

# Package ‘combi’

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**Type** Package

**Title** Compositional omics model based visual integration

**Version** 1.23.0

**Description** This explorative ordination method combines quasi-likelihood estimation, compositional regression models and latent variable models for integrative visualization of several omics datasets. Both unconstrained and constrained integration are available. The results are shown as interpretable, compositional multiplots.

**License** GPL-2

**Encoding** UTF-8

**Depends** R (>= 4.0), DBI

**RoxygenNote** 7.2.3

**Imports** ggplot2, nleqslv, phyloseq, tensor, stats, limma, Matrix (>= 1.6.0), BB, reshape2, alabama, cobs, Biobase, vegan, grDevices, graphics, methods, SummarizedExperiment

**Suggests** knitr, rmarkdown, testthat

**VignetteBuilder** knitr

**biocViews** Metagenomics, DimensionReduction, Microbiome, Visualization, Metabolomics

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|                |                                           |
|----------------|-------------------------------------------|
| <i>addLink</i> | <i>Add a link on a compositional plot</i> |
|----------------|-------------------------------------------|

---

## Description

Add a link on a compositional plot

## Usage

```
addLink(  
  DIplot,  
  links,  
  Views,  
  samples,  
  variable = NULL,  
  Dims = c(1, 2),  
  addLabel = FALSE,  
  labPos = NULL,  
  projColour = "grey",  
  latentSize = 0.25  
)
```

## Arguments

|        |                                                                                                                                                                |
|--------|----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| DIplot | A list with ggplot object where the links are to be added, and data frames with coordinates (obtained by setting <code>plot(..., returnCoords = TRUE)</code> ) |
| links  | A matrix containing either feature names (two column matrix) or approximate coordinates (four column matrix)                                                   |
| Views  | Indices or names of the views for which the links should be added                                                                                              |

|            |                                                                             |
|------------|-----------------------------------------------------------------------------|
| samples    | Sample names or approximate sample coordinates                              |
| variable   | Name of variable in environmental gradient for which link should be plotted |
| Dims       | vector of length 2 referring to the model dimensions                        |
| addLabel   | A boolean, should arrow with label be plotted?                              |
| labPos     | The position of the label, as a numeric vector of length 2                  |
| projColour | The colour of the projection, as character string                           |
| latentSize | Size of the line from the origin to the latent variable dot                 |

**Value**

A ggplot object with the links added

**Examples**

```
data(Zhang)
## Not run:
#Unconstrained
microMetaboInt = combi(
  list("microbiome" = zhangMicrobio, "metabolomics" = zhangMetabo),
  distributions = c("quasi", "gaussian"), compositional = c(TRUE, FALSE),
  logTransformGaussian = FALSE, verbose = TRUE)

## End(Not run)
load(system.file("extdata", "zhangFits.RData", package = "combi"))
Plot = plot(microMetaboInt, samDf = zhangMetavars, samCol = "ABX",
  returnCoords = TRUE)
addLink(Plot, links = cbind("OTU0565b3", "OTUa14fb5"), Views = 1,
  samples = c(1,1))
```

---

|           |                             |
|-----------|-----------------------------|
| arrayMult | <i>Array multiplication</i> |
|-----------|-----------------------------|

---

**Description**

Array multiplication

**Usage**

```
arrayMult(centralMat, outerMat, ncols = ncol(outerMat))
```

**Arguments**

|            |                                               |
|------------|-----------------------------------------------|
| centralMat | an nxp matrix                                 |
| outerMat   | an nxd matrix                                 |
| ncols      | an integer, the number of columns of outerMat |

**Value**

an nxpxd matrix, the stacked matrices of centralMat multiplied to every column of outermat

---

|              |                                                                    |
|--------------|--------------------------------------------------------------------|
| buildCentMat | <i>A function to build a centering matrix based on a dataframe</i> |
|--------------|--------------------------------------------------------------------|

---

**Description**

A function to build a centering matrix based on a dataframe

**Usage**

```
buildCentMat(object)
```

**Arguments**

object            an modelDI object or dataframe

**Value**

a centering matrix consisting of ones and zeroes, or a list with components

centMat           a centering matrix consisting of ones and zeroes

datFrame          The dataframe with factors with one level removed

---

|              |                                                                          |
|--------------|--------------------------------------------------------------------------|
| buildCompMat | <i>Build the composition matrix for a certain dimension m dimensions</i> |
|--------------|--------------------------------------------------------------------------|

---

**Description**

Build the composition matrix for a certain dimension m dimensions

**Usage**

```
buildCompMat(
  colMat,
  paramEsts,
  latentVar,
  m,
  norm = TRUE,
  id = seq_len(m),
  subtractMax = TRUE
)
```

Arguments

|             |                                                                                                                                 |
|-------------|---------------------------------------------------------------------------------------------------------------------------------|
| colMat      | The nxp independence model composition matrix                                                                                   |
| paramEsts   | The matrix of feature parameter estimates                                                                                       |
| latentVar   | The matrix of latent variables                                                                                                  |
| m           | the required dimension                                                                                                          |
| norm        | a boolean, should the composition matrix be normalized?                                                                         |
| id          | The vector of dimensions to consider                                                                                            |
| subtractMax | A boolean, should the maximum be subtracted from every composition prior to exponentiation? Recommended for numerical stability |

Value

A matrix with compositions in the rows

---

|              |                                                                     |
|--------------|---------------------------------------------------------------------|
| buildConfMat | <i>Build confounder design matrices with and without intercepts</i> |
|--------------|---------------------------------------------------------------------|

---

Description

Build confounder design matrices with and without intercepts

Usage

buildConfMat(confounders)

Arguments

|             |                                                                                                                                                                                                                                                                                                                                                                                          |
|-------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| confounders | A dataframe of confounding variables #' For the preliminary trimming, we do not include an intercept, but we do include all the levels of the factors using contrasts=FALSE: we want to do the trimming in every subgroup, so no hidden reference levels For the filtering we just use a model with an intercept and treatment coding, here the interest is only in adjusting the offset |
|-------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

Value

|                        |                                                                                                                                                                                             |
|------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| a list with components |                                                                                                                                                                                             |
| confModelMatTrim       | A confounder matrix without intercept, with all levels of factors present. This will be used to trim out taxa that have zero abundances in any subgroup defined by confounders              |
| confModelMat           | A confounder matrix with intercept, and with reference levels for factors absent. This will be used to fit the model to modify the independence model, and may include continuous variables |

---

|             |                                                                    |
|-------------|--------------------------------------------------------------------|
| buildCovMat | <i>A function to build the covariate matrix of the constraints</i> |
|-------------|--------------------------------------------------------------------|

---

### Description

A function to build the covariate matrix of the constraints

### Usage

```
buildCovMat(datFrame)
```

### Arguments

|          |                                                                                                                                                                                                                                                                                                                                                          |
|----------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| datFrame | the dataframe with which the covariate matrix is to be built<br>In this case we will 1) Include dummy's for every level of the categorical variable, and force them to sum to zero. This is needed for plotting and required for reference level independent normalization. 2) Exclude an intercept. The density function f() will provide this already. |
|----------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

### Value

|                        |                                                  |
|------------------------|--------------------------------------------------|
| a list with components |                                                  |
| covModelMat            | The model matrix                                 |
| datFrame               | The dataframe used to construct the model matrix |

---

|               |                                                                                                                                                                                              |
|---------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| buildEmptyJac | <i>Prepare an empty Jacobian matrix, with useful entries prefilled. In case of distribution "gaussian", it returns the lhs matrix of the linear system for finding the feature paramters</i> |
|---------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

---

### Description

Prepare an empty Jacobian matrix, with useful entries prefilled. In case of distribution "gaussian", it returns the lhs matrix of the linear system for finding the feature paramters

### Usage

```
buildEmptyJac(
  n,
  m,
  lower,
  distribution = "quasi",
  normal = FALSE,
  nLambda1s = 1,
  centMat = NULL,
  weights = 1
)
```

**Arguments**

|              |                                                                |
|--------------|----------------------------------------------------------------|
| n            | the number of parameters                                       |
| m            | the dimension                                                  |
| lower        | the current parameter estimates                                |
| distribution | A character string, the distributional assumption for the data |
| normal       | a boolean, are normalization restrictions in place?            |
| nLambdas     | The number of centering restrictions                           |
| centMat      | The centering matrix                                           |
| weights      | Vector of feature weights                                      |

**Value**

an empty jacobian matrix, or the lhs of the system of estimating equations

---

|                     |                                                             |
|---------------------|-------------------------------------------------------------|
| buildMarginalOffset | <i>Build an offset matrix from an marginal model object</i> |
|---------------------|-------------------------------------------------------------|

