Package ‘tigre’

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Title Transcription factor Inference through Gaussian process
Reconstruction of Expression
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utils, annotate, DBI, RSQLite
Suggests drosogenome1.db, puma, lumi, BiocStyle
Description The tigre package implements our methodology of Gaussian
process differential equation models for analysis of gene
expression time series from single input motif networks. The
package can be used for inferring unobserved transcription
factor (TF) protein concentrations from expression measurements
of known target genes, or for ranking candidate targets of a
TF.
License AGPL-3
URL https://github.com/ahonkela/tigre
BugReports https://github.com/ahonkela/tigre/issues
biocViews Microarray, TimeCourse, GeneExpression, Transcription,
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NeedsCompilation yes

R topics documented:

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Description

This package implements the method of Gao et al. (2008) and Honkela et al. (2010) for Gaussian process modelling single input motif regulatory systems with time-series expression data. The method can be used to rank potential targets of transcription factors based on such data.

Details

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License: A-GPL Version 3

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

Author(s)

Antti Honkela, Pei Gao, Jonatan Ropponen, Miika-Petteri Matikainen, Magnus Rattray, Neil D. Lawrence

Maintainer: Antti Honkela <antti.honkela@hiit.fi>
References


See Also

puma

Examples

```r
## Not run:
# Load a mmgmos preprocessed fragment of the Drosophila developmental
# time series
data(drosophila_gpsim_fragment)

# Get the target probe names
library(annotate)
aliasMapping <- getAnnMap("ALIAS2PROBE",
                        annotation(drosophila_gpsim_fragment))
twi <- get("twi", env=aliasMapping)
fbgnMapping <- getAnnMap("FLYBASE2PROBE",
                        annotation(drosophila_gpsim_fragment))
targetProbe <- get("FBgn0035257", env=fbgnMapping)

# Learn the model
model <- GPLearn(drosophila_gpsim_fragment,
                 TF=twi, targets=targetProbe,
                 useGpdisim=TRUE, quiet=TRUE)

# Plot it
GPPlot(model, nameMapping=getAnnMap("FLYBASE",
                           annotation(drosophila_gpsim_fragment)))

## End(Not run)
```

**drosophila_gpsim_fragment**

*Fragment of 12 time point Drosophila embryonic development microarray gene expression time series*

Description

Four genes from the 12 time point Drosophila embryonic development Affymetrix microarray gene expression data set by Tomancak et al. (2002).

The data has been processed using mmgmos from puma package and processData.
**Usage**

```r
data(drosophila_gpsim_fragment)
```

**Format**

An `ExpressionTimeSeries` object with 3 repeats of the 12 time points for 4 probes.

**Source**

`ftp://ftp.fruitfly.org/pub/embryo_tc_array_data/`

**References**


---

**drosophila_mmgmos_fragment**

*Fragment of 12 time point Drosophila embryonic development microarray gene expression time series*

**Description**

Four genes from the 12 time point Drosophila embryonic development Affymetrix microarray gene expression data set by Tomancak et al. (2002).

The data has been processed using `mmgmos` from the `puma` package.

**Usage**

```r
data(drosophila_mmgmos_fragment)
```

**Format**

A `puma` package `exprResult` object with 3 repeats of the 12 time points for 4 probes.

**Source**

`ftp://ftp.fruitfly.org/pub/embryo_tc_array_data/`

**References**

export.scores

Export results to an SQLite database

Description

Exports the results to an SQLite database which can then be browsed with a result browser. The function will export log likelihoods, z-scores, model figures and gene aliases.

Usage

```r
export.scores(scores, datasetName='', experimentSet='', databaseFile='database.sqlite', preprocData=NULL, models=NULL, figpath=NULL, aliasTypes=c("SYMBOL", "GENENAME", "ENTREZID"), datasetSource='', datasetDescription='', datasetSaveLocation='', datasetFigureFilename='', experimentTimestamp=as.character(Sys.Date()), figureDesc='', figurePrio=0, regulator=NULL)
```

Arguments

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>scores</td>
<td>The scoreList to export.</td>
</tr>
<tr>
<td>datasetName</td>
<td>Name of the dataset in the database.</td>
</tr>
<tr>
<td>experimentSet</td>
<td>Name of the experiment set in the database.</td>
</tr>
<tr>
<td>databaseFile</td>
<td>Filename of the database. New database is created if the file does not exist.</td>
</tr>
<tr>
<td>preprocData</td>
<td>Preprocessed data. This is required in order to generate models and figures and to calculate z-scores. Also, inserting aliases requires preprocessed data.</td>
</tr>
<tr>
<td>models</td>
<td>Learned models. If not given, the function will generate models if preprocessed data is available.</td>
</tr>
<tr>
<td>figpath</td>
<td>Figure path. If this is defined, the function will generate figures to the given path instead of inserting them to the database.</td>
</tr>
<tr>
<td>aliasTypes</td>
<td>Types of aliases that are inserted to the database.</td>
</tr>
<tr>
<td>datasetSource</td>
<td>Additional information that is inserted to the database if defined.</td>
</tr>
<tr>
<td>datasetDescription</td>
<td>Additional information that is inserted to the database if defined.</td>
</tr>
<tr>
<td>datasetSaveLocation</td>
<td>Additional information that is inserted to the database if defined.</td>
</tr>
<tr>
<td>datasetFigureFilename</td>
<td>Additional information that is inserted to the database if defined.</td>
</tr>
<tr>
<td>experimentTimestamp</td>
<td>Timestamp that is inserted to the database. The default value is current date in ISO-8601 format.</td>
</tr>
<tr>
<td>figureDesc</td>
<td>Additional information that is inserted to the database if defined.</td>
</tr>
<tr>
<td>figurePrio</td>
<td>Additional information that is inserted to the database if defined.</td>
</tr>
<tr>
<td>regulator</td>
<td>If defined, override the regulator name from scoreList.</td>
</tr>
</tbody>
</table>

