Package ‘variancePartition’

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Type Package

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Maintainer Gabriel E. Hoffman <gabriel.hoffman@mssm.edu>

Description Quantify and interpret multiple sources of biological and technical variation in gene expression experiments. Uses a linear mixed model to quantify variation in gene expression attributable to individual, tissue, time point, or technical variables. Includes dream differential expression analysis for repeated measures.

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**Author** Gabriel Hoffman [aut, cre] (<https://orcid.org/0000-0002-0957-0224>)

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### Description

Get all univariate contrasts

### Usage

`.getAllUniContrasts(formula, data)`
Arguments

- **formula**: specifies variables for the linear (mixed) model. Must only specify covariates, since the rows of exprObj are automatically used as a response. E.g.: ~ a + b + (1|c) Formulas with only fixed effects also work.
- **data**: data.frame with columns corresponding to formula.

Value

Matrix testing each variable one at a time. Contrasts are on rows.

---

**.isMixedModelFormula**  
*Check if model contains a random effect*

**Description**

Check if model contains a random effect.

**Usage**

```r
.isMixedModelFormula(formula)
```

**Arguments**

- **formula**: model formula.

---

**.standard_transform**  
*Compute standard post-processing values*

**Description**

These values are typically computed by eBayes.

**Usage**

```r
.standard_transform(fit, sigma = fit$sigma)
```

**Arguments**

- **fit**: result of dream (MArrayLM2).
- **sigma**: vector of standard errors used to compute t-statistic. Can be maximum likelihood estimates, or posterior means.

**Value**

MArrayLM2 object with values computed.
applyQualityWeights

Apply pre-specified sample weights

Description

Apply pre-specified sample weights by scaling existing precision weights.

Usage

applyQualityWeights(vobj, weights)

Arguments

vobj EList from voom or voomWithDreamWeights.
weights sample level weights

Details

Apply pre-specified sample-level weights to the existing precision weights estimated from the data. While the limma::voomWithQualityWeights function of Lui et al. (2015) estimates the sample-level weights from voom fit, here the weights are fixed beforehand.

References


See Also

limma::voomWithQualityWeights

as.data.frame.varPartResults

Convert to data.frame

Description

Convert varPartResults to data.frame

Usage

## S3 method for class 'varPartResults'
as.data.frame(x, row.names = NULL, optional = FALSE, ...)

---

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---

3
Arguments

- `x`: varPartResults
- `row.names`: pass thru to generic
- `optional`: pass thru to generic
- `...`: other arguments.

Value

data.frame

Examples

```r
# load library
# library(variancePartition)

# load simulated data:
# geneExpr: matrix of gene expression values
# info: information/metadata about each sample
data(varPartData)

# Specify variables to consider
# Age is continuous so we model it as a fixed effect
# Individual and Tissue are both categorical, so we model them as random effects
form <- ~ Age + (1 | Individual) + (1 | Tissue)

# Fit model
varPart <- fitExtractVarPartModel(geneExpr[1:5,], form, info)

# convert to matrix
as.data.frame(varPart)
```

Description

Convert varPartResults to matrix

Usage

```r
## S4 method for signature 'varPartResults'
as.matrix(x, ...)
```

Arguments

- `x`: varPartResults
- `...`: other arguments.
Value

matrix

Examples

# load library
# library(variancePartition)

# load simulated data:
# geneExpr: matrix of gene expression values
# info: information/metadata about each sample
data(varPartData)

# Specify variables to consider
# Age is continuous so we model it as a fixed effect
# Individual and Tissue are both categorical, so we model them as random effects
form <- ~ Age + (1 | Individual) + (1 | Tissue)

# Fit model
varPart <- fitExtractVarPartModel(geneExpr[1:5, ], form, info)

# convert to matrix
as.matrix(varPart)

augmentPriorCount

Augment observed read counts with prior count

Description

Augment observed read counts with prior count since log of zero counts is undefined. The prior count added to each sample is scaled so that no variance is introduced

Usage

augmentPriorCount(
  counts,
  lib.size = colSums2(counts),
  prior.count = 0.5,
  scaledByLib = FALSE
)

Arguments

counts matrix of read counts with genes as rows and samples as columns
lib.size library sizes, the sum of all ready for each sample
prior.count average prior count added to each sample.
scaledByLib if TRUE, scale pseudocount by lib.size. Else to standard constant pseudocount addition
Details

Adding prior counts removes the issue of evaluating the log of zero counts, and stabilizes the log transform when counts are very small. However, adding a constant prior count to all samples can introduced an artifact. Consider two samples each with zero counts for a given gene, but one as a library size of 1k and the other of 50k. After applying the prior count values become pc / 1k and pc / 50k. It appears that there is variance in the expression of this gene, even though no counts are observed. This is driven only by variation in the library size, which does not reflect biology. This issue is most problematic for small counts.

Instead, we make the reasonable assumption that a gene does not have expression variance unless supported sufficiently by counts in the numerator. Consider adding a different prior count to each sample so that genes with zero counts end up woth zero variance. This corresponds to adding prior.count * lib.size[i] / mean(lib.size) to sample i.

This is done in the backend of edgeR:::cpm(), but this function allows users to apply it more generally.

Value

matrix with augmented counts

See Also

edgeR::cpm()

Examples

library(edgeR)

data(varPartDEdata)

# normalize RNA-seq counts
dge <- DGEList(counts = countMatrix)
dge <- calcNormFactors(dge)

countsAugmented <- augmentPriorCount( dge$counts, dge$samples$lib.size, 1)

---

calcVarPart

Compute variance statistics

Description

Compute fraction of variation attributable to each variable in regression model. Also interpretable as the intra-class correlation after correcting for all other variables in the model.
Usage

```r
calcVarPart(fit, returnFractions = TRUE, ...)
```

## S4 method for signature 'lm'
calcVarPart(fit, returnFractions = TRUE, ...)

## S4 method for signature 'lmerMod'
calcVarPart(fit, returnFractions = TRUE, ...)

## S4 method for signature 'glm'
calcVarPart(fit, returnFractions = TRUE, ...)

## S4 method for signature 'negbin'
calcVarPart(fit, returnFractions = TRUE, ...)

## S4 method for signature 'glmerMod'
calcVarPart(fit, returnFractions = TRUE, ...)

Arguments

- `fit`: model fit from `lm()` or `lmer()`
- `returnFractions`: default: TRUE. If TRUE return fractions that sum to 1. Else return unscaled variance components.
- `...`: additional arguments (not currently used)

Details

For linear model, variance fractions are computed based on the sum of squares explained by each component. For the linear mixed model, the variance fractions are computed by variance component estimates for random effects and sum of squares for fixed effects.

For a generalized linear model, the variance fraction also includes the contribution of the link function so that fractions are reported on the linear (i.e. link) scale rather than the observed (i.e. response) scale. For linear regression with an identity link, fractions are the same on both scales. But for logit or probit links, the fractions are not well defined on the observed scale due to the transformation imposed by the link function.

The variance implied by the link function is the variance of the corresponding distribution:

- logit -> logistic distribution -> variance is $\pi^2/3$
- probit -> standard normal distribution -> variance is 1

For the Poisson distribution with rate $\lambda$, the variance is $\log(1 + 1/\lambda)$.

For the negative binomial distribution with rate $\lambda$ and shape $\theta$, the variance is $\log(1 + 1/\lambda + 1/\theta)$.

Variance decomposition is reviewed by Nakagawa and Schielzeth (2012), and expanded to other GLMs by Nakagawa, Johnson and Schielzeth (2017). See McKelvey and Zavoina (1975) for early work on applying to GLMs. Also see DeMaris (2002)

We note that Nagelkerke’s pseudo $R^2$ evaluates the variance explained by the full model. Instead, a variance partitioning approach evaluates the variance explained by each term in the model, so that
the sum of each systematic plus random term sums to 1 (Hoffman and Schadt, 2016; Nakagawa and Schielzeth, 2012).

**Value**

canCorPairs

the sum of each systematic plus random term sums to 1 (Hoffman and Schadt, 2016; Nakagawa and Schielzeth, 2012).

**Value**
fraction of variance explained / ICC for each variable in the regression model

**References**


**Examples**

```r
library(lme4)
data(varPartData)

# Linear mixed model
fit <- lmer(geneExpr[1, ] ~ (1 | Tissue) + Age, data)
calcVarPart(fit)

# Linear model
# Note that the two models produce slightly different results
# This is expected: they are different statistical estimates
# of the same underlying value
fit <- lm(geneExpr[1, ] ~ Tissue + Age, data)
calcVarPart(fit)
```

**canCorPairs**

canCorPairs

**Description**

Assess correlation between all pairs of variables in a formula

**Usage**

```r
canCorPairs(formula, data, showWarnings = TRUE)
```
Arguments

- **formula**: standard additive linear model formula (doesn’t support random effects currently, so just change the syntax)
- **data**: data.frame with the data for the variables in the formula
- **showWarnings**: default to true

Details

Canonical Correlation Analysis (CCA) is similar to correlation between two vectors, except that CCA can accommodate matrices as well. For a pair of variables, canCorPairs assesses the degree to which they co-vary and contain the same information. Variables in the formula can be a continuous variable or a discrete variable expanded to a matrix (which is done in the backend of a regression model). For a pair of variables, canCorPairs uses CCA to compute the correlation between these variables and returns the pairwise correlation matrix.

Statistically, let rho be the array of correlation values returned by the standard R function cancor to compute CCA. canCorPairs() returns \( \sqrt{\text{mean}(\rho^2)} \), which is the fraction of the maximum possible correlation. When comparing a two vectors, or a vector and a matrix, this gives the same value as the absolute correlation. When comparing two sets of categorical variables (i.e. expanded to two matrices), this is equivalent to Cramer’s V statistic.

Note that CCA returns correlation values between 0 and 1.

Value

Matrix of correlation values between all pairs of variables.

Examples

```r
# load library
# library(variancePartition)

# load simulated data:
data(varPartData)

# specify formula
form <- ~ Individual + Tissue + Batch + Age + Height

# Compute Canonical Correlation Analysis (CCA)
# between all pairs of variables
# returns absolute correlation value
C <- canCorPairs(form, info)

# Plot correlation matrix
plotCorrMatrix(C)
```
**classifyTestsF**

*Multiple Testing Genewise Across Contrasts*

**Description**

For each gene, classify a series of related t-statistics as up, down or not significant.

