Package 'TDIagree'

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Type Package

Title Assessment of Agreement using the Total Deviation Index

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Description The total deviation index (TDI) is an unscaled statistical measure used to evaluate the deviation between paired quantitative measurements when assessing the extent of agreement between different raters. It describes a boundary such that a large specified proportion of the differences in paired measurements are within the boundary (Lin, 2000) <https://pubmed.ncbi.nlm.nih.gov/10641028/>.
This R package implements some methodologies existing in the literature for TDI estimation and inference in the case of two raters.

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Description

The total deviation index (TDI) is an unscaled statistical measure used to evaluate the deviation between paired quantitative measurements when assessing the extent of agreement between different raters. It describes a boundary such that a large specified proportion of the differences in paired measurements are within the boundary (Lin, 2000). This R package implements some methodologies existing in the literature for TDI estimation and inference in the case of two raters reviewed in Perez-Jaume and Carrasco (2015).

Functions

TDI

Methods

print.tdi, plot.tdi

Datasets

AMLad

Author(s)

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Authors:

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- Josep L Carrasco (ORCID)

References

Lin, L. I. K. (2000). Total deviation index for measuring individual agreement with applications in laboratory performance and bioequivalence. Statistics in Medicine, 19(2):255-270.

| AMLad | *Acute Myeloid Leukaemia agreement data* |

Description

Acute myeloid leukaemia (AML) is a type of cancer that starts in the blood-forming cells of the bone marrow. While in adults it is the most common type of leukaemia, it is much rarer in children, accounting for 15-20% percent of paediatric leukaemia cases, which translates to 8 cases per year for every million children under the age of 15.

Minimal residual disease (MRD) is the percentage of cancer cells that remain in a person either during or after treatment when the patient is in remission (no symptoms or signs of disease). MRD aids in identifying high-risk patients so therapy can be intensified in them while deintensification of therapy can prevent long-term sequelae of chemotherapy in low-risk category patients.

MRD describes disease that can be detected using techniques other than traditional morphology, including molecular methods such as polymerase chain reaction (PCR) and immunological methods such as flow cytometry (FCM) (Chattaerjee *et al.*, 2016).

This dataset is adapted from the *Childhood Leukemia: Overcoming distance between South America and Europe Regions* (CLOSER) project, whose goal was to decrease the gap between Europe and Latin America in terms of the diagnosis, monitoring, survival, and quality of life of patients with childhood leukaemia and their caregivers. See **Source** for further information on the project. The dataset contains data from 116 paediatric patients diagnosed with AML, in which the MRD was measured twice after treatment initiation by the methods PCR and FCM.

Usage

```
AMLad
```

Format

A data frame in long format with the following columns:

id:	Patient identifier
met:	Method to quantify MRD
rep:	Replicate
mrd:	MRD (%)

Source

https://closerleukemia.eu/

References

Chatterjee, T., Mallhi, R. S., & Venkatesan, S. (2016). Minimal residual disease detection using flow cytometry: Applications in acute leukemia. Medical Journal Armed Forces India, 72(2), 152-156.

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plot.tdi	*Bland-Altman plot*

Description

This function creates a Bland-Altman plot from Altman and Bland (1983), which is used to evaluate the agreement among the quantitative measures taken by two raters. The plot displays the mean of the measurements from both raters in the x-axis and the differences between the measures taken by the two raters in the y-axis. It can also display the TDI and UB estimates from the call of the function TDI as well as the limits of agreement (LoA) from Bland and Altman (1986).

