2", "4", "6", "8", "full" or "": "allele" = "2-digit", "protein" = "4-digit", "full" and "" indicating no limit on resolution |
| rm.suffix | whether remove the suffix, e.g., for "01:22N", "N" is a suffix |

Details

Either HLA types or H1 H2 should be specified. The format of HLA types is "allele 1 / allele 2", e.g., "0512/0102". If max.resolution is specified, the HLA alleles will be trimmed with the maximum resolution.

Value

Return a [hlaAlleleClass](#) object if obj is [hlaAlleleClass](#)-type, or characters if obj is character-type.

Author(s)

Xiuwen Zheng

See Also[hlaAllele](#)

Examples

```
head(HLA_Type_Table)
dim(HLA_Type_Table) # 60 13

# make a "hlaAlleleClass" object
hla.id <- "A"
hla <- hlaAllele(HLA_Type_Table$sample.id,
  H1 = HLA_Type_Table[, paste(hla.id, ".1", sep="")],
  H2 = HLA_Type_Table[, paste(hla.id, ".2", sep="")],
  locus = hla.id, assembly="hg19")
summary(hla)

hla2 <- hlaAlleleDigit(hla, "2-digit")
summary(hla2)
```

| | |
|-----------------|----------------------------------|
| hlaAlleleSubset | <i>Get a subset of HLA types</i> |
|-----------------|----------------------------------|

Description

Get a subset of HLA types from an object of [hlaAlleleClass](#).

Usage

```
hlaAlleleSubset(hla, samp.sel=NULL)
```

Arguments

| | |
|----------|---|
| hla | an object of hlaAlleleClass |
| samp.sel | a logical vector, or an integer vector of indices |

Value

Return [hlaAlleleClass](#).

Author(s)

Xiuwen Zheng

See Also

[hlaAllele](#), [hlaAlleleDigit](#)

Examples

```

head(HLA_Type_Table)
dim(HLA_Type_Table) # 60 13

# make a "hlaAlleleClass" object
hla.id <- "A"
hla <- hlaAllele(HLA_Type_Table$sample.id,
  H1 = HLA_Type_Table[, paste(hla.id, ".1", sep="")],
  H2 = HLA_Type_Table[, paste(hla.id, ".2", sep="")],
  locus=hla.id, assembly="hg19")
summary(hla)

subhla <- hlaAlleleSubset(hla, 1:100)
summary(subhla)

```

| | |
|-----------------|---------------------------------|
| hlaAttrBagClass | <i>The class of HIBAG model</i> |
|-----------------|---------------------------------|

Description

The class of a HIBAG model, and its instance is returned from [hlaAttrBagging](#).

Value

Return a list of:

| | |
|-----------------|---|
| n.samp | the total number of training samples |
| n.snp | the total number of candidate SNP predictors |
| sample.id | the sample IDs |
| snp.id | the SNP IDs |
| snp.position | SNP position in basepair |
| snp.allele | a vector of characters with the format of "A allele/B allele" |
| snp.allele.freq | the allele frequencies |
| hla.locus | the name of HLA locus |
| hla.allele | the HLA alleles used in the model |
| hla.freq | the HLA allele frequencies |
| assembly | the human genome reference, such like "hg19" |
| model | internal use |
| appendix | an optional list: platform – supported platform(s); information – other information, like training sets, authors; warning – any warning message |

Author(s)

Xiuwen Zheng

See Also

[hlaAttrBagging](#), [hlaParallelAttrBagging](#), [hlaAttrBagObj](#)

| | |
|----------------|----------------------------|
| hlaAttrBagging | <i>Build a HIBAG model</i> |
|----------------|----------------------------|

Description

To build a HIBAG model for predicting HLA types.

Usage

```
hlaAttrBagging(hla, snp, nclassifier=100, mtry=c("sqrt", "all", "one"),
  prune=TRUE, rm.na=TRUE, verbose=TRUE, verbose.detail=FALSE)
```

Arguments

| | |
|----------------|--|
| hla | the training HLA types, an object of hlaAlleleClass |
| snp | the training SNP genotypes, an object of hlaSNPGenoClass |
| nclassifier | the total number of individual classifiers |
| mtry | a character or a numeric value, the number of variables randomly sampled as candidates for each selection. See details |
| prune | if TRUE, to perform a parsimonious forward variable selection, otherwise, exhaustive forward variable selection. See details |
| rm.na | if TRUE, remove the samples with missing HLA types |
| verbose | if TRUE, show information |
| verbose.detail | if TRUE, show more information |

Details

`mtry` (the number of variables randomly sampled as candidates for each selection): "sqrt", using the square root of the total number of candidate SNPs; "all", using all candidate SNPs; "one", using one SNP; an integer, specifying the number of candidate SNPs; $0 < r < 1$, the number of candidate SNPs is "r * the total number of SNPs".

`prune`: there is no significant difference on accuracy between parsimonious and exhaustive forward variable selections. If `prune=TRUE`, the searching algorithm performs a parsimonious forward variable selection: if a new SNP predictor reduces the current out-of-bag accuracy, then it is removed from the candidate SNP set for future searching. Parsimonious selection helps to improve the computational efficiency by reducing the searching times on non-informative SNP markers.

A parallel version of `hlaAttrBagging` is [hlaParallelAttrBagging](#).

Value

Return an object of `hlaAttrBagClass`:

| | |
|------------------------------|---|
| <code>n.samp</code> | the total number of training samples |
| <code>n.snp</code> | the total number of candidate SNP predictors |
| <code>sample.id</code> | the sample IDs |
| <code>snp.id</code> | the SNP IDs |
| <code>snp.position</code> | SNP position in basepair |
| <code>snp.allele</code> | a vector of characters with the format of "A allele/B allele" |
| <code>snp.allele.freq</code> | the allele frequencies |
| <code>hla.locus</code> | the name of HLA locus |
| <code>hla.allele</code> | the HLA alleles used in the model |
| <code>hla.freq</code> | the HLA allele frequencies |
| <code>assembly</code> | the human genome reference, such like "hg19" |
| <code>model</code> | internal use |

Author(s)

Xiuwen Zheng

References

Zheng X, Shen J, Cox C, Wakefield J, Ehm M, Nelson M, Weir BS; HIBAG – HLA Genotype Imputation with Attribute Bagging. *Pharmacogenomics Journal*. doi: 10.1038/tpj.2013.18. <http://www.nature.com/tpj/journal/v14/n2/full/tpj201318a.html>

See Also

[hlaClose](#), [hlaParallelAttrBagging](#), [summary.hlaAttrBagClass](#), [predict.hlaAttrBagClass](#)

Examples

```
# make a "hlaAlleleClass" object
hla.id <- "A"
hla <- hlaAllele(HLA_Type_Table$sample.id,
  H1 = HLA_Type_Table[, paste(hla.id, ".1", sep="")],
  H2 = HLA_Type_Table[, paste(hla.id, ".2", sep="")],
  locus=hla.id, assembly="hg19")

# divide HLA types randomly
set.seed(100)
hlatab <- hlaSplitAllele(hla, train.prop=0.5)
names(hlatab)
# "training" "validation"
summary(hlatab$training)
summary(hlatab$validation)
```

```

# SNP predictors within the flanking region on each side
region <- 500 # kb
snpid <- hlaFlankingSNP(HapMap_CEU_Geno$snp.id, HapMap_CEU_Geno$snp.position,
  hla.id, region*1000, assembly="hg19")
length(snpid) # 275

# training and validation genotypes
train.geno <- hlaGenoSubset(HapMap_CEU_Geno,
  snp.sel=match(snpid, HapMap_CEU_Geno$snp.id),
  samp.sel=match(hlatab$training$value$sample.id,
  HapMap_CEU_Geno$sample.id))
test.geno <- hlaGenoSubset(HapMap_CEU_Geno,
  samp.sel=match(hlatab$validation$value$sample.id,
  HapMap_CEU_Geno$sample.id))

# train a HIBAG model
set.seed(100)
# please use "nclassifier=100" when you use HIBAG for real data
model <- hlaAttrBagging(hlatab$training, train.geno, nclassifier=4,
  verbose.detail=TRUE)
summary(model)

# validation
pred <- predict(model, test.geno)
summary(pred)

# compare
(comp <- hlaCompareAllele(hlatab$validation, pred, allele.limit=model,
  call.threshold=0))
(comp <- hlaCompareAllele(hlatab$validation, pred, allele.limit=model,
  call.threshold=0.5))

# save the parameter file
mobj <- hlaModelToObj(model)
save(mobj, file="HIBAG_model.RData")
save(test.geno, file="testgeno.RData")
save(hlatab, file="HLASplit.RData")

# Clear Workspace
hlaClose(model) # release all resources of model
rm(list = ls())

#####

# NOW, load a HIBAG model from the parameter file
mobj <- get(load("HIBAG_model.RData"))
model <- hlaModelFromObj(mobj)

# validation
test.geno <- get(load("testgeno.RData"))

```

```

hlatab <- get(load("HLASplit.RData"))

pred <- predict(model, test.geno, type="response")
summary(pred)

# compare
(comp <- hlaCompareAllele(hlatab$validation, pred, allele.limit=model,
  call.threshold=0))
(comp <- hlaCompareAllele(hlatab$validation, pred, allele.limit=model,
  call.threshold=0.5))

# delete the temporary files
unlink(c("HIBAG_model.RData", "testgeno.RData", "HLASplit.RData"), force=TRUE)

```

hlaAttrBagObj

The class of HIBAG object

Description

The class of a HIBAG object, which can be saved in the .RData file.

