

Package ‘rxSeq’

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Description

Analysis of combined total and allele specific reads from the reciprocal cross study with RNA-seq data.

Depends MASS, VGAM, numDeriv

License GPL (>= 2)

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data.A *Sample data example for autosomal genes*

Description

This data set provides with example of experimental data for a subset of autosomal genes. The full model requires a combination of total read counts (**y**) - all the reads belonging for a gene, and finding out which of these reads we can specifically attribute to allele A or allele B - allele specific counts (**n**), separately the reads attributed specifically to allele B (**n0B**). Also, it includes the other data pieces to fit the model: **kappas** - total number of counts for each mouse, on log scale, index - specifying which cross each mouse belongs to, and geneids - Ensembl ids of genes. They, as well as the datasets simulated with **simRX** can be fitted using **proc.trecase.A** or **proc.trec.A**.

Value

index	vector defining the cross of the mouse, female - AB=1, BA=2, AA=3, BB=4, and male - AB=5, BA=6, AA=7, BB=8. If mice are of only one sex, AB=1, BA=2, AA=3, BB=4.
y	matrix of TReC counts. Note, the expected input assumes that inbred mice will be in the last columns of the table, after the last F1 mouse.
n	matrix of ASE counts for corresponding F1 mouse (classes 1, 2, 5, 6) for corresponding genes.
n0B	matrix of ASE counts belonging for allele B, for corresponding genes and mice as in n .
kappas	A parameter, specifying log(overall TReC) for each mouse.
geneids	ids of genes, if not provided, rownames of the matrix y will be used

Author(s)

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See Also

[process,readCounts](#).

Examples

```
# see total read counts (TReC) for first 2 autosomal genes of a data example:
data.A$y[1:2,]
```

data.X

*Sample data example for X chromosome genes***Description**

This data set provides with example of experimental data for a subset of autosomal genes. The full model requires a combination of total read counts (**y**) - all the reads belonging for a gene, and finding out which of these reads we can specifically attribute to allele A or allele B - allele specific counts (**n**), separately the reads attributed specifically to allele B (**n0B**). Also, **tausB** - is the *Xce* effect for each F1 mouse, which specifies the proportion of allele specific reads belonging to allele B. Also, it includes the other data pieces to fit the model: **kappas** - total number of counts for each mouse, on log scale, **index** - specifying which cross each mouse belongs to, and **geneids** - Ensembl ids of genes. They, as well as the datasets simulated with **simRX** can be fitted using **proc.trecase.X** or **proc.trec.X**.

Value

index	vector defining the cross of the mouse, female - AB=1, BA=2, AA=3, BB=4, and male - AB=5, BA=6, AA=7, BB=8. If mice are of only one sex, AB=1, BA=2, AA=3, BB=4.
y	matrix of TReC counts. Note, the expected input assumes that inbred mice will be in the last columns of the table, after the last F1 mouse.
n	matrix of ASE counts for corresponding F1 mouse (classes 1,2,5,6) for corresponding genes.
n0B	matrix of ASE counts belonging for allele B, for corresponding genes and mice as in n .
kappas	A parameter, specifying as overall TReC for the mouse, on log scale
tausB	<i>Xce</i> effect: expression of allele B relative to the overall allele specific count for each mouse. Use some allele specific counts to estimate the effect.
geneids	ids of genes, if not provided, rownames of the matrix y will be used
index	index defining which mouse belongs to which cross
y	modified total read counts
n	modified allele specific counts
n0B	modified allele specific counts, belonging to allele B
kappas	offset, defining a library size for each mouse
tausB	<i>Xce</i> effect for each mouse, for a given cross
geneids	Ensembl gene ids

Author(s)

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See Also

[process,readCounts](#).

Examples

```
# see total read counts (TReC) for first 2 X chromosome genes of a data example:
data.X$y[1:2,]
```

<code>get.tausB</code>	<i>Produce Xce estimates for mice with allele specific reads</i>
------------------------	--

Description

Xce estimation for mice with allele specific reads.

