Package 'nlmeVPC'

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Title Visual Model Checking for Nonlinear Mixed Effect Model

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Description Various visual and numerical diagnosis methods for the nonlinear mixed effect model, including visual predictive checks, numerical predictive checks, and coverage plots (Karlsson and Holford, 2008, <https://www.page-meeting.org/?abstract=1434>).

Depends R (>= 3.5.0), Hmisc

Imports quantreg, optimx, ggplot2, Rcpp, timeDate

Suggests testit

LinkingTo Rcpp, RcppArmadillo

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R topics documented:

`aqrVPC` *The visual predictive checks using the additive quantile regression (aqrVPC)*

Description

This function draws the visual predictive check (VPC) plot using additive quantile regression. The quantile regression methods are used to calculate quantiles.

Usage

```
aqrVPC(orig_data,
       sim_data,
       probs = c(0.1,0.5,0.9),
       conf.level = 0.95,
       X_name = "TIME",
       Y_name = "DV",
       MissingDV = NULL,
       plot_caption = TRUE,
       DV_point = TRUE,
       plot_flag = TRUE,
       linesize = 0.7,
       pointsize = 0.7,
       captionsize = 10,
       qss_lambda = NULL, ...)
```

Arguments

`orig_data`	A data frame of original data with X and Y variable.
`sim_data`	A matrix of simulated data with only Y values collected.
`probs`	A numeric vector of probabilities.
`conf.level`	Confidence level of the interval.
`X_name`	Name of X variable in orig_data (usually "TIME" in pharmacokinetic data).
`Y_name`	Name of Y variable in orig_data (usually "DV" in pharmacokinetic data).
`MissingDV`	Name of missing indicator variable in orig_data, which have value 1 if missing, value 0 otherwise. (usually "MDV" in pharmacokinetic data).

plot_caption	Put caption with additional information if TRUE; omit if FALSE.
DV_point	Draw point (X, Y) in the plot if TRUE; omit if FALSE.
plot_flag	Draw plot if TRUE; generate data for drawing plot if FALSE.
linesize	Size of line in the plot.
pointsize	Size of point in the plot.
captionsize	Size of caption.
qss_lambda	Smoothing parameter in quantreg::qss function. Larger lambda produces a smoother fit.
...	Arguments to be passed to methods.

Value

aqrVPC plot or the values to draw aqrVPC plot.

References

Koenker, Roger, and Kevin F. Hallock. "Quantile regression." Journal of economic perspectives 15.4 (2001): 143-156.

Jamsen, K. M., Patel, K., Nieforth, K., & Kirkpatrick, C. M. (2018). A regression approach to visual predictive checks for population pharmacometric models. CPT: pharmacometrics & systems pharmacology, 7(10), 678-686.

Examples

```
data(origdata)
data(simdata)
aqrVPC(origdata,simdata)
```

---

asVPC *The average shifted visual predictive checks (asVPC)*

Description

This function draws the average shifted visual predictive check (asVPC) plot. It calculates original and simulated data percentiles using the average shifted histogram method. After calculating percentiles with bin-related or distance-related weights, draw the VPC type plot.

Usage

```
asVPC(orig_data,
      sim_data,
      type = "CI",
      weight_method = "bin",
      N_xbin = NULL,
      N_hist = NULL,
      probs = c(0.1,0.5,0.9),
      conf.level = 0.95,
      X_name = "TIME",
      Y_name = "DV",
      MissingDV = NULL,
      DV_point = TRUE,
      CIvpc_type = "line",
      bin_grid = TRUE,
      plot_caption = TRUE,
      plot_flag = TRUE,
      linesize = 0.7,
      pointsize = 0.7,
      captionsize = 10,
      Kmethod = "cluster",
      maxK = NULL,
      beta = 0.2,
      lambda = 0.3,
      R = 4,
      C1 = 2.5,
      C2 = 7.8,...)
```

