Package 'DTA'

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Title Dynamic Transcriptome Analysis

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Depends R (>= 2.10), LSD

Imports scatterplot3d

Description Dynamic Transcriptome Analysis (DTA) can monitor the cellular response to perturbations with higher sensitivity and temporal resolution than standard transcriptomics. The package implements the underlying kinetic modeling approach capable of the precise determination of synthesis- and decay rates from individual microarray or RNAseq measurements.

License Artistic-2.0

biocViews Microarray, DifferentialExpression, GeneExpression, Transcription

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LazyLoad yes

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DTA-package *Dynamic Transcriptome Analysis*

Description

The DTA package implements all methods of the quantitative kinetic modeling approach belonging to DTA (Dynamic Transcriptome Analysis) to estimate mRNA synthesis and decay rates from individual time point measurements.

Details

Package:	DTA
Type:	Package
Version:	2.0.1
Date:	2012-03-22
License:	Artistic-2.0
LazyLoad:	yes

Author(s)

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References

C. Miller, B. Schwalb, K. Maier, D. Schulz, S. Duemcke, B. Zacher, A. Mayer, J. Sydow, L. Marcinowski, L. Doelken, D. E. Martin, A. Tresch, and P. Cramer. Dynamic transcriptome analysis measures rates of mRNA synthesis and decay in yeast. Mol Syst Biol, 7:458, 2011. M. Sun, B. Schwalb, D. Schulz, N. Pirkl, L. Lariviere, K. Maier, A. Tresch, P. Cramer. Mutual feedback between mRNA synthesis and degradation buffers transcript levels in a eukaryote. Under review. B. Schwalb, B. Zacher, S. Duemcke, D. Martin, P. Cramer, A. Tresch. Measurement of genome-wide RNA synthesis and decay rates with Dynamic Transcriptome Analysis (DTA/cDTA). Bioinformatics.

Examples

```
## see vignette or supplemental material of the given references.
```

Dm.tnumber — *The amount of thymines in the cDNA of each transcript of Drosophila Melanogaster.*

Description

The amount of thymines in the cDNA of each transcript of all Drosophila Melanogaster Ensembl transcript IDs (Flybase transcript number), to assess the uridine-dependent labeling bias and eventually correct for it.

Usage

```
Dm.tnumber
```

Format

Vector gives the number of thymines in the cDNA (uridine residues in RNA) of each Ensembl transcript ID.

Source

E. Birney, D. Andrews, M. Caccamo, Y. Chen, L. Clarke, G. Coates, T. Cox, F. Cunningham, V. Curwen, T. Cutts, T. Down, R. Durbin, X. M. Fernandez-Suarez, P. Flicek, S. Graef, M. Hammond, J. Herrero, K. Howe, V. Iyer, K. Jekosch, A. Kaehaeri, A. Kasprzyk, D. Keefe, F. Kokocinski, E. Kulesha, D. London, I. Longden, C. Melsopp, P. Meidl, B. Overduin, A. Parker, G. Proctor, A. Prlic, M. Rae, D. Rios, S. Redmond, M. Schuster, I. Sealy, S. Searle, J. Severin, G. Slater, D. Smedley, J. Smith, A. Stabenau, J. Stalker, S. Trevanion, A. Ureta- Vidal, J. Vogel, S. White, C.Woodwark, and T. J. Hubbard. Ensembl 2006. Nucleic acids research, 34(Database issue), January 2006.

Doelken2008 — *Mus Musculus and Homo Sapiens DTA experiment from Doelken et al.*

Description

R object contains all relevant *.RData files needed for the `DTA.estimate` function. For example, see vignette.

Usage

```
Doelken2008
```

Format

R object contains the following *.RData files: `Hs.phenomat` `Hs.datamat` `Hs.reliable` `Hs.enst2ensg` `Hs.tnumber` `Mm.phenomat` `Mm.datamat` `Mm.reliable` `Mm.enst2ensg` `Mm.tnumber`

Source

Doelken, L., Ruzsics, Z., Raedle, B., Friedel, C. C., Zimmer, R., Mages, J., Hoffmann, R., Dickinson, P., Forster, T., Ghazal, P., & Koszinowski, U. H. (2008). High-resolution gene expression profiling for simultaneous kinetic parameter analysis of RNA synthesis and decay. RNA 14(9), 1959-1972. E. Birney, D. Andrews, M. Caccamo, Y. Chen, L. Clarke, G. Coates, T. Cox, F. Cunningham, V. Curwen, T. Cutts, T. Down, R. Durbin, X. M. Fernandez-Suarez, P. Flicek, S. Graef, M. Hammond, J. Herrero, K. Howe, V. Iyer, K. Jekosch, A. Kaehaeri, A. Kasprzyk, D. Keefe, F. Kokocinski, E. Kulesha, D. London, I. Longden, C. Melsopp, P. Meidl, B. Overduin, A. Parker, G. Proctor, A. Prlic, M. Rae, D. Rios, S. Redmond, M. Schuster, I. Sealy, S. Searle, J. Severin, G. Slater, D. Smedley, J. Smith, A. Stabenau, J. Stalker, S. Trevanion, A. Ureta- Vidal, J. Vogel, S. White, C.Woodwark, and T. J. Hubbard. Ensembl 2006. Nucleic acids research, 34(Database issue), January 2006.

`DTA.dynamic.estimate` *Estimation of synthesis and decay rates upon perturbation*

Description

DTA.dynamic.estimate uses an experiment, given by a phenotype matrix, data matrix and the number of uridines for each gene to estimate synthesis and decay rate of the genes.

Usage

```
DTA.dynamic.estimate(phenomat = NULL,datamat = NULL,tnumber = NULL,ccl = NULL,mRNAs = NULL,reliable = N
```

Arguments

`phenomat`	A phenotype matrix, containing the design of the experiment as produced by `DTA.phenomat`. Columns are name, fraction (U=unlabebeld, L=labeled, T=total), time and nr (=replicate number). Rows represent individual experiments.
`datamat`	A matrix, containing the measurements from U, L and T, according to the design given in phenomat. Matrix should only contain the rows of phenomat as columns.
`tnumber`	Integer vector, containing the numbers of uridines. Elements should have the rownames of datamat.
`ccl`	The cell cycle length of the cells.
`mRNAs`	Estimated number of mRNAs in a cell (optional).
`reliable`	Vector of 'reliable' genes, which are used for parameter estimation.
`mediancenter`	Should the quotient Labeled/Total resp. Unlabeled/Total be rescaled to a common median over it's replicates before building the genewise median.
`usefractions`	From which fractions should the decay rate be calculated: "LandT", "UandT" or "both".
`LtoTratio`	Coefficient to rescale Labeled/Total. Is estimated from the data, if not specified. See ratiomethod.

ratiomethod	Choose the regression method to be used, possible methods are: "tls", "bias" and "lm". For details, see supplemental material of Sun et al. (see references).
largest	Percentage of largest residues from the first regression not to be used in the second regression step. For details, see supplemental material of Sun et al. (see references).
weighted	Should the regression be weighted with 1/(Total^2 + median(Total))?
relevant	Choose the arrays to be used for halflives calculation, vector due to nr (=replicate number) in phenomat.
check	If check = TRUE, control messages and plots will be generated.
error	If TRUE, the measurement error is assessed by means of an error model and resampling to gain confidence regions.
samplesize	Error model samplesize for resampling.
confidence.range	Confidence region for error model as quantiles. Interval should be between 0 and 1.
bicor	Should the labeling bias be corrected?
condition	String, to be added to the plotnames.
upper	Upper bound for labeling bias estimation. For details, see supplemental material of Sun et al. (see references).
lower	Lower bound for labeling bias estimation. For details, see supplemental material of Sun et al. (see references).
save.plots	If save.plots = TRUE, control plots will be saved.
resolution	Resolution scaling factor for plotting.
folder	Path to the folder, where to save the plots.
fileformat	Fileformat for plots to be saved. See `plotit` function (`LSD` package).
totaloverwt	Will be available in the very near future for comparative DTA data.
sr.vs.dr.folds.lims	Limits of the folds plot (dr vs sr).
te.vs.to.folds.lims	Limits of the folds plot (LT vs LE).
robust	If robust = TRUE, LE resp. LT is chosen instead of sr resp. dr.
clusters	should the dr vs sr folds be plotted with clusters, choose 'sr', 'dr' for cluster selection or 'none' to omit it
ranktime	at which time should the rankgain be calculated, default is the last column
upperquant	upper quantile for cluster selection
lowerquant	lower quantile for cluster selection
notinR	Should plots be not plotted in R.
RStudio	For RStudio users. Suppresses the opening of a new device, as RStudio allows only one.
simulation	True, if data was generated by `DTA.generate`.
sim.object	Simulation object created by `DTA.generate`.

