

Package ‘HIBAG’

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Type Package

Title HLA Genotype Imputation with Attribute Bagging

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Imports methods

Suggests parallel, knitr, gdsfmt (>= 1.2.2), SNPRelate (>= 1.1.6)

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

ByteCompile TRUE

biocViews Genetics, StatisticalMethod

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

NeedsCompilation yes

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HIBAG-package

HLA Genotype Imputation with Attribute Bagging

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

SNP genotypes of a study simulated from HapMap CEU genotypic data

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.

hlaAASeqClass	<i>Class of HLA Amino Acid Sequence Type</i>
---------------	--

Description

The definition of a class for HLA protein amino acid sequences.

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"
start.position	the start position
reference	reference sequence

The component value includes:

sample.id	sample ID
allele1	amino acid or nucleotide sequence
allele2	amino acid or nucleotide sequence
P1, ..., Pn	if applicable, a matrix of posterior probability, row – sample, column – position of amino acid

Author(s)

Xiuwen Zheng

See Also

[hlaConvSequence](#)

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), "hg38"; "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")
```

<code>hlaAlleleClass</code>	<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	if applicable, a matrix of all posterior probabilities

~

The component value includes:

sample.id	sample ID
allele1	HLA allele
allele2	HLA allele
prob	if applicable, 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", "1-field", "4-digit", "2-field", "6-digit", "3-field", "8-digit", "4-field", "allele", "protein", "full", "", "none": "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)

```

hlaAssocTest

Statistical Association Tests

Description

Perform statistical association tests via Pearson's Chi-squared test, Fisher's exact test and logistic regressions.

Usage

```

## S3 method for class 'hlaAlleleClass'
hlaAssocTest(hla, formula, data,
             model=c("dominant", "additive", "recessive", "genotype"),
             model.fit=c("glm"), prob.threshold=NaN, use.prob=FALSE, showOR=FALSE,
             verbose=TRUE, ...)
## S3 method for class 'hlaAASeqClass'
hlaAssocTest(hla, formula, data,
             model=c("dominant", "additive", "recessive", "genotype"),
             model.fit=c("glm"), prob.threshold=NaN, use.prob=FALSE, showOR=FALSE,
             show.all=FALSE, verbose=TRUE, ...)

```

Arguments

hla	an object of hlaAlleleClass
formula	an object of class "formula" (or one that can be coerced to that class): a symbolic description of the model to be fitted, e.g., $y \sim 1$, $y \sim h + a$
data	an optional data frame, list or environment containing the variables in the model. If not found in data, the variables are taken from <code>environment(formula)</code>
model	dominant, additive, recessive or genotype models: "dominant" is default
model.fit	"glm" – generalized linear regression
prob.threshold	the probability threshold to exclude individuals with low confidence scores
use.prob	if TRUE, use the posterior probabilities as weights in glm models
showOR	show odd ratio (OR) instead of log OR if TRUE
show.all	if TRUE, show both significant and non-significant results; if FALSE, only show significant results
verbose	if TRUE, show information
...	optional arguments to glm or nlme call

Details

model	description (given a specific HLA allele h)
dominant	[-/-] vs. [-/h,h/h] (0 vs. 1 in design matrix)
additive	[-] vs. [h] in Chi-squared and Fisher's exact test, the allele dosage in regressions (0: -/-, 1: -/h, 2: h/h)
recessive	[-/-,-/h] vs. [h/h] (0 vs. 1 in design matrix)
genotype	[-/-], [-/h], [h/h] (0 vs. 1 in design matrix)

In allelic associations, Chi-squared and Fisher exact tests are performed on the cross tabulation, which is constructed according to the specified model (dominant, additive, recessive and genotype).

In amino acid associations, Fisher exact test is performed on a cross tabulation with the numbers of each amino acid stratified by response variable (e.g., disease status).

In linear and logistic regressions, 95% confidence intervals are calculated based on asymptotic normality. The option `use.prob=TRUE` might be useful in the sensitivity analysis.