**Usage**

```r
classifyTestsF(object, ...)  
```

**Arguments**

- `object`: numeric matrix of t-statistics or an 'MArrayLM2' object from which the t-statistics may be extracted.
- `...`: additional arguments

**Details**

Works like `limma::classifyTestsF`, except `object` can have a list of covariance matrices `object$cov.coefficients.list`, instead of just one in `object$cov.coefficients`

**See Also**

`limma::classifyTestsF`

---

**classifyTestsF,MArrayLM2-method**

*Multiple Testing Genewise Across Contrasts*

**Description**

For each gene, classify a series of related t-statistics as up, down or not significant.

**Usage**

```r
## S4 method for signature 'MArrayLM2'
classifyTestsF(
  object,
  cor.matrix = NULL,
  df = Inf,
  p.value = 0.01,
  fstat.only = FALSE
)
```

---
### Arguments

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>object</td>
<td>numeric matrix of t-statistics or an <code>MArrayLM2</code> object from which the t-</td>
</tr>
<tr>
<td></td>
<td>statistics may be extracted.</td>
</tr>
<tr>
<td>cor.matrix</td>
<td>covariance matrix of each row of t-statistics. Defaults to the identity</td>
</tr>
<tr>
<td></td>
<td>matrix.</td>
</tr>
<tr>
<td>df</td>
<td>numeric vector giving the degrees of freedom for the t-statistics. May have</td>
</tr>
<tr>
<td></td>
<td>length 1 or length equal to the number of rows of tstat.</td>
</tr>
<tr>
<td>p.value</td>
<td>numeric value between 0 and 1 giving the desired size of the test</td>
</tr>
<tr>
<td>fstat.only</td>
<td>logical, if <code>TRUE</code> then return the overall F-statistic as for <code>FStat</code> instead</td>
</tr>
<tr>
<td></td>
<td>of classifying the test results</td>
</tr>
</tbody>
</table>

### Details

Works like limma::classifyTestsF, except object can have a list of covariance matrices `object$cov.coefficients.list`, instead of just one in `object$cov.coefficients`.

### See Also

limma::classifyTestsF

---

### Description

Collinearity score for a regression model indicating if variables are too highly correlated to give meaningful results.

### Usage

```
colinearityScore(fit)
```

### Arguments

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>fit</td>
<td>regression model fit from <code>lm()</code> or <code>lmer()</code></td>
</tr>
</tbody>
</table>

### Value

Returns the collinearity score between 0 and 1, where a score > 0.999 means the degree of collinearity is too high. This function reports the correlation matrix between coefficient estimates for fixed effects. The collinearity score is the maximum absolute correlation value of this matrix. Note that the values are the correlation between the parameter estimates, and not between the variables themselves.
Examples

```r
# load library
# library(variancePartition)

# load simulated data:
data(varPartData)
#
form <- ~ Age + (1 | Individual) + (1 | Tissue)

res <- fitVarPartModel(geneExpr[1:10, ], form, info)

# evaluate the collinearity score on the first model fit
# this reports the correlation matrix between coefficients estimates
# for fixed effects
# the collinearity score is the maximum absolute correlation value
# If the collinearity score > .999 then the variance partition
# estimates may be problematic
# In that case, a least one variable should be omitted
collinearityScore(res[[1]])
```
**diffVar**

See Also
diffVar()

Examples

```r
# library(variancePartition)
library(edgeR)
data(varPartDEdata)

# filter genes by number of counts
isexpr <- rowSums(cpm(countMatrix) > 0.1) >= 5

# Standard usage of limma/voom
dge <- DGEList(countMatrix[isexpr, ])
dge <- calcNormFactors(dge)

# make this vignette faster by analyzing a subset of genes
dge <- dge[1:1000, ]

# regression formula
form <- ~Disease

# estimate precision weights
vobj <- voomWithDreamWeights(dge, form, metadata)

# fit dream model
fit <- dream(vobj, form, metadata)
fit <- eBayes(fit)

# Compute deviation from expectation for each observation
# using model residuals
z <- deviation(fit)
z[1:4, 1:4]
```

---

**diffVar**

Test differential variance

Description

Test the association between a covariate of interest and the response’s deviation from expectation.

Usage

diffVar(
fit,
method = c("AD", "SQ"),
scale = c("leverage", "none"),
BPPARAM = SerialParam(),
)
## S4 method for signature 'MArrayLM'

```r
## S4 method for signature 'MArrayLM'

diffVar(
  fit,
  method = c("AD", "SQ"),
  scale = c("leverage", "none"),
  BPPARAM = SerialParam(),
  ...
)
```

**Arguments**

- `fit` model fit from `dream()`
- `method` transform the residuals using absolute deviation ("AD") or squared deviation ("SQ").
- `scale` scale each observation by "leverage", or no scaling ("none")
- `BPPARAM` parameters for parallel evaluation
- `...` other parameters passed to `dream()`

**Details**

This method performs a test of differential variance between two subsets of the data, in a way that generalizes to multiple categories, continuous variables and metrics of spread beyond variance. For the two category test, this method is similar to Levene’s test. This model was adapted from Phipson, et al (2014), extended to linear mixed models, and adapted to be compatible with `dream()`.

This method is composed of multiple steps where 1) a typical linear (mixed) model is fit with `dream()`, 2) residuals are computed and transformed based on an absolute value or squaring transform, 3) a second regression is performed with `dream()` to test if a variable is associated with increased deviation from expectation. Both regression take advantage of the `dream()` linear (mixed) modelling framework followed by empirical Bayes shrinkage that extends the `limma::voom()` framework.

Note that `diffVar()` takes the results of the first regression as a parameter to use as a starting point.

**Value**

`MArrayLM` object storing differential results to be passed to `topTable()`

**References**


**See Also**

`missMethyl::diffVar()`, `car::leveneTest()`
Examples

# library(variancePartition)
library(edgeR)
data(varPartDEdata)

# filter genes by number of counts
isexpr <- rowSums(cpm(countMatrix) > 0.1) >= 5

# Standard usage of limma/voom
dge <- DGEList(countMatrix[isexpr, ])
dge <- calcNormFactors(dge)

# make this vignette faster by analyzing a subset of genes
dge <- dge[1:1000, ]

# regression formula
form <- ~ Disease

# estimate precision weights
vobj <- voomWithDreamWeights(dge, form, metadata)

# fit dream model
fit <- dream(vobj, form, metadata)
fit <- eBayes(fit)

# fit differential variance model
res <- diffVar(fit)

# extract results for differential variance based on Disease
topTable(res, coef = "Disease1", number = 3)

# Box plot of top hit
# Since ASCL3 has a negative logFC,
# the deviation from expectation is *smaller* in
# Disease==1 compared to baseline.
gene <- "ENST00000325884.1 gene=ASCL3"
boxplot(vobj$E[gene, ] ~ metadata$Disease, main = gene)

dream

Differential expression with linear mixed model

Description

Fit linear mixed model for differential expression and perform hypothesis test on fixed effects as specified in the contrast matrix L.
Usage

dream(
    exprObj,
    formula,
    data,
    L,
    ddf = c("adaptive", "Satterthwaite", "Kenward-Roger"),
    useWeights = TRUE,
    control = vpcontrol,
    hideErrorsInBackend = FALSE,
    REML = TRUE,
    BPPARAM = SerialParam(),
    ...
)

Arguments

exprObj    matrix of expression data (g genes x n samples), or ExpressionSet, or EList returned by voom() from the limma package
formula    specifies variables for the linear (mixed) model. Must only specify covariates, since the rows of exprObj are automatically used as a response. e.g.: ~ a + b + (1|c) Formulas with only fixed effects also work, and lmFit() followed by contrasts.fit() are run.
data        data.frame with columns corresponding to formula
L           contrast matrix specifying a linear combination of fixed effects to test
ddf         Specify "Satterthwaite" or "Kenward-Roger" method to estimate effective degrees of freedom for hypothesis testing in the linear mixed model. Note that Kenward-Roger is more accurate, but is *much* slower. Satterthwaite is a good enough approximation for most datasets. "adaptive" (Default) uses KR for <= 20 samples.
useWeights  if TRUE, analysis uses heteroskedastic error estimates from voom(). Value is ignored unless exprObj is an EList() from voom() or weightsMatrix is specified
control     control settings for lmer()
hideErrorsInBackend default FALSE. If TRUE, hide errors in attr(.,"errors") and attr(.,"error.initial")
REML         use restricted maximum likelihood to fit linear mixed model. default is TRUE. See Details.
BPPARAM      parameters for parallel evaluation
...          Additional arguments for lmer() or lm()

Details

A linear (mixed) model is fit for each gene in exprObj, using formula to specify variables in the regression (Hoffman and Roussos, 2021). If categorical variables are modeled as random effects
(as is recommended), then a linear mixed model is used. For example if formula is \( a + b + (1|c) \), then the model is

\[
\text{fit} <- \text{lmer}( \text{exprObj}[j,] \sim a + b + (1|c), \text{data} = \text{data})
\]

useWeights=TRUE causes weightsMatrix[j,] to be included as weights in the regression model.

Note: Fitting the model for 20,000 genes can be computationally intensive. To accelerate computation, models can be fit in parallel using BiocParallel to run code in parallel. Parallel processing must be enabled before calling this function. See below.

The regression model is fit for each gene separately. Samples with missing values in either gene expression or metadata are omitted by the underlying call to lmer.

Hypothesis tests and degrees of freedom are produced by lmerTest and pbkrtest packages.

While REML=TRUE is required by lmerTest when ddf='Kenward-Roger', ddf='Satterthwaite' can be used with REML as TRUE or FALSE. Since the Kenward-Roger method gave the best power with an accurate control of false positive rate in our simulations, and since the Satterthwaite method with REML=TRUE gives p-values that are slightly closer to the Kenward-Roger p-values, REML=TRUE is the default. See Vignette "3) Theory and practice of random effects and REML".

Value

MArrayLM2 object (just like MArrayLM from limma), and the directly estimated p-value (without eBayes).

