# Package 'synergyfinder'

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**Type** Package

**Title** Calculate and Visualize Synergy Scores for Drug Combinations

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**Imports** drc (>= 2.5-12), reshape2 (>= 1.4.1), ggplot2 (>= 2.1.0), grid (>= 3.2.4), lattice (>= 0.20-33), nleqslv(>= 3.0), stats (>= 3.3.0), graphics (>= 3.3.0), grDevices (>= 3.3.0)

**Description** Efficient implementations for all the popular synergy scoring models for drug combinations, including HSA, Loewe, Bliss and ZIP and visualization of the synergy scores as either a two-dimensional or a three-dimensional interaction surface over the dose matrix.

**License** Mozilla Public License 2.0

**Encoding** UTF-8

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## R topics documented:

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.ExtendedScores *Make a smooth surface for scores*

---

### Description

Make a smooth surface for scores

### Usage

```
.ExtendedScores(scores.mat, len)
```

### Arguments

| | |
|---|---|
| scores.mat | a matrix contains scores which will be visualized |
| len | length of the interval between plotted data points. |

### Value

a matrix which

---

AddNoise *Add noise to response value*

---

### Description

Function `AddNoise` calculates and add a noise to values in response matrix. The noises obey normal distribution ~N(0, 0.001) wich are generated by fucntion `rnorm`.

### Usage

```
AddNoise(response.mat)
```

## Arguments

response.mat    A matrix. It contains the response data for one drug combination.

## Details

**Note**: If the analysis requires for reproductiblity, plesase set the random seed before calling this function.

## Value

A matrix. It contains the response value added with noises.

## Author(s)

Shuyu Zheng <shuyu.zheng@helsinki.fi>

## Examples

```
data("mathews_screening_data")
data <- ReshapeData(mathews_screening_data)
response.mat <- data$dose.response.mats[[1]]
set.seed(1)
adjusted.mat <- AddNoise(response.mat)
```

---

Bliss                          *Calculate Bliss synergy score*

---

## Description

`Bliss` calculates the synergy score matrix for a block of drug combination by using a druginteraction reference model introduced by C. I. Bliss in 1939.

## Usage

```
Bliss(response.mat)
```

## Arguments

response.mat    A drug cobination dose-response matrix. It's column name and row name are representing the concerntrations of drug added to column and row, respectively. The values in matrix indicate the inhibition rate to cell growth.

## Details

This model is a reference model for evaluating the combination effect of two drugs. The basic assumption of this model is "The expected effect of two drugs acting independently".

## Value

A matrix for synergy score calculated via reference model introduced by C. I. Bliss.

**Author(s)**

- Liye He <liye.he@helsinki.fi>
- Shuyu Zheng <shuyu.zheng@helsinki.fi>

**References**

- Yadav B, Wennerberg K, Aittokallio T, Tang J. (2015). Searching for Drug Synergy in Complex Dose-Response Landscape Using an Interaction Potency Model. Comput Struct Biotechnol J, 13:504– 513.
- Bliss, C. I. (1939). The toxicity of poisons applied jointly. Annals of Applied Biology, 26(3):585–615.

**Examples**

```
data("mathews_screening_data")
data <- ReshapeData(mathews_screening_data)
Bliss.score <- Bliss(data$dose.response.mats[[1]])
```

---

CalculateSynergy            *Calculate the synergy scores for drug combinations*

---

**Description**

CalculateSynergy is the main function for calculating synergy scores based on model(ZIP, Bliss, Loewe, and HSA) fron one dose-response **matrix**.

**Usage**

```
CalculateSynergy(data, method = "ZIP", adjusted = TRUE)
```

**Arguments**

| | |
|---|---|
| data | a list object generated by function ReshapeData. |
| method | a parameter to specify which models to use to calculate the synergy scores. Choices are "ZIP", "Bliss", "HSA" and "Loewe". Defaults to "ZIP". |
| adjusted | a logical value. If it is TRUE, the 'adjusted.response.mats' will be used to calculate synergy scores. If it is FALSE, the raw data ('dose.response.mats') will be used to calculate synergy scores. |

**Value**

a list. It contains 4 elements:

- **dose.response.mats** The original input dose-response matrix
- **adjusted.response.mats** The dose response matrix adjusted by functions: AddNoise, ImputeNA, and CorrectBaseLine.
- **drug.pairs** a data frame contains the name of the row drug, the name of the column drug, concentration unit and block IDs.
- **scores** It contains the modified response value and 4 type of synergy scores of each drug dose response pair.
- **method** the method used to calculate the synergy scores.

