Package 'chicane'

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Title Capture Hi-C Analysis Engine

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Description Toolkit for processing and calling interactions in capture Hi-C data. Converts BAM files into counts of reads linking restriction fragments, and identifies pairs of fragments that interact more than expected by chance. Significant interactions are identified by comparing the observed read count to the expected background rate from a count regression model.

Depends R (>= 3.5.0), gamlss.tr, gamlss, data.table

License GPL-2

Encoding UTF-8

LazyData true

biocViews

Imports MASS, stats, foreach, doParallel, iterators, bedr, knitr, rmarkdown

SystemRequirements bedtools

Suggests testthat, GenomicInteractions, GenomicRanges, Gviz, countreg

Additional_repositories http://R-Forge.R-project.org/

VignetteBuilder knitr

RoxygenNote 7.1.1

NeedsCompilation no

Repository CRAN

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R topics documented:

add.covariates *add.covariates*

Description

Add model covariates (trans counts and distance) to an interactions data table.

Usage

```
add.covariates(interaction.data)
```

Arguments

interaction.data	data.table with interaction data. Must contain columns bait.id, target.id, bait.chr, bait.start, bait.end, target.chr, target.start, target.end and count.

Value

Updated data table with new columns

bait.trans.count	number of trans interactions of bait fragment
target.trans.count	number of trans interactions of target fragment
distance	distance between bait and target fragment, or NA if trans

Author(s)

Erle Holgersen <Erle.Holgersen@icr.ac.uk>

Examples

```
data(bre80);
input.cols <- c('bait.id', 'target.id', 'bait.chr', 'bait.start',
'bait.end', 'target.chr', 'target.start', 'target.end', 'count');
output <- add.covariates(bre80[, input.cols, with = FALSE]);
```

`add.fragment.coordinates` *add.fragment.coordinates*

Description

Expand target and bait IDs of the form chrN:start-end to separate coordinate columns in the data table

Usage

```
add.fragment.coordinates(id.data)
```

Arguments

`id.data`	data table containing columns `target.id` and/or `bait.id` to be expanded

Value

Data table with added coordinate columns for target and bait (as applicable).

Author(s)

Erle Holgersen <Erle.Holgersen@icr.ac.uk>

Examples

```
data(bre80);
add.fragment.coordinates(bre80[, .(bait.id, target.id)]);
```

`bedtools.installed` *bedtools.installed*

Description

Check if bedtools exists in PATH

Usage

```
bedtools.installed()
```

Value

Logical indicating if bedtools was found in PATH

Author(s)

Erle Holgersen <Erle.Holgersen@icr.ac.uk>

Examples

```
bedtools.installed();
```

`bre80` *Bre80 Cell Line*

Description

A dataset containing processed data from a capture Hi-C experiment in the Bre80 normal epithelial breast tissue cell line. The experiment targeted several breast cancer risk loci, and reads that mapped to the 2q35 SNPs rs13387042 and rs16857609 are included in the dataset.

Data was prepared using the `prepare.data` function. Coordinates are GRCh38.

Usage

```
data(bre80)
```

Format

A data table object with 47,766 rows and 13 columns.

The variables are as follows:

- target.id String in chrN:start-end format identifying target fragment
- bait.id String in chrN:start-end format identifying bait fragment
- target.chr Chromosome of target fragment
- target.start Start coordinate of target fragment (zero-based)
- target.end End coordinate of target fragment
- bait.chr Chromosome of bait fragment
- bait.start Start coordinate of bait fragment (zero-based)
- bait.end End coordinate of bait fragment
- bait.to.bait Boolean indicating if the interaction is bait-to-bait (i.e. the fragment listed as target is also a bait)
- bait.trans.count The number of reads linking the bait to fragments in trans (a measure of "interactibility")
- target.trans.count The number of reads linking the target to fragments in trans (a measure of "interactibility")
- distance Distance between the midpoints of the bait and target fragments (basepairs). NA for trans interactions
- count The number of reads linking the two fragments

References

Baxter, Joseph S., et al. "Capture Hi-C identifies putative target genes at 33 breast cancer risk loci." Nature Communications 9.1 (2018): 1028.

`check.model.numerical.fit` *check.model.identifiability*

Description

Check if chicane model can be fit on a given dataset. `glm.nb` does not work when all responses are constant, or there are only two unique values and a covariate is a perfect predictor.