Usage

```
get.tausB(n, n0B, geneids, min.cnt=50, exclude.prop=.05, Xist.ID="ENSMUSG00000086503")
```

Arguments

<code>n</code>	vector of allele specific counts for each mouse
<code>n0B</code>	vector of allele specific counts for allele B
<code>geneids</code>	gene IDs
<code>min.cnt</code>	minimum number of allele specific counts
<code>exclude.prop</code>	minimum proportion of allele specific counts for each allele
<code>Xist.ID</code>	and ID of <i>Xist</i> , to exclude it from estimating <i>Xce</i> , since <i>Xce</i> would 1-tausB

Value

output - matrix of 4 rows:

<code>med.tauB</code>	taus estimated via median
<code>ave.tauB</code>	taus estimated via percent of allele B counts
<code>all.genes</code>	number of genes that had passed minimum count
<code>used.genes</code>	number of genes that had required percent of each allele

each column represent respective mouse.

Author(s)

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See Also

[process,nLogLik, data.X, rcX](#).

Examples

```
# Estimating XCE effect for each mouse for X chromosome
get.tausB(n=data.X$n, n0B=data.X$n0B, geneids=data.X$geneids)
```

nLogLik	<i>Negative log likelihood for coefficients provided in results of the fit using process function</i>
---------	---

Description

Calculates negative log(likelihood) of an X chromosome joint TReC and ASE counts model at a given set of parameters

Usage

```
nLogLik(res, rc, genei, hessian=FALSE)
```

Arguments

res	result object from process function
rc	Read count data object created by readCounts function
genei	get results for i`th gene
hessian	a logical option whether to calculate a Hessian matrix, the default values is set to FALSE.

Value

output - list(nll=-log.likelihood,hessian=hessian matrix)

Author(s)

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See Also

[process](#), [rcA](#), [readCounts](#).

Examples

```
## Not run:
# get negative-log likelihood at the given point:
nLogLik(res=trecase.X.out, rc=rcX, genei=1, hessian=TRUE)

## End(Not run)
```

process	<i>Optimization wrapper, maximizing either the joint model of total (TReC) and allele specific (ASE) counts or just TReC</i>
---------	--

Description

Performs optimization of one of four combinations: joint TReC and ASE or just TReC for autosome or X chromosome and tests with lrt test several hypotheses: additive, parent of origin, dominance, consistency of TreC and ASE additive effect, ASE only additive effect, sex, sex specific additive, dominance deviation for males.

Usage

```
process(rc, hessian=FALSE)
```

Arguments

rc	an object of class readCounts.
hessian	a flag whether Hessian matrix for these genes should be calculated, by default set to FALSE

Value

a list of following matrices (if there is only one sex, only the relevant tests and matrices are outputted):

pvals	matrix of p-values from description for each gene corresponding row
coef.full	matrix of full model fit coefficients, $-\log(\text{likelihood at these coefficients})$, phi, theta (2 overdispersion parameters used)
coef.add	matrix of additive restricted fit coefficients, $-\log(\text{likelihood at these coefficients})$, phi, theta
coef.poo	matrix of parent of origin restricted fit coefficients, $-\log(\text{likelihood at these coefficients})$, phi, theta
coef.dom	matrix of dominance restricted fit coefficients, $-\log(\text{likelihood at these coefficients})$, phi, theta
coef.same	matrix of TReC=ASE additive restricted fit coefficients, $-\log(\text{likelihood at these coefficients})$, phi, theta
coef.ase.add	matrix of ASE additive restricted fit coefficients, $-\log(\text{likelihood at these coefficients})$, phi, theta
coef.sex	matrix of sex restricted fit coefficients, $-\log(\text{likelihood at these coefficients})$, phi, theta
coef.sex.add	matrix of sex specific additive restricted fit coefficients, $-\log(\text{likelihood at these coefficients})$, phi, theta
coef.dev.dom	matrix of dominance deviation for male restricted fit coefficients, $-\log(\text{likelihood at these coefficients})$, phi, theta

errorlist a list of errors
 hess.lst a list of heessian matrices, if parameter **hessian** is set to TRUE

Author(s)

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See Also

[get.tausB,nLogLik](#), [data.X](#), [data.A](#), [rcA](#), [readCounts](#).