Arguments

orig_data	A data frame of original data with X and Y variable.
sim_data	A matrix of simulated data with only Y values collected.
type	Type of VPC graph; "CI", "percentile", or "scatter".
weight_method	The way to put weight when the average shifted values are calculated. "bin" or "distance".
N_xbin	Number of bins in X variable. If NULL, optimal number of bins are automatically calcuated using optK function.
N_hist	The number of shifted histograms.
probs	A numeric vector of probabilities.
conf.level	Confidence level of the interval.
X_name	Name of X variable in orig_data (usually "TIME" in pharmacokinetic data).
Y_name	Name of Y variable in orig_data (usually "DV" in pharmacokinetic data).
MissingDV	Name of missing indicator variable in orig_data, which have value 1 if missing, value 0 otherwise. (usually "MDV" in pharmacokinetic data).
DV_point	Draw point (X, Y) in the plot if TRUE; omit if FALSE.

CIvpc_type	Type of CI area in VPC graph; "line" or "segment".
bin_grid	Draw grid lines for binning in X variable if TRUE; omit if FALSE.
plot_caption	Put caption with additional information if TRUE; omit if FALSE.
plot_flag	Draw plot if TRUE; generate data for drawing plot if FALSE.
linesize	Size of line in the plot.
pointsize	Size of point in the plot.
captionsize	Size of caption.
Kmethod	The way to calculate the penalty in automatic binning."cluster" or "kernel".
maxK	The maximum number of bins.
beta	Additional parameter for automatic binning, used in optK function.
lambda	Additional parameter for automatic binning, used in optK function.
R	Additional parameter for automatic binning, used in optK function.
C1	Additional parameter for automatic binning, used in optK function.
C2	Additional parameter for automatic binning, used in optK function.
...	Arguments to be passed to methods.

Value

asVPC plot or the values to draw asVPC plot.

Examples

```
data(origdata)
data(simdata)
asVPC(origdata,simdata,type="CI",N_hist=3,weight_method="distance",N_xbin=8)
asVPC(origdata,simdata,type="CI",N_hist=3,weight_method="bin",N_xbin=8)
```

---

bootVPC *The bootstrap visual predictive checks.*

Description

This function draws the visual predictive check plot with bootstrapped data. It compares the distribution of the simulated data to the distribution of the bootstrap samples that draw from the observed data. This plot reflects the uncertainty of the observed data and allows for more objective comparisons with the predicted median.

Usage

```
bootVPC(orig_data,
        sim_data,
        B = 1000,
        N_xbin = NULL,
        conf.level = 0.95,
        X_name = "TIME",
        Y_name = "DV",
        subject_name = "ID",
        MissingDV = NULL,
        DV_point = TRUE,
        plot_caption = TRUE,
        plot_flag = TRUE,
        linesize = 0.7,
        pointsize = 0.7,
        Kmethod = "cluster",
        maxK = NULL,
        beta = 0.2,
        lambda = 0.3,
        R = 4,
        C1 = 2.5,
        C2 = 7.8, ...)
```

Arguments

orig_data	A data frame of original data with X and Y variable.
sim_data	A matrix of simulated data with only Y values collected.
B	Number of bootstrap samples.
N_xbin	Number of bins in X variable. If NULL, optimal number of bins are automatically calcuated using optK function.
conf.level	Confidence level of the interval.
X_name	Name of X variable in orig_data (usually "TIME" in pharmacokinetic data).
Y_name	Name of Y variable in orig_data (usually "DV" in pharmacokinetic data).
subject_name	Name of subject variable in orig_data (usually "ID" in pharmacokinetic data).
MissingDV	Name of missing indicator variable in orig_data, which have value 1 if missing, value 0 otherwise. (usually "MDV" in pharmacokinetic data).
DV_point	Draw point (X, Y) in the plot if TRUE; omit if FALSE.
plot_caption	Put caption with additional information if TRUE; omit if FALSE.
plot_flag	Draw plot if TRUE; generate data for drawing plot if FALSE.
linesize	Size of line in the plot.
pointsize	Size of point in the plot.
Kmethod	The way to calculate the penalty in automatic binning."cluster" or "kernel".
maxK	The maximum number of bins.

beta	Additional parameter for automatic binning, used in optK function.
lambda	Additional parameter for automatic binning, used in optK function.
R	Additional parameter for automatic binning, used in optK function.
C1	Additional parameter for automatic binning, used in optK function.
C2	Additional parameter for automatic binning, used in optK function.
...	Arguments to be passed to methods.