## Author(s)

- Liye He <liye.he@helsinki.fi>
- Shuyu Zheng <shuyu.zheng@helsinki.fi>

## Examples

```
data("mathews_screening_data")
data <- ReshapeData(mathews_screening_data)
scores <- CalculateSynergy(data)
```

---

CorrectBaseLine                    *Base line correction*

---

## Description

`CorrectBaseLine` adjusts the base line of drug combination dose-response matrix to make it closer to 0.

## Usage

```
CorrectBaseLine(response.mat, method = c("non", "part", "all"))
```

## Arguments

| | |
|---|---|
| response.mat | A drug cobination dose-response matrix. It's column name and row name are representing the concerntrations of drug added to column and row, respectively. The values in matrix indicate the inhibition rate to cell growth. |
| method | A character value to indicate using which method to do baseline correction. Available values ate:<br><br>• **non** means no baseline corection.<br>• **part** means only adjust the negative values in the matrix.<br>• **all** means adjust all values in the matrix. |

## Value

A matrix which base line have been adjusted.

## Author(s)

- Liye He <liye.he@helsinki.fi>
- Shuyu Zheng <shuyu.zheng@helsinki.fi>

## Examples

```
data("mathews_screening_data")
data <- ReshapeData(mathews_screening_data)
response.mat <- data$dose.response.mats[[1]]
adjusted.mat <- CorrectBaseLine(response.mat, method = "part")
```

---

ExtractSingleDrug          *Extract single drug response from matrix*

---

### Description

ExtractSingleDrug extracts the dose-response values of single drug ( drug added in column or row) from a drug combination dose-response matrix.

### Usage

```
ExtractSingleDrug(response.mat, dim = "row")
```

### Arguments

response.mat     A drug cobination dose-response matrix. It's column name and row name are representing the concerntrations of drug added to column and row, respectively. The values in matrix indicate the inhibition rate to cell growth.

dim              A character. It should be either "col" or "row" to indicate which drug's dose-response value will be extracted.

### Value

A data frame. It contains two variables:

- **dose** The concertration of drug.
- **response** The cell's response (inhibation rate) to corresponding drug concertration.

### Author(s)

Shuyu Zheng <shuyu.zheng@helsinki.fi>

### Examples

```
data("mathews_screening_data")
data <- ReshapeData(mathews_screening_data)
response.mat <- data$dose.response.mats[[1]]
drug.row <- ExtractSingleDrug(response.mat, dim = "row")
```

---

FindModelType          *Find the type of model used for fitting dose response data*

---

### Description

FindModelType will extract the model type ("LL.4" or "L.4") eventually used in funciton FitDoseResponse

### Usage

```
FindModelType(model)
```

## Arguments

| | |
|---|---|
| model | An object of class 'drc'. It is generated by function FitDoseResponse |

## Value

A character either "LL.4" or "L.4". It indicates the type of model used for fitting dose response data.

## Author(s)

Shuyu Zheng <shuyu.zheng@helsinki.fi>

## Examples

```
df <- data.frame(response = c(0, 29, 59, 60, 75, 90),
                 dose = c(0.00, 9.7656, 39.0626, 156.25, 625, 2500))
model <- FitDoseResponse(df)
model.type <- FindModelType(model)
```

---

FitDoseResponse               *Fitting single drug dose-response model*

---

## Description

Function FitDoseResponse fits dose-response model by using drm function.

## Usage

```
FitDoseResponse(data, Emin = NA, Emax = NA)
```

## Arguments

| | |
|---|---|
| data | A data frame. It contains two columns: |
| | • **conc** The concentration of drugs added in experiment. |
| | • **response** The response of cell lines to drug with different concentrations. |
| Emin | A numeric or NA. the minimal effect of the drug used in the 4-parameter log-logistic function to fit the dose-response curve. If it is not NA, it is fixed the value assigned by the user. Default setting is NA. |
| Emax | A numeric or NA. the maximal effect of the drug used in the 4-parameter log-logistic function to fit the dose-response curve. If it is not NA, it is fixed the value assigned by the user. Default setting is NA. |

## Details

Pre-fitting process: 1. Change the 0 value in concentration into 10^-10 to avoide raising error when taking log. 2. If the variance of "response" values equal to 0, add 10^-10 to the last "response" value.