Examples

```
## Not run:
# fitting X chromosome data example, for a full model, i.e. assuming we have allele specific reads:
trease.A.out = process(rc=rcA)
names(trease.A.out)
trease.A.out$pval

#alternatively for X chromosome:
trease.X.out = process(rc=rcX)
names(trease.X.out)
trease.X.out$pval

## End(Not run)
```

rcA	<i>Reformatted data for autosomal set to be used as input to process function</i>
-----	---

Description

This is an object of type `readCounts` provides with example of experimental data for a subset of autosomal genes. The full model requires a combination of total read counts (**y**) - all the reads belonging for a gene, and finding out which of these reads we can specifically attribute to allele A or allele B - allele specific counts (**n**), separately the reads attributed specifically to allele B (**n0B**). In autosomes *Xce* effect is absent, so it would be set to NULL for this dataset. Also, it includes the other data pieces to fit the model: **kappas** - total number of counts for each mouse, on log scale, **index** - specifying which cross each mouse belongs to, and **geneids** - Ensembl ids of genes. Such values also can be simulated with **simRX** can be fitted using **process** with appropriate options `chrom="X"` and `field model` to be either "full" or "short".

Value

index vector defining the cross of the mouse, female - AB=1, BA=2, AA=3, BB=4, and male - AB=5, BA=6, AA=7, BB=8. If mice are of only one sex, AB=1, BA=2, AA=3, BB=4.

<code>y</code>	matrix of TReC counts. Note, the expected input assumes that inbred mice will be in the last columns of the table, after the last F1 mouse.
<code>n</code>	matrix of ASE counts for corresponding F1 mouse (classes 1,2,5,6) for corresponding genes.
<code>n0B</code>	matrix of ASE counts belonging for allele B, for corresponding genes and mice as in <code>n</code> .
<code>kappas</code>	A parameter, specifying as overall TReC for the mouse, on log scale
<code>tausB</code>	<i>Xce</i> effect: expression of allele B relative to the overall allele specific count for each mouse. Set to NULL in autosomes.
<code>gene.switch</code>	For which genes <i>Xce</i> effect should be switched. Null for autosomes.
<code>geneids</code>	ids of genes, if not provided, rownames of the matrix <code>y</code> will be used
<code>chrom</code>	this field would be set to be "X" since this is dataset for chromosome X
<code>model</code>	set to be "full", can be modified to "short" to run a TReC oply model
<code>geneids</code>	Ensembl gene ids
<code>tech.ctrl</code>	a list of overdispersion boundaries and log(2)

Author(s)

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See Also

[process](#), [readCounts](#), [simRX](#).

Examples

```
# see total read counts (TReC) for first 2 X chromosome genes of a data example:
rcX
```

rcX

Reformatted data for chromosome X set to be used as input to process function

Description

This is an object of type `readCounts` provides with example of experimental data for a subset of X chromosome genes. The full model requires a combination of total read counts (`y`) - all the reads belonging for a gene, and finding out which of these reads we can specifically attribute to allele A or allele B - allele specific counts (`n`), separately the reads attributed specifically to allele B (`n0B`). Also, `tausB` - is the *Xce* effect for each F1 mouse, which specifies the proportion of allele specific reads belonging to allele B. Also, it includes the other data pieces to fit the model: `kappas` - total number of counts for each mouse, on log scale, index - specifying which cross each mouse belongs to, and `geneids` - Ensembl ids of genes. They, as well as the datasets simulated with `simRX` can be fitted using `process` with appropriate options `chrom="X"` and field `model` to be either "full" or "short".

Value

genes.switch=genes.switch, geneids=geneids,

index	vector defining the cross of the mouse, female - AB=1, BA=2, AA=3, BB=4, and male - AB=5, BA=6, AA=7, BB=8. If mice are of only one sex, AB=1, BA=2, AA=3, BB=4.
y	matrix of TReC counts. Note, the expected input assumes that inbred mice will be in the last columns of the table, after the last F1 mouse.
n	matrix of ASE counts for corresponding F1 mouse (classes 1,2,5,6) for corresponding genes.
n0B	matrix of ASE counts belonging for allele B, for corresponding genes and mice as in n .
kappas	A parameter, specifying as overall TReC for the mouse, on log scale
tausB	<i>Xce</i> effect: expression of allele B relative to the overall allele specific count for each mouse. Use some allele specific counts to estimate the effect.
gene.switch	For which genes <i>Xce</i> effect should be switched. Xist gene set to be switched in this set.
geneids	ids of genes, if not provided, rownames of the matrix y will be used
chrom	this field would be set to be "X" since this is dataset for chromosome X
model	set to be "full", can be modified to "short" to run a TReC oply model
geneids	Ensembl gene ids
tech.ctrl	a list of overdispersion boundaries and log(2)

Author(s)

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See Also

[process,readCounts,simRX](#).