Value

bootVPC plot or the values to draw bootVPC plot.

References

Post, T. M., et al. (2008) Extensions to the visual predictive check for facilitate model performance evaluation, Journal of pharmacokinetics and pharmacodynamics, 35(2), 185-202

Examples

```
data(origdata)
data(simdata)
bootVPC(origdata,simdata,N_xbin=8)
```

---

coverageDetailplot *The detailed coverage plot*

Description

This function draws the detailed coverage plot for the specific prediction level to check over or under estimate regions in each prediction level. The percentages of observations above the prediction interval are calculated in each bin of the independent variable. Additionally, the percentages of observations below the prediction interval are calculated. The white dots in the plot represent the expected percentages.

Usage

```
coverageDetailplot(orig_data,
                   sim_data,
                   N_xbin = NULL,
                   predL = 0.5,
                   conf.level = 0.95,
                   X_name = "TIME",
                   Y_name = "DV",
                   MissingDV = NULL,
                   Kmethod = "cluster",
```

```
maxK = NULL,
beta = 0.2,
lambda = 0.3,
R = 4,
C1 = 2.5,
C2 = 7.8, ...)
```

Arguments

orig_data	A data frame of original data with X and Y variable.
sim_data	A matrix of simulated data with only Y values collected.
N_xbin	Number of bins in X variable. If NULL, optimal number of bins are automatically calcuated using optK function.
predL	Scalar of probability
conf.level	Confidence level of the interval.
X_name	Name of X variable in orig_data (usually "TIME" in pharmacokinetic data).
Y_name	Name of Y variable in orig_data (usually "DV" in pharmacokinetic data)
MissingDV	Name of missing indicator variable in orig_data, which have value 1 if missing, value 0 otherwise. (usually "MDV" in pharmacokinetic data).
Kmethod	The way to calculate the penalty in automatic binning."cluster" or "kernel".
maxK	The maximum number of bins
beta	Additional parameter for automatic binning, used in optK function.
lambda	Additional parameter for automatic binning, used in optK function.
R	Additional parameter for automatic binning, used in optK function.
C1	Additional parameter for automatic binning, used in optK function.
C2	Additional parameter for automatic binning, used in optK function.
...	Arguments to be passed to methods.

Value

the detailed coverage plot

References

Post, T. M., et al. (2008) Extensions to the visual predictive check for facilitate model performance evaluation, Journal of pharmacokinetics and pharmacodynamics, 35(2), 185-202

Examples

```
data(origdata)
data(simdata)
coverageDetailplot(origdata,simdata,predL=0.5,N_xbin=8)
```

coverageplot *The coverage plot*

Description

The coverage plot is developed to help visually check the fitted model with the NPC result. In each level of the predicted interval, the ratios between the expected number of points (Exp) outside the prediction interval and the observed number of data (Obs) outside the prediction interval are calculated. These ratios on the upper and lower sides of the prediction interval are calculated separately.

Usage

```
coverageplot(orig_data,
             sim_data,
             N_xbin = NULL,
             pred.level = c(0,0.1,0.2,0.3,0.4,0.5,0.6,0.7,0.8,0.9),
             conf.level = 0.95,
             X_name = "TIME",
             Y_name = "DV",
             MissingDV = NULL,
             plot_flag = TRUE,
             linesize = 0.7,
             pointsize = 1.5,
             Kmethod = "cluster",
             maxK = NULL,
             beta = 0.2,
             lambda = 0.3,
             R = 4,
             C1 = 2.5,
             C2 = 7.8, ...)
```

Arguments

orig_data	A data frame of original data with X and Y variable.
sim_data	A matrix of simulated data with only Y values collected.
N_xbin	Number of bins in X variable. If NULL, optimal number of bins are automatically calculated using optK function.
pred.level	Numeric vector of probabilities.
conf.level	Confidence level of the interval.
X_name	Name of X variable in orig_data (usually "TIME" in pharmacokinetic data).
Y_name	Name of Y variable in orig_data (usually "DV" in pharmacokinetic data).
MissingDV	Name of missing indicator variable in orig_data, which have value 1 if missing, value 0 otherwise. (usually "MDV" in pharmacokinetic data).
plot_flag	Draw plot if TRUE; generate data for drawing plot if FALSE.

