

Package ‘gQTLstats’

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Title gQTLstats: computationally efficient analysis for eQTL and allied studies

Version 1.8.0

Author VJ Carey <stvjc@channing.harvard.edu>

Description computationally efficient analysis of eQTL, mQTL, dsQTL, etc.

Suggests geuvPack, geuvStore2, Rsamtools, knitr, rmarkdown, ggbio, BiocStyle, Homo.sapiens, RUnit, multtest, gwascat

Depends R (>= 3.1.0)

Imports methods, snpStats, BiocGenerics, S4Vectors (>= 0.9.25), IRanges, GenomeInfoDb, GenomicFiles, GenomicRanges, SummarizedExperiment, VariantAnnotation, Biobase, BatchJobs, gQTLBase, limma, mgecv, dplyr, AnnotationDbi, GenomicFeatures, ggplot2, reshape2, doParallel, foreach, fbase, BBmisc, beeswarm, HardyWeinberg, graphics, stats, utils, shiny, ldblock, plotly, erma

Maintainer VJ Carey <stvjc@channing.harvard.edu>

License Artistic-2.0

LazyLoad yes

VignetteBuilder knitr

BiocViews SNP, GenomeAnnotation, Genetics

NeedsCompilation no

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gQTLstats-package	<i>gQTLstats: computationally efficient analysis for eQTL and allied studies</i>
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Description

computationally efficient analysis of eQTL, mQTL, dsQTL, etc.

Details

The DESCRIPTION file:

```

Package:      gQTLstats
Title:        gQTLstats: computationally efficient analysis for eQTL and allied studies
Version:      1.8.0
Author:       VJ Carey <stvjc@channing.harvard.edu>
Description:  computationally efficient analysis of eQTL, mQTL, dsQTL, etc.
Suggests:    geuvPack, geuvStore2, Rsamtools, knitr, rmarkdown, ggbio, BiocStyle, Homo.sapiens, RUnit, multtest
Depends:      R (>= 3.1.0)
Imports:      methods, snpStats, BiocGenerics, S4Vectors (>= 0.9.25), IRanges, GenomeInfoDb, GenomicFiles, GenomicRanges
Maintainer:   VJ Carey <stvjc@channing.harvard.edu>
License:      Artistic-2.0
LazyLoad:    yes
VignetteBuilder: knitr
BiocViews:   SNP, GenomeAnnotation, Genetics

```

Index of help topics:

```

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TransStore          Instance constructor for managing trans gQTL
                    results
TransStore-class    Class '"TransStore"'
cisAssoc            test for variant-expression associations in cis
                    or generally, using VCF
clipPCs             transformations of expression data in smlSet

```

	instances
directPlot	visualize relationship between empirical and modeled FDR based on analysis of a gQTL store
enumerateByFDR	filter a ciseStore instance using an FDR threshold
eqBox2	visualization of expression or other assay measure against genotypes extracted from VCF
filtFDR	illustration of FDRsupp class
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hmm878	labeled GRanges with ChromHMM chromatin states for GM12878
manhWngr	manhattan plot with named GRanges
mixedVCFtoSnpMatrix	amalgamate called genotypes and imputed allelic dosages in VCF to SnpMatrix representation
pifdr	utility for computing plug-in FDR
qqStore	create a binned QQplot for a sharded store
queryVCF	obtain SnpMatrix from VCF genotypes
senstab	create a plottable table for eQTL sensitivity analysis visualization
setFDRfunc	estimate and store function relating association scores to approximate plug-in FDR
storeToQuantiles	extract a vector from store results as ff (out of memory reference); support statistical reductions
tqbrowser	general browsing facility for trans-gQTL
transAssoc	compute 'trans' SNP-feature associations by wrapping AllAssoc
transBrowse	shiny app to exhibit genotype:genomic feature distributions
tsByRank	harvest contents of a TransStore by rank in associations of features to SNP
txsPlot	visualize transformed FDR against transformed association statistics

This package addresses the management of map-reduce like computations for cis-association tests between DNA variants and genomic features like gene expression measurements. It makes essential use of data structures defined in package gQTLBase.

A number of experimental functions are present in the current version of the package: prep.cisAssocNB (assembles information to assess negative binomial regression in cis association testing), storeToMaxAssocBySNP (progress towards SNP-specific FDR), table_sensobj_thresh (reporting on sensitivity analysis).

Additional experimental functions are available to support scalable trans-gQTL testing TransChunk, filteredDFwPerm, and transTable operate on output of AllAssoc.

Author(s)

VJ Carey <stvjc@channing.harvard.edu>

Maintainer: VJ Carey <stvjc@channing.harvard.edu>

 cisAssoc

test for variant-expression associations in cis or generally, using VCF

Description

test for variant-expression associations in cis or generally, using VCF and RangedSummarizedExperiment representations

Usage

```

cisAssoc(summex, vcf.tf, rhs = ~1, nperm = 3, cisradius =
  50000, genome = "hg19", assayind = 1, lbmaf = 1e-06,
  lbgtf = 1e-06, dropUnivHet = TRUE, infoFields =
  c("LDAF", "SVTYPE"), simpleSNV = TRUE)
cisEsts(summex, vcf.tf, rhs = ~1, nperm = 3, cisradius =
  50000, genome = "hg19", assayind = 1, lbmaf = 1e-06,
  lbgtf = 1e-06, dropUnivHet = TRUE, infoFields =
  c("LDAF", "SVTYPE"), simpleSNV = TRUE)
cisCount(summex, vcf.tf, rhs = ~1, cisradius =
  50000, genome = "hg19", assayind = 1, lbmaf = 1e-06,
  lbgtf = 1e-06, dropUnivHet = TRUE, infoFields =
  c("LDAF", "SVTYPE"), simpleSNV = TRUE)
AllAssoc(summex, vcf.tf, variantRange, rhs = ~1, nperm = 3,
  genome = "hg19", assayind = 1, lbmaf = 1e-06, lbgtf = 1e-06,
  dropUnivHet = TRUE, infoFields = c("LDAF", "SVTYPE"))

```

Arguments

summex	a RangedSummarizedExperiment object
vcf.tf	instance of TabixFile , referring to a tabix-indexed, bgzipped VCF file
rhs	formula ‘right hand side’ for adjustments to be made as snp.rhs.tests is run on each expression vector
nperm	number of permutations to be used for plug-in FDR computation
cisradius	distance in bp around each gene body to be searched for SNP association
genome	tag suitable for use in GenomeInfoDb structures
assayind	index of assays(summex) to use for expression data retrieval
lbmaf	lower bound on MAF of SNP to retain for analysis, computed using col.summary
lbgtf	lower bound on genotype frequency of SNP to retain for analysis
dropUnivHet	logical, if TRUE, will check for columns of SnpMatrix instance that possess no values other than "NA" and "A/B". See http://www.biostars.org/p/117155/#117270
infoFields	character – VCF fields to retain in vcfInfo() part of query
simpleSNV	logical – will use simple computation of isSNV to filter variants for analysis to SNV
variantRange	GRanges instance that defines the scope of the VCF to be used for testing against all features on summex

Details

`snp.rhs.tests` is the workhorse for statistical modeling. VCF content is transformed to the byte-code (which allows for uncertain imputation) and used in fast testing.