Examples

```
# see total read counts (TReC) for first 2 X chromosome genes of a data example:
rcX
```

readCounts	<i>A list object that should be used as input to optimization process function.</i>
------------	---

Description

It should contain at least total read counts (TReC) and classification of crosses 1 to 8. To fit the full model should also have appropriate allele specific counts n and $n0B$. Also is used along with results of optimization as input to `nLogLik` function if one needs to calculate Hessian matrix.

Value

<code>index</code>	vector defining the cross of the mouse, female - AB=1, BA=2, AA=3, BB=4, and male - AB=5, BA=6, AA=7, BB=8. If mice are of only one sex, AB=1, BA=2, AA=3, BB=4.
<code>y</code>	matrix of TReC counts. Note, the expected input assumes that inbred mice will be in the last columns of the table, after the last F1 mouse.
<code>n</code>	matrix of ASE counts for corresponding F1 mouse (classes 1,2,5,6) for corresponding genes.
<code>n0B</code>	matrix of ASE counts belonging for allele B, for corresponding genes and mice as in <code>n</code> .
<code>kappas</code>	A parameter, specifying as overall TReC for the mouse, on log scale
<code>tausB</code>	<i>Xce</i> effect: expression of allele B relative to the overall allele specific count for each mouse. Set to NULL in autosomes.
<code>gene.switch</code>	For which genes <i>Xce</i> effect should be switched. Null for autosomes.
<code>geneids</code>	ids of genes, if not provided, rownames of the matrix <code>y</code> will be used
<code>chrom</code>	this field would be set to be "X" since this is dataset for chromosome X
<code>model</code>	set to be "full", can be modified to "short" to run a TReC oply model
<code>geneids</code>	Ensembl gene ids
<code>tech.ctrl</code>	a list of overdispersion boundaries and $\log(2)$

Author(s)

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See Also

[process](#), [nLogLik](#), [simRX](#).

Examples

```
# see total read counts (TReC) for first 2 X chromosome genes of a data example:
rcA = readCounts(index=data.A$index, y=data.A$y[1:2,], n=data.A$n[1:2,], n0B=data.A$n0B[1:2,],
                 kappas=data.A$kappas, geneids=data.A$geneids[1:2])
```

simRX

*Produce simulated counts***Description**

This function is producing simulated counts for the joint model with Negative-Binomial distribution for TReC and Beta-Binomial for ASE counts. The simulated dataset should be reformatted to readCounts format to be used for optimization.

Usage

```
simRX(b0f, b0m, b1f, b1m, beta_sex, beta_dom, beta_k=1, phi=1, theta=1, n=6,
      mean.base.cnt=50, range.base.cnt=60, perc.ase=.35, n.simu=1E4,
      is.X=FALSE, tauB=NULL, seed=NULL)
```

Arguments

b0f	a female additive strain effect
b0m	a male additive strain effect
b1f	a female parent of origin effect
b1m	a male parent of origin effect
beta_sex	a sex effect
beta_dom	a dominance effect
beta_k	an effect associated with the library size kappas
phi	a Negative-Binomial overdispersion, default value is 1
theta	a Beta-Binomial overdispersion, default value is 1
n	a vector defining number of mice in each cross, default value is 6
mean.base.cnt	a target expected number of counts for the base group (with no effects), default value is 50
range.base.cnt	a range in which the expected number of counts for the base group will vary, default value is 60
perc.ase	a percent reads that are allele-specific, default value is 35%
n.simu	a number of simulations, default value is 1E4
is.X	a flag if the value to be simulated is X for chromosome (otherwise autosome), default value is FALSE
tauB	a value describing allelic imbalance - <i>Xce</i> effect for the cross, default value is NULL, in which case 50% will be simulated
seed	a random seed to be set, no set by default.

Value

output - 3 matrices with one row - one gene, one column - one mouse:

index	vector defining the cross of the mouse, female - AB=1, BA=2, AA=3, BB=4, and male - AB=5, BA=6, AA=7, BB=8. If mice are of only one sex, AB=1, BA=2, AA=3, BB=4.
y	A matrix of total read counts
n	A matrix of allele specific counts
n0B	A matrix of allele specific counts associated with allele B
kappas	Offset parameter, given as overall TReC for the mouse.
tausB	In case of the simulating X chromosome the provided <i>Xce</i> effect is returned: expression of allele B relative to the overall allele specific count for each mouse.