References


Examples

# library(variancePartition)
library(BiocParallel)

# load simulated data:
# geneExpr: matrix of *normalized* gene expression values
# info: information/metadata about each sample
data(varPartData)

form <- ~ Batch + (1 | Individual) + (1 | Tissue)

# Fit linear mixed model for each gene
# run on just 10 genes for time
# NOTE: dream() runs on *normalized* data
fit <- dream(geneExpr[1:10,], form, info)
fit <- eBayes(fit)

# view top genes
topTable(fit, coef = "Batch2", number = 3)

# get contrast matrix testing if the coefficient for Batch3 is
# different from coefficient for Batch2
# Name this comparison as 'compare_3_2'
# The variable of interest must be a fixed effect
L <- makeContrastsDream(form, info, contrasts = c(compare_3_2 = "Batch3 - Batch2"))

# plot contrasts
plotContrasts(L)

# Fit linear mixed model for each gene
# run on just 10 genes for time
fit2 <- dream(geneExpr[1:10, ], form, info, L)
fit2 <- eBayes(fit2)

# view top genes for this contrast
topTable(fit2, coef = "compare_3_2", number = 3)

# Parallel processing using multiple cores with reduced memory usage
param <- SnowParam(4, "SOCK", progressbar = TRUE)
fit3 <- dream(geneExpr[1:10, ], form, info, L, BPPARAM = param)
fit3 <- eBayes(fit3)

dscchisq

## Scaled chi-square

dscchisq

### Description

Scaled chi-square density using a gamma distribution

### Usage

```r
dscchisq(x, a, b)
```

### Arguments

- **x**: vector of quantiles.
- **a**: scale
- **b**: degrees of freedom
eBayes for result of linear mixed model for with `dream()` using residual degrees of freedom approximated with `rdf.merMod()`

```r
## S4 method for signature 'MArrayLM2'
eBayes(
  fit,
  proportion = 0.01,
  stdev.coef.lim = c(0.1, 4),
  trend = FALSE,
  robust = FALSE,
  winsor.tail.p = c(0.05, 0.1)
)
```

### Arguments
- `fit`  
- `proportion`  
- `stdev.coef.lim`  
- `trend`  
- `robust`  
- `winsor.tail.p`  

### Value
results of eBayes using approximated residual degrees of freedom

### See Also
- `dream`  
- `rdf.merMod`
Effective sample size

Description
Compute effective sample size based on correlation structure in linear mixed model

Usage

```r
ESS(fit, method = "full")
```

## S4 method for signature 'lmerMod'

```r
ESS(fit, method = "full")
```

Arguments
- **fit**: model fit from `lmer()`
- **method**: "full" uses the full correlation structure of the model. The "approximate" method makes the simplifying assumption that the study has a mean of m samples in each of k groups, and computes m based on the study design. When the study design is evenly balanced (i.e. the assumption is met), this gives the same results as the "full" method.

Details
Effective sample size calculations are based on:

"full" method: if

\[ V_x = \text{var}(Y; x) \]

is the variance-covariance matrix of Y, the response, based on the covariate x, then the effective sample size corresponding to this covariate is

\[ \Sigma_{i,j}(V_x^{-1})_{i,j} \]

In R notation, this is: `sum(solve(V_x))`. In practice, this can be evaluated as `sum(w)`, where R "approximate" method: Letting m be the mean number of samples per group,

\[ k \]

be the number of groups, and

\[ \rho \]

be the intraclass correlation, the effective sample size is

\[ mk/(1 + \rho(m - 1)) \]

Note that these values are equal when there are exactly m samples in each group. If m is only an average then this an approximation.
extractVarPart

Value
effective sample size for each random effect in the model

Examples

library(lme4)
data(varPartData)

# Linear mixed model
fit <- lmer(geneExpr[1, ] ~ (1 | Individual) + (1 | Tissue) + Age, info)

# Effective sample size
ESS(fit)

extractVarPart Extract variance statistics

Description
Extract variance statistics from list of models fit with \texttt{lmer()} or \texttt{lmer()}

Usage

extractVarPart(modelList, ...)

Arguments

modelList list of \texttt{lmer()} model fits
...
other arguments

Value
data.frame of fraction of variance explained by each variable, after correcting for all others.

Examples

# library(variancePartition)

library(BiocParallel)

# load simulated data:
# geneExpr: matrix of gene expression values
# info: information/metadata about each sample
data(varPartData)

data(varPartData)

# Specify variables to consider
# Age is continuous so we model it as a fixed effect
# Individual and Tissue are both categorical, so we model them as random effects
form <- ~ Age + (1 | Individual) + (1 | Tissue)

# Step 1: fit linear mixed model on gene expression
# If categorical variables are specified, a linear mixed model is used
# If all variables are modeled as continuous, a linear model is used
# each entry in results is a regression model fit on a single gene
# Step 2: extract variance fractions from each model fit
# for each gene, returns fraction of variation attributable to each variable
# Interpretation: the variance explained by each variable
# after correction for all other variables
varPart <- fitExtractVarPartModel(geneExpr, form, info)

# violin plot of contribution of each variable to total variance
plotVarPart(sortCols(varPart))

# Advanced:
# Fit model and extract variance in two separate steps
# Step 1: fit model for each gene, store model fit for each gene in a list
results <- fitVarPartModel(geneExpr, form, info)

# Step 2: extract variance fractions
varPart <- extractVarPart(results)

fitExtractVarPartModel

Fit linear (mixed) model, report variance fractions

Description

Fit linear (mixed) model to estimate contribution of multiple sources of variation while simultaneously correcting for all other variables. Report fraction of variance attributable to each variable

Usage

fitExtractVarPartModel(
  exprObj,
  formula,
  data,
  REML = FALSE,
  useWeights = TRUE,
  control = vpcontrol,
  hideErrorsInBackend = FALSE,
  showWarnings = TRUE,
  BPPARAM = SerialParam(),
  ...
)

## S4 method for signature 'matrix'
fitExtractVarPartModel(
  exprObj,
  formula,
  data,
  REML = FALSE,
  useWeights = TRUE,
  control = vpcontrol,
  hideErrorsInBackend = FALSE,
  showWarnings = TRUE,
  BPPARAM = SerialParam(),
  ...
)

## S4 method for signature 'data.frame'
fitExtractVarPartModel(
  exprObj,
  formula,
  data,
  REML = FALSE,
  useWeights = TRUE,
  control = vpcontrol,
  hideErrorsInBackend = FALSE,
  showWarnings = TRUE,
  BPPARAM = SerialParam(),
  ...
)

## S4 method for signature 'EList'
fitExtractVarPartModel(
  exprObj,
  formula,
  data,
  REML = FALSE,
  useWeights = TRUE,
  control = vpcontrol,
  hideErrorsInBackend = FALSE,
  showWarnings = TRUE,
  BPPARAM = SerialParam(),
  ...
)

## S4 method for signature 'ExpressionSet'
fitExtractVarPartModel(
  exprObj,
  formula,
  data,
  REML = FALSE,
  useWeights = TRUE,
control = vpcontrol,
hideErrorsInBackend = FALSE,
showWarnings = TRUE,
BPPARAM = SerialParam(),
...
)

## S4 method for signature 'sparseMatrix'
fitExtractVarPartModel(
  exprObj,
  formula,
  data,
  REML = FALSE,
  useWeights = TRUE,
  control = vpcontrol,
  hideErrorsInBackend = FALSE,
  showWarnings = TRUE,
  BPPARAM = SerialParam(),
  ...
)

Arguments

exprObj matrix of expression data (g genes x n samples), or ExpressionSet, or EList returned by voom() from the limma package

formula specifies variables for the linear (mixed) model. Must only specify covariates, since the rows of exprObj are automatically used as a response. e.g.: \(~ a + b + (1|c)\)

data data.frame with columns corresponding to formula

REML use restricted maximum likelihood to fit linear mixed model. default is FALSE. See Details.

useWeights if TRUE, analysis uses heteroskedastic error estimates from voom(). Value is ignored unless exprObj is an EList() from voom() or weightsMatrix is specified

control control settings for lmer()

hideErrorsInBackend default FALSE. If TRUE, hide errors in attr(.,"errors") and attr(.,"error.initial")

showWarnings default TRUE. Indicate model failures

BPPARAM parameters for parallel evaluation

... Additional arguments for lmer() or lm()

Details

A linear (mixed) model is fit for each gene in exprObj, using formula to specify variables in the regression. If categorical variables are modeled as random effects (as is recommended), then a linear mixed model us used. For example if formula is \(~ a + b + (1|c)\), then the model is
fit <- lmer( exprObj[j,] ~ a + b + (1|c), data=data)

If there are no random effects, so formula is ~ a + b + c, a 'standard' linear model is used:
fit <- lm( exprObj[j,] ~ a + b + c, data=data)

In both cases, useWeights=TRUE causes weightsMatrix[j,] to be included as weights in the regression model.

Note: Fitting the model for 20,000 genes can be computationally intensive. To accelerate computation, models can be fit in parallel using BiocParallel to run in parallel. Parallel processing must be enabled before calling this function. See below.

The regression model is fit for each gene separately. Samples with missing values in either gene expression or metadata are omitted by the underlying call to lm/lmer.

REML=FALSE uses maximum likelihood to estimate variance fractions. This approach produced unbiased estimates, while REML=TRUE can show substantial bias. See Vignette "3) Theory and practice of random effects and REML"

Value

list() of where each entry is a model fit produced by lmer() or lm()

Examples

# load library
# library(variancePartition)

library(BiocParallel)

# load simulated data:
# geneExpr: matrix of gene expression values
# info: information/metadata about each sample
data(varPartData)

# Specify variables to consider
# Age is continuous so we model it as a fixed effect
# Individual and Tissue are both categorical, so we model them as random effects
form <- ~ Age + (1 | Individual) + (1 | Tissue)

# Step 1: fit linear mixed model on gene expression
# If categorical variables are specified, a linear mixed model is used
# If all variables are modeled as continuous, a linear model is used
# each entry in results is a regression model fit on a single gene
# Step 2: extract variance fractions from each model fit
# for each gene, returns fraction of variation attributable to each variable
# Interpretation: the variance explained by each variable
# after correction for all other variables
varPart <- fitExtractVarPartModel(geneExpr, form, info)

# violin plot of contribution of each variable to total variance
plotVarPart(sortCols(varPart))

# Note: fitExtractVarPartModel also accepts ExpressionSet
data(sample.ExpressionSet, package = "Biobase")

# ExpressionSet example
form <- ~ (1 | sex) + (1 | type) + score
info2 <- Biobase::pData(sample.ExpressionSet)
varPart2 <- fitExtractVarPartModel(sample.ExpressionSet, form, info2)

---

**fitVarPartModel**

Fit linear (mixed) model

---

**Description**

Fit linear (mixed) model to estimate contribution of multiple sources of variation while simultaneously correcting for all other variables.