Usage

```
check.model.numerical.fit(interaction.data)
```

Arguments

`interaction.data`	Data table of interaction data on which model is to be fit

Value

boolean indicating if model can be fit

`check.split.data.numerical.fit` *check.split.data.numerical.fit*

Description

Helper function to check if the chicane model can be fit on each element of a split data list.

Usage

```
check.split.data.numerical.fit(split.data)
```

Arguments

`split.data`	List of data.table objects with fragment interaction data

Value

Logical indicating if the model can be fit

chicane *chicane*

Description

Run full method for detecting significant interactions in capture Hi-C experiments, starting either from a BAM file or preprocessed data from `prepare.data`

Usage

```
chicane(
  bam = NULL,
  baits = NULL,
  fragments = NULL,
  interactions = NULL,
  replicate.merging.method = "sum",
  distribution = "negative-binomial",
  include.zeros = "none",
  bait.filters = c(0, 1),
  target.filters = c(0, 1),
  distance.bins = NULL,
  multiple.testing.correction = c("bait-level", "global"),
  adjustment.terms = NULL,
  remove.adjacent = FALSE,
  temp.directory = NULL,
  keep.files = FALSE,
  maxit = 100,
  epsilon = 1e-08,
  cores = 1,
  trace = FALSE,
  verbose = FALSE,
  interim.data.dir = NULL
)
```

Arguments

`bam`	Path to a BAM file
`baits`	Path to a BED file containing the baits
`fragments`	Path to a BED file containing all restriction fragments in the genome
`interactions`	Data table or path to a text file detailing fragment interactions, typically from `prepare.data`. Can be used instead of bam/baits/fragments specification if the text files have already been prepared.
`replicate.merging.method`	Method that should be used for merging replicates, if applicable
`distribution`	Name of distribution of the counts. Options are 'negative-binomial', 'poisson', 'truncated-poisson', and 'truncated-negative-binomial'

include.zeros String specifying what zero counts to include. Options are none (default), cis, and all.

bait.filters Vector of length two, where the first element corresponds to the lower-end filter and the second to the upper-end filter. When global multiple testing correction is performed, altering the bait filtering settings may affect the number of significant results.

target.filters Vector of length two, giving lower and higher filter, respectively. Changing this filtering setting may affect multiple testing correction by altering the number of tests performed.

distance.bins Number of bins to split distance into. Models are fit separately in each bin.

multiple.testing.correction
String specifying how multiple testing correction should be performed, by bait or globally.

adjustment.terms
Character vector of extra terms to adjust for in the model fit.

remove.adjacent
Logical indicating whether to remove all reads mapping to adjacent restriction fragments.

temp.directory Directory where temporary files should be stored. Defaults to current directory.

keep.files Logical indicating whether to keep temporary files

maxit Maximum number of IWLS iterations for fitting the model (passed to glm.control)

epsilon Positive convergence tolerance for Poisson and negative binomial models. Passed to glm.control

cores Integer value specifying how many cores to use to fit model for cis-interactions.

trace Logical indicating if output should be produced for each of model fitting procedure. Passed to glm.control or gamlss.control

verbose Logical indicating whether to print progress reports.

interim.data.dir
Path to directory to store intermediate QC data and plots. NULL indicate skip intermediate results.

Value

Data table with columns

target.id String in chrN:start-end format identifying target fragment

bait.id String in chrN:start-end format identifying bait fragment

target.chr Chromosome of target fragment

target.start Start coordinate of target fragment (zero-based)

target.end End coordinate of target fragment

bait.chr Chromosome of bait fragment

bait.start Start coordinate of bait fragment (zero-based)

bait.end End coordinate of bait fragment

bait.to.bait	Boolean indicating if the interaction is bait-to-bait (i.e. the fragment listed as target is also a bait)
bait.trans.count	The number of reads linking the bait to fragments in trans (a measure of "interactibility")
target.trans.count	The number of reads linking the target to fragments in trans (a measure of "interactibility")
distance	Distance between the midpoints of the bait and target fragments (basepairs). NA for trans interactions
count	The number of reads linking the two fragments
expected	The expected number of reads linking the two fragments under the fitted model
p.value	P-value for test of the observed number of reads significantly exceeding the expected count
q.value	FDR-corrected p-value

Author(s)

Erle Holgersen <Erle.Holgersen@icr.ac.uk>

Examples

```
if( bedtools.installed() ) {
  # start from BAM file
  bam <- system.file('extdata', 'Bre80_2q35.bam', package = 'chicane');
  baits <- system.file('extdata', '2q35.bed', package = 'chicane');
  fragments <- system.file('extdata', 'GRCh38_HindIII_chr2.bed.gz', package = 'chicane');
  results <- chicane(
bam = bam,
baits = baits,
fragments = fragments
);
}

# start from pre-processed data
data(bre80);
results <- chicane(interactions = bre80);
```

---

combine.replicates *combine.replicates*

Description

Merge biological replicates.