Value

Return a data.frame with

[-]	the number of haplotypes not carrying the specified HLA allele
[h]	the number of haplotype carrying the specified HLA allele
%. [-], ...	case/disease proportion in the group [-], ...
[-/-]	the number of individuals or haplotypes not carrying the specified HLA allele
[-/h]	the number of individuals or haplotypes carrying one specified HLA allele
[-/h]	the number of individuals or haplotypes carrying two specified HLA alleles
[-/h,h/h]	the number of individuals or haplotypes carrying one or two specified HLA alleles
[-/-,-/h]	the number of individuals or haplotypes carrying at most one specified HLA allele
%. [-/-], ...	case/disease proportion in the group [-/-], ...
avg. [-/-], ...	outcome average in the group [-/-], ...
chisq.st	the value the chi-squared test statistic
chisq.p	the p-value for the Chi-squared test
fisher.p	the p-value for the Fisher's exact test
h.est	the coefficient estimate of HLA allele
h.25%, h.75%	the 95% confidence interval for HLA allele
h.pval	p value for HLA allele

Author(s)

Xiuwen Zheng

See Also

[hlaConvSequence](#), [summary.hlaAASeqClass](#)

Examples

```

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")

set.seed(1000)
n <- nrow(hla$value)
dat <- data.frame(case = c(rep(0, n/2), rep(1, n/2)), y = rnorm(n),
  pc1 = rnorm(n))

hlaAssocTest(hla, case ~ 1, data=dat)
hlaAssocTest(hla, case ~ 1, data=dat, model="additive")
hlaAssocTest(hla, case ~ 1, data=dat, model="recessive")
hlaAssocTest(hla, case ~ 1, data=dat, model="genotype")

hlaAssocTest(hla, y ~ 1, data=dat)
hlaAssocTest(hla, y ~ 1, data=dat, model="genotype")

hlaAssocTest(hla, case ~ h, data=dat)
hlaAssocTest(hla, case ~ h + pc1, data=dat)
hlaAssocTest(hla, case ~ h + pc1, data=dat, showOR=TRUE)

hlaAssocTest(hla, y ~ h, data=dat)
hlaAssocTest(hla, y ~ h + pc1, data=dat)
hlaAssocTest(hla, y ~ h + pc1, data=dat, showOR=TRUE)

hlaAssocTest(hla, case ~ h, data=dat, model="additive")
hlaAssocTest(hla, case ~ h, data=dat, model="recessive")
hlaAssocTest(hla, case ~ h, data=dat, model="genotype")

```

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

Build a HIBAG model

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](#):

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

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), "hg38"; "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)
```

hlaCheckAllele	<i>Check SNP alleles</i>
----------------	--------------------------

Description

Check SNP reference and non-reference alleles.

Usage

```
hlaCheckAllele(allele1, allele2)
```

Arguments

allele1	two alleles for the first individual, like <code>c("A/G", "C/G")</code>
allele2	two alleles for the second individual, like <code>c("A/G", "C/G")</code>

Value

Return a logical vector, where TRUE indicates the alleles are matching at that locus.

Author(s)

Xiuwen Zheng

See Also

[hlaCheckSNPs](#)

Examples

```
hlaCheckAllele(c("A/G", "T/G", "0/A"), c("G/A", "C/A", "G/0"))
```

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 c("rs2523442", "rs9257863", ...)
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](#)

hlaCombineAllele	<i>Combine two datasets of HLA types</i>
------------------	--

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

<code>TrueHLA</code>	an object of <code>hlaAlleleClass</code> , the true HLA types
<code>PredHLA</code>	an object of <code>hlaAlleleClass</code> , the predicted HLA types
<code>allele.limit</code>	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, <code>hlaAttrBagClass</code> or <code>hlaAttrBagObj</code>
<code>call.threshold</code>	the call threshold for posterior probability, i.e., call or no call is determined by whether <code>prob >= call.threshold</code> or not
<code>max.resolution</code>	"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
<code>output.individual</code>	if TRUE, output accuracy for each individual
<code>verbose</code>	if TRUE, show information

Value

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

`overall` (`data.frame`):

<code>total.num.ind</code>	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

n.call the number of individuals with call
 call.rate overall call rate

confusion (matrix): a confusion matrix.
 detail (data.frame):

allele HLA alleles
 train.num the number of training haplotypes
 train.freq the training haplotype frequencies
 valid.num the number of validation haplotypes
 valid.freq the validation haplotype frequencies
 call.rate the call rates for HLA alleles
 accuracy allele accuracy
 sensitivity sensitivity
 specificity specificity
 ppv positive predictive value
 npv negative predictive value
 miscall the most likely miss-called alleles
 miscall.prop the proportions of the most likely miss-called allele in all miss-called alleles

individual (data.frame):

sample.id sample id
 true.hla the true HLA type
 pred.hla the prediction of HLA type
 accuracy 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))

```

hlaConvSequence

Conversion From HLA Alleles to Amino Acid Sequences

Description

Convert (P-coded or G-coded) HLA alleles to amino acid sequences.

