

Package ‘SeqVarTools’

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Type Package

Title Tools for variant data

Description An interface to the fast-access storage format for VCF data provided in SeqArray, with tools for common operations and analysis.

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SeqVarTools-package *Tools for Variant Analysis*

Description

This package provides tools for data exploration and analysis of variants, extending the functionality of the package [SeqArray](#).

Details

[SeqArray](#) provides an alternative to the Variant Call Format (VCF) for storage of variants called from sequencing data, enabling efficient storage, fast access to subsets of the data, and rapid computation.

SeqVarTools provides an interface to the [SeqArray](#) storage format with tools for many common tasks in variant analysis and integration with basic S4 classes in Bioconductor.

Author(s)

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allele-methods *Extract allele information from a GDS object*

Description

Extract reference and alternate alleles and allele counts from a GDS object.

Usage

```
## S4 method for signature 'SeqVarGDSClass'  
refChar(gdsobj)  
## S4 method for signature 'SeqVarGDSClass'  
altChar(gdsobj, n=0)  
## S4 method for signature 'SeqVarGDSClass'  
nAlleles(gdsobj)
```

Arguments

`gdsobj` A [SeqVarGDSClass](#) object with VCF data.

`n` An integer indicating which alternate allele to return. `n=0` returns a comma-separated string of all alternate alleles.

Details

These methods parse the "allele" field of a GDS object.

Value

`refChar` returns a character vector of reference alleles.

`altChar` returns a character vector of alternate alleles. If `n=0`, multiple alternate alleles are represented as a comma-separated string. If `n>0`, only the `n`th alternate allele is returned.

`nAlleles` returns an integer vector of the number of alleles (reference and alternate) for each variant.

Author(s)

Stephanie Gogarten

See Also

[SeqVarGDSClass](#), [applyMethod](#)

Examples

```
gds <- seqOpen(seqExampleFileName("gds"))  
table(refChar(gds))  
table(altChar(gds))  
table(altChar(gds, n=1))  
table(altChar(gds, n=2), useNA="ifany")  
table(nAlleles(gds))  
seqClose(gds)
```

alleleFrequency *Allele frequency*

Description

Calculate allele frequency for each variant

Usage

```
## S4 method for signature 'SeqVarGDSCClass'  
alleleFrequency(gdsobj, n=0, use.names=FALSE)
```

Arguments

gdsobj	A SeqVarGDSCClass object with VCF data.
n	An integer indicating which allele to calculate the frequency of. n=0 is the reference allele, n=1 is the first alternate allele, and so on.
use.names	A logical indicating whether to assign variant IDs as names of the output vector.

Details

Frequency can be calculated over any allele, specified by the argument n. Default is the reference allele frequency (n=0).

Value

A numeric vector of allele frequencies.

Author(s)

Stephanie Gogarten

See Also

[SeqVarGDSCClass](#), [applyMethod](#), [heterozygosity](#)

Examples

```
gds <- seqOpen(seqExampleFileName("gds"))  
head(alleleFrequency(gds))  
head(alleleFrequency(gds, n=1))  
head(alleleFrequency(gds, n=2))  
seqClose(gds)
```

```
alternateAlleleDetection
      alternateAlleleDetection
```

Description

Calculate rates of detecting minor alleles given a “gold standard” dataset

Usage

```
## S4 method for signature 'SeqVarData,SeqVarData'
alternateAlleleDetection(gdsobj, gdsobj2, match.samples.on=c("subject.id", "subject.id"), verbose)
```

Arguments

`gdsobj` A [SeqVarData](#) object with VCF data.

`gdsobj2` A [SeqVarData](#) object with VCF data to be used as the “gold standard”.

`match.samples.on` A length-2 character vector indicating the column to be used for matching in each dataset’s `sampleData` annotation

`verbose` A logical indicating whether to print progress messages.

Details

Calculates the accuracy of detecting alternate alleles in one dataset (`gdsobj`) given a “gold standard” dataset (`gdsobj2`). Samples are matched using the `match.samples.on` argument. The first element of `match.samples.on` indicates the column to be used as the subject identifier for the first dataset, and the second element is the column to be used for the second dataset. Variants are matched on position and alleles using bi-allelic SNVs only. Genotype dosages are recoded to count the same allele if the reference allele in one dataset is the alternate allele in the other dataset. If a variant in one dataset matches to multiple variants in the second dataset, then only the first match will be used. If a variant is missing in either dataset for a given sample pair, that sample pair is ignored for that variant. To exclude certain variants or samples from the calculate, use [seqSetFilter](#) to set appropriate filters on each `gds` object.

This test is positive if an alternate allele was been detected. Results are returned on an allele level, such that:

TP, TN, FP, and FN are calculated as follows:

		genoData2		
		aa	Ra	RR
genoData1	aa	2TP	1TP + 1FP	2FP
	Ra	1TP + 1FN	1TN + 1TP	1TN + 1FP
	RR	2FN	1FN + 1TN	2TN

where “R” indicates a reference allele and “a” indicates an alternate allele.