Model choice: First use "L.4" model to fit the raw data. If error or waring occurs, use "LL.4" model to fit log(raw data).

**Value**

An object of class 'drc'. It contains imformation of fitted model.

**Author(s)**

- Liye He <liye.he@helsinki.fi>
- Shuyu Zheng <shuyu.zheng@helsinki.fi>

**References**

Seber, G. A. F. and Wild, C. J (1989) hrefhttps://onlinelibrary.wiley.com/doi/book/10.1002/0471725315Nonlinear Regression, New York: Wiley \& Sons (p. 330).

**Examples**

```
df <- data.frame(response = c(0, 29, 59, 60, 75, 90),
                 dose = c(0.00, 9.7656, 39.0626, 156.25, 625, 2500))
model <- FitDoseResponse(df)
```

---

HSA                         *Calculate HSA synergy score*

---

**Description**

HSA calculates the synergy score matrix for a block of drug combination by using Highest Single Agent (HSA) reference model.

**Usage**

```
HSA(response.mat)
```

**Arguments**

response.mat    A drug cobination dose-response matrix. It's column name and row name are representing the concerntrations of drug added to column and row, respectively. The values in matrix indicate the inhibition rate to cell growth.

**Details**

This model is a reference model for evaluating the combination effect of two drugs. The basic assumption of this model is "The reference effect of drug combination is the maximal single drug effect".

**Value**

A matrix for synergy score calculated via Highest Single Agent (HSA).

**Author(s)**

- Liye He <liye.he@helsinki.fi>
- Shuyu Zheng <shuyu.zheng@helsinki.fi>

## References

- Yadav B, Wennerberg K, Aittokallio T, Tang J.(2015). Searching for Drug Synergy in Complex Dose-Response Landscape Using an Interaction Potency Model.Comput Struct Biotechnol J, 13:504– 513.

- Berenbaum MC. (1989). What is synergy? Pharmacol Rev 1990 Sep;41(3):422.

## Examples

```
data("mathews_screening_data")
data <- ReshapeData(mathews_screening_data)
HSA.score <- HSA(data$dose.response.mats[[1]])
```

---

ImputeNA                *Impute missing value with nearest values*

---

## Description

Function `ImputeNA` does missing value imputation by assigning the average of values in nearest 4 cells (top, bottom, left, right) to the NA cell. This pocess will be done repeadly until there is no missing values in the matrix.

## Usage

```
ImputeNA(response.mat)
```

## Arguments

response.mat    A matrix which has missing value.

## Value

A matrix which is same as input matrix except the missing values are imputed.

## Author(s)

Shuyu Zheng <shuyu.zheng@helsinki.fi>

## Examples

```
data("mathews_screening_data")
data <- ReshapeData(mathews_screening_data)
response.mat <- data$dose.response.mats[[1]]
# introduce some NA values into matrix
response.mat[3:4, 3:5] <- NA
adjusted.mat <- ImputeNA(response.mat)
```

---

kriging                          *Kriging*

---

## Description

This function interpolates a zero mean Gaussian random field using the simple kriging predictor.

## Usage

```
kriging(
  data,
  data.coord,
  krig.coord,
  cov.mod = "whitmat",
  sill,
  range,
  smooth,
  smooth2 = NULL,
  grid = FALSE,
  only.weights = FALSE
)
```

## Arguments

| | |
|---|---|
| data | A numeric vector or matrix. If data is a matrix then the simple kriging predictor is given for each realisation, i.e., each row of data. |
| data.coord | A numeric vector or matrix specifying the coordinates of the observed data. If data.coord is a matrix, each row must corresponds to one location. |
| krig.coord | A numeric vector or matrix specifying the coordinates where the kriging predictor has to be computed. If krig.coord is a matrix, each row must correspond to one location. |
| cov.mod | A character string specifying the covariance function family. Must be one of "whitmat", "powexp", "cauchy", "bessel" or "caugen" for the Whittle-Matern, the powered exponential, the Cauchy, the Bessel or the generalized Cauchy covariance families. |
| sill, range, smooth, smooth2 | |
| | Numerics specifiying the sill, range, smooth and, if any, the second smooth parameters of the covariance function. |
| grid | logical. Does krig.coord specifies a grid? |
| only.weights | Logical. Should only the kriging weights be computed? If FALSE, the kriging predictor isn't computed. |

## Value

A list with components

- coord The coordinates where the kriging predictor has been computed;
- krig.est The kriging predictor estimates;
- grid Does coord define a grid?;
- weights A matrix giving the kriging weights: each column corresponds to one prediction location.

| Loewe | *Calculate Loewe synergy score* |
|---|---|

## Description

Loewe calculates the synergy score matrix from a dose-response matrix by using a druginteraction reference model introduced by Loewe in 1953.