`distToGene` is a helper function that should be replaced with something from the Bioconductor annotation subsystem

Value

`cisAssoc`: a `GRanges-class` instance with `mcols` including `chisq`, `permScore`...

`cisCount`: enumerate locations in VCF that would be tested

Note

`seqlevelsStyle` for `summex` and `vcf.tf` content must agree

Author(s)

VJ Carey <stvjd@channing.harvard.edu>

Examples

```
require(GenomeInfoDb)
require(geuvPack)
require(Rsamtools)
#
# obtain geuvadis expression measures as FPKM
#
data(geuFPKM)
#
# confine the chromosome 20
#
lgeu = geuFPKM[ which(seqnames(geuFPKM)=="chr20"), ]
seqlevelsStyle(lgeu) = "NCBI"
#
# acquire subset of genotypes on chr20
#
tf20 = TabixFile(system.file("vcf/c20exch.vcf.gz", package="gQTLstats"))
if (require(VariantAnnotation)) scanVcfHeader(tf20)
#
# perform a general technical confounder correction, and confine
# attention to CEU samples
#
lgeue = clipPCs(lgeu[,which(lgeu$popcode=="CEU")], 1:2)
#
# obtain all score test statistics for SNP:gene pairs at radius 50k
#
set.seed(1234)
litc = cisAssoc(lgeue[c(162,201),], tf20, nperm=2, lbmaf=.05, cisradius=50000)
#
# obtain all estimates for SNP:gene pairs at radius 50k
#
set.seed(1234)
lite = cisEsts(lgeue[c(162,201),], tf20, nperm=2, lbmaf=.05, cisradius=50000)
summary(litc$chisq)
mysr = range(litc)
```

```

#
# compute the plug-in FDR
#
litc$pfdr = gQTLstats:::pfdr(litc$chisq, c(litc$permScore_1, litc$permScore_2))
litc[which(litc$pfdr < .01)]
#
# trans association testing. leave to the user the question of
# whether a test is actually cis
#
lita = AllAssoc(geuFPKM[1:10,], tf20, mysr)
lita3 = AllAssoc(geuFPKM[11:20,], tf20, mysr)
#lita5 = AllAssoc(geuFPKM[21:30,], tf20, mysr)
#
# This retains the top 5 (default) associations per SNP
#
n1 = gQTLstats:::collapseToBuf(lita, lita3)
#n1 = collapseToBuf(n1, lita5)

```

clipPCs

transformations of expression data in smlSet instances

Description

transformations of expression data in smlSet instances or assay data in RangedSummarizedExperiment

Usage

```

clipPCs(x, inds2drop, center = TRUE)

regressOut(x, rhs, ...)

```

Arguments

x	a RangedSummarizedExperiment object
inds2drop	Vector of PCs to be eliminated by setting the associated diagonal elements in the SVD to zero before recomposing the matrix of expression values. If the value 0 is present in inds2drop, the smlSet is returned unchanged, with a message.
center	logical, passed to prcomp
rhs	formula fragment (no dependent variable) used to form residuals in a reexpression of the expression matrix; variable bindings found in pData of an ExpressionSet or colData of a RangedSummarizedExperiment
...	arguments passed to lmFit

Details

clipPCs is an operation on the $n \times p$ transposed matrix X of expression data. The singular value decomposition $X = UDV^t$ is formed, the diagonal elements of D corresponding to inds2drop are set to zero yielding the diagonal matrix E , and then $Y = UEV^t$ is computed and transposed to replace the expression data.

regressOut obtains residuals after genewise regression of expression on the design matrix specified by the rhs; [lmFit](#) is used to compute coefficients, linear predictions and residuals.

Value

a [RangedSummarizedExperiment](#) object

Author(s)

VJ Carey <stvjc@channing.harvard.edu>

References

The use of PCA-based adjustments to remove mass extraneous effects from expression matrices has been criticized in work of Oliver Stegle and Jeffrey Leek, who offer Bayesian PEER and SVA respectively as alternative solutions.

Examples

```
if(require(geuvPack)){
  data(geuFPKM)
  cg = clipPCs(geuFPKM, 1:10)
  ro = regressOut(cg, ~popcode)
  ro
}
```

directPlot	<i>visualize relationship between empirical and modeled FDR based on analysis of a gQTL store</i>
------------	---

Description

visualize relationship between empirical and modeled FDR based on analysis of a gQTL store

Usage

```
directPlot(FDRsupp)
```

Arguments

FDRsupp instance of [FDRsupp-class](#)

Details

This plot is used to show the degree of fit between a smooth model relating modeled FDR to empirical FDR, and the empirical FDR themselves. It should be used in conjunction with [txsPlot](#).

It is possible for an implausible squiggly model to yield perfect agreement for all empirical FDR estimates. See the example.

Examples

```
data(filtFDR)
directPlot(filtFDR)
```

enumerateByFDR *filter a ciseStore instance using an FDR threshold*

Description

filter a ciseStore instance using an FDR threshold

Usage

```
enumerateByFDR(store, fdrsupp, threshold = 0.05, filter=force,
               ids=NULL, trimToUnit=TRUE)
```

Arguments

store	instance of ciseStore-class
fdrsupp	instance of FDRsupp-class
threshold	upper bound on FDR to be included
filter	The FDR can be computed for any association score. To return only records satisfying a given filter, supply the filter function here. It may be desirable to carry a filter function from the storeToFDR stage, and this may be considered in future versions.
ids	if NULL, process all results in store, otherwise limit attention to jobs with id values in ids
trimToUnit	plug-in FDR estimates can sometimes lie outside [0,1] owing to sparsity or defects of extrapolation; if this parameter is TRUE, estimated FDR values outside [0,1] are moved to the nearest boundary

Details

uses [storeApply](#), which will use BiocParallel infrastructure when available

Value

A GRanges instance with store contents to which estFDR is appended for each range. The estFDR quantity is predicted using the GAM model held in the FDRsupp instance.

