

Package ‘GGtools’

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Title software and data for analyses in genetics of gene expression

Version 5.4.0

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Description software and data for analyses in genetics of gene expression and/or DNA methylation

Suggests GGdata, illuminaHumanv1.db, SNPlocs.Hsapiens.dbSNP.20120608, multtest, aod, rmeta

Depends R (>= 2.14), GGBase (>= 3.19.7), data.table, parallel

Imports methods, utils, stats, BiocGenerics, snpStats, ff, Rsamtools, AnnotationDbi, Biobase, bit, VariantAnnotation, hexbin, rtracklayer, Gviz, stats4, S4Vectors, IRanges, GenomeInfoDb, GenomicRanges, iterators, Biostrings, ROCR, biglm, ggplot2, reshape2

Enhances MatrixEQTL, Homo.sapiens, foreach, doParallel, gwascat

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License Artistic-2.0

biocViews Genetics, GeneExpression, GeneticVariability, SNP

LazyLoad yes

Collate AllClasses.R AllGenerics.R eqtlTests.R managers.R topFeats.R gwSnpTests.R snpsCisToGenes.R relocate.R topSnps.R snplocsDefault.R transutils.R vcfutils.R eqtlEstimates.R alleq.R meta.R eqME.R meta.all.R best.trans.eQTLs.R meta.transScores.R summInfra.R bindmaf.R fdr.all.cis.R pifdr.R getFDR.R cisConfig.R thinclass.R harvest.R scoredist.R binqq.R gffprocess.R cisEqTools.R modutils.R seqinfo.R pureSensSoft.R cisa.R scan.R basicappraise.R Eqappr.R

NeedsCompilation no

R topics documented:

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GGtools-package *software and data for analyses in genetics of gene expression*

Description

software and data for analyses in genetics of gene expression

Details

Package: GGtools
Version: 4.2.26
Suggests: GGdata, illuminaHumanv1.db
Depends: R (>= 2.14), GGBase (>= 3.16.1)
Imports: methods, snpStats, ff, IRanges, GenomicRanges, AnnotationDbi, Biobase, Rsamtools, bit, VariantAnnotation
License: Artistic-2.0
LazyLoad: yes
Packaged: 2012-01-18 03:39:51 UTC; stvjc
Collate: AllClasses.R AllGenerics.R eqtlTests.R managers.R topFeats.R gwSnpTests.R snpsCisToGenes.R relocate.R top
Built: R 2.15.0; ; 2012-02-06 17:22:52 UTC; unix

Index:

best.cis.eQTLs	collect genewise best scoring eQTL
eqtlTests	compute association statistics between all probes and SNP in an smlSet instance
eqtlTestsManager-class	Class "'eqtlTestsManager'"
ex	ExpressionSet instance for illustrating integrative smlSet container
getCisMap	create, using Bioconductor annotation resources, a structure that enumerates SNP in the vicinity of ('cis' to) genes
gwSnpTests	execute a series of tests for association between genotype and expression
strMultPop	serialization of a table from Stranger's multipopulation eQTL report
hg19.si.df	data frame representation of seqinfo for Homo.sapiens at hg19 build

The package depends on GGBase, which includes additional infrastructure for integrative data structures and data filtering.

Author(s)

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See Also

[getSS](#) for acquiring containers for integrative data on genetics of expression.

Examples

```
## Not run:
# acquire chromosome 20 genotypes and all expression data for
# 90 CEU samples as published at Wellcome Trust GENEVAR and
# HapMap phase II
c20 = getSS("GGtools", "20")
# perform a focused eQTL search
t1 = gwSnpTests(genesym("CPNE1")~male, c20)
# get best hits
topSnpS(t1)

## End(Not run)
```

All.cis	<i>functions that compute score tests for all SNP cis to genes, with flexible filtering</i>
---------	---

Description

function that computes score tests for all SNP cis to genes, with flexible filtering

Usage

```
cisScores( config = new("CisConfig"), ... )
All.cis( config = new("CisConfig"), ... )
addgwhit(ans, traitFilter=force, vname="isgwashit")
add878(ans)
inflammFilter(gwtagger)
```

Arguments

config	instance of class CisConfig-class
...	passed to eqtlTests
ans	cisRun-like entity to which additional annotation will be bound by addgwhit or add878
gwtagger	GRanges like gwastagger in gwascat data elements
traitFilter	function that returns a gwastagger-like GRanges, see inflammFilter
vname	name to be used for new data.table column added by addgwhit

Details

cisScores (All.cis) returns score statistics for associations of all SNP cis to genes, in a GRanges instance, with range names given by probes; metadata supplied SNP location, name, and score

cisAssoc targets SummarizedExperiment instances for molecular phenotype measures and VCF for variant data

addgwhit and add878 will use GWAS hit information or ChromHMM labeling to annotation ranges

Value

for cisScores: instance of [cisRun-class](#)

for cisAssoc: a GRanges with information on observed and permuted test scores per locus/feature pair

Author(s)

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Examples

```
## Not run:

cc = new("CisConfig")
chrnames(cc) = "21"
genome(cc) = "hg19"
lkp = try(library(parallel))
if (!inherits(lkp, "try-error")) {
  nc = min(10, detectCores())
  options(mc.cores=nc)
  geneApply(cc) = mclapply
}
estimates(cc) = FALSE
set.seed(1234)
unix.time(f1 <- cisScores( cc ))

#
# demonstrate adding annotation on chromatin state and gwas status
#
eprops = function(ans) {
#
# only adds fields to values() of the input
#
data(hmm878)
ac = as.character
eqr = GRanges(ac(seqnames(ans)), IRanges(ans$snlocs, width=1))
fo = findOverlaps(eqr, hmm878)
chromcat878 = factor(rep("none", length(ans)), levels=c(unique(hmm878$name), "none"))
chromcat878[ queryHits(fo) ] = factor(hmm878$name[subjectHits(fo)])
ans$chromcat878 = chromcat878

if (require(gwascat)) {
  data(gwastagger)
```

```

    isgwashit = 1*(overlapsAny(eqr, gwastagger) | ans$snp
    ans$isgwashit = isgwashit
  }
  ans
}
extraProps(cc) = eprops
set.seed(1234)
unix.time(f2 <- cisScores( cc ))
#
#
inflammFilter # to make more restrictive predicate for prediction

## End(Not run)

```

 appraise

appraisal for eQTL prediction models

Description

appraisal for eQTL prediction models

Usage

```

appraise(dtab,
  discretize = TRUE,
  reduceToSNP = TRUE,
  prefix,
  folder = paste0(prefix, "_APPROUT"),
  discfmlas_in = GGtools:::.discfmlas.demo,
  txlist = list(
    distcats = function(x) {
      cut(x$mindist, c(-1, seq(0, 200001, 50000)))
    },
    fdrcats = function(x) {
      fdrfac = cut(x$fdr, c(-.01, .05, .1, .25, .5, 1.01))
      relevel(fdrfac, "(0.5,1.01]")
    },
    mafcats = function(x) {
      maffac = cut(x$MAF, c(-0.01, .05, .1, .25, .51))
      relevel(maffac, "(-0.01,0.05]")
    },
    caddcats = function(x){
      cut(x$PHRED, c(-.01, 5, seq(10, 30, 10 ), 60))
    }
  ),
  cutts = c(-0.01, seq(0.015, .12, .015), .15),
  names2check= GGtools:::.standardNames, maxit=30,
  savePinfer=FALSE)
# bindgwava( gwavadt, eqdt )

```

Arguments

<code>dtab</code>	data.table instance as created by transforming <code>cisRun</code> to <code>GRanges</code> and then to <code>data.table</code> , and then adding CADD PHRED scores if available. If CADD PHRED scores are not available, the default formulas should not be used.
<code>discretize</code>	logical telling whether binning to factors defined in <code>txlist</code> should be performed
<code>reduceToSNP</code>	logical telling whether ranges should be reduced to unique SNP and FDR re-computed
<code>prefix</code>	character atom used to prefix objects saved and folder for result objects
<code>folder</code>	folder name suffix
<code>discfmlas_in</code>	named list of model formulae
<code>txlist</code>	named list of functions that are used to bin certain quantitative features of SNP
<code>cutts</code>	numeric vector of thresholds for tabulation and discrete calibration
<code>names2check</code>	if NULL, ignored; if a character vector, function will fail unless <code>all(names2check %in% names(dtab))</code>
<code>maxit</code>	numeric passed to <code>bigglm</code> as control parameter for maximum number of iterations to use in modeling gwas hit probabilities
<code>savePinfer</code>	logical specifying whether the inferred probabilities of GWAS involvement are retained

Details

The `appraise` function wraps many tasks used to appraise eQTL collections in terms of predictive capacity. Details will be provided.

Value

A folder is opened and objects are written representing the test set (`data.table` on SNPs on even chromosomes), the coefficients of predictive models built on training set (SNPs on odd chromosomes), coefficients of linear regressions of binary test outcomes for calibrating the model on test data, and ROC AUC measures.

`bindgwava` uses simple `data.table` operations with `match` to add three columns to `eqdt`, `gwava_tss`, `gwava_unmat`, and `gwava_regi`

Author(s)

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b1 *mcwBestCis instances, integrative analysis output containers generated by GGtools vignette*

Description

integrative analysis output containers generated by GGtools vignette

Usage

data(b1)

Format

The format is:

Formal class 'mcwBestCis' [package "GGtools"] with 9 slots
 ..@ scoregr :Formal class 'GRanges' [package "GenomicRanges"] with 6 slots
@ seqnames :Formal class 'Rle' [package "IRanges"] with 4 slots
@ values : Factor w/ 1 level "20": 1
@ lengths : int 50
@ elementMetadata: NULL
@ metadata : list()
@ ranges :Formal class 'IRanges' [package "IRanges"] with 6 slots
@ start : int [1:50] 24280834 61665697 352356 61679079 45286150 55187941 38766161
 10871477 56570242 13304639 ...
@ width : int [1:50] 2090785 2005619 2021461 2001901 2129211 2007692 2038197
 2035767 2012068 2013675 ...
@ NAMES : chr [1:50] "GI_34147330-S" "hmm26961-S" "GI_17149835-I" "GI_31077201-S"
 S" ...
@ elementType : chr "integer"
@ elementMetadata: NULL
@ metadata : list()
@ strand :Formal class 'Rle' [package "IRanges"] with 4 slots
@ values : Factor w/ 3 levels "+","-","*": 3
@ lengths : int 50
@ elementMetadata: NULL
@ metadata : list()
@ elementMetadata:Formal class 'DataFrame' [package "IRanges"] with 6 slots
@ rownames : NULL
@ nrows : int 50
@ listData :List of 6
\$ score : num [1:50] 36.5 16.8 16.7 14.8 9.8 ...
\$ snpid : chr [1:50] "rs6037097" "rs3810504" "rs13043344" "rs13044229" ...
\$ snploc : int [1:50] 25347221 62678549 544417 61738288 46369894 56551001
 38879237 12177765 57565943 15056960 ...
\$ radiusUsed: num [1:50] 1e+06 1e+06 1e+06 1e+06 1e+06 1e+06 1e+06 1e+06 1e+06
 1e+06 ...


```

.. .. .. ..$ nsnp : int [1:50] 1387 783 2382 766 2157 2238 1658 2459 1675 1868 ...
.. .. .. ..$ fdr : num [1:50] 0 0 0 0.25 0.717 ...
.. .. .. ..@ elementType : chr "ANY"
.. .. .. ..@ elementMetadata: NULL
.. .. .. ..@ metadata : list()
.. .. ..@ seqinfo :Formal class 'Seqinfo' [package "GenomicRanges"] with 4 slots
.. .. .. ..@ seqnames : chr "20"
.. .. .. ..@ seqlengths : int NA
.. .. .. ..@ is_circular: logi NA
.. .. .. ..@ genome : chr NA
.. .. ..@ metadata : list()
..@ allperm : num [1:100] 15.8 13.9 13.8 13.2 13 ...
..@ extra : NULL
..@ chromUsed: chr "20"
..@ theCall : language best.cis.eQTLs(smpack = "GGdata", rhs = ~male, folderstem = "db2", radius
= 1e+06, chrnames = "20", geneApply = mclapply, snpnopk = snplocsDefault(), ...
..@ smFilter :function (x)
.. .. attr(*, "srcref")=Class 'srcref' atomic [1:8] 413 8 413 50 8 50 4 4
.. .. .. attr(*, "srcfile")=Classes 'srcfilecopy', 'srcfile' <environment: 0xf5c0cc0>
..@ nperm : num 2
..@ globalMap:<environment: 0xf5c0538>
..@ testCount: int 83969

