

Package ‘ACME’

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Title Algorithms for Calculating Microarray Enrichment (ACME)

Author Sean Davis <sdavis2@mail.nih.gov>

Maintainer Sean Davis <sdavis2@mail.nih.gov>

Depends R (>= 2.10), Biobase (>= 2.5.5), methods, BiocGenerics

Imports graphics, stats

Description ACME (Algorithms for Calculating Microarray Enrichment) is a set of tools for analysing tiling array ChIP/chip, DNase hypersensitivity, or other experiments that result in regions of the genome showing ``enrichment". It does not rely on a specific array technology (although the array should be a ``tiling" array), is very general (can be applied in experiments resulting in regions of enrichment), and is very insensitive to array noise or normalization methods. It is also very fast and can be applied on whole-genome tiling array experiments quite easily with enough memory.

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ACMECalcSet-class	<i>Class "ACMECalcSet"</i>
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Description

A subclass of [ACMESet](#) that can also store the parameters and results of an ACME calculation

Objects from the Class

Objects can be created by calls of the form `new("ACMECalcSet", assayData, phenoData, featureData, experimentData, annotation, cutpoints, threshold, exprs, vals, ...)`. In addition to the constraints defined by [ACMESet](#), this class can also hold the results (in the `assayDataElement` `vals`) and the threshold and cutpoints from an ACME `do.aGFF.calc` run

Slots

cutpoints: Object of class "numeric" The values of the cutpoints used in an analysis by `do.aGFF.calc`, one per sample.
threshold: Object of class "numeric" The threshold used in an analysis.
assayData: Object of class "AssayData". See [ExpressionSet](#) for details.
phenoData: Object of class "AnnotatedDataFrame" See [ExpressionSet](#) for details.
featureData: Object of class "AnnotatedDataFrame" See [ExpressionSet](#) for details.
experimentData: Object of class "MIAME" See [ExpressionSet](#) for details.
annotation: Object of class "character" See [ExpressionSet](#) for details.
__classVersion__: Object of class "Versions" See [ExpressionSet](#) for details.

Extends

Class "[ACMESet](#)", directly. Class "[ExpressionSet](#)", by class "ACMESet", distance 2. Class "[eSet](#)", by class "ACMESet", distance 3. Class "[VersionedBiobase](#)", by class "ACMESet", distance 4. Class "[Versioned](#)", by class "ACMESet", distance 5.

Methods

cutpoints signature(`x = "ACMECalcSet"`): A simple getter for the cutpoints.
plot signature(`x = "ACMECalcSet"`): A convenience plotting method that also takes sample and chrom
show signature(`object = "ACMECalcSet"`): A show method
threshold signature(`x = "ACMECalcSet"`): A simple getter for the threshold
vals signature(`x = "ACMECalcSet"`): an accessor for the p-values from a run of `do.aGFF.calc`. Returns a matrix with samples in columns and probes in rows.

Author(s)

Sean Davis <sdavis2@mail.nih.gov>

See Also

[ACMESet](#)

Examples

```
showClass("ACMECalcSet")
data(example.agff)
b <- do.aGFF.calc(example.agff, thresh=0.95, window=1000)
b
head(vals(b))
threshold(b)
cutpoints(b)
```

ACMESet-class

Class "ACMESet"

Description

An extension of ExpressionSet to deal with ACME data including chromosome locations

Objects from the Class

Objects can be created by calls of the form `new("ACMESet", assayData, phenoData, featureData, experimentData, annotation, exprs, ...)`. The `exprs` assayDataElement stores the data. The `featureData` slot stores the chromosome location. In practice, the `data.frame` underlying the `featureData` MUST contain three columns named `chromosome`, `start`, and `end`; this is enforced by the class validity method.

Slots

assayData: Object of class "AssayData". See [ExpressionSet](#) for details.
phenoData: Object of class "AnnotatedDataFrame" See [ExpressionSet](#) for details.
featureData: Object of class "AnnotatedDataFrame" See [ExpressionSet](#) for details.
experimentData: Object of class "MIAME" See [ExpressionSet](#) for details.
annotation: Object of class "character" See [ExpressionSet](#) for details.
__classVersion__: Object of class "Versions" See [ExpressionSet](#) for details.

