

Package ‘cccrm’

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Title Concordance Correlation Coefficient for Repeated (and Non-Repeated) Measures

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Imports nlme, dplyr, Deriv, tidyselect, progressr, furrr, nlmeU, parallelly, purrr, tidyr, lifecycle, future, MASS, ggplot2

Description Estimates the Concordance Correlation Coefficient to assess agreement. The scenarios considered are non-repeated measures, non-longitudinal repeated measures (replicates) and longitudinal repeated measures. It also includes the estimation of the one-way intraclass correlation coefficient also known as reliability index. The estimation approaches implemented are variance components and U-statistics approaches. Description of methods can be found in Fleiss (1986) <[doi:10.1002/9781118032923](https://doi.org/10.1002/9781118032923)> and Carrasco et al. (2013) <[doi:10.1016/j.cmpb.2012.09.002](https://doi.org/10.1016/j.cmpb.2012.09.002)>.

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Contents

| | |
|------------------|---|
| bdaw | 2 |
| bfat | 2 |
| bpres | 3 |
| ccclon | 4 |

| | |
|---------------------------|----|
| ccclonw | 5 |
| cccUst | 6 |
| cccvc | 7 |
| ccc_est_by_time | 8 |
| ccc_sim_data | 10 |
| ccc_vc | 12 |
| lme_model | 16 |
| sim_power_ccc | 18 |
| Ztest | 20 |

| | |
|--------------|-----------|
| Index | 22 |
|--------------|-----------|

| | |
|------|------------------------|
| bdaw | <i>Blood draw data</i> |
|------|------------------------|

Description

Plasma cortisol area under curve (AUC) was calculated from the trapezoidal rule over the 12-h period of the hourly blood draws. The subjects were required to repeat the process in five visits. The aim of the agreement study was to assess how well the plasma cortisol AUC from hourly measurements agreed with plasma cortisol AUC that was measured every two hours.

Usage

bdaw

Format

A data frame with the following columns:

SUBJ Subject identifier

VNUM Visit number

AUC Area under the curve

MET Device identifier

| | |
|------|----------------------|
| bfat | <i>Body fat data</i> |
|------|----------------------|

Description

Percentage body fat was estimated from skinfold calipers and DEXA on a cohort of 90 adolescent girls. Skinfold caliper and DEXA measurements were taken at ages 12.5, 13 and 13.5. The objective was to determine the amount of agreement between the skinfold caliper and DEXA measurements of percentage body fat.

Usage

bfat

Format

A data frame with the following columns:

SUBJECT Subject identifier**VISITNO** Visit number**BF** Percentage body fat**MET** Device identifier

bpres

*Blood pressure data***Description**

Systolic and diastolic blood pressure was measured in a sample of 384 subjects using a handle mercury sphygmomanometer device and an automatic device. The blood pressure was simultaneously measured twice by each instrument, thus every subject had four measurements, two by each method.

Usage

bpres

Format

A data frame with the following columns:

ID Subject identifier**SIS** Systolic blood pressure in mmHg**DIA** Diastolic blood pressure in mmHg**METODE** Device identifier**NM** Identifier of replicates**ALTURA** Height in cm**EDAD** Age in years**FRECUENC** Heart rate**INFOR_AR** Have the subject been informed about he is hypertense?**PESO** Weight in Kg**SEXO** Gender. 1 for Male. 2 for Female**TA** Was the subject's blood pressure measured the last year? 1=Yes, 2=No, 9=Unknown**TNSI_MED** Does the subject receive treatment for hypertension? 1=Yes, 2=No, 3=Doubtful, 8=not applicable, 9=Insufficient data.

| | |
|--------|---|
| ccclon | <i>Concordance Correlation Coefficient estimated by Variance Components</i> |
|--------|---|

Description

Concordance Correlation Coefficient for longitudinal repeated measures estimated by variance components

Usage

```
ccclon(  
  dataset,  
  ry,  
  rind,  
  rtime,  
  rmet,  
  covar = NULL,  
  rho = 0,  
  cl = 0.95,  
  control.lme = list()  
)
```