Examples

```
## Not run:
require(geuvStore2)
require(gQTLBase)
st = makeGeuvStore2()
data(filtFDR)
filtEnum = enumerateByFDR( st, filtFDR,
  filter=function(x)x[which(x$mindist <= 500000 & x$MAF >= 0.05)] )
names(metadata(filtEnum))
filtEnum[order(filtEnum$chisq, decreasing=TRUE)[1:2]]

## End(Not run) # not really essential
```

eqBox2	<i>visualization of expression or other assay measure against genotypes extracted from VCF</i>
--------	--

Description

visualization of expression or other assay measure against genotypes extracted from VCF

Usage

```
eqBox2(gene, se, tf, snpgr, genome = "hg19", forceRs=TRUE, ...)
eqDesc2(gene, se, tf, snpgr, genome = "hg19", forceRs=TRUE)
eqBox3(gene, se, tf, snpgr, geneAnno, genome = "hg19", forceRs = TRUE,
      ...)
```

Arguments

gene	an element of rownames(se) from which a vector of assay values will be created
se	a RangedSummarizedExperiment object
tf	instance of class TabixFile-class , defining paths to a tabix-indexed VCF and index file
snpgr	instance of GRanges-class identifying the SNP to be visualized
genome	tag identifying reference genome
forceRs	In the 1000 genomes VCF, there are sometimes variants identified with DELLY that are grabbed by readVcf on an SNV address. Set forceRs to TRUE to retain only variants with 'rs' in the name. Has no effect if readVcf extracts only a single variant.
geneAnno	named vector, geneAnno[<i>gene</i>] will be used to annotate display
...	extra arguments passed to beeswarm

Details

In 1.5.4, altered to supply beeswarm data visualization in addition to boxplot. Use additional option `corral="gutter"` to reduce horizontal sprawl in large samples.

Examples

```
require(Rsamtools)
require(SummarizedExperiment)
mygr = GRanges("1", IRanges(54683925, width=1))
gene = "ENSG00000231581.1"
library(geuvPack)
data(geuFPKM)
#tf = gtpath(1)
tf = TabixFile(system.file("vcf/small_1.vcf.gz", package="gQTLstats"))
eqBox2(gene, se=geuFPKM, tf, mygr )
eqDesc2(gene, se=geuFPKM, tf, mygr )
```

FDRsupp-class	Class "FDRsupp"
---------------	-----------------

Description

Support for FDR computations with ciseStore instances

Objects from the Class

Objects can be created by calls of the form `new("FDRsupp", ...)`.

Slots

tab: Object of class "data.frame" a table with association scores and plug-in FDR estimates evaluated on selected score values

FDRfunc: Object of class "function" a function of one argument with input association score and output the corresponding FDR estimate

FDRmodel: Object of class "gam" that was fit to elements of tab

filterUsed: Object of class "function" a copy of the function used for filtering the store to create the FDRfunc element.

sessinfo: sessionInfo() value at time of construction

theCall: instance of class "call" showing call leading to construction

Methods

getFDRfunc signature(x = "FDRsupp"): extract the FDR approximating function, a function of one (vector) argument assumed to represent association scores, evaluating to the plug-in FDR estimates corresponding to these scores

getTab signature(x = "FDRsupp"): extract the table of association scores and empirical FDR estimates

Note

Typically the FDRfunc function is constructed using a smooth model relating the estimated FDR to association scores.

Examples

```
showClass("FDRsupp")
```

filtFDR	<i>illustration of FDRsupp class</i>
---------	--------------------------------------

Description

illustration of FDRsupp class

Usage

```
data("filtFDR")
```

Format

A FDRsupp object.

Details

filtFDR was constructed on geuvStore contents, filtering to MAF at least five percent and radius at most 500kbp. rawFDR uses the entire geuvStore contents, with 1Mbp radius and 1 percent MAF lower bound

Examples

```
data(filtFDR)
filtFDR
```

gQTLs	<i>use SummarizedExperiment to manage a collection of gQTL results of interest</i>
-------	--

Description

use SummarizedExperiment to manage a collection of gQTL results of interest

Usage

```
gQTLs(filtgr, se, tf, genome = "hg19", forceRs = TRUE, chunksize = 50)
gQTLswarm(se, ind, covar = NULL, inpch = 19, xlab, ylab, featTag="probeid", ...)
```

Arguments

filtgr	a GRanges instance typically obtained by filtering a ciseStore instance
se	SummarizedExperiment with individual level expression and sample-level data from which filtgr statistics were derived; for gQTLswarm, output of gQTLs
tf	TabixFile for VCF on which filtgr statistics are based
genome	tag for readVcf
forceRs	if TRUE insist that snp ids include 'rs'
chunksize	VCF processing proceeds via foreach in chunks of size chunksize

ind	index into rows of se to be used for visualization, must be length 1
covar	a character string indicating a variable in colData(se) to be used to color the points
inpch	pch setting for dots in swarm
xlab	xlabel for beeswarm plot, defaults to snp id as recovered from rowRanges(se)\$snp
ylab	ylabel for beeswarm plot, defaults to probe id as recovered from rowRanges(se)\$probeid
featTag	element of mcols(rowRanges(se)) used to find ylab text, defaults to 'probeid', 'symbol' is often preferred
...	passed to <code>beeswarm</code>

Value

a SummarizedExperiment instance with two assays, the first is genotype the second is expression