Value

`DTA.dynamic.estimate` returns a list, where each entry contains the estimation results for all replicates of one timecourse timepoint. Each result contains the following entries

`triples`	Mapping of each fraction and experiment to its corresponding column in the data matrix.
`plabel`	The labeling efficiency. For details, see the vignette.
`LtoTratio`	Estimated ratio of labeled to total fraction.
`UtoTratio`	Estimated ratio of unlabeled to total fraction.
`LtoUratio`	Estimated ratio of labeled to unlabeled fraction.
`correcteddatamat`	Labeling bias corrected data matrix.
`drmat`	Decay rates for each replicate. The last column gives the median decay rates.
`dr`	Median decay rates. The last column of drmat.
`dr.confidence`	Confidence regions of decay rates.
`hlmat`	Half-lives for each replicate. The last column gives the median half-lifes.
`hl`	Median half-lives. The last column of hlmat.
`hl.confidence`	Confidence regions of half-lives.
`TEmat`	Total expression for each replicate. The last column gives the median total expression values.
`TE`	Median total expression values. The last column of TEmat.
`TE.confidence`	Confidence regions of total expression values.
`LEmat`	Labeled expression for each replicate. The last column gives the median labeled expression values.
`LE`	Median labeled expression values. The last column of LEmat.
`LE.confidence`	Confidence regions of labeled expression values.
`UEmat`	Unlabeled expression for each replicate. The last column gives the median unlabeled expression values. (Only if unlabeled values exist in the experiment)
`UE`	Median unlabeled expression values. The last column of UEmat. (Only if unlabeled values exist in the experiment)
`UE.confidence`	Confidence regions of unlabeled expression values.
`srmat`	Synthesis rates for each replicate. The last column gives the median synthesis rates.
`sr`	Median synthesis rates. The last column of srmat.
`sr.confidence`	Confidence regions of synthesis rates.
`LtoTmat`	Labeled to total ratio for each replicate. The last column gives the median labeled to total ratios.
`LtoT`	Median labeled to total ratios. The last column of LtoTmat.
`LtoT.confidence`	Confidence regions of labeled to total ratios.

UtoTmat	Unlabeled to total ratio for each replicate. The last column gives the median unlabeled to total ratios.
UtoT	Median unlabeled to total ratios. The last column of UtoTmat.
UtoT.confidence	Confidence regions of unlabeled to total ratios.
Rsrmat	Rescaled synthesis rates for each replicate, if parameter mRNAs is specified. The last column gives the median synthesis rates.
Rsr	Rescaled median synthesis rates. The last column of Rsrmat.
globaldrmat	Decay rate for each replicate. Reciprocally weighted by the total expression. Last element contains (weighted) median decay rate.
globaldr	(Weighted) median decay rate.

Author(s)

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References

C. Miller, B. Schwalb, K. Maier, D. Schulz, S. Duemcke, B. Zacher, A. Mayer, J. Sydow, L. Marcinowski, L. Doelken, D. E. Martin, A. Tresch, and P. Cramer. Dynamic transcriptome analysis measures rates of mRNA synthesis and decay in yeast. Mol Syst Biol, 7:458, 2011. M. Sun, B. Schwalb, D. Schulz, N. Pirkl, L. Lariviere, K. Maier, A. Tresch, P. Cramer. Mutual feedback between mRNA synthesis and degradation buffers transcript levels in a eukaryote. Under review. B. Schwalb, B. Zacher, S. Duemcke, D. Martin, P. Cramer, A. Tresch. Measurement of genome-wide RNA synthesis and decay rates with Dynamic Transcriptome Analysis (DTA/cDTA). Bioinformatics.

See Also

heatscatter, plotit, tls

Examples

```
dataPath = system.file("data", package="DTA")
load(file.path(dataPath, "Miller2011dynamic.RData"))

### for control plots set 'check = TRUE' ###

res = DTA.dynamic.estimate(Sc.phenomat.dynamic,Sc.datamat.dynamic,Sc.tnumber,ccl = 150,mRNAs = 60000,reliable = S
```

`DTA.dynamic.generate` *Simulation of DTA experiments upon perturbation*

Description

DTA.dynamic.generate produces the phenotype matrix and the matrix containing the simulated data according to the given parameters.

Usage

```
DTA.dynamic.generate(duration = 60,lab.duration = 6,tnumber = NULL,plabel = NULL,nrgenes = 5000,median
```

Arguments

`duration`	duration of the whole time course (min)
`lab.duration`	labeling duration for single experiments (min)
`tnumber`	Integer vector containing the number of uridine residues for each gene. If NULL, tnumber is sampled from an F-distribution within the function.
`plabel`	The labeling efficiency. If NULL, plabel is set to 0.005 within the function. For details, see supplemental material of Sun et al. (see references).
`nrgenes`	The number of genes the simulated experiment will have (will be cropped if it exceeds the length of tnumber).
`mediantime.halflives`	the median of the half life distribution
`mediantime.synthesisrates`	the median of the synthesis rates distribution (counts/cell/cellcycle)
`n`	the number of cells N(0)
`ccl`	The cell cycle length (in minutes).
`check`	if check=TRUE, control messages will be generated
`plots`	if plots = TRUE, control plots will be plotted
`save.plots`	if save.plots = TRUE, control plots will be saved
`folder`	folder, where to save the plots
`condition`	to be added to the plotnames
`addformat`	additional fileformat for plots to be saved
`sdnoise`	The amount of measurement noise (proportional to expression strength).
`nobias`	Should a labeling bias be added?
`unspecific.LtoU`	Proportion of labeled RNAs that unspecifically end up in the unlabeled fraction.
`unspec.LtoU.weighted`	Should unspecific proportion of labeled to unlabeled depend linearly on the length of the RNA?

`unspecific.UtoL`
: Proportion of unlabeled RNAs that unspecifically end up in the labeled fraction.

`unspec.UtoL.weighted`
: Should unspecific proportion of unlabeled to labeled depend linearly on the length of the RNA?

`mu.values.mat`
: if the data should be generated using given synthesis rates, this matrix must contain the respective values for each gene

`mu.breaks.mat`
: timepoints of synthesis rate changes, this matrix must contain the respective values for each gene, only needed when mu.values.mat is given (one column less than mu.values.mat)

`lambda.values.mat`
: if the data should be generated using given decay rates, this matrix must contain the respective values for each gene

`lambda.breaks.mat`
: timepoints of decay rate changes, this matrix must contain the respective values for each gene, only needed when lambda.values.mat is given (one column less than lambda.values.mat)

`truehalflives`
: If the data should be generated using a given half-life distribution, this vector must contain the respective values for each gene.

`truesynthesisrates`
: If the data should be generated using a given synthesis rates distribution, this vector must contain the respective values for each gene

`genenames`
: An optional list of gene names.

Value

DTA.dynamic.generate returns a list, containing the following entries

`phenomat`
: A matrix, containing the design of the experiment as produced by `DTA.phenomat`.

`datamat`
: A matrix, containing the simulated measurements from U, L and T, according to the design given in phenomat.

`tnumber`
: Integer vector containing the number of uridine residues for each gene.

`ccl`
: The cell cycle length (in minutes).

`truemus`
: A vector, containing the true synthesis rates.

`truemusaveraged`
: A vector, containing the true synthesis rates, averaged over the labeling period.

`truelambdas`
: A vector, containing the true decay rates.

`truelambdasaveraged`
: A vector, containing the true decay rates, averaged over the labeling period.

`truehalflives`
: A vector, containing the true half-lives.

`truehalflivesaveraged`
: A vector, containing the true half-lives, averaged over the labeling period.

`trueplabel`
: The true labeling efficiency. For details, see supplemental material of Sun et al. (see references).

truecomplete	A vector, containing the true amount of total RNA.
truelambdas	A vector, containing the true decay rates.
truemus	A vector, containing the true synthesis rates.
truehalflives	A vector, containing the true half-lives.
trueplabel	The true labeling efficiency. For details, see supplemental material of Miller et al. (see references).
truear	The true parameter ar. For details, see supplemental material of Miller et al. (see references).
truebr	The true parameter br. For details, see supplemental material of Miller et al. (see references).
truecr	The true parameter cr. For details, see supplemental material of Miller et al. (see references).
truecrbyar	The true parameter cr/ar. For details, see supplemental material of Miller et al. (see references).
truecrbybr	The true parameter cr/br. For details, see supplemental material of Miller et al. (see references).
truebrbyar	The true parameter br/ar. For details, see supplemental material of Miller et al. (see references).
trueLasymptote	The true parameter asymptote (labeled bias). For details, see supplemental material of Miller et al. (see references).
trueUasymptote	The true parameter asymptote (unlabeled bias). For details, see supplemental material of Miller et al. (see references).