linesize	Size of line in the plot.
pointsize	Size of point in the plot.
Kmethod	The way to calculate the penalty in automatic binning."cluster" or "kernel".
maxK	Yhe maximum number of bins.
beta	Additional parameter for automatic binning, used in optK function.
lambda	Additional parameter for automatic binning, used in optK function.
R	Additional parameter for automatic binning, used in optK function.
C1	Additional parameter for automatic binning, used in optK function.
C2	Additional parameter for automatic binning, used in optK function.
...	arguments to be passed to methods

Value

coverage plot

References

Holford N, & Karlsson M. (2008). "A tutorial on visual predictive checks, abstr 1434." Annual Meeting of the Populations Approach Group in Europe. www.page-meeting.org. 2008.

Examples

```
data(origdata)
data(simdata)
coverageplot(origdata,simdata,N_xbin=8)
```

FindBestCut *Find the best cutoff values of binning for the visual predictive checks.*

Description

By various rules, find the best cutoff values for a given number of bins.

Usage

```
FindBestCut(X,
            K,
            beta = 0.2, ...)
```

Arguments

X	A numeric vector to divide into K bins.
K	Number of bins.
beta	Additional parameter in the penalty. For more detailed explanation, see reference.
...	Arguments to be passed to methods.

Value

The best cutoff values to make K bins using X and the minimum within sums of square values for the binning

References

Lavielle, M. and Bleakley, K. (2011). Automatic data binning for improved visual diagnosis of pharmacometric models. Journal of pharmacokinetics and pharmacodynamics, 38(6), 861-871.

VPC automatic binning algorithm in PsN 5.0.0 manual.

Examples

```
data(origdata)
FindBestCut(origdata$TIME,K=10)
```

---

findQuantile *Find quantiles of the original data.*

Description

Find quantiles of the original data.

Usage

```
findQuantile(Y,
             X,
             X_bin,
             probs=c(0.1,0.5,0.9),...)
```

Arguments

Y	A numeric vector whose sample quantiles are wanted.
X	A numeric vector corresponding to Y.
X_bin	Binning result from makeCOVbin function.
probs	A numeric vector of probabilities.
...	Arguments to be passed to methods.

Value

quantiles of Y using X_bin

Examples

```
data(origdata)
CUT = FindBestCut(origdata$TIME,8)$cutoffs
time_bin = makeCOVbin(origdata$TIME,K=8,cutoffs = CUT)
findQuantile(origdata$DV,origdata$TIME,X_bin=time_bin)
```

`findSIMQ` *Find quantiles of the simulated data using Rcpp*

Description

Find quantiles of the simulated data using Rcpp

Usage

```
findSIMQ(SIM,
        X,
        Xbin,
        probs,
        confLevel,
        approx)
```

Arguments

`SIM`	A matrix of simulated data with only Y values collected.
`X`	A numeric vector corresponding to Y
`Xbin`	Binning result from makeCOVbin function
`probs`	A numeric vector of probabilities
`confLevel`	Confidence level of the interval.
`approx`	Arguments to be passed to methods

Value

quantiles of SIM using xbin

Examples

```
data(origdata)
data(simdata)
CUT = FindBestCut(origdata$TIME,8)$cutoffs
time_bin = makeCOVbin(origdata$TIME,K=8,cutoffs = CUT)
findSIMQ(simdata,origdata$TIME,Xbin=time_bin,probs=c(0.1,0.5,0.9),
confLevel=0.95,approx=FALSE)
```

`findSIMQuantile` *Find quantiles of the simulated data.*

Description

Find quantiles of the simulated data.