---

**Description**

Build an offset matrix from an marginal model object

**Usage**

```
buildMarginalOffset(indepModel, invLink)
```

**Arguments**

|            |                                   |
|------------|-----------------------------------|
| indepModel | The fitted marginal model, a list |
| invLink    | The inverse link function         |

**Value**

an offset matrix of the size of the data

---

|         |                                          |
|---------|------------------------------------------|
| buildMu | <i>A function to build the mu matrix</i> |
|---------|------------------------------------------|

---

**Description**

A function to build the mu matrix

**Usage**

```
buildMu(offSet, latentVar, paramEsts, distribution, paramMatrix = FALSE)
```

**Arguments**

|                                    |                                                             |
|------------------------------------|-------------------------------------------------------------|
| offSet                             | the offset matrix                                           |
| latentVar, paramEsts, distribution | Latent variables, parameter estimates and distribution type |
| paramMatrix                        | A boolean, are feature parameters provided as matrix        |

**Value**

The mean matrix

---

|                |                                     |
|----------------|-------------------------------------|
| buildMuMargins | <i>Build the marginal mu matrix</i> |
|----------------|-------------------------------------|

---

**Description**

Build the marginal mu matrix

**Usage**

```
buildMuMargins(x, otherMargin, col)
```

**Arguments**

|             |                                                       |
|-------------|-------------------------------------------------------|
| x           | The marginal parameters begin estimated               |
| otherMargin | The parameters of the other margin                    |
| col         | A logical, are the column parameters being estimated? |

**Value**

a matrix of means

---

|                  |                                                     |
|------------------|-----------------------------------------------------|
| buildOffsetModel | <i>Build a marginal offset matrix given a model</i> |
|------------------|-----------------------------------------------------|

---

**Description**

Build a marginal offset matrix given a model

**Usage**

```
buildOffsetModel(modelObj, View, distributions, compositional)
```

**Arguments**

|                              |                                        |
|------------------------------|----------------------------------------|
| modelObj                     | a modelDI object                       |
| View                         | The view for which to build the offset |
| distributions, compositional | belong to the view                     |

**Value**

The offset matrix

---

|            |                                                                                        |
|------------|----------------------------------------------------------------------------------------|
| checkAlias | <i>Check for alias structures in a dataframe, and throw an error when one is found</i> |
|------------|----------------------------------------------------------------------------------------|

---

**Description**

Check for alias structures in a dataframe, and throw an error when one is found

**Usage**

```
checkAlias(datFrame, covariatesNames)
```

**Arguments**

|                 |                                                  |
|-----------------|--------------------------------------------------|
| datFrame        | the data frame to be checked for alias structure |
| covariatesNames | The names of the variables to be considered      |

**Value**

Throws an error when an alias structure is detected, returns invisible otherwise

---

|                   |                                                                     |
|-------------------|---------------------------------------------------------------------|
| checkMeanVarTrend | <i>Quickly check if the mean variance trend provides a good fit</i> |
|-------------------|---------------------------------------------------------------------|

---

**Description**

Quickly check if the mean variance trend provides a good fit

**Usage**

```
checkMeanVarTrend(data, meanVarFit = "spline", returnTrend = FALSE, ...)
```

**Arguments**

|             |                                                                                   |
|-------------|-----------------------------------------------------------------------------------|
| data        | Data in any acceptable format (see details ?combi)                                |
| meanVarFit  | The type of mean variance fit, either "cubic" or "spline"                         |
| returnTrend | A boolean, should the estimated trend be returned (TRUE) or only plotted (FALSE)? |
| ...         | passed on to the estMeanVarTrend() function                                       |

**Value**

A plot object

**Examples**

```
data(Zhang)
par(mfrow = c(1,2))
lapply(list("microbiome" = zhangMicrobio, "metabolome" = zhangMetabo),
  checkMeanVarTrend)
par(mfrow = c(1,1))
```

---

|                   |                                                                              |
|-------------------|------------------------------------------------------------------------------|
| checkMonotonicity | <i>Check for monotonicity in compositional datasets fro given dimensions</i> |
|-------------------|------------------------------------------------------------------------------|

---

**Description**

Check for monotonicity in compositional datasets fro given dimensions

**Usage**

```
checkMonotonicity(modelObj, Dim)
```

**Arguments**

|          |                           |
|----------|---------------------------|
| modelObj | The combi fit             |
| Dim      | The dimensions considered |

**Value**

A boolean matrix indicating monotonicity for every feature

---

|       |                                             |
|-------|---------------------------------------------|
| combi | <i>Perform model-based data integration</i> |
|-------|---------------------------------------------|

---

**Description**

Perform model-based data integration

**Usage**

```
combi(  
  data,  
  M = 2L,  
  covariates = NULL,  
  distributions,  
  compositional,  
  maxIt = 300L,  
  tol = 0.001,  
  verbose = FALSE,  
  prevCutOff = 0.95,  
  minFraction = 0.1,  
  logTransformGaussian = TRUE,  
  confounders = NULL,  
  compositionalConf = rep(FALSE, length(data)),  
  nleq.control = list(maxit = 1000L, cndtol = 1e-16),  
  record = TRUE,  
  weights = NULL,  
  fTol = 1e-05,  
  meanVarFit = "spline",  
  maxFeats = 2000,  
  dispFreq = 10L,  
  allowMissingness = FALSE,  
  biasReduction = TRUE,  
  maxItFeat = 20L,  
  initPower = 1  
)
```

**Arguments**

|               |                                                                                            |
|---------------|--------------------------------------------------------------------------------------------|
| data          | A list of data objects with the same number of samples. See details.                       |
| M             | the required dimension of the fit, a non-negative integer                                  |
| covariates    | a dataframe of n samples with sample-specific variables.                                   |
| distributions | a character vector describing which distributional assumption should be used. See details. |

|                      |                                                                                                                                                                                                              |
|----------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| compositional        | A logical vector with the same length as "data", indicating if the datasets should be treated as compositional                                                                                               |
| maxIt                | an integer, the maximum number of iterations                                                                                                                                                                 |
| tol                  | A small scalar, the convergence tolerance                                                                                                                                                                    |
| verbose              | Logical. Should verbose output be printed to the console?                                                                                                                                                    |
| prevCutOff           | a scalar, the prevalence cutoff for the trimming.                                                                                                                                                            |
| minFraction          | a scalar, each taxon's total abundance should equal at least the number of samples n times minFraction, otherwise it is trimmed.                                                                             |
| logTransformGaussian | A boolean, should the gaussian data be logtransformed, i.e. are they log-normal?                                                                                                                             |
| confounders          | A dataframe or a list of dataframes with the same length as data. In the former case the same dataframe is used for conditioning, In the latter case each view has its own conditioning variables (or NULL). |
| compositionalConf    | A logical vector with the same length as "data", indicating if the datasets should be treated as compositional when correcting for confounders. Numerical problems may occur when set to TRUE                |
| nleq.control         | A list of arguments to the nleqslv function                                                                                                                                                                  |
| record               | A boolean, should intermediate estimates be stored? Can be useful to check convergence                                                                                                                       |
| weights              | A character string, either 'marginal' or 'uniform', indicating rhow the feature parameters should be weighted in the normalization                                                                           |
| fTol                 | The tolerance for solving the estimating equations                                                                                                                                                           |
| meanVarFit           | The type of mean variance fit, see details                                                                                                                                                                   |
| maxFeats             | The maximal number of features for a Newton-Raphson procedure to be feasible                                                                                                                                 |
| dispFreq             | An integer, the period after which the variances should be reestimated                                                                                                                                       |
| allowMissingness     | A boolean, should NA values be allowed?                                                                                                                                                                      |
| biasReduction        | A boolean, should bias reduction be applied to allow for confounder correction in groups with all zeroes? Not guaranteed to work                                                                             |
| maxItFeat            | Integers, the maximum allowed number of iterations in the estimation of the feature parameters                                                                                                               |
| initPower            | The power to be applied to the residual matrix used to calculate the starting value. Must be positive; can be tweaked in case of numerical problems (i.e. infinite values returned by nleqslv)               |

## Details

Data can be provided as raw matrices with features in the columns, or as phyloseq, Summarized-Experiment or ExpressionSet objects. Estimation of independence model and view wise parameters can be parametrized. See `?BiocParallel::bplapply` and `?BiocParallel::register`. `meanVarFit = "spline"` yields a cubic spline fit for the abundance-variance trend, `"cubic"` gives a third degree polynomial. Both converge to the diagonal line with slope 1 for small means. Distribution can be either `"quasi"` for quasi likelihood or `"gaussian"` for Gaussian data