Author(s)

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References

C. Miller, B. Schwalb, K. Maier, D. Schulz, S. Duemcke, B. Zacher, A. Mayer, J. Sydow, L. Marcinowski, L. Dolken, D. E. Martin, A. Tresch, and P. Cramer. Dynamic transcriptome analysis measures rates of mRNA synthesis and decay in yeast. Mol Syst Biol, 7:458, 2011. M. Sun, B. Schwalb, D. Schulz, N. Pirkl, L. Lariviere, K. Maier, A. Tresch, P. Cramer. Mutual feedback between mRNA synthesis and degradation buffers transcript levels in a eukaryote. Under review. B. Schwalb, B. Zacher, S. Duemcke, D. Martin, P. Cramer, A. Tresch. Measurement of genome-wide RNA synthesis and decay rates with Dynamic Transcriptome Analysis (DTA/cDTA). Bioinformatics.

Examples

```
nrgenes = 5000
truesynthesisrates = rf(nrgenes,5,5)*18
steady = rep(1,nrgenes)
shock = 1/pmax(rnorm(nrgenes,mean = 8,sd = 4),1)
induction = pmax(rnorm(nrgenes,mean = 8,sd = 4),1)
changes.mat = cbind(steady,shock,shock*induction)
```

```
mu.values.mat = changes.mat*truesynthesisrates
mu.breaks.mat = cbind(rep(12,nrgenes),rep(18,nrgenes))
truehalflives = rf(nrgenes,15,15)*12
truelambdas = log(2)/truehalflives
changes.mat = cbind(steady,shock,shock*induction,steady)
lambda.values.mat = changes.mat*truelambdas
lambda.breaks.mat = cbind(rep(12,nrgenes),rep(18,nrgenes),rep(27,nrgenes))

### it takes several min to build sim.object (depends on the number of genes 'nrgenes') ###

sim.object = DTA.dynamic.generate(duration = 36,lab.duration = 6,nrgenes = nrgenes,mu.values.mat = mu.values.mat,m

### for control plots set 'check = TRUE' ###

res = DTA.dynamic.estimate(simulation = TRUE,sim.object = sim.object,check = FALSE)
```

`DTA.estimate` *Estimation of synthesis and decay rates*

Description

DTA.estimate uses an experiment, given by a phenotype matrix, data matrix and the number of uridines for each gene to estimate synthesis and decay rate of the genes.

Usage

```
DTA.estimate(phenomat = NULL,datamat = NULL,tnumber = NULL,reliable = NULL,ccl = NULL,mRNAs = NULL,medi
```

Arguments

`phenomat`	A phenotype matrix, containing the design of the experiment as produced by `DTA.phenomat`. Columns are name, fraction (U=unlabebeld, L=labeled, T=total), time and nr (=replicate number). Rows represent individual experiments.
`datamat`	A matrix, containing the measurements from U, L and T, according to the design given in phenomat. Matrix should only contain the rows of phenomat as columns.
`tnumber`	Integer vector, containing the numbers of uridine residues for each transcript. Elements should have the rownames of datamat.
`ccl`	The cell cycle length of the cells (optional). Is not modeled, if not set.
`mRNAs`	Estimated number of mRNAs in a cell (optional).
`reliable`	Vector of 'reliable' genes, which are used for parameter estimation.
`mediancenter`	Should the quotient Labeled/Total resp. Unlabeled/Total be rescaled to a common median over it's replicates before building the genewise median.
`usefractions`	From which fractions should the decay rate be calculated: "LandT", "UandT" or "both".

LtoTratio	Coefficient to rescale Labeled/Total. Is estimated from the data, if not specified. See ratiomethod. Altering this parameter leads to a altered median half-life. For details, see supplemental material of Sun et al. (see references).
ratiomethod	Choose the regression method to be used, possible methods are: "tls", "bias" and "lm". For details, see supplemental material of Sun et al. (see references). Method to estimate the parameter LtoTratio, which determines the median half-life of the sample.
largest	Percentage of largest residues from the first regression not to be used in the second regression step. For details, see supplemental material of Sun et al. (see references).
weighted	Should the regression be weighted with 1/(Total^2 + median(Total))?
relevant	Choose the arrays to be used for halflives calculation, vector due to nr (=replicate number) in phenomat. If not set, all arrays are used.
check	If check = TRUE, control messages and plots will be generated.
error	If TRUE, the measurement error is assessed by means of an error model and resampling to gain confidence regions.
samplesize	Error model samplesize for resampling.
confidence.range	Confidence region for error model as quantiles. Interval should be between 0 and 1.
bicor	Should the labeling bias be corrected?
condition	String, to be added to the plotnames if saved.
upper	Upper bound for labeling bias estimation. For details, see supplemental material of Sun et al. (see references).
lower	Lower bound for labeling bias estimation. For details, see supplemental material of Sun et al. (see references).
save.plots	If save.plots = TRUE, control plots will be saved. Please check folder writability.
resolution	Resolution scaling factor for plotting. (Scaled with 72dpi.)
notinR	If TRUE, plots are not plotted in R.
RStudio	For RStudio users. Suppresses the opening of a new device, as RStudio allows only one.
folder	Path to the folder, where to save the plots. Needs to be writable.
fileformat	Fileformat for plots to be saved. See plotit function (LSD package). Save the plot as "jpeg", "png", "bmp", "tiff", "ps" or "pdf".
totaloverwt	Only needed when mRNAs is set. Should give the factor by which the total mRNA of the condition outreaches that of the reference (comparative DTA data).
simulation	True, if data was generated by DTA.generate.
sim.object	Simulation object created by DTA.generate.

Value

`DTA.estimate` returns a list, where each entry contains the estimation results for all replicates of one labeling time. Each result contains the following entries

`triples`	Mapping of each fraction and experiment to its corresponding column in the data matrix.
`plabel`	The labeling efficiency. For details, see supplemental material of Sun et al. (see references).
`LtoTratio`	Estimated ratio of labeled to total fraction.
`UtoTratio`	Estimated ratio of unlabeled to total fraction.
`LtoUratio`	Estimated ratio of labeled to unlabeled fraction.
`correcteddatamat`	Labeling bias corrected data matrix.
`drmat`	Decay rates for each replicate. The last column gives the median decay rates.
`dr`	Median decay rates. The last column of drmat.
`dr.confidence`	Confidence regions of decay rates.
`hlmat`	Half-lives for each replicate. The last column gives the median half-lifes.
`hl`	Median half-lives. The last column of hlmat.
`hl.confidence`	Confidence regions of half-lives.
`TEmat`	Total expression for each replicate. The last column gives the median total expression values.
`TE`	Median total expression values. The last column of TEmat.
`TE.confidence`	Confidence regions of total expression values.
`LEmat`	Labeled expression for each replicate. The last column gives the median labeled expression values.
`LE`	Median labeled expression values. The last column of LEmat.
`LE.confidence`	Confidence regions of labeled expression values.
`UEmat`	Unlabeled expression for each replicate. The last column gives the median unlabeled expression values. (Only if unlabeled values exist in the experiment)
`UE`	Median unlabeled expression values. The last column of UEmat. (Only if unlabeled values exist in the experiment)
`UE.confidence`	Confidence regions of unlabeled expression values.
`srmat`	Synthesis rates for each replicate. The last column gives the median synthesis rates.
`sr`	Median synthesis rates. The last column of srmat.
`sr.confidence`	Confidence regions of synthesis rates.
`LtoTmat`	Labeled to total ratio for each replicate. The last column gives the median labeled to total ratios.
`LtoT`	Median labeled to total ratios. The last column of LtoTmat.
`LtoT.confidence`	Confidence regions of labeled to total ratios.

UtoTmat	Unlabeled to total ratio for each replicate. The last column gives the median unlabeled to total ratios.
UtoT	Median unlabeled to total ratios. The last column of UtoTmat.
UtoT.confidence	Confidence regions of unlabeled to total ratios.
Rsrmat	Rescaled synthesis rates for each replicate, if parameter mRNAs is specified. The last column gives the median synthesis rates.
Rsr	Rescaled median synthesis rates. The last column of Rsrmat.
globaldrmat	Decay rate for each replicate. Reciprocally weighted by the total expression. Last element contains (weighted) median decay rate.
globaldr	(Weighted) median decay rate.

Author(s)

Bjoern Schwalb <schwalb@lmb.uni-muenchen.de>

References

C. Miller, B. Schwalb, K. Maier, D. Schulz, S. Duemcke, B. Zacher, A. Mayer, J. Sydow, L. Marcinowski, L. Doelken, D. E. Martin, A. Tresch, and P. Cramer. Dynamic transcriptome analysis measures rates of mRNA synthesis and decay in yeast. Mol Syst Biol, 7:458, 2011. M. Sun, B. Schwalb, D. Schulz, N. Pirkl, L. Lariviere, K. Maier, A. Tresch, P. Cramer. Mutual feedback between mRNA synthesis and degradation buffers transcript levels in a eukaryote. Under review. B. Schwalb, B. Zacher, S. Duemcke, D. Martin, P. Cramer, A. Tresch. Measurement of genome-wide RNA synthesis and decay rates with Dynamic Transcriptome Analysis (DTA/cDTA). Bioinformatics.