Usage

```
combine.replicates(replicates, method = c("sum", "weighted-sum"))
```

Arguments

replicates	list of data table objects from prepare.data
method	string specifying the method for merging replicates. Options are 'sum' and 'weighted-sum'.

Details

The parameter method determines which method is used for merging replicates. Available options are weighted-sum and sum.

'weighted-sum' implements the size factor scaling approach used in DEseq, rounded to the closest integer. See Anders and Huber 2010 for details.

'sum' is the naive sum of counts across biological replicates.

Value

Data table object containing merged data, where counts are stored in colums

count.i	count of interaction in ith replicate
count	count after merging replicates

References

Anders, Simon, and Wolfgang Huber. "Differential expression analysis for sequence count data." *Genome biology* 11.10 (2010): R106.

Examples

```
if( bedtools.installed() ) {
  # preprocess data
  bam <- system.file('extdata', 'Bre80_2q35.bam', package = 'chicane');
  baits <- system.file('extdata', '2q35.bed', package = 'chicane');
  fragments <- system.file('extdata', 'GRCh38_HindIII_chr2.bed.gz', package = 'chicane');
  input.data <- prepare.data(
  bam = bam,
  baits = baits,
  fragments = fragments
  );

  # combined two datasets into one
  merged <- combine.replicates(list(input.data, input.data));
 }
```

`compare.replicates` *compare.replicates*

Description

Compare replicates in a pairwise manner and further stratified by distance

Usage

```
compare.replicates(interaction.data = NULL, output.directory = "./")
```

Arguments

`interaction.data`
: A named vector specifying paths to files created using {prepare.data()}

`output.directory`
: Path to the output directory where pairwise plots are generated

Value

TRUE if pairwise plots were successfully created

Author(s)

Syed Haider

Examples

```
# TODO
```

`convert.bam` *convert.bam*

Description

Convert a BAM file to a format that can be used for replicate merging.

Note: This function does not process data enough to be used for interaction calling. Use `prepare.data` for full preprocessing.

Usage

```
convert.bam(bam, baits, fragments, temp.directory = NULL, keep.files = FALSE)
```

Arguments

bam	Path to a BAM file
baits	Path to a BED file containing the baits
fragments	Path to a BED file containing all restriction fragments in the genome
temp.directory	Directory where temporary files should be stored. Defaults to current directory.
keep.files	Logical indicating whether to keep temporary files

Author(s)

Erle Holgersen <Erle.Holgersen@icr.ac.uk>

See Also

prepare.data

---

convert.hicup.digest.bed

convert.hicup.digest.bed

Description

Convert a HiCUP digest file to BED format.

Usage

```
convert.hicup.digest.bed(hicup.digest, file.name = "")
```

Arguments

hicup.digest	Path to HiCUP digest
file.name	Path to output file. A blank string indicates output to the console.

Examples

```
hicup.digest <- system.file('extdata', 'HiCUP_digest_example.txt', package = 'chicane');
convert.hicup.digest.bed(hicup.digest);
```

convert.standard.format *convert.standard.format*

Description

Create a file in standard format for cross compatability including with WashU Epigenome Browser.

Usage

```
convert.standard.format(chicane.results, file.name = "")
```

Arguments

chicane.results	Path to CHiCANE interaction calls file
file.name	Path to output file

Value

TRUE if output files are created successfully

Author(s)

Andrea Gillespie, Syed Haider

Examples

```
chicane.results <- system.file(
   'extdata', 'T47D_2q35_filtered_chicane_calls.txt',
   package = 'chicane'
   );
 output.file = file.path(tempdir(), 'temp_standard_format.txt');
convert.standard.format(chicane.results, file.name = output.file);
```

convert.to.one.based *convert.to.one.based*

Description

Convert zero-based region in format chr:start-end to 1-based

Usage

```
convert.to.one.based(id)
```

Arguments

id	string in format chr:start-end

Value

one-converted ID

`create.locus.plot` *create.locus.plot*

Description

Create a file compatible with WashU Epigenome Browser from CHiCANE interaction calls.

