

Package ‘gwascat’

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Title representing and modeling data in the EMBL-EBI GWAS catalog

Version 2.15.0

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Description Represent and model data in the EMBL-EBI GWAS catalog.

Enhances SNPlocs.Hsapiens.dbSNP144.GRCh37

Depends R (>= 3.5.0), Homo.sapiens

Imports methods, BiocGenerics, S4Vectors (>= 0.9.25), IRanges, GenomeInfoDb, GenomicRanges (>= 1.29.6), snpStats, Biostrings, Rsamtools, rtracklayer, gQTLstats, Gviz, VariantAnnotation, AnnotationHub, AnnotationDbi, GenomicFeatures, graph, ggbio, ggplot2, SummarizedExperiment

Suggests DO.db, DT, utils, knitr, RBGL, RUnit

VignetteBuilder utils, knitr

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

License Artistic-2.0

LazyData no

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gwascat-package	<i>representing and modeling data in the NHGRI GWAS catalog</i>
-----------------	---

Description

representing and modeling data in the NHGRI GWAS catalog, using GRanges and allied infrastructure

Details

```

Package:    gwascat
Version:    1.7.3
Suggests:
Depends:    R (>= 3.0.0), methods, IRanges, GenomicRanges
Imports:
License:    Artistic-2.0
LazyLoad:   yes

```

Index:

```
gwaswloc-class      Class "gwaswloc"
```

The GWAS catalog management has migrated to EMBL/EBI. Use `data(ebicat38)` for an image dated 3 August 2015. Use `makeCurrentGwascat()` to get a more recent image. Use `data(ebicat37)` for a GRCh37 (or hg19) liftOver result. Use `data(ebicat37UCSC)` for an image with hg19 as genome tag and UCSC seqnames.

The data objects

```
'g17SM' 'gg17N' 'gw6.rs_17' 'low17' 'rules_6.0_1kg_17' 'gwrngs'
```

are described in vignettes.

The `DataFrame` function is imported from `IRanges`.

The `SnpMatrix-class` is used to represent data related to rule-based imputation, using the `impute.snps` function.

`si.hs.38` is a `Seqinfo-class` instance for hg38.

`nodeData` (and `nodes`, `ugraph`, `subGraph`, `adj`) are exported for use in the vignettes.

Author(s)

VJ Carey <stvjc@channing.harvard.edu>

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

References

<http://www.ebi.ac.uk/gwas/>

Partial support from the Computational Biology Group at Genentech, Inc.

Examples

```
data(ebicat38)
ebicat38
```

bindcadd_snv	<i>bind CADD scores of Kircher et al. 2014 to a GRanges instance</i>
--------------	--

Description

bind CADD scores of Kircher et al. 2014 to a GRanges instance; by default will use HTTP access at UW

Usage

```
bindcadd_snv(gr, fn = "http://krishna.gs.washington.edu/download/CADD/v1.0/1000G.tsv.gz")
```

Arguments

gr	query ranges to which CADD scores should be bound
fn	path to Tabix-indexed bgzipped TSV of CADD as distributed at krishna.gs.washington.edu on 1 April 2014

Details

joins CADD fields at addresses that match query; the CADD fields for query ranges that are not matched are set to NA

Value

GRanges instance with additional fields as obtained in the CADD resource

Note

This software developed in part with support from Genentech, Inc.

Author(s)

VJ Carey <stvjc@channing.harvard.edu>

References

M Kircher, DM Witten, P Jain, BJ O’Roak, GM Cooper, J Shendure, A general framework for estimating the relative pathogenicity of human genetic variants, Nature Genetics Feb 2014, PMID 24487276

Examples

```

if (interactive()) {
  data(ebicat37)
  g2 = as(ebicat37, "GRanges")
  bindcadd_snv( g2[which(seqnames(g2)=="chr2")][1:20] )
}