Extends

Class "[ExpressionSet](#)", directly. Class "[eSet](#)", by class "ExpressionSet", distance 2. Class "[VersionedBiobase](#)", by class "ExpressionSet", distance 3. Class "[Versioned](#)", by class "ExpressionSet", distance 4.

Methods

- chromosome** signature(object = "ACMESet"): Accessor for the chromosome. Returns a vector of chromosomes.
- end** signature(x = "ACMESet"): Accessor for the end location for a probe. If that is not known, this could be set to the same value as the start location.
- plot** signature(x = "ACMESet"): A convenience plotting method that takes a sample name and chrom as well.
- start** signature(x = "ACMESet"): Accessor for the start location for a probe.

Author(s)

Sean Davis <sdavis2@mail.nih.gov>

See Also

[ExpressionSet](#), [ACMECalcSet](#)

Examples

```
showClass("ACMESet")
data(example.agff)
example.agff
head(chromosome(example.agff))
head(start(example.agff))
head(end(example.agff))
```

aGFF-class

Class for storing GFF-like data

Description

The GFF format is quite versatile while remaining simple. This class simply stores the annotation associated with a set of GFF files from the same regions of the genome along with some information about the samples from which the data came and the data (from the "score" column of the GFF file) themselves.

Objects from the Class

Objects can be created by calls of the form `new("aGFF", ...)`. Also, the `read.resultsGFF()` function returns aGFF objects.

Slots

- annotation:** Object of class "data.frame" with two columns absolutely necessary, "Chromosome" and "Location". Other columns can be included.
- data:** Object of class "matrix" of the same number of rows as the annotation slot and the same number of columns as the number of rows in the samples slot, containing data for later analysis
- samples:** Object of class "data.frame" for describing the samples, one row per sample

Methods

plot signature(x = "aGFF"): to plot a region along the genome.

print signature(x = "aGFF"): simple method to display summary of aGFF object

show signature(object = "aGFF"): simple method to display summary of aGFF object

Author(s)

Sean Davis

See Also

[read.resultsGFF](#) and [aGFFCalc-class](#)

Examples

```
# Load an example
data(example.agff)
example.agff
```

aGFFCalc-class

Class "aGFFCalc"

Description

Store results of ACME calculations

Objects from the Class

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

Slots

call: Object of class "call", contains the exact call to `do.aGFF.calc`, for historical purposes

threshold: Object of class "numeric", the threshold used in the calculation

cutpoints: Object of class "numeric", the data value above which probes were considered positive

vals: Object of class "matrix", equivalent in size to the original data matrix, containing the calculated p-values from the ACME algorithm

annotation: Object of class "data.frame", currently a copy of the original annotation, possibly reordered in chromosome order

data: Object of class "matrix", the original data, possibly reordered

samples: Object of class "data.frame", sample metadata

Extends

Class "aGFF", directly.

Methods

plot signature(x = "aGFFCalc", ask=FALSE): plot the results of an ACME calculation
print signature(x = "aGFFCalc"): brief overview of the object
show signature(object = "aGFFCalc"): brief overview of the object

Author(s)

Sean Davis <sdavis2@mail.nih.gov>

See Also

[do.aGFF.calc](#), [aGFF-class](#)

Examples

```
data(example.agff)
example.agffcalc <- do.aGFF.calc(example.agff,window=1000,thresh=0.9)
example.agffcalc
```

do.aGFF.calc	<i>Perform ACME calculation</i>
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Description

This function performs the moving window chi-square calculation. It is written in C, so is quite fast.

Usage

```
do.aGFF.calc(x, window, thresh)
```

Arguments

x	An aGFF class object
window	An integer value, representing the number of basepairs to include in the windowed chi-square calculation
thresh	The quantile of the data distribution for each sample that will be used to classify a probe as positive

Details

A window size on the order of 2-3 times the average size of fragments from sonication, digestion, etc. and containing at least 8-10 probes is the recommended size. Larger size windows are probably more sensitive, but obviously reduce the accuracy with which boundaries of signal can be called.