Value

A list of:

| | |
|-----------------|---|
| n.samp | the total number of training samples |
| n.snp | the total number of candidate SNP predictors |
| sample.id | the sample IDs |
| snp.id | the SNP IDs |
| snp.position | SNP position in basepair |
| snp.allele | a vector of characters with the format of "A allele/B allele" |
| snp.allele.freq | the allele frequencies |
| hla.locus | the name of HLA locus |
| hla.allele | the HLA alleles used in the model |
| hla.freq | the HLA allele frequencies |
| assembly | the human genome reference, such like "hg19" |
| classifiers | a list of all classifiers (described as follows) |
| appendix | platform – supported platform(s); information – other information, like training sets, authors; warning – any warning message |

classifiers has the following components:

| | |
|----------|---|
| samp.num | the number of copies of samples in a bootstrap sample |
|----------|---|

| | |
|--------------|--|
| haplos | a data.frame of haplotype frequencies freq – haplotype frequency hla – a HLA allele haplo – a SNP haplotype, with an entry value 0 standing for B (ZERO A allele), 1 for A (ONE A allele) |
| snpidx | the SNP indices used in this classifier |
| outofbag.acc | the out-of-bag accuracy of this classifier |

Author(s)

Xiuwen Zheng

See Also

[hlaAttrBagging](#), [hlaParallelAttrBagging](#), [hlaModelToObj](#), [hlaModelFiles](#), [hlaAttrBagClass](#)

| | |
|-------------|--------------------------------------|
| hlaBED2Geno | <i>Convert from PLINK BED format</i> |
|-------------|--------------------------------------|

Description

To convert a PLINK BED file to an object of [hlaSNPGenoClass](#).

Usage

```
hlaBED2Geno(bed.fn, fam.fn, bim.fn, rm.invalid.allele=FALSE,
            import.chr="xMHC", assembly="auto", verbose=TRUE)
```

Arguments

| | |
|-------------------|--|
| bed.fn | binary file, genotype information |
| fam.fn | family, individual information, etc |
| bim.fn | extended MAP file: two extra cols = allele names |
| rm.invalid.allele | if TRUE, remove SNPs with invalid alleles |
| import.chr | the chromosome, "1" .. "22", "X", "Y", "XY", "MT", "xMHC", or "", where "xMHC" implies the extended MHC on chromosome 6, and "" for all SNPs |
| assembly | the human genome reference: "hg18", "hg19" (default), "hg20"; "auto" refers to "hg19"; "auto-silent" refers to "hg19" without any warning |
| verbose | if TRUE, show information |

Value

Return an object of [hlaSNPGenoClass](#).

Author(s)

Xiuwen Zheng

See Also[hlaGeno2PED](#), [hlaGDS2Geno](#)**Examples**

```
# Import a PLINK BED file
bed.fn <- system.file("extdata", "HapMap_CEU.bed", package="HIBAG")
fam.fn <- system.file("extdata", "HapMap_CEU.fam", package="HIBAG")
bim.fn <- system.file("extdata", "HapMap_CEU.bim", package="HIBAG")

hapmap.ceu <- hlaBED2Geno(bed.fn, fam.fn, bim.fn, assembly="hg19")
summary(hapmap.ceu)

# Or

hapmap.ceu <- hlaBED2Geno(bed.fn, fam.fn, bim.fn, assembly="hg19",
  rm.invalid.allele=TRUE, import.chr="6")
summary(hapmap.ceu)
```

hlaCheckSNPs

*Check the SNP predictors in a HIBAG model***Description**

Check the SNP predictors in a HIBAG model, by calculating the overlapping between the model and SNP genotypes.

Usage

```
hlaCheckSNPs(model, object,
  match.type=c("RefSNP+Position", "RefSNP", "Position"), verbose=TRUE)
```

Arguments

| | |
|------------|--|
| model | an object of hlaAttrBagClass , or an object of hlaAttrBagObj |
| object | a genotype object of hlaSNPGenoClass , or a character vector like <code>c("rs2523442", "rs9257863", ...)</code> |
| match.type | "RefSNP+Position" (by default) – using both of RefSNP IDs and positions; "RefSNP" – using RefSNP IDs only; "Position" – using positions only |
| verbose | if TRUE, show information |

Value

Return a data.frame for individual classifiers:

| | |
|---------------|--|
| NumOfValidSNP | the number of non-missing SNPs in an individual classifier |
| NumOfSNP | the number of SNP predictors in an individual classifier |
| fraction | NumOfValidSNP / NumOfSNP |

Author(s)

Xiuwen Zheng

See Also

[hlaAttrBagging](#), [predict.hlaAttrBagClass](#)

Examples

```
# make a "hlaAlleleClass" object
hla.id <- "DQB1"
hla <- hlaAllele(HLA_Type_Table$sample.id,
  H1 = HLA_Type_Table[, paste(hla.id, ".1", sep="")],
  H2 = HLA_Type_Table[, paste(hla.id, ".2", sep="")],
  locus=hla.id, assembly="hg19")

# training genotypes
region <- 100 # kb
snpid <- hlaFlankingSNP(HapMap_CEU_Geno$snp.id, HapMap_CEU_Geno$snp.position,
  hla.id, region*1000, assembly="hg19")
train.geno <- hlaGenoSubset(HapMap_CEU_Geno,
  snp.sel = match(snpid, HapMap_CEU_Geno$snp.id))

# train a HIBAG model
set.seed(1000)
model <- hlaAttrBagging(hla, train.geno, nclassifier=2)
print(model)

hlaCheckSNPs(model, train.geno)

# close the HIBAG model explicitly
hlaClose(model)
```

hlaClose

Dispose a model object

Description

Release all resources stored in the [hlaAttrBagClass](#) object. The HIBAG package allows up to 256 [hlaAttrBagClass](#) objects stored in memory.

Usage

```
hlaClose(model)
```

Arguments

model an object of [hlaAttrBagClass](#)

Value

None.

Author(s)

Xiuwen Zheng

See Also

[hlaAttrBagging](#), [summary.hlaAttrBagClass](#)

Examples

```
# make a "hlaAlleleClass" object
hla.id <- "DQB1"
hla <- hlaAllele(HLA_Type_Table$sample.id,
  H1 = HLA_Type_Table[, paste(hla.id, ".1", sep="")],
  H2 = HLA_Type_Table[, paste(hla.id, ".2", sep="")],
  locus=hla.id, assembly="hg19")

# training genotypes
region <- 100 # kb
snpid <- hlaFlankingSNP(HapMap_CEU_Geno$snp.id, HapMap_CEU_Geno$snp.position,
  hla.id, region*1000, assembly="hg19")
train.geno <- hlaGenoSubset(HapMap_CEU_Geno,
  snp.sel = match(snpid, HapMap_CEU_Geno$snp.id))

# train a HIBAG model
set.seed(1000)
model <- hlaAttrBagging(hla, train.geno, nclassifier=2)
print(model)

# close the HIBAG model explicitly
hlaClose(model)
```

hlaCombineAllele *Combine two datasets of HLA types*

Description

Get a subset of HLA types from an object of [hlaAlleleClass](#).

Usage

```
hlaCombineAllele(H1, H2)
```

Arguments

H1 the first [hlaAlleleClass](#) object
H2 the second [hlaAlleleClass](#) object

Value

Return [hlaAlleleClass](#).

Author(s)

Xiuwen Zheng

See Also

[hlaAllele](#), [hlaAlleleSubset](#)

Examples

```
head(HLA_Type_Table)
dim(HLA_Type_Table) # 60 13

# make a "hlaAlleleClass" object
hla.id <- "C"
hla <- hlaAllele(HLA_Type_Table$sample.id,
  HLA_Type_Table[, paste(hla.id, ".1", sep="")],
  HLA_Type_Table[, paste(hla.id, ".2", sep="")],
  locus=hla.id, assembly="hg19")
summary(hla)

subhla1 <- hlaAlleleSubset(hla, 1:100)
summary(subhla1)
subhla2 <- hlaAlleleSubset(hla, 201:300)
summary(subhla2)

H <- hlaCombineAllele(subhla1, subhla2)
summary(H)
```

hlaCombineModelObj *Combine two HIBAG models together*

Description

Merge two objects of [hlaAttrBagObj](#) together, which is useful for building an ensemble model in parallel.

Usage

```
hlaCombineModelObj(obj1, obj2)
```

Arguments

obj1 an object of [hlaAttrBagObj](#)
obj2 an object of [hlaAttrBagObj](#)

Value

Return an object of [hlaAttrBagObj](#).

Author(s)

Xiuwen Zheng

See Also

[hlaAttrBagging](#), [hlaModelFiles](#)

Examples

```
# make a "hlaAlleleClass" object
hla.id <- "A"
hla <- hlaAllele(HLA_Type_Table$sample.id,
  H1 = HLA_Type_Table[, paste(hla.id, ".1", sep="")],
  H2 = HLA_Type_Table[, paste(hla.id, ".2", sep="")],
  locus=hla.id, assembly="hg19")

# SNP predictors within the flanking region on each side
region <- 500 # kb
snpid <- hlaFlankingSNP(HapMap_CEU_Geno$snp.id, HapMap_CEU_Geno$snp.position,
  hla.id, region*1000, assembly="hg19")
length(snpid) # 275

# training genotypes
train.geno <- hlaGenoSubset(HapMap_CEU_Geno,
  snp.sel = match(snpid, HapMap_CEU_Geno$snp.id))

# train a HIBAG model
```

```

set.seed(100)
m1 <- hlaAttrBagging(hla, train.geno, nclassifier=1)
m2 <- hlaAttrBagging(hla, train.geno, nclassifier=1)

m1.obj <- hlaModelToObj(m1)
m2.obj <- hlaModelToObj(m2)

m.obj <- hlaCombineModelObj(m1.obj, m2.obj)
summary(m.obj)

```

hlaCompareAllele *Evaluate prediction accuracies*

Description

To evaluate the overall accuracy, sensitivity, specificity, positive predictive value, negative predictive value.

Usage

```

hlaCompareAllele(TrueHLA, PredHLA, allele.limit=NULL, call.threshold=NaN,
  max.resolution="", output.individual=FALSE, verbose=TRUE)

```

Arguments

| | |
|-------------------|--|
| TrueHLA | an object of hlaAlleleClass , the true HLA types |
| PredHLA | an object of hlaAlleleClass , the predicted HLA types |
| allele.limit | a list of HLA alleles, the validation samples are limited to those having HLA alleles in <code>allele.limit</code> , or NULL for no limit. <code>allele.limit</code> could be character-type, hlaAttrBagClass or hlaAttrBagObj |
| call.threshold | the call threshold for posterior probability, i.e., call or no call is determined by whether <code>prob >= call.threshold</code> or not |
| max.resolution | "2-digit", "4-digit", "6-digit", "8-digit", "allele", "protein", "2", "4", "6", "8", "full" or "": "allele" = "2-digit", "protein" = "4-digit", "full" and "" indicating no limit on resolution |
| output.individual | if TRUE, output accuracy for each individual |
| verbose | if TRUE, show information |

Value

Return a `list(overall, confusion, detail)`, or `list(overall, confusion, detail, individual)` if `output.individual=TRUE`.