Usage

```
findSIMQuantile(sim_data,
                X,
                X_bin,
                probs = c(0.1,0.5,0.9),
                conf.level = 0.95,
                approx = FALSE, ...)
```

Arguments

`sim_data`	A matrix of simulated data with only Y values collected.
`X`	A numeric vector corresponding to Y.
`X_bin`	Binning result from makeCOVbin function.
`probs`	A numeric vector of probabilities.
`conf.level`	Confidence level of the interval.
`approx`	Arguments to be passed to methods
`...`	Arguments to be passed to methods

Value

quantiles of sim_data using X_bin

Examples

```
data(origdata)
data(simdata)
CUT = FindBestCut(origdata$TIME,8)$cutoffs
time_bin = makeCOVbin(origdata$TIME,K=8,cutoffs = CUT)
findSIMQuantile(simdata,origdata$TIME,X_bin=time_bin)
```

`makeCOVbin` *Discretise numeric data into categorical data*

Description

Discretise numeric value into a categorical variable using the user-defined breaks. If cutoffs and the number of bins (K) is NULL, find the best number of bins using the optK function and find the best cutoff values using the FindBestCut function.

Usage

```
makeCOVbin(X,
           K,
           cutoffs,
           adjust0bin = TRUE, ...)
```

Arguments

`X`	A numeric vector corresponding to Y.
`K`	Number of bins.
`cutoffs`	A numeric vector of two or more unique cut points.
`adjust0bin`	Adjust bin with 0 observation if TRUE.
`...`	Arguments to be passed to methods.

Value

The result of binning and the summary of the binning results

References

Lavielle, M. and Bleakley, K. (2011). Automatic data binning for improved visual diagnosis of pharmacometric models. Journal of pharmacokinetics and pharmacodynamics, 38(6), 861-871.

Examples

```
data(origdata)
CUT = FindBestCut(origdata$TIME,8)$cutoffs
makeCOVbin(origdata$TIME,K=8,cutoffs=CUT)
```

NumericalCheck *The numerical predictive checks*

Description

This function calculates the numerical predictive checks for each prediction level. For a given level of prediction, the predicted interval is calculated using the simulated data, and the number of observed data below the predicted interval is counted. The expected number of points below the predicted interval is also calculated and compared to the observed number.

Usage

```
NumericalCheck(orig_data,
               sim_data,
               N_xbin = NULL,
               pred.level = c(0,0.1,0.2,0.3,0.4,0.5,0.6,0.7,0.8,0.9),
               conf.level = 0.95,
               X_name = "TIME",
               Y_name = "DV",
               MissingDV = NULL,
               Kmethod = "cluster",
               maxK = NULL,
               beta = 0.2,
               lambda = 0.3,
               R = 4,
               C1 = 2.5,
               C2 = 7.8, ...)
```

Arguments

orig_data	A data frame of original data with X and Y variable.
sim_data	A matrix of simulated data with only Y values collected.
N_xbin	Number of bins in X variable. If NULL, optimal number of bins are automatically calcuated using optK function.
pred.level	Numeric vector of probabilities.
conf.level	Confidence level of the interval.
X_name	Name of X variable in orig_data (usually "TIME" in pharmacokinetic data).
Y_name	Name of Y variable in orig_data (usually "DV" in pharmacokinetic data).
MissingDV	Name of missing indicator variable in orig_data, which have value 1 if missing, value 0 otherwise. (usually "MDV" in pharmacokinetic data).
Kmethod	The way to calculate the penalty in automatic binning."cluster" or "kernel".
maxK	The maximum number of bins.
beta	Additional parameter for automatic binning, used in optK function.
lambda	Additional parameter for automatic binning, used in optK function.

R	Additional parameter for automatic binning, used in optK function.
C1	Additional parameter for automatic binning, used in optK function.
C2	Additional parameter for automatic binning, used in optK function.
...	Arguments to be passed to methods.

Value

The result of numerical predictive check

References

Holford N, & Karlsson M. (2008). "A tutorial on visual predictive checks, abstr 1434." Annual Meeting of the Populations Approach Group in Europe. www.page-meeting.org. 2008.

Harling, Uekcert, K. 2018. VPC and NPC User Guide. ICON plc.

https://github.com/UUPharmacometrics/PsN/releases/download/4.9.0/vpc_npc_userguide.pdf.