Value

A data frame with the following columns:

variant.id.1	variant id from the first dataset
variant.id.2	matched variant id from the second dataset
n.samples	the number of samples with non-missing data for this variant
true.pos	the number of alleles that are true positives for this variant
true.neg	the number of alleles that are true negatives for this variant
false.pos	the number of alleles that are false positives for this variant
false.neg	the number of alleles that are false negatives for this variant

Author(s)

Adrienne Stilp

See Also

[SeqVarGDSCClass](#)

Examples

```
## Not run:
gds1 <- seqOpen(gdsfile.1) # dataset to test, e.g. sequencing
sample1 <- data.frame(subject.id=c("a", "b", "c"), sample.id=c("A", "B", "C"), stringsAsFactors=F)
seqData1 <- SeqVarData(gds1, sampleData=sample1)

gds2 <- seqOpen(gdsfile.2) # gold standard dataset, e.g. array genotyping
sample2 <- data.frame(subject.id=c("b", "c", "d"), sample.id=c("B", "C", "D"), stringsAsFactors=F)
seqData2 <- SeqVarData(gds2, sampleData=sample2)

res <- alleleDetectionAccuracy(seqData1, seqData2)

## End(Not run)
```

applyMethod

Apply method to GDS object

Description

Apply a method to a subset of variants and/or samples in a GDS object

Usage

```
## S4 method for signature 'SeqVarGDSCClass,function,character'
applyMethod(gdsobj, FUN, variant, sample=NULL, ...)
## S4 method for signature 'SeqVarGDSCClass,function,numeric'
applyMethod(gdsobj, FUN, variant, sample=NULL, ...)
## S4 method for signature 'SeqVarGDSCClass,function,GRanges'
applyMethod(gdsobj, FUN, variant, sample=NULL, ...)
## S4 method for signature 'SeqVarGDSCClass,function,missing'
applyMethod(gdsobj, FUN, variant, sample=NULL, ...)
```

Arguments

<code>gdsobj</code>	A SeqVarGDSClass object with VCF data.
<code>FUN</code>	A method or function to be applied to <code>gdsobj</code> .
<code>variant</code>	A vector of <code>variant.id</code> values or a <code>GRanges</code> object defining the variants to be included in the call to <code>FUN</code> .
<code>sample</code>	A vector of <code>sample.id</code> values defining the samples to be included in the call to <code>FUN</code> .
<code>...</code>	Additional arguments, passed to <code>FUN</code> .

Details

`applyMethod` applies a method or function `FUN` to the subset of variants defined by `variant` and samples defined by `sample` in a GDS object.

If a filter was previously set with [seqSetFilter](#), it will be saved and reset after the call to `applyMethod`.

Value

The result of the call to `FUN`.

Author(s)

Stephanie Gogarten

See Also

[SeqVarGDSClass](#)

Examples

```
gds <- seqOpen(seqExampleFileName("gds"))
variant.id <- seqGetData(gds, "variant.id")
sample.id <- seqGetData(gds, "sample.id")
applyMethod(gds, getGenotype, variant.id[1:5], sample.id[1:10])

library(GenomicRanges)
chrom <- seqGetData(gds, "chromosome")
pos22 <- seqGetData(gds, "position")[chrom == 22]
ranges <- GRanges(seqnames="22", IRanges(min(pos22), max(pos22)))
applyMethod(gds, heterozygosity, ranges, margin="by.sample")
applyMethod(gds, heterozygosity, ranges, margin="by.variant")

seqClose(gds)
```

countSingletons	<i>Count singletons</i>
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Description

Count singleton variants for each sample

Usage

```
## S4 method for signature 'SeqVarGDSCClass'  
countSingletons(gdsobj, use.names=FALSE)
```

Arguments

gdsobj	A SeqVarGDSCClass object with VCF data.
use.names	A logical indicating whether to assign variant IDs as names of the output vector.

Details

A singleton variant is a variant in which only one sample has a non-reference allele. For each sample, countSingletons finds the number of variants for which that sample has the only non-reference allele.

Value

A vector of the number of singleton variants per sample.

Author(s)

Stephanie Gogarten

See Also

[SeqVarGDSCClass](#), [applyMethod](#), [alleleFrequency](#)

Examples

```
gds <- seqOpen(seqExampleFileName("gds"))  
head(countSingletons(gds))  
seqClose(gds)
```

duplicateDiscordance *Duplicate discordance*

Description

Find discordance rate for duplicate sample pairs

Usage

```
## S4 method for signature 'SeqVarData,missing'
duplicateDiscordance(gdsobj, match.samples.on="subject.id", check.phase=FALSE, verbose=TRUE)
## S4 method for signature 'SeqVarData,SeqVarData'
duplicateDiscordance(gdsobj, obj2, match.samples.on=c("subject.id", "subject.id"), match.variants
```

Arguments

gdsobj	A SeqVarData object with VCF data.
obj2	A SeqVarData object with VCF data.
match.samples.on	Character string or vector of strings indicating which column should be used for matching samples. See details.
match.variants.on	Character string of length one indicating how to match variants. See details.
discordance.type	Character string describing how discordances should be calculated. See details.
check.phase	A logical indicating whether phase should be considered when calculating discordance.
by.variant	Calculate discordance by variant, otherwise by sample
verbose	A logical indicating whether to print progress messages.

Details

For calls that involve only one gds file, duplicate discordance is calculated by sample pair and by variant. If there are more than two samples per subject in `samples`, only the first two samples are used and a warning message is printed. If `check.phase=TRUE`, variants with mismatched phase are considered discordant. If `check.phase=FALSE`, phase is ignored.

For calls that involve two gds files, duplicate discordance is calculated by matching sample pairs and variants between the two data sets. Only biallelic SNVs are considered in the comparison. Variants can be matched using chromosome and position only (`match.variants.on="position"`) or by using chromosome, position, and alleles (`match.variants.on="alleles"`). If matching on alleles and the reference allele in the first dataset is the alternate allele in the second dataset, the genotype dosage will be recoded so the same allele is counted before making the comparison. If a variant in one dataset maps to multiple variants in the other dataset, only the first pair is considered for the comparison. Discordances can be calculated using either genotypes (`discordance.type = "genotype"`) or heterozygote/homozygote status (`discordance.type = "hethom"`). The latter is a method to calculate discordance that does not require alleles to be measured on the same strand in both datasets, so it is probably best to also set `match.variants.on = "position"` if using the "hethom" option.