`overall` (data.frame):

`total.num.ind` the total number of individuals

| | |
|---|---|
| <code>crt.num.ind</code> | the number of individuals with correct HLA types |
| <code>crt.num.haplo</code> | the number of chromosomes with correct HLA alleles |
| <code>acc.ind</code> | the proportion of individuals with correctly predicted HLA types (i.e., both of alleles are correct, the accuracy of an individual is 0 or 1.) |
| <code>acc.haplo</code> | the proportion of chromosomes with correctly predicted HLA alleles (i.e., the accuracy of an individual is 0, 0.5 or 1, since an individual has two alleles.) |
| <code>call.threshold</code> | call threshold, if it is NaN, no call threshold is executed |
| <code>n.call</code> | the number of individuals with call |
| <code>call.rate</code> | overall call rate |
| confusion (matrix): a confusion matrix. | |
| detail (data.frame): | |
| <code>allele</code> | HLA alleles |
| <code>train.num</code> | the number of training haplotypes |
| <code>train.freq</code> | the training haplotype frequencies |
| <code>valid.num</code> | the number of validation haplotypes |
| <code>valid.freq</code> | the validation haplotype frequencies |
| <code>call.rate</code> | the call rates for HLA alleles |
| <code>accuracy</code> | allele accuracy |
| <code>sensitivity</code> | sensitivity |
| <code>specificity</code> | specificity |
| <code>ppv</code> | positive predictive value |
| <code>npv</code> | negative predictive value |
| <code>miscall</code> | the most likely miss-called alleles |
| <code>miscall.prop</code> | the proportions of the most likely miss-called allele in all miss-called alleles |
| individual (data.frame): | |
| <code>sample.id</code> | sample id |
| <code>true.hla</code> | the true HLA type |
| <code>pred.hla</code> | the prediction of HLA type |
| <code>accuracy</code> | accuracy, 0, 0.5, or 1 |

Author(s)

Xiuwen Zheng

See Also[hlaAttrBagging](#), [predict.hlaAttrBagClass](#), [hlaReport](#)

Examples

```

# make a "hlaAlleleClass" object
hla.id <- "A"
hla <- hlaAllele(HLA_Type_Table$sample.id,
  H1 = HLA_Type_Table[, paste(hla.id, ".1", sep="")],
  H2 = HLA_Type_Table[, paste(hla.id, ".2", sep="")],
  locus=hla.id, assembly="hg19")

# divide HLA types randomly
set.seed(100)
hlatab <- hlaSplitAllele(hla, train.prop=0.5)
names(hlatab)
# "training" "validation"
summary(hlatab$training)
summary(hlatab$validation)

# SNP predictors within the flanking region on each side
region <- 500 # kb
snpid <- hlaFlankingSNP(HapMap_CEU_Geno$snp.id, HapMap_CEU_Geno$snp.position,
  hla.id, region*1000, assembly="hg19")
length(snpid) # 275

# training and validation genotypes
train.geno <- hlaGenoSubset(HapMap_CEU_Geno,
  snp.sel=match(snpid, HapMap_CEU_Geno$snp.id),
  samp.sel=match(hlatab$training$value$sample.id,
  HapMap_CEU_Geno$sample.id))
test.geno <- hlaGenoSubset(HapMap_CEU_Geno,
  samp.sel=match(hlatab$validation$value$sample.id,
  HapMap_CEU_Geno$sample.id))

# train a HIBAG model
set.seed(100)
model <- hlaAttrBagging(hlatab$training, train.geno, nclassifier=4,
  verbose.detail=TRUE)
summary(model)

# validation
pred <- predict(model, test.geno)
# compare
(comp <- hlaCompareAllele(hlatab$validation, pred, allele.limit=model,
  call.threshold=0))
(comp <- hlaCompareAllele(hlatab$validation, pred, allele.limit=model,
  call.threshold=0.5))

```

hlaErrMsg

The last error message

Description

Return the last error message.

Usage

```
hlaErrMsg()
```

Value

Character

Author(s)

Xiuwen Zheng

Examples

```
hlaErrMsg()
```

| | |
|----------------|-----------------------------------|
| hlaFlankingSNP | <i>SNP IDs in Flanking Region</i> |
|----------------|-----------------------------------|

Description

To select SNPs in the flanking region of a specified HLA locus.

Usage

```
hlaFlankingSNP(snp.id, position, hla.id, flank.bp=500*1000, assembly="auto")
```

Arguments

| | |
|----------|---|
| snp.id | a vector of SNP IDs |
| position | a vector of positions |
| hla.id | the name of HLA locus |
| flank.bp | the size of flanking region on each side in basepair |
| assembly | the human genome reference: "hg18", "hg19" (default), "hg20"; "auto" refers to "hg19"; "auto-silent" refers to "hg19" without any warning |

Details

hla.id is "A", "B", "C", "DRB1", "DRB5", "DQA1", "DQB1", "DPB1" or "any".

Value

Return allele frequencies.

Author(s)

Xiuwen Zheng

See Also

[hlaGenoSubset](#), [hlaLociInfo](#)

Examples

```
# make a "hlaAlleleClass" object
hla.id <- "A"
hla <- hlaAllele(HLA_Type_Table$sample.id,
  H1 = HLA_Type_Table[, paste(hla.id, ".1", sep="")],
  H2 = HLA_Type_Table[, paste(hla.id, ".2", sep="")],
  locus=hla.id, assembly="hg19")

# training genotypes
region <- 500 # kb
snpid <- hlaFlankingSNP(HapMap_CEU_Geno$snp.id, HapMap_CEU_Geno$snp.position,
  hla.id, region*1000, assembly="hg19")

train.geno <- hlaGenoSubset(HapMap_CEU_Geno,
  snp.sel = match(snpid, HapMap_CEU_Geno$snp.id),
  samp.sel = match(hla$training$value$sample.id, HapMap_CEU_Geno$sample.id))
summary(train.geno)
```

hlaGDS2Geno

Convert from SNP GDS format

Description

To convert a SNP GDS file to an object of [hlaSNPGenoClass](#).

Usage

```
hlaGDS2Geno(gds.fn, rm.invalid.allele=FALSE, import.chr="xMHC",
  assembly="auto", verbose=TRUE)
```

Arguments

| | |
|--------------------------------|--|
| <code>gds.fn</code> | the SNP GDS file used by the SNPRelate package |
| <code>rm.invalid.allele</code> | if TRUE, remove SNPs with invalid alleles |
| <code>import.chr</code> | the chromosome, "1" .. "22", "X", "Y", "XY", "MT", "xMHC", or "", where "xMHC" implies the extended MHC on chromosome 6, and "" for all SNPs |
| <code>assembly</code> | the human genome reference: "hg18", "hg19" (default), "hg20"; "auto" refers to "hg19"; "auto-silent" refers to "hg19" without any warning |
| <code>verbose</code> | if TRUE, show information |

Value

Return an object of [hlaSNPGenoClass](#).

Author(s)

Xiuwen Zheng

See Also[hlaGeno2PED](#), [hlaBED2Geno](#)**Examples**

```
# Import a SNP GDS file
fn <- system.file("extdata", "HapMap_CEU_Chr6.gds", package="HIBAG")

geno <- hlaGDS2Geno(fn, assembly="hg18",
  rm.invalid.allele=TRUE, import.chr="6")

summary(geno)
```

`hlaGeno2PED`*Convert to PLINK PED format*

Description

Convert an object of [hlaSNPGenoClass](#) to a file of PLINK PED format.

Usage

```
hlaGeno2PED(geno, out.fn)
```

Arguments

| | |
|---------------------|--|
| <code>geno</code> | a genotype object of hlaSNPGenoClass |
| <code>out.fn</code> | the file name of output ped file |

Details

Two files ".map" and ".ped" are created.

Value

None.

Author(s)

Xiuwen Zheng

See Also[hlaBED2Geno](#)

Examples

```
# make a "hlaAlleleClass" object
hla.id <- "A"
hla <- hlaAllele(HLA_Type_Table$sample.id,
  H1 = HLA_Type_Table[, paste(hla.id, ".1", sep="")],
  H2 = HLA_Type_Table[, paste(hla.id, ".2", sep="")],
  max.resolution=4, locus=hla.id, assembly="hg19")

# training genotypes
region <- 500 # kb
snpid <- hlaFlankingSNP(HapMap_CEU_Geno$snp.id, HapMap_CEU_Geno$snp.position,
  hla.id, region*1000, assembly="hg19")

train.geno <- hlaGenoSubset(HapMap_CEU_Geno,
  snp.sel = match(snpid, HapMap_CEU_Geno$snp.id))

hlaGeno2PED(train.geno, "test")

# delete the temporary files
unlink(c("test.map", "test.ped"), force=TRUE)
```

hlaGenoAFreq

Allele Frequency

Description

To calculate the allele frequencies from genotypes or haplotypes.

Usage

```
hlaGenoAFreq(obj)
```

Arguments

obj an object of [hlaSNPGenoClass](#)

Value

Return allele frequencies.

Author(s)

Xiuwen Zheng

See Also

[hlaGenoAFreq](#), [hlaGenoMFreq](#), [hlaGenoMRate](#), [hlaGenoMRate_Samp](#)

Examples

```
summary(HapMap_CEU_Geno)

summary(hlaGenoAFreq(HapMap_CEU_Geno))
```

| | |
|----------------|---|
| hlaGenoCombine | <i>Combine two genotypic data sets into one</i> |
|----------------|---|

Description

To combine two genotypic data sets into one dataset.

Usage

```
hlaGenoCombine(geno1, geno2,
  match.type=c("RefSNP+Position", "RefSNP", "Position"),
  allele.check=TRUE, same.strand=FALSE, verbose=TRUE)
```

Arguments

| | |
|--------------|--|
| geno1 | the first genotype object of hlaSNPGenoClass |
| geno2 | the second genotype object of hlaSNPGenoClass |
| match.type | "RefSNP+Position" (by default) – using both of RefSNP IDs and positions; "RefSNP" – using RefSNP IDs only; "Position" – using positions only |
| allele.check | if TRUE, call hlaGenoSwitchStrand to check and then switch allele pairs if needed |
| same.strand | TRUE assuming alleles are on the same strand (e.g., forward strand); otherwise, FALSE not assuming whether on the same strand or not |
| verbose | show information, if TRUE |

Details

The function merges two SNP dataset geno1 and geno2, and returns a SNP dataset consisting of the SNP intersect between geno1 and geno2, and having the same SNP information (allele and position) as geno1.