Usage

```
## S3 method for class 'tdi'
plot(
  x,
  tdi = FALSE,
  ub = FALSE,
  loa = FALSE,
  method = NULL,
  ub.pc = NULL,
  p = NULL,
  loess = FALSE,
  method.col = NULL,
  loa.col = "#c27d38",
  loess.col = "#cd2c35",
  legend = FALSE,
  inset = c(-0.24, 0),
  main = "Bland-Altman plot",
  xlab = "Mean",
  ylab = "Difference",
  xlim = NULL,
  ylim = NULL,
  ...
)
```

Arguments

x	input object of class tdi resulting from a call of the function TDI.
tdi	logical indicating whether the $\pm$TDI estimate(s) should be added to the plot as solid lines. Default is FALSE.
ub	logical indicating whether the $\pm$UB estimate(s) should be added to the plot as a dashed lines. Default is FALSE.

loa	logical indicating whether the LoA should be added to the plot as dotted lines. Default is FALSE.
method	name of the method(s) for which the TDI or the UB estimates will be added to the plot. If both tdi and ub are set to FALSE, this argument is ignored. This argument is not case-sensitive and is passed to match.arg. The default value, NULL, indicates that, for the measures specified, all the methods for which the TDI (and/or UB) has been computed in the call of the function TDI are to be added to the plot.
ub.pc	name of the technique for the estimated UB to be added from the method of Perez-Jaume and Carrasco (2015). Possible values are: p_db, n_db, e_db, b_db, p_cb, n_cb, e_cb and b_cb. The bootstrap approach (differences or cluster) is indicated with "db" and "cb" and the strategy (based on percentiles, the normal distribution, the empirical method or the BC_a) is indicated with "p", "n", "e" and "b". The default value, NULL, indicates that the first estimated UB is to be added to the plot.
p	value of the proportion for which the TDI and/or UB (depending on the value of the arguments tdi and ub) are to be added to the plot. If both tdi and ub are set to FALSE, this argument is ignored. The default value, NULL, indicates that only the first proportion passed to the call of the function TDI is to be considered.
loess	logic indicating whether a smooth curve computed by loess should be added to the plot as a dotdashed curve. Default is FALSE.
method.col	colour palette to be used in the drawing of TDIs and/or UBs. A colour should be indicated for every method asked. It is assumed that the colours are passed in the same order as the methods passed to method. If both tdi and ub are set to FALSE, this argument is ignored. The default value, NULL, indicates that the following palette should be used: "#f3df6c", "#9c964a", "#f4b5bd" and "#85d4e3" corresponding to the options "Choudhary P", "Escaramis et al.", "Choudhary NP" and "Perez-Jaume and Carrasco" of method, respectively.
loa.col	colour to be used in the drawing of the LoA. If loa is set to FALSE, this argument is ignored. Default is "#c27d38".
loess.col	colour to be used in the drawing of the loess smooth curve. If loess is set to FALSE, this argument is ignored. Default is "#cd2c35".
legend	logical indicating whether a legend should be added outside the plot. If all tdi, ub and loa are set to FALSE, this argument is ignored. Default is FALSE.
inset	specifies how far the legend is inset from the plot margins (to be passed to inset argument in legend). Default is c(-0.25, 0), recommended for 24" screens with default plot window. For 13" screens, c(-0.34, 0) is recommended.

main	overall title for the plot (to be passed to main argument in plot). Default is "Bland-Altman plot".
xlab	a label for the x-axis (to be passed to xlab argument in plot). Default is "Mean".
ylab	a label for the y-axis (to be passed to ylab argument in plot). Default is "Difference".
xlim	the x limits of the plot (to be passed to xlim argument in plot). The default value, NULL, indicates that the range of the mean values should be used.
ylim	the y limits of the plot (to be passed to ylim argument in plot). The default value, NULL, indicates that the range of the differences values should be used.
...	other graphical parameters (to be passed to plot).

Details

The LoA are computed using the formula $\bar{d} \pm z_{1-\frac{\alpha}{2}} \cdot \mathrm{sd}(d)$, where $z_{1-\frac{\alpha}{2}}$ is the $(1 - \frac{\alpha}{2})$-th quantile of the standard normal distribution, d is the vector containing the differences between the two raters and $\bar{d}$ represents their mean.

Value

A Bland-Altman plot of the data in x with a solid black line at differences $= 0$, with differences considered as first level $-$ second level of the variable met in the call of the function [TDI](TDI).

Note

A call to [par](par) is used in this method. Notice that the arguments font.lab and las are always set to 2 and 1 respectively. Moreover, if legend is TRUE, mar is set to c(4, 4, 2, 9).