## Usage

```
Loewe(response.mat, quiet = TRUE, drug.col.model = NULL, drug.row.model = NULL)
```

## Arguments

| | |
|---|---|
| response.mat | A drug cobination dose-response matrix. It's column name and row name are representing the concerntrations of drug added to column and row, respectively. The values in matrix indicate the inhibition rate to cell growth. |
| quiet | A logical value. If it is TRUE then the warning message will not show during calculation. |
| drug.col.model | (optional) a character. It indicates the model used for fitting dose-response curve for drug added to columns. |
| drug.row.model | (optional) a character. It indicates the model type used for fitting dose-response curve for drug added to rows. |

## Details

Loewe model is a reference model for evaluating the combination effect of two drugs. The basic assumption of this model is "The referece effect of drug combination is the expected effect of a drug combined with itself".

The optional arguments drug.col.model, drug.row.model are designed for reuse the single drug dose response model fitting results, if it has been down before. Functions FitDoseResponse and ExtractSingleDrug could be used to calculate these arguments.

## Value

A matrix for Synergy score calculated via reference model introduced by Loewe, S.

## Author(s)

- Liye He <liye.he@helsinki.fi>
- Jing Tang <jing.tang@helsinki.fi>
- Shuyu Zheng <shuyu.zheng@helsinki.fi>

## References

- Yadav B, Wennerberg K, Aittokallio T, Tang J.(2015). Searching for Drug Synergy in Complex Dose-Response Landscape Using an Interaction Potency Model.Comput Struct Biotechnol J, 13:504– 513.
- [Loewe, 1953] Loewe, S. (1953). The problem of synergism and antagonism of combined drugs. Arzneimittelforschung, 3(6):285–290.

## Examples

```
# No single drug fitted modle before
data("mathews_screening_data")
data <- ReshapeData(mathews_screening_data)
response.mat <- data$dose.response.mats[[1]]
Loewe.score <- Loewe(response.mat)

# Single drug dose response models have been fitted before.
drug.row.model <- FitDoseResponse(ExtractSingleDrug(response.mat, dim="row"))
drug.col.model <- FitDoseResponse(ExtractSingleDrug(response.mat, dim="col"))
Loewe.score2 <- Loewe(response.mat, drug.col.model=drug.col.model,
                      drug.row.model=drug.row.model)
```

---

mathews_screening_data
                          *A high-throughput drug combination screening data*

---

### Description

A recent drug combination screening for the treatment of diffuse large B-cell lymphoma (DLBCL).

### Format

A data frame with the following columns: block_id, drug_row, drug_col, conc_r, conc_c, response, conc_r_unit, conc_c_unit.

### References

Mathews Griner LA, Guha R, Shinn P, Young RM, Keller JM, et al. High-throughput combinatorial screening identifies drugs that cooperate with ibrutinib to kill activated B-cell-like diffuse large B-cell lymphoma cells. Proc Natl Acad Sci USA 2014; 111:2349-54.

---

PlotDoseResponse          *Visualize the drug combination dose-response data*

---

### Description

A function to visualize the drug combination dose-response data

### Usage

```
PlotDoseResponse(
  data,
  adjusted = TRUE,
  pair.index = NULL,
  color.low.response = "green",
  color.point = "red",
  color.high.response = "red",
  color.conc = "red",
  save.file = FALSE,
```

```
    file.type = "pdf",
    file.name = NULL,
    ...
)
```