```

Details

As created in GGtools.Rnw vignette code, with sharply curtailed searches

Examples

```

data(b1)
b1

```

best.cis.eQTLs

collect genewise best scoring eQTL

Description

collect genewise best scoring eQTL

Usage

```

best.cis.eQTLs(smpack = "GGdata", rhs = ~1,
  folderstem = "cisScratch", radius = 50000,
  shortfac = 100,
  chrnames = as.character(1:22),
  smchrpref = "", gchrpref = "", schrpref = "ch",

```

```

geneApply = lapply, geneannopk = "illuminaHumanv1.db",
snpannopk = snplocsDefault(),
smFilter = function(x) nsFilter(MAFFilter(x, lower = 0.05), var.cutoff = 0.97), nperm = 2,
useME=FALSE, excludeRadius=NULL, exFilter=function(x)x,
keepMapCache=FALSE, getDFFITs=FALSE, Ssgen = GGBase::getSS)

```

```

All.cis.eQTLs(maxfdr = 0.05, inbestcis = NULL, smpack = "GGdata",
  rhs = ~1, folderstem = "cisScratch", radius = 50000,
  shortfac = 100,
  chrnames = as.character(1:22),
  smchrpref = "", gchrpref = "", schrpref = "ch",
  geneApply = lapply, geneannopk = "illuminaHumanv1.db",
  snpannopk = snplocsDefault(),
  smFilter4cis = function(x) nsFilter(MAFFilter(clipPCs(x,
    1:10), lower = 0.05), var.cutoff = 0.85),
  smFilter4all = function(x) MAFFilter(clipPCs(x,
    1:10), lower = 0.05),
  nperm = 2, excludeRadius=NULL, exFilter=function(x)x,
  Ssgen = GGBase::getSS)

```

```

meta.best.cis.eQTLs(smpackvec = c("GGdata", "hmyriB36"), rhslist = list(~1,
  ~1), folderstem = "cisScratch", radius = 50000, shortfac = 100,
  chrnames = as.character(1:22), smchrpref = "", gchrpref = "",
  schrpref = "ch", geneApply = lapply, geneannopk = "illuminaHumanv1.db",
  snpannopk = snplocsDefault(), SMFilterList = list(
  function(x) nsFilter(MAFFilter(x, lower = 0.05), var.cutoff = 0.97),
  function(x) nsFilter(MAFFilter(x, lower = 0.05), var.cutoff = 0.97) ),
  exFilterList = list(function(x)x, function(x)x),
  nperm = 2, excludeRadius=NULL)

```

```

meta.All.cis.eQTLs(minchisq, smpackvec = c("GGdata", "hmyriB36"),
  rhslist = list(~1, ~1), folderstem = "cisScratch",
  radius = 50000, shortfac=100, chrnames = as.character(1:22), smchrpref = "",
  gchrpref = "", schrpref = "ch", geneApply = lapply,
  geneannopk = "illuminaHumanv1.db",
  snpannopk = snplocsDefault(),
  SMFilterList = list(function(x) nsFilter(MAFFilter(x,
    lower = 0.05), var.cutoff = 0.97), function(x)
    nsFilter(MAFFilter(x, lower = 0.05), var.cutoff =
    0.97)),
  exFilterList = list(function(x) x, function(x)
    x),
  nperm = 2)

```

```

chromsUsed(x)

```

```

fdr(x)

```

fullreport(x, type, ...)

getAll(x)

getBest(x)

getCall(x)

Arguments

smpack	character string naming a package to which <code>getSS</code> can be applied to extract <code>smlSet-class</code> instances
smpackvec	vector of character strings naming packages that can be used as <code>smpack</code> values in a series of <code>best.cis.eQTLs</code> calls, one per population for meta-analysis
rhs	R model formula, with no dependent variable, that will be used with <code>snp.rhs.tests</code> to adjust GWAS tests for each expression probe
rhslist	a list of model formulae to be used as <code>rhs</code> in a series of <code>best.cis.eQTLs</code> calls, one per population for meta-analysis
folderstem	prefix of the folder name to be used to hold <code>ff</code> archives of test results
radius	coding extent of each gene will be extended in both directions by <code>radius</code> bases, and only SNP within these limits are used for selecting best hits for the gene
shortfac	a numeric that will scale up the chi-squared statistic before it is converted to short integer for storage in <code>ff</code> array
chrnames	character vector of chromosome identifiers, to be manipulated for certain query resolutions by the following parameters
smchrpref	prefix to convert <code>chrnames</code> into appropriate tokens for indexing <code>smlSet</code> elements as collected from the package named by parameter <code>smpack</code>
gchrpref	prefix to convert <code>chrnames</code> into appropriate tokens for obtaining gene metadata; in future this may need to be a string transformation function
schrpref	prefix to convert <code>chrnames</code> into appropriate tokens for use with <code>getSNPlocs</code> for the SNP location information package identified in <code>snpnopack</code> parameter below
geneApply	an <code>lapply</code> like function, defaults to <code>lapply</code>
geneannopk	character string, name of a <code>*.db</code> annotation package that annotates probe identifiers; or see <code>getCisMap</code> for additional possibilities concerning <code>FDb.*</code> complex token values for newer annotation formats
snpnopk	character string, name of <code>SNPlocs.Hsapiens.dbSNP.*</code> package for obtaining; global function <code>snplocsDefault()</code> can be used to get a nominally current package name
smFilter	function accepting and returning an <code>smlSet-class</code> instance
SMFilterList	list of functions, one element per <code>smlSet</code> package used in meta analysis, accepting and returning an <code>smlSet-class</code> instance

minchisq	threshold on test statistic value that must be met to include records on SNPs in the All.cis.eQTLs report
nperm	number of permutations to be used for plug-in FDR computation
useME	logical; if TRUE, use the rudimentary interface to the MatrixEQTL package from A. Shabalin on CRAN
maxfdr	Used in All.cis.eQTLs. The process of identifying “best” cis eQTL per probe leads to a probe-specific FDR. In All.cis.eQTLs we enumerate all probes and all SNP with FDR at most maxfdr, not just the best scoring SNP per probe.
inbestcis	Used in All.cis.eQTLs. An instance of <code>mcwBestCis</code> that can be used to speed up the extraction of All.cis eQTL.
smFilter4cis	Used in All.cis.eQTLs. A function accepting and returning an <code>smlSet</code> instance. When <code>inbestcis</code> parameter is NULL, this filter will be used for identifying the best SNP per probe.
smFilter4all	Used in All.cis.eQTLs. A function accepting and returning an <code>smlSet</code> instance. This filter will be used for identifying the best SNP per probe. This filter should not affect the number of probes.
x	instance of <code>mcwBestCis</code>
type	character, either 'data.frame' or 'GRanges'
excludeRadius	numeric, defaulting to NULL; if non-null, defines radius around gene region that is excluded for cis SNP scoring; must be less than radius
keepMapCache	logical, if TRUE, returned <code>mcwBestCis</code> object will include an environment loaded with chromosome-specific lists of maps from genes to cis SNP names; if FALSE, the <code>mapCache</code> environment returned will be empty – NB, this feature has been found to add too much volume to returned objects and is suspended...
exFilter	this function is passed to <code>getSS</code> ; see Details
exFilterList	for metaanalytic applications, a list of functions in correspondence with the elements of <code>smpackvec</code> to be passed to <code>getSS</code> ; see Details
getDFFITS	logical; a component storing max DFFITS value for each gene will be retained if this argument TRUE
...	not used
SSgen	function to be used to create <code>smlSet</code> instance for testing – in general, <code>GG-Base::getSS</code> has been used to pull the <code>ExpressionSet</code> and <code>Snpmatrix</code> data from a named package, but in some cases a specialize task is needed to create the desired <code>smlSet</code> . Whatever is passed to <code>SSgen</code> must return an <code>smlSet</code> instance.

Details

`geneApply` can be set to `parallel::mclapply`, for example, in a multicore context.

`mcwBestCis` stands for 'multi-chromosome-wide best cis' eQTL report container.

It is possible that the filtering processes should be broken into genotype filtering and expression probe filtering.

`fdr(x)` will return a numeric vector of plug-in FDR estimates corresponding to probe:association tests as ordered in the `fullreport` of a `*Cis` container. More metadata should be attached to the output of this function.

exFilter may seem redundant with smFilter, but its existence allows simpler management of multitissue expression archives (which may have several records per individual) with germ line genotype data (which will have only one record per individual). In this setting, use exFilter to select records for the tissue of interest; this will occur early in the smlSet generation process.