Note

very preliminary

Examples

```
require(Rsamtools)
tf = TabixFile(system.file("vcf/litv.vcf.gz", package="gQTLstats"))
data(sigInlit) # 33 loci with significant cis eQTL on a specific filtering
library(geuvPack)
data(geuFPKM)
require(doParallel)
registerDoSEQ()
gdem = gQTLs(sigInlit, geuFPKM, tf, genome = "hg19")
gQTLswarm(gdem, 1, "popcode")
```

hmm878

labeled GRanges with ChromHMM chromatin states for GM12878

Description

labeled GRanges with ChromHMM chromatin states for GM12878

Usage

```
data(hmm878)
```

Format

The format is:

```
Formal class 'GRanges' [package "GenomicRanges"] with 6 slots
..@ seqnames :Formal class 'Rle' [package "IRanges"] with 4 slots
.. ..@ values : Factor w/ 23 levels "chr1","chr2",...: 1 2 3 4 5 6 7 8 9 10 ...
.. ..@ lengths : int [1:23] 54467 46499 37617 25155 30071 34846 29420 24506 24123 27263 ...
.. ..@ elementMetadata: NULL
.. ..@ metadata : list()
..@ ranges :Formal class 'IRanges' [package "IRanges"] with 6 slots
```

```

.. ..@ start : int [1:571339] 10001 10601 11138 11738 11938 12138 14538 20338 22138 22938
...
.. ..@ width : int [1:571339] 600 537 600 200 200 2400 5800 1800 800 4000 ...
.. ..@ NAMES : NULL
.. ..@ elementType : chr "integer"
.. ..@ elementMetadata: NULL
.. ..@ metadata : list()
..@ strand :Formal class 'Rle' [package "IRanges"] with 4 slots
.. ..@ values : Factor w/ 3 levels "+","-","*": 3
.. ..@ lengths : int 571339
.. ..@ elementMetadata: NULL
.. ..@ metadata : list()
..@ elementMetadata:Formal class 'DataFrame' [package "IRanges"] with 6 slots
.. ..@ rownames : NULL
.. ..@ nrows : int 571339
.. ..@ listData :List of 4
.. .. ..$ name : chr [1:571339] "15_Repetitive/CNV" "13_Heterochrom/lo" "8_Insulator" "11_Weak_Txn"
...
.. .. ..$ score : num [1:571339] 0 0 0 0 0 0 0 0 0 0 ...
.. .. ..$ itemRgb : chr [1:571339] "#F5F5F5" "#F5F5F5" "#0ABEFE" "#99FF66" ...
.. .. ..$ thick :Formal class 'IRanges' [package "IRanges"] with 6 slots
.. .. .. ..@ start : int [1:571339] 10001 10601 11138 11738 11938 12138 14538 20338 22138
22938 ...
.. .. .. ..@ width : int [1:571339] 600 537 600 200 200 2400 5800 1800 800 4000 ...
.. .. .. ..@ NAMES : NULL
.. .. .. ..@ elementType : chr "integer"
.. .. .. ..@ elementMetadata: NULL
.. .. .. ..@ metadata : list()
.. .. ..@ elementType : chr "ANY"
.. .. ..@ elementMetadata: NULL
.. .. ..@ metadata : list()
..@ seqinfo :Formal class 'Seqinfo' [package "GenomicRanges"] with 4 slots
.. ..@ seqnames : chr [1:23] "chr1" "chr2" "chr3" "chr4" ...
.. ..@ seqlengths : int [1:23] 249250621 243199373 198022430 191154276 180915260 171115067
159138663 146364022 141213431 135534747 ...
.. ..@ is_circular : logi [1:23] FALSE FALSE FALSE FALSE FALSE FALSE ...
.. ..@ genome : chr [1:23] "hg19" "hg19" "hg19" "hg19" ...
..@ metadata :List of 1
.. ..$ url : chr "http://genome.ucsc.edu/cgi-bin/hgFileUi?g=wgEncodeBroadHmm&db=hg19"

```

Details

acquired using `rtracklayer` import from the bed file given at `metadata(hmm878)[["url"]]`

Source

see details

References

Ernst J, Kellis M. Discovery and characterization of chromatin states for systematic annotation of the human genome. *Nat Biotechnol.* 2010 Aug;28(8):817-25.

Ernst J, Kheradpour P, Mikkelsen TS, Shores N, Ward LD, Epstein CB, Zhang X, Wang L, Issner R, Coyne M et al. Mapping and analysis of chromatin state dynamics in nine human cell types. *Nature*. 2011 May 5;473(7345):43-9.

Examples

```
data(hmm878)
table(hmm878$name)
```

manhWngr

manhattan plot with named GRanges

Description

manhattan plot with named GRanges

Usage

```
manhWngr(store, probeid = "ENSG00000183814.10", sym = "LIN9", fdrsupp, namedGR, slstyle = "NCBI", ...)
```

Arguments

store	instance of ciseStore-class
probeid	name of feature identifier to use for cis association
sym	symbol for feature identifier
fdrsupp	instance of FDRsupp-class
namedGR	GRanges instance with 'name' in mcols element
slstyle	seqlevelsStyle
xlab.in	x axis label
ylab.in	y axis label
applyFDRfilter	if TRUE, use the filter defined in the filterUsed element of the object supplied as fdrsupp on the output
...	additional arguments for plotting

Examples

```
require(geuvStore2)
require(gQTLBase)
store = makeGeuvStore2()
data(hmm878)
data(filtFDR)
manhWngr(store, fdrsupp=filtFDR, namedGR=hmm878)
```

mixedVCFtoSnpMatrix	<i>amalgamate called genotypes and imputed allelic dosages in VCF to SnpMatrix representation</i>
---------------------	---

Description

amalgamate called genotypes and imputed allelic dosages in VCF to SnpMatrix representation

Usage

```
mixedVCFtoSnpMatrix(vcf, preferGT = TRUE)
```

Arguments

vcf	object inheriting from CollapsedVCF-class
preferGT	logical. VCF allows loci for samples to be reported in various formats, and a given locus can have a call tagged GT and a genotype probability or likelihood representation tagged GP or GL. genotypeToSnpMatrix has an uncertain parameter that, if TRUE, will transform GP or GL content to allelic dose. Note that only the "first" dosage type appearing in the header will be transformed. Thus if GP is first in the header but a given locus is tagged only with GL, the genotype for this locus will be recorded as NA.