Author(s)

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See Also

[process,readCounts](#).

Examples

```
# simulating autosomal data:
dat.A = simRX(b0f=.5, b0m=.6, b1f=.3, b1m=.4, beta_sex=.1, beta_dom=.1, n.simu=1E1)
names(dat.A)
# simulating autosomal data:
dat.X = simRX(b0f=.5, b0m=.6, b1f=.3, b1m=.4, beta_sex=.1, beta_dom=.1, n.simu=1E1,
             is.X=TRUE, tauB=.3)
names(dat.X)
```

trecase.A.out

Example of results produced by optimizing step using process function on autosomal genes. Structured as a list.

Description

A list containing test results as well as parameter estimates for joint model evaluated by process function for autosomal genes.

Value

a list of following matrices (if there is only one sex, only the relevant tests and matrices are outputted)
:

<code>pvals</code>	matrix of p-values from description for each gene corresponding row
<code>coef.full</code>	matrix of full model fit coefficients, $-\log(\text{likelihood at these coefficients})$, ϕ , θ (2 overdispersion parameters used)
<code>coef.add</code>	matrix of additive restricted fit coefficients, $-\log(\text{likelihood at these coefficients})$, ϕ , θ
<code>coef.poo</code>	matrix of parent of origin restricted fit coefficients, $-\log(\text{likelihood at these coefficients})$, ϕ , θ
<code>coef.dom</code>	matrix of dominance restricted fit coefficients, $-\log(\text{likelihood at these coefficients})$, ϕ , θ
<code>coef.same</code>	matrix of TReC=ASE additive restricted fit coefficients, $-\log(\text{likelihood at these coefficients})$, ϕ , θ
<code>coef.ase.add</code>	matrix of ASE additive restricted fit coefficients, $-\log(\text{likelihood at these coefficients})$, ϕ , θ
<code>coef.sex</code>	matrix of sex restricted fit coefficients, $-\log(\text{likelihood at these coefficients})$, ϕ , θ
<code>coef.sex.add</code>	matrix of sex specific additive restricted fit coefficients, $-\log(\text{likelihood at these coefficients})$, ϕ , θ
<code>coef.dev.dom</code>	matrix of dominance deviation for male restricted fit coefficients, $-\log(\text{likelihood at these coefficients})$, ϕ , θ
<code>errorlist</code>	a list of errors
<code>hess.lst</code>	a list of heessian matrices, if parameter hessian is set to TRUE

Author(s)

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See Also

[process](#), [rCA](#), [data.A](#).

Examples

```
names(trecase.A.out)
```

trecase.X.out *Example of results produced by optimizing step using process function on X chromosome genes. Structured as a list.*

Description

A list containing test results as well as parameter estimates for joint model evaluated by process function for autosomal genes.

Value

a list of following matrices (if there is only one sex, only the relevant tests and matrices are outputted):

pvals	matrix of p-values from description for each gene corresponding row
coef.full	matrix of full model fit coefficients, -log(likelihood at these coefficients),phi, theta (2 overdispersion parameters used)
coef.add	matrix of additive restricted fit coefficients, -log(likelihood at these coefficients),phi, theta
coef.poo	matrix of parent of origin restricted fit coefficients, -log(likelihood at these coefficients),phi, theta
coef.dom	matrix of dominance restricted fit coefficients, -log(likelihood at these coefficients),phi, theta
coef.same	matrix of TReC=ASE additive restricted fit coefficients, -log(likelihood at these coefficients),phi, theta
coef.ase.add	matrix of ASE additive restricted fit coefficients, -log(likelihood at these coefficients),phi, theta
coef.sex	matrix of sex restricted fit coefficients, -log(likelihood at these coefficients),phi, theta
coef.sex.add	matrix of sex specific additive restricted fit coefficients, -log(likelihood at these coefficients),phi, theta
coef.dev.dom	matrix of dominance deviation for male restricted fit coefficients, -log(likelihood at these coefficients),phi, theta
errorlist	a list of errors
hess.lst	a list of heessian matrices, if parameter hessian is set to TRUE

Author(s)

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See Also

[process](#), [rcX](#), [data.X](#).

trecase.X.out

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Examples

```
names(trecase.X.out)
```

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