**Value**

An object of the "combi" class, containing all information on the data integration and fitting procedure

**Examples**

```
data(Zhang)
#The method works on several datasets at once, and simply is not very fast.
#Hence the "Not run" statement
## Not run:
#Unconstrained
microMetaboInt = combi(
  list("microbiome" = zhangMicrobio, "metabolomics" = zhangMetabo),
  distributions = c("quasi", "gaussian"), compositional = c(TRUE, FALSE),
  logTransformGaussian = FALSE, verbose = TRUE)
#Constrained
microMetaboIntConstr = combi(
  list("microbiome" = zhangMicrobio, "metabolomics" = zhangMetabo),
  distributions = c("quasi", "gaussian"), compositional = c(TRUE, FALSE),
  logTransformGaussian = FALSE, covariates = zhangMetavars, verbose = TRUE)

## End(Not run)
```

---

convPlot

---

*Plot the convergence of the different parameter estimates in a line plot*


---

**Description**

Plot the convergence of the different parameter estimates in a line plot

**Usage**

```
convPlot(
  model,
  latent = is.null(View),
  nVars = Inf,
  Dim = 1L,
  View = NULL,
  size = 0.125
)
```

**Arguments**

|        |                                                                         |
|--------|-------------------------------------------------------------------------|
| model  | A fitted modelDI object                                                 |
| latent | A boolean, should latent variable trajectory be plotted                 |
| nVars  | An integer, the number of variables to plot. By default all are plotted |
| Dim    | An integer, the dimension to be plotted                                 |

|      |                                                                                       |
|------|---------------------------------------------------------------------------------------|
| View | An integer or character string, indicating the view to be plotted (if latent = FALSE) |
| size | The line size (see ?geom_path)                                                        |

**Value**

A ggplot object containing the convergence plot

**Examples**

```
## Not run:
data(Zhang)
#Unconstrained
microMetaboInt = combi(
  list("microbiome" = zhangMicrobio, "metabolomics" = zhangMetabo),
  distributions = c("quasi", "gaussian"), compositional = c(TRUE, FALSE),
  logTransformGaussian = FALSE, verbose = TRUE)
## End(Not run)
load(system.file("extdata", "zhangFits.RData", package = "combi"))
convPlot(microMetaboInt)
convPlot(microMetaboInt, Dim = 2)
convPlot(microMetaboInt, View = "microbiome")
```

---

deriv2LagrangianFeatures

*The score function to estimate the latent variables*

---

**Description**

The score function to estimate the latent variables

**Usage**

```
deriv2LagrangianFeatures(
  x,
  data,
  distribution,
  offSet,
  latentVars,
  numVar,
  paramEstsLower,
  mm,
  Jac,
  meanVarTrend,
  weights,
  compositional,
  indepModel,
  ...
)
```

**Arguments**

|                                                           |                                                                    |
|-----------------------------------------------------------|--------------------------------------------------------------------|
| x                                                         | parameter estimates                                                |
| data                                                      | A list of data matrices                                            |
| distribution, compositional, meanVarTrend, offSet, numVar | Characteristics of the view                                        |
| latentVars                                                | A vector of latent variables                                       |
| paramEstsLower                                            | lower dimension estimates                                          |
| mm                                                        | the current dimension                                              |
| Jac                                                       | a prefab jacobian                                                  |
| weights                                                   | The normalization weights                                          |
| indepModel                                                | the independence model                                             |
| ...                                                       | Additional arguments passed on to the score and jacobian functions |

**Value**

A vector of length n, the evaluation of the score functions of the latent variables

---

deriv2LagrangianLatentVars

*The jacobian function to estimate the latent variables*

---

**Description**

The jacobian function to estimate the latent variables

**Usage**

```
deriv2LagrangianLatentVars(
  x,
  data,
  distributions,
  offsets,
  paramEsts,
  paramMats,
  numVars,
  latentVarsLower,
  n,
  m,
  Jac,
  numSets,
  meanVarTrends,
  links,
  varPosts,
  indepModels,
  compositional,
  ...
)
```

**Arguments**

|                                                                                                                                  |                                                       |
|----------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------|
| x                                                                                                                                | The current estimates of the latent variables         |
| distributions, links, compositional, data, meanVarTrends, offsets, numVars, numSets, paramMats, paramEsts, varPosts, indepModels |                                                       |
| latentVarsLower                                                                                                                  | Characteristics of the views                          |
| n, m                                                                                                                             | The parameter estimates of the lower dimensions       |
| Jac                                                                                                                              | integers, number of samples and dimensions            |
| Jac                                                                                                                              | an empty jacobian matrix                              |
| ...                                                                                                                              | arguments to the jacobian function, currently ignored |

**Value**

A vector of length n, the evaluation of the score functions of the latent variables

---

deriv2LagrangianLatentVarsConstr

*The score function to estimate the latent variables*

---

**Description**

The score function to estimate the latent variables

**Usage**

```
deriv2LagrangianLatentVarsConstr(
  x,
  data,
  distributions,
  offsets,
  paramEsts,
  paramMats,
  numVars,
  latentVarsLower,
  nn,
  m,
  Jac,
  numSets,
  meanVarTrends,
  links,
  numCov,
  covMat,
  nLambda1s,
  varPosts,
  compositional,
  indepModels,
  ...
)
```

**Arguments**

|                                                                                                  |                                                       |
|--------------------------------------------------------------------------------------------------|-------------------------------------------------------|
| x                                                                                                | The current estimates of the latent variables         |
| distributions, data, links, compositional, meanVarTrends, offsets, numVars, paramMats, paramEsts |                                                       |
| latentVarsLower                                                                                  | Characteristics of the view                           |
|                                                                                                  | The parameter estimates of the lower dimensions       |
| nn                                                                                               | number of samples                                     |
| m, numSets, varPosts, indepModels                                                                |                                                       |
|                                                                                                  | other arguments                                       |
| Jac                                                                                              | an empty jacobian matrix                              |
| numCov                                                                                           | The number of covariates                              |
| covMat                                                                                           | the covariates matrix                                 |
| nLambda1s                                                                                        | The number of centering restrictions                  |
| ...                                                                                              | arguments to the jacobian function, currently ignored |

**Value**

A vector of length nn, the evaluation of the score functions of the latent variables

---

derivLagrangianFeatures

*The score function to estimate the feature parameters*

---

**Description**

The score function to estimate the feature parameters

**Usage**

```
derivLagrangianFeatures(
  x,
  data,
  distribution,
  offSet,
  latentVars,
  numVar,
  paramEstsLower,
  mm,
  indepModel,
  meanVarTrend,
  weights,
  compositional,
  ...
)
```

**Arguments**

|                                                                                       |                                                       |
|---------------------------------------------------------------------------------------|-------------------------------------------------------|
| x                                                                                     | current parameter estimates                           |
| data                                                                                  | A list of data matrices                               |
| distribution, compositional, meanVarTrend, offSet, numVar, indepModel, paramEstsLower | Characteristics of the view                           |
| latentVars                                                                            | A vector of latent variables                          |
| mm                                                                                    | the current dimension                                 |
| weights                                                                               | The normalization weights                             |
| ...                                                                                   | arguments to the jacobian function, currently ignored |

**Value**

A vector with the evaluation of the score functions of the feature parameters

---

derivLagrangianLatentVars

*The score function to estimate the latent variables*

---

**Description**

The score function to estimate the latent variables

**Usage**

```
derivLagrangianLatentVars(
  x,
  data,
  distributions,
  offsets,
  paramEsts,
  paramMats,
  numVars,
  n,
  m,
  numSets,
  meanVarTrends,
  links,
  varPosts,
  latentVarsLower,
  compositional,
  indepModels,
  ...
)
```

**Arguments**

|                                                                                                                         |                                                       |
|-------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------|
| x                                                                                                                       | The current estimates of the latent variables         |
| n                                                                                                                       | The number of samples                                 |
| m                                                                                                                       | The dimensions                                        |
| numSets                                                                                                                 | The number of views                                   |
| latentVarsLower                                                                                                         | The parameter estimates of the lower dimensions       |
| compositional, links, indepModels, meanVarTrends, numVars, distributions, data, offsets, varPosts, paramMats, paramEsts | Lists of information on all the views                 |
| ...                                                                                                                     | arguments to the jacobian function, currently ignored |

**Value**

A vector of length n, the evaluation of the score functions of the latent variables