Usage

```
create.locus.plot(
  genome = "hg38",
  chr = NULL,
  start = NULL,
  end = NULL,
  gene.data = NULL,
  genomic.features = NULL,
  feature.name = NULL,
  fdr.filter = 0.05,
  interaction.data = NULL,
  file.name = NULL,
  height = 5.5,
  width = 8.5,
  track.heights = c(0.2, 0.5, 0.8, 0.5, 1.5, 2),
  ...
)
```

Arguments

genome	Name of genome build (e.g. 'hg38' or 'hg37')
chr	Chromosome number for desired locus including 'chr' (e.g. 'chr1')
start	Start coordinate of desired locus
end	End coordinate of desired locus
gene.data	Path to chosen genome annotation file in .gtf format
genomic.features	Path to BED file with coordinates of desired feature track
feature.name	Title to appear above genomic features
fdr.filter	Q-value filter threshold for interaction calls to be included

interaction.data	Path to unfiltered CHiCANE calls output
file.name	Path to output file
height	Height in inches for desired plot
width	Width in inches of desired plot
track.heights	Vector of length 6 indicating desired height of individual tracks
...	Any additional parameters to Gviz::plotTracks

Value

TRUE if plot was successfully created

Author(s)

Andrea Gillespie, Syed Haider

Examples

```
# In order to conserve memory only significant interactions are included in example
# interaction.data file. However, in order to show raw counts, unfiltered calls should be
# included and only significant interactions (as set by fdr.filter) wil be displayed

gene.data <- system.file('extdata', 'gencode_2q35.gtf', package = 'chicane');
genomic.features <- system.file('extdata', '2q35.bed', package = 'chicane');
interaction.data <- system.file(
  'extdata', 'T47D_2q35_filtered_chicane_calls.txt',
  package = 'chicane'
  );
file.name <- file.path(tempdir(), "chr2_interactions.pdf");


create.locus.plot(
   genome = 'hg38',
   chr = 'chr2',
   start = 216600000,
   end = 217200000,
   gene.data = gene.data,
   genomic.features = genomic.features,
   feature.name = 'baits',
   interaction.data = interaction.data,
   file.name = file.name,
   collapseTranscripts = TRUE,
   shape = "arrow"
   );
```

create.modelfit.plot *create.modelfit.plot*

Description

create a plot representing model's fit

Usage

```
create.modelfit.plot(model, file.name = NULL, resolution = 300)
```

Arguments

model	An object of fitted model
file.name	A string specifying plotting file name
resolution	A numeric specifying plot's resolution

Value

TRUE if plot was successfully created

Author(s)

Syed Haider

distance.bin *distance.bin*

Description

Assign distances to a meaningful category

Usage

```
distance.bin(distance)
```

Arguments

distance	Vector of distances that should be mapped to a distance bin

Value

vector of same length as distance containing assigned distance bins

distance.split *distance.split*

Description

Split interaction data into subsets that are large enough for the chicane model to be fit (see Details), based on distance. This step allows the distance term in the model to be fit in a piecewise linear fashion.

Usage

```
distance.split(
  interaction.data,
  distance.bins = NULL,
  min.rows.bin = 50,
  verbose = FALSE
)
```

Arguments

interaction.data	Data table of interaction data, typically from prepare.data
distance.bins	Number of distance bins desired. If NULL, a number is chosen to ensure that the negative binomial can be fit in all bins.
min.rows.bin	The minimum number of expected rows in a distance bin. Ignored if distance.bins is set
verbose	Logical indicating whether to print progress reports

Details

Fitting glm.nb fails when there is a lack of overdispersion in the data. The chicane method contains logic to catch these errors and instead fit a Poisson model. However, to avoid this happening more than necessary, an attempt is made to avoid distance splits that will clearly result in numerical errors. This includes bins of data where the count is the same for all rows, or a covariate is a perfect predictor of count.