**Usage**

```r
fitVarPartModel(
  exprObj,
  formula,
  data,
  REML = FALSE,
  useWeights = TRUE,
  fxn = identity,
  control = vpcontrol,
  hideErrorsInBackend = FALSE,
  showWarnings = TRUE,
  BPPARAM = SerialParam(),
  ...
)
```

## S4 method for signature 'matrix'

```r
fitVarPartModel(
  exprObj,
  formula,
  data,
  REML = FALSE,
  useWeights = TRUE,
  fxn = identity,
  control = vpcontrol,
  hideErrorsInBackend = FALSE,
  showWarnings = TRUE,
  BPPARAM = SerialParam(),
  ...
)
```
## S4 method for signature 'data.frame'
fitVarPartModel(
  exprObj,
  formula,
  data,
  REML = FALSE,
  useWeights = TRUE,
  fxn = identity,
  control = vpcontrol,
  hideErrorsInBackend = FALSE,
  showWarnings = TRUE,
  BPPARAM = SerialParam(),
  ...
)

## S4 method for signature 'EList'
fitVarPartModel(
  exprObj,
  formula,
  data,
  REML = FALSE,
  useWeights = TRUE,
  fxn = identity,
  control = vpcontrol,
  hideErrorsInBackend = FALSE,
  showWarnings = TRUE,
  BPPARAM = SerialParam(),
  ...
)

## S4 method for signature 'ExpressionSet'
fitVarPartModel(
  exprObj,
  formula,
  data,
  REML = FALSE,
  useWeights = TRUE,
  fxn = identity,
  control = vpcontrol,
  hideErrorsInBackend = FALSE,
  showWarnings = TRUE,
  BPPARAM = SerialParam(),
  ...
)

## S4 method for signature 'sparseMatrix'
fitVarPartModel(
  exprObj,
fitVarPartModel

```r
fit <- lmer( exprObj[j,] ~ a + b + (1|c), data=data)
```

If there are no random effects, so formula is ~ a + b + c, a 'standard' linear model is used:

```r
fit <- lm( exprObj[j,] ~ a + b + c, data=data)
```

In both cases, useWeights=TRUE causes weightsMatrix[j,] to be included as weights in the regression model.
Note: Fitting the model for 20,000 genes can be computationally intensive. To accelerate computation, models can be fit in parallel using BiocParallel to run in parallel. Parallel processing must be enabled before calling this function. See below.

The regression model is fit for each gene separately. Samples with missing values in either gene expression or metadata are omitted by the underlying call to lm/lmer.

Since this function returns a list of each model fit, using this function is slower and uses more memory than fitExtractVarPartModel().

REML=FALSE uses maximum likelihood to estimate variance fractions. This approach produced unbiased estimates, while REML=TRUE can show substantial bias. See Vignette "3) Theory and practice of random effects and REML”

Value

list() of where each entry is a model fit produced by lmer() or lm() (n)  

Examples

# load library
# library(variancePartition)
library(BiocParallel)

# load simulated data:
# geneExpr: matrix of gene expression values
# info: information/metadata about each sample
data(varPartData)

# Specify variables to consider
# Age is continuous so we model it as a fixed effect
# Individual and Tissue are both categorical, so we model them as random effects
form <- ~ Age + (1 | Individual) + (1 | Tissue)

# Step 1: fit linear mixed model on gene expression
# If categorical variables are specified, a linear mixed model is used
# If all variables are modeled as continuous, a linear model is used
# each entry in results is a regression model fit on a single gene
# Step 2: extract variance fractions from each model fit
# for each gene, returns fraction of variation attributable to each variable
# Interpretation: the variance explained by each variable
# after correction for all other variables
varPart <- fitExtractVarPartModel(geneExpr, form, info)

# violin plot of contribution of each variable to total variance
# also sort columns
plotVarPart(sortCols(varPart))

# Advanced:
# Fit model and extract variance in two separate steps
# Step 1: fit model for each gene, store model fit for each gene in a list
results <- fitVarPartModel(geneExpr, form, info)
# Step 2: extract variance fractions
varPart <- extractVarPart(results)

# Note: fitVarPartModel also accepts ExpressionSet
data(sample.ExpressionSet, package = "Biobase")

# ExpressionSet example
form <- ~ (1 | sex) + (1 | type) + score
info2 <- Biobase::pData(sample.ExpressionSet)
results2 <- fitVarPartModel(sample.ExpressionSet, form, info2)

---

**getContrast**

*Extract contrast matrix for linear mixed model*

**Description**

Extract contrast matrix, L, testing a single variable. Contrasts involving more than one variable can be constructed by modifying L directly.

**Usage**

getContrast(exprObj, formula, data, coefficient)

**Arguments**

- **exprObj**: matrix of expression data (g genes x n samples), or ExpressionSet, or EList returned by voom() from the limma package.
- **formula**: specifies variables for the linear (mixed) model. Must only specify covariates, since the rows of exprObj are automatically used as a response. e.g.: ~ a + b + (1|c) Formulas with only fixed effects also work.
- **data**: data.frame with columns corresponding to formula.
- **coefficient**: the coefficient to use in the hypothesis test.

**Value**

Contrast matrix testing one variable.

**Examples**

# load simulated data:
# geneExpr: matrix of gene expression values
# info: information/metadata about each sample
data(varPartData)

# get contrast matrix testing if the coefficient for Batch2 is zero
# The variable of interest must be a fixed effect
getTreat <- ~ Batch + (1 | Individual) + (1 | Tissue)
L <- getContrast(geneExpr, form, info, "Batch3")

# get contrast matrix testing if Batch3 - Batch2 = 0
form <- ~ Batch + (1 | Individual) + (1 | Tissue)
L <- getContrast(geneExpr, form, info, c("Batch3", "Batch2"))

# To test against Batch1 use the formula:
# ~ 0 + Batch + (1|Individual) + (1|Tissue)
# to estimate Batch1 directly instead of using it as the baseline

getTreat

Test if coefficient is different from a specified value

Description

Test if coefficient is different from a specified value

Usage

getTreat(fit, lfc = log2(1.2), coef = 1, number = 10, sort.by = "p")

## S4 method for signature 'MArrayLM'
getTreat(fit, lfc = log2(1.2), coef = 1, number = 10, sort.by = "p")

## S4 method for signature 'MArrayLM2'
getTreat(fit, lfc = log2(1.2), coef = 1, number = 10, sort.by = "p")

Arguments

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>fit</td>
<td>fit</td>
</tr>
<tr>
<td>lfc</td>
<td>a minimum log2-fold-change below which changes not considered scientifically meaningful</td>
</tr>
<tr>
<td>coef</td>
<td>which coefficient to test</td>
</tr>
<tr>
<td>number</td>
<td>number of genes to return</td>
</tr>
<tr>
<td>sort.by</td>
<td>column to sort by</td>
</tr>
</tbody>
</table>

Value

results of getTreat
Examples

data(varPartData)

form <- ~ Age + Batch + (1 | Individual) + (1 | Tissue)

fit <- dream(geneExpr, form, info)
fit <- eBayes(fit)

coef <- "Age"

# Evaluate treat()/topTreat() in a way that works seamlessly for dream()
getTreat(fit, lfc = log2(1.03), coef, sort.by = "none", number = 3)

get_prediction  Compute predicted value of formula for linear (mixed) model

Description

Compute predicted value of formula for linear (mixed) model for with lm or lmer

Usage

get_prediction(fit, formula)

## S4 method for signature 'lmerMod'
get_prediction(fit, formula)

## S4 method for signature 'lm'
get_prediction(fit, formula)

Arguments

fit       model fit with lm or lmer
formula   formula of fixed and random effects to predict

Details

Similar motivation as lme4:::predict.merMod(), but that function cannot use just a subset of the fixed effects: it either uses none or all. Note that the intercept is included in the formula by default. To exclude it from the prediction use ~ 0 + ... syntax

Value

Predicted values from formula using parameter estimates from fit linear (mixed) model
**Examples**

```r
library(lme4)

# Linear model
fit <- lm(Reaction ~ Days, sleepstudy)

# prediction of intercept
gget_prediction(fit, ~1)

# prediction of Days without intercept
gget_prediction(fit, ~ 0 + Days)

# Linear mixed model

# fit model
fm1 <- lmer(Reaction ~ Days + (Days | Subject), sleepstudy)

# predict Days, but exclude intercept
gget_prediction(fm1, ~ 0 + Days)

# predict Days and (Days | Subject) random effect, but exclude intercept
gget_prediction(fm1, ~ 0 + Days + (Days | Subject))
```

---

**ggColorHue**

*Default colors for ggplot*

**Description**

Return an array of n colors the same as the default used by ggplot2

**Usage**

`ggColorHue(n)`

**Arguments**

- `n` number of colors

**Value**

array of colors of length n

**Examples**

`ggColorHue(4)`
hatvalues,MArrayLM-method

Compute hatvalues

Description

Compute hatvalues from dream fit

Usage

## S4 method for signature 'MArrayLM'
hatvalues(model, vobj, ...)

## S4 method for signature 'MArrayLM2'
hatvalues(model, ...)

Arguments

model    model fit from dream()
vobj     EList returned by voom() or voomWithDreamWeights().
... other arguments, currently ignored

isRunableFormula

Test if formula is full rank on this dataset

Description

Test if formula is full rank on this dataset

Usage

isRunableFormula(exprObj, formula, data)

Arguments

exprObj    expression object
formula    formula
data        data
**Description**

Construct the contrast matrix corresponding to specified contrasts of a set of parameters. Each specified set of contrast weights must sum to 1.