```

gwastagger

data on 1000 genomes SNPs that 'tag' GWAS catalog entries

Description

data on 1000 genomes SNPs that 'tag' GWAS catalog entries

Usage

```
data(gwastagger)
```

Format

The format is:

```

Formal class 'GRanges' [package "GenomicRanges"] with 6 slots
..@ seqnames :Formal class 'Rle' [package "IRanges"] with 4 slots
.. ..@ values : Factor w/ 24 levels "chr1","chr2",...: 1 2 3 4 5 6 7 8 9 10 ...
.. ..@ lengths : int [1:22] 24042 23740 21522 14258 14972 34101 12330 11400 8680 15429 ...
.. ..@ elementMetadata: NULL
.. ..@ metadata : list()
..@ ranges :Formal class 'IRanges' [package "IRanges"] with 6 slots
.. ..@ start : int [1:297579] 986111 988364 992250 992402 995669 999686 1005579 1007450
1011209 1011446 ...
.. ..@ width : int [1:297579] 1 1 1 1 1 1 1 1 1 1 ...
.. ..@ 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 297579
.. ..@ elementMetadata: NULL
.. ..@ metadata : list()
..@ elementMetadata:Formal class 'DataFrame' [package "IRanges"] with 6 slots
.. ..@ rownames : NULL
.. ..@ nrows : int 297579
.. ..@ listData :List of 3
.. .. ..$ tagid : chr [1:297579] "rs28479311" "rs3813193" "chr1:992250" "rs60442576" ...
.. .. ..$ R2 : num [1:297579] 0.938 0.994 0.969 1 1 ...
.. .. ..$ baseid : chr [1:297579] "rs3934834" "rs3934834" "rs3934834" "rs3934834" ...
.. ..@ elementType : chr "ANY"
.. ..@ elementMetadata: NULL
.. ..@ metadata : list()
..@ seqinfo :Formal class 'Seqinfo' [package "GenomicRanges"] with 4 slots

```

```

.. ..@ seqnames : chr [1:24] "chr1" "chr2" "chr3" "chr4" ...
.. ..@ seqlengths : int [1:24] 249250621 243199373 198022430 191154276 180915260 171115067
159138663 146364022 141213431 135534747 ...
.. ..@ is_circular: logi [1:24] FALSE FALSE FALSE FALSE FALSE FALSE ...
.. ..@ genome : chr [1:24] "hg19" "hg19" "hg19" "hg19" ...
..@ metadata : list()

```

Details

This GRanges instance includes locations for 297000 1000 genomes SNP that have been identified as exhibiting LD with NHGRI GWAS SNP as of September 2013. The tagid field tells the name of the tagging SNP, the baseid field is the SNP identifier for the GWAS catalog entry, the R2 field tells the value of R-squared relating the distributions of the tagging SNP and the GWAS entry. Only tagging SNP with R-squared 0.8 or greater are included. A self-contained R-based procedure should emerge in 2014.

Source

NHGRI GWAS catalog; plink is used with the 1000 genomes VCF in a perl routine by Michael McGeachie, Harvard Medical School;

Examples

```

data(gwastagger)
gwastagger[1:5]
data(ebicat37)
mean(ebicat37$SNPS %in% gwastagger$baseid)
# ideally, all GWAS SNP would be in our tagging ranges as baseid
query <- setdiff(ebicat37$SNPS, gwastagger$baseid)
# relatively recent catalog additions
sort(table(ebicat37[which(ebicat37$SNPS %in% query)]$DATE.ADDED.TO.CATALOG), decreasing=TRUE)[1:10]

```

gwaswloc-class

Class "gwaswloc"

Description

A container for GRanges instances representing information in the NHGRI GWAS catalog.

Objects from the Class

Objects can be created by calls of the form `new("gwaswloc", ...)`. Any GRanges instance can be supplied.

Slots

extractDate: character set manually in .onAttach code to indicate date of retrieval of base table
seqnames: Object of class "Rle" typically representing chromosome numbers of loci associated with specific traits
ranges: Object of class "IRanges" genomic coordinates for locus
strand: Object of class "Rle" identifier of chromosome strand

elementMetadata: Object of class "DataFrame" general [DataFrame-class](#) instance providing attributes for the locus-trait association

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 "[GenomicRanges_OR_missing](#)", by class "GRanges", distance 3. Class "[GenomicRanges_OR_GRangesList](#)", by class "GRanges", distance 3. Class "[Annotated](#)", by class "GRanges", distance 4.