See Also

heatscatter, plotit, tls

Examples

```
dataPath = system.file("data", package="DTA")
load(file.path(dataPath, "Miller2011.RData"))

### for control plots set 'check = TRUE' ###

res = DTA.estimate(Sc.phenomat,Sc.datamat,Sc.tnumber,ccl = 150,mRNAs = 60000,reliable = Sc.reliable,check = FALSE)
```

DTA.generate *Simulation of DTA experiments*

Description

DTA.generate produces the phenotype matrix and the matrix containing the simulated data according to the given parameters.

Usage

```
DTA.generate(timepoints, tnumber = NULL, plabel = NULL, nrgenes = 5000, mediantime = 12, ccl = 150, delay
```

Arguments

timepoints	Integer vector containing the labeling times for which the samples should be generated.
tnumber	Integer vector containing the number of uridine residues for each gene. If NULL, tnumber is sampled from an F-distribution within the function.
plabel	The labeling efficiency. If NULL, plabel is set to 0.005 within the function. For details, see supplemental material of Sun et al. (see references).
nrgenes	The number of genes the simulated experiment will have (will be cropped if it exceeds the length of tnumber).
mediantime	The median of the randomly drawn half-life distribution.
ccl	The cell cycle length (in minutes).
delaytime	Estimates the delay between the moment of 4sU/4tU labeling and actual incorporation of it into mRNA.
sdnoise	The amount of measurement noise (proportional to expression strength).
nobias	Should a labeling bias be added?
unspecific.LtoU	Proportion of labeled RNAs that unspecifically end up in the unlabeled fraction.
unspec.LtoU.weighted	Should unspecific proportion of labeled to unlabeled depend linearly on the length of the RNA?
unspecific.UtoL	Proportion of unlabeled RNAs that unspecifically end up in the labeled fraction.
unspec.UtoL.weighted	Should unspecific proportion of unlabeled to labeled depend linearly on the length of the RNA?
truehalflives	If the data should be generated using a given half-life distribution, this vector must contain the respective values for each gene.
truecomplete	If the data should be generated using a given expression distribution, this vector must contain the respective values for each gene.
genenames	An optional list of gene names.
cDTA	cDTA = FALSE does not rescale L and U.

Value

DTA.generate returns a list, containing the following entries

phenomat	A matrix, containing the design of the experiment as produced by DTA.phenomat.
datamat	A matrix, containing the simulated measurements from U, L and T, according to the design given in phenomat.
tnumber	Integer vector containing the number of uridine residues for each gene.
ccl	The cell cycle length (in minutes).
truecomplete	A vector, containing the true amount of total RNA.
truelambdas	A vector, containing the true decay rates.
truemus	A vector, containing the true synthesis rates.
truehalflives	A vector, containing the true half-lives.
trueplabel	The true labeling efficiency. For details, see supplemental material of Miller et al. (see references).
truear	The true parameter ar. For details, see supplemental material of Miller et al. (see references).
truebr	The true parameter br. For details, see supplemental material of Miller et al. (see references).
truecr	The true parameter cr. For details, see supplemental material of Miller et al. (see references).
truecrbyar	The true parameter cr/ar. For details, see supplemental material of Miller et al. (see references).
truecrbybr	The true parameter cr/br. For details, see supplemental material of Miller et al. (see references).
truebrbyar	The true parameter br/ar. For details, see supplemental material of Miller et al. (see references).
trueLasymptote	The true parameter asymptote (labeled bias). For details, see supplemental material of Miller et al. (see references).
trueUasymptote	The true parameter asymptote (unlabeled bias). For details, see supplemental material of Miller et al. (see references).

Author(s)

Bjoern Schwalb <schwalb@lmb.uni-muenchen.de>

References

C. Miller, B. Schwalb, K. Maier, D. Schulz, S. Duemcke, B. Zacher, A. Mayer, J. Sydow, L. Marcinowski, L. Doelken, D. E. Martin, A. Tresch, and P. Cramer. Dynamic transcriptome analysis measures rates of mRNA synthesis and decay in yeast. Mol Syst Biol, 7:458, 2011. M. Sun, B. Schwalb, D. Schulz, N. Pirkl, L. Lariviere, K. Maier, A. Tresch, P. Cramer. Mutual feedback between mRNA synthesis and degradation buffers transcript levels in a eukaryote. Under review. B. Schwalb, B. Zacher, S. Duemcke, D. Martin, P. Cramer, A. Tresch. Measurement of genome-wide RNA synthesis and decay rates with Dynamic Transcriptome Analysis (DTA/cDTA). Bioinformatics.

Examples

```
sim.object = DTA.generate(timepoints=rep(c(6,12),2))

### for control plots set 'check = TRUE' ###

res.sim = DTA.estimate(ratiomethod = "bias",simulation = TRUE,sim.object = sim.object,check = FALSE)
```

DTA.map.it *Mapping function to switch between different identifiers.*

Description

DTA.map.it can map different kinds of identifiers in a matrix or a vector given by mapping vector.

Usage

```
DTA.map.it(mat,map = NULL,check = TRUE)
```

Arguments

mat	Matrix or vector with numerical entries.
map	Vector of identifiers to map to, named by identifiers to map from.
check	Should check protocol be printed.

Author(s)

Bjoern Schwalb <schwalb@lmb.uni-muenchen.de>

References

M. Sun, B. Schwalb, D. Schulz, N. Pirkl, L. Lariviere, K. Maier, A. Tresch, P. Cramer. Mutual feedback between mRNA synthesis and degradation buffers transcript levels in a eukaryote. Under review. B. Schwalb, B. Zacher, S. Duemcke, D. Martin, P. Cramer, A. Tresch. Measurement of genome-wide RNA synthesis and decay rates with Dynamic Transcriptome Analysis (DTA/cDTA). Bioinformatics.

Examples

```
### see vignette examples or reference:
### B. Schwalb, B. Zacher, S. Duemcke, D. Martin, P. Cramer, A. Tresch.
### Measurement of genome-wide RNA synthesis and decay rates with Dynamic Transcriptome Analysis (DTA/cDTA). Bioinf
```

DTA.normalize *cDTA normalization procedure.*

Description

DTA.normalize can normalize expression values from a certain species to the median of values from a reference species.

Usage

```
DTA.normalize(mat,reliable = NULL,logscale = FALSE,protocol = FALSE,center = FALSE)
```

Arguments

mat	Expression matrix.
reliable	The rows to be used, i.e. identifiers of the reference species to normalize on.
logscale	Is the matrix in log-scale ?
protocol	Should a protocol be printed ?
center	Should the center be 0 (log-scale) or 1 (absolute scale). Otherwise the median of the medians is taken.

Author(s)

Bjoern Schwalb <schwalb@lmb.uni-muenchen.de>

References

M. Sun, B. Schwalb, D. Schulz, N. Pirkl, L. Lariviere, K. Maier, A. Tresch, P. Cramer. Mutual feedback between mRNA synthesis and degradation buffers transcript levels in a eukaryote. Under review. B. Schwalb, B. Zacher, S. Duemcke, D. Martin, P. Cramer, A. Tresch. Measurement of genome-wide RNA synthesis and decay rates with Dynamic Transcriptome Analysis (DTA/cDTA). Bioinformatics.

Examples

```
### see vignette examples or reference:
### B. Schwalb, B. Zacher, S. Duemcke, D. Martin, P. Cramer, A. Tresch.
### Measurement of genome-wide RNA synthesis and decay rates with Dynamic Transcriptome Analysis (DTA/cDTA). Bioinf
```

DTA.phenomat *Create a phenomat that suits your experiment.*

Description

DTA.phenomat creates a phenomat for a given experimental design, i.e. used labeling times.

Usage

```
DTA.phenomat(timepoints, timecourse = NULL)
```

Arguments

timepoints	The respective labeling times of the measured samples.
timecourse	Vector giving the order for timecourse DTA data.

Value

A matrix, containing the design of the experiment. Columns are name, fraction (U=unlabebeld, L=labeled, T=total), time and nr (=replicate number). Rows represent individual experiments. For timecourse data, an additional column of the order of the underlying timecourse data can be added via timecourse.