**Usage**

```r
makeContrastsDream(
  formula,
  data,
  ..., 
  contrasts = NULL,
  suppressWarnings = FALSE,
  nullOnError = FALSE
)
```

**Arguments**

- `formula`: specifies variables for the linear (mixed) model. Must only specify covariates, since the rows of exprObj are automatically used as a response. e.g.: `~ a + b + (1|c)` Formulas with only fixed effects also work
- `data`: data.frame with columns corresponding to formula
- `...`: expressions, or character strings which can be parsed to expressions, specifying contrasts
- `contrasts`: character vector specifying contrasts
- `suppressWarnings`: (default FALSE). suppress warnings for univariate contrasts
- `nullOnError`: (default FALSE). When a contrast entry is invalid, throw warning and return NULL for that contrast entry

**Details**

This function expresses contrasts between a set of parameters as a numeric matrix. The parameters are usually the coefficients from a linear (mixed) model fit, so the matrix specifies which comparisons between the coefficients are to be extracted from the fit. The output from this function is usually used as input to `dream()`.

This function creates a matrix storing the contrasts weights that are applied to each coefficient. Consider a variable `v` with levels `c('A', 'B', 'C')`. A contrast comparing `A` and `B` is `'vA - vB'` and tests whether the difference between these levels is different than zero. Coded for the 3 levels this has weights `c(1, -1, 0)`. In order to compare `A` to the other levels, the contrast is `'vA - (vB + vC)/2` so that `A` is compared to the average of the other two levels. This is encoded as `c(1, -0.5, -0.5)`. This type of proper matching in testing multiple levels is enforced by ensuring that
the contrast weights sum to 1. Based on standard regression theory only weighted sums of the estimated coefficients are supported.

This function is inspired by `limma::makeContrasts()` but is designed to be compatible with linear mixed models for `dream()`

Names in ... and contrasts will be used as column names in the returned value.

Value

matrix of linear contrasts between regression coefficients

See Also

`plotContrasts()`

Examples

```r
# load library
# library(variancePartition)

library(BiocParallel)

# load simulated data:
# geneExpr: matrix of gene expression values
# info: information/metadata about each sample
data(varPartData)

form <- ~ 0 + Batch + (1 | Individual) + (1 | Tissue)

# Define contrasts
# Note that for each contrast, the weights sum to 1
L <- makeContrastsDream(form, info, contrasts = c(Batch1_vs_2 = "Batch1 - Batch2", Batch3_vs_4 = "Batch3 - Batch4", Batch1_vs_34 = "Batch1 - (Batch3 + Batch4)/2"))

# show contrasts matrix
L

# Plot to visualize contrasts matrix
plotContrasts(L)

# Fit linear mixed model for each gene
# run on just 10 genes for time
fit <- dream(geneExpr[1:10, ], form, info, L = L)

# examine contrasts after fitting
head(coef(fit))

# show results from first contrast
topTable(fit, coef = "Batch1_vs_2")

# show results from second contrast
topTable(fit, coef = "Batch3_vs_4")
```
Class \texttt{MArrayLM2}

\textbf{Description}

Evaluate multivariate tests on results from \texttt{dream()} using \texttt{vcov()} to compute the covariance between estimated regression coefficients across multiple responses. A joint test to see if the coefficients are jointly different from zero is performed using meta-analysis methods that account for the covariance.

\textbf{Usage}

\begin{verbatim}
mvTest(fit, vobj, features, coef, method = c("FE.empirical", "FE", "RE2C", "tstat", "hotelling", "sidak", "fisher"), shrink.cov = TRUE, BPPARAM = SerialParam(), ... )
\end{verbatim}

\begin{verbatim}
## S4 method for signature 'MArrayLM,EList,vector'
mvTest(fit, vobj, features, coef, method = c("FE.empirical", "FE", "RE2C", "tstat", "hotelling", "sidak", "fisher"), shrink.cov = TRUE, BPPARAM = SerialParam(), ... )
\end{verbatim}
mvTest

## S4 method for signature 'MArrayLM,EList,missing'
mvTest(
  fit,
  vobj,
  features,
  coef,
  method = c("FE.empirical", "FE", "RE2C", "tstat", "hotelling", "sidak", "fisher"),
  shrink.cov = TRUE,
  BPPARAM = SerialParam(),
  ...
)

## S4 method for signature 'MArrayLM,EList,list'
mvTest(
  fit,
  vobj,
  features,
  coef,
  method = c("FE.empirical", "FE", "RE2C", "tstat", "hotelling", "sidak", "fisher"),
  shrink.cov = TRUE,
  BPPARAM = SerialParam(),
  ...
)

## S4 method for signature 'mvTest_input,ANY,ANY'
mvTest(
  fit,
  vobj,
  features,
  coef,
  method = c("FE.empirical", "FE", "RE2C", "tstat", "hotelling", "sidak", "fisher"),
  shrink.cov = TRUE,
  BPPARAM = SerialParam(),
  ...
)

## S4 method for signature 'MArrayLM,matrix,ANY'
mvTest(
  fit,
  vobj,
  features,
  coef,
  method = c("FE.empirical", "FE", "RE2C", "tstat", "hotelling", "sidak", "fisher"),
  shrink.cov = TRUE,
  BPPARAM = SerialParam(),
  ...
)
Arguments

- **fit**: MArrayLM or MArrayLM2 returned by dream()
- **vobj**: matrix or EList object returned by voom()
- **features**: a) indeces or names of features to perform multivariate test on, b) list of indeces or names. If missing, perform joint test on all features.
- **coef**: name of coefficient or contrast to be tested
- **method**: statistical method used to perform multivariate test. See details. 'FE' is a fixed effect test that models the covariance between coefficients. 'FE.empirical' use compute empirical p-values by sampling from the null distribution and fitting with a gamma. 'RE2C' is a random effect test of heterogeneity of the estimated coefficients that models the covariance between coefficients, and also incorporates a fixed effects test too. 'tstat' combines the t-statistics and models the covariance between coefficients. 'hotelling' performs the Hotelling T2 test. 'sidak' returns the smallest p-value and accounting for the number of tests. 'fisher' combines the p-value using Fisher’s method assuming independent tests.
- **shrink.cov**: shrink the covariance matrix between coefficients using the Schafer-Strimmer method
- **BPPARAM**: parameters for parallel evaluation
- **...**: other arguments

Details

See package remaCor for details about the remaCor::RE2C() test, and see remaCor::LS() for details about the fixed effect test. When only 1 feature is selected, the original p-value is returned and the test statistic is set to NA.

For the "RE2C" test, the final test statistic is the sum of a test statistic for the mean effect (stat.FE) and heterogeneity across effects (stat.het). mvTest() returns 0 if stat.het is negative in extremely rare cases.

Value

Returns a data.frame with the statistics from each test, the pvalue from the test, n_features, method, and Lambda from the Schafer-Strimmer method to shrink the estimated covariance. When shrink.cov=FALSE, Lambda = 0.

Examples

```R
# library(variancePartition)
library(edgeR)
library(BiocParallel)

data(varPartDEdata)

# normalize RNA-seq counts
dge <- DGEList(counts = countMatrix)
dge <- calcNormFactors(dge)
```
# specify formula with random effect for Individual
form <- ~ Disease + (1 | Individual)

# compute observation weights
vobj <- voomWithDreamWeights(dge[1:20, ], form, metadata)

# fit dream model
fit <- dream(vobj, form, metadata)
fit <- eBayes(fit)

# Multivariate test of features 1 and 2
mvTest(fit, vobj, 1:2, coef = "Disease1")

# Test multiple sets of features
lst <- list(a = 1:2, b = 3:4)
mvTest(fit, vobj, lst, coef = "Disease1", BPPARAM = SnowParam(2))

---

### mvTest_input-class

**Class mvTest_input**

**Description**

Class mvTest_input work is with iterRowsSplit()

---

### plotCompareP

**Compare p-values from two analyses**

**Description**

Plot -log10 p-values from two analyses and color based on donor component from variancePartition analysis

**Usage**

```r
plotCompareP(
  p1,
  p2,
  vpDonor,
  dupcorvalue,
  fraction = 0.2,
  xlabel = bquote(duplicateCorrelation ~ (-log[10] ~ p)),
  ylabel = bquote(dream ~ (-log[10] ~ p))
)
```
Arguments

p1  p-value from first analysis
p2  p-value from second analysis
vpDonor  donor component for each gene from variancePartition analysis
dupcorvalue  scalar donor component from duplicateCorrelation
fraction  fraction of highest/lowest values to use for best fit lines
xlabel  for x-axis
ylabel  label for y-axis

Value

ggplot2 plot

Examples

# load library
# library(variancePartition)

library(BiocParallel)

# load simulated data:
# geneExpr: matrix of gene expression values
# info: information/metadata about each sample
data(varPartData)

# Perform very simple analysis for demonstration

# Analysis 1
form <- ~Batch
fit <- dream(geneExpr, form, info)
fit <- eBayes(fit)
res <- topTable(fit, number = Inf, coef = "Batch3")

# Analysis 2
form <- ~ Batch + (1 | Tissue)
fit2 <- dream(geneExpr, form, info)
res2 <- topTable(fit2, number = Inf, coef = "Batch3")

# Compare p-values
plotCompareP(res$P.Value, res2$P.Value, runif(nrow(res)), .3)
plotContrasts

Plot representation of contrast matrix

Description
Plot contrast matrix to clarify interpretation of hypothesis tests with linear contrasts

Usage
plotContrasts(L)

Arguments
L contrast matrix

Details
This plot shows the contrasts weights that are applied to each coefficient.
Consider a variable \( v \) with levels c('A', 'B', 'C'). A contrast comparing A and B is \( vA - vB \) and tests whether the difference between these levels is different than zero. Coded for the 3 levels this has weights \( c(1, -1, 0) \). In order to compare A to the other levels, the contrast is \( vA - (vB + vC)/2 \) so that A is compared to the average of the other two levels. This is encoded as \( c(1, -0.5, -0.5) \). This type of proper matching in testing multiple levels is enforced by ensuring that the contrast weights sum to 1. Based on standard regression theory only weighted sums of the estimated coefficients are supported.