Value

An object of [hlaSNPGenoClass](#).

Author(s)

Xiuwen Zheng

See Also

[hlaMakeSNPGeno](#), [hlaGenoSubset](#)

Examples

```
# import a PLINK BED file
bed.fn <- system.file("extdata", "HapMap_CEU.bed", package="HIBAG")
fam.fn <- system.file("extdata", "HapMap_CEU.fam", package="HIBAG")
bim.fn <- system.file("extdata", "HapMap_CEU.bim", package="HIBAG")
hapmap.ceu <- hlaBED2Geno(bed.fn, fam.fn, bim.fn, assembly="hg19")

# combine two datasets together
geno <- hlaGenoCombine(HapMap_CEU_Geno, hapmap.ceu)
summary(geno)
```

hlaGenoLD

Composite Linkage Disequilibrium

Description

To calculate composite linkage disequilibrium (r^2) between HLA locus and SNP markers.

Usage

```
hlaGenoLD(hla, geno)
```

Arguments

| | |
|------|---|
| hla | an object of hlaAlleleClass |
| geno | an object of hlaSNPGenoClass , or a vector or matrix for SNP data |

Value

Return a vector of linkage disequilibrium (r^2) for each SNP marker.

Author(s)

Xiuwen Zheng

References

Weir BS, Cockerham CC: Complete characterization of disequilibrium at two loci; in Feldman MW (ed): Mathematical Evolutionary Theory. Princeton, NJ: Princeton University Press, 1989.

Zaykin, D. V., Pudovkin, A., and Weir, B. S. (2008). Correlation-based inference for linkage disequilibrium with multiple alleles. *Genetics* 180, 533-545.

Examples

```

# plot linkage disequilibrium
ymax <- 0.16
plot(NA, NA, xlab="SNP Position (in KB)",
     ylab="Composite Linkage Disequilibrium (r2)",
     xlim=range(HapMap_CEU_Geno$snp.position)/1000, ylim=c(0, ymax),
     main="Major Histocompatibility Complex")

hla.list <- c("A", "C", "DQA1")
col.list <- 1:3

# for-loop
for (i in 1:3)
{
  hla.id <- hla.list[i]

  # make a "hlaAlleleClass" object
  hla <- hlaAllele(HLA_Type_Table$sample.id,
                  H1 = HLA_Type_Table[, paste(hla.id, ".1", sep="")],
                  H2 = HLA_Type_Table[, paste(hla.id, ".2", sep="")],
                  locus=hla.id, assembly="hg19")

  # linkage disequilibrium between HLA locus and SNP markers
  ld <- hlaGenoLD(hla, HapMap_CEU_Geno)

  # draw
  points(HapMap_CEU_Geno$snp.position/1000, ld, pch="*", col=i)
  x <- (hla$pos.start/1000 + hla$pos.end/1000)/2
  abline(v=x, col=col.list[i], lty=3, lwd=2.5)
  points(x, ymax, pch=25, col=7, bg=col.list[i], cex=1.5)
}
legend("topleft", col=col.list, pt.bg=col.list, text.col=col.list, pch=25,
      legend=paste("HLA -", hla.list))

```

hlaGenoMFreq

Minor Allele Frequency

Description

To calculate the minor allele frequencies from genotypes or haplotypes.

Usage

```
hlaGenoMFreq(obj)
```

Arguments

obj an object of [hlaSNPGenoClass](#)

Value

Return minor allele frequencies.

Author(s)

Xiuwen Zheng

See Also

[hlaGenoAFreq](#), [hlaGenoMFreq](#), [hlaGenoMRate](#), [hlaGenoMRate_Samp](#)

Examples

```
summary(HapMap_CEU_Geno)
```

```
summary(hlaGenoMFreq(HapMap_CEU_Geno))
```

hlaGenoMRate

Missing Rates Per SNP

Description

To calculate the missing rates from genotypes or haplotypes per SNP.

Usage

```
hlaGenoMRate(obj)
```

Arguments

obj an object of [hlaSNPGenoClass](#)

Value

Return missing rates per SNP.

Author(s)

Xiuwen Zheng

See Also

[hlaGenoAFreq](#), [hlaGenoMFreq](#), [hlaGenoMRate](#), [hlaGenoMRate_Samp](#)

Examples

```
summary(HapMap_CEU_Geno)
```

```
summary(hlaGenoMRate(HapMap_CEU_Geno))
```

| | |
|-------------------|---------------------------------|
| hlaGenoMRate_Samp | <i>Missing Rates Per Sample</i> |
|-------------------|---------------------------------|

Description

To calculate the missing rates from genotypes or haplotypes per sample.

Usage

```
hlaGenoMRate_Samp(obj)
```

Arguments

obj an object of [hlaSNPGenoClass](#)

Value

Return missing rates per sample.

Author(s)

Xiuwen Zheng

See Also

[hlaGenoAFreq](#), [hlaGenoMFreq](#), [hlaGenoMRate](#), [hlaGenoMRate_Samp](#)

Examples

```
summary(HapMap_CEU_Geno)
summary(hlaGenoMRate_Samp(HapMap_CEU_Geno))
```

| | |
|---------------|----------------------------------|
| hlaGenoSubset | <i>Get a subset of genotypes</i> |
|---------------|----------------------------------|

Description

To get a subset of genotypes from a [hlaSNPGenoClass](#) object.

Usage

```
hlaGenoSubset(genoobj, samp.sel=NULL, snp.sel=NULL)
```

Arguments

| | |
|-----------------------|--|
| <code>genoobj</code> | a genotype object of hlaSNPGenoClass |
| <code>samp.sel</code> | a logical vector, or an integer vector of indices |
| <code>snp.sel</code> | a logical vector, or an integer vector of indices |

Details

`genoobj$genotype` is a numeric matrix, with an entry value 0 standing for BB (ZERO A allele), 1 for AB (ONE A allele), 2 for AA (TWO A alleles) and others for missing values (missing genotypes are usually set to be NA).

Value

Return a [hlaSNPGenoClass](#) object, and it is a list:

| | |
|---------------------------|---|
| <code>genotype</code> | a genotype matrix, “# of SNPs” - by - “# of individuals” |
| <code>sample.id</code> | a vector of sample IDs |
| <code>snp.id</code> | a vector of SNP IDs |
| <code>snp.position</code> | a vector of SNP positions in basepair |
| <code>snp.allele</code> | a vector of characters with the format of “A allele/B allele” |

Author(s)

Xiuwen Zheng

See Also

[hlaMakeSNPGeno](#), [hlaGenoCombine](#)

Examples

```
summary(HapMap_CEU_Geno)

geno <- hlaGenoSubset(HapMap_CEU_Geno,
  snp.sel = (hlaGenoMFreq(HapMap_CEU_Geno)>0.10))
summary(geno)
```

hlaGenoSwitchStrand *Allele switching*

Description

Determine the ordered pair of A and B alleles, using the allele information provided by template.

Usage

```
hlaGenoSwitchStrand(target, template,  
    match.type=c("RefSNP+Position", "RefSNP", "Position"),  
    same.strand=FALSE, verbose=TRUE)
```

Arguments

| | |
|-------------|--|
| target | an object of hlaSNPGenoClass |
| template | a genotypic object of hlaSNPGenoClass , a model object of hlaAttrBagClass or a model object of hlaAttrBagObj |
| match.type | "RefSNP+Position" (by default) – using both of RefSNP IDs and positions; "RefSNP" – using RefSNP IDs only; "Position" – using positions only |
| same.strand | TRUE assuming alleles are on the same strand (e.g., forward strand); otherwise, FALSE not assuming whether on the same strand or not |
| verbose | show information, if TRUE |

Details

The A/B pairs of target are determined using the information from template.

Value

Return a [hlaSNPGenoClass](#) object consisting of the SNP intersect between target and template.

Author(s)

Xiuwen Zheng

See Also

[hlaMakeSNPGeno](#), [hlaGenoSubset](#)

Examples

```
summary(HapMap_CEU_Geno)
# A/C A/G C/T G/T
# 136 655 632 141

# import a PLINK BED file
bed.fn <- system.file("extdata", "HapMap_CEU.bed", package="HIBAG")
fam.fn <- system.file("extdata", "HapMap_CEU.fam", package="HIBAG")
bim.fn <- system.file("extdata", "HapMap_CEU.bim", package="HIBAG")
hapmap.ceu <- hlaBED2Geno(bed.fn, fam.fn, bim.fn, assembly="hg19")
summary(hapmap.ceu)
# A/C A/G A/T C/G C/T G/T
# 332 1567 64 111 1510 348

# combine two datasets together
geno <- hlaGenoSwitchStrand(HapMap_CEU_Geno, hapmap.ceu)
summary(geno)
# There are 1564 SNPs in common.
# The allele pairs of 763 SNPs need to be switched.
# A/C A/G C/T G/T
# 104 505 496 109
```

hlaLociInfo

HLA Locus Information

Description

To get the starting and ending positions in basepair of HLA loci.

Usage

```
hlaLociInfo(assembly=c("auto", "auto-silent", "hg18", "hg19", "hg20",
"unknown"))
```

Arguments

assembly the human genome reference: "hg18", "hg19" (default), "hg20"; "auto" refers to "hg19"; "auto-silent" refers to "hg19" without any warning

Value

Return a data frame include the genomic locations.

Author(s)

Xiuwen Zheng

References

NCBI Resources: <http://www.ncbi.nlm.nih.gov/gene>, HLA Nomenclature: <http://hla.alleles.org/genes/index.html>

Examples

```
hlaLociInfo()
```

| | |
|----------------|-----------------------------------|
| hlaMakeSNPGeno | <i>Make a SNP genotype object</i> |
|----------------|-----------------------------------|

Description

To create a `hlaSNPGenoClass` object (SNP genotypic object).