A threshold of between 0.9 and 0.99 seems empirically to be adequate. If one plots the histogram of data values and there is an obvious better choice (such as a bimodal distribution, with one peak representing enrichment), a more data-driven approach may yield better results.

Value

An object of class aGFFCalc

Author(s)

Sean Davis <sdavis2@mail.nih.gov>

Examples

```
data(example.agff)
example.agffcalc <- do.aGFF.calc(example.agff,window=1000,thresh=0.9)
example.agffcalc
```

example.agff

An example ACME data structure of class ACMESet

Description

An ACMESet data structure from two Nimblegen arrays, custom tiled to include multiple HOX genes.

Usage

```
data(example.agff)
```

Format

The format is: chr "example.agff"

Source

From Scacheri et al., Plot Genet, 2006. Pubmed ID 16604156

Examples

```
data(example.agff)
example.agff
```

findClosestGene

Find closest refseq gene

Description

This function is used to find the nearest refseq transcript(s) to a point in the genome specified. Note that it is limited to the refseq transcripts listed at genome.ucsc.edu, where this function goes for information.

Usage

```
findClosestGene(chrom, pos, genome = "hg17", position = "txStart")
```

Arguments

chrom	Usually specified like 'chr1', 'chr2', etc.
pos	A position in base pairs in the genome
genome	Something like 'hg16', 'hg17', 'mm6', etc.
position	The location to measure distance from: one of 'txStart', 'txEnd', 'cdsStart', 'cdsEnd'

Details

The first time the function is run, it checks to see if the refflat table for the given genome is present in the package environment. If not, it downloads it to the /tmp directory and gunzips it (using [getRefflat](#)). It is then stored so that in future calls, there is no re-download required.

Value

A data frame with the gene name, refseq id(s), txStart, txEnd, cdsStart, cdsEnd, exon count, and distance. Note that distance is measured as pos-position, so negative values mean that the point in the gene is to the left of the point specified in the function call (with the p-tel on the left).

Note

The function may return more than one transcript, as several transcripts may have the same start site

Author(s)

Sean Davis <sdavis2@mail.nih.gov>

Examples

```
findClosestGene('chr1', 100000000, 'hg17')
```

findRegions

Find all regions in data above p-value threshold

Description

After the ACME calculation, each probe is associated with a p-value of enrichment. However, one often wants the contiguous regions associated with runs of p-values above a given p-value threshold.

Usage

```
findRegions(x, thresh = 1e-04)
```

Arguments

x	An ACMESetCalc object
thresh	The p-value threshold

Details

Runs of p-values above the p-value threshold will be reported as one "region". These can be used for downstream analyses, export to browsers, submitted for transcription factor binding enrichment analyses, etc.

Value

A data frame with these columns:

Length	The length of the region in probes
TF	Either TRUE or FALSE; TRUE regions represent regions of enrichment while FALSE regions are the regions between the TRUE regions
StartInd	The starting Index of the region
EndInd	The ending Index of the region
Sample	The sample containing the region
Chromosome	The Chromosome of the region
Start	The starting basepair of the region
End	The ending basepair of the region
Median	The median p-value in the region
Mean	The mean p-value in the region

Author(s)

Sean Davis <sdavis2@mail.nih.gov>

See Also

[do.aGFF.calc](#), [findClosestGene](#)

Examples

```
data(example.agff)
example.agffcalc <- do.aGFF.calc(example.agff,window=1000,thresh=0.9)
foundregions <- findRegions(example.agffcalc,thresh=0.001)
foundregions[1:6,]
```

generics

Generics defined within ACME

Description

See methods descriptions for details.