Value

an instance of `mcwBestCis`

Author(s)

VJ Carey <stvjc@channing.harvard.edu>

Examples

```
getClass("mcwBestCis")
## Not run:
best.cis.eQTLs(chrnames="20")

## End(Not run)
```

best.trans.eQTLs	<i>collect strongest trans SNP-gene associations in a buffer of size K genes per SNP</i>
------------------	--

Description

collect strongest trans SNP-gene associations in a buffer of size K genes per SNP

Usage

```
best.trans.eQTLs(smpack, rhs, genechrnum, snpchrnum, K = 20,
  targdirpref = "tsco", batchsize = 200, radius = 2e+06, genequeryprefix = "",
  snploadprefix = "chr", snplocprefix = "chr", geneannopk, snpannopk,
  exFilter = function(x) x, smFilter = function(x) x,
  geneApply = lapply, SGen = GGBase::getSS)
```

Arguments

smpack	character string naming a package from which <code>smlSet-class</code> instances can be generated using <code>getSS</code>
rhs	passed to <code>snp.rhs.tests</code> for covariate or stratification adjustments; for permutation analysis, covariates should be handled via <code>regressOut</code>
genechrnum	character vector of chromosome identifiers for genes, typically as <code>character(1:22)</code> for somatic genes in human studies
snpchrnum	specific chromosome identifier for all SNP to be analyzed

K	the size of the buffer: scores will be recorded for the most strongly associated K genes for each SNP
targdirpref	character string where buffer data will be held in ff archives
batchsize	passed to <code>ffrowapply</code> as scores are filtered from comprehensive testing to fill the buffer
radius	numeric: for same-chromosome tests, tests will not be performed for SNP-gene combinations with base-pair proximity smaller than radius
genequeryprefix	string: used when the numeric chromosome identifier requires a prefix like 'chr' for annotation query resolution on gene location
snploadprefix	string: used when the package identified in <code>smpack</code> requires a prefix to the <code>snpchrnum</code> token for <code>getSS</code> retrieval of <code>smlSet</code> instance
snplocprefix	string: used when the numeric chromosome identifier requires a prefix like 'chr' for annotation query resolution on SNP location
geneannopk	package to be used for <code>CHRLOC</code> and <code>CHRLOCEND</code> queries for genes
snpannopk	package to be used to resolve <code>getSNPlocs</code> calls
exFilter	function returning an <code>smlSet</code> instance, operating on expression component prior to <code>smFilter</code> application and eQTL testing
smFilter	function returning an <code>smlSet</code> instance, operating on the full <code>smlSet</code>
geneApply	lapply-like function, typically <code>mclapply</code> or the like
SSgen	function to be used to create <code>smlSet</code> instance for testing – in general, <code>GG-Base::getSS</code> has been used to pull the <code>ExpressionSet</code> and <code>SnpMatrix</code> data from a named package, but in some cases a specialize task is needed to create the desired <code>smlSet</code> . Whatever is passed to <code>SSgen</code> must return an <code>smlSet</code> instance.

Value

instance of `transManager-class`

Author(s)

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Examples

```
## Not run:
if (.Platform$OS.type != "windows") { # ff overwrites failing 5.IX.12
  nsFilter2 = function(sms, var.cutoff=.5) {
    alliq = apply(exprs(sms),1,IQR)
    qs = quantile(alliq,var.cutoff, na.rm=TRUE)
    sms[ which(alliq > qs), ]
  }
  thefilt = function(x) GTFfilter( nsFilter2( clipPCs(x, 1:10), var.cutoff=.95 ), lower=.05 )
  tfile = tempfile()
  tfold = dir.create(tfile)
  t1 = best.trans.eQTLs( "GGdata", ~1, as.character(20:22), "22",
```

```

geneannopk="illuminaHumanv1.db", snpannopk= snplocsDefault(),
smFilter=thefilt, snploadprefix="", snplocprefix="ch", targdirpref=tfile)
tt1 = transTab(t1)
tt1o = tt1[ order(tt1[, "sumchisq"], decreasing=TRUE), ][1:10,]
tt1o
}

## End(Not run)

```

bindmaf

bind testing metadata to a best.cis.eQTLs result

Description

bind testing metadata to a best.cis.eQTLs result

Usage

```

meta.bindmaf (smpackvec=c("GGdata", "hmyriB36"),
smchr="20", obj, usemaxMAF=FALSE, SSgen=GGBase::getSS)

```

Arguments

smpackvec	a vector of candidate package names (potential smpack arguments to getSS for metaanalysis across populations or tissues)
smchr	the chromosome name as used in the names of the <code>smlist</code> output for the <code>getSS</code> result
obj	an instance of <code>mcwBestCis-class</code> generated using the package named in <code>smpack</code>
usemaxMAF	if TRUE, label a SNP with maximum MAF observed across populations, otherwise compute the MAF for the combined genotypes across populations represented by the various <code>smlSet</code> instances generated with the <code>smpackvec</code> spec.
SSgen	function to be used to create <code>smlSet</code> instance for testing – in general, <code>GGBase::getSS</code> has been used to pull the <code>ExpressionSet</code> and <code>SnpMatrix</code> data from a named package, but in some cases a specialize task is needed to create the desired <code>smlSet</code> . Whatever is passed to <code>SSgen</code> must return an <code>smlSet</code> instance.

Details

computes the MAF of most highly associated SNP per gene, and distance between that SNP and the transcription limits of the gene, assigning 0 for this if the SNP lies within the transcription limits

Value

a `GRanges` instance

Note

This will be used to stratify the permuted scores.

Examples

```
## Not run:
b1 = best.cis.eQTLs(chr="20") # sharply filtered
b1b = bindmaf(obj=b1)

## End(Not run)
```

cgff2dt	<i>translate the GFF3 from a ciseqByCluster/processgff output into a serialized data.table instance, compute genome-wide plug-in FDR, and update the GFF3 with this FDR</i>
---------	---

Description

translate the GFF3 from a ciseqByCluster/processgff output into a serialized data.table instance, compute genome-wide plug-in FDR, and update the GFF3 with this FDR

Usage

```
cgff2dt(gff3, tiling, addHitTest = TRUE, addcc878 = TRUE)
```

Arguments

gff3	character string naming a tabix-indexed, bgzipped output of gffprocess
tiling	output of simpleTiling
addHitTest	logical, telling whether to add a column on coincidence of SNP with the gwastagger ranges
addcc878	logical, telling whether to add a column on coincidence of SNP with the hmm878 ranges, using the inferred chromatin state as factor level

Note

assumes unix utilites zcat, paste and bgzip are available

Examples

```
##---- Should be DIRECTLY executable !! ----
##-- ==> Define data, use random,
##--or do help(data=index) for the standard data sets.

## The function is currently defined as
function (gff3, tiling)
{
  require(foreach)
  require(Rsamtools)
  stopifnot(is(tiling, "GRanges"))
  basen = gsub(".gff3.gz", "", gff3)
```



```

th = headerTabix(gff3)
orderedChr = th$seqnames
lgr = foreach(i = 1:length(tiling)) %dopar% {
  gc()
  cat(i)
  lk = try(import.gff3(gff3, which = tiling[i]))
  if (inherits(lk, "try-error"))
    lk = NULL
  if (!is.null(lk))
    lk = as.data.table(as.data.frame(lk))
  lk
}
bad = sapply(lgr, is.null)
if (any(bad))
  lgr = lgr[-which(bad)]
ans = do.call(rbind, lgr)
ans$snlocs = as.numeric(ans$snlocs)
ans$ests = as.numeric(ans$ests)
ans$se = as.numeric(ans$se)
ans$oldfdr = as.numeric(ans$fdr)
ans$MAF = as.numeric(ans$MAF)
ans$dist.mid = as.numeric(ans$dist.mid)
nperm = length(grep("permS", names(ans)))
pnames = paste("permScore_", 1:nperm, sep = "")
for (i in 1:nperm) ans[[pnames[i]]] = as.numeric(ans[[pnames[i]]])
ans$mindist = as.numeric(ans$mindist)
print(date())
ans$fdr = pifdr(ans$score, c(ans$permScore_1, ans$permScore_2,
  ans$permScore_3))
print(date())
obn = paste0(basen, "_dt")
assign(obn, ans)
save(list = obn, file = paste0(obn, ".rda"))
gwfdr = ans$fdr
gwch = ans$seqnames
gwsnp = ans$snp
gwprobeid = ans$probeid
sgwfdr = split(gwfdr, gwch)
sgwfdr = unlist(sgwfdr[orderedChr])
nn = tempfile()
fdrt = file(nn, "w")
writeLines(c(c(" ", " ", " "), paste("; gwfdr=", round(sgwfdr,
  6), sep = "")), con = fdrt)
close(fdrt)
chkb = system(paste0("zcat ", gff3, " | paste -d ' ' - ",
  nn, " | bgzip > ", gsub(".gff3", "wm1f.gff3", gff3)))
if (!(chkb == 0))
  warning(paste("final system zcat-paste-bgzip returned non-zero: chkb=",
    chkb))
invisible(chkb)
}

```

 cisAssoc

test for variant-expression associations in cis, using VCF

Description

test for variant-expression associations in cis, using VCF and SummarizedExperiment representations

Usage

```
cisAssoc(summex, vcf.tf, rhs = ~1,
         nperm = 3, cisradius = 50000,
         genome = "hg19", assayind = 1, lbmaf = 1e-06,
         dropUnivHet = TRUE)
```

```
data(lgeu) # obtains an example SummarizedExperiment
```

Arguments

summex	instance of SummarizedExperiment-class
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 use
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

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.

Value

a [GRanges-class](#) instance with mcols including chisq, permScore...

Note

seqlevelsStyle for summex and vcf.tf content must agree

Author(s)

VJ Carey <stvjd@channing.harvard.edu>

Examples

```
data(lgeu) # small excerpt from GEUVADIS FPKM
tf20 = TabixFile(system.file("vcf/c20exch.vcf.gz", package="GGtools"))
if (require(VariantAnnotation)) scanVcfHeader(tf20)
lgeue = clipPCs(lgeu[,which(lgeu$popcode=="CEU")], 1:2)
litc = cisAssoc(lgeue, tf20, nperm=2, lbmaf=.05, cisradius=50000)
summary(litc$chisq)
litc$pifdr = pifdr(litc$chisq, c(litc$permScore_1, litc$permScore_2))
litc[which(litc$pifdr < .01)]
```

CisConfig-class	Class "CisConfig"
-----------------	-------------------

Description

Object specifying configuration of cis-eQTL search, to be used with All.cis

Objects from the Class

Objects can be created by calls of the form `new("CisConfig")`. Use replacement methods to update the fields.

Slots

smpack: character string identifying package holding the expression and genotype data; see [getSS](#)

genome: character string identifying genome build in use

rhs: Object of class "formula" right hand side for calls to [snp.rhs.tests](#)

nperm: Object of class "integer" number of permutations for plug in FDR

folderStem: Object of class "character" string used for scratch space folders, relative to current folder

radius: Object of class "integer" radius of search

shortfac: Object of class "integer" scores are scaled up by this factor so that precision can be retained in short integer representation

chrnames: Object of class "character" string identifying chromosome label used in gene annotation retrieval – typically length 1

smchrpref: Object of class "character" prefix to be attached to chromosome label in chrnames to pick out the element of [smlSet-class](#) instance used in testing

gchrpref: Object of class "character" prefix on chrnames token to be used for gene location retrievals

schrpref: Object of class "character" prefix on chrnames token to be used with [SNPlocs](#) package for retrieval of SNP locations

geneApply: Object of class "function" iterator over genes, could be lapply or mclapply

geneannopk: Object of class "character" Bioconductor annotation package for gene locations, typically for expression array

snpannopk: Object of class "character" Bioconductor dbSNP annotation package

smFilter: Object of class "function" function to be applied to smlSet instance that yields an smlSet instance with required contents; could apply MAF restriction for example by calling MAFilter

exFilter: Object of class "function" function that is run right after smlSet is materialized, permitting replacement or filtering of expression data, when, for example, the ExpressionSet includes multiple tissue types

keepMapCache: Object of class "logical" for enhancing processing of gene-SNP cis mapping with a global cache

SSgen: Object of class "function" function that accepts name of an expression+SnpMatrix package (as generated by [externalize](#)), a chromosome tag (chrnames prefixed by smchrpref), and a function, and returns an smlSet instance

excludeRadius: Object of class "integerOrNULL" which will determine what interval about the gene is excluded for cis testing; 0 should exclude all within-gene SNP, but needs testing

estimates: Object of class "logical" if TRUE, estimates and standard errors (expanded and reduced in storage as a short int, using shortfac) are generated and retained

extraProps: Object of class "function" this function is applied to the cisScores output before it is returned, to bind additional metadata to the ranges if desired. Defaults to function(x)x.

useME: Object of class "logical" if TRUE, use the statistics generated by [Matrix_eQTL_engine](#) for association testing.