Usage

```
hlaMakeSNPGeno(genotype, sample.id, snp.id, snp.position,
               A.allele, B.allele, assembly="auto")
```

Arguments

| | |
|--------------|---|
| genotype | a genotype matrix, “# of SNPs” - by - “# of individuals” |
| sample.id | a vector of sample IDs |
| snp.id | a vector of SNP IDs |
| snp.position | a vector of SNP positions |
| A.allele | a vector of A alleles in the SNP list |
| B.allele | a vector of B alleles in the SNP list |
| assembly | the human genome reference: "hg18", "hg19" (default), "hg20"; "auto" refers to "hg19"; "auto-silent" refers to "hg19" without any warning |

Details

genotype is a numeric matrix, with an entry value 0 standing for BB (ZERO A allele), 1 for AB (ONE A allele), 2 for AA (TWO A alleles) and others for missing values (missing genotypes are usually set to be NA).

Value

Return a `hlaSNPGenoClass` object, and it is a list:

| | |
|--------------|---|
| genotype | a genotype matrix, “# of SNPs” - by - “# of individuals” |
| sample.id | a vector of sample IDs |
| snp.id | a vector of SNP IDs |
| snp.position | a vector of SNP positions in basepair |
| snp.allele | a vector of characters with the format of “A allele/B allele” |
| assembly | the human genome reference |

Author(s)

Xiuwen Zheng

See Also

[hlaGenoSubset](#), [hlaGenoCombine](#)

Examples

```
summary(HapMap_CEU_Geno)

allele <- strsplit(HapMap_CEU_Geno$snp.allele, "/")
A.allele <- sapply(allele, function(x) { x[1] })
B.allele <- sapply(allele, function(x) { x[2] })

geno <- hlaMakeSNPGeno(HapMap_CEU_Geno$genotype, HapMap_CEU_Geno$sample.id,
  HapMap_CEU_Geno$snp.id, HapMap_CEU_Geno$snp.position, A.allele, B.allele,
  assembly="hg19")

summary(geno)
```

hlaModelFiles

Load a model object from files

Description

To load HIBAG models from a list of files, and merge all together.

Usage

```
hlaModelFiles(fn.list, action.missingfile=c("ignore", "stop"), verbose=TRUE)
```

Arguments

| | |
|--------------------|---|
| fn.list | a vector of file names |
| action.missingfile | "ignore", ignore the missing files, by default; "stop", stop if missing |
| verbose | if TRUE, show information |

Value

Return [hlaAttrBagObj](#).

Author(s)

Xiuwen Zheng

See Also

[hlaAttrBagging](#), [hlaModelToObj](#)

Examples

```
# make a "hlaAlleleClass" object
hla.id <- "C"
hla <- hlaAllele(HLA_Type_Table$sample.id,
  H1 = HLA_Type_Table[, paste(hla.id, ".1", sep="")],
  H2 = HLA_Type_Table[, paste(hla.id, ".2", sep="")],
  locus=hla.id, assembly="hg19")

# training genotypes
region <- 100 # kb
snpid <- hlaFlankingSNP(HapMap_CEU_Geno$snp.id, HapMap_CEU_Geno$snp.position,
  hla.id, region*1000, assembly="hg19")
train.geno <- hlaGenoSubset(HapMap_CEU_Geno,
  snp.sel = match(snpid, HapMap_CEU_Geno$snp.id),
  samp.sel = match(hla$value$sample.id, HapMap_CEU_Geno$sample.id))

#
# train HIBAG models
#
set.seed(1000)

model1 <- hlaAttrBagging(hla, train.geno, nclassifier=1)
mobj1 <- hlaModelToObj(model1)
save(mobj1, file="tm1.RData")

model2 <- hlaAttrBagging(hla, train.geno, nclassifier=1)
mobj2 <- hlaModelToObj(model2)
save(mobj2, file="tm2.RData")

model3 <- hlaAttrBagging(hla, train.geno, nclassifier=1)
mobj3 <- hlaModelToObj(model3)
save(mobj3, file="tm3.RData")

# load all of mobj1, mobj2 and mobj3
mobj <- hlaModelFiles(c("tm1.RData", "tm2.RData", "tm3.RData"))
summary(mobj)

# delete the temporary files
unlink(c("tm1.RData", "tm2.RData", "tm3.RData"), force=TRUE)
```

hlaModelFromObj

Conversion between the in-memory model and the object that can be saved in a file

Description

Build a model [hlaAttrBagClass](#) from an object of [hlaAttrBagObj](#) which is stored in an R object file, or convert [hlaAttrBagClass](#) to [hlaAttrBagObj](#).

Usage

```
hlaModelFromObj(obj)
hlaModelToObj(model)
```

Arguments

| | |
|-------|--|
| obj | an object of hlaAttrBagObj |
| model | an object of hlaAttrBagClass |

Value

[hlaModelFromObj](#) returns [hlaAttrBagClass](#), and [hlaModelToObj](#) returns [hlaAttrBagObj](#).

Author(s)

Xiuwen Zheng

See Also

[hlaAttrBagging](#)

Examples

```
# make a "hlaAlleleClass" object
hla.id <- "DQB1"
hla <- hlaAllele(HLA_Type_Table$sample.id,
  H1 = HLA_Type_Table[, paste(hla.id, ".1", sep="")],
  H2 = HLA_Type_Table[, paste(hla.id, ".2", sep="")],
  locus=hla.id, assembly="hg19")

# training genotypes
region <- 100 # kb
snpid <- hlaFlankingSNP(HapMap_CEU_Geno$snp.id, HapMap_CEU_Geno$snp.position,
  hla.id, region*1000, assembly="hg19")
train.geno <- hlaGenoSubset(HapMap_CEU_Geno,
  snp.sel = match(snpid, HapMap_CEU_Geno$snp.id))

# train a HIBAG model
set.seed(1000)
model <- hlaAttrBagging(hla, train.geno, nclassifier=2)
print(model)

mobj <- hlaModelToObj(model)

is(model)
is(mobj)
```



```
# close the HIBAG model explicitly
hlaClose(model)
```

| | |
|-------------|---|
| hlaOutOfBag | <i>Out-of-bag estimation of overall accuracy, per-allele sensitivity, etc</i> |
|-------------|---|

Description

Out-of-bag estimation of overall accuracy, per-allele sensitivity, specificity, positive predictive value, negative predictive value and call rate.

Usage

```
hlaOutOfBag(model, hla, snp, call.threshold=NaN, verbose=TRUE)
```

Arguments

| | |
|----------------|---|
| model | an object of hlaAttrBagClass or hlaAttrBagObj |
| hla | the training HLA types, an object of hlaAlleleClass |
| snp | the training SNP genotypes, an object of hlaSNPGenoClass |
| call.threshold | the specified call threshold; if NaN, no threshold is used |
| verbose | if TRUE, show information |

Value

Return [hlaAlleleClass](#).

Author(s)

Xiuwen Zheng

See Also

[hlaCompareAllele](#), [hlaReport](#)

Examples

```
# make a "hlaAlleleClass" object
hla.id <- "A"
hla <- hlaAllele(HLA_Type_Table$sample.id,
  H1 = HLA_Type_Table[, paste(hla.id, ".1", sep="")],
  H2 = HLA_Type_Table[, paste(hla.id, ".2", sep="")],
  locus=hla.id, assembly="hg19")

# SNP predictors within the flanking region on each side
region <- 500 # kb
```

```

snpid <- hlaFlankingSNP(HapMap_CEU_Geno$snp.id, HapMap_CEU_Geno$snp.position,
  hla.id, region*1000, assembly="hg19")
length(snpid) # 275

# training and validation genotypes
geno <- hlaGenoSubset(HapMap_CEU_Geno,
  snp.sel = match(snpid, HapMap_CEU_Geno$snp.id),
  samp.sel = match(hla$value$sample.id, HapMap_CEU_Geno$sample.id))

# train a HIBAG model
set.seed(100)
# please use "nclassifier=100" when you use HIBAG for real data
model <- hlaAttrBagging(hla, geno, nclassifier=4)
summary(model)

# out-of-bag estimation
(comp <- hlaOutOfBag(model, hla, geno, call.threshold=NaN, verbose=TRUE))

# report
hlaReport(comp, type="txt")

hlaReport(comp, type="tex")

hlaReport(comp, type="html")

```

hlaParallelAttrBagging

Build a HIBAG model via parallel computation

Description

To build a HIBAG model for predicting HLA types via parallel computation.

Usage

```

hlaParallelAttrBagging(cl, hla, snp, auto.save="",
  nclassifier=100, mtry=c("sqrt", "all", "one"), prune=TRUE, rm.na=TRUE,
  stop.cluster=FALSE, verbose=TRUE)

```

Arguments

| | |
|-------------|---|
| cl | a cluster object, created by the package parallel or snow ; if NULL is given, a uniprocessor implementation will be performed |
| hla | training HLA types, an object of hlaAlleleClass |
| snp | training SNP genotypes, an object of hlaSNPGenoClass |
| auto.save | specify a autosaved file, see details |
| nclassifier | the total number of individual classifiers |

| | |
|--------------|--|
| mtry | a character or a numeric value, the number of variables randomly sampled as candidates for each selection. See details |
| prune | if TRUE, to perform a parsimonious forward variable selection, otherwise, exhaustive forward variable selection. See details |
| rm.na | if TRUE, remove the samples with missing HLA types |
| stop.cluster | TRUE: stop cluster nodes after computing |
| verbose | if TRUE, show information |

Details

mtry (the number of variables randomly sampled as candidates for each selection): "sqrt", using the square root of the total number of candidate SNPs; "all", using all candidate SNPs; "one", using one SNP; an integer, specifying the number of candidate SNPs; $0 < r < 1$, the number of candidate SNPs is "r * the total number of SNPs".

prune: there is no significant difference on accuracy between parsimonious and exhaustive forward variable selections. If prune = TRUE, the searching algorithm performs a parsimonious forward variable selection: if a new SNP predictor reduces the current out-of-bag accuracy, then it is removed from the candidate SNP set for future searching. Parsimonious selection helps to improve the computational efficiency by reducing the searching times of non-informative SNP markers.

If auto.save="", the function returns a HIBAG model (an object of [hlaAttrBagClass](#)); otherwise, there is no return.

