Package ‘gprege’

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Title Gaussian Process Ranking and Estimation of Gene Expression
  time-series
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Suggests spam
Description The gprege package implements the methodology described in
  Kalaitzis & Lawrence (2011) "A simple approach to ranking differentially
  expressed gene expression time-courses through Gaussian process regression".
  The software fits two GPs with the an RBF (+ noise diagonal) kernel on each
  profile. One GP kernel is initialised with a short lengthscale hyperparameter,
  signal variance as the observed variance and a zero noise variance. It is
  optimised via scaled conjugate gradients (netlab). A second GP has fixed
  hyperparameters: zero inverse-width, zero signal variance and noise
  variance as the observed variance. The log-ratio of marginal likelihoods of
  the two hypotheses acts as a score of differential expression for the profile.
  Comparison via ROC curves is performed against BATS (Angelini et.al, 2007).
  A detailed discussion of the ranking approach and dataset used can be found in
  the paper (http://www.biomedcentral.com/1471-2105/12/180).
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R topics documented:

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Description

This package implements the method of Kalaitzis and Lawrence (2011) for Gaussian process modelling gene expression time-series data. The method can be used to filter quiet genes and quantify differential expression in time-series expression ratios.

Details

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For details of using the package please refer to the Vignette.

Author(s)

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References


See Also
demGpCov2D, demGpSample, demInterpolation, demOptimiseGp, demRegression

Examples

## see demTp63Gp1.R
**compareROC**

**Make ROC plots.**

**Description**

This rocStats wrapper superimposes ROC curves on a plot to analyse the output performance of a method-A, and optionally compare it with that of a method-B, based on some ground thruth labels.

**Usage**

```r
compareROC(output, groundTruthLabels, compareToRanking)
```

**Arguments**

- `output` (vector): The output of ranking scores returned by method-A for each data-point.
- `groundTruthLabels` (vector): A binary vector that contains the ground truth (e.g., which genes are members of the top-100 ground truth list).
- `compareToRanking` (matrix): A matrix where each column is the output vector of ranking scores returned by another competing method.

**Value**

- `area` (vector): A scalar. The area under the ROC curve of method-A.

**See Also**

- `rocStats`

**Examples**

```r
data(FragmentDellaGattaData) ## Load demo data.
compareROC(output=rnorm(length(DGatta_labels_byTSNI))>0, groundTruthLabels=DGatta_labels_byTSNI)
```

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**DellaGattaData**

*Fragment dataset of 13 time-point mouse microarray time series of gene expression ratios and and a ranking list of TP63 targets suggested by TSNI.*

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**Description**

`exprs_tp63_RMA` 100 gene reporters of 13 time-points mouse Affymetrix microarray gene expression coming from a study on primary mouse keratinocytes with an induced activation of the TRP63 transcription factor (GEO-accession number: GSE10562, see Source section), where a reverse-engineering algorithm was developed (TSNI: time-series network identification) to infer the direct targets of TRP63 (Della Gatta et al. 2008). The data has been processed using `rma` (affy) and the profiles are centred (zero-mean) across the timepoints.
DGatta_labels_byTSNI, DGatta_labels_byTSNItop100  
a ranking list suggested based on TSNI is provided. The inferred direct targets were biologically confirmed by correlation with ChIP-Seq binding regions; therefore the list is used as a noisy ground truth. See Source section.

genesymbols  
Names of the genes that the transcript_IDs (in exprs_tp63_RMA) correspond to.

gpregeOutput  
Its field 'rankingScores' contains log-marginal likelihood ratios, used as ranking scores, for each gene reporter in exprs_tp63_RMA. This is the output from a run of gprege on the full DellaGatta dataset (see demTp63Gp1.R) and stored here for convenience.

Usage

data(FragmentDellaGattaData)

Source

GEO: http://www.ncbi.nlm.nih.gov/geo/, TSNI ranking: genome.cshlp.org/content/suppl/2008/05/05/gr.073601.107.DC1/DellaGatta_SupTable1.xls

References


demTp63Gp1  
gprege on TP63 expression time-series.

Description

Demo script of Gaussian Process Regression and Estimation of Gene Expression on TP63 time-series data (see gprege.m). See Kalaitzis & Lawrence (2011) for a detailed discussion of the ranking algorithm and dataset used.

Usage

demTp63Gp1(fulldataset=FALSE)

Arguments

fulldataset  
(Logical) TRUE downloads and uses the full dataset.

See Also

gprege

Examples

demTp63Gp1(fulldataset=FALSE)
**BATS rankings (Angelini, 2007)**

**Case 1:** Delta error prior  
**Case 2:** Inverse Gamma error prior  
**Case 3:** Double Exponential error prior

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**Description**

- **DGdat_p63_case1_GL**  
  Case 1: Delta error prior
- **DGdat_p63_case2_GL**  
  Case 2: Inverse Gamma error prior
- **DGdat_p63_case3_GL**  
  Case 3: Double Exponential error prior

**Usage**

```r
data(DGdat_p63)
```

**Source**

  TSNI ranking: [genome.cshlp.org/content/suppl/2008/05/05/gr.073601.107.DC1/DellaGatta_SupTable1.xls](http://genome.cshlp.org/content/suppl/2008/05/05/gr.073601.107.DC1/DellaGatta_SupTable1.xls)

**References**


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**exhaustivePlot**

*Plot of the LML function by exhaustive search.*

**Description**

Exhaustively searches the hyperparameter space by a grid, whose resolution is passed as an argument, and plots the LML function for every point in the space.