Details

emulates output from [genotypeToSnpMatrix](#)

Value

list with elements genotypes and map

Author(s)

VJ Carey

See Also

[genotypeToSnpMatrix](#)

Examples

```
fn = system.file("vcf/polytypeSNV.vcf", package="gQTLstats")
require("VariantAnnotation")
require("snpStats")
vv = readVcf(fn, genome="hg19") # only 4th SNP will have dosage coding
mixedVCFtoSnpMatrix(vv)$genotypes@.Data
```

pifdr *utility for computing plug-in FDR*

Description

utility for computing plug-in FDR

Usage

```
pifdr( obs, perms, trimToUnit = TRUE, ... )
pifdr2( obs, perms, trimToUnit = TRUE, expandPerms=TRUE, ... )
```

Arguments

obs	observed association scores
perms	vector of association scores under permutation; length should be integer multiple of length(obs)
trimToUnit	logical, if TRUE, values greater than 1 are replaced by 1. Such values can occur, for example, with relatively small sample sizes.
expandPerms	With certain pair-specific filtering operations, the number of scores obtained after permutation may not be a multiple of the number of observed scores. If TRUE, the scores obtained under permutation are sampled with replacement to simplify computation of plug-in FDR.
...	extra arguments ignored

Details

Revised 12/30/13 to employ hist() to rapidly bin the permuted values.

Value

vector of plug-in FDR estimates congruent to obs

References

Hastie Tibshirani and Friedman Elements of Statistical Learning ch 18.7

Examples

```
set.seed(1234)
op = par(no.readonly=TRUE)
par(mfrow=c(2,2))
X = c(rchisq(30000,1),rchisq(300,10))
Y = rchisq(30300*3,1)
qqplot(Y, X, xlab="null", ylab="observed")
hist(pp <- pifdr(X,Y), xlab="plug-in FDR", main=" ")
library(multtest)
rawp = 1-pchisq(X, 1)
MT <- mt.rawp2adjp(rawp)
MT2 = MT[[1]][order(MT[[2]]),]
plot(MT2[, "BH"], pp, xlab="BH FDR", ylab="plug-in FDR")
par(op)
```

qqStore	<i>create a binned QQplot for a sharded store</i>
---------	---

Description

create a binned QQplot for a sharded store with association and permutation statistics

Usage

```
qqStore(st, ids = NULL,
        .probs = c(0, seq(0.6, 0.8, 0.2), 0.9, 0.95, 0.99, 0.999, 0.9999, 1),
        xlim.in = c(0.2, 75), lowfac = 0.5, xlab = "Permutation distribution",
        ylab = "Distribution of score statistic", countpos = 50,
        plot.it = TRUE, doab = TRUE, scoreField = "chisq",
        permField = "permScore_1", ...)
```

Arguments

st	instance of ciseStore-class
ids	optional job id vector; if NULL, all jobs used
.probs	vector of probabilities for use with quantile evaluation, as provided in ffbase , using storeToQuantiles
xlim.in	xlim setting for QQplot
lowfac	we use a log-log plot, and the first quantile (as prescribed in .probs) is often close to zero; we reassign it to lowfac*(second quantile)
xlab	label
ylab	label
countpos	where on the x axis will we stack the information on bin counts
plot.it	logical, if FALSE, a list is returned with elements on quantile values and bin counts
doab	logical prescribing drawing of line of identity
scoreField	tag in store naming the statistic, typically 'chisq', can also be 'tstat' for GTEEx
permField	tag in store naming the field holding statistics on realizations from permutation distribution
...	passed to storeToQuantiles

Value

invisibly returns list with elements qx, qy, counts, fracs

Examples

```
## Not run:
library(geuvStore2)
library(gQTLBase)
gs = makeGeuvStore2()
qqStore(gs) #, ids=partialIds()[1:20])

## End(Not run)
```

queryVCF	<i>obtain SnpMatrix from VCF genotypes</i>
----------	--

Description

obtain SnpMatrix from VCF genotypes

Usage

```
queryVCF(gr, vcf.tf, samps, genome = "hg19", getSM = TRUE,
          snvOnly=TRUE)
```

Arguments

gr	GRanges instance; SNPs lying within will be processed
vcf.tf	TabixFile instance pointing to VCF
samps	samples to be retained
genome	tag identifying build
getSM	logical; if FALSE, genotypeToSnpMatrix will not be run and only the output of readVcf is returned.
snvOnly	logical, if TRUE, will confine results to SNV

Value

a list of length two

readout	output of readVcf
sm	output of genotypeToSnpMatrix run on the read result

Examples

```
require(Rsamtools)
tf20 = TabixFile(system.file("vcf/c20exch.vcf.gz", package="gQTLstats"))
require(geuvPack)
data(geuFPKM)
lgeu = geuFPKM[ which(seqnames(geuFPKM)=="chr20"),
               which(geuFPKM$popcode=="CEU") ]
seqlevelsStyle(lgeu) = "NCBI"
rng = rowRanges(lgeu)[232] # CPNE1
myq = queryVCF( rng, tf20, samps=colnames(lgeu), genome="hg19" )
myq
```

senstab	<i>create a plottable table for eQTL sensitivity analysis visualization</i>
---------	---

Description

create a plottable table for eQTL sensitivity analysis visualization

Usage

```
senstab(x, filt = force)
## S3 method for class 'senstab'
plot(x, ...)
```

Arguments

x	a list generated by a process analogous to the sensitivity survey exhibited in the example below
filt	a function that operates on and returns a data.frame; typically will select rows based on values of fields 'MAF' and 'radius'
...	extra arguments passed to plot

Details

sensByProbe is a list structure; for information on this and other elements of sensitivity analysis workflow, see extensive non-executed code in example below

Value

an instance of the S3 class 'senstab', 'data.frame'