Usage

```

hlaConvSequence(hla=character(), locus=NULL,
  method=c("protein", "protein_reference"),
  code=c("exact", "P.code", "G.code", "P.code.merge", "G.code.merge"),
  region=c("auto", "all", "P.code", "G.code"), release=c("v3.22.0"),
  replace=NULL)

```

Arguments

hla	characters, or an object of hlaAlleleClass , at least 4-digit or 2-field (P-coded) HLA alleles
locus	"A", "B", "C", "DRB1", "DQA1", "DQB1", "DPB1" or "DPA1"
method	"protein": returns protein sequence alignments, "protein_reference": returns the protein sequence alignment reference

code	"exact": requires full resolution; "P.code": allows ambiguous alleles according to P code; "G.code": allows ambiguous alleles according to G code; "P.code.merge" and "G.code.merge" merge multiple ambiguous allele sequences by masking unknown or ambiguous amino acid an asterisk
region	"all": returns all amino acid or nucleotide sequences; "P.code", "G.code": returns the exon 2 and 3 for HLA class I, and the exon 2 for HLA class II alleles; "auto": region="all" if code=="exact", region="P.code" if code=="P.code" "P.code.merge", region="G.code" if code=="G.code" "G.code.merge"
release	"v3.22.0" – IPD-IMGT/HLA 3.22.0 database (2015-10-07)
replace	NULL, or a character vector, like c("09:02"="107:01"), any "09:02" will be replaced by "107:01"

Details

The P or G codes for reporting of ambiguous allele typings can be found: http://hla.alleles.org/alleles/p_groups.html or http://hla.alleles.org/alleles/g_groups.html. The protein sequences for each HLA alleles could be found: http://hla.alleles.org/alleles/text_index.html.

Due to allelic ambiguity, multiple alleles are assigned to a 2-field P-coded allele or 3-field G-coded allele. For HLA Class I alleles, identity in the 'antigen binding domains' is based on identical protein sequences as encoded by exons 2 and 3. For HLA Class II alleles this is based on identical protein sequences as encoded by exon 2. P codes and G codes encode the same protein sequence for the peptide binding domains (exon 2 and 3 for HLA class I and exon 2 only for HLA class II alleles).

1. the sequence is displayed as a hyphen "-" where it is identical to the reference.
2. an insertion or deletion is represented by a period ".".
3. an unknown or ambiguous position in the alignment is represented by an asterisk "*".
4. a capital X is used for the 'stop' codons in protein alignments.

<http://hla.alleles.org/alleles/formats.html>

HLA class I and II sequence alignments (Text Index): http://hla.alleles.org/alleles/text_index.html

WARNING: if you are not familiar with HLA nomenclature, you might consult with the package author or anyone who is familiar with HLA sequence alignments.

Value

Return an object of [hlaAASeqClass](#) or a list of characters. NULL or NA in the list indicates no matching.

Author(s)

Xiuwen Zheng

References

The licence and disclaimer of distributed HLA data: Creative Commons Attribution-NoDerivs Licence (<http://hla.alleles.org/terms.html>).

Robinson J, Halliwell JA, Hayhurst JH, Flicek P, Parham P, Marsh SGE: The IPD and IMGT/HLA database: allele variant databases. *Nucleic Acids Research*. 2015 43:D423-431

Robinson J, Malik A, Parham P, Bodmer JG, Marsh SGE: IMGT/HLA - a sequence database for the human major histocompatibility complex. *Tissue Antigens*. 2000 55:280-7

See Also

[hlaAlleleSubset](#)