Arguments

| | |
|-------------|--|
| dataset | an object of class <code>data.frame</code> . |
| ry | Character string. Name of the outcome in the data set. |
| rind | Character string. Name of the subject variable in the data set. |
| rtime | Character string. Name of the time variable in the data set. |
| rmet | Character string. Name of the method variable in the data set. |
| covar | Character vector. Name of covariates to include in the linear mixed model as fixed effects. |
| rho | Within subject correlation structure. A value of 0 (default option) stands for compound symmetry and 1 is used for autorregressive of order 1 structure. |
| cl | Confidence level. |
| control.lme | A list of control values for the estimation algorithm used in <code>lme</code> function. For further details see <code>lme</code> help. |

Details

This function has been deprecated. See [ccc_vc](#).

| | |
|---------|---|
| ccclonw | <i>Concordance Correlation Coefficient estimated by Variance Components</i> |
|---------|---|

Description

Concordance Correlation Coefficient for longitudinal repeated measures estimated by variance components

Usage

```
ccclonw(
  dataset,
  ry,
  rind,
  rtime,
  rmet,
  vecD,
  covar = NULL,
  rho = 0,
  cl = 0.95,
  control.lme = list()
)
```

Arguments

| | |
|-------------|--|
| dataset | an object of class <code>data.frame</code> . |
| ry | Character string. Name of the outcome in the data set. |
| rind | Character string. Name of the subject variable in the data set. |
| rtime | Character string. Name of the time variable in the data set. |
| rmet | Character string. Name of the method variable in the data set. |
| vecD | Vector of weights. The length of the vector must be the same as the number of repeated measures. |
| covar | Character vector. Name of covariates to include in the linear mixed model as fixed effects. |
| rho | Within subject correlation structure. A value of 0 (default option) stands for compound symmetry and 1 is used for autorregressive of order 1 structure. |
| cl | Confidence level. |
| control.lme | A list of control values for the estimation algorithm used in <code>lme</code> function. For further details see <code>lme</code> help. |

Details

This function has been deprecated. See [ccc_vc](#).

| | |
|--------|--|
| cccUst | <i>Repeated Measures Concordance Correlation Coefficient estimated by U-statistics</i> |
|--------|--|

Description

Estimation of the concordance correlation coefficient for repeated measurements using the U-statistics approach. The function is also applicable for the non-repeated measurements scenario.

Usage

```
cccUst(dataset, ry, rmet, rtime = NULL, Dmat = NULL, delta = 1, cl = 0.95)
```

Arguments

| | |
|---------|---|
| dataset | An object of class <code>data.frame</code> . |
| ry | Character string. Name of the outcome in the data set. |
| rmet | Character string. Name of the method variable in the data set. |
| rtime | Character string. Name of the time variable in the data set. |
| Dmat | Matrix of weights. |
| delta | Power of the differences. A value of 0 provides an estimate that is comparable to a repeated measures version of kappa index. |
| cl | Confidence level. |

Value

A vector that includes the point estimate, confidence interval and standard error of the CCC. Additionally the Fisher's Z-transformation value and its standard error are also provided.

References

- King, TS and Chinchilli, VM. (2001). A generalized concordance correlation coefficient for continuous and categorical data. *Statistics in Medicine*, 20, 2131:2147.
- King, TS; Chinchilli, VM; Carrasco, JL. (2007). A repeated measures concordance correlation coefficient. *Statistics in Medicine*, 26, 3095:3113.
- Carrasco, JL; Phillips, BR; Puig-Martinez, J; King, TS; Chinchilli, VM. (2013). Estimation of the concordance correlation coefficient for repeated measures using SAS and R. *Computer Methods and Programs in Biomedicine*, 109, 293-304.

Examples

```
# Non-longitudinal scenario
newdat=bpres[bpres$NM==1,]
estccc=cccUst(newdat,"DIA","METODE")
estccc

estccc=cccUst(bdaw,"AUC","MET","VNUM")
estccc

estccc=cccUst(bfat,"BF","MET","VISITNO",Dmat=diag(c(2,1,1)))
estccc
```

cccvc

Concordance Correlation Coefficient estimated by Variance Components

Description

Estimation of the concordance correlation coefficient for non-repeated measurements and non-longitudinal repeated measurements (replicates) using the variance components from a linear mixed model. The appropriate intraclass correlation coefficient is used as estimator of the concordance correlation coefficient.