Value

List where each element corresponds to a specified distance bin, and the final one corresponding to trans-interactions (if present)

Examples

```
data(bre80);
distance.split(bre80);
```

`fill.in.zeros` *fill.in.zeros*

Description

Add zero counts to interaction data

Usage

```
fill.in.zeros(interaction.data, baits, fragments)

fill.in.zeroes(interaction.data, baits, fragments)
```

Arguments

`interaction.data`	Data table containing interaction data
`baits`	Vector of bait IDs used in the experiment, in format chrN:start-end
`fragments`	Vector of potential fragments the baits can link up to, in format chrN:start-end

Value

Data table containing origiina

Examples

```
data(bre80);
bait.file <- system.file('extdata', '2q35.bed', package = 'chicane');
fragment.file <- system.file('extdata', 'GRCh38_HindIII_chr2.bed.gz', package = 'chicane');
results <- fill.in.zeros(
bre80,
baits = read.bed(bait.file),
fragments = read.bed(fragment.file)
);
```

`filter.fragments` *filter.fragments*

Description

Filter low and high-interacting restriction fragments based on the total number of trans counts

Usage

```
filter.fragments(
  interaction.data,
  bait.filters = c(0, 1),
  target.filters = c(0, 1),
  verbose = FALSE
)
```

Arguments

interaction.data	Data table containing interactions
bait.filters	Vector of length two, where the first element corresponds to the lower-end filter and the second to the upper-end filter. When global multiple testing correction is performed, altering the bait filtering settings may affect the number of significant results.
target.filters	Vector of length two, giving lower and higher filter, respectively. Changing this filtering setting may affect multiple testing correction by altering the number of tests performed.
verbose	Logical indicating whether to print progress reports.

Value

Data table containing fragments that passed all filters

Author(s)

Erle Holgersen <Erle.Holgersen@icr.ac.uk>

Examples

```
# filter out lowest 10% of baits
filter.fragments(bre80, bait.filters = c(0.1, 1))
```

---

fit.glm *fit.glm*

Description

Fit GLM according to a specified distribution. This needs to be done separately from `glm` in order to include negative binomial and truncated distributions as options.

Usage

```
fit.glm(
  formula,
  data,
  distribution = c("negative-binomial", "poisson", "truncated-poisson",
    "truncated-negative-binomial"),
  start = NULL,
  init.theta = NULL,
  maxit = 100,
  epsilon = 1e-08,
  trace = FALSE
)
```

Arguments

formula	Formula specifying model of interest
data	Data frame containing variables specified in formula
distribution	Name of distribution of the counts. Options are 'negative-binomial', 'poisson', 'truncated-poisson', and 'truncated-negative-binomial'
start	Starting values for model coefficients
init.theta	Initial value of theta if fitting the negative binomial distribution
maxit	Maximum number of IWLS iterations for fitting the model (passed to glm.control)
epsilon	Positive convergence tolerance for Poisson and negative binomial models. Passed to glm.control
trace	Logical indicating if output should be produced for each of model fitting procedure. Passed to glm.control or gamlss.control

Value

List with elements

model	model object
expected.values	vector of expected values for each element in original data
p.values	vector of p-values for test of significantly higher response than expected

---

fit.model *fit.model*

Description

Fit negative binomial model to obtain p-values for interactions.

Usage

```
fit.model(
  interaction.data,
  distance.bins = NULL,
  distribution = "negative-binomial",
  bait.filters = c(0, 1),
  target.filters = c(0, 1),
  adjustment.terms = NULL,
  maxit = 100,
  epsilon = 1e-08,
  cores = 1,
  trace = FALSE,
  verbose = FALSE,
  interim.data.dir = NULL
)
```

Arguments

interaction.data	data.table object containing interaction counts. Must contain columns distance, count, and bait_trans_count.
distance.bins	Number of bins to split distance into. Models are fit separately in each bin.
distribution	Name of distribution of the counts. Options are 'negative-binomial', 'poisson', 'truncated-poisson', and 'truncated-negative-binomial'
bait.filters	Vector of length two, where the first element corresponds to the lower-end filter and the second to the upper-end filter. When global multiple testing correction is performed, altering the bait filtering settings may affect the number of significant results.
target.filters	Vector of length two, giving lower and higher filter, respectively. Changing this filtering setting may affect multiple testing correction by altering the number of tests performed.
adjustment.terms	Character vector of extra terms to adjust for in the model fit.
maxit	Maximum number of IWLS iterations for fitting the model (passed to glm.control)
epsilon	Positive convergence tolerance for Poisson and negative binomial models. Passed to glm.control
cores	Integer value specifying how many cores to use to fit model for cis-interactions.
trace	Logical indicating if output should be produced for each of model fitting procedure. Passed to glm.control or gamlss.control
verbose	Logical indicating whether to print progress reports.
interim.data.dir	Path to directory to store intermediate QC data and plots.