MEpvot: Object of class "numeric" used if useME slot is set to TRUE: p-value output threshold for retaining association test statistic generated by [Matrix_eQTL_engine](#); defaults to 0.5. Higher values lead to higher volumes and longer times to completion.

Methods

chrnames signature(x = "CisConfig"): ...

chrnames<- signature(object = "CisConfig", value = "character"): ...

estimates signature(x = "CisConfig"): ...

estimates<- signature(object = "CisConfig", value = "logical"): ...

excludeRadius signature(x = "CisConfig"): ...

excludeRadius<- signature(object = "CisConfig", value = "integer"): ...

exFilter signature(x = "CisConfig"): ...

exFilter<- signature(object = "CisConfig", value = "function"): ...

gchrpref signature(x = "CisConfig"): ...

gchrpref<- signature(object = "CisConfig", value = "character"): ...

geneannopk signature(x = "CisConfig"): ...

geneannopk<- signature(object = "CisConfig", value = "character"): ...

geneApply signature(x = "CisConfig"): ...

```

geneApply<- signature(object = "CisConfig", value = "function"): ...
initialize signature(.Object = "CisConfig"): ...
keepMapCache signature(x = "CisConfig"): ...
keepMapCache<- signature(object = "CisConfig", value = "logical"): ...
radius signature(x = "CisConfig"): ...
radius<- signature(object = "CisConfig", value = "integer"): ...
rhs signature(x = "CisConfig"): ...
rhs<- signature(object = "CisConfig", value = "function"): ...
schrpref signature(x = "CisConfig"): ...
schrpref<- signature(object = "CisConfig", value = "character"): ...
shortfac signature(x = "CisConfig"): ...
shortfac<- signature(object = "CisConfig", value = "integer"): ...
show signature(object = "CisConfig"): ...
smchrpref signature(x = "CisConfig"): ...
smchrpref<- signature(object = "CisConfig", value = "character"): ...
smFilter signature(x = "CisConfig"): ...
smFilter<- signature(object = "CisConfig", value = "function"): ...
snpannopk signature(x = "CisConfig"): ...
snpannopk<- signature(object = "CisConfig", value = "character"): ...
SSgen signature(x = "CisConfig"): ...
SSgen<- signature(object = "CisConfig", value = "function"): ...

```

Examples

```
showClass("CisConfig")
```

ciseqByCluster

end-to-end cluster-based cis-eQTL search, and allied utilities

Description

end-to-end cluster-based cis-eQTL search, and allied utilities

Usage

```

ciseqByCluster(cl, pack = "yr1kgv", outprefix = "yrirun",
  finaltag = "partyri100k", chromsToRun = 1:22,
  targetfolder = "/freshdata/YRI_3", radius = 100000L, nperm = 3L, ncoresPerNode = 8,
  numPctoFilter = 10, lowerMAF = 0.02, geneannopk = "lumiHumanAll.db",
  snpannopk = "SNPlocs.Hsapiens.dbSNP.20120608", smchrpref = "chr",
  tmpForSort = "/tmp", numtiles = 200,
  postProcCores = 12, reqlist = NULL)

```

Arguments

<code>cl</code>	instance of S3 cluster class from parallel package
<code>pack</code>	character string naming package to which <code>getSS</code> can be applied to generate <code>smlSet-class</code> instances
<code>outprefix</code>	character string used to prefix names of output GFF3 files
<code>finaltag</code>	character string used to prefix names of final amalgamated GFF3 and <code>data.table</code> instances
<code>chromsToRun</code>	numeric tags of chromosomes to be analyzed
<code>targetfolder</code>	character string naming folder where GFF3 will be deposited
<code>radius</code>	extent of search around gene model in bp
<code>nperm</code>	number of permutations for plug-in FDR computation (usually a small integer)
<code>ncoresPerNode</code>	number of cores for multicore testing: chromosomes map to nodes, genes map to cores
<code>numPctoFilter</code>	number of PCs to be removed through <code>clipPCs</code>
<code>lowerMAF</code>	lower bound on MAF of SNP to be included for testing
<code>geneannopk</code>	character string naming Bioconductor package with annotation for expression probe identifiers
<code>snpannopk</code>	character string naming Bioconductor package with annotation for SNP locations
<code>smchrpref</code>	character prefix converting <code>chromsToRun</code> elements to basenames of <code>rda</code> files harboring <code>SnpMatrix</code> instances
<code>tmpForSort</code>	the assembly of final resources employs <code>unix sort</code> , and substantial temporary space can be required; this parameter tells where the temp files will reside
<code>numtiles</code>	number of tiles into which the genome in use will be sliced for parallel processing in final assembly
<code>postProcCores</code>	numeric establishing number of cores to use for final assembly of annotated output
<code>reqlist</code>	rescue request, see Details section

Details

purpose is to maximize throughput of cis-eQTL testing in a two-level concurrent computing environment, where a cluster as defined in package `parallel` has nodes to which half-chromosomes will be dispatched; each node is assumed to be multicore and genes are mapped to cores during the iteration process.

the `reqlist` parameter consists of a list of elements (chromosome name, subchromosome token, and handler) to be used for completing a partial run

Value

a set of GFF3 files encoding all cis associations with location and various metadata

See Also

[gffprocess](#), [cgff2dt](#)

Examples

```
#none yet
```

cisRun-class	Class "cisRun"
--------------	----------------

Description

manage results of All.cis eQTL analysis

Objects from the Class

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

Slots

`seqnames`: Object of class "Rle" ~~

`ranges`: Object of class "IRanges" – will document the range searched for each probe/gene – therefore the values returned are addresses of gene extent minus/plus radius at each end

`strand`: Object of class "Rle" ~~

`elementMetadata`: Object of class "DataFrame" ~~

`seqinfo`: Object of class "Seqinfo" ~~

`metadata`: Object of class "list" ~~

Extends

Class "[GRanges](#)", directly. Class "[GenomicRanges](#)", by class "GRanges", distance 2. Class "[Vector](#)", by class "GRanges", distance 3. Class "[GenomicRangesORmissing](#)", by class "GRanges", distance 3. Class "[GenomicRangesORGRangesList](#)", by class "GRanges", distance 3.

Class "[Annotated](#)", by class "GRanges", distance 4.

Methods

No methods defined with class "cisRun" in the signature.

Note

intent is to simplify output of cis eQTL testing in a GRanges instance

Author(s)

VJ Carey <stvjc@channing.harvard.edu>

Examples

```
showClass("cisRun")
```

collectBest	<i>given a collection of All.cis outputs (cisRun instances) compute FDRs for various filterings</i>
-------------	---

Description

given a collection of All.cis outputs (cisRun instances) compute FDRs for various filterings

Usage

```
collectBest(fns,
  targetname = "harvest",
  mafs = c(0.01, 0.02, 0.025, 0.03333, 0.05, 0.075, 0.1),
  hidists = c(10000, 25000, 50000, 75000, 1e+05, 250000), interimSaves=FALSE)

collectFiltered( fns, targetname="harvest",
  mafs = c(.01, .02, .025, .03333, .05, .075, .1),
  hidists = c(10000, 25000, 50000, 75000, 100000, 250000),
  filterFun = cis.FDR.filter.best, filtApplier=lapply,
  interimSaves=FALSE)
```

Arguments

fns	names of .rda with the cisRun outputs
targetname	basename of rda file to be emitted
mafs	lower bounds on MAF for filtering
hidists	upper bounds on cis radius for filtering
filterFun	function like GGtools:::cis.FDR.filter.best
filtApplier	function like lapply
interimSaves	logical, if TRUE save list at each maf/dist transition

Details

[pifdr](#) is repeatedly used to generate conditional plugin FDR for different filtering criteria

Value

a list of lists is written to disk incrementally, as the job can be long running

Note

This is the workhorse of sensitivity analysis. Permits counting of genes with eQTL at selected FDR for various criteria on cis radius and MAF.

Examples

```
## Not run:
#
# contents of fns are two chromosomes of cis runs for CEU
#
fns = dir(system.file("rdas", package="GGtools"), full=TRUE)
cc = collectBest(fns, maf=c(.01, .05), hidists=c(10000, 50000))
sapply(cc, sapply, function(x) sum(x$fdr <= 0.01))
#
# this tells us which to keep
#
kp = cc[["0.05"]][["50000"]]
kp = kp[kp$fdr <= 0.01,]
#
# the hits are in the table above; the following function
# retrieves the initial scores giving rise to the filtered
# hits
#
pullHits = function(fns, atts) {
  tmp = lapply(fns, function(x) get(load(x)))
  k1 = lapply(tmp, function(x) paste(names(x), x$snp, sep=":"))
  atk = paste(atts$genes, atts$bestsnp, sep=":")
  tmp = lapply(1:length(tmp), function(x) tmp[[x]][ match( atk, k1[[x]], nomatch=0 ) ])
  curans = do.call(c, lapply(tmp, as, "GRanges"))
  newword = match( atk, paste(names(curans), curans$snp, sep=":"))
  newfdr = atts$fdr[newword]
  curans$fdr = newfdr
  curans
}
pullHits( fns, kp )
#
#
#
# after executing code in example for All.cis (protected by dontrun)
# and running save(f1, file="f1.rda"), the following will work
# genewise max score
cf1 = collectFiltered("f1.rda", maf=.02, hidists=25000, targetname="gwise")
# SNPwise scores, all
cf2 = collectFiltered("f1.rda", maf=.02, hidists=25000, targetname="swise",
  filterFun = cis.FDR.filter.SNPcentric.complete )
# SNPwise scores, best per SNP when SNP is cis to multiple genes
cf3 = collectFiltered("f1.rda", maf=.02, hidists=25000, targetname="swise2",
  filterFun = cis.FDR.filter.SNPcentric )

## End(Not run) # end dontrun
```

concatCis	<i>combine a list of cisRun instances to a single instance</i>
-----------	--

Description

combine a list of cisRun instances to a single instance, with ad hoc metadata combination

Usage

```
concatCis(crl)
```

Arguments

crl list of instances of [cisRun-class](#)

Details

the metadata for the output is a list with elements call and config as required, derived from first element of the input; the extras component holds the metadata elements of the remaining input list elements

Value

a cisRun instance

Examples

```
## Not run:  
example(All.cis)  
concatCis(f1, f1)  
  
## End(Not run)
```

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

Description

Manage the appraisal of an eQTL search

Objects from the Class

Objects can be created by calls of the form `new("EqAppr", ...)`, or via `buildEqAppr()`