---

derivLagrangianLatentVarsConstr

*The score function to estimate the latent variables*

---

**Description**

The score function to estimate the latent variables

**Usage**

```
derivLagrangianLatentVarsConstr(
  x,
  data,
  distributions,
  offsets,
  paramEsts,
  numVars,
  latentVarsLower,
  n,
  m,
  numSets,
  meanVarTrends,
  links,
  covMat,
  numCov,
  centMat,
  nLambda1s,
  varPosts,
  compositional,
```

```

    indepModels,
    paramMats,
    ...
)

```

### Arguments

|                                                                                                                         |                                                       |
|-------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------|
| x                                                                                                                       | The current estimates of the latent variables         |
| latentVarsLower                                                                                                         | The parameter estimates of the lower dimensions       |
| n                                                                                                                       | The number of samples                                 |
| m                                                                                                                       | The dimensions                                        |
| numSets                                                                                                                 | The number of views                                   |
| covMat                                                                                                                  | The covariance matrix                                 |
| numCov                                                                                                                  | The number of covariates                              |
| centMat                                                                                                                 | A centering matrix                                    |
| nLambdas                                                                                                                | The number of dummy variables                         |
| compositional, links, indepModels, meanVarTrends, numVars, distributions, data, offsets, varPosts, paramMats, paramEsts | Lists of information on all the views                 |
| ...                                                                                                                     | arguments to the jacobian function, currently ignored |

### Value

A vector of length n, the evaluation of the score functions of the latent variables

---

estFeatureParameters    *Estimate the feature parameters*

---

### Description

Estimate the feature parameters

### Usage

```

estFeatureParameters(
  paramEsts,
  lambdasParams,
  seqSets,
  data,
  distributions,
  offsets,
  nCores,
  m,
  JacFeatures,

```

```

    meanVarTrends,
    latentVars,
    numVars,
    control,
    weights,
    compositional,
    indepModels,
    fTol,
    allowMissingness,
    maxItFeat,
    ...
)

```

### Arguments

|                  |                                                                    |
|------------------|--------------------------------------------------------------------|
| paramEsts        | Current list of parameter estimates for the different views        |
| lambdasParams    | The lagrange multipliers                                           |
| seqSets          | A vector with view indices                                         |
| data             | A list of data matrices                                            |
| distributions    | A character vector describing the distributions                    |
| offsets          | A list of offset matrices                                          |
| nCores           | The number of cores to use in multithreading                       |
| m                | The dimension                                                      |
| JacFeatures      | An empty Jacobian matrix                                           |
| meanVarTrends    | The mean-variance trends of the different views                    |
| latentVars       | A vector of latent variables                                       |
| numVars          | The number of variables                                            |
| control          | A list of control arguments for the nleqslv function               |
| weights          | The normalization weights                                          |
| compositional    | A list of booleans indicating compositionality                     |
| indepModels      | A list of independence model                                       |
| fTol             | A convergence tolerance                                            |
| allowMissingness | A boolean indicating whether missing values are allowed            |
| maxItFeat        | An integer, the maximum number of iterations                       |
| ...              | Additional arguments passed on to the score and jacobian functions |

### Value

A vector with estimates of the feature parameters

---

|               |                                                              |
|---------------|--------------------------------------------------------------|
| estIndepModel | <i>Estimate the independence model belonging to one view</i> |
|---------------|--------------------------------------------------------------|

---

**Description**

Estimate the independence model belonging to one view

**Usage**

```
estIndepModel(
  data,
  distribution,
  compositional,
  maxIt,
  tol,
  link,
  invLink,
  meanVarFit,
  newtonRaphson,
  dispFreq,
  ...
)
```

**Arguments**

|               |                                                                                                                    |
|---------------|--------------------------------------------------------------------------------------------------------------------|
| data          | a list of data matrices with the same number of samples <i>n</i> in the rows. Also phyloseq objects are acceptable |
| distribution  | a character string describing which distributional assumption should be used.                                      |
| compositional | A logical indicating if the dataset should be treated as compositional                                             |
| maxIt         | an integer, the maximum number of iterations                                                                       |
| tol           | A small scalar, the convergence tolerance                                                                          |
| link, invLink | link and inverse link function                                                                                     |
| meanVarFit    | mean variance model                                                                                                |
| newtonRaphson | a boolean, should newton-raphson be used                                                                           |
| dispFreq      | An integer, frequency of dispersion estimation                                                                     |
| ...           | passed on to the estOff() function                                                                                 |

**Value**

A list with elements

|           |                                                      |
|-----------|------------------------------------------------------|
| rowOff    | The row offsets                                      |
| colOff    | The column offsets                                   |
| converged | A logical flag, indicating whether the fit converged |
| iter      | An integer, the number of iterations                 |

---

|               |                                      |
|---------------|--------------------------------------|
| estLatentVars | <i>Estimate the latent variables</i> |
|---------------|--------------------------------------|

---

**Description**

Estimate the latent variables

**Usage**

```
estLatentVars(latentVars, lambdasLatent, constrained, fTol, ...)
```

**Arguments**

|               |                                                                |
|---------------|----------------------------------------------------------------|
| latentVars    | A vector of latent variables                                   |
| lambdasLatent | A vector of Lagrange multipliers                               |
| constrained   | A boolean, is the ordination constrained?                      |
| fTol          | The convergence tolerance                                      |
| ...           | additional arguments passed on to score and jacobian functions |

**Value**

A vector of length n, the estimates of the latent variables

---

|                 |                                                   |
|-----------------|---------------------------------------------------|
| estMeanVarTrend | <i>Estimate a column-wise mean-variance trend</i> |
|-----------------|---------------------------------------------------|

---

**Description**

Estimate a column-wise mean-variance trend

**Usage**

```
estMeanVarTrend(
  data,
  meanMat,
  baseAbundances,
  libSizes,
  plot = FALSE,
  meanVarFit,
  degree = 2L,
  constraint = "none",
  ...
)
```

**Arguments**

|                |                                                                                          |
|----------------|------------------------------------------------------------------------------------------|
| data           | the data matrix with n rows                                                              |
| meanMat        | the estimated mean matrix                                                                |
| baseAbundances | The baseline abundances                                                                  |
| libSizes       | Library sizes                                                                            |
| plot           | A boolean, should the trend be plotted?                                                  |
| meanVarFit     | A character string describing the type of trend to be fitted: either "spline" or "cubic" |
| degree         | The degree of the spline                                                                 |
| constraint     | Constraint to the spline                                                                 |
| ...            | additional arguments passed on to the plot() function                                    |

**Value**

|                        |                                                               |
|------------------------|---------------------------------------------------------------|
| A list with components |                                                               |
| meanVarTrend           | An smoothed trend function, that can map a mean on a variance |
| meanVarTrendDeriv      | A derivative function of this                                 |

---

 estOff

---

*Estimate the row/column parameters of the independence model*


---

**Description**

Estimate the row/column parameters of the independence model

**Usage**

```
estOff(
  data,
  distribution,
  rowOff,
  colOff,
  meanVarTrend,
  col,
  newtonRaphson,
  libSizes,
  ...
)
```

**Arguments**

|                |                                                                                                               |
|----------------|---------------------------------------------------------------------------------------------------------------|
| data           | a list of data matrices with the same number of samples $n$ in the rows. Also phyloseq objects are acceptable |
| distribution   | a character string describing which distributional assumption should be used.                                 |
| rowOff, colOff | current row and column offset estimates                                                                       |
| meanVarTrend   | The estimated mean-variance trend                                                                             |
| col            | A logical, should column offsets be estimated                                                                 |
| newtonRaphson  | A boolean, should Newton-Raphson be used to solve the estimating equations                                    |
| libSizes       | The library sizes, used to evaluate the mean-variance trend                                                   |
| ...            | passed onto nleqslv                                                                                           |

**Value**

The estimated marginal parameters

---

|               |                                               |
|---------------|-----------------------------------------------|
| extractCoords | <i>Extract coordinates from fitted object</i> |
|---------------|-----------------------------------------------|

---

**Description**

Extract coordinates from fitted object

**Usage**

```
extractCoords(modelObj, Dim)
```

**Arguments**

|          |                         |
|----------|-------------------------|
| modelObj | The fitted model        |
| Dim      | the required dimensions |

**Value**

A list with components (matrices with two columns)

|             |                        |
|-------------|------------------------|
| latentData  | The latent variables   |
| featureData | The feature parameters |
| varData     | The variables          |

**Examples**

```

data(Zhang)
## Not run:
#Unconstrained
microMetaboInt = combi(
  list("microbiome" = zhangMicrobio, "metabolomics" = zhangMetabo),
  distributions = c("quasi", "gaussian"), compositional = c(TRUE, FALSE),
  logTransformGaussian = FALSE, verbose = TRUE)

## End(Not run)
#Load the fits
load(system.file("extdata", "zhangFits.RData", package = "combi"))
extractCoords(microMetaboInt, Dim = c(1,2))