Usage

```
vals(x, ...)
chromosome(object, ...)
end(x, ...)
start(x, ...)
plot(x, y, ...)
cutpoints(x, ...)
threshold(x, ...)
```

Arguments

<code>x</code>	An ACMESet or ACMECalcSet object (for cutpoints and threshold)
<code>object</code>	An ACMESet or ACMECalcSet object (for cutpoints and threshold)
<code>y</code>	Treated as missing for plotting these types of objects
<code>...</code>	Passed into method

Details

These are all getters for ACMESet and ACMECalcSet objects.

Value

See methods descriptions for details

Author(s)

Sean Davis <sdavis2@mail.nih.gov>

See Also

[ACMESet](#), [ACMECalcSet](#)

Examples

```
data(example.agff)
head(chromosome(example.agff))
head(end(example.agff))
head(start(example.agff))
```

getRefflat

Get the refflat table from ucsc for the given genome

Description

Fetches the refflat table from ucsc, stores in temp dir and then gunzips it and reads it in.

Usage

```
getRefflat(genome = "hg17")
```

Arguments

<code>genome</code>	The genome code from ucsc, like 'hg16', 'mm6', etc.
---------------------	---

Value

A data frame mirroring the UCSC table structure.

Author(s)

Sean Davis <sdavis2@mail.nih.gov>

References

<http://genome.ucsc.edu>

See Also

[findClosestGene](#)

Examples

```
rf <- getRefflat('hg17')
```

read.resultsGFF	<i>Read Nimblegen GFF files</i>
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Description

A GFF format file is a quite flexible format for storing genomic data. Nimblegen uses these format files as one format for making chip-chip data available. This function reads these files, one per experiment and creates a resulting aGFF-class object.

Usage

```
read.resultsGFF(fnames, path = ".", samples = NULL, notes = NULL, skip = 0, sep = "\t", quote = "\"",
```

Arguments

fnames	A vector of filenames
path	The path to the filenames
samples	A data.frame containing sample information, one row per sample, in the same order as the files in fnames
notes	A character vector for notes—not currently stored
skip	Number of lines to skip if the file contains a header
sep	The field separator—should be a tab character for gff files, but can be set if necessary.
quote	The text quote character—again not used for gff file, typically
...	...

Details

The output is an ACMESet object.

Value

A single ACMESet object.

Author(s)

Sean Davis <sdavis2@mail.nih.gov>

References

<http://www.sanger.ac.uk/Software/formats/GFF/>

See Also

[ACMESet](#)

Examples

```
datdir <- system.file('extdata',package='ACME')
fnames <- dir(datdir)
example.agff <- read.resultsGFF(fnames,path=datdir)
```

write.bedGraph	<i>Write bedGraph format tracks for UCSC genome browser</i>
----------------	---

Description

Generate bedGraph format files for the UCSC genome browser. This function will write the bed-Graph files associated with a aGFFcalc object. There will be either one or two files (default two) representing the raw data and the calculated data (which is output as $-\log_{10}(\text{val})$ for visualization purposes for EACH sample).

Usage

```
write.bedGraph(x, raw = TRUE, vals = TRUE, directory = ".")
```

Arguments

x	An ACMESet or ACMECalcSet object
raw	Boolean. Create a file for the raw data?
vals	Boolean. Create a file for the calculated p-values?
directory	Give a directory for storing the files

Author(s)

Sean Davis

Examples

```
data(example.agff)
write.bedGraph(example.agff)
```

write.sgr	<i>Write Affy IGB .sgr format files</i>
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Description

The affy Integrated Genome Browser (IGB) is a powerful, fast browser for genomic data. The file format is simple (three columns: chromosome, location, and score) to generate. This function will write the sgr files associated with a aGFFcalc object. There will be either one or two files (default two) representing the raw data and the calculated data (which is output as $-\log_{10}(\text{val})$ for visualization purposes).

Usage

```
write.sgr(x, raw = TRUE, vals = TRUE, directory = ".")
```

Arguments

x	An ACMESet or ACMECalcSet object
raw	Boolean. Create a file for the raw data?
vals	Boolean. Create a file for the calculated p-values?
directory	Give a directory for storing the files

Author(s)

Sean Davis

Examples

```
data(example.agff)
write.sgr(example.agff)
```

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