Details

Fit a negative binomial model for obtaining p-value for interactions. The data is first sorted by distance, and models are fit separately in each quantile of the distance-sorted data.

Value

Interactions data with expected number of interactions and p-values added.

Examples

```
data(bre80);
fit.model(bre80);
```

`get.combination.count` *get.combination.count*

Description

Calculate the number of possible combinations between baits and fragments, excluding self-ligations and only counting bait-to-bait interactions once (e.g. a-b, not b-a)

Usage

```
get.combination.count(baits, fragments, cis.only = FALSE)
```

Arguments

`baits`	vector of bait IDs in form chrN:start-end
`fragments`	vector of fragment IDs in form chrN:start-end
`cis.only`	logical indicating whether cis-interactions only should be considered

Value

total number of possible combinations

`get.components` *get.components*

Description

Split a fragment in format chr:start-end to a list of corresponding elements

Usage

```
get.components(id)
```

Arguments

id	string in format chr:start-end

Value

list with entries 'chr', 'start', 'end'

---

get.distance *get.distance*

Description

Calculate distance between bait and target region

Usage

```
get.distance(interaction.data)
```

Arguments

interaction.data	data.table with interaction data. Must contain columns bait.chr, bait.start, bait.end, target.chr, target.start, target.end

Value

vector of absolute distances (NA for trans-interactions)

Examples

```
data(bre80);
input.cols <- c('bait.chr', 'bait.start', 'bait.end',
'target.chr', 'target.start', 'target.end');
get.distance( bre80[, input.cols, with = FALSE]);
```

get.id.components *get.id.components*

Description

Split a segment ID in form chrN:start-end into its different components

Usage

```
get.id.components(id)
```

Arguments

id	segment ID of form chrN:start-end

Value

A character vector of length three, where the elements are chromosome, start, and end, respectively. If id is a vector, a list of the same length is returned

Examples

```
get.id.components('chrX:6-30');
get.id.components(c('3:4-10', '22:1000-20000'))
```

get.interaction.id *get.interaction.id*

Description

Generate a unique identifying ID for each interaction

Usage

```
get.interaction.id(bait, other.end, bait.to.bait, zero.based = FALSE)
```

Arguments

bait	id of bait in format chr:start-end
other.end	id of other end in format chr:start-end
bait.to.bait	logical indicating whether both ends are baits
zero.based	logical indicating if IDs are zero-based

Value

string identifying interaction

get.trans.counts *get.trans.counts*

Description

Calculate the number of trans-interactions per fragment, accounting for the fact that baits can be listed either as bait or target.

Usage

```
get.trans.counts(interaction.data)
```

Arguments

interaction.data	Data table containing interactions

Value

Data table with columns `fragment.id` and `trans.count`.

fragment.id	ID of restriction fragment in chrN:start-end format
trans.count	Number of trans interactions involving the fragment

Examples

```
data(bre80);
get.trans.counts(bre80[, .(bait.chr, target.chr, bait.id, target.id, count)]);
```

is.glm.nb.maxiter.warning *is.glm.nb.maxiter.warning*

Description

Check if a warning object is an iteration limit reached warning from `glm.nb`

Usage

```
is.glm.nb.maxiter.warning(w)
```

Arguments

w	Warning object

Value

Logical indicating if warning matches iteration limit reached warning

is.glm.nb.theta.error *check.glm.nb.theta.error*

Description

Check if an error matches the error raised by `glm.nb` due to an inflated theta estimate. This happens when the variance of the negative binomial does not exceed the mean (i.e. there is no overdispersion). In such cases, the Poisson distribution may be a suitable alternative.

Usage

```
is.glm.nb.theta.error(e)
```

Arguments

`e`	Error object

Value

Boolean indicating if error matches

is.glm.nb.theta.warning *is.glm.nb.theta.warning*

Description

Check if a warning matches the square root warning raised by `glm.nb` due to an inflated theta estimate. This happens when the variance of the negative binomial does not exceed the mean (i.e. there is no overdispersion). In such cases, the Poisson distribution may be a suitable alternative.