```

---

|             |                                                                                                                        |
|-------------|------------------------------------------------------------------------------------------------------------------------|
| extractData | <i>Helper function to extract data matrix from phyloseq, expressionset objects etc. Also filters out all zero rows</i> |
|-------------|------------------------------------------------------------------------------------------------------------------------|

---

**Description**

Helper function to extract data matrix from phyloseq, expressionset objects etc. Also filters out all zero rows

**Usage**

```
extractData(data, logTransformGaussian = TRUE)
```

**Arguments**

|                      |                                                                            |
|----------------------|----------------------------------------------------------------------------|
| data                 | The list of data objects, either matrix, phyloseq or ExpressionSet objects |
| logTransformGaussian | A boolean, should array data be logtransformed                             |

**Value**

the raw data matrices, samples in the rows

**Examples**

```

data(Zhang)
matrixList = extractData(list("microbiome" = zhangMicrobio,
  "metabolome" = zhangMetabo))

```

---

|            |                                                                     |
|------------|---------------------------------------------------------------------|
| extractMat | <i>A function to extract a data matrix from a number of objects</i> |
|------------|---------------------------------------------------------------------|

---

### Description

A function to extract a data matrix from a number of objects

### Usage

```
extractMat(Y, ...)

## S4 method for signature 'ExpressionSet'
extractMat(Y, logTransformGaussian, ...)

## S4 method for signature 'SummarizedExperiment'
extractMat(Y, ...)

## S4 method for signature 'matrix'
extractMat(Y, ...)
```

### Arguments

|                      |                                                                    |
|----------------------|--------------------------------------------------------------------|
| Y                    | a phyloseq or eSet object, or another object, or a raw data matrix |
| ...                  | additional arguments for the extractor function                    |
| logTransformGaussian | A boolean, should array data be logtransformed                     |

### Value

A data matrix with samples in the rows and features in the columns

---

|                   |                                                   |
|-------------------|---------------------------------------------------|
| filterConfounders | <i>Filter out the effect of known confounders</i> |
|-------------------|---------------------------------------------------|

---

### Description

Filter out the effect of known confounders

Usage

```
filterConfounders(  
  confMat,  
  data,  
  distribution,  
  link,  
  invLink,  
  compositional,  
  control,  
  meanVarTrend,  
  offSet,  
  numVar,  
  marginModel,  
  biasReduction,  
  allowMissingness  
)
```

Arguments

- confMat            A confounder design matrix
- data              data matrix
- distribution, link, invLink, compositional, meanVarTrend, offSet, numVar, marginModel      Characteristics of the view
- control           A list of control elements to the nleqslv function
- biasReduction    A boolean, should bias reduction be applied
- allowMissingness      A boolean, are missing values allowed?

Value

Parameter estimates accounting for the effects of the confounders

---

|                  |                                                                       |
|------------------|-----------------------------------------------------------------------|
| getInflLatentVar | <i>Extract the influence on the estimation of the latent variable</i> |
|------------------|-----------------------------------------------------------------------|

---

Description

Extract the influence on the estimation of the latent variable

Usage

```
getInflLatentVar(score, InvJac, i)
```

Arguments

|        |                      |
|--------|----------------------|
| score  | The score matrix     |
| InvJac | The inverse Jacobian |
| i      | the sample index     |

Value

The influence of all observations on the i-th latent variable

---

|                 |                                                                      |
|-----------------|----------------------------------------------------------------------|
| gramSchmidtOrth | <i>Gram schmidt orhtogonalize a with respect to b, and normalize</i> |
|-----------------|----------------------------------------------------------------------|

---

Description

Gram schimdt orhtogonalize a with respect to b, and normalize

Usage

```
gramSchmidtOrth(a, b, weights = 1, norm = TRUE)
```

Arguments

|         |                                             |
|---------|---------------------------------------------|
| a       | the vector to be orthogonalized             |
| b       | the vector to be orthogonalized to          |
| weights | weights vector                              |
| norm    | a boolean, should the result be normalized? |

Value

The orthogonalized vector

---

|            |                                                                  |
|------------|------------------------------------------------------------------|
| indentPlot | <i>Functions to indent the plot to include the entire labels</i> |
|------------|------------------------------------------------------------------|

---

Description

Functions to indent the plot to include the entire labels

Usage

```
indentPlot(plt, xInd = 0, yInd = 0)
```

**Arguments**

|      |                                                                                                                                          |
|------|------------------------------------------------------------------------------------------------------------------------------------------|
| plt  | a ggplot object                                                                                                                          |
| xInd | a scalar or a vector of length 2, specifying the indentation left and right of the plot to allow for the labels to be printed entirely   |
| yInd | a a scalar or a vector of length 2, specifying the indentation top and bottom of the plot to allow for the labels to be printed entirely |

**Value**

a ggplot object, squared

---

|          |                                                  |
|----------|--------------------------------------------------|
| inflPlot | <i>A ggplot line plot showing the influences</i> |
|----------|--------------------------------------------------|

---

**Description**

A ggplot line plot showing the influences

**Usage**

```
inflPlot(
  modelObj,
  plotType = ifelse(length(modelObj$data) <= 2, "pointplot", "boxplot"),
  pointFun = "sum",
  lineSize = 0.07,
  Dim = 1,
  samples = seq_len(nrow(if (is.null(modelObj$covariates)) modelObj$latentVars else
    modelObj$alphas)),
  ...
)
```

**Arguments**

|          |                                                             |
|----------|-------------------------------------------------------------|
| modelObj | The fitted data integration                                 |
| plotType | The type of plot requested, see details                     |
| pointFun | The function to calculate the summary measure to be plotted |
| lineSize | The line size                                               |
| Dim      | The dimension required                                      |
| samples  | index vector of which samples to be plotted                 |
| ...      | additional arguments passed on to the influence() function  |

## Details

The options for plotType are: "pointPlot": Dot plot of total influence per view and sample, "boxplot": plot boxplot of influence of all observations per view and sample, "boxplotSingle": boxplot of log absolute total influence per view, "lineplot": line plot of total influence per view and sample. In the pointplot, dots crosses represent parameter estimates

## Value

A ggplot object

## Examples

```
data(Zhang)
#Unconstrained
microMetaboInt = combi(
  list("microbiome" = zhangMicrobio, "metabolomics" = zhangMetabo),
  distributions = c("quasi", "gaussian"), compositional = c(TRUE, FALSE),
  logTransformGaussian = FALSE, verbose = TRUE)
#Constrained
microMetaboIntConstr = combi(
  list("microbiome" = zhangMicrobio, "metabolomics" = zhangMetabo),
  distributions = c("quasi", "gaussian"), compositional = c(TRUE, FALSE),
  logTransformGaussian = FALSE, covariates = zhangMetavars, verbose = TRUE)
load(system.file("extdata", "zhangFits.RData", package = "combi"))
inflPlot(microMetaboInt)
#Constrained
inflPlot(microMetaboIntConstr)
```

---

influence.combi

*Evaluate the influence function*

---

## Description

Evaluate the influence function

## Usage

```
## S3 method for class 'combi'
influence(modelObj, samples = is.null(View), Dim = 1, View = NULL)
```

## Arguments

|           |                                                                          |
|-----------|--------------------------------------------------------------------------|
| modelObj  | The model object                                                         |
| samples   | A boolean, should we look at sample variables? Throws an error otherwise |
| Dim, View | Integers, the dimension and views required                               |

**Details**

Especially the influence of the different views on the latent variable or gradient estimation may be of interest. The influence values are not all calculated. Rather, the score values and inverse jacobian are returned so they can easily be calculated

**Value**

A list with components

|        |                                      |
|--------|--------------------------------------|
| score  | The evaluation of the score function |
| InvJac | The inverted jacobian matrix         |

---

|                |                                                      |
|----------------|------------------------------------------------------|
| jacConfounders | <i>Jacobian when estimating confounder variables</i> |
|----------------|------------------------------------------------------|

---

**Description**

Jacobian when estimating confounder variables

**Usage**

```
jacConfounders(
  confMat,
  data,
  distribution,
  x,
  meanVarTrend,
  offSet,
  CompMat,
  libSizes,
  allowMissingness
)
```

**Arguments**

|                             |                                             |
|-----------------------------|---------------------------------------------|
| data, confMat, meanVarTrend | Characteristics of the views                |
| distribution, offSet        | distribution and offset of the view         |
| x                           | the parameter estimates                     |
| libSizes, CompMat           | Library sizes and relative abundance        |
| allowMissingness            | a boolean, should missing values be allowed |