## Arguments

| | |
|---|---|
| data | a list object generated by function [ReshapeData](#). |
| adjusted | a logical value. If it is FALSE, original response matrix will be plotted. If it is TRUE, adjusted response matrix will be plotted. |
| pair.index | a parameter to specify which drug combination if there are many drug combinations in the data. By default, it is NULL so that the visualization of all the drug combinations in the data is returned. |
| color.low.response | |
| | a charactor in R color format. It indicates the color for the response lower than 0. Default setting is "green". |
| color.point | a charactor in R color format. It indicates the color for the data point in the plot. Default setting is "red". |
| color.high.response | |
| | a charactor in R color format. It indicates the color for the response higher than 0. Default setting is "red". |
| color.conc | a charactor in R color format. It indicates the color for the concentrations label for axises. Default setting is "red". |
| save.file | a parameter to specify if the visualization results are saved as pdf files in current working directory or not. If it is FALSE, the results are returned as a list of the plots. It is FALSE by default. |
| file.type | a character. It indicates the format of files you want to save as. Default is "pdf". Available values are "jpeg", "bmp", "png", "tiff", "pdf". |
| file.name | a character vector. It indicates the file names, if user chose to save the plot to local directory.If it is not defined by user, a default name will be assigned. |
| ... | further graphical parameters from [plot](#) for plotting the single drug dose-response curve. Use e.g., cex.lab to change the axis label size and cex.axis to change the tick size of axises. |

## Value

NULL. The plot will be saved into a local file if save.file = TRUE. If save.file = FALSE, the plot will be printed in default graphic device.

## Author(s)

- Liye He <liye.he@helsinki.fi>,
- Shuyu Zheng <shuyu.zheng@helsinki.fi>

## Examples

```
data("mathews_screening_data")
data <- ReshapeData(mathews_screening_data)
PlotDoseResponse(data)
```

PlotSynergy                           *Drug interaction landscape*

**Description**

A function to visualize the synergy scores for drug combinations as 2D or 3D interaction landscape over the dose-response matrix.

**Usage**

```
PlotSynergy(
  data,
  type = "2D",
  save.file = FALSE,
  pair.index = NULL,
  len = 3,
  legend.start = NULL,
  legend.end = NULL,
  row.range = NULL,
  col.range = NULL,
  color.low.value = "green",
  color.high.value = "red",
  file.name = NULL,
  file.type = "pdf"
)
```

**Arguments**

| | |
|---|---|
| data | a list object generated by function `CalculateSynergy`. |
| type | a parameter to specify the type of the interaction landscape, 2D, 3D or both. By default, 2D interaction landscape is returned. |
| save.file | a logical parameter to specify if the interaction landscape is saved as a pdf file in the current working directory or returned as an R object. By default, it is FALSE. |
| pair.index | a parameter to specify which drug combination if there are many drug combinations in the data. By default, it is NULL so that the synergy score visualization of all the drug combinations in the data is returned. |
| len | a parameter to specify how many values need to be predicted between two concentrations. It is used to control the smoothness of the synergy surface in the plot. |
| legend.start | a parameter to specify the starting point of the legend. By defualt, it is NULL so the legend starting point is fixed by the data automatically. |
| legend.end | a parameter to specify the ending point of the legend. By defualt, it is NULL so the legend ending point is fixed by the data automatically. |
| row.range | a parameter to specify the starting and ending concentration of the drug on y-axis. Use e.g., c(1, 3) to specify that only from 1st to 3rd concentrations of the drug on y-axis are used. By default, it is NULl so all the concentrations are used. |

col.range    a parameter to specify the starting and ending concentration of the drug on x-axis. Use e.g., c(1, 3) to specify that only from 1st to 3rd concentrations of the drug on x-axis are used. By default, it is NULl so all the concentrations are used.

color.low.value

a charactor in R color format. It indicates the color for the synergy score lower than 0. Default setting is "green".

color.high.value

a charactor in R color format. It indicates the color for the synergy score higher than 0. Default setting is "red".

file.name    a character vector. It indicates the file names, if user chose to save the plot to local directory.If it is not defined by user, a default name will be assigned.

file.type    a character. It indicates the format of files you want to save as. Default is "pdf". Available values are "jpeg", "bmp", "png", "tiff", "pdf".

## Value

a numeric value. It is the summarized synergy score.

## Author(s)

- Liye He <liye.he@helsinki.fi>
- Shuyu Zheng <shuyu.zheng@helsinki.fi>

## Examples

```
data("mathews_screening_data")
data <- ReshapeData(mathews_screening_data)
scores <- CalculateSynergy(data)
PlotSynergy(scores, "2D")
PlotSynergy(scores, "3D", save.file = TRUE, file.name = c("plot1", "plot2"))
```

---

ReshapeData                 *Pre-processe the response data for furhter calculation and plot*

---

## Description

A function to transform the response data from data frame format to dose-response matrices. Several processes could be chose to add noise, impute missing values or correct base line to the dose-response matrix.