Examples

```
data(origdata)
data(simdata)
NumericalCheck(origdata,simdata,N_xbin=8)$NPC
```

---

optK *Find the optimal number of bins*

Description

This function automatically finds the optimal number of bins using dynamic programming.

Usage

```
optK(X,
     Kmethod = "cluster",
     maxK = 10,
     beta = 0.2,
     lambda = 0.3,
     R = 4,
     C1 = 2.5,
     C2 = 7.8, ...)
```

Arguments

X	Numeric vector corresponding to Y.
Kmethod	The way to calculate the penalty in automatic binning."cluster" or "kernel".
maxK	The maximum number of bins.
beta	Additional parameter for automatic binning. For more detailed explanation, see reference.
lambda	Additional parameter for automatic binning. For more detailed explanation, see reference.
R	Additional parameter for automatic binning. For more detailed explanation, see reference.
C1	Additional parameter for automatic binning. For more detailed explanation, see reference.
C2	Additional parameter for automatic binning. For more detailed explanation, see reference.
...	Arguments to be passed to methods.

Value

The optimal number of bins, the result of binning, and the summary of binning including the penalty values up to the maximum number of bins are returned.

References

Lavielle, M. and Bleakley, K. (2011). Automatic data binning for improved visual diagnosis of pharmacometric models. Journal of pharmacokinetics and pharmacodynamics, 38(6), 861-871.

Examples

```
data(origdata)
optK(origdata$TIME)
```

---

origdata *Pharmacokinetics of Theophylline with a different schedule of time.*

Description

The simulated Theoph data frame has 132 rows and 3 columns of data from an experiment on the pharmacokinetics of theophylline.

Arguments

ID	An ordered factor with levels 1, ..., 12 identifying the subject on whom the observation was made. The ordering is by increasing the maximum concentration of theophylline observed.
TIME	Time since drug administration when the sample was drawn (hr).
DV	Theophylline concentration in the sample (mg/L).

Examples

```
data(origdata)
dim(origdata)
```

---

quantVPC *The quantified visual predictive check plot (QVPC)*

Description

The quantified visual predictive check visually represents actual and unavailable observations around predicted medians, regardless of the density or shape of the observed data distribution, through the form of a percent.

Usage

```
quantVPC(orig_data,
         sim_data,
         N_xbin = NULL,
         prob = 0.5,
         X_name = "TIME",
         Y_name = "DV",
         MissingDV = NULL,
         Kmethod = "cluster",
         maxK = NULL,
         beta = 0.2,
         lambda = 0.3,
         R = 4,
         C1 = 2.5,
         C2 = 7.8, ...)
```

Arguments

orig_data	A data frame of original data with X and Y variable.
sim_data	A matrix of simulated data with only Y values collected.
N_xbin	Number of bins in X variable. If NULL, optimal number of bins are automatically calcuated using optK function.
prob	Scalar of probability.

X_name	Name of X variable in orig_data (usually "TIME" in pharmacokinetic data).
Y_name	Name of Y variable in orig_data (usually "DV" in pharmacokinetic data).
MissingDV	Name of missing indicator variable in orig_data, which have value 1 if missing, value 0 otherwise. (usually "MDV" in pharmacokinetic data).
Kmethod	The way to calculate the penalty in automatic binning."cluster" or "kernel".
maxK	The maximum number of bins.
beta	Additional parameter for automatic binning, used in optK function.
lambda	Additional parameter for automatic binning, used in optK function.
R	Additional parameter for automatic binning, used in optK function.
C1	Additional parameter for automatic binning, used in optK function.
C2	Additional parameter for automatic binning, used in optK function.
...	Arguments to be passed to methods.