Examples

```

hlaConvSequence(locus="A", method="protein_reference")
hlaConvSequence(c("01:01", "02:02", "01:01:01G", "01:01:01:01", "07"),
  locus="A")
hlaConvSequence(c("01:01", "02:02", "01:01:01G", "01:01:01:01", "07"),
  locus="A", code="P.code")
hlaConvSequence(c("01:01", "02:02", "01:01:01G", "01:01:01:01", "07"),
  locus="A", code="P.code.merge")

hlaConvSequence(locus="DPB1", method="protein_reference")
hlaConvSequence(c("09:01", "09:02"), locus="DPB1", replace=c("09:02"="107:01"))
hlaConvSequence(c("09:01", "09:02"), locus="DPB1", code="P.code",
  replace=c("09:02"="107:01"))
hlaConvSequence(c("09:01", "09:02"), locus="DPB1", code="P.code.merge",
  replace=c("09:02"="107:01"))

hlaConvSequence(locus="DQB1", method="protein_reference")
hlaConvSequence(c("05:01:01:01", "06:01:01"), locus="DQB1")
hlaConvSequence(c("05:01", "06:01"), locus="DQB1", code="P.code")
hlaConvSequence(c("05:01", "06:01"), locus="DQB1", code="P.code.merge")

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")

(v <- hlaConvSequence(hla, code="P.code.merge"))
summary(v)

v <- hlaConvSequence(hla, code="P.code.merge", region="all")
summary(v)

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")

(v <- hlaConvSequence(hla, code="P.code.merge"))
summary(v)

v <- hlaConvSequence(hla, code="P.code.merge", region="all")
summary(v)

```

hlaErrMsg	<i>The last error message</i>
-----------	-------------------------------

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",
  pos.start=NA_integer_, pos.end=NA_integer_)
```

Arguments

snp.id	a vector of SNP IDs
position	a vector of positions
hla.id	the name of HLA locus, or "any" for other genes
flank.bp	the size of flanking region on each side in basepair
assembly	the human genome reference: "hg18", "hg19" (default), "hg38"; "auto" refers to "hg19"; "auto-silent" refers to "hg19" without any warning
pos.start	the start position of the gene
pos.end	the end position of the gene

Details

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

Value

Return selected SNP IDs from `snp.id`.

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)

## customize positions
snpid <- hlaFlankingSNP(HapMap_CEU_Geno$snp.id, HapMap_CEU_Geno$snp.position,
  "any", 500*1000, pos.start=29457816, pos.end=30450205)
```

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

`gds.fn` the SNP GDS file used by the SNPRelate package
`rm.invalid.allele` 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), "hg38"; "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-digit", 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(NaN, NaN, 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	<i>Minor Allele Frequency</i>
--------------	-------------------------------

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	<i>Missing Rates Per SNP</i>
--------------	------------------------------

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

genoobj a genotype object of [hlaSNPGenoClass](#)
samp.sel a logical vector, or an integer vector of indices
snp.sel 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:

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”

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", "hg38",  
"unknown"))
```

Arguments

`assembly` the human genome reference: "hg18", "hg19" (default), "hg38"; "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`*Make a SNP genotype object*

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), "hg38"; "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	<i>Load a model object from files</i>
---------------	---------------------------------------

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	<i>Conversion between the in-memory model and the object that can be saved in a file</i>
-----------------	--

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

Out-of-bag estimation of overall accuracy, per-allele sensitivity, etc

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 <code>data.frame</code> 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))
```



```

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	<i>Get sample IDs from HLA types with a filter</i>
-----------------	--

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	<i>Get SNP IDs and positions</i>
----------	----------------------------------

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 character 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), "hg38"; "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

```

hlaPredict(object, snp, cl=NULL,
  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)
## 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" or "hlaAASeqClass" object***Description**

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

Usage

```
## S3 method for class 'hlaAlleleClass'
summary(object, verbose=TRUE, ...)
## S3 method for class 'hlaAASeqClass'
summary(object, poly.only=TRUE, head=0L,
  verbose=TRUE, ...)
```

Arguments

object	an object of hlaAlleleClass or hlaAASeqClass
poly.only	if TRUE, only show the amino acid positions with polymorphism; otherwise, show all sequences
head	show the first head rows of cross tabulation, or 0L for all rows
verbose	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, if object is [hlaAlleleClass](#); a matrix of cross tabulation of amino acids at each position, if object is [hlaAASeqClass](#).

Author(s)

Xiuwen Zheng

See Also

[hlaAllele](#), [hlaConvSequence](#)

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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