Usage

```
is.glm.nb.theta.warning(w)
```

Arguments

`w`	Warning object

Value

Boolean indicating if warning matches

model.rows.sanity.check *model.rows.sanity.check*

Description

Check that the model fit contains the same number of rows as the data used to fit it, and throw an error if not

Usage

```
model.rows.sanity.check(model.data, model)
```

Arguments

model.data	Data used to fit model
model	Resulting negative binomial model object

Value

None

model.try.catch *model.try.catch*

Description

Internal function for fitting model within a tryCatch loop, handling numerical errors gracefully.

Usage

```
model.try.catch(
  model.formula,
  data,
  distribution = "negative-binomial",
  maxit = 100,
  epsilon = 1e-08,
  init.theta = NULL,
  start = NULL,
  trace = FALSE,
  verbose = FALSE
)
```

Arguments

model.formula	formula
data	model data
distribution	Name of distribution of the counts. Options are 'negative-binomial', 'poisson', 'truncated-poisson', and 'truncated-negative-binomial'
maxit	Maximum number of IWLS iterations for fitting the model (passed to glm.control)
epsilon	Positive convergence tolerance for Poisson and negative binomial models. Passed to glm.control
init.theta	Initial value of theta in negative binomial model
start	starting values of coefficients in linear predictor
trace	Logical indicating if output should be produced for each of model fitting procedure. Passed to glm.control or gamlss.control
verbose	Logical indicating whether to print progress reports.

Value

List with elements

model	model object. Set to NULL if no model could be fit.
expected.values	vector of expected values for each element in original data, or vector of NAs if no model could be fit
p.values	vector of p-values for test of significantly higher response than expected, or vector of NAs if no model could be fit

---

multiple.testing.correct

multiple.testing.correct

Description

Perform multiple testing correction on p-values from interaction test. By default, multiple testing correction is applied per bait. To change this to a global multiple testing correction, set bait.level = FALSE.

Usage

```
multiple.testing.correct(interaction.data, bait.level = TRUE)
```

Arguments

interaction.data	Data table of interaction calls. Must contain columns p.value and bait.id.
bait.level	Logical indicating whether multiple testing correction should be performed per bait.

Value

Original data table with new column

`q.value` FDR-corrected p-value

Examples

```
## Not run:
data(bre80);
 results <- fit.model(bre80);
 adjusted.results <- multiple.testing.correct(results);

## End(Not run)
```

`prepare.data` *prepare.data*

Description

Prepare data for running interaction calling. Takes a BAM file and baits and restriction fragments as input, and returns a data table with data ready for analysis.

Usage

```
prepare.data(
  bam,
  baits,
  fragments,
  replicate.merging.method = "sum",
  include.zeros = c("none", "cis", "all"),
  remove.adjacent = FALSE,
  temp.directory = NULL,
  keep.files = FALSE,
  verbose = FALSE
)
```

Arguments

`bam`	Path to a BAM file
`baits`	Path to a BED file containing the baits
`fragments`	Path to a BED file containing all restriction fragments in the genome
`replicate.merging.method`	Method that should be used for merging replicates, if applicable
`include.zeros`	String specifying what zero counts to include. Options are none (default), cis, and all.

remove.adjacent	Logical indicating whether to remove all reads mapping to adjacent restriction fragments.
temp.directory	Directory where temporary files should be stored. Defaults to current directory.
keep.files	Logical indicating whether to keep temporary files
verbose	Logical indicating whether to print progress reports.

Value

Data table object with columns

target.id	String in chrN:start-end format identifying target fragment
bait.id	String in chrN:start-end format identifying bait fragment
target.chr	Chromosome of target fragment
target.start	Start coordinate of target fragment (zero-based)
target.end	End coordinate of target fragment
bait.chr	Chromosome of bait fragment
bait.start	Start coordinate of bait fragment (zero-based)
bait.end	End coordinate of bait fragment
bait.to.bait	Boolean indicating if the interaction is bait-to-bait (i.e. the fragment listed as target is also a bait)
count	The number of reads linking the two fragments
bait.trans.count	The number of reads linking the bait to fragments in trans (a measure of "interactibility")
target.trans.count	The number of reads linking the target to fragments in trans (a measure of "interactibility")
distance	Distance between the midpoints of the bait and target fragments (basepairs). NA for trans interactions