Examples

```
## Not run:
#
# illustration of sensitivity analysis using BatchJobs
#
# assume the following content in 'parms.R' (uncommented)
# MAFS = c(.03, .04, .05, .075, .10, .125, .15)
# dists = c(5000, 7500, 10000, 15000, 20000,
#           25000, 50000, 100000, 250000, 500000, 750000, 1000000)
# parms = expand.grid(MAFS, dists)
library(BatchJobs) # for bigStore manip
library(gQTLstats)

# could use multilevel parallelism here
# because it is a somewhat large, fragile job, BatchJobs
# is a relevant tool for iteration. but storeToFDRByProbe is
# already using bplapply. so register 3 cores for it
# and specify 15 cpu for BatchJobs in .BatchJobs.R

sens1 = makeRegistry("sens1", file.dir="sens1",
  packages=c("gQTLstats", "dplyr"),
  src.files="parms.R") # note parms.R
```

```

sens4One = function(z) {
  load("../bigStore.rda") # get a ciseStore instance
  ans = storeToFDRByProbe(bigStore, xprobs=seq(.01,.99,.01), # xprobs
                          # needs to be chosen with care
  filter=function(x) x[which(x$MAF >= parms[z,1] &
                             x$mindist <= parms[z,2])])
  ans = setFDRfunc(ans, span=.35) # span can be important
  list(fdrsups=ans, parms=parms[z,])
}

batchMap(sens1, sens4One, 1:nrow(parms))
submitJobs(sens1)

# now loadResult(sens1) or the equivalent can be the input to sensstab()
# as in the example to continue here:

## End(Not run)
library(gQTLstats)
data(sensByProbe)
ptab = t(sapply(sensByProbe, function(x)as.numeric(x[[2]])))
unique(ptab[,1]) # MAFs used
unique(ptab[,2]) # radii used
# here we filter away some extreme values of the design space
tab = sensstab(sensByProbe, filt=function(x) {
  x[ x$radius > 10000 & x$ radius < 500000 & x$MAF > .03, ]
} )
plot(tab)

```

setFDRfunc	<i>estimate and store function relating association scores to approximate plug-in FDR</i>
------------	---

Description

estimate and store function relating association scores to approximate plug-in FDR

Usage

```
setFDRfunc(FDRsupp, fudge = 1e-06, zthresh = 30, maxch = 30, ...)
```

Arguments

FDRsupp	instance of FDRsupp-class
fudge	if FDR is zero, a log or logistic transform will fail; we add the small positive number fudge to avoid this
zthresh	for association scores greater than this value, a hard value of FDR 0 is assigned
maxch	the model for the functional relationship between association and FDR is subset to observations for which association chisq score is no greater than 1.1*maxch
...	arguments passed to s for the smooth model relating association score to FDR at selected quantiles of the association score distribution

Value

returns an updated [FDRsupp-class](#) instance

Examples

```
data(filtFDR)
filtFDR2 = setFDRfunc(filtFDR)
```

storeToStats	<i>extract a vector from store results as ff (out of memory reference); support statistical reductions</i>
--------------	--

Description

extract a vector from store results as ff (out of memory reference); support statistical reductions

Usage

```
storeToQuantiles(store, field,
  probs=c(seq(0,.999,.001), 1-(c(1e-4,1e-5,1e-6,1e-7))),
  ids = NULL, ..., checkField = FALSE, filter=force)
storeToHist(store, getter = function(x)
  as.numeric(S4Vectors::as.matrix(mcols(x)[,
  grep("permScore", names(mcols(x)))])), breaks, ids =
  NULL, filter = force)
storeToFDR(store, xprobs = c(seq(0, 0.999, 0.001), 1 - (c(1e-04,
  1e-05, 1e-06, 1e-07))), xfield = "chisq", getter =
  function(x) as.numeric(S4Vectors::as.matrix(mcols(x)[,
  grep("permScore", names(mcols(x)))])), filter = force,
  .id4coln=1, ids=NULL)
```

Arguments

store	instance of ciseStore-class
field	character tag, length one, must be name of a numeric field in the result set (typically something like 'chisq' in the GRanges generated by cisAssoc)
xfield	as field, for FDR computation, see Details.
ids	job ids to be used; if NULL, process all jobs
breaks	boundaries of histogram bins
...	supplied to makeRegistry for a temporary registry: typically will be a vector of package names if additional packages are needed to process results
checkField	if TRUE steps will be taken to verify that the tag to which 'field' evaluates is present in result in the first job
probs	numeric vector of probabilities with values in [0,1]. See quantile.ff .
xprobs	percentiles of the empirical distribution of the association statistic at which FDR estimates are recorded.
getter	function of a single argument that extracts a numeric vector of association scores obtained under permutation

x	instance of FDRsupp
filter	function accepting and returning GRanges instance, executed when cisAssoc result is loaded to modify that result, defaults to no-op
.id4coln	job id to be used for initial probe to determine names of fields in mcols of all jobs

Details

uses current BatchJobs configuration to parallelize extraction; reduceResults could be used for a sequential solution

Value

storeToQuantiles and storeToHist return objects analogous to those returned by stats::quantile and graphics::hist.

However, it should be noted that storeToQuantiles will use the `quantile.ff` of `ffbase`. For vectors of modest length, this can disagree with results of `base::quantile` by a few percent.

storeToFDR and storeToFDRByProbe return an instance of FDRsupp class

Note

uses `ffbase::c.ff` explicitly to concatenate outputs; there is no guarantee of order among elements

Examples

```
## Not run:
stopifnot(require(geuvStore2))
require(BatchJobs)
require(gQTLBase)
store = makeGeuvStore2()
library(doParallel)
if (.Platform$OS.type == "windows") {
  registerDoSEQ()
} else registerDoParallel(cores=max(c(detectCores()-1,1)))
smchisq = storeToFF( store, "chisq", ids=store@validJobs[1:3])
smchisq
if (.Platform$OS.type != "windows") { # avoid timeout
  qs = storeToQuantiles( store, "chisq", ids = store@validJobs[1:5],
    probs=seq(.1,.9,.1) )
  qs
  hh = storeToHist( store, ids = store@validJobs[1:5], breaks=
    c(0,qs,1e9) )
  hh$counts
  fd = storeToFDR( store, xprobs=c(seq(.05,.95,.05),.99,.999) )
  tail(getTab(fd),4)
  sss = storeToFDRByProbe( store , xprobs=c(seq(.05,.95,.05),.99) )
  tail(getTab(sss),4)
}

## End(Not run)
```

tqbrowser	<i>general browsing facility for trans-gQTL</i>
-----------	---

Description

Provide a general browsing facility for trans-gQTL.