References

Altman, D. G., & Bland, J. M. (1983). Measurement in medicine: the analysis of method comparison studies. Journal of the Royal Statistical Society Series D: The Statistician, 32(3), 307-317.

Bland, J. M., & Altman, D. (1986). Statistical methods for assessing agreement between two methods of clinical measurement. The Lancet, 327(8476), 307-310.

Perez-Jaume, S., & Carrasco, J. L. (2015). A non-parametric approach to estimate the total deviation index for non-normal data. Statistics in Medicine, 34(25), 3318-3335.

Examples

```
# normal data
set.seed(2025)

n <- 100
y_A1 <- rnorm(n, 50, 10) # rater A, replicate 1
y_A2 <- rnorm(n, 50, 10) # rater A, replicate 2
y_B1 <- rnorm(n, 30, 15) # rater B, replicate 1
```

```
        y_B2 <- rnorm(n, 30, 15) # rater B, replicate 2

        ex_data <- data.frame(y = c(y_A1, y_A2, y_B1, y_B2), rater = factor(rep(c("A", "B"), each = 2*n)),
                        replicate = factor(rep(rep(1:2, each = n), 2)), subj = factor(rep(1:n, 4)))

        tdi <- TDI(ex_data, y, subj, rater, replicate, p = c(0.8, 0.9),
                method = c("Choudhary P", "Escaramis et al.",
                            "Choudhary NP", "Perez-Jaume and Carrasco"),
                R = 1000)
    plot(tdi)

    # enhance plot
    plot(tdi, xlim = c(10, 70), ylim = c(-60, 80), pch = 16, tdi = TRUE, ub = TRUE,
        method = c("es", "pe"), ub.pc = "b_cb", loa = TRUE, loa.col = "red", legend = TRUE)

    # non-normal data
    tdi.aml <- TDI(AMLad, mrd, id, met, rep, p = c(0.85, 0.95), boot.type = "cluster",
                    dec.est = 4, R = 1000)
    plot(tdi.aml)

    # enhance plot
    plot(tdi.aml, method = c("choudhary p", "pe"), tdi = TRUE, ub = TRUE, legend = TRUE,
        main = "Bland-Altman plot of the MRD")
```

---

print.tdi   *Printing tdi objects*

Description

A nice gt table containing the values computed with the function TDI.

Usage

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

Arguments

x   input object of class tdi resulting from a call of the function [TDI](#).

...   currently not in use

Value

A nice **gt** table containing the values computed with the function [TDI](#). The number of decimals for the estimates and the proportions correspond to the arguments dec.est and dec.p of the function [TDI](#), respectively.

Examples

```
# normal data
set.seed(2025)

n <- 100
y_A1 <- rnorm(n, 50, 10) # rater A, replicate 1
y_A2 <- rnorm(n, 50, 10) # rater A, replicate 2
y_B1 <- rnorm(n, 30, 15) # rater B, replicate 1
y_B2 <- rnorm(n, 30, 15) # rater B, replicate 2

ex_data <- data.frame(y = c(y_A1, y_A2, y_B1, y_B2), rater = factor(rep(c("A", "B"), each = 2*n)),
                replicate = factor(rep(rep(1:2, each = n), 2)), subj = factor(rep(1:n, 4)))

tdi <- TDI(ex_data, y, subj, rater, replicate, p = c(0.8, 0.9),
          method = c("Choudhary P", "Escaramis et al.",
                     "Choudhary NP", "Perez-Jaume and Carrasco"),
          R = 1000)
tdi

# non-normal data
tdi.aml <- TDI(AMLad, mrd, id, met, rep, p = c(0.85, 0.95), boot.type = "cluster",
              dec.est = 4, R = 1000)
tdi.aml
```

TDI   *TDI estimation and inference*

Description

This function implements the estimation of the TDI and its corresponding $100(1 - \alpha)\%$ upper bound (UB), where α is the significance level, using the methods proposed by Choudhary (2007), Escaramis *et al.* (2010), Choudhary (2010) and Perez-Jaume and Carrasco (2015) in the case of two raters. See **Details** and **References** for further information about these methods.