Author(s)

Miika-Petteri Matikainen, Antti Honkela
See Also

GPRankTargets, GPRankTFs.

Examples

```r
## Not run:
# Load a mmgmos preprocessed fragment of the Drosophila developmental
time series
data(drosophila_gpsim_fragment)

# FBgn names of target genes
targets <- c('FBgn0003486', 'FBgn0033188', 'FBgn0035257')
# Load gene annotations
library(annotate)
aliasMapping <- getAnnMap("ALIAS2PROBE",
  annotation(drosophila_gpsim_fragment))

# Get the probe identifier for TF 'twi'
twi <- get("twi", env=aliasMapping)
# Load alternative gene annotations
fbgnMapping <- getAnnMap("FLYBASE2PROBE",
  annotation(drosophila_gpsim_fragment))

# Get the probe identifiers for target genes
targetProbes <- mget(targets, env=fbgnMapping)

# Rank the targets, filtering weakly expressed genes with average
# expression z-score below 1.8
scores <- GPRankTargets(drosophila_gpsim_fragment, TF=twi,
  testTargets=targetProbes,
  options=list(quiet=TRUE),
  filterLimit=1.8)

# Export data from scoreList and preprocessed data to a database
export.scores(scores, datasetName="Drosophila",
  experimentSet='GPSIM/GPDISIM',
  database='database.sqlite',
  preprocData=drosophila_gpsim_fragment,
  aliasTypes=c('SYMBOL', 'GENENAME', 'FLYBASE', 'ENTREZID'))

## End(Not run)
```

ExpressionTimeSeries-class

Class to contain time series expression assays

Description

Container for time series expression assays and experimental metadata. ExpressionTimeSeries
class is derived from ExpressionSet, and requires fields experiments and modeltime in phenoData.

Extends

Directly extends class ExpressionSet.
Objects from the Class

```r
new("ExpressionTimeSeries")
new("ExpressionTimeSeries", phenoData = new("AnnotatedDataFrame"), featureData = new("AnnotatedDataFrame"), ... annotation = character(0), protocolData = phenoData[,integer(0)], exprs = new("matrix"), var.exprs = new("matrix"))
```

This creates an `ExpressionTimeSeries` with `assayData` implicitly created to contain `exprs` and `var.exprs`.

```r
new("ExpressionTimeSeries", assayData = assayDataNew(exprs=new("matrix")), phenoData = new("AnnotatedDataFrame"), ...)
```

This creates an `ExpressionTimeSeries` with `assayData` provided explicitly. In this form, the only required named argument is `assayData`.

`ExpressionTimeSeries` instances are usually created through `new("ExpressionTimeSeries", ...). Usually the arguments to new include `exprs` (a matrix of expression data, with features corresponding to rows and samples to columns), `var.exprs`, `phenoData`, `featureData`, `experimentData`, `annotation`, and `protocolData`. `phenoData`, `featureData`, `experimentData`, `annotation`, and `protocolData` can be missing, in which case they are assigned default values.

Slots

- **assayData**: Inherited from `ExpressionSet`. The models in `gpsim` package assume that `exprs` contains absolute (i.e. non-logarithmic) expression values. The member `var.exprs` may contain variances of the values.
- **phenoData**: Inherited from `ExpressionSet`. The following fields are required: `experiments` which contains integers from 1 to N with measurements from the same biological assay having the same number; `modeltime` which contains observation times in model units.
- **featureData**: Inherited from `ExpressionSet`.
- **experimentData**: Inherited from `ExpressionSet`.
- **annotation**: Inherited from `ExpressionSet`.
- **protocolData**: Inherited from `ExpressionSet`.
- **__classVersion__**: Inherited from `ExpressionSet`.

Methods

See also methods for `ExpressionSet`.

- `var.exprs(object)`, `var.exprs(object)<- value` Access and set `var.exprs`
- `initialize("ExpressionTimeSeries")` Object instantiation, used by `new`; not to be called directly by the user.

Author(s)

Antti Honkela, Jonatan Ropponen

See Also

`processData`, `processRawData`.

Examples

```r
showClass("ExpressionTimeSeries")
```
**expTransform**

Constrains a parameter.

**Description**

contains commands to constrain parameters to be positive via exponentiation or within a fixed interval via the sigmoid function.