Author(s)

Bjoern Schwalb <schwalb@lmb.uni-muenchen.de>

Examples

```
### phenomat for 2 replicates of 6 and 12 min labeling duration resp.
DTA.phenomat(c(6,12))

### phenomat for three adjacent timepoints measured in 2 replicates
DTA.phenomat(rep(6,6),timecourse = 1:3)
```

DTA.plot.it *Plots in any format and any quality*

Description

DTA.plot.it can save plots in any format and any quality in addition to show them in R devices

Usage

```
DTA.plot.it(filename,sw = 1,sh = 1,sres = 1,plotsfkt,ww = 7,wh = 7,pointsize = 12,dev.pointsize = 8,pape
```

Arguments

filename	Name of the plot to be saved without the format type suffix.
sw	Scaling factor of width. Scaled with 480px.
sh	Scaling factor of height. Scaled with 480px.
sres	Scaling factor of the resolution. Scaled with 72dpi.
plotsfkt	Function of plots to be plotted.
ww	Width of window. Needed only for plotting in R or if filformat = "pdf" or "ps". See pdf or ps.
wh	Height of window. Needed only for plotting in R or if filformat = "pdf" or "ps". See pdf or ps.
pointsize	The default pointsize of plotted text, interpreted as big points (1/72 inch) for plots to be saved.
dev.pointsize	Pointsize of plotted text, interpreted as big points (1/72 inch) for display in R.
paper	Needed only if filformat = "pdf" or "ps". See pdf or ps.
quality	Needed only if filformat = "jpeg". See jpeg.
units	Needed only if filformat = "jpeg", "png", "bmp" or "tiff". See corresponding function.
bg	Backgroundcolor.
fileformat	Save the plot as "jpeg", "png", "bmp", "tiff", "ps" or "pdf".
saveit	Should plot be saved.
notinR	Should plot be not plotted in R.
RStudio	For RStudio users. Suppresses the opening of a new device, as RStudio allows only one.
addformat	Should plot be saved additionally in another format, "jpeg", "png", "bmp", "tiff", "ps" or "pdf".

Author(s)

Bjoern Schwalb <schwalb@lmb.uni-muenchen.de>

Examples

```
plotsfkt = function(){
par(mfrow = c(1,2))
plot(1:10)
plot(10:1)
}
DTA.plot.it(filename = "test",plotsfkt = plotsfkt,saveit = TRUE)

dev.off()
```

Hs.datamat — *Gene expression profiles of the Homo Sapiens DTA experiment from Doelken et al.*

Description

This matrix contains the RNA intensity values for each gene across each RNA fraction and their replicate measurements of the Homo Sapiens DTA experiment from Doelken et al.

Usage

```
Hs.datamat
```

Format

The column names of the matrix give the cel-file name and the row names the Ensembl gene IDs.

Source

Doelken, L., Ruzsics, Z., Raedle, B., Friedel, C. C., Zimmer, R., Mages, J., Hoffmann, R., Dickinson, P., Forster, T., Ghazal, P., & Koszinowski, U. H. (2008). High-resolution gene expression profiling for simultaneous kinetic parameter analysis of RNA synthesis and decay. RNA 14(9), 1959-1972.

Hs.enst2ensg — *Mapping of Homo Sapiens gene and transcript identifiers.*

Description

Mapping from Ensembl transcript IDs to Ensembl gene IDs of Homo Sapiens.

Usage

```
Hs.enst2ensg
```

Format

Vector gives the Ensembl gene IDs, names the Ensembl transcript IDs.

Source

E. Birney, D. Andrews, M. Caccamo, Y. Chen, L. Clarke, G. Coates, T. Cox, F. Cunningham, V. Curwen, T. Cutts, T. Down, R. Durbin, X. M. Fernandez-Suarez, P. Flicek, S. Graef, M. Hammond, J. Herrero, K. Howe, V. Iyer, K. Jekosch, A. Kaehaeri, A. Kasprzyk, D. Keefe, F. Kokocinski, E. Kulesha, D. London, I. Longden, C. Melsopp, P. Meidl, B. Overduin, A. Parker, G. Proctor, A. Prlic, M. Rae, D. Rios, S. Redmond, M. Schuster, I. Sealy, S. Searle, J. Severin, G. Slater, D. Smedley, J. Smith, A. Stabenau, J. Stalker, S. Trevanion, A. Ureta- Vidal, J. Vogel, S. White, C.Woodwark, and T. J. Hubbard. Ensembl 2006. Nucleic acids research, 34(Database issue), January 2006.

Hs.phenomat — *Design of the Homo Sapiens DTA experiment from Doelken et al.*

Description

The phenotype matrix `Hs.phenomat` contains information about the experimental design. It is comprised of the filename, the type of RNA fraction measured (T, U or L), the labeling time and the replicate number.

Usage

```
Hs.phenomat
```

Format

The phenomat is a matrix comprised of the file name, the type of RNA fraction mesasured (T, U or L, `fraction` column), the labeling time (`time`,`timeframe` column) and the replicate number (`nr` column). Rows in this matrix represent the individual experiments.

Source

Doelken, L., Ruzsics, Z., Raedle, B., Friedel, C. C., Zimmer, R., Mages, J., Hoffmann, R., Dickinson, P., Forster, T., Ghazal, P., & Koszinowski, U. H. (2008). High-resolution gene expression profiling for simultaneous kinetic parameter analysis of RNA synthesis and decay. RNA 14(9), 1959-1972.

Hs.reliable — *Gene identifiers valid for parameter estimation from the Homo Sapiens Doelken et al. DTA experiment.*

Description

Ensembl gene IDs, that passed certain criteria among the Homo Sapiens Doelken et al. DTA experiment to be considered valid for parameter estimation. For details, see vignette.

Usage

```
Hs.reliable
```

Format

Vector of Ensembl gene IDs that can be passed to `DTA.estimate` for parameter estimation.

Source

Doelken, L., Ruzsics, Z., Raedle, B., Friedel, C. C., Zimmer, R., Mages, J., Hoffmann, R., Dickinson, P., Forster, T., Ghazal, P., & Koszinowski, U. H. (2008). High-resolution gene expression profiling for simultaneous kinetic parameter analysis of RNA synthesis and decay. RNA 14(9), 1959-1972.

`Hs.tnumber` *The amount of thymines in the cDNA of each transcript of Homo Sapiens.*

Description

The amount of thymines in the cDNA of each transcript of all Homo Sapiens Ensembl transcript IDs, to assess the uridine-dependent labeling bias and eventually correct for it.

Usage

```
Hs.tnumber
```

Format

Vector gives the number of thymines in the cDNA (uridine residues in RNA) of each Ensembl transcript ID.

Source

E. Birney, D. Andrews, M. Caccamo, Y. Chen, L. Clarke, G. Coates, T. Cox, F. Cunningham, V. Curwen, T. Cutts, T. Down, R. Durbin, X. M. Fernandez-Suarez, P. Flicek, S. Graef, M. Hammond, J. Herrero, K. Howe, V. Iyer, K. Jekosch, A. Kaehaeri, A. Kasprzyk, D. Keefe, F. Kokocinski, E. Kulesha, D. London, I. Longden, C. Melsopp, P. Meidl, B. Overduin, A. Parker, G. Proctor, A. Prlic, M. Rae, D. Rios, S. Redmond, M. Schuster, I. Sealy, S. Searle, J. Severin, G. Slater, D. Smedley, J. Smith, A. Stabenau, J. Stalker, S. Trevanion, A. Ureta- Vidal, J. Vogel, S. White, C.Woodwark, and T. J. Hubbard. Ensembl 2006. Nucleic acids research, 34(Database issue), January 2006.

`Miller2011` *Saccharomyces Cerevisiae wild-type DTA experiment from Miller et al.*

Description

R object contains all relevant *.RData files needed for the `DTA.estimate` function. For example, see vignette.

Usage

```
Miller2011
```

Format

R object contains the following *.RData files: `Sc.phenomat` `Sc.datamat` `Sc.reliable` `Sc.tnumber`

Source

C. Miller, B. Schwalb, K. Maier, D. Schulz, S. Duemcke, B. Zacher, A. Mayer, J. Sydow, L. Marcinowski, L. Doelken, D. E. Martin, A. Tresch, and P. Cramer. Dynamic transcriptome analysis measures rates of mRNA synthesis and decay in yeast. Mol Syst Biol, 7:458, 2011. E. Birney, D. Andrews, M. Caccamo, Y. Chen, L. Clarke, G. Coates, T. Cox, F. Cunningham, V. Curwen, T. Cutts, T. Down, R. Durbin, X. M. Fernandez-Suarez, P. Flicek, S. Graef, M. Hammond, J. Herrero, K. Howe, V. Iyer, K. Jekosch, A. Kaehaeri, A. Kasprzyk, D. Keefe, F. Kokocinski, E. Kulesha, D. London, I. Longden, C. Melsopp, P. Meidl, B. Overduin, A. Parker, G. Proctor, A. Prlic, M. Rae, D. Rios, S. Redmond, M. Schuster, I. Sealy, S. Searle, J. Severin, G. Slater, D. Smedley, J. Smith, A. Stabenau, J. Stalker, S. Trevanion, A. Ureta- Vidal, J. Vogel, S. White, C.Woodwark, and T. J. Hubbard. Ensembl 2006. Nucleic acids research, 34(Database issue), January 2006.