Slots

meta: Object of class "ApprMeta" basic descriptive information about source analysis
sens: Object of class "ApprSens" outputs of sensitivity analysis
pruned: Object of class "ApprRes" outputs of appraisal for LD-pruned predictions
unpruned: Object of class "ApprRes" outputs of general appraisal without LD pruning

Methods

calfig signature(x = "EqAppr", ind = "character"): Additional arguments can be specified:
ind index or name of model to be plotted
hfudgetxt distance to move rendered fractions relative to bin x coordinate
tickend maximum value at which axis tick mark will be plotted
tickgap axis will have ticks at seq(0, tickend, tickgap)
yimin ylim setting for rendering
xlimin xlim setting for rendering
fraccex cex setting for fraction rendering
fuselast if data are sparse in entries of high predicted probability, you can fuse the nearby cells up to the end – pick fuselast=2 for final 2 cells, 3 for final 3 and so on
getModnames signature(x = "EqAppr"): obtain the list of strings used to name different appraisal models
getPruned signature(x = "EqAppr"): get the ApprRes instance corresponding to the LD-pruned loci
getUnpruned signature(x = "EqAppr"): get the ApprRes instance for all loci in use
getSens signature(x = "EqAppr"): get sensitivity analysis results
show signature(object = "EqAppr"): concise report

Examples

```
showClass("EqAppr")
```

 eqBox

descriptive plot of expression against genotype for cisAssoc results

Description

descriptive plot of expression against genotype for cisAssoc results

Usage

```
eqBox(gene, snp, se, tf, radius=1e6, genome="hg19", ...)
eqDesc(gene, snp, se, tf, radius=1e6, genome="hg19", ...)
```

Arguments

gene	identifier of gene in SummarizedExperiment se, must be present in rownames(se)
snp	identifier of variant in VCF referenced by tf
se	SummarizedExperiment instance
tf	TabixFile reference for a VCF file that has been bgzipped and tabix-indexed
radius	in order to limit the VCF import, we filter variants to those within a radius around the selected gene – it is assumed that the selected snp will exist in that region (we can't extract SNP by name from vcf...)
genome	a simple genome identifier tag
...	(not used with eqDesc) will embellish plot; xlab and ylab already taken care of

Details

The chromosome names in the VCF and the seqlevelsStyle of the Summarized Experiment must match.

Value

eqBox produces a boxplot for all categories (including NA) of genotype. eqDesc tabulates the genotype calls in categories.

Examples

```
if (require(VariantAnnotation)) {
  data(lgeu)
  lgeue = lgeu[,which(lgeu$popcode=="CEU")]
  tf20 = TabixFile(system.file("vcf/c20exch.vcf.gz", package="GGtools"))
  eqBox("ENSG00000126005.10", "rs2425038", lgeue, tf20 )
}
```

 eqsens_dt

support for sensitivity analyses related to eQTL enumerations

Description

support for sensitivity analyses related to eQTL enumerations

Usage

```
eqsens_dt(dtab, filtgen = filtgen.maf.dist, by = c("pairs", "snps", "probes")[1],
  targfdrs = c(0.05, 0.01, 0.005),
  parmslist = list(mafs = c(0.025, 0.05, 0.075, 0.1, 0.125),
    dists = c(1000, 5000, 10000, 25000, 50000, 1e+05)),
    renameChisq = TRUE)
filtgen.maf.dist (maf.dist, validate.tab = function(tab) all(c("mindist",
  "MAF", "score") %in% colnames(tab)))
```

```
update_fdr_filt(tab, filt = function(x) x, by = c("pairs", "snps",
"probes")[1])
plotsens(eqsout, ylab = "count of eQTL at given FDR",
title = "cis radius in bp")
```

Arguments

dtab	data.table instance as generated by converting a cisScores GRanges. In general it will need to have column names score, MAF, mindist, and columns with names permScore_1,
filtgen	a function that generates a closure. The function returned by <code>filtgen</code> will be a function of one argument that filters an input data.table. The environment of the returned function will possess bindings used to define the filtering operation. <code>filtgen.maf.dist</code> , documented here, is a working example.
by	character atom describing the level of aggregation for sensitivity analysis. eQTL searches generally involve cartesian products of sets of SNPs and sets of genes, and if all elements of these products are of interest, set by to "pairs". For sensitivity analysis in which per-SNP associations are measured by choosing the maximum association statistic for all genes cis to the SNP, set by to "snps". For per-gene associations, with scores maximized over all SNPs cis to genes, use "probes".
targfdrs	numeric vector of FDR levels for which enumerations are performed.
parmslist	list of numeric vectors giving thresholds for use in filtering tests using <code>filtgen</code>
maf.dist	numeric vector of length two giving thresholding values for MAF and cis distance for filtering association tests
validate.tab	function of one argument, assumed to be a data.table instance, that can be used to check whether filtering conditions are feasible before attempting to filter; should return TRUE if they are, FALSE otherwise.
tab	data.table instance as generated by converting a cisScores
filt	function of one argument that operates on a data.table instance to reduce the rows to a desired set; parameters of filtering task are established in the environment of <code>filt</code>
eqsout	matrix as output by <code>eqsens_dt</code>
ylab	text string to be used to label Y axis on the left
title	text string to label top of plot
renameChisq	Some utilities fail to generate 'score' for observed association statistic, but report as 'chisq'. If TRUE and such a column name is found in <code>dtab</code> , <code>setnames</code> will be run to rename to 'score'.

Details

The objective is to generate data for tabulation or visualization of sensitivity analyses, and the scope of sensitivity analysis can be established in various ways. This software is mostly intended as a framework.

Value

eqsens_dt returns a data.frame instance with enumerations of eQTL at various FDR thresholds for various settings of tuning parameters

update_fdr_filt revises (using `pifdr`) the `fdr` field of an input `data.table` instance using variable score as observed value, and permuted values furnished by the variables named with `permScore` as leading substring

Note

To do: allow filtering on the number of permutations to be used in FDR calculation.

Author(s)

VJ Carey <stvjc@channing.harvard.edu>

Examples

```
## Not run:
example(cisScores) # would generate f1
names(f1) = NULL
eqsens_dt( data.table(as(f1, "data.frame")) )

## End(Not run)
```

eqtlTests	<i>compute association statistics between all probes and SNP in an smlSet instance</i>
-----------	--

Description

compute association statistics (or point estimates and standard errors) between all probes and SNP in an `smlSet` instance, using out-of-memory storage; the basic test statistics are generated by the `snp.rhs.tests` function of the `snpStats` package

Usage

```
eqtlTests(smlSet, rhs = ~1 - 1, runname = "foo",
  targdir = "foo", geneApply = lapply,
  shortfac = 100,
  checkValid = TRUE, useUncertain = TRUE,
  glmfamily = "gaussian", doFFSUMM = FALSE)

eqtlEstimates(smlSet, rhs = ~1 - 1, runname = "foo",
  targdir = "fooe", geneApply = lapply,
  shortfac = 10000,
  checkValid = TRUE, useUncertain = TRUE,
  glmfamily = "gaussian")
```

Arguments

smlSet	instance of smlSet
rhs	fragment of a standard formula, minus a dependent variable (i.e., starts with tilde); bindings will be sought in <code>pData(smlSet)</code>
runname	string used to identify output ff files
targdir	string naming the folder where ff outputs will reside
geneApply	analog to <code>lapply</code> to drive iteration over probes
shortfac	ff contents will be multiplied by this quantity and stored as short integers
checkValid	logical, will apply <code>validObject</code> to <code>smlSet</code> if TRUE
useUncertain	logical, passed as <code>uncertain</code> parameter to snp.rhs.tests to specify whether uncertain genotypes will be used (as 'dosage' in GLM fitting)
glmfamily	family specification for snp.rhs.tests
doFFSUMM	logical indicating whether ff archives will be retained for <code>col.summary</code> outputs for SNPs

Details

The purpose of the `eqtlTests` function is to allow very substantial eQTL search processes to occur with R. For several million SNP and tens of thousands of probes, the storage of test results requires attention to parsimony. The storage occurs out of memory, using the `ff` package, and employs short integers to represent chi squared statistics. These are scaled up prior to storage, and will be scaled down prior to use.

`eqtlEstimates` will use compact storage for both the point estimates and standard errors of association estimated under an additive genetic model

Note: [snp.rhs.estimate](#)s will emit a warning whenever the parameters are not estimable. These warnings are suppressed by temporary setting of `options()[['warn']]` to zero.

Value

returns an instance of `eqtlTestsManager`

Author(s)

VJ Carey <stvjc@channing.harvard.edu>

Examples

```
hm2ceuSMS = getSS("GGtools", c("20"), renameChrs=c("chr20"))
library(illuminaHumanv1.db)
cptag = get("CPNE1", revmap(illuminaHumanv1SYMBOL))
indc = which(featureNames(hm2ceuSMS) == cptag[1])
#
# get a set of additional genes on chr20
all20 = get("20", revmap(illuminaHumanv1CHR))
g20 = unique(c(all20[1:10], cptag))
#
```

```

hm = hm2ceuSMS[probeId(g20),] # reduce problem
td = tempdir()
curd = getwd()
setwd(td)
time.lapply = unix.time(e1 <- eqtlTests( hm, ~male ))
time.lapply
e1
# best chisq(1) for CPNE1
topFeats(probeId(cptag), e1)
setwd(curd)

```

eqtlTests.me	<i>use MatrixEQTL computations and statistics as a back end to GGtools eqtlTests</i>
--------------	--

Description

use MatrixEQTL computations and statistics as a back end to GGtools eqtlTests

Usage

```

eqtlTests.me(smlSet, rhs = ~1, runname = "20",
  targdir = "cisScratch.me", pvot = 0.5, geneApply = lapply,
  shortfac = 100, checkValid = TRUE, useUncertain = TRUE,
  glmfamily = "gaussian", scoretx = abs,
  matrixEQTL.engine.control =
  list(output_file_name = "/dev/null",
    useModel = modelLINEAR,
    errorCovariance = numeric(),
    verbose = FALSE,
    pvalue.hist = FALSE),
  snpSlicedData.control = .slicedDataDefaults,
  geneSlicedData.control = .slicedDataDefaults,
  covarSlicedData.control = .slicedDataDefaults,
  covariates_file_name = character())

```

Arguments

smlSet	instance of smlSet-class
rhs	formula for adjustment of tests for covariates or stratification, see snp.rhs.tests
runname	tag used to distinguish emitted files
targdir	folder where ff archives will reside
pvot	setting for pvOutputThreshold in Matrix_eQTL_engine
geneApply	lapply-like function for iteration over genes, mclapply is suitable when in multicore environments
shortfac	scaling factor to increase precision when test results are stored as short ints in ff

checkValid	logical to check validity of input smlSet
useUncertain	logical informing snp.rhs.tests that imputed real-valued B allele counts may be present among genotype data
glmfamily	family specification for snp.rhs.tests
scoretx	function to be applied to MatrixEQTL statistics. Defaults to abs, for signless association testing
matrixEQTL.engine.control	list of parameters passed to Matrix_eQTL_engine
snpSlicedData.control	list of parameters used to define SlicedData-class instances
geneSlicedData.control	list of parameters used to define SlicedData-class instances
covarSlicedData.control	list of parameters used to define SlicedData-class instances
covariates_file_name	if covariates are to be used with MatrixEQTL testing engine, they reside in this file. regressOut can be used to avoid this if plug-in FDR are to be used