**Usage**

expTransform(x, transform)
sigmoidTransform(x, transform)
boundedTransform(x, transform, bounds)

**Arguments**

- **x** input argument.
- **transform** type of transform, 'atox' maps a value into the transformed space (i.e. makes it positive). 'xtoa' maps the parameter back from transformed space to the original space. 'gradfact' gives the factor needed to correct gradients with respect to the transformed parameter.
- **bounds** a 2-vector of bounds of allowed values in boundedTransform

**Value**

Return value as selected by transform

**See Also**

generateModels(modelOptimise)

**Examples**

# Transform unconstrained parameter -4 to a positive value
expTransform(-4, 'atox')

# Transform a bounded parameter in (1,3) to an unconstrained one
boundedTransform(2, 'xtoa', c(1, 3))

**generateModels**

Generating models with the given data

**Description**

'generateModels' recreates models based on the parameters stored in a scoreList.

**Usage**

generateModels(preprocData, scores)
GPLearn

Arguments

preprocData  The preprocessed data to be used.
scores      A scoreList object containing data of the models to be generated.

Value

'generateModels' returns a list of the generated models.

Author(s)

Antti Honkela, Jonatan Ropponen

See Also

GPLearn, GPRankTargets, GPRankTFs, scoreList.

Examples

## Not run:
# Load a mmgmos preprocessed fragment of the Drosophila developmental
time series
data(drosophila_gpsim_fragment)

# Get the target probe names
targets <- c("FBgn0003486", "FBgn0033188", "FBgn0035257")
library(annotate)
aliasMapping <- getAnnMap("ALIAS2PROBE",
annotation(drosophila_gpsim_fragment))
twi <- get("twi", env=aliasMapping)
fbgnMapping <- getAnnMap("FLYBASE2PROBE",
annotation(drosophila_gpsim_fragment))
targetProbes <- mget(targets, env=fbgnMapping)

scores <- GPRankTargets(drosophila_gpsim_fragment, TF=twi,
testTargets=targetProbes,
options=list(quiet=TRUE),
filterLimit=1.8)

models <- generateModels(drosophila_gpsim Fragment, scores)

## End(Not run)

GPLearn  Fit a GP model

Description

Forms an optimized model of the desired genes. The function can form a model with GPsim or GPdisim and it's also possible to use initial parameters or fix parameters for future use. The genes can also be filtered based on ratios calculated from the expression values. The given data can also be searched for the data of specific genes.
GPLearn

Usage

GPLearn(preprocData, TF = NULL, targets = NULL,
  useGpdisim = !is.null(TF), randomize = FALSE, addPriors = FALSE,
  fixedParams = FALSE, initParams = NULL, initialZero = TRUE,
  fixComps = NULL, dontOptimise = FALSE,
  allowNegativeSensitivities = FALSE, quiet = FALSE,
  gpsimOptions = NULL, allArgs = NULL)

Arguments

preprocData  The preprocessed data to be used.
TF  The probe corresponding to the transcription factor (TF) mRNA if TF protein translation model is used, or NULL (default) if the translation model is not used.
targets  The target genes of the model.
useGpdisim  A logical value determining whether a model of translation is included. By default TRUE if TF is set, FALSE if TF is unset.
randomize  A logical value determining whether the parameters of the model are randomized before optimization.
addPriors  A logical value determining whether priors are added to the model.
fixedParams  A logical value determining whether the initial parameters are fixed.
initParams  The initial parameters for the model. In combination with fixedParams a value NA denotes parameters to learn.
initalZero  Assume a zero initial TF protein concentration, default = TRUE.
fixComps  The blocks of the kernel the parameters of which are to be fixed. To be used together with fixedParams and initParams.
dontOptimise  Just create the model, do not run optimisation.
allowNegativeSensitivities  Allow sensitivities to go negative. This is an experimental feature, and the negative values have no physical interpretation.
quiet  Suppress optimiser output.
gpsimOptions  Internal: additional options to pass to gp[di]simCreate.
allArgs  A list of arguments that can be used to override ones with the same name.

Value

Returns the optimized model.

Author(s)

Antti Honkela, Pei Gao, Jonatan Ropponen, Magnus Rattray, Neil D. Lawrence

See Also

GPRankTargets, GPRankTFs.
Example

# Load a mmgmos preprocessed fragment of the Drosophila developmental
# time series
data(drosophila_gpsim_fragment)

# Get the target probe names
library(annotate)
aliasMapping <- getAnnMap("ALIAS2PROBE",
    annotation(drosophila_gpsim_fragment))
twi <- get("twi", env=aliasMapping)
fbgnMapping <- getAnnMap("FLYBASE2PROBE",
    annotation(drosophila_gpsim_fragment))
targetProbe <- get("FBgn0035257", env=fbgnMapping)

# Create the model but do not optimise (rarely needed...)
model <- GPLearn(drosophila_gpsim_fragment,
    TF=twi, targets=targetProbe,
    useGpdisim=TRUE, quiet=TRUE,
    dontOptimise=TRUE)

## Not run:
# Create and learn the model
model <- GPLearn(drosophila_gpsim_fragment,
    TF=twi, targets=targetProbe,
    useGpdisim=TRUE, quiet=TRUE)

## End(Not run)

GPModel-class

A container for gpsim models

Description

The class is a container for the internal representation of models used by the gpsim package.