Value

Return an object of [hlaAttrBagClass](#) if auto.save is specified.

Author(s)

Xiuwen Zheng

References

Zheng X, Shen J, Cox C, Wakefield J, Ehm M, Nelson M, Weir BS; HIBAG – HLA Genotype Imputation with Attribute Bagging. Pharmacogenomics Journal. doi: 10.1038/tpj.2013.18. <http://www.nature.com/tpj/journal/v14/n2/full/tpj201318a.html>

See Also

[hlaAttrBagging](#), [hlaClose](#)

Examples

```
# make a "hlaAlleleClass" object
hla.id <- "A"
hla <- hlaAllele(HLA_Type_Table$sample.id,
  H1 = HLA_Type_Table[, paste(hla.id, ".1", sep="")],
  H2 = HLA_Type_Table[, paste(hla.id, ".2", sep="")],
  locus=hla.id, assembly="hg19")
```

```

# divide HLA types randomly
set.seed(100)
hlatab <- hlaSplitAllele(hla, train.prop=0.5)
names(hlatab)
# "training" "validation"
summary(hlatab$training)
summary(hlatab$validation)

# SNP predictors within the flanking region on each side
region <- 500 # kb
snpid <- hlaFlankingSNP(HapMap_CEU_Geno$snp.id, HapMap_CEU_Geno$snp.position,
  hla.id, region*1000, assembly="hg19")
length(snpid) # 275

# training and validation genotypes
train.geno <- hlaGenoSubset(HapMap_CEU_Geno,
  snp.sel = match(snpid, HapMap_CEU_Geno$snp.id),
  samp.sel = match(hlatab$training$value$sample.id,
    HapMap_CEU_Geno$sample.id))
test.geno <- hlaGenoSubset(HapMap_CEU_Geno,
  samp.sel=match(hlatab$validation$value$sample.id,
    HapMap_CEU_Geno$sample.id))

#####

library(parallel)

# use option cl.core to choose an appropriate cluster size.
cl <- makeCluster(getOption("cl.cores", 2))
set.seed(100)

# train a HIBAG model in parallel
# please use "nclassifier=100" when you use HIBAG for real data
hlaParallelAttrBagging(cl, hlatab$training, train.geno, nclassifier=4,
  auto.save="tmp_model.RData", stop.cluster=TRUE)

mobj <- get(load("tmp_model.RData"))
summary(mobj)
model <- hlaModelFromObj(mobj)

# validation
pred <- predict(model, test.geno)
summary(pred)

# compare
hlaCompareAllele(hlatab$validation, pred, allele.limit=model)$overall

# since 'stop.cluster=TRUE' used in 'hlaParallelAttrBagging'
# need a new cluster
cl <- makeCluster(getOption("cl.cores", 2))

```

```
pred <- predict(model, test.geno, cl=cl)
summary(pred)

# stop parallel nodes
stopCluster(cl)

# delete the temporary file
unlink(c("tmp_model.RData"), force=TRUE)
```

hlaPredMerge *Merge prediction results from multiple HIBAG models*

Description

Return an object of [hlaAlleleClass](#), which contains predicted HLA types.

Usage

```
hlaPredMerge(..., weight=NULL, equivalence=NULL)
```

Arguments

| | |
|-------------|--|
| ... | The object(s) of hlaAlleleClass , having a field of 'postprob', and returned by <code>predict(..., type="response+prob", vote="majority")</code> |
| weight | the weight used for each prediction; if NULL, equal weights |
| equivalence | a data.frame with two columns, the first column for new equivalent alleles, and the second for the alleles possibly existed in the object(s) passed to this function |

Details

Calculate a new probability matrix for each pair of HLA alleles, by averaging (posterior) probabilities from all models with specified weights. If equivalence is specified, multiple alleles might be collapsed into one class.

Value

Return a [hlaAlleleClass](#) object.

Author(s)

Xiuwen Zheng

See Also

[hlaAttrBagging](#), [hlaAllele](#), [predict.hlaAttrBagClass](#)

Examples

```

# make a "hlaAlleleClass" object
hla.id <- "A"
hla <- hlaAllele(HLA_Type_Table$sample.id,
  H1 = HLA_Type_Table[, paste(hla.id, ".1", sep="")],
  H2 = HLA_Type_Table[, paste(hla.id, ".2", sep="")],
  locus=hla.id, assembly="hg19")

# divide HLA types randomly
set.seed(100)
hlatab <- hlaSplitAllele(hla, train.prop=0.5)
names(hlatab)
# "training" "validation"
summary(hlatab$training)
summary(hlatab$validation)

# SNP predictors within the flanking region on each side
region <- 500 # kb
snpid <- hlaFlankingSNP(HapMap_CEU_Geno$snp.id, HapMap_CEU_Geno$snp.position,
  hla.id, region*1000, assembly="hg19")
length(snpid) # 275

# training and validation genotypes
train.geno <- hlaGenoSubset(HapMap_CEU_Geno,
  snp.sel=match(snpid, HapMap_CEU_Geno$snp.id),
  samp.sel=match(hlatab$training$value$sample.id,
    HapMap_CEU_Geno$sample.id))
test.geno <- hlaGenoSubset(HapMap_CEU_Geno,
  samp.sel=match(hlatab$validation$value$sample.id,
    HapMap_CEU_Geno$sample.id))

# train HIBAG models
set.seed(100)

# please use "nclassifier=100" when you use HIBAG for real data
m1 <- hlaAttrBagging(hlatab$training, train.geno, nclassifier=2,
  verbose.detail=TRUE)
m2 <- hlaAttrBagging(hlatab$training, train.geno, nclassifier=2,
  verbose.detail=TRUE)

# validation
pd1 <- predict(m1, test.geno, type="response+prob", vote="majority")
pd2 <- predict(m2, test.geno, type="response+prob", vote="majority")

hlaCompareAllele(hlatab$validation, pd1)$overall

hlaCompareAllele(hlatab$validation, pd2)$overall

# merge predictions from multiple models, by voting from all classifiers
pd <- hlaPredMerge(pd1, pd2, weight=c(1,1))

```

```
hlaCompareAllele(hlatab$validation, pd)$overall
```

hlaPublish *Finalize a HIBAG model*

Description

Finalize a HIBAG model by removing unused SNP predictors and adding appendix information (platform, training set, authors, warning, etc)

Usage

```
hlaPublish(mobj, platform=NULL, information=NULL, warning=NULL,  
          rm.unused.snp=TRUE, anonymize=TRUE, verbose=TRUE)
```

Arguments

| | |
|---------------|---|
| mobj | an object of hlaAttrBagObj or hlaAttrBagClass |
| platform | the text of platform information |
| information | the other information, like authors |
| warning | any warning message |
| rm.unused.snp | if TRUE, remove unused SNPs from the model |
| anonymize | if TRUE, remove sample IDs |
| verbose | if TRUE, show information |

Value

Returns a new object of [hlaAttrBagObj](#).

Author(s)

Xiuwen Zheng

See Also

[hlaModelFromObj](#), [hlaModelToObj](#)

Examples

```

# make a "hlaAlleleClass" object
hla.id <- "A"
hla <- hlaAllele(HLA_Type_Table$sample.id,
  H1 = HLA_Type_Table[, paste(hla.id, ".1", sep="")],
  H2 = HLA_Type_Table[, paste(hla.id, ".2", sep="")],
  locus=hla.id, assembly="hg19")

# training genotypes
region <- 250 # kb
snpid <- hlaFlankingSNP(HapMap_CEU_Geno$snp.id, HapMap_CEU_Geno$snp.position,
  hla.id, region*1000, assembly="hg19")
train.geno <- hlaGenoSubset(HapMap_CEU_Geno,
  snp.sel = match(snpid, HapMap_CEU_Geno$snp.id),
  samp.sel = match(hla$value$sample.id, HapMap_CEU_Geno$sample.id))

#
# train a HIBAG model
#
set.seed(1000)

# please use "nclassifier=100" when you use HIBAG for real data
model <- hlaAttrBagging(hla, train.geno, nclassifier=2, verbose.detail=TRUE)
summary(model)
length(model$snp.id)

mobj <- hlaPublish(model,
  platform = "Illumina 1M Duo",
  information = "Training set -- HapMap Phase II")
model2 <- hlaModelFromObj(mobj)
length(mobj$snp.id)
mobj$appendix
summary(mobj)

p1 <- predict(model, train.geno)
p2 <- predict(model2, train.geno)

# check
cbind(p1$value, p2$value)

```

hlaReport

Format a report

Description

Create a report for evaluating prediction accuracies.

Usage

```
hlaReport(object, export.fn="", type=c("txt", "tex", "html", "markdown"),
          header=TRUE)
```

Arguments

| | |
|-----------|---|
| object | an object returned by hlaCompareAllele |
| export.fn | a file name for output, or "" for stdout |
| type | "txt" – tab-delimited text format; "tex" – tex format using the 'longtable' package; "html" – html file |
| header | if TRUE, output the header of text file associated corresponding format |

Value

None.

Author(s)

Xiuwen Zheng

See Also

[hlaCompareAllele](#)

Examples

```
# make a "hlaAlleleClass" object
hla.id <- "A"
hla <- hlaAllele(HLA_Type_Table$sample.id,
  H1 = HLA_Type_Table[, paste(hla.id, ".1", sep="")],
  H2 = HLA_Type_Table[, paste(hla.id, ".2", sep="")],
  locus=hla.id, assembly="hg19")

# divide HLA types randomly
set.seed(100)
hlatab <- hlaSplitAllele(hla, train.prop=0.5)
names(hlatab)
# "training" "validation"
summary(hlatab$training)
summary(hlatab$validation)

# SNP predictors within the flanking region on each side
region <- 500 # kb
snpid <- hlaFlankingSNP(HapMap_CEU_Geno$snp.id, HapMap_CEU_Geno$snp.position,
  hla.id, region*1000, assembly="hg19")
length(snpid) # 275

# training and validation genotypes
train.geno <- hlaGenoSubset(HapMap_CEU_Geno,
  snp.sel = match(snpid, HapMap_CEU_Geno$snp.id),
```

```

    samp.sel = match(hlatab$training$value$sample.id,
                    HapMap_CEU_Geno$sample.id)
test.geno <- hlaGenoSubset(HapMap_CEU_Geno,
                          samp.sel=match(hlatab$validation$value$sample.id,
                                          HapMap_CEU_Geno$sample.id))

# train a HIBAG model
set.seed(100)
# please use "nclassifier=100" when you use HIBAG for real data
model <- hlaAttrBagging(hlatab$training, train.geno, nclassifier=4,
                       verbose.detail=TRUE)
summary(model)

# validation
pred <- predict(model, test.geno)
# compare
(comp <- hlaCompareAllele(hlatab$validation, pred, allele.limit=model,
                          call.threshold=0))

# report
hlaReport(comp, type="txt")

hlaReport(comp, type="tex")

hlaReport(comp, type="html")

hlaReport(comp, type="markdown")

```

hlaSampleAllele

Get sample IDs from HLA types with a filter

Description

Get sample IDs from HLA types limited to a set of HLA alleles.