Methods

[**signature**(x = "gwaswloc"): a character argument to the bracket will be assumed to be a dbSNP identifier for a SNP locus, and records corresponding to this SNP are extracted; numeric indexes are supported as for [GRanges-class](#) instances.

getRsids **signature**(x = "gwaswloc"): extract all dbSNP identifiers as a character vector

getTraits **signature**(x = "gwaswloc"): extract all traits (NHGRI term 'Disease/Trait') as a character vector

subsetByChromosome **signature**(x = "gwaswloc"): select records by chromosome, a vector of chromosomes may be supplied

subsetByTraits **signature**(x = "gwaswloc"): select all records corresponding to a given vector of traits

Note

In gwascat package 1.9.6 and earlier, the globally accessible gwaswloc instance gwrngs was created upon attachment. This is no longer the case.

Author(s)

VJ Carey <stvjc@channing.harvard.edu>

References

<http://www.ebi.ac.uk/gwas/>

Examples

```
showClass("gwaswloc")
```

 gwce2gviz

Prepare salient components of GWAS catalog for rendering with Gviz

Description

Prepare salient components of GWAS catalog for rendering with Gviz

Usage

```
gwce2gviz(basegr, contextGR = GRanges(seqnames =
  "chr17", IRanges(start = 37500000, width = 1e+06)),
  txrefpk = "TxDb.Hsapiens.UCSC.hg19.knownGene", genome
  = "hg19", genesympk = "Homo.sapiens", plot.it = TRUE,
  maxmlp = 25)
```

Arguments

basegr	gwaswloc instance containing information about GWAS in catalog
contextGR	A GRanges instance delimiting the visualization in genomic coordinates
txrefpk	a TxDb package, typically
genesympk	string naming annotationDbi .db package
genome	character tag like 'hg19'
plot.it	logical, if FALSE, just return list
maxmlp	maximum value of $-10 \log p$ – winsorization of all larger values is performed, modifying the contents of Pvalue_mlp in the elementMetadata for the call

Examples

```
args(gwce2gviz)
#gwascat:::onAttach("", "gwascat")
data(ebicat37)
seqlevelsStyle(ebicat37) = "UCSC"
gwce2gviz(ebicat37)
```

 gwdf_2012_02_02

internal data frame for NHGRI GWAS catalog

Description

convenience container for imported table from NHGRI GWAS catalog

Usage

```
data("gwdf_2014_09_08")
```

Format

A data frame with 17832 observations on the following 34 variables.

'Date Added to Catalog' a character vector

PUBMEDID a numeric vector

'First Author' a character vector

Date a character vector

Journal a character vector

Link a character vector

Study a character vector

'Disease/Trait' a character vector

'Initial Sample Size' a character vector

'Replication Sample Size' a character vector

Region a character vector

Chr_id a character vector

Chr_pos a character vector

'Reported Gene(s)' a character vector

Mapped_gene a character vector

Upstream_gene_id a character vector

Downstream_gene_id a character vector

Snps_gene_ids a character vector

Upstream_gene_distance a character vector

Downstream_gene_distance a character vector

'Strongest SNP-Risk Allele' a character vector

SNPs a character vector

Merged a character vector

Snps_id_current a character vector

Context a character vector

Intergenic a character vector

'Risk Allele Frequency' a character vector

'p-Value' a character vector

Pvalue_mlog a character vector

'p-Value (text)' a character vector

'OR or beta' a character vector

'95% CI (text)' a character vector

'Platform [SNPs passing QC]' a character vector

CNV a character vector

Note

In versions prior to 1.9.6, The `.onAttach` function specifies which data frame is transformed to GRanges. This is now managed manually.

Source

<http://www.ebi.ac.uk/gwas/>

Examples

```
## Not run:
data(gwdf_2014_09_08)
# try gwascats::gwdf2GRanges on this data.frame

## End(Not run)
```

ldtagr	<i>expand a list of variants by including those in a VCF with LD exceeding some threshold</i>
--------	---

Description

expand a list of variants by including those in a VCF with LD exceeding some threshold

Usage

```
ldtagr(snprng, tf, samples, genome = "hg19", lbmaf = 0.05, lbR2 = 0.8, radius = 1e+05)
```