Usage

```
tqbrowser(mae, felname, gelname, tiling, tsbra,
  annovec, band.init = "6q12", ermaset, gwascats, ...)
```

Arguments

mae	Instance of MultiAssayExperiment-class
felname	character naming the element of mae holding assay features
gelname	character naming the element of mae holding a VcfStack-class instance for genotypes
tiling	a tiling of the genome used to partition large genotype resource
tsbra	an instance of the output of tsByRankAccum that collects association statistics and metadata on general searches for genotype-feature association
annovec	a named character vector mapping between identifiers used to identify features in <code>experiments(mae)[[felname]]</code> and tokens to be used in display – the names of annovec are the rownames to be translated to the associated value in the display.
band.init	an initial tile selection
ermaset	instance of ErmaSet-class
gwascats	instance of gwaswloc-class
...	not currently used

Details

starts a shiny app

Author(s)

VJ Carey <stvjc@channing.harvard.edu>

Examples

```
if (interactive()) {
  oa = options()$example.ask
  options(example.ask=FALSE)
  #
  # this example assumes you have a working internet connection
  # it will collect genotype information from a S3 bucket
  # where 1000 genomes VCF resides
  #
  # obtain infrastructure
  #
```

```

# message("note: as of Dec 17 2016 this function will trigger transient errors... ignore them") # solved with
message("loading packages...")
packs = c("VariantAnnotation", "GenomicFiles", "ggvis", "plotly",
  "Rsamtools", "GenomeInfoDb", "geuvPack", "shiny", "ggplot2",
  "MultiAssayExperiment", "AnnotationHub", "ldblock", "erma")
suppressPackageStartupMessages({
r = sapply(packs, require, character.only=TRUE)
})
stopifnot(all(r))

# use S3 bucket to get genotypes, create VcfStack wrapper
#
message("create VcfStack...")
tf17 = ldblock::s3_1kg("17")
vcst = VcfStack(c("17"=path(tf17)))
seqlevelsStyle(vcst) = "NCBI"

# obtain expression data for GEUVADIS samples
#
message("obtain expression data...")
if (!exists("geuFPKM")) data(geuFPKM)
data(gen2sym)
seqlevelsStyle(geuFPKM) = "NCBI"
#
# bind to MAE
#
e1 = ExperimentList(list(geu=geuFPKM, vcst=vcst))
message("create MultiAssayExperiment...")
suppressWarnings({ # samples don't line up between expression and genotype, we know this
mae = MultiAssayExperiment(e1, pData=colData(e1[[1]]))
})
#
# obtain and clean up cytoband representation
# cyto37n created as follows:
#ah = AnnotationHub()
#cyto37 = ah[["AH5012"]]
#seqlevelsStyle(cyto37) = "NCBI"
#cyto37 = as(cyto37, "GRanges")
#sn = as.character(seqnames(cyto37))
#mcols(cyto37)$name = paste0(sn, mcols(cyto37)$name)
#names(cyto37) = mcols(cyto37)$name
#seqlengths(cyto37)["MT"] = 16569
message("obtain cytoband index...")
data(cyto37n)
data(tbgaOrmdl3) # saved output of tsByRankAccum, giving association scores
#
message("obtain gwas catalog...")
library(gwascat)
data(ebicat37)
# obtain chromatin state calls from erma
message("obtain chromatin state calls...")
erset = makeErmaSet()
#
# target and invoke browser
#
okba = c("17q12", "17q21.1", "17q21.2")
on.exit(options(example.ask=oa))

```

```
print(tqbrowser( mae, "geu", "vcf", cyto37n[okba],
  tbga0rmdl3, gen2sym, band.init="17q12", ermaset=erset, gwascat=ebicat37 ))
} # end interactivity check
```

transAssoc	<i>compute 'trans' SNP-feature associations by wrapping AllAssoc</i>
------------	--

Description

compute 'trans' SNP-feature associations by wrapping AllAssoc, retaining only the strongest associations (and similarly filtered association scores computed under permutation)

Usage

```
transAssoc(variantGR, exSE, vcfgen, bufsize = 10, nperm = 3, exChLen = 2 * bufsize, ...)
```

Arguments

variantGR	GRanges instance establishing scope of variants to test
exSE	SummarizedExperiment instance, all of whose features will be tested for association with all SNP
vcfgen	a function returning a path to a tabix-indexed VCF file from which SNP genotypes will be extracted
bufsize	Size of 'buffer' used to retain largest feature association scores encountered during the search. The scores and the names of associated genes are retained in 'scorebuf' and 'elnames' components of output GRanges
nperm	number of permutations of features against genotypes to be performed for realizing null distribution of association scores
exChLen	size of chunks of exSE to be tested through calls to AllAssoc; this is intended to allow control of RAM usage
...	arguments passed to AllAssoc

Value

a GRanges with mcols including

Examples

```
## Not run: # requires access to 1KG S3
library(geuvPack)
data(geuFPKM)
seqlevelsStyle(geuFPKM) = "NCBI"
mysr = GRanges("20", IRanges(33000055, 33020055))
genome(mysr) = "hg19"
tt = transAssoc(mysr, geuFPKM[1:16,],
  bufsize=3, exChLen=4, vcfgen=function(x)gtpath(paste0("chr", x)) )
colnames(mcols(tt))
table(as.character(mcols(tt)$elnames))

## End(Not run)
```

transBrowse

shiny app to exhibit genotype:genomic feature distributions

Description

exhibit genotype:genomic feature distributions with a shiny app

Usage

```
transBrowse(tbg, anno, tivcf, se, title = "trans eQTL")
transBrowse2(tbga, annovec, tivcf, se, title = "trans eQTL", maxrank=3)
```

Arguments

tbg	filtered output of <code>tsByRankAccum</code> , see example
tbga	filtered output of <code>tsByRankAccum</code> , see example
anno	a vector with 'feature symbols' (e.g., gene symbols) as values and 'feature names' (elements of rownames of <code>se</code> , e.g., ENSEMBLE gene ids) as names
annovec	a vector with 'feature symbols' (e.g., gene symbols) as values and 'feature names' (elements of rownames of <code>se</code> , e.g., ENSEMBLE gene ids) as names
tivcf	reference to Tabix-indexed VCF
se	SummarizedExperiment instance with rowname coincident with <code>anno</code> and <code>tbg[["allfeats"]]</code>
title	optional string for title panel
maxrank	<code>transBrowse2</code> works with the <code>tsByRankAccum</code> function that collects scores down to a specified rank. This parameter specifies the boundary.

Details

This function is under development. The intention is to allow convenient visualization of off-chromosome genotype-feature relationships. `AllAssoc` collects association scores SNP-wise, and saves the largest "K" scores obtained, along with feature identity and location metadata. The largest score obtained for a given SNP is the rank 1 association, the next largest is rank 2, and so on.