`Miller2011dynamic` *Saccharomyces Cerevisiae salt stress DTA experiment from Miller et al.*

Description

R object contains all relevant *.RData files needed for the `DTA.estimate` function. For example, see vignette.

Usage

```
Miller2011dynamic
```

Format

R object contains the following *.RData files: `Sc.phenomat.dynamic` `Sc.datamat.dynamic` `Sc.reliable.dynamic` `Sc.tnumber`

Source

C. Miller, B. Schwalb, K. Maier, D. Schulz, S. Duemcke, B. Zacher, A. Mayer, J. Sydow, L. Marcinowski, L. Doelken, D. E. Martin, A. Tresch, and P. Cramer. Dynamic transcriptome analysis measures rates of mRNA synthesis and decay in yeast. Mol Syst Biol, 7:458, 2011. E. Birney, D. Andrews, M. Caccamo, Y. Chen, L. Clarke, G. Coates, T. Cox, F. Cunningham, V. Curwen, T. Cutts, T. Down, R. Durbin, X. M. Fernandez-Suarez, P. Flicek, S. Graef, M. Hammond, J. Herrero, K. Howe, V. Iyer, K. Jekosch, A. Kaehaeri, A. Kasprzyk, D. Keefe, F. Kokocinski, E. Kulesha, D. London, I. Longden, C. Melsopp, P. Meidl, B. Overduin, A. Parker, G. Proctor, A. Prlic, M. Rae, D. Rios, S. Redmond, M. Schuster, I. Sealy, S. Searle, J. Severin, G. Slater, D. Smedley, J. Smith, A. Stabenau, J. Stalker, S. Trevanion, A. Ureta- Vidal, J. Vogel, S. White, C.Woodwark, and T. J. Hubbard. Ensembl 2006. Nucleic acids research, 34(Database issue), January 2006.

Mm.datamat — *Gene expression profiles of the Mus Musculus DTA experiment from Doelken et al.*

Description

This matrix contains the RNA intensity values for each gene across each RNA fraction and their replicate measurements of the Mus Musculus DTA experiment from Doelken et al.

Usage

```
Mm.datamat
```

Format

The column names of the matrix give the cel-file name and the row names the Ensembl gene IDs.

Source

Doelken, L., Ruzsics, Z., Raedle, B., Friedel, C. C., Zimmer, R., Mages, J., Hoffmann, R., Dickinson, P., Forster, T., Ghazal, P., & Koszinowski, U. H. (2008). High-resolution gene expression profiling for simultaneous kinetic parameter analysis of RNA synthesis and decay. RNA 14(9), 1959-1972.

Mm.enst2ensg — *Mapping of Mus Musculus gene and transcript identifiers.*

Description

Mapping from Ensembl transcript IDs to Ensembl gene IDs of Mus Musculus.

Usage

```
Mm.enst2ensg
```

Format

Vector gives the Ensembl gene IDs, names the Ensembl transcript IDs.

Source

E. Birney, D. Andrews, M. Caccamo, Y. Chen, L. Clarke, G. Coates, T. Cox, F. Cunningham, V. Curwen, T. Cutts, T. Down, R. Durbin, X. M. Fernandez-Suarez, P. Flicek, S. Graef, M. Hammond, J. Herrero, K. Howe, V. Iyer, K. Jekosch, A. Kaehaeri, A. Kasprzyk, D. Keefe, F. Kokocinski, E. Kulesha, D. London, I. Longden, C. Melsopp, P. Meidl, B. Overduin, A. Parker, G. Proctor, A. Prlic, M. Rae, D. Rios, S. Redmond, M. Schuster, I. Sealy, S. Searle, J. Severin, G. Slater, D. Smedley, J. Smith, A. Stabenau, J. Stalker, S. Trevanion, A. Ureta- Vidal, J. Vogel, S. White, C.Woodwark, and T. J. Hubbard. Ensembl 2006. Nucleic acids research, 34(Database issue), January 2006.

Mm.phenomat — *Design of the Mus Musculus DTA experiment from Doelken et al.*

Description

The phenotype matrix `Mm.phenomat` contains information about the experimental design. It is comprised of the filename, the type of RNA fraction measured (T, U or L), the labeling time and the replicate number.

Usage

```
Mm.phenomat
```

Format

The phenomat is a matrix comprised of the file name, the type of RNA fraction mesasured (T, U or L, `fraction` column), the labeling time (`time`,`timeframe` column) and the replicate number (`nr` column). Rows in this matrix represent the individual experiments.

Source

Doelken, L., Ruzsics, Z., Raedle, B., Friedel, C. C., Zimmer, R., Mages, J., Hoffmann, R., Dickinson, P., Forster, T., Ghazal, P., & Koszinowski, U. H. (2008). High-resolution gene expression profiling for simultaneous kinetic parameter analysis of RNA synthesis and decay. RNA 14(9), 1959-1972.

Mm.reliable — *Gene identifiers valid for parameter estimation from the Mus Musculus Doelken et al. DTA experiment.*

Description

Ensembl gene IDs, that passed certain criteria among the Mus Musculus Doelken et al. DTA experiment to be considered valid for parameter estimation. For details, see vignette.

Usage

```
Mm.reliable
```

Format

Vector of Ensembl gene IDs that can be passed to `DTA.estimate` for parameter estimation.

Source

Doelken, L., Ruzsics, Z., Raedle, B., Friedel, C. C., Zimmer, R., Mages, J., Hoffmann, R., Dickinson, P., Forster, T., Ghazal, P., & Koszinowski, U. H. (2008). High-resolution gene expression profiling for simultaneous kinetic parameter analysis of RNA synthesis and decay. RNA 14(9), 1959-1972.

`Mm.tnumber` *The amount of thymines in the cDNA of each transcript of Mus Musculus.*

Description

The amount of thymines in the cDNA of each transcript of all Mus Musculus Ensembl transcript IDs, to assess the uridine-dependent labeling bias and eventually correct for it.

Usage

```
Mm.tnumber
```

Format

Vector gives the number of thymines in the cDNA (uridine residues in RNA) of each Ensembl transcript ID.

Source

E. Birney, D. Andrews, M. Caccamo, Y. Chen, L. Clarke, G. Coates, T. Cox, F. Cunningham, V. Curwen, T. Cutts, T. Down, R. Durbin, X. M. Fernandez-Suarez, P. Flicek, S. Graef, M. Hammond, J. Herrero, K. Howe, V. Iyer, K. Jekosch, A. Kaehaeri, A. Kasprzyk, D. Keefe, F. Kokocinski, E. Kulesha, D. London, I. Longden, C. Melsopp, P. Meidl, B. Overduin, A. Parker, G. Proctor, A. Prlic, M. Rae, D. Rios, S. Redmond, M. Schuster, I. Sealy, S. Searle, J. Severin, G. Slater, D. Smedley, J. Smith, A. Stabenau, J. Stalker, S. Trevanion, A. Ureta- Vidal, J. Vogel, S. White, C.Woodwark, and T. J. Hubbard. Ensembl 2006. Nucleic acids research, 34(Database issue), January 2006.

`Pol.phenomat` *Design of the Saccharomyces Cerevisiae rpb1-N488D (Slow Polymerase) cDTA experiment from Sun et al.*

Description

The phenotype matrix `Pol.phenomat` contains information about the experimental design. It is comprised of the filename, the type of RNA fraction measured (T, U or L), the labeling time and the replicate number.

Usage

```
Pol.phenomat
```

Format

The phenomat is a matrix comprised of the file name, the type of RNA fraction mesasured (T, U or L, `fraction` column), the labeling time (`time`,`timeframe` column) and the replicate number (`nr` column). Rows in this matrix represent the individual experiments.

Source

M. Sun, B. Schwalb, D. Schulz, N. Pirkl, L. Lariviere, K. Maier, A. Tresch, P. Cramer. Mutual feedback between mRNA synthesis and degradation buffers transcript levels in a eukaryote. Under review.

`Raw.datamat` *Gene expression profiles of the Saccharomyces Cerevisiae rpb1-N488D (Slow Polymerase) and wild-type cDTA experiment from Sun et al.*

Description

This matrix contains the RNA intensity values for each gene across each RNA fraction and their replicate measurements of the Saccharomyces Cerevisiae rpb1-N488D (Slow Polymerase) and wild-type cDTA experiment from Sun et al.

Usage

```
Raw.datamat
```

Format

The column names of the matrix give the cel-file name and the row names the affymetrix IDs.