Arguments

snprng	a named GRanges for a single SNP. The name must correspond to the name that will be assigned by <code>genotypeToSnpMatrix</code> to the corresponding column of a SnpMatrix.
tf	TabixFile instance pointing to a bgzipped tabix-indexed VCF file
samples	a vector of sample identifiers, if excluded, all samples used
genome	tag like 'hg19'
lbmaf	lower bound on variant MAF to allow consideration
lbR2	lower bound on R squared for regarding SNP to be incorporated
radius	radius of search in bp around the input range

Details

uses `snpStats ld()`

Value

a GRanges with names corresponding to 'new' variants and mcols fields 'paramRangeID' (base variant input) and 'R2'

Note

slow but safe approach. probably a matrix method could be substituted using the nice sparse approach already in `snpStats`

Author(s)

VJ Carey

Examples

```
require(GenomicRanges)
cand = GRanges("1", IRanges(113038694, width=1))
names(cand) = "rs883593"
require(VariantAnnotation)
expath = dir(system.file("vcf", package="gwascat"), patt=".*exon.*gz$", full=TRUE)
tf = TabixFile(expath)
ldtagr( cand, tf, lbR2 = .8)
# should do with 1000 genomes in S3 bucket and gwascat
```

locon6

location information for 10000 SNPs probed on Affy GW 6.0

Description

location information for 10000 SNPs probed on Affy GW 6.0

Usage

```
data(locon6)
```

Format

A data frame with 10000 observations on the following 3 variables.

dbsnp_rs_id a character vector

chrom a character vector

physical_pos a numeric vector

Details

extracted from pd.genomewidesnp.6 v 1.4.0; for demonstration purposes

Examples

```
data(locon6)
str(locon6)
```

makeCurrentGwascat	<i>read NHGRI GWAS catalog table and construct associated GRanges instance</i>
--------------------	--

Description

read NHGRI table and construct associated GRanges instance

Usage

```
makeCurrentGwascat(table.url =  
  "http://www.ebi.ac.uk/gwas/api/search/downloads/alternative",  
  fixNonASCII = TRUE, genome="GRCh38",  
  withOnt = TRUE)
```

Arguments

table.url	string identifying the .txt file curated at EBI/EMBL
fixNonASCII	logical, if TRUE, non-ASCII characters as identified by iconv will be replaced by asterisk
genome	character string: 'GRCh38' is default and yields current image as provided by EMBL/EBI; 'GRCh37' yields a realtime liftOver to hg19 coordinates, via AnnotationHub storage of the chain files. Any other value yields an error.
withOnt	logical indicating whether 'alternative' (ontology-present, includes repetition of loci with one:many ontological mapping) or 'full' (ontology-absent, one record per locus report) version of distributed table

Details

records for which clear genomic position cannot be determined are dropped from the ranges instance
an effort is made to use reasonable data types for GRanges metadata, so some qualifying characters such as (EA) in Risk allele frequency field will simply be omitted during coercion of contents of that field to numeric.

Value

a GRanges instance

Author(s)

VJ Carey

Examples

```
# if you have good internet access  
if (interactive()) {  
  newcatr = makeCurrentGwascat()  
  newcatr  
}
```

obo2graphNEL	<i>convert a typical OBO text file to a graphNEL instance (using Term elements)</i>
--------------	---

Description

convert a typical OBO text file to a graphNEL instance (using Term elements)

Usage

```
obo2graphNEL(obo, kill = "\\[Typedef\\]", killTrailSp=TRUE)
node2uri(nn)
uri2node(us)
```

Arguments

obo	string naming a file in OBO format
nn	node name for converted graph, generally of form EFO:nnnnnnn
us	URI string from GWAS catalog annotation MAPPED_TRAIT_URI
kill	entity types to be excluded from processing – probably this should be in a 'keep' form, but for now this works.
killTrailSp	In the textual version of EFO ca. Aug 2015, there is a trailing blank in the tag field defining EFO:0000001, which is not present in references to this term. Set this to TRUE to eliminate this, or graphNEL construction will fail to validate.

Details

Very rudimentary list and grep operations are used to retain sufficient information to map the DAG to a graphNEL, using formal term identifiers as node names and 'is-a' relationships as edges, and term names and other metadata are assigned to nodeData components.

Value

a graphNEL instance

Note

The OBO for Human Disease ontology is serialized as text with this package.