Objects from the Class

Objects can be created by calls of the form new("GPModel", model).

Slots

model: A model object used internally by the code of the gpsim package
type: Type of the model object

Methods

modelStruct(object), modelStruct(object)<- value Access and set the internal model structure
modelType(object) Access the internal type values
show(object) Informatively display object contents.
is.GPModel(object) Check if object is a GPModel.
initialize("GPModel") Object instantiation, used by new; not to be called directly by the user.
GPPlot

Author(s)
Antti Honkela, Jonatan Ropponen

See Also
GPLearn, GPRankTargets, GPRankTFs, generateModels, modelExtractParam, modelLogLikelihood.

Examples
showClass("GPModel")

GPPlot

Plot GP(DI)SIM models

Description
Plots GP(DI)SIM models.

Usage
GPPlot(data, savepath = '\Var\Var', nameMapping = NULL, predt = NULL, fileOutput=FALSE, plotTime=NULL)

Arguments
data
The model to plot as returned by GPLearn.
savepath
The location in the file system where the images are saved.
nameMapping
The annotation used for mapping the names of the genes for the figures.
predt
The set of time points to use in plotting (default: the time interval covering the data).
fileOutput
Is the plot being saved to a file? If yes, do not open new interactive devices for each plot.
plotTime
The times of observations to use in the plot. Should usually not be changed!

Details
The function plots the fitted expression level of the transcription factor (if applicable), the inferred activity of the transcription factor, and the fitted expression level of the target(s).

Author(s)
Antti Honkela

See Also
GPLearn.
GPRankTargets

Examples

## Not run:
# Load a mmgmos preprocessed fragment of the Drosophila developmental # time series
data(drosophila_gpsim_fragment)

# Get the target probe names
library(annotate)
aliasMapping <- getAnnMap("ALIAS2PROBE", 
  annotation(drosophila_gpsim_fragment))
twi <- get('twi', env=aliasMapping)
fbgnMapping <- getAnnMap("FLYBASE2PROBE", 
  annotation(drosophila_gpsim_fragment))
targetProbe <- get('FBgn0035257', env=fbgnMapping)

# Learn the model
model <- GPLearn(drosophila_gpsim_fragment,
  TF=twi, targets=targetProbe,
  useGpdisim=TRUE, quiet=TRUE)

# Plot it
GPPlot(model, nameMapping=getAnnMap("FLYBASE", 
  annotation(drosophila_gpsim_fragment)))

## End(Not run)

GPRankTargets

Ranking possible target genes or regulators

Description

GPRankTargets ranks possible target genes by forming optimized models with a fixed transcription factor, a set of known target genes and targets to be tested. The transcription factor and the known targets are always included in the models while the tested targets are tested by including them in the models one at a time. The function determines itself whether to use GPSIM or GPDISIM based on the input arguments.

Usage

GPRankTargets(preprocData, TF = NULL, knownTargets = NULL, 
  testTargets = NULL, filterLimit = 1.8, 
  returnModels = FALSE, options = NULL, 
  scoreSaveFile = NULL, 
  datasetName = "", experimentSet = "")
GPRankTFs(preprocData, TFs, targets, 
  filterLimit = 1.8, returnModels = FALSE, options = NULL, 
  scoreSaveFile = NULL, datasetName = "", experimentSet = "")

Arguments

preprocData The preprocessed data to be used.
TF

The transcription factor (TF) probe present in all models when TF protein translation model is used. Set to NULL (default) when translation model is not used.

knownTargets

The target genes present in all models.

testTargets

Target genes that are tested by including them in the models one at a time. Can be names of genes, or a set of indices in preprocData.

filterLimit

Genes with an average expression $z$-score above this figure are accepted after filtering. If this value is 0, all genes will be accepted.

returnModels

A logical value determining whether the function returns the calculated models.

options

A list of additional arguments to pass to GPLearn.

scoreSaveFile

Name of file to save the scores to after processing each gene.

TFs

The transcription factors that are tested by including them in the models one at a time.

targets

The target genes present in all models.

datasetName

For exporting the scores using `export.scores`: Name of the dataset in the database.

experimentSet

For exporting the scores using `export.scores`: Name of the experiment set in the database.

Details

The models are formed by calling `GPLearn`. If there is no value given to the transcription factor, a model without protein translation is used. Without protein translation model, some known targets are needed. If known targets are given, a model is first created with only the transcription factor and the known targets. The parameters extracted from this model are used as initial parameters of the models with test targets.

`GPRankTFs` is very similar to `GPRankTargets`, except it loops over candidate regulators, not candidate targets.

Value

The function returns a `scoreList` containing the genes, parameters and log-likelihoods of the models. If `returnModels` is true, the function returns a list of the calculated models.

Author(s)

Antti Honkela, Jonatan Ropponen, Magnus Rattray, Neil D. Lawrence

See Also

`GPLearn`, `scoreList`, `generateModels`, `export.scores`.