Examples

```
if( bedtools.installed() ) {
  bam <- system.file('extdata', 'Bre80_2q35.bam', package = 'chicane');
  baits <- system.file('extdata', '2q35.bed', package = 'chicane');
  fragments <- system.file('extdata', 'GRCh38_HindIII_chr2.bed.gz', package = 'chicane');
  input.data <- prepare.data(
bam = bam,
baits = baits,
fragments = fragments
);
 }
```

read.bed *read.bed*

Description

Read a BED file and return regions in chrN:start-end format

Usage

```
read.bed(bed.path, zero.based = TRUE)
```

Arguments

bed.path	Path to bed file
zero.based	Whether to return ID in zero-based coordinates

Value

vector of region IDs

Examples

```
bait.file <- system.file('extdata', '2q35.bed', package = 'chicane');
baits <- read.bed(bait.file);
```

run.model.fitting *run.model.fitting*

Description

Run model fitting procedure for either bait-to-bait or other interactions. Meant for internal use only.

Usage

```
run.model.fitting(
  interaction.data,
  distance.bins = NULL,
  distribution = "negative-binomial",
  bait.to.bait = FALSE,
  adjustment.terms = NULL,
  maxit = 100,
  epsilon = 1e-08,
  cores = 1,
  trace = FALSE,
  verbose = FALSE,
  interim.data.dir = NULL
)
```

Arguments

interaction.data	data.table object containing interaction counts. Must contain columns distance, count, and bait_trans_count.
distance.bins	Number of bins to split distance into. Models are fit separately in each bin.
distribution	Name of distribution of the counts. Options are 'negative-binomial', 'poisson', 'truncated-poisson', and 'truncated-negative-binomial'
bait.to.bait	Logical indicating if model should be fit as bait-to-bait
adjustment.terms	Characted vector of extra terms to adjust for in the model fit
maxit	Maximum number of IWLS iterations for fitting the model (passed to `glm.control`)
epsilon	Positive convergence tolerance for Poisson and negative binomial models. Passed to `glm.control`
cores	Integer value specifying how many cores to use to fit model for cis-interactions.
trace	Logical indicating if output should be produced for each of model fitting procedure. Passed to `glm.control` or `gamlss.control`
verbose	Logical indicating whether to print progress reports.
interim.data.dir	Path to directory to store intermediate QC data and plots.

Value

Interactions data with expeceted number of interactions and p-values added.

---

smart.split *smart.split*

Description

Split a data frame into a prespecified number of bins, using `split` and `cut`. Unlike the default R functions, this does not fail when asked to split the data into a single bin.

Usage

```
smart.split(dat, bins)
```

Arguments

dat	Data frame or data table to be split
bins	Number of bins to split data into

Value

List with `bins` elements. Each element corresponds to one portion of the data

stratified.enrichment.sample *stratified.enrichment.sample*

Description

Generate a stratified sample matching distance distribution of significant interactions.

Usage

```
stratified.enrichment.sample(nonsignificant.results, significant.results)
```

Arguments

nonsignificant.results	Data table containing non-significant interactions that should be sampled from
significant.results	Data table of significant results. Used to determine size of strata in stratified sampling procedure.

test.enrichment *test.enrichment*

Description

test.enrichment

Usage

```
test.enrichment(
  interaction.data,
  feature.bed,
  significance.cutoff = 0.05,
  span = 0,
  n = 1000,
  remove.bait.to.bait = TRUE
)
```

Arguments

interaction.data	Data table containing details on interactions
feature.bed	BED file with regions of features
significance.cutoff	q-value threshold for significant interactions

span	Distance around target restriction fragment to consider. If set to zero (default), only features that overlap with the restriction fragment itself are considered.
n	Number of random samples to consider
remove.bait.to.bait	Logical specifying whether to exclude bait-to-bait interactions

Value

list with elements

observed	observed overlap between significant interactions and features
random	vector of length n giving overlap between random samples and features

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Examples

```
if( bedtools.installed() ) {
  data(bre80);
  ctcf.bed <- system.file('extdata', 'T47D_chr2_CTCF.bed.gz', package = 'chicane');

  results <- chicane(interactions = bre80);
  test.enrichment(results, ctcf.bed, significance.cutoff = 0.25);
}
```

---

verify.interaction.data

verify.interaction.data

Description

Verify that interaction.data object is in expected format. Throws an error if object does not fit requirements.

Usage

```
verify.interaction.data(interaction.data)
```

Arguments

interaction.data	Object to be verified.

Value

None

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