The argument `match.samples.on` can be used to select which column in the `sampleData` of the input `SeqVarData` object should be used for matching samples. For one gds file, `match.samples.on` should be a single string. For two gds files, `match.samples.on` should be a length-2 vector of character strings, where the first element is the column to use for the first gds object and the second element is the column to use for the second gds file.

To exclude certain variants or samples from the calculate, use `seqSetFilter` to set appropriate filters on each gds object.

Value

For calls involving one gds file, a list with the following elements:

- `by.variant` A data.frame with the number of discordances for each variant, the number of sample pairs with non-missing data, and the discordance rate (`num.discord / num.pair`). Row names are variant ids.
- `by.subject` A data.frame with the sample ids for each pair, the number of discordances, the number of non-missing variants, and the discordance rate (`num.discord / num.var`). Row.names are `subject.id` (as given in `samples`).

For calls involving two gds files, A data frame with the following columns, depending on whether `by.variant=TRUE` or `FALSE`:

- `subjectID` currently, this is the sample ID (`by.variant=FALSE` only)
- `sample.id.1/variant.id.1`
 sample id or variant id in the first gds file
- `sample.id.2/variant.id.1`
 sample id or variant id in the second gds file
- `n.variants/n.samples`
 the number of non-missing variants or samples that were compared
- `n.concordant` the number of concordant variants
- `n.alt` the number of variants involving the alternate allele in either sample
- `n.alt.conc` the number of concordant variants involving the alternate allele in either sample
- `n.het.ref` the number of mismatches where one call is a heterozygote and the other is a reference homozygote
- `n.het.alt` the number of mismatches where one call is a heterozygote and the other is an alternate homozygote
- `n.ref.alt` the number of mismatches where the calls are opposite homozygotes

Author(s)

Stephanie Gogarten, Adrienne Stilp

See Also

[SeqVarData](#), [applyMethod](#)

Examples

```

require(Biobase)

gds <- seqOpen(seqExampleFileName("gds"))

## the example file has one sample per subject, but we
## will match the first four samples into pairs as an example
sample.id <- seqGetData(gds, "sample.id")
samples <- AnnotatedDataFrame(data.frame(data.frame(subject.id=rep(c("subj1", "subj2"), times=45),
                                             sample.id=sample.id,
                                             stringsAsFactors=FALSE)))
seqData <- SeqVarData(gds, sampleData=samples)

# set a filter on the first four samples
seqSetFilter(seqData, sample.id=sample.id[1:4])

disc <- duplicateDiscordance(seqData)
head(disc$by.variant)
disc$by.subject
seqClose(gds)

```

getGenotype

Get genotype data

Description

Get matrix of genotype values from a GDS object as VCF-style character strings

Usage

```

## S4 method for signature 'SeqVarGDSCClass'
getGenotype(gdsobj, use.names=TRUE)
## S4 method for signature 'SeqVarGDSCClass'
getGenotypeAlleles(gdsobj, use.names=TRUE, sort=FALSE)
## S4 method for signature 'SeqVarGDSCClass'
refDosage(gdsobj, use.names=TRUE)
## S4 method for signature 'SeqVarGDSCClass'
altDosage(gdsobj, use.names=TRUE)
## S4 method for signature 'SeqVarGDSCClass,numeric'
alleleDosage(gdsobj, n=0, use.names=TRUE)
## S4 method for signature 'SeqVarGDSCClass,list'
alleleDosage(gdsobj, n, use.names=TRUE)

```

Arguments

gdsobj	A SeqVarGDSCClass object with VCF data.
use.names	A logical indicating whether to assign sample and variant IDs as dimnames of the resulting matrix.
sort	Logical for whether to sort alleles lexicographically ("G/T" instead of "T/G").
n	An integer, vector, or list indicating which allele(s) to return dosage for. n=0 is the reference allele, n=1 is the first alternate allele, and so on.

Details

In `getGenotype`, genotypes are coded as in the VCF file, where "0/0" is homozygous reference, "0/1" is heterozygous for the first alternate allele, "0/2" is heterozygous for the second alternate allele, etc.

Separators are "/" for unphased and "|" for phased. If `sort=TRUE`, all returned genotypes will be unphased. Missing genotypes are coded as NA.

Only diploid genotypes (the first two alleles at a given site) are returned.

If the argument `n.toAlleleDosage` is a single integer, the same allele is counted for all variants. If `n` is a vector with `length=number of variants in the current filter`, a different allele is counted for each variant. If `n` is a list, more than one allele can be counted for each variant. For example, if `n[[1]]=c(1, 3)`, genotypes "0/1" and "0/3" will each have a dosage of 1 and genotype "1/3" will have a dosage of 2.

Value

`getGenotype` and `getGenotypeAlleles` return a character matrix with dimensions `[sample,variant]` containing diploid genotypes.

`getGenotype` returns alleles as "0", "1", "2", etc. indicating reference and alternate alleles.

`getGenotypeAlleles` returns alleles as "A", "C", "G", "T". `sort=TRUE` sorts lexicographically, which may be useful for comparing genotypes with data generated using a different reference sequence.

`refDosage` returns an integer matrix with the dosage of the reference allele: 2 for two copies of the reference allele ("0/0"), 1 for one copy of the reference allele, and 0 for two alternate alleles.