Details

provisional interface

Value

see [eqtlTests](#)

Note

intended for simple comparisons

References

Shabalin et al Bioinformatics (OUP) 2012

Examples

```
if (require(MatrixEQTL)) {  
  g22 = nsFilter( chrFilter( getSS("GGdata", "22"), "22" ), var.cutoff = .8 )  
  m22 = eqtlTests.me(g22)  
}
```

 eqtlTestsManager-class

 Class "eqtlTestsManager"

Description

manage out-of-memory elements of an eQTL search

Objects from the Class

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

Slots

fffile: Object of class "ff_matrix" chisquared statistics stored as short ints in ff out of memory file

call: Object of class "call" audit of creation call

sess: Object of class "ANY" session info structure at time of creation

exdate: Object of class "ANY" date at time of creation

shortfac: Object of class "numeric" number by which chisq stats are multiplied to allow recovery of precision

geneanno: Object of class "character" string naming annotation package relevant for probe identifier translation

df: Object of class "numeric" degrees of freedom of chisq stats

summaryList: Object of class "list" list of genotype statistical summaries

Methods

[signature(x = "eqtlTestsManager", i = "ANY", j = "ANY", drop = "ANY"): extract chisq statistics properly rescaled from short int to double

show signature(object = "eqtlTestsManager"): concise report

topFeats signature(feats = "probeId", mgr = "eqtlTestsManager"): extract highest scores for SNP associated with given probeId

topFeats signature(feats = "rsid", mgr = "eqtlTestsManager"): extract highest scores for probes associated with given SNP

Note

instances are created by [eqtlTests](#)

Author(s)

VJ Carey <stvjc@channing.harvard.edu>

Examples

```
showClass("eqtlTestsManager")
```

ex

*ExpressionSet instance for illustrating integrative smlSet container***Description**

ExpressionSet instance for illustrating integrative smlSet container

Usage

data(eset)

Format

The format is: Formal class 'ExpressionSet' [package "Biobase"] with 7 slots ..@ experimentData :Formal class 'MIAME' [package "Biobase"] with 13 slots

```

.. ..@ name : chr ""
.. ..@ lab : chr ""
.. ..@ contact : chr ""
.. ..@ title : chr ""
.. ..@ abstract : chr ""
.. ..@ url : chr ""
.. ..@ pubMedIds : chr ""
.. ..@ samples : list()
.. ..@ hybridizations : list()
.. ..@ normControls : list()
.. ..@ preprocessing : list()
.. ..@ other : list()
.. ..@ .__classVersion__:Formal class 'Versions' [package "Biobase"] with 1 slots
.. .. .@ .Data:List of 2
.. .. .$. : int [1:3] 1 0 0
.. .. .$. : int [1:3] 1 1 0
.. ..@ assayData :<environment: 0x10bf12948>
.. ..@ phenoData :Formal class 'AnnotatedDataFrame' [package "Biobase"] with 4 slots
.. .. .@ varMetadata :'data.frame': 7 obs. of 1 variable:
.. .. .$. labelDescription: chr [1:7] "hapmap family id" "hapmap person id" "id of mother of this
person" "id of father of this person" ...
.. .. .@ data :'data.frame': 90 obs. of 7 variables:
.. .. .$. famid : int [1:90] 1341 1341 1341 1340 1340 1340 1340 1341 1341 ...
.. .. .$. persid : int [1:90] 14 2 13 9 10 2 11 1 11 1 ...
.. .. .$. mothid : int [1:90] 0 14 0 0 0 12 0 10 0 12 ...
.. .. .$. fathid : int [1:90] 0 13 0 0 0 11 0 9 0 11 ...
.. .. .$. sampid : Factor w/ 90 levels "NA06985","NA06991",...: 1 2 3 4 5 6 7 8 9 10 ...
.. .. .$. isFounder: logi [1:90] TRUE FALSE TRUE TRUE TRUE FALSE ...
.. .. .$. male : logi [1:90] FALSE FALSE TRUE TRUE FALSE FALSE ...
.. .. .@ dimLabels : chr [1:2] "sampleNames" "sampleColumns"
.. ..@ .__classVersion__:Formal class 'Versions' [package "Biobase"] with 1 slots
.. .. .@ .Data:List of 1

```

```

.. .. .. .. .$ : int [1:3] 1 1 0
..@ featureData :Formal class 'AnnotatedDataFrame' [package "Biobase"] with 4 slots
.. .. ..@ varMetadata :'data.frame': 0 obs. of 1 variable:
.. .. .. .$ labelDescription: chr(0)
.. .. ..@ data :'data.frame': 47293 obs. of 0 variables
.. .. ..@ dimLabels : chr [1:2] "featureNames" "featureColumns"
.. .. ..@ __classVersion__:Formal class 'Versions' [package "Biobase"] with 1 slots
.. .. .. ..@ .Data:List of 1
.. .. .. .. .$ : int [1:3] 1 1 0
..@ annotation : chr "illuminaHumanv1.db"
..@ protocolData :Formal class 'AnnotatedDataFrame' [package "Biobase"] with 4 slots
.. .. ..@ varMetadata :'data.frame': 0 obs. of 1 variable:
.. .. .. .$ labelDescription: chr(0)
.. .. ..@ data :'data.frame': 90 obs. of 0 variables
.. .. ..@ dimLabels : chr [1:2] "sampleNames" "sampleColumns"
.. .. ..@ __classVersion__:Formal class 'Versions' [package "Biobase"] with 1 slots
.. .. .. ..@ .Data:List of 1
.. .. .. .. .$ : int [1:3] 1 1 0
..@ __classVersion__:Formal class 'Versions' [package "Biobase"] with 1 slots
.. .. ..@ .Data:List of 4
.. .. .. .$ : int [1:3] 2 14 0
.. .. .. .$ : int [1:3] 2 13 7
.. .. .. .$ : int [1:3] 1 3 0
.. .. .. .$ : int [1:3] 1 0 0

```

Details

Expression data harvested in 2007 from GENEVAR

ftp://ftp.sanger.ac.uk/pub/genevar/CEU_parents_norm_march2007.zip

Examples

```
data(eset) # yields ExpressionSet instance called ex
```

getCisMap

create, using Bioconductor annotation resources, a structure that enumerates SNP in the vicinity of ('cis' to) genes

Description

create a structure that enumerates SNP in the vicinity of ('cis' to) genes

Usage

```
getCisMap(radius = 50000, gchr = "20",
          schr = "ch20", geneannopk = "illuminaHumanv1.db",
          snpannopk = snplocsDefault(),
          as.GRangesList = FALSE, excludeRadius=NULL)
```

Arguments

radius	How far, in bases, up or down stream from the asserted coding region limits to include SNP
gchr	the token to be used to acquire locations for probes on a specified chromosome, using revmap([dbpk]CHR)
schr	the token to be used to acquire locations for SNP on a specified chromosome, using getSNPLocs
geneannopk	character string naming a Bioconductor .db expression chip annotation package; or a complex string with first part naming a Bioconductor FDb.* annotation package, colon separator, and a second string naming the getter hook that when called returns a GRanges with names corresponding to features and ranges corresponding to feature extents. For example "FDb.InfiniumMethylation.hg19:get27k" is valid. Note that in this case, gchr must have prefix "chr".
snpannopk	character string naming a Bioconductor SNPlocs.* SNP metadata package
as.GRangesList	logical telling whether a GRangesList should be returned
excludeRadius	numeric or NULL: radius of interval around gene extent from which SNP will be excluded, required to be less than radius

Details

This is a utility that the developer would rather not export. The complexity of harmonizing queries among probe and SNP annotation resources leads to a somewhat fragile product. Users who have their own gene ranges and SNP locations can examine the namelist component of the output of the default call to see what is expected for the *.cis.eQTLs function. For the set of chromosomes to be analyzed, there will be a list of chromosome specific namelist-like lists.

Value

Instance of cisMap class, which will retain SNP location, gene range, and radius information for auditing.

Examples

```
## Not run:
  getCisMap()

## End(Not run)
```

gffprocess	<i>transform a collection of gff3 into a single tabix-indexed gff3</i>
------------	--

Description

process a collection of gff3 into a single tabix-indexed gff3 using unix utilities to minimize memory requirements

Usage

```
gffprocess(basename = "fullyri100k", n_in = 44, headpatt = "_1A", tmpForSort = "/freshdata/tmp")
```

Arguments

basename	basename of the resulting .gff3.gz(.tbi) file
n_in	number of gff3 files to be processed – used for consistency check against length(dir(patt="gff3"))
headpatt	pattern to identify file for the 'top' gff3 to be used as the contents are concatenated
tmpForSort	name of a folder that unix sort will use as a temporary directory

Details

The purpose of this utility is to exploit unix shell tools to unify a collection of gff3 files generated using `link{All.cis}`. The use case is cluster-based per-chromosome (or split chromosome) cis-testing generating a large number of GRanges that are transformed to gff3 to allow targeted interrogation.

Value

Used for side effects. Will fail if any unix utility call via `system()` returns nonzero value. Returns NULL otherwise.

Author(s)

VJ Carey <stvjc@channing.harvard.edu>

gwSnpTests	<i>execute a series of tests for association between genotype and expression</i>
------------	--

Description

execute a series of tests for association between genotype and expression

Usage

```
gwSnpTests(sym, sms, ...)  
topSnps(x, n=10)
```

Arguments

sym	instance of probeId or genesym
sms	instance of smlSet-class
x	instance of gwSnpScreenResult
n	integer, number of test results to be reported, sorted decreasing from the most significant
...	not used

Details

The plot method for [gwSnpScreenResult](#) instances takes a second argument, the name of a Bioconductor `SNPlocs.*` package.

Value

an instance of the [gwSnpScreenResult](#) class, to be examined by `topSnps`

Note

The most basic application yields one d.f. chi-squared statistics based on score tests.