Examples

```r
## Not run:
# Load a mmgmos preprocessed fragment of the Drosophila developmental
data time series
data(drosophila_gpsim_fragment)

# Get the target probe names
targets <- c("FBgn0003406", "FBgn0033188", "FBgn0035257")
library(annotate)
```
gpsimCreate <- function(Ngenes, Ntf, times, y, yvar, options, genes=NULL, annotation=NULL) {
  # Create a GPSIM/GPDISIM model.
  # Description
  # creates a model for single input motifs with Gaussian processes.
  # Usage
  # gsimCreate(Ngenes, Ntf, times, y, yvar, options, genes=NULL, annotation=NULL)
  # gpdisimCreate(Ngenes, Ntf, times, y, yvar, options, genes=NULL, annotation=NULL)
  # Arguments
  # Ngenes number of genes to be modelled in the system.
  # Ntf number of proteins to be modelled in the system.
  # times the time points where the data is to be modelled.
  # y the values of each gene at the different time points.
  # yvar the variances of each gene at the different time points.
  # options options structure (optional).
  # genes names of the probes the model is for
  # annotation (optional) annotation for the probe names
  # Details
  # These functions are meant to be used through GPLearn.
  # Value
  # model model structure containing default parameterisation.
  # See Also
  # modelExtractParam, modelOptimise, GPLearn.
}

## End(Not run)
Compute the kernel given the parameters and X.

Usage

\[
kernCompute(kern, x, x2) \\
kernDiagCompute(kern, x)
\]

Arguments

- **kern**: kernel structure to be computed.
- **x**: first or only input data matrix (rows are data points) to the kernel computation.
- **x2**: (optional) second input matrix to the kernel computation (forms the columns of the kernel).

Details

- \( K \leftarrow \text{kernCompute}(\text{kern}, X) \) computes a kernel matrix for the given kernel type given an input data matrix.
- \( K \leftarrow \text{kernCompute}(\text{kern}, X1, X2) \) computes a kernel matrix for the given kernel type given two input data matrices, one for the rows and one for the columns.
- \( K \leftarrow \text{kernDiagCompute}(\text{kern}, X) \) computes the diagonal of a kernel matrix for the given kernel.
- \( K \leftarrow *X*\text{kernCompute}(\text{kern1}, \text{kern2}, X) \) \( K \leftarrow *X*\text{kernCompute}(\text{kern1}, \text{kern2}, X1, X2) \) same as above, but for cross combinations of two kernels, \text{kern1} and \text{kern2}.

Value

- **K**: computed elements of the kernel structure.
- **Kd**: vector containing computed diagonal elements of the kernel structure.

See Also

- kernCreate

Examples

\[
kern \leftarrow \text{kernCreate}(1, 'rbf') \\
K \leftarrow \text{kernCompute}(\text{kern}, \text{as.matrix}(3:8))
\]
kernCreate

Initialise a kernel structure.

Description

Initialise a kernel structure.

Usage

kernCreate(x, kernType, kernOptions=NULL)

Arguments

- **x**: If list, array or matrix: input data values (from which kernel will later be computed). If scalar: input dimension of the design matrix (i.e. number of features in the design matrix).
- **kernType**: Type of kernel to be created, some standard types are 'rbf', 'white', 'sim' and 'disim'. If a list of the form list(type='cmpnd', comp=c('rbf', 'rbf', 'white')) is used a compound kernel based on the sum of the individual kernels will be created. Parameters can be passed to kernels using type list(type='parametric', options=list(opt=val), realType=...) where realType is the type that would be used otherwise.
- **kernOptions**: (optional) list of kernel options

Details

kern <- kernCreate(X, type) input points and a kernel type.

kern <- kernCreate(dim, type) creates a kernel matrix structure given the dimensions of the design matrix and the kernel type.

The *KernParamInit functions perform initialisation specific to different types of kernels. They should not be called directly.

Value

kern: The kernel structure.

See Also

kernDisplay, modelTieParam.

Examples

# Create a multi kernel with two rbf blocks with bounded inverse widths
invWidthBounds <- c(0.5, 2)
kernType <- list(type="multi", comp=list())
for (i in 1:2)
  kernType$comp[[i]] <- list(type="parametric", realType="rbf",
                           options=list(isNormalised=TRUE,
                                          inverseWidthBounds=invWidthBounds))
kern <- kernCreate(1, kernType)

# Tie the inverse with parameters of the component RBF kernels
kern <- modelTieParam(kern, list(tieWidth="inverseWidth"))
kernDisplay(kern)
kernDiagGradX  

*Compute the gradient of the kernel wrt X.*

**Description**

computes the gradient of the (diagonal of the) kernel matrix with respect to the elements of the design matrix given in X.

**Usage**

```
kernDiagGradX(kern, x)  
kernGradX(kern, x, x2)
```

**Arguments**

- `kern`: the kernel structure for which gradients are being computed.
- `x`: if only argument: the input data in the form of a design matrix, if two arguments: row locations against which gradients are being computed.
- `x2` (optional): column locations against which gradients are being computed.