`altDosage` returns an integer matrix with the dosage of any alternate allele: 2 for two alternate alleles ("1/1", "1/2", etc.), 1 for one alternate allele, and 0 for no alternate allele (homozygous reference).

`alleleDosage` with an integer argument returns an integer matrix with the dosage of the specified allele only: 2 for two copies of the allele ("0/0" if `n=0`, "1/1" if `n=1`, etc.), 1 for one copy of the specified allele, and 0 for no copies of the allele.

`alleleDosage` with a list argument returns a list of sample x allele matrices with the dosage of each specified allele for each variant.

Author(s)

Stephanie Gogarten

See Also

[SeqVarGDSCClass](#), [applyMethod](#), [seqGetData](#), [seqSetFilter](#), [alleleFrequency](#)

Examples

```
gds <- seqOpen(seqExampleFileName("gds"))
variant.id <- seqGetData(gds, "variant.id")
sample.id <- seqGetData(gds, "sample.id")
seqSetFilter(gds, variant.id=variant.id[1:5],
             sample.id=sample.id[1:10])
getGenotype(gds)
getGenotypeAlleles(gds)
refDosage(gds)
altDosage(gds)
```

```
alleleDosage(gds, n=0)
alleleDosage(gds, n=1)
alleleDosage(gds, n=c(0,1,0,1,0))
alleleDosage(gds, n=list(0,c(0,1),0,c(0,1),1))
seqClose(gds)
```

getVariableLengthData *Get variable-length data*

Description

Get data with multiple values per sample from a GDS object and return as an array

Usage

```
## S4 method for signature 'SeqVarGDSCClass,character'
getVariableLengthData(gdsobj, var.name, use.names=TRUE)
```

Arguments

gdsobj	A SeqVarGDSCClass object with VCF data.
var.name	Character string with name of the variable, most likely "annotation/format/VARIABLE_NAME".
use.names	A logical indicating whether to assign sample and variant IDs as dimnames of the resulting matrix.

Details

Data which are indicated as having variable length (possibly different numbers of values for each variant) in the VCF header are stored as variable-length data in the GDS file. Each such data object has two components, "length" and "data." "length" indicates how many values there are for each variant, while "data" is a matrix with one row per sample and columns defined as all values for variant 1, followed by all values for variant 2, etc.

getVariableLengthData converts this format to a 3-dimensional array, where the length of the first dimension is the maximum number of values in "length," and the remaining dimensions are sample and variant. Missing values are given as NA. If the first dimension of this array would have length 1, the result is converted to a matrix.

Value

An array with dimensions [n, sample, variant] where n is the maximum number of values possible for a given sample/variant cell. If n=1, a matrix with dimensions [sample,variant].

Author(s)

Stephanie Gogarten

See Also

[SeqVarGDSCClass](#), [applyMethod](#), [seqGetData](#)

Examples

```

file <- system.file("extdata", "gl_chr1.gds", package="SeqVarTools")
gds <- seqOpen(file)
## genotype likelihood
gl <- seqGetData(gds, "annotation/format/GL")
names(gl)
gl$length
## 3 values per variant - likelihood of RR,RA,AA genotypes
dim(gl$data)
## 85 samples (rows) and 9 variants with 3 values each - 27 columns

gl.array <- getVariableLengthData(gds, "annotation/format/GL")
dim(gl.array)
## 3 genotypes x 85 samples x 9 variants
head(gl.array[1,,])
head(gl.array[2,,])
head(gl.array[3,,])

## genotype dosage
ds <- seqGetData(gds, "annotation/format/DS")
names(ds)
ds$length
## 1 value per variant
dim(ds$data)
## 85 samples (rows) and 9 variants (columns)

ds.array <- getVariableLengthData(gds, "annotation/format/DS")
dim(ds.array)
## 85 samples x 9 variants
head(ds.array)

seqClose(gds)

```

heterozygosity

Heterozygosity and Homozygosity

Description

Calculate heterozygosity and homozygosity by variant or by sample

Usage

```

## S4 method for signature 'SeqVarGDSClass'
heterozygosity(gdsobj, margin=c("by.variant", "by.sample"), use.names=FALSE)
## S4 method for signature 'SeqVarGDSClass'
homozygosity(gdsobj, allele=c("any", "ref", "alt"), margin=c("by.variant", "by.sample"), use.names=FALSE)
## S4 method for signature 'SeqVarGDSClass'
hethom(gdsobj, use.names=FALSE)

```

Arguments

`gdsobj` A [SeqVarGDSClass](#) object with VCF data.

margin	Possible values are "by.variant" or "by.sample," indicating whether the calculation should be done over all samples for each variant, or over all variants for each sample.
use.names	A logical indicating whether to assign variant or samples IDs as names of the output vector.
allele	Possible values are "any", "ref," or "alt," indicating which alleles to consider when calculating homozygosity.

Details

heterozygosity calculates the fraction of heterozygous genotypes in a GDS object, either by variant or by sample.

homozygosity calculates the rate of homozygous genotypes in a GDS object, either by sample or by variant. If allele="any", all homozygous genotypes are considered (reference or any alternate allele). If allele="ref", only reference homozygotes are considered. If allele="alt", any alternate allele homozygote is considered. For example, "ref" will count "0/0" genotypes only, "alt" will count "1/1", "2/2", etc. (but not "0/0"), and "any" will count all of the above.

hethom calculates the ratio of heterozygous genotypes to alternate homozygous genotypes by sample.

Value

A numeric vector of heterozygosity or homozygosity rates. If margin="by.variant", the vector will have length equal to the number of variants in the GDS object. If margin="by.sample", the vector will have length equal to the number of samples.