**Usage**

```r
exhaustivePlot(y, x, xstar, options, maxwidth, res, nlevels)
```

**Arguments**

- **y**  
  the target (output) data.
- **x**  
  the input data matrix.
- **xstar**  
  the points to predict function values.
- **options**  
  options structure as defined by gpOptions.m.
- **maxwidth**  
  maximum lengthscale to search for.
- **res**  
  The search resolution. Number of points to plot for in the search range.
- **nlevels**  
  Number of contour levels.
Value
area Area under the ROC curve of method-A.

See Also
rocStats

Examples
noiseLevel <- 0.2
noiseVar <- noiseLevel^2
options <- gpOptions()
options$kern$comp <- list('rbf','white')
## Create data set
l <- 9; x <- matrix(seq(0,240,by=20), ncol=1)
tureKern <- kernCreate(x, 'rbf')
trueKern$inverseWidth <- 1/(20^2) ## Characteristic inverse-width.
K <- kernCompute(trueKern, x) + diag(dim(x)[1])*noiseVar
## Sample some true function values.
y <- gaussSamp(Sigma=K, numSamps=1)
xTest <- as.matrix(seq(0, 240, length=200))
graphics.off(); dev.new(); plot.new(); dev.new(); plot.new()
exhaustivePlot(y, x, xTest, options=options, maxwidth=100, res=50, nlevels=75)

Description
Fits two GPs with the an RBF (+ noise diagonal) kernel on each profile. One GP kernel is initialised with a short lengthscale hyperparameter, signal variance as the observed variance and a zero noise variance. It is optimised via scaled conjugate gradients (netlab). The other GP has fixed hyperparameters with a zero inverse-width, zero signal variance and noise variance as the observed variance. The log-ratio of marginal likelihoods of the two hypotheses acts as a score of differential expression for the profile. Comparison via ROC curves is performed against BATS (Angelini et.al, 2007). See Kalaitzis & Lawrence (2011) for a detailed discussion of the ranking algorithm and dataset used.

Usage
gprege(data, inputs, gpregeOptions)

Arguments
data The matrix of gene expression profiles; one profile per row.
inputs Inputs (timepoints) to the GP.
gpregeOptions Options list for gprege with fields
    explore Logical. TRUE operates in a user interactive mode. Used for examining individual gene expression profiles.
    labels A binary vector. TRUE specifies whether the corresponding profile comes from a differentially expressed gene (usually from a ground truth).
indexRange  A numeric vector. Range of indices of profiles on which the function should operate. Useful for selective exploration of specific profiles, e.g. only genes marked as differentially expressed in a ground truth list.

interpolatedT  A numeric vector. New timepoints to interpolate for each profile, based on the estimated function values.

iters  A scalar. The number of iterations for scaled-conjugate gradients (SCG) optimisation.

display  Logical. Display gradient and LML information on each SCG iteration.

inithypers  The matrix of hyperparameter configurations as its rows. Each row has the following format: [inverse-lengthscale percent-signal-variance percent-noise-variance] The first row corresponds to a (practically constant) function with a very large lengthscale. Such a function will account for 0 percent of the observed variance in the expression profile (hence 0 for signal) and explain it as noise (hence 1 for noise). Subsequent rows (initialisations for SCG optimisation) correspond to functions of various lengthscales that explain all the observed variance as signal. A reasonable lengthscale would be roughly in line with the time-point sampling intervals.

exhaustPlotRes  A scalar. The search resolution. Used for interactive mode (explore == 1).

exhaustPlotLevels  A scalar. Number of contour levels in the exhaustive plot. Used for interactive mode (explore == 1).

exhaustPlotMaxWidth  A scalar. the maximum lengthscale to search for. Used for interactive mode (explore == 1).

Value

gpregeOutput  Output list with fields:

signalvar  A numeric vector of the vertical lengthscales of the optimised RBF kernel; one for each profile.

noisevar  A numeric vector. Similar to signalvar, but for the noise hyperparameter.

width  A numeric vector. Similar to signalvar and noisevar, but for the horizontal lengthscales of the RBF.

LMLs  A numeric vector of log-marginal likelihoods of the GP; one for each profile.

interpolatedData  A matrix of the extended dataset with interpolated values as the augmenting columns.

rankingScores  A numeric vector of the ranking scores, based on the log-ratio of marginal likelihoods.

See Also

gpOptions, gpCreate, gpExpandParam, gpOptimise, gpExtractParam, gpLogLikelihood, gpPosterior

Examples

## see demTp63Gp1.R
data(FragmentDellaGattaData) ## Load demo data.
## Setup other gprege options.
gpregeOptions = list(indexRange=(1:2), explore=TRUE, exhaustPlotRes=30, exhaustPlotLevels=10,
## rocStats

### Make ROC curve data.

**Description**

Computes the points on an ROC curve by varying a threshold on the sorted outputs of the method in question.

**Usage**

```r
rocStats(outputs, groundTruthLabels, decreasing = TRUE)
```

**Arguments**

- `outputs`: A numeric vector with the outputs of the evaluated method (e.g. likelihoods from `gprege`).
- `groundTruthLabels`: A binary vector than contains the ground truth (e.g. which genes belong in the top-100 ground truth list).
- `decreasing`: Logical. TRUE sorts outputs by decreasing order.

**Value**

- `stats`: A list of numeric variables with the necessary statistics to compute an ROC curve, a precision-recall curve, etc.

**Examples**

```r
## see compareROC.R
data(FragmentDellaGattaData) ## Load demo data.
rocStats(gpregeOutput$rankingScores, DGatta_labels_byTSNItop100, decreasing=TRUE)
```
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