Value
ggplot2 object

See Also
makeContrastsDream()

Examples

```r
# load library
# library(variancePartition)

# load simulated data:
# geneExpr: matrix of gene expression values
# info: information/metadata about each sample
data(varPartData)

# 1) get contrast matrix testing if the coefficient for Batch2 is different from Batch3
form <- ~ Batch + (1 | Individual) + (1 | Tissue)
L <- makeContrastsDream(form, info, contrasts = c(Batch_3_vs_2 = "Batch3 - Batch2"))
```
# plot contrasts
plotContrasts(L)

## Usage

```r
plotCorrMatrix(
    C, 
    dendrogram = "both", 
    sort = TRUE, 
    margins = c(13, 13), 
    key.xlab = "correlation", 
    ...
)
```

## Arguments

- `C` correlation matrix: R or R^2 matrix
- `dendrogram` character string indicating whether to draw 'both' or none'
- `sort` sort rows and columns based on clustering
- `margins` spacing of plot
- `key.xlab` label of color gradient
- `...` additional arguments to heatmap.2

## Description

Plot correlation matrix

## Value

Image of correlation matrix

## Examples

```r
# simulate simple matrix of 10 variables
mat <- matrix(rnorm(1000), ncol = 10)

# compute correlation matrix
C <- cor(mat)

# plot correlations
```
plotCorrMatrix(C)

# plot squared correlations
plotCorrMatrix(C^2, dendrogram = "none")

---

**plotCorrStructure**  **plotCorrStructure**

---

**Description**
Plot correlation structure of a gene based on random effects

**Usage**

```r
plotCorrStructure(
  fit,
  varNames = names(coef(fit)),
  reorder = TRUE,
  pal = colorRampPalette(c("white", "red", "darkred")),
  hclust.method = "complete"
)
```

**Arguments**
- `fit` linear mixed model fit of a gene produced by `lmer()` or `fitVarPartModel()`
- `varNames` variables in the metadata for which the correlation structure should be shown. Variables must be random effects
- `reorder` how to reorder the rows/columns of the correlation matrix. `reorder=FALSE` gives no reorder. `reorder=TRUE` reorders based on `hclust`. `reorder` can also be an array of indices to reorder the samples manually
- `pal` color palette
- `hclust.method` clustering methods for `hclust`

**Value**
Image of correlation structure between each pair of experiments for a single gene

**Examples**

```r
# load library
# library(variancePartition)

library(BiocParallel)

# load simulated data:
data(varPartData)
```
# specify formula
form <- ~ Age + (1 | Individual) + (1 | Tissue)

# fit and return linear mixed models for each gene
fitList <- fitVarPartModel(geneExpr[1:10, ], form, info)

# Focus on the first gene
fit <- fitList[[1]]

# plot correlation structure based on Individual, reordering samples with hclust
plotCorrStructure(fit, "Individual")

# don't reorder
plotCorrStructure(fit, "Individual", reorder = FALSE)

# plot correlation structure based on Tissue, reordering samples with hclust
plotCorrStructure(fit, "Tissue")

# don't reorder
plotCorrStructure(fit, "Tissue", FALSE)

# plot correlation structure based on all random effects
# reorder manually by Tissue and Individual
idx <- order(info$Tissue, info$Individual)
plotCorrStructure(fit, reorder = idx)

# plot correlation structure based on all random effects
# reorder manually by Individual, then Tissue
idx <- order(info$Individual, info$Tissue)
plotCorrStructure(fit, reorder = idx)

---

**plotPercentBars**

*Bar plot of gene fractions*

**Description**

Bar plot of fractions for a subset of genes

**Usage**

```r
plotPercentBars(
  x,
  col = c(ggColorHue(ncol(x) - 1), "grey85"),
  genes = rownames(x),
  width = NULL,
  ...
)
```
## S4 method for signature 'matrix'
plotPercentBars(
  x,
  col = c(ggColorHue(ncol(x) - 1), "grey85"),
  genes = rownames(x),
  width = NULL,
  ...
)

## S4 method for signature 'data.frame'
plotPercentBars(
  x,
  col = c(ggColorHue(ncol(x) - 1), "grey85"),
  genes = rownames(x),
  width = NULL,
  ...
)

## S4 method for signature 'varPartResults'
plotPercentBars(
  x,
  col = c(ggColorHue(ncol(x) - 1), "grey85"),
  genes = rownames(x),
  width = NULL,
  ...
)

### Arguments

- **x**: object storing fractions
- **col**: color of bars for each variable
- **genes**: name of genes to plot
- **width**: specify width of bars
- **...**: other arguments

### Value

Returns ggplot2 barplot

### Examples

```r
# library(variancePartition)
library(BiocParallel)

# load simulated data:
# geneExpr: matrix of gene expression values
# info: information/metadata about each sample
data(varPartData)
```
# Specify variables to consider
form <- ~ Age + (1 | Individual) + (1 | Tissue)

# Fit model
varPart <- fitExtractVarPartModel(geneExpr, form, info)

# Bar plot for a subset of genes showing variance fractions
plotPercentBars(varPart[1:5, ])

# Move the legend to the top
plotPercentBars(varPart[1:5, ]) + theme(legend.position = "top")

---

**plotStratify**

**plotStratify**

**Description**

Plot gene expression stratified by another variable

**Usage**

```r
plotStratify(
  formula,
  data,
  xlab,
  ylab,
  main,
  sortBy,
  colorBy,
  sort = TRUE,
  text = NULL,
  text.y = 1,
  text.size = 5,
  pts.cex = 1,
  ylim = NULL,
  legend = TRUE,
  x.labels = FALSE
)
```

**Arguments**

- `formula`: specify variables shown in the x- and y-axes. Y-axis should be continuous variable, x-axis should be discrete.
- `data`: data.frame storing continuous and discrete variables specified in formula
- `xlab`: label x-axis. Defaults to value of xval
plotStratify

- **ylab**: label y-axis. Defaults to value of yval
- **main**: main label
- **sortBy**: name of column in geneExpr to sort samples by. Defaults to xval
- **colorBy**: name of column in geneExpr to color box plots. Defaults to xval
- **sort**: if TRUE, sort boxplots by median value, else use default ordering
- **text**: plot text on the top left of the plot
- **text.y**: indicate position of the text on the y-axis as a fraction of the y-axis range
- **text.size**: size of text
- **pts.cex**: size of points
- **ylim**: specify range of y-axis
- **legend**: show legend
- **x.labels**: show x axis labels

**Value**

ggplot2 object

**Examples**

```r
# Note: This is a newer, more convenient interface to plotStratifyBy()

# load library
# library(variancePartition)

# load simulated data:
data(varPartData)

# Create data.frame with expression and Tissue information for each sample
GE <- data.frame(Expression = geneExpr[,], Tissue = info$Tissue)

# Plot expression stratified by Tissue
plotStratify(Expression ~ Tissue, GE)

# Omit legend and color boxes grey
plotStratify(Expression ~ Tissue, GE, colorBy = NULL)

# Specify colors
col <- c(B = "green", A = "red", C = "yellow")
plotStratify(Expression ~ Tissue, GE, colorBy = col, sort = FALSE)
```
**Description**

Plot gene expression stratified by another variable

**Usage**

```r
plotStratifyBy(
  geneExpr,  
  xval,  
  yval,  
  xlab = xval,  
  ylab = yval,  
  main = NULL,  
  sortBy = xval,  
  colorBy = xval,  
  sort = TRUE,  
  text = NULL,  
  text.y = 1,  
  text.size = 5,  
  pts.cex = 1,  
  ylim = NULL,  
  legend = TRUE,  
  x.labels = FALSE
)
```

**Arguments**

- `geneExpr`: data.frame of gene expression values and another variable for each sample. If there are multiple columns, the user can specify which one to use.
- `xval`: name of column in geneExpr to be used along x-axis to stratify gene expression.
- `yval`: name of column in geneExpr indicating gene expression.
- `xlab`: label x-axis. Defaults to value of xval.
- `ylab`: label y-axis. Defaults to value of yval.
- `main`: main label.
- `sortBy`: name of column in geneExpr to sort samples by. Defaults to xval.
- `colorBy`: name of column in geneExpr to color box plots. Defaults to xval.
- `sort`: if TRUE, sort box plots by median value, else use default ordering.
- `text`: plot text on the top left of the plot.
- `text.y`: indicate position of the text on the y-axis as a fraction of the y-axis range.
- `text.size`: size of text.
**plotVarianceEstimates**

pts.cex    size of points
ylim      specify range of y-axis
legend   show legend
x.labels  show x axis labels

**Value**

ggplot2 object

**Examples**

```r
# load library
# library(variancePartition)

# load simulated data:
data(varPartData)

# Create data.frame with expression and Tissue information for each sample
GE <- data.frame(Expression = geneExpr[, ], Tissue = info$Tissue)

# Plot expression stratified by Tissue
plotStratifyBy(GE, "Tissue", "Expression")

# Omit legend and color boxes grey
plotStratifyBy(GE, "Tissue", "Expression", colorBy = NULL)

# Specify colors
col <- c(B = "green", A = "red", C = "yellow")
plotStratifyBy(GE, "Tissue", "Expression", colorBy = col, sort = FALSE)
```

---

**plotVarianceEstimates  Plot Variance Estimates**

**Description**

Plot Variance Estimates

**Usage**

```r
plotVarianceEstimates(
  fit,      
  fitEB,    
  var_true = NULL,  
  xmax = quantile(fit$sigma^2, 0.999)
)
```
plotVarPart

Arguments

- **fit**: model fit from `dream()`
- **fitEB**: model fit from `eBayes()`
- **var_true**: array of true variance values from simulation (optional)
- **xmax**: maximum value on the x-axis

Description

Violin plot of variance fraction for each gene and each variable

Usage

```r
plotVarPart(
  obj,
  col = c(ggColorHue(ncol(obj) - 1), "grey85"),
  label.angle = 20,
  main = "",
  ylab = "",
  convertToPercent = TRUE,
  ...
)
```

---

**Violin plot of variance fractions**

---

```r
## S4 method for signature 'matrix'
plotVarPart(
  obj,
  col = c(ggColorHue(ncol(obj) - 1), "grey85"),
  label.angle = 20,
  main = "",
  ylab = "",
  convertToPercent = TRUE,
  ...
)

## S4 method for signature 'data.frame'
plotVarPart(
  obj,
  col = c(ggColorHue(ncol(obj) - 1), "grey85"),
  label.angle = 20,
  main = "",
  ylab = "",
  convertToPercent = TRUE,
  ...
)
```
## S4 method for signature 'varPartResults'

plotVarPart(
  obj,
  col = c(ggColorHue(ncol(obj) - 1), "grey85"),
  label.angle = 20,
  main = "",
  ylab = "",
  convertToPercent = TRUE,
  ...
)

### Arguments

- **obj**: varParFrac object returned by fitExtractVarPart or extractVarPart
- **col**: vector of colors
- **label.angle**: angle of labels on x-axis
- **main**: title of plot
- **ylab**: text on y-axis
- **convertToPercent**: multiply fractions by 100 to convert to percent values

### Value

Makes violin plots of variance components model. This function uses the graphics interface from ggplot2. Warnings produced by this function usually ggplot2 warning that the window is too small.