## Usage

```
ReshapeData(
  data,
  impute = TRUE,
  noise = TRUE,
  correction = "non",
  data.type = "viability"
)
```

**Arguments**

| | |
|---|---|
| data | drug combination response data in a data frame format |
| impute | a logical value. If it is TRUE, the NA values will be imputed by ImputeNA. Default is TRUE. |
| noise | a logical value. It indicates whether or not adding noise to to the "response" values in the matrix. Default is TRUE. |
| correction | a character. This argument is extended from the argument method of CorrectBaseLine function. There are three available valuse: non, part, all. The default setting is non. |
| data.type | a parameter to specify the response data type which can be either "viability" or "inhibition". |

**Details**

The input data must contain the following columns: block_id, drug_row, drug_col, response, conc_r, conc_c, conc_r_unit, conc_c_unit.

**Value**

a list of the following components:

- **dose.response.mats** a list of the dose-response matrices with %inhibition as the response data. Row names and column names are drug concentrations.

- **adjusted.response.mats** The dose response matrix adjusted. The processes are chosen by arguments impute, noise, and correction. If no process was chosen, the final result will not contain this result.

- **drug.pairs** a data frame contains the name of the row drug, the name of the column drug, concentration unit and block IDs.

**Author(s)**

- Liye He <liye.he@helsinki.fi>
- Shuyu Zheng <shuyu.zheng@helsinki.fi>

**Examples**

```
data("mathews_screening_data")
# set a random number seed for generating the noises
set.seed(1)
data <- ReshapeData(mathews_screening_data)
```

---

ZIP                                    *Calculate Delta synergy score based on ZIP model*

---

**Description**

ZIP calculates the $\Delta$ score matrix from a dose-response matrix by using Zero Interaction Potency (ZIP) method.

## Usage

```
ZIP(response.mat, quiet = TRUE, drug.row.model = NULL, drug.col.model = NULL)
```

## Arguments

| | |
|---|---|
| response.mat | A drug cobination dose-response matrix. It's column name and row name are representing the concerntrations of drug added to column and row, respectively. The values in matrix indicate the inhibition rate to cell growth. |
| quiet | A logical value. If it is TRUE then the warning message will not show during calculation. |
| drug.row.model | (optional) a character. It indicates the model type used for fitting dose-response curve for drug added to rows. |
| drug.col.model | (optional) a character. It indicates the model used for fitting dose-response curve for drug added to columns. |

## Details

Zero Interaction Potency (ZIP) is a reference model for evaluating the conbimation effect of two drugs. It captures the effect of drug combination by comparing the change in the potency of the dose-response curves between individual drugs and their combinations.

The optional arguments `drug.col.model`, `drug.row.model` are designed for reuse the single drug dose response model fitting results, if it has been down before. Functions `FitDoseResponse` and `ExtractSingleDrug` could be used to calculate these arguments.

## Value

A matrix of $\Delta$ score calculated via Zero Interaction Potency (ZIP) method.

## Author(s)

- Liye He <liye.he@helsinki.fi>
- Jing Tang <jing.tang@helsinki.fi>
- Shuyu Zheng <shuyu.zheng@helsinki.fi>

## References

- Yadav B, Wennerberg K, Aittokallio T, Tang J. (2015). Searching for Drug Synergy in Complex Dose-Response Landscape Using an Interaction Potency Model. Comput Struct Biotechnol J, 13:504– 513.

## Examples

```
# No single drug fitted modle before
data("mathews_screening_data")
data <- ReshapeData(mathews_screening_data)
response.mat <- data$dose.response.mats[[1]]
ZIP.score <- ZIP(response.mat)

# Single drug dose response models have been fitted before.
drug.row.model <- FitDoseResponse(ExtractSingleDrug(response.mat, dim="row"))
drug.col.model <- FitDoseResponse(ExtractSingleDrug(response.mat, dim="col"))
```

```
ZIP.score2 <- ZIP(response.mat[-1, -1], drug.col.model=drug.col.model,
                  drug.row.model=drug.row.model)
```

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