Author(s)

VJ Carey <stvjc@channing.harvard.edu>

Examples

```
s20 = getSS("GGtools", "20")  
t1 = gwSnpTests(genesym("CPNE1")~male, s20)  
topSnps(t1)  
## Not run:  
plot(t1, snplocsDefault())  
  
## End(Not run)
```

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, Shoresh 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)

```

pifdr

utility for computing plug-in FDR

Description

utility for computing plug-in FDR

Usage

```

pifdr( obs, perms, legacy=FALSE, trimToUnit = TRUE, ... )

```

Arguments

obs	observed association scores
perms	vector of association scores under permutation; length should be integer multiple of length(obs)
legacy	logical, if TRUE, use the approximate version of pifdr() available before 12/30/2013, with additional arguments if desired
trimToUnit	logical, if TRUE, values greater than 1 are replaced by 1. Such values can occur, for example, with relatively small sample sizes.
...	extra arguments passed if legacy is TRUE

Details

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

Use legacy=TRUE to obtain the approximate implementation, for which the following remarks held: “As currently implemented the algorithm is quadratic in length(obs). While it is possible to get a unique FDR value for every element of obs, an approximate approach yields practically identical precision and by default this will be used for obs with length 2000 or more. In this case, [approx](#) is used with rule=2 to interpolate from the grid-based FDR estimates back to the data values.” Additional parameters npts and applier may be supplied if legacy is set to TRUE.

npts defined the number of points spanning the range of obs to be used for a lossy grid-based computation only used if length(obs)>npts.

applier is to be an sapply-like function.

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)
```

qqhex	<i>obtain qqplot coordinates for the specific case of comparing a given distribution to that of multiple realizations from a permutation distribution, and bin these coordinates using hexbin, useful for very large samples</i>
-------	--

Description

obtain qqplot coordinates for the specific case of comparing a given distribution to that of multiple realizations from a permutation distribution, and bin these coordinates using hexbin, useful for very large samples

Usage

```

binnedQQ(dt, nxbins=20,
  ylim=c(0,76), xlim=c(0,30), end45=5, thrs=c(0,.001,.005,.01,.05),
  tempmar = c(6,4,4,5), ...)
qqhex(sco, p1, p2, p3, fdr, nxbins = 20, thrs = c(0, 0.001, 0.005, 0.01, 0.05))
binqq(qqob, ylim = c(0, 76), xlim = c(0, 30), end45=5, ...)

```

Arguments

dt	a data.table instance with association scores and scores obtained under permutation along with FDR, as returned by cgff2dt or ciseqByCluster
sco	numeric vector of observed statistics
p1	realization of null distribution for sco, independent of p2 and p3
p2	realization of null distribution for sco, independent of p1 and p3
p3	realization of null distribution for sco, independent of p1 and p2
fdr	vector of FDR associated with elements of sco
nxbins	number of bins to be used for samples from the null distribution
thrs	vector of thresholds in FDR to be used for ruling the plot
qqob	for binhex() , output of qqhex
ylim	vertical limits of rendering
xlim	horizontal limits of rendering
end45	a segment is drawn from (0,0) to (end45,end45) to depict the line of identity
tempmar	numerical vector with 4 elements serving as a temporary setting of the mar parameter of par
...	not currently used

Value

for [qqhex](#), a list with elements

hb	output of hexbin
thrs	vector of input thrs
scothrs	vector of observed statistics corresponding to FDRs in thrs

Examples

```

opar = par(no.readonly=TRUE)
set.seed(123)
x = c(rchisq(9000,1), rchisq(1000,12))
nn = lapply(1:3, function(x) rchisq(10000,1))
fd = pifdr(x, unlist(nn))
qqh = qqhex(x, nn[[1]], nn[[2]], nn[[3]], fd)
par(mar=c(4,4,4,7))
binqq(qqh,xlim=c(0,10), ylim=c(0,20))
mtext(4, "FDR")
par(opar)

```

richNull	<i>bind metadata concerning SNP allele frequency and other aspects of optimized cis-eQTL association to an mcwBestCis instance</i>
----------	--

Description

bind metadata concerning SNP allele frequency and other aspects of optimized cis-eQTL association to an mcwBestCis instance, to allow conditional FDR computation

Usage

```

richNull(..., MAF1b = 0.01, npc = 10, radius = 250000, nperm = 1,
  innerFilt = function(x) x, outerFilt = function(x) x)

meta.richNull(..., MAF1b=.01, npc=10, radius=250000,
  nperm=1, innerFilt=function(x)x, outerFilt=function(x)x)
#
# internally:
#
# bigfilt = function(z)
#   outerFilt(MAFfilter(clipPCs(permEx(innerFilt(z))), 1:npc), lower=MAF1b))
#

```

Arguments

...	should provide bindings for smpack and chrnames, which will be used to obtain gene/probe locations; see getSS for information on smpack settings. meta.richNull allows a vector of smpack values bound to smpackvec
MAF1b	lower bound on SNP MAF for null distribution evaluation
npc	number of expression principal components to be removed
radius	radius used for testing
nperm	This establishes how many permutations of expression against genotype will be performed for this process.
innerFilt	function immediately applied to generated smlSet instances

outerFilt function applied to generated smlSet instances after clipPCs and MAFfilter are applied in that order

Details

The purpose of richNull is to obtain realizations from the permutation distribution of cis-eQTL association statistics, binding information on the characteristics of the optimal results with the scores. This allows us to use conditioning with the realizations from the permutation distribution.

Value

richNull returns a list of nperm mcwBestCis instances with additional metadata bound in

Author(s)

Vince Carey <stvjc@channing.harvard.edu>

sampsInVCF	<i>enumerate samples available in a VCF file</i>
------------	--

Description

enumerate samples available in a VCF file

Usage

```
sampsInVCF(tf)
```

Arguments

tf instance of [TabixFile](#) referring to a tabix-indexed VCF

Value

vector of available sample identifiers

Note

This package exports [TabixFile](#) for the sake of the example below.

Examples

```
tf = TabixFile(system.file("vcf/CEU.exon.2010_09.genotypes.vcf.gz", package="GGtools"))
sampsInVCF(tf)
```

scoresCis	<i>visualize a gene model with cis-eQTL association scores (-log FDR by default) on the basis of a ciseqByCluster data.table output</i>
-----------	---

Description

visualize a gene model with cis-eQTL association scores (-log FDR by default) on the basis of a ciseqByCluster data.table output

Usage

```
scoresCis(sym = "ORMDL3", cisRun,
  cisannopk = "lumiHumanAll.db", radius = 1e+05, pad = 1000,
  txScore = function(x) -log10(x + (1e-05)), ylim = c(0, 4),
  genometag = "hg19", plot.it = TRUE, laxistag = "-log10 FDR: ", ...)
```

Arguments

sym	gene symbol to be resolved into probe id using cisannopk
cisRun	data.table output of ciseqByCluster
cisannopk	Annotation resource, often a ChipDb instance
radius	radius to be added to gene model for display, should typically agree with that used in the search
pad	some extra space
txScore	function that will transform fdr for rendering
ylim	vertical limits for fdr display
genometag	coordinates from this build of genome
plot.it	logical dictating whether plotTracks will be run
laxistag	token used to tell what units are used on vertical axis
...	not used

Value

a list of Gviz tracks, invisibly returned

See Also

The Bioconductor workflow on cloud-enabled cis-eQTL analysis.

sensanal	<i>Summarize information from a collection of eQTL searches for sensitivity assessment</i>
----------	--

Description

Summarize information from a collection of eQTL searches for sensitivity assessment

Usage

```
sensanal(object, fdrbound)
```

Arguments

object	instance of sensiCisInput-class
fdrbound	numeric upper bound on FDR for declarations of eQTL yield

Details

Sensitivity analysis for cis-eQTL search involves checking effects of scope of search, allele frequency filtering, and adjustment for expression heterogeneity on eQTL declarations. In this version, we focus on collections of outputs of [best.cis.eQTLs](#), to which the values of tuning parameters are bound. These collections are identified in a [sensiCisInput-class](#) instance, and the `sensanal` function processes these outputs into a [sensiCisOutput-class](#) instance for tabulation and visualization.

Value

a [sensiCisOutput-class](#) instance

Author(s)

VJ Carey <stvjc@channing.harvard.edu>

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

Description

Manage references to collections of cis-eQTL searches for sensitivity analysis.

Objects from the Class

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

Slots

cisMgrFiles: Object of class "character": a vector of filenames, each file is an instance of class [mcwBestCis-class](#)

cisMgrProperties: Object of class "list" one vector with named elements per element of cisMgrFiles, with components rad, excl, maf, nperm, npc; see details below.

probeannopk: Object of class "character", identifying a bioconductor probe annotation package that can be used to map probe identifiers to other vocabularies or feature value sets

Methods

sensanal signature(object = "sensiCisInput", fdrbound = "numeric"): generates an instance of [sensiCisOutput-class](#) with summarization of sensitivities

show signature(object = "sensiCisInput"): concise rendering

Note

This version of sensitivity analysis support is rudimentary and involves manual construction of metadata that should be extractable from analysis outputs. The radius of the cis search (and radius of excluded interior if used) are identified as elements named rad and excl in the cisMgrProperties vectors; additional elements maf, nperm, and npc define the lower bound for minor allele frequency, number of permutations for plug-in FDR computation, and number of principal components removed to adjust for expression heterogeneity in the associated cis-eQTL search.

Examples

```
showClass("sensiCisInput")
```

```
sensiCisOutput-class  Class "sensiCisOutput"
```

Description

This class helps to manage the results from a collection of cis-eQTL searches.

Objects from the Class

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

Slots

byGene: Object of class "GRanges", organized to provide ranges for genes and their best associated cis SNP

bySNP: Object of class "GRanges" organized to provide easy access to genomic coordinates of SNP found to be most strongly associated with a gene in cis

tabAtFDRB: Object of class "ANY" a flattened table that defines tuning parameters and eQTL yield for a collection of searches

input: Object of class "sensiCisInput" : object that describes the files and parameter settings used for the sensitivity analysis

thecall: Object of class "call": the call generating this instance

fdrbound: Object of class "numeric": gives the upper bound on FDR for declaring an eQTL

sessionInfo: Object of class "ANY": describes state of system in which the object was made.

Methods

show signature(object = "sensiCisOutput"): concise rendering with hints

Author(s)

VJ Carey <stvjc@channing.harvard.edu>

Examples

```
showClass("sensiCisOutput")
```

simpleTiling	<i>create a GRanges with a tiling of the human genome</i>
--------------	---

Description

create a GRanges with a tiling of the human genome

Usage

```
simpleTiling(ntile)
```

Arguments

ntile

Examples

```
##---- Should be DIRECTLY executable !! ----
##-- ==> Define data, use random,
##--or do help(data=index) for the standard data sets.

## The function is currently defined as
function (ntile)
{
  require(Homo.sapiens)
  hsi = seqinfo(Homo.sapiens)[paste0("chr", 1:22), ]
  GenomicRanges::unlist(tileGenome(hsi, ntile = 100))
}
```

snplocsDefault	<i>name the default SNPlocs.Hsapiens.dbSNP.* package</i>
----------------	--

Description

generate a string naming the default SNPlocs.Hsapiens.dbSNP.* package for use with GGtools

Usage

```
snplocsDefault()
```

Details

allows centralized specification of SNPlocs resource package

Value

a character string, see example

Examples

```
snplocsDefault()
```

strMultiPop	<i>serialization of a table from Stranger's multipopulation eQTL report</i>
-------------	---

Description

serialization of a table from Stranger's multipopulation eQTL report

Usage

```
data(strMultiPop)
```

Format

A data frame with 39649 observations on the following 12 variables.

rsid a factor with levels rs...

genesym a factor with levels 37865 39692 ABC1 ABCD2 ABHD4 ACAS2 ...

illv1pid a factor with levels GI_10047105-S GI_10092611-A GI_10190705-S GI_10567821-S
GI_10835118-S GI_10835186-S ...

snpChr a numeric vector

snpCoordB35 a numeric vector

probeMidCoorB35 a numeric vector

snp2probe a numeric vector
 minuslog10p a numeric vector
 adjR2 a numeric vector
 assocGrad a numeric vector
 permThresh a numeric vector
 popSet a factor with levels CEU-CHB-JPT CEU-CHB-JPT-YRI CHB-JPT

Details

imported from the PDF(!) distributed by Stranger et al as supplement to PMID 17873874

Source

PMID 17873874 supplement

References

PMID 17873874 supplement

Examples

```
data(strMultiPop)
strMultiPop[1:2,]
```

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

Description

Instances from this class can be input to the transScores function to control a trans-eQTL search.