Author(s)

Stephanie Gogarten

See Also

[SeqVarGDSClass](#), [applyMethod](#), [alleleFrequency](#)

Examples

```
gds <- seqOpen(seqExampleFileName("gds"))
head(heterozygosity(gds, margin="by.variant"))
head(homozygosity(gds, allele="any", margin="by.variant"))
head(homozygosity(gds, allele="ref", margin="by.variant"))
head(homozygosity(gds, allele="alt", margin="by.variant"))

## Het/Hom Non-Ref by sample
head(hethom(gds))

seqClose(gds)
```

`hwe`*Exact test for Hardy-Weinberg equilibrium*

Description

Performs an exact test for Hardy-Weinberg equilibrium on Single-Nucleotide Variants

Usage

```
## S4 method for signature 'SeqVarGDSCClass'  
hwe(gdsobj, permute=FALSE)
```

Arguments

<code>gdsobj</code>	A SeqVarGDSCClass object with VCF data.
<code>permute</code>	A logical indicating whether to permute the genotypes to get a set of p-values under the null hypothesis.

Details

HWE calculations are performed with the [HWEExact](#) function in the [GWASExactHW](#) package.

`permute=TRUE` will permute the genotypes prior to running the test. This can be useful for obtaining a set of expected values under the null hypothesis to compare to the observed values.

P values are set to NA for all multiallelic and monomorphic variants.

Value

A data.frame with the following columns:

<code>variant.id</code>	The unique identifier for the variant
<code>nAA</code>	The number of reference homozygotes
<code>nAa</code>	The number of heterozygotes
<code>naa</code>	The number of alternate homozygotes
<code>afreq</code>	The reference allele frequency
<code>p</code>	p values for the exact test
<code>f</code>	The inbreeding coefficient, $1 - \text{observed heterozygosity} / \text{expected heterozygosity}$

Author(s)

Stephanie Gogarten

See Also

[SeqVarGDSCClass](#), [applyMethod](#)

Examples

```
gds <- seqOpen(seqExampleFileName("gds"))
## autosomal variants only
auto <- seqGetData(gds, "chromosome") %in% 1:22
var.auto <- seqGetData(gds, "variant.id")[auto]
hw <- applyMethod(gds, hwe, variant=var.auto)
head(hw)
sum(is.na(hw$p))
range(hw$p, na.rm=TRUE)
seqClose(gds)
```

inbreedCoeff	<i>Inbreeding coefficient</i>
--------------	-------------------------------

Description

Calculates the inbreeding coefficient by variant or by sample

Usage

```
## S4 method for signature 'SeqVarGDSCClass'
inbreedCoeff(gdsobj, margin=c("by.variant", "by.sample"), use.names=FALSE)
```

Arguments

gdsobj	A SeqVarGDSCClass object with VCF data.
margin	Possible values are "by.variant" or "by.sample," indicating whether the calculation should be done over all samples for each variant, or over all variants for each sample.
use.names	A logical indicating whether to assign variant or sample IDs as names of the output vector.

Details

For inbreeding coefficients by variant, calculates $1 - \text{observed heterozygosity} / \text{expected heterozygosity}$.

For individual inbreeding coefficients (`margin="by.sample"`), calculates Visscher's estimator described in Yang et al. (2010).

Value

Values for the inbreeding coefficient.

Author(s)

Xiuwen Zheng, Stephanie Gogarten

References

Yang J, Benyamin B, McEvoy BP, Gordon S, Henders AK, Nyholt DR, Madden PA, Heath AC, Martin NG, Montgomery GW, Goddard ME, Visscher PM. 2010. Common SNPs explain a large proportion of the heritability for human height. *Nat Genet.* 42(7):565-9. Epub 2010 Jun 20.

See Also

[SeqVarGDSCClass](#), [applyMethod](#)

Examples

```
gds <- seqOpen(seqExampleFileName("gds"))
f <- inbreedCoeff(gds, margin="by.variant")
range(f, na.rm=TRUE)

ic <- inbreedCoeff(gds, margin="by.sample")
range(ic)
seqClose(gds)
```

isSNV

Flag single nucleotide variants

Description

Flag single nucleotide variants

Usage

```
## S4 method for signature 'SeqVarGDSCClass'
isSNV(x, biallelic=TRUE)
```

Arguments

x A [SeqVarGDSCClass](#) object with VCF data.
biallelic A logical indicating whether only biallelic SNVs are considered.

Details

If `biallelic=TRUE`, a variant is considered a single nucleotide variant (SNV) if there is one reference allele and one alternate allele, each one base in length. If `biallelic=FALSE`, there may be multiple alternate alleles, each one base in length.

Setting `biallelic=TRUE` is considerably faster for large data sets.

Value

A logical vector indicating which variants are SNVs.

Author(s)

Stephanie Gogarten

See Also

[SeqVarGDSCClass](#), [allele-methods](#), [applyMethod](#)

Examples

```
gds <- seqOpen(seqExampleFileName("gds"))
table(isSNV(gds))
seqClose(gds)
```

isVariant	<i>Locate variant samples across sites</i>
-----------	--

Description

Locate which samples are variant for each site in a GDS object

Usage

```
## S4 method for signature 'SeqVarGDSClass'  
isVariant(gdsobj, use.names=FALSE)
```

Arguments

gdsobj	A SeqVarGDSClass object with VCF data.
use.names	A logical indicating whether to assign sample and variant IDs as dimnames of the resulting matrix.

Details

Each sample/site cell of the resulting matrix is TRUE if the genotype at that location for that sample contains an alternate allele. A genotype of "0/0" is not variant, while genotypes "0/1", "1/0", "0/2", etc. are variant.

