Package ‘SeqVarTools’

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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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Extract allele information from a GDS object

Description

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

### Usage

```r
## 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

```r
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**

Calculate allele frequency for each variant.

## Usage

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

### Arguments

- `gdsobj`: A `SeqVarGDSClass` 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

`SeqVarGDSClass`, `applyMethod`, `heterozygosity`

### Examples

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

**Description**

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

**Usage**

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

**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:

<table>
<thead>
<tr>
<th>aa</th>
<th>Ra</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>2TP</td>
<td>1TP + 1FP</td>
<td>2FP</td>
</tr>
<tr>
<td>1TP + 1FN</td>
<td>1TN + 1TP</td>
<td>1TN + 1FP</td>
</tr>
<tr>
<td>2FN</td>
<td>1FN + 1TN</td>
<td>2TN</td>
</tr>
</tbody>
</table>

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

**Value**

A data frame with the following columns:
applyMethod

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
SeqVarGDSClass

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 'SeqVarGDSClass,function,character'
applyMethod(gdsobj, FUN, variant, sample=NULL, ...)

## S4 method for signature 'SeqVarGDSClass,function,numeric'
applyMethod(gdsobj, FUN, variant, sample=NULL, ...)

## S4 method for signature 'SeqVarGDSClass,function,GRanges'
applyMethod(gdsobj, FUN, variant, sample=NULL, ...)

## S4 method for signature 'SeqVarGDSClass,function,missing'
applyMethod(gdsobj, FUN, variant, sample=NULL, ...)

**applyMethod**

Arguments

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

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

```r
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  

Count singletons

Description

Count singleton variants for each sample

Usage

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

Arguments

- `gdsobj`: A `SeqVarGDSClass` 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

`SeqVarGDSClass`, `applyMethod`, `alleleFrequency`

Examples

```r
gds <- seqOpen(seqExampleFileName("gds"))
head(countSingletons(gds))
seqClose(gds)
```
**duplicateDiscordance**  
Duplicate discordance

**Description**

Find discordance rate for duplicate sample pairs

**Usage**

```r
## 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.on=c("alleles", "position"), discordance.type=c("genotype", "hethom"), by.variant=FALSE, verbose=TRUE)
```

**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`
getGenotype

Examples

```r
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)

seqClose(gds)
```

getGenotype  Get genotype data

Description

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

Usage

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

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.
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.
getGenotype

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 to alleleDosage 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

SeqVarGDSClass, 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])
geetGenotype(gds)
geetGenotypeAlleles(gds)
refDosage(gds)
altDosage(gds)
getVariableLengthData

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 'SeqVarGDSClass,character'
getVariableLengthData(gdsobj, var.name, use.names=TRUE)

Arguments

gdsobj  A SeqVarGDSClass 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
SeqVarGDSClass, applyMethod, seqGetData
heterozygosity

Examples

```r
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**

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

**Arguments**

- `gdsobj` A `SeqVarGDClass` object with VCF data.
heterozygosity

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**

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

**Arguments**

- `gdsobj`: A `SeqVarGDSClass` object with VCF data.
- `permute`: 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 `HWExact` 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:

- `variant.id`: The unique identifier for the variant
- `nAA`: The number of reference homozygotes
- `nAa`: The number of heterozygotes
- `naa`: The number of alternate homozygotes
- `afreq`: The reference allele frequency
- `p`: p values for the exact test
- `f`: The inbreeding coefficient, 1 - observed heterozygosity / expected heterozygosity

**Author(s)**

Stephanie Gogarten

**See Also**

`SeqVarGDSClass`, `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)

Description

Calculates the inbreeding coefficient by variant or by sample

Usage

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

Arguments

gdsobj A \texttt{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 sample IDs as names of the output vector.

Details

For inbreeding coefficients by variant, calculates 1 - observed heterozygosity / expected heterozygosity.
For individual inbreeding coefficients (\texttt{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

See Also

SeqVarGDSClass, applyMethod

Examples

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

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

isSNV

Flag single nucleotide variants

Description

Flag single nucleotide variants

Usage

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

Arguments

- `x` A `SeqVarGDSClass` 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

SeqVarGDSClass, allele-methods, applyMethod

Examples

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

Locate variant samples across sites

Description

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

Usage

```r
## 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

```r
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

Description

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

Usage

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

Arguments

- **gdsobj**: A `SeqVarGDSClass` 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

`SeqVarGDSClass`, `applyMethod`, `seqApply`

Examples

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

**Mendelian errors**

**Description**

Detect Mendelian errors

**Usage**

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

**Arguments**

- `gdsobj`: A `SeqVarGDSClass` 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**

`SeqVarGDSClass`, `applyMethod`
missingGenotypeRate

Examples

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

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)
Principal Component Analysis

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

Usage
```r
## 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

See Also
- `SeqVarGDSClass`, `applyMethod`

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

**Pedigree for example data**

**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**

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

---

refFrac  

**Reference allele fraction**

**Description**

Calculate fraction of reference allele reads
Usage

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

Arguments

- `gdsobj`: A `SeqVarGDSClass` object with VCF data.
- `FUN`: The function to apply over heterozygote calls (mean or median).
- `use.names`: A logical indicating whether to assign variant or samples IDs as names of the output vector.
- `variant.id`: A vector of variant.ids to plot.
- `highlight`: A list of sample.ids to highlight with sequential integers on each plot
- `...`: 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

`SeqVarGDSClass`, `applyMethod`

Examples

```r
gdsfile <- system.file("extdata", "hapmap_exome_chr22.gds", package="SeqVarTools")
gds <- seqOpen(gdsfile)
RF <- refFrac(gds)
dim(RF)
```
regression 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
gdsobj A SeqVarData object
outcome A character string with the name of the column in sampleData(gdsobj) containing the outcome variable
covar A character vector with the name of the column(s) in sampleData(gdsobj) containing the covariates
model.type the type of model to be run. "linear" uses lm, "logistic" uses glm with family=binomial(), and "firth" uses logistf.

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

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

**Author(s)**

Stephanie Gogarten

**See Also**

SeqVarData, seqSetFilter, lm, glm, logistf

**Examples**

```r
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)
```

**Description**

Extends SeqVarGDSClass to include annotation for samples and variants.

**Details**

A SeqVarData object adds an AnnotatedDataFrame for both samples and variants to a SeqVarGDSClass object.

**Constructor**

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

gds can be either the filename of a sequencing GDS file or an existing SeqVarGDSClass 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

setVariantID

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

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

Details

If by.sample=FALSE (the default), \texttt{titv} calculates the transition/transversion ratio (TiTv) over all samples.
If by.sample=TRUE, \texttt{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

\texttt{SeqVarGDSClass}, \texttt{applyMethod}, \texttt{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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