Usage

```
TDI(data, y, id, met, rep = NA,
    method = c("Choudhary P", "Escaramis et al.",
               "Choudhary NP", "Perez-Jaume and Carrasco"),
    p = 0.9, ub = TRUE, boot.type = c("differences", "cluster"),
    type = 8, R = 10000, dec.p = 2, dec.est = 3,
    choose.model.ch.p = TRUE, var.equal = TRUE,
    choose.model.es = TRUE, int = FALSE, tol = 10^(-8), add.es = NULL,
    alpha = 0.05)
```

Arguments

data	name of the dataset containing at least 3 columns (measurement, subject effect, rater effect).
y	continuous measurement column name.
id	subject effect column name. Must be a factor.
met	rater effect column name. Must be a factor.
rep	replicate effect column name. Must be a factor. When there are no replicates use rep = NA. Default is NA.
method	name of the method(s) to estimate the TDI and UB. Options: "Choudhary P" (Choudhary, 2007), "Escaramis et al." (Escaramis *et al.*, 2010), "Choudhary NP" (Choudhary, 2010) and "Perez-Jaume and Carrasco" (Perez-Jaume and Carrasco, 2015). This argument is not case-sensitive and is passed to match.arg. Default is c("Choudhary P", "Escaramis et al.", "Choudhary NP", "Perez-Jaume and Carrasco"), so all approaches are executed by default.
p	a value or vector of the proportions for estimation of the TDI, where $0 < p < 1$. Commonly, $p \geq 0.80$. Default is 0.90.
ub	logical asking whether the UBs should be computed. Default is TRUE.
boot.type	name of the bootstrap approach(es) to be used in the method of Perez-Jaume and Carrasco (2015). There are two different options when there are replicates: to bootstrap the vector of the within-subject differences ("differences") or to bootstrap at subject level ("cluster"). This is, not all the differences coming from the same subject need to be bootstrapped together in the first one but all the measurements from the same subjects have to be bootstrapped together in the second one. This argument is passed to match.arg Default is c("differences", "cluster"), so all approaches are executed by default.
type	in the method of Perez-Jaume and Carrasco (2015), a quantile is calculated to obtain the estimation of the TDI. This argument is an integer between 1 and 9 selecting one of the nine quantile algorithms (to be passed to quantile). Recommended 8 for continuous data and 3 for discrete data. Default is 8.
R	in the method of Perez-Jaume and Carrasco (2015), bootstrap is used for the estimation of the UB. This argument chooses the number of bootstrap replicates (to be passed to boot). Default is 10000.
dec.p	number of decimals to display for p in the method print.tdi. Default is 2.
dec.est	number of decimals to display for the estimates in the method print.tdi. Up to 4 decimals. Default is 3.

choose.model.ch.p

> in the parametric method of Choudhary (2007) two methods can be fit, one with equal residual homoscedasticity between raters and one with unequal residual homoscedasticity. This argument, if TRUE, chooses the model with the minimum AIC. If FALSE, the argument var.equal must be specified.
> Default is TRUE.

var.equal   logical asking if there is residual homoscedasticity between raters to choose the model in the parametric method of Choudhary (2007). If choose.model.ch.p is set to TRUE, this argument is ignored.
Default is TRUE.

choose.model.es

> in the method of Escaramis *et al.* (2010) two methods can be fit, one including the subject–rater interaction and one that does not. The model with interaction only applies to data with replicates. This argument, if TRUE, chooses the model with the minimum AIC. If FALSE, the argument int must be specified.
> Default is TRUE.

int   logical asking if there is interaction between subjects and methods to choose the model in the method of Escaramis *et al.* (2010). The model with interaction only applies to data with replicates. If choose.model.es is set to TRUE, this argument is ignored.
Default is FALSE.

tol   tolerance to be used in the method of Escaramis *et al.* (2010).
Default is 10^(-8).

add.es   name of the columns in data that will be added to the model (as fixed effects) of the method of Escaramis *et al.* (2010). It must be passed as a column name or vector of column names.
The default value, NULL, indicates that no extra variables are to be added in the model.

alpha   significance level for inference on the TDI.
Default is 0.05.