**Value**

the jacobian matrix

---

|                    |                                                         |
|--------------------|---------------------------------------------------------|
| jacConfoundersComp | <i>Jacobian for conditioning under compositionality</i> |
|--------------------|---------------------------------------------------------|

---

**Description**

Jacobian for conditioning under compositionality

**Usage**

```
jacConfoundersComp(  
  x,  
  confMat,  
  data,  
  meanVarTrend,  
  marginModel,  
  allowMissingness,  
  biasReduction,  
  subtractMax = TRUE  
)
```

**Arguments**

- x                    the parameter estimates
- confMat, data, meanVarTrend                    arguments belonging to views
- marginModel, biasReduction, subtractMax                    The marginal mode, and booleans indicating bias reduction and maximum subtraction
- allowMissingness                    a boolean, should missing values be allowed

**Value**

the jacobian matrix

---

|             |                                                                                 |
|-------------|---------------------------------------------------------------------------------|
| jacFeatures | <i>Evaluate the jacobian for estimating the feature parameters for one view</i> |
|-------------|---------------------------------------------------------------------------------|

---

**Description**

Evaluate the jacobian for estimating the feature parameters for one view

**Usage**

```
jacFeatures(
  latentVars,
  data,
  distribution,
  paramEsts,
  meanVarTrend,
  offSet,
  compositional,
  indepModel,
  m,
  paramEstsLower,
  allowMissingness,
  ...
)
```

**Arguments**

|                                                                                          |                                                                    |
|------------------------------------------------------------------------------------------|--------------------------------------------------------------------|
| latentVars                                                                               | A vector of latent variables                                       |
| data                                                                                     | A list of data matrices                                            |
| distribution, compositional, meanVarTrend, offSet, paramEsts, paramEstsLower, indepModel | Characteristics of each view                                       |
| m                                                                                        | dimension                                                          |
| allowMissingness                                                                         | a boolean, are missing values allowed?                             |
| ...                                                                                      | Additional arguments passed on to the score and jacobian functions |

**Value**

The jacobian matrix

---

|               |                                                                              |
|---------------|------------------------------------------------------------------------------|
| jacLatentVars | <i>Evaluate the jacobian for estimating the latent variable for one view</i> |
|---------------|------------------------------------------------------------------------------|

---

**Description**

Evaluate the jacobian for estimating the latent variable for one view

**Usage**

```
jacLatentVars(
  latentVar,
  data,
  distribution,
  paramEsts,
```

```

    paramMats,
    offSet,
    meanVarTrend,
    n,
    varPosts,
    mm,
    indepModel,
    latentVarsLower,
    compositional,
    allowMissingness,
    ...
)

```

### Arguments

|                                                                                                     |                                                                |
|-----------------------------------------------------------------------------------------------------|----------------------------------------------------------------|
| latentVar                                                                                           | the latent variable estimates                                  |
| distribution, data, varPosts, compositional, meanVarTrend, offSet, paramEsts, paramMats, indepModel | Characteristics of each view                                   |
| n                                                                                                   | the number of samples                                          |
| mm                                                                                                  | the current dimension                                          |
| latentVarsLower                                                                                     | the lower dimensional latent variables                         |
| allowMissingness                                                                                    | a boolean, should missing values be allowed                    |
| ...                                                                                                 | additional arguments passed on to score and jacobian functions |

### Value

The diagonal of the jacobian matrix

---

|                     |                                                                                                         |
|---------------------|---------------------------------------------------------------------------------------------------------|
| jacLatentVarsConstr | <i>Evaluate the jacobian for estimating the latent variable for one view for constrained ordination</i> |
|---------------------|---------------------------------------------------------------------------------------------------------|

---

### Description

Evaluate the jacobian for estimating the latent variable for one view for constrained ordination

### Usage

```

jacLatentVarsConstr(
  latentVar,
  data,
  distribution,
  paramEsts,

```

```

    offSet,
    meanVarTrend,
    numCov,
    covMat,
    varPosts,
    compositional,
    mm,
    indepModel,
    latentVarsLower,
    ...
  )

```

### Arguments

|                            |                                                                |
|----------------------------|----------------------------------------------------------------|
| latentVar                  | current latent variable estimates                              |
| distribution,              | compositional, meanVarTrend, offSet, paramEsts,                |
| indepModel, varPosts, data |                                                                |
|                            | Characteristics of each view                                   |
| numCov                     | the number of covariates                                       |
| covMat                     | the covariates matrix                                          |
| mm                         | the dimension                                                  |
| latentVarsLower            | latent variable estimates of lower dimensions                  |
| ...                        | additional arguments passed on to score and jacobian functions |

### Value

The jacobian matrix

---

|            |                                                       |
|------------|-------------------------------------------------------|
| plot.combi | <i>Make multiplots of the data integration object</i> |
|------------|-------------------------------------------------------|

---

### Description

Make multiplots of the data integration object

### Usage

```

## S3 method for class 'combi'
plot(
  x,
  ...,
  Dim = c(1, 2),
  samDf = NULL,
  samShape = NULL,
  samCol = NULL,

```

```

featurePlot = "threshold",
featNum = 15L,
samColValues = NULL,
manExpFactorTaxa = 0.975,
featSize = switch(featurePlot, threshold = 2.5, points = samSize * 0.7, density = 0.35),
crossSize = 4,
manExpFactorVar = 0.975,
varNum = nrow(x$alphas),
varSize = 2.5,
samSize = 1.75,
featCols = c("darkblue", "darkgreen", "grey10", "turquoise4", "blue", "green", "grey",
  "cornflowerblue", "lightgreen", "grey75"),
strokeSize = 0.05,
warnMonotonicity = FALSE,
returnCoords = FALSE,
squarePlot = TRUE,
featAlpha = 0.5,
featShape = 8,
xInd = 0,
yInd = 0,
checkOverlap = FALSE,
shapeValues = (21:(21 + length(unique(samDf[[samShape]]))))
)

```

## Arguments

|                                                                                                                        |                                                                                                                                                               |
|------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <code>x</code>                                                                                                         | the fit                                                                                                                                                       |
| <code>...</code>                                                                                                       | additional arguments, currently ignored                                                                                                                       |
| <code>Dim</code>                                                                                                       | the dimensions to be plotted                                                                                                                                  |
| <code>samDf</code>                                                                                                     | a dataframe of sample variables                                                                                                                               |
| <code>samShape</code>                                                                                                  | A variable name from <code>samDf</code> used to shape the samples                                                                                             |
| <code>samCol</code>                                                                                                    | A variable name from <code>samDf</code> used to colour the samples                                                                                            |
| <code>featurePlot</code>                                                                                               | A character string, either "threshold", "points" or "density". See details                                                                                    |
| <code>featNum</code> , <code>varNum</code>                                                                             | The number of features and variables to plot                                                                                                                  |
| <code>samColValues</code>                                                                                              | Colours for the samples                                                                                                                                       |
| <code>manExpFactorTaxa</code> , <code>manExpFactorVar</code>                                                           | Expansion factors for taxa and variables, normally calculated natively                                                                                        |
| <code>featSize</code> , <code>crossSize</code> , <code>varSize</code> , <code>samSize</code> , <code>strokeSize</code> | Size parameters for the features (text, dots or density contour lines), central cross, variable labels, sample dots, sample strokes and feature contour lines |
| <code>featCols</code>                                                                                                  | Colours for the features                                                                                                                                      |
| <code>warnMonotonicity</code>                                                                                          | A boolean, should a warning be thrown when the feature proportions of compositional views do not all vary monotonically with all latent variables?            |
| <code>returnCoords</code>                                                                                              | A boolean, should coordinates be returned, e.g. for use in third party software                                                                               |

|              |                                                            |
|--------------|------------------------------------------------------------|
| squarePlot   | A boolean, should the axes be square? Strongly recommended |
| featAlpha    | Controls the transparency of the features                  |
| featShape    | Shape of feature dots when featurePlot = "points"          |
| xInd, yInd   | x and y indentations                                       |
| checkOverlap | A boolean, should overlapping labels be omitted?           |
| shapeValues  | the shapes, as numeric values                              |

## Details

It is usually impossible to plot all features with their labels. Therefore, the default option of the 'featurePlot' parameter is "threshold", whereby only the 'featNum' features furthest away from the origin are shown. Alternatively, the "points" or "density" options are available to plot all features as a point or density cloud, but without labels.