Value

A logical matrix with dimensions [sample,site] which is TRUE for cells where the genotype contains an alternate allele.

Author(s)

Stephanie Gogarten

See Also

[SeqVarGDSClass](#), [applyMethod](#), [getGenotype](#)

Examples

```
gds <- seqOpen(seqExampleFileName("gds"))  
variant.id <- seqGetData(gds, "variant.id")  
sample.id <- seqGetData(gds, "sample.id")  
applyMethod(gds, isVariant, variant.id[1:5], sample.id[1:10])  
applyMethod(gds, isVariant, variant.id[1:5], sample.id[1:10], use.names=TRUE)  
seqClose(gds)
```

meanBySample	<i>Mean value by sample</i>
--------------	-----------------------------

Description

Calculate the mean value of a variable by sample over all variants

Usage

```
## S4 method for signature 'SeqVarGDSCClass'  
meanBySample(gdsobj, var.name, use.names=FALSE)
```

Arguments

gdsobj	A SeqVarGDSCClass object with VCF data.
var.name	Character string with name of the variable, most likely "annotation/format/VARIABLE_NAME".
use.names	A logical indicating whether to assign sample IDs as names of the output vector.

Details

Mean values by variant can be calculated using `seqApply(gdsobj, var.name, mean, na.rm=TRUE)`. Currently `seqApply` can only be used with the option `margin="by.variant"`. This method provides a way to calculate mean values by sample.

Value

A numeric vector of mean values.

Author(s)

Stephanie Gogarten

See Also

[SeqVarGDSCClass](#), [applyMethod](#), [seqApply](#)

Examples

```
gds <- seqOpen(seqExampleFileName("gds"))  
head(meanBySample(gds, "annotation/format/DP", use.names=TRUE))  
seqClose(gds)
```

mendelErr	<i>Mendelian errors</i>
-----------	-------------------------

Description

Detect Mendelian errors

Usage

```
## S4 method for signature 'SeqVarGDSCClass'  
mendelErr(gdsobj, pedigree, use.names=FALSE,  
autosomes=1:22, xchrom="X", ychrom="Y", verbose=TRUE)
```

Arguments

gdsobj	A SeqVarGDSCClass object with VCF data.
pedigree	A data.frame with columns (family, individ, father, mother, sex, sample.id). "sex" column should have values "M"/"F". "sample.id" values should correspond to "sample.id" in gdsobj.
use.names	A logical indicating whether to assign variant IDs as names of the output vector.
autosomes	A vector with chromosome values in gdsobj corresponding to autosomes.
xchrom	The chromosome value in gdsobj corresponding to the X chromosome.
ychrom	The chromosome value in gdsobj corresponding to the Y chromosome.
verbose	A logical indicating whether to print the number of samples selected for each trio.

Details

Mendelian errors are detected for each trio in pedigree. Duos (mother or father missing) are included. The pedigree must have only one sample per individual.

Value

A list with the following elements:

by.variant	An integer vector with the number of mendelian errors detected for each variant. If use.names=TRUE, the vector will be named with variant IDs.
by.trio	An integer vector with the number of mendelian errors detected for each trio. The vector will be named with the sample ID of the child in each trio.

Author(s)

Stephanie Gogarten

See Also

[SeqVarGDSCClass](#), [applyMethod](#)

Examples

```
gds <- seqOpen(seqExampleFileName("gds"))
data(pedigree)
err <- mendelErr(gds, pedigree)
table(err$by.variant)
err$by.trio
seqClose(gds)
```

missingGenotypeRate *Missing genotype rate*

Description

Calculate missing genotype rate by variant or by sample

Usage

```
## S4 method for signature 'SeqVarGDSClass'
missingGenotypeRate(gdsobj, margin=c("by.variant", "by.sample"), use.names=FALSE)
```

Arguments

gdsobj	A SeqVarGDSClass object with VCF data.
margin	Possible values are "by.variant" or "by.sample," indicating whether the calculation should be done over all samples for each variant, or over all variants for each sample.
use.names	A logical indicating whether to assign variant IDs as names of the output vector.

Details

Calculates the fraction of missing genotypes in a GDS object, either by variant or by sample.

Value

A numeric vector of missing genotype rates. If `margin="by.variant"`, the vector will have length equal to the number of variants in the GDS object. If `margin="by.sample"`, the vector will have length equal to the number of samples.

Author(s)

Stephanie Gogarten

See Also

[SeqVarGDSClass](#), [applyMethod](#), [getGenotype](#)

Examples

```
gds <- seqOpen(seqExampleFileName("gds"))
head(missingGenotypeRate(gds, margin="by.variant"))
head(missingGenotypeRate(gds, margin="by.sample"))
seqClose(gds)
```

pca *Principal Component Analysis*

Description

Calculates the eigenvalues and eigenvectors of a SeqVarGDSClass object with Principal Component Analysis

Usage

```
## S4 method for signature 'SeqVarGDSClass'  
pca(gdsobj, eigen.cnt=32)
```

Arguments

gdsobj A [SeqVarGDSClass](#) object with VCF data.
eigen.cnt An integer indicating how many eigenvalues and eigenvectors to return.

Details

Calculates the genetic covariance matrix and finds the eigen decomposition.

Value

A list with two elements:

eigenval A vector of length eigen.cnt with eigenvalues
eigenvect A matrix of dimension ("selected samples", eigen.cnt).

Author(s)

Xiuwen Zheng, Stephanie Gogarten

References

Patterson N, Price AL, Reich D (2006) Population structure and eigenanalysis. PLoS Genetics 2:e190.