**Value**

- `gX`: the gradients of the diagonal with respect to each element of X. The returned matrix has the same dimensions as X.
- `gX2`: the returned gradients. The gradients are returned in a matrix which is numData x numInputs x numData. Where numData is the number of data points and numInputs is the number of input dimensions in X.

**See Also**

- `kernGradient`

**Examples**

```
kern <- kernCreate(1, 'mlp')  
g <- kernDiagGradX(kern, as.matrix(3:8))
```

---

**kernGradient**  

*Compute the gradient wrt the kernel parameters.*

**Description**

Compute the gradient wrt the kernel parameters.

**Usage**

```
kernGradient(kern, x, ...)
```
Arguments

kern
the kernel structure for which the gradients are being computed.

x
the input locations for which the gradients are being computed, specifically those associated with the rows of the kernel matrix if there are two arguments of input locations.

... optional arguments including potentially: the input locations associated with the columns of the kernel matrix; matrix of partial derivatives of the function of interest with respect to the kernel matrix. With single input, the argument takes the form of a square matrix of dimension numData, where numData is the number of rows in x, with two input arguments the matrix should have the same number of rows as the first and the same number of columns as the second has rows.

Details

\[ g \leftarrow \text{kernGradient}(\text{kern}, x, \text{partial}) \]

computes the gradient of functions with respect to the kernel parameters. As well as the kernel structure and the input positions, the user provides a matrix PARTIAL which gives the partial derivatives of the function with respect to the relevant elements of the kernel matrix.

\[ g \leftarrow \text{kernGradient}(\text{kern}, x_1, x_2, \text{partial}) \]

computes the derivatives as above, but input locations are now provided in two matrices associated with rows and columns of the kernel matrix.

\[ g \leftarrow \text{*X*kernGradient}(\text{kern}_1, \text{kern}_2, x, \text{partial}) \]

same as above, but for cross combinations of two kernels, \text{kern}_1 and \text{kern}_2.

Value

\[ g \]

gradients of the function of interest with respect to the kernel parameters. The ordering of the vector should match that provided by the function \text{kernExtractParam}.

See Also

\text{kernCompute}, \text{kernExtractParam}.

Examples

\[
\begin{align*}
\text{kern} & \leftarrow \text{kernCreate}(1, \text{'rbf'}) \\
\text{g} & \leftarrow \text{kernGradient}(\text{kern}, \text{as.matrix}(\text{c}(1, 4)), \text{array}(1, \text{c}(2, 2)))
\end{align*}
\]

\text{lnDiffErfs}

\text{Helper function for computing the log of difference}

Description

Helper function for computing the log of difference

Usage

\text{lnDiffErfs}(x_1, x_2)
modelDisplay

Display a model.

Description

displays the parameters of the model/kernel and the model/kernel type to the console.

Usage

modelDisplay(model, ...)

Arguments

model the model/kernel structure to be displayed.
... (optional) indent level for the display.

See Also

modelExtractParam

Examples

# Load a mmgmos preprocessed fragment of the Drosophila developmental
# time series
data(drosophila_gpsim_fragment)

# The probe identifier for TF 'twi'
twi <- "143396_at"
# The probe identifier for the target gene
targetProbe <- "152715_at"

# Create the model, but do not optimise
model <- GPLearn(drosophila_gpsim_fragment,
  TF=twi, targets=targetProbe,
  useGpdisim=TRUE, quiet=TRUE,

Arguments

x1 argument of the positive erf
x2 argument of the negative erf

Details

v <- lnDiffErfs(x1, x2) computes the log of the difference of two erfs in a numerically stable manner.

Value

v list(c(log(abs(\(\text{erf}(x1) - \text{erf}(x2))\)), sign(\(\text{erf}(x1) - \text{erf}(x2))\)))

Examples

lnDiffErfs(100, 10)
modelExpandParam

```
dontOptimise=TRUE)
```

# Display the initial model
modelDisplay(model)

---

**modelExpandParam**

*Update a model structure with new parameters or update the posterior processes.*

**Description**

Update a model structure or component with new parameters, or update the posterior processes.

**Usage**

```
modelExpandParam(model, params)
modelUpdateProcesses(model, predt=NULL)
```

**Arguments**

- `model`: the model structure to be updated.
- `params`: vector of parameters.
- `predt`: (optional) a vector of times to infer the posterior at. By default this is 100 points spanning the time range of the data.

**Details**

- `model <- modelExpandParam(model1, params)` returns a model structure filled with the parameters in the given vector. This is used as a helper function to enable parameters to be optimised in, for example, the optimisation functions.
- `model <- modelUpdateProcesses(model)` updates posterior processes of the given model.

**Value**

- `model`: updated model structure.

**See Also**

GPLearn, modelExtractParam

**Examples**

```r
## Not run:
# Learn the model
model <- GPLearn(...)
params <- modelExtractParam(model, only.values=TRUE)
params[1] <- 0
new_model <- modelExpandParam(model, params)
new_model <- modelUpdateProcesses(new_model)

## End(Not run)
```
modelExtractParam  

Extract the parameters of a model.