## Value

A ggplot object containing the plot

## Examples

```
data(Zhang)
## Not run:
#Unconstrained
microMetaboInt = combi(
  list("microbiome" = zhangMicrobio, "metabolomics" = zhangMetabo),
  distributions = c("quasi", "gaussian"), compositional = c(TRUE, FALSE),
  logTransformGaussian = FALSE, verbose = TRUE)
#Constrained
microMetaboIntConstr = combi(
  list("microbiome" = zhangMicrobio, "metabolomics" = zhangMetabo),
  distributions = c("quasi", "gaussian"), compositional = c(TRUE, FALSE),
  logTransformGaussian = FALSE, covariates = zhangMetavars, verbose = TRUE)
## End(Not run)
#Load the fits
load(system.file("extdata", "zhangFits.RData", package = "combi"))
plot(microMetaboInt)
plot(microMetaboInt, samDf = zhangMetavars, samCol = "ABX")
#Plot all features as points or density
plot(microMetaboInt, samDf = zhangMetavars, samCol = "ABX",
  featurePlot = "points")
plot(microMetaboInt, samDf = zhangMetavars, samCol = "ABX",
  featurePlot = "density")
#Constrained
plot(microMetaboIntConstr, samDf = zhangMetavars, samCol = "ABX")
```

---

|            |                                                                                                          |
|------------|----------------------------------------------------------------------------------------------------------|
| polyHorner | <i>Horner's method to evaluate a polynomial, copied from the polynom package. the most efficient way</i> |
|------------|----------------------------------------------------------------------------------------------------------|

---

**Description**

Horner's method to evaluate a polynomial, copied from the polynom package. the most efficient way

**Usage**

```
polyHorner(coefs, x)
```

**Arguments**

|       |                                              |
|-------|----------------------------------------------|
| coefs | the polynomial coefficients                  |
| x     | the input values for the polynomial function |

**Value**

the evaluated polynomial

---

|               |                                                                                                                                    |
|---------------|------------------------------------------------------------------------------------------------------------------------------------|
| predictSpline | <i>A custom spline prediction function, extending linearly with a slope such that prediction never drops below first bisectant</i> |
|---------------|------------------------------------------------------------------------------------------------------------------------------------|

---

**Description**

A custom spline prediction function, extending linearly with a slope such that prediction never drops below first bisectant

**Usage**

```
predictSpline(
  fit,
  newdata,
  linX,
  coefsQuad,
  deriv = 0L,
  meanVarFit,
  minFit,
  new.knots,
  degree
)
```

**Arguments**

|            |                                                                              |
|------------|------------------------------------------------------------------------------|
| fit        | The existing spline fit                                                      |
| newdata    | points in which the spline needs to be evaluated                             |
| linX       | The x at which the fit becomes linear and intersects the diagonal line       |
| coefsQuad  | parameters of a quadratic fit                                                |
| deriv      | An integer. Which derivative is required?                                    |
| meanVarFit | A character string, indicating which type of mean variance fit is being used |
| minFit     | The lower bound of the cubic fit                                             |
| new.knots  | The knots at which the spline is to be evaluated                             |
| degree     | The degree of the polynomial fit                                             |

**Value**

The evaluation of the spline, i.e. the predicted variance

---

|               |                                    |
|---------------|------------------------------------|
| prepareJacMat | <i>prepare the jacobian matrix</i> |
|---------------|------------------------------------|

---

**Description**

prepare the jacobian matrix

**Usage**

```
prepareJacMat(mu, data, meanVarTrend, CompMat, libSizes)
```

**Arguments**

|              |                         |
|--------------|-------------------------|
| mu           | the mean matrix         |
| data         | the count matrix        |
| meanVarTrend | The mean variance trend |
| CompMat      | The compisition matrix  |
| libSizes     | The library sizes       |

**Value**

the matrix which can be summed over

---

|                   |                                                                  |
|-------------------|------------------------------------------------------------------|
| prepareJacMatComp | <i>prepare the jacobian for the latent variabls compostional</i> |
|-------------------|------------------------------------------------------------------|

---

**Description**

prepare the jacobian for the latent variabls compostional

**Usage**

```
prepareJacMatComp(mu, paramEsts, CompMat0, meanVarTrend, data, libSizes)
```

**Arguments**

|              |                             |
|--------------|-----------------------------|
| mu           | the mean matrix             |
| paramEsts    | Current parameter estimates |
| CompMat0     | The compisition matrix      |
| meanVarTrend | The mean variance trend     |
| data         | the count matrix            |
| libSizes     | The library sizesv          |

**Value**

The empty jacobian matrix with entries maximally filled out

---

|                 |                                                                                     |
|-----------------|-------------------------------------------------------------------------------------|
| prepareScoreMat | <i>Prepare a helper matrix for score function evaluation under quasi-likelihood</i> |
|-----------------|-------------------------------------------------------------------------------------|

---

**Description**

Prepare a helper matrix for score function evaluation under quasi-likelihood

**Usage**

```
prepareScoreMat(data, mu, meanVarTrend, CompMat, libSizes)
```

**Arguments**

|              |                         |
|--------------|-------------------------|
| data         | the count matrix        |
| mu           | the mean matrix         |
| meanVarTrend | The mean variance trend |
| CompMat      | The compisition matrix  |
| libSizes     | The library sizes       |

**Value**

The helper matrix

---

|             |                                              |
|-------------|----------------------------------------------|
| print.combi | <i>Print an overview of a fitted combi x</i> |
|-------------|----------------------------------------------|

---

**Description**

Print an overview of a fitted combi x

**Usage**

```
## S3 method for class 'combi'
print(x, ...)
```

**Arguments**

|     |                                      |
|-----|--------------------------------------|
| x   | a fitted combi x                     |
| ... | Further arguments, currently ignored |

**Value**

An overview of the number of dimensions, views and parameters, type of ordination and importance parameters

**Examples**

```
data(Zhang)
## Not run:
#Unconstrained
microMetaboInt = combi(
  list("microbiome" = zhangMicrobio, "metabolomics" = zhangMetabo),
  distributions = c("quasi", "gaussian"), compositional = c(TRUE, FALSE),
  logTransformGaussian = FALSE, verbose = TRUE)
#Constrained
microMetaboIntConstr = combi(
  list("microbiome" = zhangMicrobio, "metabolomics" = zhangMetabo),
  distributions = c("quasi", "gaussian"), compositional = c(TRUE, FALSE),
  logTransformGaussian = FALSE, covariates = zhangMetavars, verbose = TRUE)
## End(Not run)
#Load the fits
load(system.file("extdata", "zhangFits.RData", package = "combi"))
print(microMetaboInt)
print(microMetaboIntConstr)
#Or simply
microMetaboInt
```

---

|               |                                                  |
|---------------|--------------------------------------------------|
| quasiJacIndep | <i>The jacobian for column offset estimation</i> |
|---------------|--------------------------------------------------|

---

**Description**

The jacobian for column offset estimation

**Usage**

```
quasiJacIndep(x, data, otherMargin, meanVarTrend, col, libSizes, ...)
```

**Arguments**

|              |                                                 |
|--------------|-------------------------------------------------|
| x            | the initial guess for the current margin        |
| data         | the data matrix                                 |
| otherMargin  | The other margin                                |
| meanVarTrend | the function describing the mean-variance trend |
| col          | A logical, is the column being estimated?       |
| libSizes     | The library sizes                               |
| ...          | passed on to prepareJacMat                      |

**Value**

the jacobian matrix

---

|                 |                                                                                  |
|-----------------|----------------------------------------------------------------------------------|
| quasiScoreIndep | <i>Quasi score equations for column offset parameters of sequence count data</i> |
|-----------------|----------------------------------------------------------------------------------|

---

**Description**

Quasi score equations for column offset parameters of sequence count data

**Usage**

```
quasiScoreIndep(x, data, otherMargin, meanVarTrend, col, libSizes, ...)
```

**Arguments**

|              |                                                 |
|--------------|-------------------------------------------------|
| x            | the initial guess for the current margin        |
| data         | the data matrix                                 |
| otherMargin  | The other margin                                |
| meanVarTrend | the function describing the mean-variance trend |
| col          | A logical, is the column being estimated?       |
| libSizes     | The library sizes                               |
| ...          | passed on to prepareJacMat                      |

**Value**

the evaluated estimating equation

---

rowMultiply

*A function to efficiently row multiply a matrix and a vector*


---

**Description**

A function to efficiently row multiply a matrix and a vector

**Usage**

```
rowMultiply(matrix, vector)
```

**Arguments**

matrix            a numeric matrix of dimension a-by-b

vector            a numeric vector of length b  
                      $t(t(matrix)*vector)$  but then faster