Source

M. Sun, B. Schwalb, D. Schulz, N. Pirkl, L. Lariviere, K. Maier, A. Tresch, P. Cramer. Mutual feedback between mRNA synthesis and degradation buffers transcript levels in a eukaryote. Under review.

`Sc.affy2ensg` *Mapping of SaccharomycesCerevisiae Affymetrix Yeast 2.0 and gene identifiers.*

Description

Mapping from Affymetrix Yeast 2.0 IDs to Ensembl gene IDs of SaccharomycesCerevisiae.

Usage

```
Sc.affy2ensg
```

Format

Vector gives the Ensembl gene IDs, names the Affymetrix Yeast 2.0 IDs.

Source

M. Sun, B. Schwalb, D. Schulz, N. Pirkl, L. Lariviere, K. Maier, A. Tresch, P. Cramer. Mutual feedback between mRNA synthesis and degradation buffers transcript levels in a eukaryote. Under review.

`Sc.datamat` *Gene expression profiles of the Saccharomyces Cerevisiae wild-type DTA experiment from Miller et al.*

Description

This matrix contains the RNA intensity values for each gene across each RNA fraction and their replicate measurements of the Saccharomyces Cerevisiae wild-type DTA experiment from Miller et al.

Usage

```
Sc.datamat
```

Format

The column names of the matrix give the cel-file name and the row names the Ensembl gene IDs.

Source

C. Miller, B. Schwalb, K. Maier, D. Schulz, S. Duemcke, B. Zacher, A. Mayer, J. Sydow, L. Marcinowski, L. Doelken, D. E. Martin, A. Tresch, and P. Cramer. Dynamic transcriptome analysis measures rates of mRNA synthesis and decay in yeast. Mol Syst Biol, 7:458, 2011.

`Sc.datamat.dynamic` *Gene expression profiles of the Saccharomyces Cerevisiae salt stress DTA experiment from Miller et al.*

Description

This matrix contains the RNA intensity values for each gene across each RNA fraction and their replicate measurements of the Saccharomyces Cerevisiae salt stress DTA experiment from Miller et al.

Usage

```
Sc.datamat.dynamic
```

Format

The column names of the matrix give the cel-file name and the row names the Ensembl gene IDs.

Source

C. Miller, B. Schwalb, K. Maier, D. Schulz, S. Duemcke, B. Zacher, A. Mayer, J. Sydow, L. Marcinowski, L. Doelken, D. E. Martin, A. Tresch, and P. Cramer. Dynamic transcriptome analysis measures rates of mRNA synthesis and decay in yeast. Mol Syst Biol, 7:458, 2011.

`Sc.ensg.reliable` *Gene identifiers valid for parameter estimation from the Saccharomyces Cerevisiae Sun et al. cDTA experiment.*

Description

Ensembl gene IDs, that passed certain criteria among the Saccharomyces Cerevisiae Sun et al. cDTA experiment to be considered valid for parameter estimation. For details, see Sun et al (Materials and Methods).

Usage

```
Sc.ensg.reliable
```

Format

Vector of Ensembl gene IDs that can be passed to `DTA.estimate` for parameter estimation.

Source

M. Sun, B. Schwalb, D. Schulz, N. Pirkl, L. Lariviere, K. Maier, A. Tresch, P. Cramer. Mutual feedback between mRNA synthesis and degradation buffers transcript levels in a eukaryote. Under review.

`Sc.phenomat` *Design of the Saccharomyces Cerevisiae wild-type DTA experiment from Miller et al.*

Description

The phenotype matrix `Sc.phenomat` contains information about the experimental design. It is comprised of the filename, the type of RNA fraction measured (T, U or L), the labeling time and the replicate number.

Usage

```
Sc.phenomat
```

Format

The phenomat is a matrix comprised of the file name, the type of RNA fraction mesasured (T, U or L, `fraction` column), the labeling time (`time`,`timeframe` column) and the replicate number (`nr` column). Rows in this matrix represent the individual experiments.

Source

C. Miller, B. Schwalb, K. Maier, D. Schulz, S. Duemcke, B. Zacher, A. Mayer, J. Sydow, L. Marcinowski, L. Doelken, D. E. Martin, A. Tresch, and P. Cramer. Dynamic transcriptome analysis measures rates of mRNA synthesis and decay in yeast. Mol Syst Biol, 7:458, 2011.

`Sc.phenomat.dynamic` *Design of the Saccharomyces Cerevisiae salt stress DTA experiment from Miller et al.*

Description

The phenotype matrix `Sc.phenomat.dynamic` contains information about the experimental design. It is comprised of the filename, the type of RNA fraction measured (T, U or L), the labeling time, the replicate number and an additional number indicating the timecourse order.

Usage

```
Sc.phenomat.dynamic
```

Format

The phenomat is a matrix comprised of the file name, the type of RNA fraction mesasured (T, U or L, `fraction` column), the labeling time (`time`,`timeframe` column), the replicate number (`nr` column) and a number indicating the timecourse order (`timecourse` column). Rows in this matrix represent the individual experiments.

Source

C. Miller, B. Schwalb, K. Maier, D. Schulz, S. Duemcke, B. Zacher, A. Mayer, J. Sydow, L. Marcinowski, L. Doelken, D. E. Martin, A. Tresch, and P. Cramer. Dynamic transcriptome analysis measures rates of mRNA synthesis and decay in yeast. Mol Syst Biol, 7:458, 2011.

Sc.reliable — *Gene identifiers valid for parameter estimation from the Saccharomyces Cerevisiae Miller et al. wild-type DTA experiment.*

Description

Ensembl gene IDs, that passed certain criteria among the Saccharomyces Cerevisiae Miller et al. wild-type DTA experiment to be considered valid for parameter estimation. For details, see supplemental material Miller et al.

Usage

```
Sc.reliable
```

Format

Vector of Ensembl gene IDs that can be passed to `DTA.estimate` for parameter estimation.

Source

C. Miller, B. Schwalb, K. Maier, D. Schulz, S. Duemcke, B. Zacher, A. Mayer, J. Sydow, L. Marcinowski, L. Doelken, D. E. Martin, A. Tresch, and P. Cramer. Dynamic transcriptome analysis measures rates of mRNA synthesis and decay in yeast. Mol Syst Biol, 7:458, 2011.

Sc.reliable.dynamic — *Gene identifiers valid for parameter estimation from the Saccharomyces Cerevisiae Miller et al. salt stress DTA experiment.*

Description

Ensembl gene IDs, that passed certain criteria among the Saccharomyces Cerevisiae Miller et al. salt stress DTA experiment to be considered valid for parameter estimation. For details, see supplemental material Miller et al.

Usage

```
Sc.reliable.dynamic
```

Format

Vector of Ensembl gene IDs that can be passed to `DTA.estimate` for parameter estimation.

Source

C. Miller, B. Schwalb, K. Maier, D. Schulz, S. Duemcke, B. Zacher, A. Mayer, J. Sydow, L. Marcinowski, L. Doelken, D. E. Martin, A. Tresch, and P. Cramer. Dynamic transcriptome analysis measures rates of mRNA synthesis and decay in yeast. Mol Syst Biol, 7:458, 2011.

`Sc.ribig.ensg` *Ribosome biogenesis genes.*

Description

ORF identifiers (Ensembl Gene ID) found to be associated with ribosome biogenesis, rRNA processing etc.

Usage

```
Sc.ribig.ensg
```

Format

Vector of ORF identifiers (Ensembl Gene ID).

Source

P. Jorgensen, I. RupeAi, J. R. Sharom, L. Schneper, J. R. Broach, and M. Tyers. A dynamic transcriptional network communicates growth potential to ribosome synthesis and critical cell size. Genes & Development, 18(20):2491-2505, October 2004.

`Sc.rpg.ensg` *Ribosomal protein genes.*

Description

ORF identifiers (Ensembl Gene ID) encoding for ribosomal protein genes.

Usage

```
Sc.rpg.ensg
```

Format

Vector of ORF identifiers (Ensembl Gene ID).

Source

A. Nakao, M. Yoshihama, and N. Kenmochi. RPG: the Ribosomal Protein Gene database. Nucleic acids research, 32(Database issue), January 2004.

Sc.stress.ensg *ISA stress module.*

Description

ORF identifiers (Ensembl Gene ID) found to be associated with stress response by the iterative signature algorithm.

Usage

```
Sc.stress.ensg
```

Format

Vector of ORF identifiers (Ensembl Gene ID).

Source

J. Ihmels, G. Friedlander, S. Bergmann, O. Sarig, Y. Ziv, and N. Barkai. Revealing modular organization in the yeast transcriptional network. Nature genetics, 31(4):370-377, August 2002.

Sc.tf.ensg *Transcription factors.*

Description

ORF identifiers (Ensembl Gene ID) encoding for transcription factors.