See Also

[SeqVarGDSClass](#), [applyMethod](#)

Examples

```
gds <- seqOpen(seqExampleFileName("gds"))  
pca <- pca(gds)  
pca$eigenval  
head(pca$eigenvect)  
seqClose(gds)
```

pedigree	<i>Pedigree for example data</i>
----------	----------------------------------

Description

Pedigree for example data files in SeqArray.

Usage

```
pedigree
```

Format

A data.frame with the following columns.

family Family ID

individ Individual ID

father Father ID

mother Mother ID

sex Sex

sample.id sample.id in VCF/GDS files

Details

There is one trio in the pedigree.

Source

HapMap

Examples

```
data(pedigree)
head(pedigree)
gds <- seqOpen(seqExampleFileName("gds"))
setdiff(seqGetData(gds, "sample.id"), pedigree$sample.id)
seqClose(gds)
```

refFrac	<i>Reference allele fraction</i>
---------	----------------------------------

Description

Calculate fraction of reference allele reads

Usage

```
## S4 method for signature 'SeqVarGDSCClass'
refFrac(gdsobj, use.names=TRUE)
## S4 method for signature 'SeqVarGDSCClass'
refFracOverHets(gdsobj, FUN=mean, use.names=TRUE)
## S4 method for signature 'SeqVarGDSCClass'
refFracPlot(gdsobj, variant.id, highlight=NULL, ...)
```

Arguments

<code>gdsobj</code>	A SeqVarGDSCClass object with VCF data.
<code>FUN</code>	The function to apply over heterozygote calls (mean or median).
<code>use.names</code>	A logical indicating whether to assign variant or samples IDs as names of the output vector.
<code>variant.id</code>	A vector of variant.ids to plot.
<code>highlight</code>	A list of sample.ids to highlight with sequential integers on each plot
<code>...</code>	Additional arguments passed to plot .

Details

The variable "annotation/format/AD" (allelic depth) is required to compute the reference allele fraction.

`refFracPlot` generates plots of total unfiltered depth (sum over "AD" for all alleles) versus reference allele fraction. Points are color-coded by called genotype: teal = reference homozygote, orange = heterozygote including the reference allele, fuschia = heterozygote with two alternate alleles, purple = alternate homozygote, black = missing. Darker colors indicate a higher density of points. Vertical black line is at 0.5, vertical orange line is the median reference allele fraction for ref/alt heterozygotes. Values significantly different from 0.5 (after applying a Bonferroni correction) are plotted with triangles.

Value

`refFrac` returns a sample by variant array of the reference allele fraction, defined as `ref_depth / total_depth`.

`refFracOverHets` returns the mean (or other function, e.g. median) of reference allele depth (per variant) over all samples called as heterozygotes.

Author(s)

Stephanie Gogarten

See Also

[SeqVarGDSCClass](#), [applyMethod](#)

Examples

```
gdsfile <- system.file("extdata", "hapmap_exome_chr22.gds", package="SeqVarTools")
gds <- seqOpen(gdsfile)
RF <- refFrac(gds)
dim(RF)
```

```

samples <- seqGetData(gds, "sample.id")
refFracPlot(gds, variant.id=5:6,
            highlight=list(samples[2:3], samples[4:5]))
seqClose(gds)

```

regression

Linear or logistic regression

Description

Run linear or logistic regression on variants

Usage

```

## S4 method for signature 'SeqVarData'
regression(gdsobj, outcome, covar=NULL,
           model.type=c("linear", "logistic", "firth"))

```

Arguments

<code>gdsobj</code>	A SeqVarData object
<code>outcome</code>	A character string with the name of the column in <code>sampleData(gdsobj)</code> containing the outcome variable
<code>covar</code>	A character vector with the name of the column(s) in <code>sampleData(gdsobj)</code> containing the covariates
<code>model.type</code>	the type of model to be run. "linear" uses lm , "logistic" uses glm with <code>family=binomial()</code> , and "firth" uses logistf .

Value

a data.frame with the following columns (if applicable):

<code>variant.id</code>	variant identifier
<code>n</code>	number of samples with non-missing data
<code>n0</code>	number of controls (outcome=0) with non-missing data
<code>n1</code>	number of cases (outcome=1) with non-missing data
<code>freq</code>	reference allele frequency
<code>freq0</code>	reference allele frequency in controls
<code>freq1</code>	reference allele frequency in cases
<code>Est</code>	beta estimate for genotype
<code>SE</code>	standard error of beta estimate for the genotype
<code>Wald.Stat</code>	chi-squared test statistic for association
<code>Wald.pval</code>	p-value for association
<code>PPL.Stat</code>	firth only: profile penalized likelihood test statistic for association
<code>PPL.pval</code>	firth only: p-value for association

Author(s)

Stephanie Gogarten

See Also[SeqVarData](#), [seqSetFilter](#), [lm](#), [glm](#), [logistf](#)**Examples**

```
gds <- seqOpen(seqExampleFileName("gds"))

## create some phenotype data
library(Biobase)
sample.id <- seqGetData(gds, "sample.id")
n <- length(sample.id)
df <- data.frame(sample.id,
  sex=sample(c("M", "F"), n, replace=TRUE),
  age=sample(18:70, n, replace=TRUE),
  phen=rnorm(n),
  stringsAsFactors=FALSE)
meta <- data.frame(labelDescription=c("sample identifier",
  "sex", "age", "phenotype"), row.names=names(df))
sample.data <- AnnotatedDataFrame(df, meta)
seqData <- SeqVarData(gds, sample.data)

## select samples and variants
seqSetFilter(gds, sample.id=sample.id[1:50], variant.id=1:10)

res <- regression(seqData, outcome="phen", covar=c("sex", "age"))
res
seqClose(gds)
```

SeqVarData*SeqVarData*

Description

Extends [SeqVarGDSCClass](#) to include annotation for samples and variants.