Value

quantVPC plot

References

Post, T.M., et al. (2008) Extensions to the visual predictive check for facilitate model performance evaluation, Journal of pharmacokinetics and pharmacodynamics, 35(2), 185-202

Examples

```
data(origdata)
data(simdata)
quantVPC(origdata,simdata,prob=0.5,N_xbin=8)
```

---

simdata *Simulation data*

Description

Simulation data from the fitted model of the origdata

Examples

```
data(simdata)
dim(simdata)
```

VPCgraph *The original visual predictive check plot (VPC)*

Description

This function draws the original visual predictive check plot proposed by Holford & Karlsson (2008). The visual predictive check plot is a graphical comparison of the distribution of observations and simulated data from the fitted model. In the "scatter" type of the VPC plot, dots indicate the observed data. Two dashed blue lines and one solid line represent profiles of percentiles of the simulated data. If the fitted model represents the observed data well, most observed data are between two dashed blue lines. In the "percentile" type of the VPC plot, profiles of percentiles from the observed data are compared to profiles of percentiles from the simulated data. Red lines represent profiles from the observed data, and blue lines represent profiles from the simulated data. If the fitted model represents the observed data well, two profiles in each percentile - one from the original data and the other from the simulated data - are similar. In the "CI" type of the VPC plot, sky blue and pink areas represent the confidence areas of the profile in each percentile. These confidence areas were calculated from the simulated data. In this plot, it is necessary to verify that the profiles of the original data are in confidence areas of each profile from the simulated data in each percentile. If each percentile line of the observed data is in the corresponding confidence area, this can be evidence that the fitted model represents the observed data quite well. Otherwise, the fitted model needs to be improved.

Usage

```
VPCgraph(orig_data,
         sim_data,
         type = "CI",
         N_xbin = NULL,
         probs = c(0.1,0.5,0.9),
         conf.level = 0.95,
         X_name = "TIME",
         Y_name = "DV",
         MissingDV = NULL,
         DV_point = TRUE,
         CIvpc_type = "line",
         bin_grid = TRUE,
         plot_caption = TRUE,
         plot_flag = TRUE,
         linesize = 0.7,
         pointsize = 0.7,
         captionsize = 10,
         Kmethod = "cluster",
         maxK = NULL,
         beta = 0.2,
         lambda = 0.3,
         R = 4,
         C1 = 2.5,
```

```
            C2 = 7.8, ...)
```

Arguments

orig_data	A data frame of original data with X and Y variable.
sim_data	A matrix of simulated data with only Y values collected.
type	Type of VPC graph; "CI", "percentile", or "scatter".
N_xbin	Number of bins in X variable. If NULL, optimal number of bins are automatically calcuated using optK function.
probs	A numeric vector of probabilities.
conf.level	Confidence level of the interval.
X_name	Name of X variable in orig_data (usually "TIME" in pharmacokinetic data).
Y_name	Name of Y variable in orig_data (usually "DV" in pharmacokinetic data).
MissingDV	Name of missing indicator variable in orig_data, which have value 1 if missing, value 0 otherwise. (usually "MDV" in pharmacokinetic data).
DV_point	Draw point (X, Y) in the plot if TRUE; omit if FALSE.
CIvpc_type	Type of CI area in VPC graph; "line" or "segment".
bin_grid	Draw grid lines for binning in X variable if TRUE; omit if FALSE.
plot_caption	Put caption with additional information if TRUE; omit if FALSE.
plot_flag	Draw plot if TRUE; generate data for drawing plot if FALSE.
linesize	Size of line in the plot.
pointsize	Size of point in the plot.
captionsize	Size of caption .
Kmethod	The way to calculate the penalty in automatic binning."cluster" or "kernel".
maxK	The maximum number of bins.
beta	Additional parameter for automatic binning, used in optK function.
lambda	Additional parameter for automatic binning, used in optK function.
R	Additional parameter for automatic binning, used in optK function.
C1	Additional parameter for automatic binning, used in optK function.
C2	Additional parameter for automatic binning, used in optK function.
...	Arguments to be passed to methods.

Value

Visual predictive check plot or the values to draw VPC plot.

References

Holford N, & Karlsson M. (2008). "A tutorial on visual predictive checks, abstr 1434." Annual Meeting of the Populations Approach Group in Europe. www.page-meeting.org. 2008.

Harling, Uekcert, K. 2018. VPC and NPC User Guide. ICON plc.

https://github.com/UUPharmacometrics/PsN/releases/download/4.9.0/vpc_npc_userguide.pdf.

Examples

```
data(origdata)
data(simdata)
VPCgraph(origdata,simdata,type="CI",X_name="TIME",Y_name="DV",N_xbin=8)
```

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