Objects from the Class

Instances from this class can be input to the transScores function to control a trans-eQTL search. Objects can be created by calls of the form `new("TransConfig")`.

Slots

snpchr: Object of class "character" identifies the name of the chromosome harboring SNP that will all be used (subject to filtering by `smFilter` function) in transcriptome-wide searches for associated transcripts
gbuFSIZE: Object of class "integer", scores for the top `gbuFSIZE` genes are retained as the search proceeds
batchsize: Object of class "integer" used in processing ff-based archives for association scores
smpack: Object of class "character", tells the name of the installed package used for retrieval of expression-genotype data using `getSS`

rhs: Object of class "formula", formula used in `snp.rhs.tests`; typically not used. If plug-in FDR is desired, adjustments should be executed in a `regressOut` call .

folderStem: Object of class "character", name of a folder where interim results are sequestered.

radius: Object of class "integer", defines region around SNP within which genes are considered 'cis' so tests are not conducted.

shortfac: Object of class "integer" see documentation for [CisConfig-class](#)

chrnames: Object of class "character" see documentation for [CisConfig-class](#)

smchrpref: Object of class "character" see documentation for [CisConfig-class](#)

chrpref: Object of class "character" see documentation for [CisConfig-class](#)

schrpref: Object of class "character" see documentation for [CisConfig-class](#)

geneApply: Object of class "function" see documentation for [CisConfig-class](#)

geneannopk: Object of class "character" see documentation for [CisConfig-class](#)

snpannopk: Object of class "character" see documentation for [CisConfig-class](#)

smFilter: Object of class "function" see documentation for [CisConfig-class](#)

exFilter: Object of class "function" see documentation for [CisConfig-class](#)

keepMapCache: Object of class "logical" see documentation for [CisConfig-class](#)

SSgen: Object of class "function" see documentation for [CisConfig-class](#)

excludeRadius: Object of class "integerOrNULL" see documentation for [CisConfig-class](#)

estimates: Object of class "logical" see documentation for [CisConfig-class](#)

Extends

Class "[CisConfig](#)", directly.

Methods

batchsize signature(x = "TransConfig"): ...

batchsize<- signature(object = "TransConfig", value = "integer"): ...

gbufsize signature(x = "TransConfig"): ...

gbufsize<- signature(object = "TransConfig", value = "integer"): ...

show signature(object = "TransConfig"): ...

snpchr signature(x = "TransConfig"): ...

snpchr<- signature(object = "TransConfig", value = "character"): ...

Examples

```
showClass("TransConfig")
```

transeqByCluster *convenience functions for trans-eQTL testing*

Description

convenience functions for trans-eQTL testing, one assuming a parallel-based cluster instance is available, one assuming a chromosome's SNPs will all be candidates for testing

Usage

```
transeqByCluster(cl,
  snpchrs = c("chr21", "chr22"),
  exchrs = 1:22, baseconf,
  targname = "transrun_", nperm = 1, inseed = 1234, ...)
```

```
transeqByChrom(snpchr = "chr22",
  exchrs = 1:22, baseconf, targname = "transrun_",
  nperm = 1, inseed = 1234, ...)
```

Arguments

cl	cluster instance as defined by the parallel package makeCluster API
snpchrs	character vector of tokens to be used to enumerate chromosomes harboring SNP for testing
snpchr	character atom, for transeqByChrom, the chromosome on which testing will be conducted
exchrs	enumeration of chromosomes harboring expression measures to be checked for trans association with SNPs
baseconf	an instance of TransConfig-class
targname	folder where scratch results are computed
nperm	number of permutations to be used for plug-in FDR
inseed	seed to be set before permutations are attempted, in conjunction with RNGkind("L'Ecuyer-CMRG")
...	not used

Details

the [TransConfig-class](#) instance determines most of the details of the testing procedure

Value

a data.frame with test results as chisq, and permScore* with scores obtained after permuting expression against genotype

transManager-class *Class "transManager"*

Description

simple container for manager of transScores output

Objects from the Class

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

Slots

base: Object of class "list" includes ff references for scores and indices of genes corresponding to scores, and other metadata about the run

Methods

show signature(object = "transManager"): simple reporter

See Also

[transTab](#)

Examples

```
showClass("transManager")
```

transScores *obtain the top trans associations for each SNP in an smlSet*

Description

obtain the top trans associations for each SNP in an smlSet

Usage

```
transScores( tconfig )
```

```
transScores.legacy(smpack, snpchr = "chr1", rhs, K = 20, targdirpref = "tsco", geneApply = lapply,
  chrnames = paste("chr", as.character(1:22), sep = ""), geneRanges = NULL, snpRanges = NULL,
  radius = 2e+06, renameChrs = NULL, probesToKeep = NULL, batchsize = 200,
  genegran = 50, shortfac = 10, wrapperEndo = NULL,
  geneannopk = "illuminaHumanv1.db",
  snpannopk = snplocsDefault(), gchrpref = "",
  schrpref = "ch", exFilter=function(x)x,
```

```

smFilter=function(x)x,
SSgen=GGBase::getSS)

meta.transScores (smpackvec = c("GGdata", "hmyriB36"),
  snpchr = "22", rhsList=list(~1, ~1), K = 20, targdirpref = "mtsco",
  geneApply = lapply, chrnames = as.character(21:22),
  radius = 2e+06, renameChrs=NULL,
  probesToKeep=NULL, batchsize=200, genegran=50, shortfac=10, wrapperEndo=NULL,
  geneannopk = "illuminaHumanv1.db", snpannopk = snplocsDefault(),
  gchrpref = "", schrpref="ch",
  exFilterList= list(function(x)x, function(x)x),
  SMFilterList = list(function(x)x, function(x)x),
  SSgen = GGBase::getSS)

```

Arguments

tconfig	instance of TransConfig-class
smpack	name of package holding eset.rda providing 'ex' ExpressionSet when loaded, and holding SnpMatrix instances in inst/parts
smpackvec	vector of names of package holding eset.rda providing 'ex' ExpressionSet when loaded, and holding SnpMatrix instances in inst/parts
snpchr	name or vector of chromosome names of SNPs of interest
rhs	right hand side of snp.rhs.tests model for which expression is left hand side, e.g., covariates other than genotype
rhsList	list of right hand side of snp.rhs.tests model for which expression is left hand side, e.g., covariates other than genotype, one per element of smpackvec
K	number of most highly associated features to be retained
targdirpref	prefix of target folder name (passed to eqtlTests)
geneApply	passed to eqtlTests
chrnames	names of chromosomes harboring genes that will be tested for association with genotype
geneRanges	list of GRanges-class instances containing chromosomal coordinate defined regions occupied by genes, with regions partitioned by chromosomes, and list element names as given in chrnames above
snpRanges	list of GRanges-class instances with SNP addresses
radius	radius within which an association is considered cis and therefore the corresponding test statistic is set to zero
renameChrs	passed to getSS
probesToKeep	passed to getSS
batchsize	defines batch size for ffrowapply
genegran	passed to eqtlTests
shortfac	passed to eqtlTests

wrapperEndo	a function accepting and returning an smlSet instance, evaluated before numerical analysis of associations, which will be executed on the output of this function
gchrpref	prefix to convert chrnames into appropriate tokens for obtaining gene metadata; in future this may need to be a string transformation function
schrpref	prefix to convert chrnames into appropriate tokens for use with getSNPLocs for the SNP location information package identified in snpannopack parameter below
geneannopk	character string naming a Bioconductor .db expression chip annotation package
snpannopk	character string naming a Bioconductor SNPLocs.* SNP metadata package
exFilter	function to transform ExpressionSet component of retrieved smlSet, to reduce probe sets in use, for example
smFilter	function to transform smlSet instance before use; filter can affect genotypes in smList(x)[[1]], for example
exFilterList	list of functions serving as exFilters for each of the elements of smpackvec
SMFilterList	list of functions servicing as wrapperEndos for each of the elements of smpackvec
SSgen	function to be used to create smlSet instance for testing – in general, GG-Base::getSS has been used to pull the ExpressionSet and SnpMatrix data from a named package, but in some cases a specialize task is needed to create the desired smlSet. Whatever is passed to SSgen must return an smlSet instance.

Value

a list with elements	
scores	an S by K ff matrix where S is number of SNPs, K is number of best features to be retained, with element s,k the kth largest score statistic among association tests computed for SNP s
inds	an S by K ff matrix with s,k element telling which element of guniv (see below) is the gene giving the kth largest score statistic for association
guniv	the vector of gene identifiers defining the universe of genes tested
snpname	vector of SNP identifiers
call	the call used to create the result

Author(s)

VJ Carey <stvjc@channing.harvard.edu>

Examples

```
## Not run:
library(GGdata)
# need to define the geneRanges and snpRanges ...
transScores("GGdata", "20", renameChrs="chr20", chrnames="chr21")

## End(Not run)
```

transTab	<i>tabulate results of transScores run</i>
----------	--

Description

tabulate results of transScores run

Usage

```
transTab(x, snps2keep, ...)
```

Arguments

x	a transManager instance.
snps2keep	character vector used for filtering snps whose scores will be retained; intersection with snps named in x will be used.
...	not used

Value

data.frame instance

Author(s)

VJ Carey <stvjc@channing.harvard.edu>

vcf2sm	<i>generate a SnpMatrix instance on the basis of a VCF (4.0) file</i>
--------	---

Description

generate a SnpMatrix instance on the basis of a VCF (4.0) file.

Usage

```
vcf2sm(tbxfi, ..., gr, nmetacol)
```

Arguments

tbxfi	instance of TabixFile-class
...	not used
gr	instance of GRanges-class
nmetacol	numeric: tells number of columns used in each record as locus-level metadata

Details

This function is relevant only for diallelic SNP. If any base call is denoted '.', the associated genotype is set to missing (raw 0), even if the nonmissing call is ALT, implying at least one ALT.

Value

an instance of `SnpMatrix-class`

Author(s)

VJ Carey <stvjc@channing.harvard.edu>

References

http://www.1000genomes.org/wiki/doku.php?id=1000_genomes:analysis:vcf4.0

Examples

```
# SRC: ftp://ftp.1000genomes.ebi.ac.uk/vol1/ftp/pilot_data/release/2010_07/exon/CEU.exon.2010_03.genotypes.vcf.gz
vref = system.file("vcf/CEU.exon.2010_09.genotypes.vcf.gz", package="GGtools")
gg = GenomicRanges::GRanges(seqnames="1", IRanges::IRanges(10e6,20e6))
vcf2sm(Rsamtools::TabixFile(vref), gr=gg, nmetacol=9L)
```

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