Usage

```
hlaSampleAllele(TrueHLA, allele.limit=NULL, max.resolution="")
```

Arguments

| | |
|----------------|--|
| TrueHLA | an object of hlaAlleleClass |
| allele.limit | a list of HLA alleles, the validation samples are limited to those having HLA alleles in <code>allele.limit</code> , or NULL for no limit. <code>allele.limit</code> could be character-type, hlaAttrBagClass or hlaAttrBagObj |
| max.resolution | "2-digit", "4-digit", "6-digit", "8-digit", "allele", "protein", "2", "4", "6", "8", "full" or "": "allele" = "2-digit", "protein" = "4-digit", "full" and "" mean no limit on resolution |

Value

Return a list of sample IDs.

Author(s)

Xiuwen Zheng

See Also

[hlaCompareAllele](#)

Examples

```
# make a "hlaAlleleClass" object
hla.id <- "A"
hla <- hlaAllele(HLA_Type_Table$sample.id,
  HLA_Type_Table[, paste(hla.id, ".1", sep="")],
  HLA_Type_Table[, paste(hla.id, ".2", sep="")],
  locus=hla.id, assembly="hg19")
summary(hla)

hlaSampleAllele(hla)

hlaSampleAllele(hla, allele.limit=c(
  "01:01", "02:01", "02:06", "03:01", "11:01", "23:01"))
```

| | |
|-----------------|-----------------------------------|
| hlaSNPGenoClass | <i>The class of SNP genotypes</i> |
|-----------------|-----------------------------------|

Description

The class of SNP genotypes, and its instance is returned from [hlaMakeSNPGeno](#).

Value

There are five components:

| | |
|--------------|---|
| genotype | a genotype matrix, “# of SNPs” - by - “# of individuals” |
| sample.id | a vector of sample IDs |
| snp.id | a vector of SNP IDs |
| snp.position | a vector of SNP positions in basepair |
| snp.allele | a vector of characters with a format of “A allele/B allele” |
| assembly | the human genome reference, such like "hg19" |

Author(s)

Xiuwen Zheng

See Also

[hlaMakeSNPGeno](#)

hlaSNPID

Get SNP IDs and positions

Description

Get the information of SNP ID with or without position.

Usage

```
hlaSNPID(obj, type=c("RefSNP+Position", "RefSNP", "Position"))
```

Arguments

| | |
|------|--|
| obj | a genotypic object of hlaSNPGenoClass , a model object of hlaAttrBagClass or a model object of hlaAttrBagObj |
| type | "RefSNP+Position" (by default), "RefSNP" or "Position" |

Value

If type = "RefSNP+Position", return `paste(obj$snp.id, obj$snp.position, sep="-")`; if type = "RefSNP", return `obj$snp.id`; otherwise, return `obj$snp.position`.

Author(s)

Xiuwen Zheng

See Also

[hlaGenoSwitchStrand](#), [hlaGenoCombine](#)

Examples

```
x <- hlaSNPID(HapMap_CEU_Geno)
head(x)

x <- hlaSNPID(HapMap_CEU_Geno, "RefSNP")
head(x)

x <- hlaSNPID(HapMap_CEU_Geno, "Position")
head(x)
```

| | |
|----------------|------------------------------------|
| hlaSplitAllele | <i>Divide the samples randomly</i> |
|----------------|------------------------------------|

Description

Divide the samples to the training and validation sets randomly.

Usage

```
hlaSplitAllele(HLA, train.prop=0.5)
```

Arguments

| | |
|------------|---|
| HLA | an object of hlaAlleleClass |
| train.prop | the proportion of training set |

Details

The algorithm tries to divide each HLA alleles into training and validation sets randomly with a training proportion `train.prop`.

Value

Return a list:

| | |
|------------|---|
| training | an object of hlaAlleleClass |
| validation | an object of hlaAlleleClass |

Author(s)

Xiuwen Zheng

See Also

[hlaAllele](#)

Examples

```
# make a "hlaAlleleClass" object
hla.id <- "A"
hla <- hlaAllele(HLA_Type_Table$sample.id,
  H1 = HLA_Type_Table[, paste(hla.id, ".1", sep="")],
  H2 = HLA_Type_Table[, paste(hla.id, ".2", sep="")],
  locus=hla.id, assembly="hg19")

# divide HLA types randomly
set.seed(100)
hlatab <- hlaSplitAllele(hla, train.prop=0.5)
names(hlatab)
```

```
# "training"  "validation"
summary(hlatab$training)
summary(hlatab$validation)
```

hlaSubModelObj *Get a subset of individual classifiers*

Description

Get the first n individual classifiers.

Usage

```
hlaSubModelObj(obj, n)
```

Arguments

obj an object of [hlaAttrBagObj](#)
n an integer, get the first n individual classifiers

Value

Return an object of [hlaAttrBagObj](#).

Author(s)

Xiuwen Zheng

See Also

[hlaAttrBagging](#)

Examples

```
# make a "hlaAlleleClass" object
hla.id <- "C"
hla <- hlaAllele(HLA_Type_Table$sample.id,
  H1 = HLA_Type_Table[, paste(hla.id, ".1", sep="")],
  H2 = HLA_Type_Table[, paste(hla.id, ".2", sep="")],
  locus=hla.id, assembly="hg19")

# training genotypes
region <- 50 # kb
snpid <- hlaFlankingSNP(HapMap_CEU_Geno$snp.id, HapMap_CEU_Geno$snp.position,
  hla.id, region*1000, assembly="hg19")
train.geno <- hlaGenoSubset(HapMap_CEU_Geno,
  snp.sel = match(snpid, HapMap_CEU_Geno$snp.id))

# train a HIBAG model
```

```
set.seed(1000)
# please use "nclassifier=100" when you use HIBAG for real data
model <- hlaAttrBagging(hla, train.geno, nclassifier=2, verbose.detail=TRUE)
mobj <- hlaModelToObj(model)
summary(mobj)

newmobj <- hlaSubModelObj(mobj, 1)
summary(newmobj)
```

| | |
|-----------------|-------------------------------|
| hlaUniqueAllele | <i>Get unique HLA alleles</i> |
|-----------------|-------------------------------|

Description

Get unique HLA alleles, which are in ascending order.

Usage

```
hlaUniqueAllele(hla)
```

Arguments

hla character-type HLA alleles, or a [hlaAlleleClass](#) object

Details

Each HLA allele name has a unique number corresponding to up to four sets of digits separated by colons. The name designation depends on the sequence of the allele and that of its nearest relative. The digits before the first colon describe the type, which often corresponds to the serological antigen carried by an allotype. The next set of digits are used to list the subtypes, numbers being assigned in the order in which DNA sequences have been determined. Alleles whose numbers differ in the two sets of digits must differ in one or more nucleotide substitutions that change the amino acid sequence of the encoded protein. Alleles that differ only by synonymous nucleotide substitutions (also called silent or non-coding substitutions) within the coding sequence are distinguished by the use of the third set of digits. Alleles that only differ by sequence polymorphisms in the introns or in the 5' or 3' untranslated regions that flank the exons and introns are distinguished by the use of the fourth set of digits.

In addition to the unique allele number there are additional optional suffixes that may be added to an allele to indicate its expression status. Alleles that have been shown not to be expressed, 'Null' alleles have been given the suffix 'N'. Those alleles which have been shown to be alternatively expressed may have the suffix 'L', 'S', 'C', 'A' or 'Q'.

<http://hla.alleles.org/nomenclature/index.html>

Value

Return a vector of HLA alleles

Author(s)

Xiuwen Zheng

See Also[hlaAllele](#), [hlaAlleleDigit](#)**Examples**

```
# make a "hlaAlleleClass" object
hla.id <- "A"
hla <- hlaAllele(HLA_Type_Table$sample.id,
  H1 = HLA_Type_Table[, paste(hla.id, ".1", sep="")],
  H2 = HLA_Type_Table[, paste(hla.id, ".2", sep="")],
  locus=hla.id, assembly="hg19")
summary(hla)
hlaUniqueAllele(hla)

hlaUniqueAllele(c("01", "01:03", "01:01", "03:05", "03:01G",
  "03:05P", "03:104:01", "104:01"))
```

HLA_Type_Table*Four-digit HLA types of a study simulated from HapMap CEU*

Description

A data.frame object including HLA-A, B, C, DRB1, DQA1 and DQB1 loci of 60 samples.

Usage

```
HLA_Type_Table
```

Value

A data.frame

References

A high-resolution HLA and SNP haplotype map for disease association studies in the extended human MHC. de Bakker PI, McVean G, Sabeti PC, Miretti MM, Green T, Marchini J, Ke X, Monsuur AJ, Whittaker P, Delgado M, Morrison J, Richardson A, Walsh EC, Gao X, Galver L, Hart J, Hafler DA, Pericak-Vance M, Todd JA, Daly MJ, Trowsdale J, Wijmenga C, Vyse TJ, Beck S, Murray SS, Carrington M, Gregory S, Deloukas P, Rioux JD. Nat Genet. 2006 Oct;38(10):1166-72. Epub 2006 Sep 24.

plot.hlaAttrBagObj *Plot a HIBAG model*

Description

To show a scatterplot of the numbers of individual classifiers and SNP positions.