**Details**

Memory intensive but that does not matter with given matrix sizes

**Value**

a matrix, row multiplied by the vector

---

scaleCoords

*A helper function to rescale coordinates*


---

**Description**

A helper function to rescale coordinates

**Usage**

```
scaleCoords(featsCoords, latentData, manExpFactorTaxa, featNum = NULL)
```

**Arguments**

featsCoords        the feature coordinates to be rescaled

latentData         latent variables

manExpFactorTaxa    an expansion factor

featNum            the number of features to retain

**Value**

The rescaled feature coordinates

---

|                  |                                                 |
|------------------|-------------------------------------------------|
| scoreConfounders | <i>Score functions for confounder variables</i> |
|------------------|-------------------------------------------------|

---

**Description**

Score functions for confounder variables

**Usage**

```
scoreConfounders(  
  x,  
  data,  
  distribution,  
  offSet,  
  confMat,  
  meanVarTrend,  
  allowMissingness,  
  libSizes,  
  CompMat  
)
```

**Arguments**

- x                    the parameter estimates
- data, distribution, offSet, confMat, meanVarTrend  
                     Characteristics of the views
- allowMissingness    a boolean, should missing values be allowed
- libSizes, CompMat    Library sizes and relative abunance

**Value**

The evaluation of the estimating equations

---

|                      |                                                                |
|----------------------|----------------------------------------------------------------|
| scoreConfoundersComp | <i>Score equations for conditioning under compositionality</i> |
|----------------------|----------------------------------------------------------------|

---

**Description**

Score equations for conditioning under compositionality

**Usage**

```
scoreConfoundersComp(  
  x,  
  confMat,  
  data,  
  meanVarTrend,  
  marginModel,  
  biasReduction,  
  allowMissingness,  
  subtractMax = TRUE  
)
```

**Arguments**

|                  |                                                                                                                   |
|------------------|-------------------------------------------------------------------------------------------------------------------|
| x                | Confounder parameter estimates                                                                                    |
| confMat          | confounder matrix                                                                                                 |
| data             | data                                                                                                              |
| meanVarTrend     | mean variance trend                                                                                               |
| marginModel      | marginal models                                                                                                   |
| biasReduction    | A boolean, should a bias reduced estimation be applied?                                                           |
| allowMissingness | A boolean, are missing values allowed                                                                             |
| subtractMax      | A boolean, should the maximum be subtracted before softmax transformation?<br>Recommended for numerical stability |

**Value**

The evaluation of the estimating equations

---

|                    |                                                                                                       |
|--------------------|-------------------------------------------------------------------------------------------------------|
| scoreFeatureParams | <i>Evaluate the score functions for the estimation of the feature parameters for a single dataset</i> |
|--------------------|-------------------------------------------------------------------------------------------------------|

---

## Description

Evaluate the score functions for the estimation of the feature parameters for a single dataset

## Usage

```
scoreFeatureParams(
  x,
  data,
  distribution,
  offSet,
  latentVar,
  meanVarTrend,
  mm,
  indepModel,
  compositional,
  paramEstsLower,
  allowMissingness,
  ...
)
```

## Arguments

|                                                                                     |                                                                    |
|-------------------------------------------------------------------------------------|--------------------------------------------------------------------|
| x                                                                                   | the parameter estimates                                            |
| data, distribution, offSet, meanVarTrend, indepModel, compositional, paramEstsLower | Characteristics of the views                                       |
| latentVar                                                                           | the latent variables                                               |
| mm                                                                                  | the dimension                                                      |
| allowMissingness                                                                    | a boolean, should missing values be allowed                        |
| ...                                                                                 | Additional arguments passed on to the score and jacobian functions |

## Value

A vector with evaluated score function

---

|                 |                                                                                                     |
|-----------------|-----------------------------------------------------------------------------------------------------|
| scoreLatentVars | <i>Evaluate the score functions for the estimation of the latent variables for a single dataset</i> |
|-----------------|-----------------------------------------------------------------------------------------------------|

---

## Description

Evaluate the score functions for the estimation of the latent variables for a single dataset

## Usage

```
scoreLatentVars(
  data,
  distribution,
  paramEsts,
  paramMats,
  offSet,
  latentVar,
  meanVarTrend,
  constrained = FALSE,
  covMat = NULL,
  varPosts,
  compositional,
  indepModel,
  mm,
  latentVarsLower,
  allowMissingness,
  ...
)
```

## Arguments

|                                                                                                     |                                                                |
|-----------------------------------------------------------------------------------------------------|----------------------------------------------------------------|
| data, distribution, offSet, meanVarTrend, indepModel, varPosts, paramEsts, paramMats, compositional | Characteristics of the views                                   |
| latentVar                                                                                           | the latent variable estimates                                  |
| constrained                                                                                         | a boolean, is this a constrained analysis                      |
| covMat                                                                                              | a matrix of constraining covariates                            |
| mm                                                                                                  | the current dimension                                          |
| latentVarsLower                                                                                     | the lower dimensional latent variables                         |
| allowMissingness                                                                                    | a boolean, should missing values be allowed                    |
| ...                                                                                                 | additional arguments passed on to score and jacobian functions |

## Value

A vector of length n, with evaluated score function

---

|      |                                                                               |
|------|-------------------------------------------------------------------------------|
| seqM | <i>A small auxiliary function for the indices of the lagrange multipliers</i> |
|------|-------------------------------------------------------------------------------|

---

**Description**

A small auxiliary function for the indices of the lagrange multipliers

**Usage**

```
seqM(y, normal = TRUE, nLambdas = 1)
```

**Arguments**

|          |                                                  |
|----------|--------------------------------------------------|
| y        | an integer, the current dimension                |
| normal   | a logical, is there a normalization restriction? |
| nLambdas | the number of centering restrictions             |

**Value**

a vector containing the ranks of the current lagrangian multipliers

---

|                   |                                                                      |
|-------------------|----------------------------------------------------------------------|
| trimOnConfounders | <i>Trim based on confounders to avoid taxa with only zero counts</i> |
|-------------------|----------------------------------------------------------------------|

---

**Description**

Trim based on confounders to avoid taxa with only zero counts

**Usage**

```
trimOnConfounders(confounders, data, prevCutOff, minFraction, n)
```

**Arguments**

|             |                                                                                                                                                 |
|-------------|-------------------------------------------------------------------------------------------------------------------------------------------------|
| confounders | a n x t confounder matrix                                                                                                                       |
| data        | the data matrix                                                                                                                                 |
| prevCutOff  | a scalar between 0 and 1, the prevalence cut off                                                                                                |
| minFraction | a scalar between 0 and 1, each taxon's total abundance should equal at least the number of samples n times minFraction, otherwise it is trimmed |
| n           | the number of samples<br>Should be called prior to fitting the independence model                                                               |

**Value**

A trimmed data matrix n x p'

---

|             |                                                                                          |
|-------------|------------------------------------------------------------------------------------------|
| zhangMetabo | <i>Metabolomes of mice that underwent Pulsed Antibiotic Treatment (PAT) and controls</i> |
|-------------|------------------------------------------------------------------------------------------|

---

**Description**

Metabolome of mice that underwent Pulsed Antibiotic Treatment (PAT) and controls

**Usage**

data(Zhang)

**Format**

SummarizedExperiment with metabolome data

**zhangMetabo** The metabolome data as a SummarizedExperiment object

**Source**

<https://www.ibdmdb.org/>

---

|               |                                                          |
|---------------|----------------------------------------------------------|
| zhangMetavars | <i>Baseline sample variables of PAT and control mice</i> |
|---------------|----------------------------------------------------------|

---

**Description**

Baseline covariates of PAT mice and healthy controls

**Usage**

data(Zhang)

**Format**

A dataframe with baseline sample variables

**zhangMetavars** The metadata on the mice

**Source**

<https://www.ibdmdb.org/>

---

|               |                                                                                          |
|---------------|------------------------------------------------------------------------------------------|
| zhangMicrobio | <i>Microbiomes of mice that underwent Pulsed Antibiotic Treatment (PAT) and controls</i> |
|---------------|------------------------------------------------------------------------------------------|

---

**Description**

Microbiome of mice that underwent Pulsed Antibiotic Treatment (PAT) and controls. The data were extracted from the source <https://www.ibdmdb.org/>, and then only the samples matching between microbiome and metabolome were retained.

**Usage**

```
data(Zhang)
```

**Format**

A phyloseq object containing microbiome data

**zhangMicrobio** The microbiome dataset pruned for matches with the metabolome object

**Source**

<https://www.ibdmdb.org/>

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