Examples

```
## Not run:
# consider the following filtering utility
tbfilt = function(tbg, seqnames="17", minMAF=.1, minabsodist = 1e7,
  nrec=1000) {
  tbg = tbg[ which(as.character(seqnames(tbg)) %in% seqnames.) ]
  tbg = tbg[ which(tbg$MAF > minMAF & abs(tbg$obsdist) > minabsodist) ]
  tbg[ order(tbg$scores, decreasing=TRUE) ][1:nrec]
}
#
registerDoSEQ()
library(geuvStore2)
r17 = g17transRegistry()
g17 = TransStore(list(r17))
tbg = tbfilt(tsByRankAccum(g17, 3, mcol2keep=c("REF", "snp", "MAF"))) # 1000 records
tf17 = ldblock::s3_1kg("17") # uses S3 bucket
```

```

require(geuvPack)
require(shiny)
if (!exists("geuFPKM")) data(geuFPKM)
if (!exists("gencodeV12")) data(gencodeV12)
data(gen2sym)
transBrowse2( tbg, gen2sym, tf17, geuFPKM, title="trans GEUV chr17")

## End(Not run) # end dontrun

```

TransStore

Instance constructor for managing trans gQTL results

Description

Instance constructor for managing trans gQTL results

Usage

```

TransStore(regs, paths = NULL)
tsIndex.reg(tsin, ind)

```

Arguments

regs	a list of Registry instances, typically one per (variant-oriented) chromosome
paths	if desired, paths to folders for which loadRegistry succeeds, used instead of regs
tsin	a TransStore instance
ind	index of registry to index

Details

tsIndex.reg is experimental, producing a hash mapping snps to registry job identifiers, to support rapid store-level retrieval of locus-specific findings.

Value

instance of [TransStore-class](#)

Examples

```

if (require(geuvStore2) && require(doParallel)) {
  registerDoSEQ()
  r17 = g17transRegistry()
  r18 = g18transRegistry()
  g1718 = TransStore(list(r17, r18))
  g1718
}

```

TransStore-class	<i>Class "TransStore"</i>
------------------	---------------------------

Description

Manage collection of related trans-gQTL results in BatchJobs registries, typically one per chromosome

Objects from the Class

Objects can be created by calls of the form `new("TransStore", ...)`.

Slots

`allRegistries`: Object of class "list" containing [Registry](#) instances
`numSubmitted`: Object of class "numeric" records number of jobs submitted for each registry
`numDone`: Object of class "numeric" records number of jobs completed for each registry
`nloci`: Object of class "numeric" records number of loci with test results for each registry
`jobinfos`: Object of class "list" records results of [getJobInfo](#) for each registry

Methods

describe signature(object = "TransStore"): summarize information about a store

Examples

```
showClass("TransStore")
```

tsByRank	<i>harvest contents of a TransStore by rank in associations of features to SNP</i>
----------	--

Description

Harvest contents of a TransStore by rank in associations of features to SNP.

Usage

```
tsByRankAccum(tsin, maxrank = 3, mcol2keep=c("REF", "ALT", "snp", "MAF", "z.HWE"), filt=force)
```

Arguments

tsin	An instance of TransStore-class
maxrank	The maximum rank of association scores to retrieve, cumulatively. Each variant has been tested for association with each genomic feature (e.g., gene in a typical expression QTL study), but only the top ranking associations are recorded for each variant. If maxrank=k, for each variant, this function retrieves the features exhibiting the kth largest association recorded over all features, along with all k-1 larger association scores.

`mcol2keep` a character vector of metadata columns to retain

`filt` a function accepting a GRanges and returning a GRanges. The mcols of the GRanges to be processed will have elements `c(mcol2keep, "scorebuf", "elnames", "dist")`, where the latter two are matrices with number of columns equal to the bufsize of the `transAssoc` call that generated `ts`. Only SNP-specific elements can be used to define the filter.

Details

`tsByRankAccum_sing` and other functions with suffix `_sing` were developed for the case of a single permutation

`getTransRegistries()` accesses objects packaged for demonstration purposes

Value

A `GRanges` instance.

Examples

```
if (require(doParallel)) {
  registerDoSEQ()
  lit = TransStore(getTransRegistries()) # very limited slice
  tbga = tsByRankAccum(lit, maxrank=5)
  plot(ecdf(as.numeric(data.matrix(tbga$permscoresByRank1))), ylim=c(.99,1),
       main="eCDF of permutation dist. of association, by variant rank")
  exr = paste0("permscoresByRank", 2:5)
  for (i in 1:4)
    lines(ecdf(as.numeric(data.matrix(mcols(tbga)[[exr[i]]]))), col=i+1)
  legend(200, .994, lty=1, col=1:5, legend=paste("rank", 1:5))
  plot(ecdf(as.numeric(data.matrix(tbga$permscoresByRank1[,1]))), ylim=c(.99,1),
       main="between-permutation variation")
  lines(ecdf(as.numeric(data.matrix(tbga$permscoresByRank1[,2]))), col=2)
  lines(ecdf(as.numeric(data.matrix(tbga$permscoresByRank1[,3]))), col=3)
  lines(ecdf(as.numeric(data.matrix(tbga$permscoresByRank5[,1]))), col=4)
  lines(ecdf(as.numeric(data.matrix(tbga$permscoresByRank5[,2]))), col=5)
  lines(ecdf(as.numeric(data.matrix(tbga$permscoresByRank5[,3]))), col=6)
  legend(200, .994, col=1:6, lty=1, legend=c("rank 1 (perm 1)", "(2)", "(3)",
      "rank 5 (perm 1)", "(2)", "(3)"))
  # head(tbga,2)
  # consider the following filtering utility
  # tbfilt = function(tbg, seqnames.="17", minMAF=.1, minabsodist = 1e7,
  #   nrec=1000) {
  #   tbg = tbg[ which(as.character(seqnames(tbg)) %in% seqnames.) ]
  #   tbg = tbg[ which(tbg$MAF > minMAF) ]
  #   tbg[ order(tbg$scores, decreasing=TRUE) ][1:nrec]
  # }
}
```

txsPlot

visualize transformed FDR against transformed association statistics

Description

visualize transformed FDR against transformed association statistics

Usage

```
txsPlot(FDRsupp, xmax=50)
```

Arguments

FDRsupp	an instance of FDRsupp-class
xmax	upper bound on xlim for display

Examples

```
data(filtFDR)  
txsPlot(filtFDR)
```

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