### Examples

```r
# load library
# library(variancePartition)

library(BiocParallel)

# load simulated data:
# geneExpr: matrix of gene expression values
# info: information/metadata about each sample
data(varPartData)

# Specify variables to consider
# Age is continuous so we model it as a fixed effect
# Individual and Tissue are both categorical, so we model them as random effects
form <- ~ Age + (1 | Individual) + (1 | Tissue)

varPart <- fitExtractVarPartModel(geneExpr, form, info)

# violin plot of contribution of each variable to total variance
```
**Description**

Residual degrees of freedom

**Usage**

```r
df(fit)
```

**Arguments**

- `fit` model fit from `lm()`, `glm()`, `lmer()`

**See Also**

- `rdf.merMod`

**Examples**

```r
library(lme4)

fit <- lm(Reaction ~ Days, sleepstudy)
df(fit)
```

---

**Description**

For a linear model with \(n\) samples and \(p\) covariates, \(\frac{RSS}{\sigma^2} \sim \chi^2_\nu\) where \(\nu = n - p\) is the residual degrees of freedom. In the case of a linear mixed model, the distribution is no longer exactly a chi-square distribution, but can be approximated with a chi-square distribution.

Given the hat matrix, \(H\), that maps between observed and fitted responses, the approximate residual degrees of freedom is \(\nu = \text{tr}((I - H)^T(I - H))\). For a linear model, this simplifies to the well known form \(\nu = n - p\). In the more general case, such as a linear mixed model, the original form simplifies only to \(n - 2\text{tr}(H) + \text{tr}(HH)\) and is an approximation rather than being exact. The third term here is quadratic in the number of samples, \(n\), and can be computationally expensive to evaluate for larger datasets. Here we develop a linear time algorithm that takes advantage of the fact that \(H\) is low rank.

\(H\) is computed as \(A^T A + B^T B\) for \(A=CL\) and \(B=CR\) defined in the code. Since \(A\) and \(B\) are low rank, there is no need to compute \(H\) directly. Instead, the terms \(\text{tr}(H)\) and \(\text{tr}(HH)\) can be computed using the eigen decompositions of \(AA^T\) and \(BB^T\) which is linear time in the number of samples.
Usage

rdf.merMod(model, method = c("linear", "quadratic"))

Arguments

model An object of class merMod
method Use algorithm that is "linear" (default) or quadratic time in the number of samples

Details

Compute the approximate residual degrees of freedom from a linear mixed model.

Value

residual degrees of freedom

See Also

rdf_from_matrices

Examples

library(lme4)

# Fit linear mixed model
fit <- lmer(Reaction ~ Days + (Days | Subject), sleepstudy)

# Evaluate the approximate residual degrees of freedom
rdf.merMod(fit)

rdf_from_matrices

Fast approximate residual degrees of freedom

Description

Defining $H = A^T A + B^T B$ where $A$ and $B$ are low rank, compute $n - 2\text{tr}(H) + \text{tr}(HH)$ in $O(np^2)$ instead of $O(n^2p^2)$.

Usage

rdf_from_matrices(A, B)

Arguments

A a matrix or sparseMatrix
B a matrix or sparseMatrix
### reOnly

**See Also**

`rdf.merMod`

---

### Description

Adapted from `lme4::reOnly`

### Usage

```r
reOnly(f, response = FALSE)
```

### Arguments

- `f`  
  formula

- `response`  
  (FALSE) is there a response in the formula

---

### residuals,MArrayLM-method

**residuals for MArrayLM**

---

### Description

residuals for MArrayLM

### Usage

```r
## S4 method for signature 'MArrayLM'
residuals(object, y, ..., type = c("response", "pearson"))
```

### Arguments

- `object`  
  MArrayLM object from dream

- `y`  
  EList object used in `dream()`

- `...`  
  other arguments, currently ignored

- `type`  
  compute either response or pearson residuals

### Value

results of residuals
residuals,MArrayLM2-method

residuals for MArrayLM2

Description
residuals for MArrayLM2

Usage
## S4 method for signature 'MArrayLM2'
residuals(object, y, type = c("response", "pearson"), ...)

Arguments
- object: MArrayLM2 object from dream
- y: EList object used in dream()
- type: compute either response or pearson residuals
- ...: other arguments, currently ignored

Value
results of residuals

residuals,VarParFitList-method

Residuals from model fit

Description
Extract residuals for each gene from model fit with fitVarPartModel()

Usage
## S4 method for signature 'VarParFitList'
residuals(object, ...)

Arguments
- object: object produced by fitVarPartModel()
- ...: other arguments.

Details
If model is fit with missing data, residuals returns NA for entries that were missing in the original data
Value

Residuals extracted from model fits stored in object

Examples

# load library
# library(variancePartition)

library(BiocParallel)

# load simulated data:
# geneExpr: matrix of gene expression values
# info: information/metadata about each sample
data(varPartData)

# Specify variables to consider
# Age is continuous so we model it as a fixed effect
# Individual and Tissue are both categorical, so we model them as random effects
form <- ~ Age + (1 | Individual) + (1 | Tissue)

# Fit model
modelFit <- fitVarPartModel(geneExpr, form, info)

# Extract residuals of model fit
res <- residuals(modelFit)

residuals.MArrayLM2 Residuals for result of dream

Description

Residuals for result of dream

Usage

residuals.MArrayLM2(object, y, ..., type = c("response", "pearson"))

Arguments

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>object</td>
<td>See ?stats::residuals</td>
</tr>
<tr>
<td>y</td>
<td>EList object used in dream()</td>
</tr>
<tr>
<td>...</td>
<td>See ?stats::residuals</td>
</tr>
<tr>
<td>type</td>
<td>compute either response or pearson residuals</td>
</tr>
</tbody>
</table>
shrinkageMetric  

*Shrinkage metric for eBayes*

**Description**

Evaluates the coefficient from the linear regression of \( s2.post \sim \sigma^2 \). When there is no shrinkage, this value is 1. Values less than 1 indicate the amount of shrinkage.

**Usage**

```r
shrinkageMetric(sigmaSq, s2.post)
```

**Arguments**

- `sigmaSq`: maximum likelihood residual variance for every gene
- `s2.post`: empirical Bayes posterior estimate of residual variance for every gene

**Details**

Shrinkage metric for eBayes quantifying the amount of shrinkage that is applied to shrink the maximum likelihood residual variance to the empirical Bayes posterior estimate

---

sortCols  

*Sort variance partition statistics*

**Description**

Sort columns returned by `extractVarPart()` or `fitExtractVarPartModel()`

**Usage**

```r
sortCols(
  x,
  FUN = median,
  decreasing = TRUE,
  last = c("Residuals", "Measurement.error"),
  ...
)
```

```r
## S4 method for signature 'matrix'
sortCols(
  x,
  FUN = median,
  decreasing = TRUE,
  last = c("Residuals", "Measurement.error"),
)```
## S4 method for signature 'data.frame'
\texttt{sortCols(}
  \texttt{x, FUN = median, decreasing = \texttt{TRUE},}
  \texttt{last = c("Residuals", "Measurement.error"), \ldots)}
\texttt{)}

## S4 method for signature 'varPartResults'
\texttt{sortCols(}
  \texttt{x, FUN = median, decreasing = \texttt{TRUE},}
  \texttt{last = c("Residuals", "Measurement.error"), \ldots)}
\texttt{)}

### Arguments

\texttt{x} \hspace{1cm} \text{object returned by \texttt{extractVarPart()} or \texttt{fitExtractVarPartModel()}}
\texttt{FUN} \hspace{1cm} \text{function giving summary statistic to sort by. Defaults to median}
\texttt{decreasing} \hspace{1cm} \text{logical. Should the sorting be increasing or decreasing?}
\texttt{last} \hspace{1cm} \text{columns to be placed on the right, regardless of values in these columns}
\ldots \hspace{1cm} \text{other arguments to sort}

### Value

\texttt{data.frame} with columns sorted by mean value, with Residuals in last column

### Examples

# library(variancePartition)

library(BiocParallel)

# load simulated data:
# geneExpr: matrix of gene expression values
# info: information/metadata about each sample
data(varPartData)

# Specify variables to consider
# Age is continuous so we model it as a fixed effect
# Individual and Tissue are both categorical, so we model them as random effects
form <- ~ Age + (1 | Individual) + (1 | Tissue)
# Step 1: fit linear mixed model on gene expression
# If categorical variables are specified, a linear mixed model is used
# If all variables are modeled as continuous, a linear model is used
# each entry in results is a regression model fit on a single gene
# Step 2: extract variance fractions from each model fit
# for each gene, returns fraction of variation attributable to each variable
# Interpretation: the variance explained by each variable
# after correction for all other variables
varPart <- fitExtractVarPartModel(geneExpr, form, info)

# violin plot of contribution of each variable to total variance
# sort columns by median value
plotVarPart(sortCols(varPart))

---

topTable

Table of Top Genes from Linear Model Fit

Description

topTable generic

topTable generic MArrayLM

topTable generic MArrayLM2

Usage

topTable(
  fit,
  coef = NULL,
  number = 10,
  genelist = fit$genes,
  adjust.method = "BH",
  sort.by = "B",
  resort.by = NULL,
  p.value = 1,
  lfc = 0,
  confint = FALSE
)

## S4 method for signature 'MArrayLM'
topTable(
  fit,
  coef = NULL,
  number = 10,
  genelist = fit$genes,
  adjust.method = "BH",
  sort.by = "p",

resort.by = NULL,
p.value = 1,
lfc = 0,
confint = FALSE
)

## S4 method for signature 'MArrayLM2'
topTable(
  fit,
  coef = NULL,
  number = 10,
  genelist = fit$genes,
  adjust.method = "BH",
  sort.by = "p",
  resort.by = NULL,
  p.value = 1,
  lfc = 0,
  confint = FALSE
)

Arguments

<table>
<thead>
<tr>
<th>fit</th>
<th>fit</th>
</tr>
</thead>
<tbody>
<tr>
<td>coef</td>
<td>coef</td>
</tr>
<tr>
<td>number</td>
<td>number</td>
</tr>
<tr>
<td>genelist</td>
<td>genelist</td>
</tr>
<tr>
<td>adjust.method</td>
<td>adjust.method</td>
</tr>
<tr>
<td>sort.by</td>
<td>sort.by</td>
</tr>
<tr>
<td>resort.by</td>
<td>resort.by</td>
</tr>
<tr>
<td>p.value</td>
<td>p.value</td>
</tr>
<tr>
<td>lfc</td>
<td>lfc</td>
</tr>
<tr>
<td>confint</td>
<td>confint</td>
</tr>
</tbody>
</table>

Value

- results of toptable
- results of toptable
- results of toptable

VarParCIList-class  

Class VarParCIList

Description

Class VarParCIList
Description

Class VarParFitList

Description

Class varParFrac

Description

Linear mixed model confidence intervals

Fit linear mixed model to estimate contribution of multiple sources of variation while simultaneously correcting for all other variables. Then perform parametric bootstrap sampling to get a 95% confidence intervals for each variable for each gene.

Usage