Usage

```
## S3 method for class 'hlaAttrBagObj'  
plot(x, xlab=NULL, ylab=NULL,  
     locus.color="red", locus.lty=2, locus.cex=1.25, assembly="auto", ...)  
## S3 method for class 'hlaAttrBagClass'  
plot(x, ...)
```

Arguments

| | |
|-------------|---|
| x | an object of hlaAttrBagObj |
| xlab | the label of X-axis |
| ylab | the label of Y-axis |
| locus.color | the color of text and line for HLA locus |
| locus.lty | the type of line for HLA locus |
| locus.cex | the font size of HLA locus |
| assembly | the human genome reference: "hg18", "hg19" (default), "hg20"; "auto" refers to "hg19"; "auto-silent" refers to "hg19" without any warning |
| ... | further arguments passed to or from other methods |

Value

None

Author(s)

Xiuwen Zheng

See Also

[print.hlaAttrBagObj](#), [summary.hlaAttrBagObj](#)

Examples

```
# make a "hlaAlleleClass" object
hla.id <- "C"
hla <- hlaAllele(HLA_Type_Table$sample.id,
  H1 = HLA_Type_Table[, paste(hla.id, ".1", sep="")],
  H2 = HLA_Type_Table[, paste(hla.id, ".2", sep="")],
  locus=hla.id, assembly="hg19")

# training genotypes
region <- 100 # kb
snpid <- hlaFlankingSNP(HapMap_CEU_Geno$snp.id, HapMap_CEU_Geno$snp.position,
  hla.id, region*1000, assembly="hg19")
train.geno <- hlaGenoSubset(HapMap_CEU_Geno,
  snp.sel = match(snpid, HapMap_CEU_Geno$snp.id))

# train a HIBAG model
set.seed(1000)
# please use "nclassifier=100" when you use HIBAG for real data
model <- hlaAttrBagging(hla, train.geno, nclassifier=2, verbose.detail=TRUE)
plot(model)
```

predict.hlaAttrBagClass

HIBAG model prediction (in parallel)

Description

To predict HLA type based on a HIBAG model (in parallel).

Usage

```
## S3 method for class 'hlaAttrBagClass'
predict(object, snp, cl,
  type=c("response", "prob", "response+prob"), vote=c("prob", "majority"),
  allele.check=TRUE, match.type=c("RefSNP+Position", "RefSNP", "Position"),
  same.strand=FALSE, verbose=TRUE, ...)
```

Arguments

| | |
|--------|---|
| object | a model of hlaAttrBagClass |
| snp | a genotypic object of hlaSNPGenoClass |
| cl | a cluster object, created by the package parallel or snow ; if NULL is given, a uniprocessor implementation will be performed |
| type | "response": return the best-guess type plus its posterior probability; "prob": return all posterior probabilities; "response+prob": return the best-guess and all posterior probabilities |

| | |
|--------------|--|
| vote | "prob" (default behavior) – make a prediction based on the averaged posterior probabilities from all individual classifiers; "majority" – majority voting from all individual classifiers, where each classifier votes for an HLA type |
| allele.check | if TRUE, check and then switch allele pairs if needed |
| match.type | "RefSNP+Position" (by default) – using both of RefSNP IDs and positions; "RefSNP" – using RefSNP IDs only; "Position" – using positions only |
| same.strand | TRUE assuming alleles are on the same strand (e.g., forward strand); otherwise, FALSE not assuming whether on the same strand or not |
| verbose | if TRUE, show information |
| ... | further arguments passed to or from other methods |

Details

If more than 50% of SNP predictors are missing, a warning will be given.

When `match.type="RefSNP+Position"`, the matching of SNPs requires both RefSNP IDs and positions. A lower missing fraction may be gained by matching RefSNP IDs or positions only. Call `predict(..., match.type="RefSNP")` or `predict(..., match.type="Position")` for this purpose. It might be safe to assume that the SNPs with the same positions on the same genome reference (e.g., hg19) are the same variant albeit the different RefSNP IDs. Any concern about SNP mismatching should be emailed to the genotyping platform provider.

Value

Return a [hlaAlleleClass](#) object with posterior probabilities of predicted HLA types, or a matrix of pairwise possible HLA types with all posterior probabilities. If `type = "response+prob"`, return a [hlaAlleleClass](#) object with a matrix of `postprob` for the probabilities of all pairs of alleles. If a probability matrix is returned, `colnames` is `sample.id` and `rownames` is an unordered pair of HLA alleles.

Author(s)

Xiuwen Zheng

See Also

[hlaAttrBagging](#), [hlaAllele](#), [hlaCompareAllele](#), [hlaParallelAttrBagging](#)

Examples

```
# make a "hlaAlleleClass" object
hla.id <- "A"
hla <- hlaAllele(HLA_Type_Table$sample.id,
  H1 = HLA_Type_Table[, paste(hla.id, ".1", sep="")],
  H2 = HLA_Type_Table[, paste(hla.id, ".2", sep="")],
  locus=hla.id, assembly="hg19")

# divide HLA types randomly
set.seed(100)
```

```

hlatab <- hlaSplitAllele(hla, train.prop=0.5)
names(hlatab)
# "training" "validation"
summary(hlatab$training)
summary(hlatab$validation)

# SNP predictors within the flanking region on each side
region <- 500 # kb
snpid <- hlaFlankingSNP(HapMap_CEU_Geno$snp.id, HapMap_CEU_Geno$snp.position,
  hla.id, region*1000, assembly="hg19")
length(snpid) # 275

# training and validation genotypes
train.geno <- hlaGenoSubset(HapMap_CEU_Geno,
  snp.sel=match(snpid, HapMap_CEU_Geno$snp.id),
  samp.sel=match(hlatab$training$value$sample.id,
    HapMap_CEU_Geno$sample.id))
test.geno <- hlaGenoSubset(HapMap_CEU_Geno,
  samp.sel=match(hlatab$validation$value$sample.id,
    HapMap_CEU_Geno$sample.id))

# train a HIBAG model
set.seed(100)
model <- hlaAttrBagging(hlatab$training, train.geno, nclassifier=4,
  verbose.detail=TRUE)
summary(model)

# validation
pred <- predict(model, test.geno)
# compare
(comp <- hlaCompareAllele(hlatab$validation, pred, allele.limit=model,
  call.threshold=0))
(comp <- hlaCompareAllele(hlatab$validation, pred, allele.limit=model,
  call.threshold=0.5))

```

print.hlaAttrBagClass Summarize a “hlaAttrBagClass” or “hlaAttrBagObj” object.

Description

Summarize an object of [hlaAttrBagClass](#) or [hlaAttrBagObj](#).

Usage

```

## S3 method for class 'hlaAttrBagClass'
print(x, ...)
## S3 method for class 'hlaAttrBagObj'
print(x, ...)
## S3 method for class 'hlaAttrBagClass'
summary(object, show=TRUE, ...)

```

```
## S3 method for class 'hlaAttrBagObj'
summary(object, show=TRUE, ...)
```

Arguments

| | |
|--------|---|
| x | an object of hlaAttrBagClass or hlaAttrBagObj |
| object | an object of hlaAttrBagClass or hlaAttrBagObj |
| show | if TRUE, show information |
| ... | further arguments passed to or from other methods |

Value

print returns NULL.

summary.hlaAttrBagClass and summary.hlaAttrBagObj return a list:

| | |
|----------------|---|
| num.classifier | the total number of classifiers |
| num.snp | the total number of SNPs |
| snp.id | SNP IDs |
| snp.position | SNP position in basepair |
| snp.hist | the number of classifier for each SNP, and it could be used for SNP importance |
| info | a data.frame for the average number of SNPs (num.snp), haplotypes (num.haplo), out-of-bag accuracies (accuracy) among all classifiers: mean, standard deviation, min, max |

Author(s)

Xiuwen Zheng

See Also

[plot.hlaAttrBagClass](#), [plot.hlaAttrBagObj](#)

Examples

```
# make a "hlaAlleleClass" object
hla.id <- "C"
hla <- hlaAllele(HLA_Type_Table$sample.id,
  H1 = HLA_Type_Table[, paste(hla.id, ".1", sep="")],
  H2 = HLA_Type_Table[, paste(hla.id, ".2", sep="")],
  locus=hla.id, assembly="hg19")

# training genotypes
region <- 100 # kb
snpid <- hlaFlankingSNP(HapMap_CEU_Geno$snp.id, HapMap_CEU_Geno$snp.position,
  hla.id, region*1000, assembly="hg19")
train.geno <- hlaGenoSubset(HapMap_CEU_Geno,
  snp.sel = match(snpid, HapMap_CEU_Geno$snp.id))
```

```
# train a HIBAG model
set.seed(1000)
# please use "nclassifier=100" when you use HIBAG for real data
model <- hlaAttrBagging(hla, train.geno, nclassifier=2, verbose.detail=TRUE)
print(model)
```

summary.hlaAlleleClass

Summarize a "hlaAlleleClass" object

Description

Show the information of a [hlaAlleleClass](#) object.

Usage

```
## S3 method for class 'hlaAlleleClass'
summary(object, show=TRUE, ...)
```

Arguments

| | |
|--------|---|
| object | an object of hlaAlleleClass |
| show | if TRUE, show information |
| ... | further arguments passed to or from other methods |

Value

Return a data.frame of count and frequency for each HLA allele.

Author(s)

Xiuwen Zheng

See Also

[hlaAllele](#)

Examples

```
# make a "hlaAlleleClass" object
hla.id <- "A"
hla <- hlaAllele(HLA_Type_Table$sample.id,
  H1 = HLA_Type_Table[, paste(hla.id, ".1", sep="")],
  H2 = HLA_Type_Table[, paste(hla.id, ".2", sep="")],
  locus=hla.id, assembly="hg19")
summary(hla)
```

```
summary.hlaSNPGenoClass
```

Summarize a SNP dataset

Description

Summarize the genotypic dataset.

Usage

```
## S3 method for class 'hlaSNPGenoClass'  
summary(object, show=TRUE, ...)
```

Arguments

| | |
|--------|--|
| object | a genotype object of hlaSNPGenoClass |
| show | if TRUE, print information |
| ... | further arguments passed to or from other methods |

Value

None.

Author(s)

Xiuwen Zheng

See Also

[hlaMakeSNPGeno](#), [hlaGenoSubset](#)

Examples

```
summary(HapMap_CEU_Geno)
```

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