Details

A `SeqVarData` object adds an [AnnotatedDataFrame](#) for both samples and variants to a [SeqVarGDSCClass](#) object.

Constructor

`SeqVarData(gds, sampleData, variantData)`: Returns a `SeqVarData` object.

`gds` can be either the filename of a sequencing GDS file or an existing [SeqVarGDSCClass](#) object.

`sampleData` must be an [AnnotatedDataFrame](#) with a column `sample.id` matching `sample.id` in the GDS file. If this argument is missing, a data frame with only `sample.id` will be created.

`variantData` must be an [AnnotatedDataFrame](#) with a column `variant.id` matching `variant.id` in the GDS file. If this argument is missing, a data frame with only `variant.id` will be created.

Accessors

sampleData(x), sampleData(x)<- value: Get or set the [AnnotatedDataFrame](#) with sample data. If a sample filter has been applied with [seqSetFilter](#), only selected samples will be returned. value must include all samples.

variantData(x), variantData(x)<- value: Get or set the [AnnotatedDataFrame](#) with variant data. If a variant filter has been applied with [seqSetFilter](#), only selected variants will be returned. value must include all variants.

granges(x): Return a [GRanges](#) object with the columns of variantData as metadata columns.

See [SeqVarGDSClass](#) for additional methods.

Author(s)

Stephanie Gogarten

See Also

[SeqVarGDSClass](#), [seqVCF2GDS](#), [seqOpen](#), [seqGetData](#), [seqSetFilter](#), [seqApply](#), [seqClose](#)

Examples

```
gds <- seqOpen(seqExampleFileName("gds"))

## create sample annotation
library(Biobase)
sample.id <- seqGetData(gds, "sample.id")
sex <- sample(c("M","F"), length(sample.id), replace=TRUE)
phenotype <- rnorm(length(sample.id), mean=10)
samp <- data.frame(sample.id, sex, phenotype, stringsAsFactors=FALSE)
meta <- data.frame(labelDescription=c("unique sample identifier",
  "sex (M=male, f=female)", "example phenotype"),
  row.names=names(samp), stringsAsFactors=FALSE)
sample.data <- AnnotatedDataFrame(samp, meta)

seqData <- SeqVarData(gds, sample.data)

## add another annotation column
sample.data$site <- sample(letters, length(sample.id), replace=TRUE)
varMetadata(sample.data)["site", "labelDescription"] <- "study site"
sampleData(seqData) <- sample.data

## set a filter
seqSetFilter(seqData, sample.id=sample.id[1:10])
nrow(sampleData(seqData))

seqClose(seqData)
```

setVariantID

Change the variant ID of a GDS file

Description

Replace the variable "variant.id" in a GDS file with a user-supplied unique vector of the same length.

Usage

```
setVariantID(gdsfile, variant.id)
```

Arguments

`gdsfile` A character string with the file path of a GDS file.
`variant.id` A vector with the new variant IDs.

Details

A VCF file created by [seqVCF2GDS](#) creates a variable "variant.id" containing sequential integers to identify each variant. `setVariantID` allows the user to replace these values with something more meaningful. The replacement values in `variant.id` must be unique and have the same length as the original "variant.id" vector.

Using character values for `variant.id` may affect performance for large datasets.

Author(s)

Stephanie Gogarten

See Also

[SeqVarGDSClass](#), [seqVCF2GDS](#)

Examples

```
oldfile <- system.file("extdata", "gl_chr1.gds", package="SeqVarTools")
newfile <- tempfile()
file.copy(oldfile, newfile)

gds <- seqOpen(newfile)
rsID <- seqGetData(gds, "annotation/id")
seqClose(gds)

setVariantID(newfile, rsID)
gds <- seqOpen(newfile)
seqGetData(gds, "variant.id")
head(getGenotype(gds))
seqClose(gds)

unlink(newfile)
```

titv

Transition/Transversion Ratio

Description

Calculate transition/transversion ratio overall or by sample

Usage

```
## S4 method for signature 'SeqVarGDSClass'
titv(gdsobj, by.sample=FALSE, use.names=FALSE)
```

Arguments

<code>gdsobj</code>	A SeqVarGDSClass object with VCF data.
<code>by.sample</code>	A logical indicating whether TiTv should be calculated by sample or overall for the entire GDS object.
<code>use.names</code>	A logical indicating whether to assign sample IDs as names of the output vector (if <code>by.sample=TRUE</code>).

Details

If `by.sample=FALSE` (the default), `titv` calculates the transition/transversion ratio (TiTv) over all samples.

If `by.sample=TRUE`, `titv` calculates TiTv over all variant genotypes (heterozygous or homozygous non-reference) for each sample.

Value

A single value for TiTv if `by.sample=FALSE`. If `by.sample=TRUE`, a numeric vector containing TiTv for each sample.

Author(s)

Stephanie Gogarten

See Also

[SeqVarGDSClass](#), [applyMethod](#), [isVariant](#)

Examples

```
gds <- seqOpen(seqExampleFileName("gds"))
titv(gds)
titv(gds, by.sample=TRUE)

## apply to a subset of variants
library(GenomicRanges)
chrom <- seqGetData(gds, "chromosome")
pos22 <- seqGetData(gds, "position")[chrom == 22]
ranges <- GRanges(seqnames="22", IRanges(min(pos22), max(pos22)))
applyMethod(gds, titv, ranges)

seqClose(gds)
```

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