Usage

```
Sc.tf.ensg
```

Format

Vector of ORF identifiers (Ensembl Gene ID).

Source

K. D. MacIsaac, T. Wang, D. B. Gordon, D. K. Gifford, G. D. Stormo, and E. Fraenkel. An improved map of conserved regulatory sites for saccharomyces cerevisiae. BMC Bioinformatics, 7:113, 2006.

`Sc.tnumber` *The amount of thymines in the cDNA of each transcript of Saccharomyces Cerevisiae.*

Description

The amount of thymines in the cDNA of each transcript of all Saccharomyces Cerevisiae Ensembl transcript IDs (ORF identifier), to assess the uridine-dependent labeling bias and eventually correct for it.

Usage

```
Sc.tnumber
```

Format

Vector gives the number of thymines in the cDNA (uridine residues in RNA) of each Ensembl transcript ID.

Source

E. Birney, D. Andrews, M. Caccamo, Y. Chen, L. Clarke, G. Coates, T. Cox, F. Cunningham, V. Curwen, T. Cutts, T. Down, R. Durbin, X. M. Fernandez-Suarez, P. Flicek, S. Graef, M. Hammond, J. Herrero, K. Howe, V. Iyer, K. Jekosch, A. Kaehaeri, A. Kasprzyk, D. Keefe, F. Kokocinski, E. Kulesha, D. London, I. Longden, C. Melsopp, P. Meidl, B. Overduin, A. Parker, G. Proctor, A. Prlic, M. Rae, D. Rios, S. Redmond, M. Schuster, I. Sealy, S. Searle, J. Severin, G. Slater, D. Smedley, J. Smith, A. Stabenau, J. Stalker, S. Trevanion, A. Ureta- Vidal, J. Vogel, S. White, C.Woodwark, and T. J. Hubbard. Ensembl 2006. Nucleic acids research, 34(Database issue), January 2006.

`Sp.affy.reliable` *Gene identifiers valid for cDTA normalization from the Saccharomyces Cerevisiae Sun et al. cDTA experiment.*

Description

Ensembl gene IDs, that passed certain criteria among the Saccharomyces Cerevisiae Sun et al. cDTA experiment to be considered valid for cDTA normalization. For details, see Sun et al (Materials and Methods).

Usage

```
Sp.affy.reliable
```

Format

Vector of Schizosaccharomyces Pombe affymetrix IDs that can be passed to `DTA.normalize` for cDTA normalization of the Saccharomyces Cerevisiae identifiers.

Source

M. Sun, B. Schwalb, D. Schulz, N. Pirkl, L. Lariviere, K. Maier, A. Tresch, P. Cramer. Mutual feedback between mRNA synthesis and degradation buffers transcript levels in a eukaryote. Under review.

`Sp.tnumber` *The amount of thymines in the cDNA of each transcript of Schizosaccharomyces Pombe.*

Description

The amount of thymines in the cDNA of each transcript of all Schizosaccharomyces Pombe Ensembl transcript IDs (ORF identifier), to assess the uridine-dependent labeling bias and eventually correct for it.

Usage

```
Sp.tnumber
```

Format

Vector gives the number of thymines in the cDNA (uridine residues in RNA) of each Ensembl transcript ID.

Source

E. Birney, D. Andrews, M. Caccamo, Y. Chen, L. Clarke, G. Coates, T. Cox, F. Cunningham, V. Curwen, T. Cutts, T. Down, R. Durbin, X. M. Fernandez-Suarez, P. Flicek, S. Graef, M. Hammond, J. Herrero, K. Howe, V. Iyer, K. Jekosch, A. Kaehaeri, A. Kasprzyk, D. Keefe, F. Kokocinski, E. Kulesha, D. London, I. Longden, C. Melsopp, P. Meidl, B. Overduin, A. Parker, G. Proctor, A. Prlic, M. Rae, D. Rios, S. Redmond, M. Schuster, I. Sealy, S. Searle, J. Severin, G. Slater, D. Smedley, J. Smith, A. Stabenau, J. Stalker, S. Trevanion, A. Ureta- Vidal, J. Vogel, S. White, C.Woodwark, and T. J. Hubbard. Ensembl 2006. Nucleic acids research, 34(Database issue), January 2006.

`Sun2011` *Saccharomyces Cerevisiae rpb1-N488D (Slow Polymerase) and wild-type cDTA experiment from Sun et al.*

Description

R object contains all relevant *.RData files needed for the `DTA.estimate` function. For example, see Schwalb et al.

Usage

```
Sun2011
```

Format

R object contains the following *.RData files: `Raw.datamat` `Sp.affy.reliable` `Sc.affy2ensg` `Wt.phenomat` `Pol.phenomat` `Sc.ensg.reliable` `Sc.tnumber`

Source

M. Sun, B. Schwalb, D. Schulz, N. Pirkl, L. Lariviere, K. Maier, A. Tresch, P. Cramer. Mutual feedback between mRNA synthesis and degradation buffers transcript levels in a eukaryote. Under review. B. Schwalb, B. Zacher, S. Duemcke, D. Martin, P. Cramer, A. Tresch. Measurement of genome-wide RNA synthesis and decay rates with Dynamic Transcriptome Analysis (DTA/cDTA). Bioinformatics. E. Birney, D. Andrews, M. Caccamo, Y. Chen, L. Clarke, G. Coates, T. Cox, F. Cunningham, V. Curwen, T. Cutts, T. Down, R. Durbin, X. M. Fernandez-Suarez, P. Flicek, S. Graef, M. Hammond, J. Herrero, K. Howe, V. Iyer, K. Jekosch, A. Kaehaeri, A. Kasprzyk, D. Keefe, F. Kokocinski, E. Kulesha, D. London, I. Longden, C. Melsopp, P. Meidl, B. Overduin, A. Parker, G. Proctor, A. Prlic, M. Rae, D. Rios, S. Redmond, M. Schuster, I. Sealy, S. Searle, J. Severin, G. Slater, D. Smedley, J. Smith, A. Stabenau, J. Stalker, S. Trevanion, A. Ureta- Vidal, J. Vogel, S. White, C.Woodwark, and T. J. Hubbard. Ensembl 2006. Nucleic acids research, 34(Database issue), January 2006.

`tls` *Weighted Total Least Square Regression.*

Description

Weigthed total least square regression according to Golub and Van Loan (1980) in SIAM J.Numer.Anal Vol 17 No.6.

Usage

```
tls(formula, D = NULL, T = NULL, precision = .Machine$double.eps)
```

Arguments

`formula`	An object of class formula.
`D`	Diagonal weigth matrix. Default weights are set to 1.
`T`	Diagonal weigth matrix. Default weights are set to 1.
`precision`	Smallest possible numeric value on this machine (default).

Value

`tls` returns a lm object.

Author(s)

Sebastian Duemcke <duemcke@lmb.uni-muenchen.de>

References

Golub, G.H. and Van Loan, C.F. (1980). An analysis of the total least squares problem. SIAM J. Numer. Anal., 17:883-893.

Examples

```
f = 1.5 # true ratio
a = rnorm(5000)
b = f*a
a = a + rnorm(5000,sd=0.5)
b = b + rnorm(5000,sd=0.5)

coeff.tls = coef(tls(b ~ a + 0))
coeff.lm1 = coef(lm(b ~ a + 0))
coeff.lm2 = 1/coef(lm(a ~ b + 0))

heatscatter(a,b)
abline(0,coeff.lm1,col="red",pch=19,lwd=2)
abline(0,coeff.lm2,col="orange",pch=19,lwd=2)
abline(0,coeff.tls,col="green",pch=19,lwd=2)
abline(0,f,col="grey",pch=19,lwd=2,lty=2)
legend("topleft", c("Least-squares regr. (y ~ x + 0)", "Least-squares regr. (x ~ y + 0)", "Total Least-squares regr.

results = c(coeff.tls,coeff.lm1,coeff.lm2)
names(results) = c("coeff.tls","coeff.lm1","coeff.lm2")
print(results)
```

`Wt.phenomat` *Design of the Saccharomyces Cerevisiae wild-type cDTA experiment from Sun et al.*

Description

The phenotype matrix `Wt.phenomat` contains information about the experimental design. It is comprised of the filename, the type of RNA fraction measured (T, U or L), the labeling time and the replicate number.

Usage

```
Wt.phenomat
```

Format

The phenomat is a matrix comprised of the file name, the type of RNA fraction mesasured (T, U or L, `fraction` column), the labeling time (`time`,`timeframe` column) and the replicate number (`nr` column). Rows in this matrix represent the individual experiments.

Source

M. Sun, B. Schwalb, D. Schulz, N. Pirkl, L. Lariviere, K. Maier, A. Tresch, P. Cramer. Mutual feedback between mRNA synthesis and degradation buffers transcript levels in a eukaryote. Under review.

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