Details

The methods of Choudhary (2007) and Escaramis *et al.* (2010) are parametric methods based on linear mixed models that assume normality of the data and linearity between the response and the effects (subjects, raters and random errors). The linear mixed models are fitted using the function [lme](#) from the nlme package. The methods of Choudhary (2010) and Perez-Jaume and Carrasco (2015) are non-parametric methods based on the estimation of quantiles of the absolute value of the differences between raters. Non-parametric methods are recommended when dealing with skewed data or other non-normally distributed data, such as count data. In situations of normality, parametric methods are recommended. See **References** for further details.

Value

An object of class tdi, which is a list with five components:

result an object of class data.frame with the TDI estimates and UBs of the methods specified for every proportion.

`fitted.models` a list with the fitted models of the parametric methods of Choudhary (2007) and Escaramis *et al.* (2010).

`params` a list with the values dec.est, dec.p, ub, `method` and `alpha` to be used in the method [print.tdi](#) and in the method [plot.tdi](#).

`data.long` an object of class data.frame with columns y, id, met (and rep if it applies) with the values of the measurement, subject identifiers, rater (and replicate number if it applies) from the original data frame provided.

`data.wide` an object of class data.frame with either:

- columns id, y_met1, y_met2 (in the case of no replicates) with the measurements of each method.
- columns id, y_met1rep1,..., y_met1rep$m$, y_met2rep1,..., y_met2rep$m$, with the measurements of each method and each replicate, where m is the number of replicates.

Numbers 1 and 2 after met correspond to the first and second level of the column met in data, respectively. Numbers 1,..., m after rep correspond to the first,..., m-th level of the column rep in data, respectively.

References

Efron, B., & Tibshirani, R. (1993). An Introduction to the Bootstrap; Chapman and Hall. Inc.: New York, NY, USA, 914.

Lin, L. I. K. (2000). Total deviation index for measuring individual agreement with applications in laboratory performance and bioequivalence. Statistics in Medicine, 19(2):255-270.

Choudhary, P. K. (2007). A tolerance interval approach for assessment of agreement with left censored data. Journal of Biopharmaceutical Statistics, 17(4), 583-594.

Escaramis, G., Ascaso, C., & Carrasco, J. L. (2010). The total deviation index estimated by tolerance intervals to evaluate the concordance of measurement devices. BMC Medical Research Methodology, 10, 1-12.

Choudhary, P. K. (2010). A unified approach for nonparametric evaluation of agreement in method comparison studies. The International Journal of Biostatistics, 6(1).

Perez-Jaume, S., & Carrasco, J. L. (2015). A non-parametric approach to estimate the total deviation index for non-normal data. Statistics in Medicine, 34(25), 3318-3335.

See Also

[print.tdi](#), [plot.tdi](#)

Examples

```
# normal data, parametric methods more suitable
set.seed(2025)

n <- 100
y_A1 <- rnorm(n, 50, 10) # rater A, replicate 1
y_A2 <- rnorm(n, 50, 10) # rater A, replicate 2
y_B1 <- rnorm(n, 30, 15) # rater B, replicate 1
y_B2 <- rnorm(n, 30, 15) # rater B, replicate 2
```

```
ex_data <- data.frame(y = c(y_A1, y_A2, y_B1, y_B2), rater = factor(rep(c("A", "B"), each = 2*n)),
                replicate = factor(rep(rep(1:2, each = n), 2)), subj = factor(rep(1:n, 4)))

tdi <- TDI(ex_data, y, subj, rater, replicate, p = c(0.8, 0.9),
           method = c("Choudhary P", "Escaramis et al.",
                      "Choudhary NP", "Perez-Jaume and Carrasco"),
           R = 1000)
tdi$result
tdi$fitted.models
tdi$data.long
tdi$data.wide

# non-normal data, non-parametric methods more suitable
tdi.aml <- TDI(AMLad, mrd, id, met, rep, p = c(0.85, 0.95), boot.type = "cluster",
               dec.est = 4, R = 1000)
tdi.aml$result
tdi.aml$fitted.models
tdi.aml$data.long
tdi.aml$data.wide
```

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