Description

Extract parameters from the model into a vector of parameters for optimisation.

Usage

modelExtractParam(model, only.values=TRUE, untransformed.values=FALSE)

Arguments

model  
the model structure containing the parameters to be extracted.

only.values  
include parameter names in the returned vector.

untransformed.values  
return actual values, not transformed values used by the optimisers.

Value

param  
vector of parameters extracted from the model.

See Also

modelExpandParam

Examples

# Load a mmgmos preprocessed fragment of the Drosophila developmental # time series  
data(drosophila_gpsim_fragment)

# The probe identifier for TF 'twi'  
twi <- "143396_at"

# The probe identifier for the target gene  
targetProbe <- "152715_at"

# Create the model, but do not optimise  
model <- GPLearn(drosophila_gpsim_fragment,  
TF=twi, targets=targetProbe,  
useGpdissim=TRUE, quiet=TRUE,  
dontOptimise=TRUE)

# Get the initial parameter values  
params <- modelExtractParam(model, only.values=FALSE)
modelGradient

Model log-likelihood/objective error function and its gradient.

Description

modelGradient gives the gradient of the objective function for a model. By default the objective function (modelObjective) is a negative log likelihood (modelLogLikelihood).

Usage

modelObjective(params, model, ...)
modelLogLikelihood(model)
modelGradient(params, model, ...)

Arguments

params parameter vector to evaluate at.
model model structure.
... optional additional arguments.

Value

g the gradient of the error function to be minimised.

v the objective function value (lower is better).
ll the log-likelihood value.

See Also

modelOptimise.

Examples

# Load a mmgmos preprocessed fragment of the Drosophila developmental
# time series
data(drosophila_gpsim_fragment)

# The probe identifier for TF 'twi'
twi <- "143396_at"
# The probe identifier for the target gene
targetProbe <- "152715_at"

# Create the model but do not optimise
model <- GPLearn(drosophila_gpsim_fragment,
    TF=twi, targets=targetProbe,
    useGpdisim=TRUE, quiet=TRUE,
    dontOptimise=TRUE)
params <- modelExtractParam(model, only.values=FALSE)
ll <- modelLogLikelihood(model)
paramValues <- modelExtractParam(model, only.values=TRUE)
modelGradient(paramValues, model)
modelTieParam

Tie parameters of a model together.

Description

groups of parameters of a model to be seen as one parameter during optimisation of the model.

Usage

modelTieParam(model, paramsList)

Arguments

model
  the model for which parameters are being tied together.
paramsList
  indices of parameters to group together. The indices are provided in a list. Each element in the list contains a vector of indices of parameters that should be considered as one parameter. Each group of parameters in each cell should obviously be mutually exclusive. Alternatively, the specification may consist of strings, which are interpreted as regular expressions that are matched against the parameter names returned by modelExtractParam or kernExtractParam, as appropriate for the current object.

Value

model
  the model with the parameters grouped together.

See Also

modelExtractParam, modelExpandParam, modelGradient.

Examples

# Create a multi kernel with two rbf blocks with bounded inverse widths
invWidthBounds <- c(0.5, 2)
kernType <- list(type="multi", comp=list())
for (i in 1:2)
  kernType$comp[[i]] <- list(type="parametric", realType="rbf",
                           options=list(isNormalised=TRUE,
                                         inverseWidthBounds=invWidthBounds))
kern <- kernCreate(1, kernType)

# Tie the inverse with parameters of the component RBF kernels
kern <- modelTieParam(kern, list(tieWidth="inverseWidth"))
kernDisplay(kern)
optimiDefaultConstraint

*Returns function for parameter constraint.*

**Description**

returns the current default function for constraining a parameter.

**Usage**

```r
optimiDefaultConstraint(constraint)
```

**Arguments**

- `constraint` is the type of constraint you want to place on the parameter, options include 'positive' (gives an 'exp' constraint) and 'zeroone' (gives a 'sigmoid' constraint).

**Value**

- `val` is a list with two components: 'func' for the name of function used to apply the constraint, and 'hasArgs' for a boolean flag if the function requires additional arguments.

**See Also**

`expTransform`, `sigmoidTransform`.

**Examples**

```r
optimiDefaultConstraint('positive')
optimiDefaultConstraint('bounded')
```

---

plotTimeseries

*Plot ExpressionTimeSeries data*

**Description**

Plots ExpressionTimeSeries data.

**Usage**

```r
plotTimeseries(data, nameMapping = NULL)
```

**Arguments**

- `data` is An ExpressionTimeSeries object.
- `nameMapping` is The annotation used for mapping the names of the genes for the figures. By default, the SYMBOL annotation for the array is used, if available.
Details

The function plots the expression levels from an ExpressionTimeSeries object and the associated standard deviations. If the object includes multiple time series, they will be plotted in the same figure, but slightly shifted.

Author(s)

Antti Honkela

See Also

processData.