```r
varPartConfInf(
  exprObj,
  formula,
  data,
  REML = FALSE,
  useWeights = TRUE,
  control = vpcontrol,
  nsim = 1000,
  ...
)
```
Arguments

exprObj: matrix of expression data (g genes x n samples), or ExpressionSet, or EList returned by voom() from the limma package

formula: specifies variables for the linear (mixed) model. Must only specify covariates, since the rows of exprObj are automatically used as a response. e.g.: ~ a + b + (1|c)

data: data.frame with columns corresponding to formula

REML: use restricted maximum likelihood to fit linear mixed model. default is FALSE. Strongly discourage against changing this option, but here for compatibility.

useWeights: if TRUE, analysis uses heteroskedastic error estimates from voom(). Value is ignored unless exprObj is an EList from voom() or weightsMatrix is specified

control: control settings for lmer()

nsim: number of bootstrap datasets

... Additional arguments for lmer() or lm()

Details

A linear mixed model is fit for each gene, and bootMer() is used to generate parametric bootstrap confidence intervals. use.u=TRUE is used so that the \( \hat{u} \) values from the random effects are used as estimated and are not re-sampled. This gives confidence intervals as if additional data were generated from these same current samples. Conversely, use.u=FALSE assumes that this dataset is a sample from a larger population. Thus it simulates \( \hat{u} \) based on the estimated variance parameter. This approach gives confidence intervals as if additional data were collected from the larger population from which this dataset is sampled. Overall, use.u=TRUE gives smaller confidence intervals that are appropriate in this case.

Value

list() of where each entry is the result for a gene. Each entry is a matrix of the 95% confidence interval of the variance fraction for each variable

Examples

# load library
# library(variancePartition)

library(BiocParallel)

# load simulated data:
# geneExpr: matrix of gene expression values
# info: information/metadata about each sample
data(varPartData)

# Specify variables to consider
# Age is continuous so we model it as a fixed effect
# Individual and Tissue are both categorical, so we model them as random effects
form <- ~ Age + (1 | Individual) + (1 | Tissue)
# Compute bootstrap confidence intervals for each variable for each gene
resCI <- varPartConfInf(geneExpr[1:5, ], form, info, nsim = 100)

## varPartData

### Simulation dataset for examples

#### Description

A simulated dataset of gene expression and metadata
A simulated dataset of gene counts
A simulated dataset of gene counts
A simulated dataset of gene counts

#### Usage

data(varPartData)
data(varPartData)
data(varPartData)
data(varPartData)
data(varPartData)

#### Format

A dataset of 100 samples and 200 genes
A dataset of 100 samples and 200 genes
A dataset of 100 samples and 200 genes
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#### Details

- geneCounts gene expression in the form of RNA-seq counts
- geneExpr gene expression on a continuous scale
- info metadata about the study design
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varPartDEdata

- geneCounts gene expression in the form of RNA-seq counts
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A simulated dataset of gene counts

Description

- geneCounts gene expression in the form of RNA-seq counts
- geneExpr gene expression on a continuous scale
- info metadata about the study design

Usage

data(varPartData)

data(varPartData)

Format

A dataset of 24 samples and 19,364 genes

varPartResults-class

Class varPartResults

Description

Class varPartResults
vcov,MArrayLM-method  

Co-variance matrix for dream() fit

Description
Define generic vcov() for result of lmFit() and dream()

Usage

## S4 method for signature 'MArrayLM'
vcov(object, vobj, coef)

Arguments

- **object**  MArrayLM object return by lmFit() or dream()
- **vobj**   EList object returned by voom()
- **coef**  name of coefficient to be extracted

Value

  variance-covariance matrix

vcov,MArrayLM2-method  

Co-variance matrix for dream() fit

Description
Define generic vcov() for result of lmFit() and dream()

Usage

## S4 method for signature 'MArrayLM2'
vcov(object, vobj, coef)

Arguments

- **object**  MArrayLM object return by lmFit() or dream()
- **vobj**   EList object returned by voom()
- **coef**  name of coefficient to be extracted

Value

  variance-covariance matrix
vcovSqrt

**Sqrt of co-variance matrix for dream() fit**

**Description**
Define generic vcovSqrt() for result of lmFit() and dream()

**Usage**

```r
documentization for vcovSqrt()
```

**Arguments**

- **object**: MArrayLM object return by lmFit() or dream()
- **vobj**: EList object returned by voom()
- **coef**: name of coefficient to be extracted
- **approx**: use fast approximation

**Value**
Computes factor of covariance matrix so that vcov(object) is the same as crossprod(vcovSqrt(object))

**Examples**

```r
# load simulated data:
# geneExpr: matrix of normalized* gene expression values
# info: information/metadata about each sample
data(varPartData)

form <- ~Batch

fit <- dream(geneExpr[1:2, ], form, info)
fit <- eBayes(fit)

# Compute covariance directly
Sigma <- vcov(fit, geneExpr[1:2, ])

# Compute factor of covariance
S <- crossprod(vcovSqrt(fit, geneExpr[1:2, ]))
```
**voomWithDreamWeights**  
*Transform RNA-Seq Data Ready for Linear Mixed Modelling with dream()*

**Description**

Transform count data to log2-counts per million (logCPM), estimate the mean-variance relationship and use this to compute appropriate observation-level weights. The data are then ready for linear mixed modelling with `dream()`. This method is the same as `limma::voom()`, except that it allows random effects in the formula.

**Usage**

```r
voomWithDreamWeights(
  counts,
  formula,
  data,
  lib.size = NULL,
  normalize.method = "none",
  span = 0.5,
  weights = NULL,
  prior.count = 0.5,
  plot = FALSE,
  save.plot = FALSE,
  rescaleWeightsAfter = TRUE,
  BPPARAM = SerialParam(),
  ...
)
```

**Arguments**

- `counts`  
a numeric matrix containing raw counts, or an ExpressionSet containing raw counts, or a DGEList object. Counts must be non-negative and NAs are not permitted.

- `formula`  
specifies variables for the linear (mixed) model. Must only specify covariates, since the rows of exprObj are automatically used as a response. e.g.: `~ a + b + (1|c)` Formulas with only fixed effects also work, and `lmFit()` followed by `contrasts.fit()` are run.

- `data`  
data.frame with columns corresponding to formula

- `lib.size`  
numeric vector containing total library sizes for each sample. Defaults to the normalized (effective) library sizes in counts if counts is a DGEList or to the columnwise count totals if counts is a matrix.

- `normalize.method`  
the microarray-style normalization method to be applied to the logCPM values (if any). Choices are as for the method argument of `normalizeBetweenArrays` when the data is single-channel. Any normalization factors found in counts will still be used even if `normalize.method="none".`
voomWithDreamWeights

span width of the lowess smoothing window as a proportion. Setting span="auto" uses fANCOVA::loess.as() to estimate the tuning parameter from the data

weights Can be a numeric matrix of individual weights of same dimensions as the counts, or a numeric vector of sample weights with length equal to ncol(counts)

prior.count average count to be added to each observation to avoid taking log of zero. The count applied to each sample is normalized by library size so given equal log CPM for a gene with zero counts across multiple samples

plot logical, should a plot of the mean-variance trend be displayed?

save.plot logical, should the coordinates and line of the plot be saved in the output?

rescaleWeightsAfter default = TRUE, should the output weights be scaled by the input weights

BPPARAM parameters for parallel evaluation

... other arguments are passed to lmer.

Details

Adapted from voom() in limma v3.40.2

Value

An EList object just like the result of limma::voom()

See Also

limma::voom()

Examples

# library(variancePartition)
library(edgeR)
library(BiocParallel)

data(varPartDEdata)

# normalize RNA-seq counts
dge <- DGEList(counts = countMatrix)
dge <- calcNormFactors(dge)

# specify formula with random effect for Individual
form <- ~ Disease + (1 | Individual)

# compute observation weights
vobj <- voomWithDreamWeights(dge[1:20, ], form, metadata)

# fit dream model
res <- dream(vobj, form, metadata)
res <- eBayes(res)

# extract results
topTable(res, coef = "Disease1", number = 3)

### Description
Enable subsetting on MArrayLM2 object. Same as for MArrayLM, but apply column subsetting to df.residual and cov.coefficients.list

### Arguments
- **object**: MArrayLM2
- **i**: row
- **j**: col

### Value
subset
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