Author(s)

VJ Carey <stvjc@channing.harvard.edu>

References

For use with human disease ontology, http://www.obofoundry.org/cgi-bin/detail.cgi?id=disease_ontology

Examples

```
data(efo.obo.g)
hn = nodes(efo.obo.g)[1:5]
hn
nodeData(efo.obo.g, hn[5])
```

riskyAlleleCount	<i>given a matrix of subjects x SNP calls, count number of risky alleles</i>
------------------	--

Description

given a matrix of subjects x SNP calls, count number of risky alleles for various conditions, relative to NHGRI GWAS catalog

Usage

```
riskyAlleleCount(callmat, matIsAB = TRUE, chr,
  gwvl , snpap = "SNPlocs.Hsapiens.dbSNP144.GRCh37",
  gencode = c("A/A", "A/B", "B/B"))
```

Arguments

callmat	matrix with subjects as rows, SNPs as columns; entries can be generic A/A, A/B, B/B, or specific nucleotide calls
matIsAB	logical, FALSE if nucleotide codes are present, TRUE if generic call codes are present; in the latter case, <code>gwascat::ABmat2nuc</code> will be run
chr	code for chromosome, should work with the SNP annotation <code>getSNPlocs</code> function, so likely "ch[nn]"
gwvl	an instance of <code>gwaswloc</code>
snpap	name of a Bioconductor <code>SNPlocs.Hsapiens.dbSNP.*</code> package
gencode	codes used for generic SNP call

Value

matrix with rows corresponding to subjects , columns corresponding to SNP

Examples

```
data(gg17N) # translated from GGdata chr 17 calls using ABmat2nuc
data(ebicat37)
library(GenomeInfoDb)
seqlevelsStyle(ebicat37) = "UCSC"
h17 = riskyAlleleCount(gg17N, matIsAB=FALSE, chr="ch17", gwvl=ebicat37)
h17[1:5,1:5]
table(as.numeric(h17))
```

topTraits	<i>operations on GWAS catalog</i>
-----------	-----------------------------------

Description

operations on GWAS catalog

Usage

```
topTraits (gwwl, n=10, tag="DISEASE/TRAIT")  
locs4trait(gwwl, trait, tag="DISEASE/TRAIT")  
chklocs(chrtag="20", gwwl)
```

Arguments

gwwl	instance of gwaswloc
n	numeric, number of traits to report
tag	character, name of field to be used for trait enumeration
trait	character, trait to use for filtering
chrtag	character, chromosome identifier

Value

topTraits returns a character vector of most frequently occurring traits in the database

locs4trait returns a [gwaswloc](#) object with records defining associations to the specified trait

chklocs returns a logical that is TRUE when the asserted locations of SNP in the GWAS catalog agree with the locations given in the dbSNP package SNPlocs.Hsapiens.dbSNP144.GRCh37

Author(s)

VJ Carey <stvjc@channing.harvard.edu>

Examples

```
data(ebicat38)  
topTraits(ebicat38)
```

traitsManh	<i>use ggbio facilities to display GWAS results for selected traits in genomic coordinates</i>
------------	--

Description

use ggbio facilities to display GWAS results for selected traits in genomic coordinates

Usage

```
traitsManh(gwr, selr = GRanges(seqnames = "chr17", IRanges(3e+07, 5e+07)), traits = c("Asthma", "Par"))
```

Arguments

<code>gwr</code>	GRanges instance as managed by the gwaswloc container design, with Disease.Trait and Pvalue_mlog among elementMetadata columns
<code>selr</code>	A GRanges instance to restrict the gwr for visualization. Not tested for noncontiguous regions.
<code>traits</code>	Character vector of traits to be exhibited; GWAS results with traits not among these will be labeled "other".
<code>truncmlp</code>	Maximum value of $-\log_{10} p$ to be displayed; in the raw data this ranges to the hundreds and can cause bad compression.
<code>...</code>	not currently used

Details

uses a ggbio autoplot

Value

autoplot value

Note

An xlab is added, concatenating genome tag with seqnames tag.

Author(s)

VJ Carey <stvjc@channing.harvard.edu>

Examples

```
# do a p-value truncation if you want to reduce compression
## Not run: # ggbio July 2018
data(ebicat38)
library(GenomeInfoDb)
seqlevelsStyle(ebicat38) = "UCSC"
traitsManh(ebicat38)

## End(Not run)
```

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