Examples

# Load a mmgmos preprocessed fragment of the Drosophila developmental time series
data(drosophila_gpsim_fragment)

# Plot the first two genes
plotTimeseries(drosophila_gpsim_fragment[1:2,])

processData  Processing expression time series

Description

processData further processes time series data preprocessed by puma or lumi.
processRawData performs similar processing for other data.
Both functions return ExpressionTimeSeries objects that can be used as input for the functions GPLearn and GPRankTargets.

Usage

processData(data, times = NULL, experiments = NULL, do.normalisation = TRUE)
processRawData(rawData, times, experiments = NULL, is.logged = TRUE, do.normalisation = ifelse(is.logged, TRUE, FALSE))

Arguments

data The preprocessed data from mmgMOS in the puma package (an exprResult object) or from the lumi package (a LumiBatch object).
rawData Raw data matrix to be used. Each row corresponds to a gene and each column to a data point.
times Observation times of each data point. If unspecified or NULL, processData attempts to infer this from phenoData(data) field containing 'time' in the name.
experiments The replicate structure of the data indicating which expression data points arise from which experiments. This should be an array in integers from 1 to N with length equal to the number of data points. By default all the data points are assumed to be from same replicate.
is.logged Indicates whether the expression values are on log scale or not. Normalisation of non-logged data is unsupported.

do.normalisation Indicates whether to perform the normalisation.

Details
The expression data (and percentiles, if available) are normalized by equalising the mean of log-expression in each time points. In processData, a normal distribution is then fitted into the data with distfit.

Value
An ExpressionTimeSeries object containing all provided information.

Author(s)
Antti Honkela, Jonatan Ropponen

See Also
GPLearn, GPRankTargets.

Examples
```r
## Load a mmgmos preprocessed fragment of the Drosophila developmental time series
data(drosophila_mmgmos_fragment)

## Process the data (3 experiments containing 12 time points each)
drosophila_gpsim_fragment <- processData(drosophila_mmgmos_fragment,
                                         experiments=rep(1:3, each=12))
```

---

**SCGoptim**  
Optimise the given function using (scaled) conjugate gradients.

**Description**
Optimise the given function using (scaled) conjugate gradients.

**Usage**
```r
optimDefaultOptions()
SCGoptim(x, fn, grad, options, ...)
CGoptim(x, fn, grad, options, ...)
modelOptimise(model, options, ...)
```
Arguments

model  
the model to be optimised.
x  
initial parameter values.
fn  
objective function to minimise
grad  
gradient function of the objective
options  
options structure like one returned by optimiDefaultOptions. The fields are interpreted as:
option[1]: number of iterations
option[2]: interval for the line search
option[3]: tolerance for x to terminate the loop
option[4]: tolerance for fn to terminate the loop
option$display: option of showing the details of optimisation
...  
extra arguments to pass to fn and grad

Value

options  
an options structure
newParams  
optimised parameter values
model  
the optimised model.

See Also

modelObjective, modelGradient

Examples

```r
## Not run to speed up package checks
# model <- GPLearn(..., dontOptimise=TRUE)
# options <- optimiDefaultOptions()
# model <- modelOptimise(model, options)
```

scoreList-class  
Class “scoreList”

Description

'scoreList' is an object which contain the genes, parameters, log-likelihoods and arguments of models. With the data in a scoreList item and the original data used for creating the models, the models can be reconstructed with the function 'generateModels'.

Objects from the Class

Objects can be created by calls of the form scoreList(params, loglikelihoods, genes, modelArgs, knownTargets, sharedModel).

Slots

params: The parameters of the models.
loglikelihoods: The log-likelihoods of the models.
baseloglikelihoods: The log-likelihoods of corresponding null models.
genres: The genes used in the models.
modelArgs: A list of arguments used to generate the models.

knownTargets: The list of known targets used in the ranking.

TF: The TF used in the ranking.

sharedModel: Shared model for known targets.

datasetName: Dataset name, used when exporting scores to a database.

experimentSet: Experiment set name, used when exporting scores to a database.

Methods

Class-specific methods:

write.scores(object, ...) Writes the log-likelihoods and null log-likelihoods. Accepts any options write.table does.

genes(object), genes(object)<- value Access and set genes

knownTargets(object), knownTargets(object)<- value Access and set knownTargets

loglikelihoods(object), loglikelihoods(object)<- value Access and set loglikelihoods

baseloglikelihoods(object), baseloglikelihoods(object)<- value Access and set baseloglikelihoods

modelArgs(object), modelArgs(object)<- value Access and set modelArgs

params(object), params(object)<- value Access and set params

sharedModel(object), sharedModel(object)<- value Access and set sharedModel

TF(object), TF(object)<- value Access and set TF

datasetName(object), datasetName(object)<- value Access and set datasetName

experimentSet(object), experimentSet(object)<- value Access and set experimentSet

Standard generic methods:

object[(index)] Conducts subsetting of the scoreList.

c(object, ...) Concatenates scoreLists.

length(object) Returns the length of the list.

show(object) Informatively display object contents.

sort(object, decreasing=FALSE) Sort the list according to log-likelihood

Author(s)

Antti Honkela, Jonatan Ropponen

See Also

GPRankTargets, GPRankTFs, generateModels, write.table.

Examples

showClass("scoreList")
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