Usage

```
cccvc(
  dataset,
  ry,
  rind,
  rmet,
  covar = NULL,
  int = FALSE,
  cl = 0.95,
  control.lme = list()
)
```

Arguments

| | |
|---------|--|
| dataset | an object of class <code>data.frame</code> . |
| ry | Character string. Name of the outcome in the data set. |
| rind | Character string. Name of the subject variable in the data set. |
| rmet | Character string. Name of the method variable in the data set. |
| covar | Character vector. Name of covariates to include in the linear mixed model as fixed effects. |
| int | Binary indicating if the subject-method interaction has to be included in the model when analyzing the non-longitudinal setting (defaults to <code>FALSE</code>). |

| | |
|--------------------------|---|
| <code>cl</code> | Confidence level. |
| <code>control.lme</code> | A list of control values for the estimation algorithm used in <code>lme</code> function. For further details see <code>lme</code> help. |

Details

This function has been deprecated. See [ccc_vc](#).

| | |
|------------------------------|---|
| <code>ccc_est_by_time</code> | <i>Concordance Correlation Coefficient estimation by variance components.</i> |
|------------------------------|---|

Description

Estimation of the non-longitudinal concordance correlation coefficient at each time using the variance components approach.

Usage

```
ccc_est_by_time(
  dataset,
  ry,
  rind,
  rmet,
  rtime,
  covar = NULL,
  int = F,
  cl = 0.95,
  control.lme = list(),
  future_seed = TRUE,
  transf = "F2",
  workers = 15,
  plotit = TRUE,
  test = FALSE,
  nboot = 500,
  adj.method = "holm",
  ...
)
```

Arguments

| | |
|----------------------|---|
| <code>dataset</code> | an object of class <code>data.frame</code> . |
| <code>ry</code> | Character string. Name of the outcome in the data set. |
| <code>rind</code> | Character string. Name of the subject variable in the data set. |
| <code>rmet</code> | Character string. Name of the method variable in the data set. |
| <code>rtime</code> | Character string. Name of the time variable in the data set. |

| | |
|-------------|---|
| covar | Character vector. Name of covariates to include in the linear mixed model as fixed effects. |
| int | Binary indicating if the subject-method interaction has to be included in the model when analyzing the non-longitudinal setting (defaults to FALSE). |
| cl | Confidence level. |
| control.lme | A list of control values for the estimation algorithm used in lme function. For further details see lme help. |
| future_seed | Logical/Integer. The seed to be used for parallelization. Further details in furr_options . |
| transf | Character string. Whether to apply a transformation of the coefficient for inference. Valid options are: "F" for Fisher's Z-transformation; "F2" For Fisher's Z-transformation setting m=2 (default); "KG" Konishi-Gupta transformation; "None", no transformation is applied. See *Details* for further information. |
| workers | Integer. Number of cores to be used for parallelization. Default is 15. Capped to number of available cores minus 1. |
| plotit | Logical. If TRUE it generates a plot with the CCC and their confidence intervals for each time. |
| test | Logical. If TRUE the equality of CCCs is assessed. Default to FALSE. |
| nboot | Number of bootstrap resamples. |
| adj.method | Character string. Correction method for pairwise comparisons. See p.adjust |
| ... | To pass further arguments. |

Details

The concordance correlation coefficient is estimated using the variance components approach. Confidence intervals are built using the asymptotic Normal distribution approach. Variance-covariance matrix of CCC estimates is estimated by non-parametric balanced randomized cluster bootstrap approach (Davison and Hinkley, 1997; Field and Welsh, 2007). Overall equality of CCCs is tested following the non-parametric bootstrap approach suggested in Vanbelle (2017).

Value

A ccc class object. Generic function `summary` show a summary of the results. The output is a list with the following components:

- `ccc`. CCC estimates at each level of time variable.
- `plot`. Plot of the CCC along with their confidence intervals.
- `res_test`. Test of equality of CCCs.
- `ph_table`. Pairwise comparison of CCCs.

References

Davison A.C., Hinkley D.V. (1997). *Bootstrap Methods and Their Application*. Cambridge: Cambridge University Press.

Field, C.A., Welsh, A.H. (2007). Bootstrapping Clustered Data. *Journal of the Royal Statistical Society. Series B (Statistical Methodology)* 69(3):369-390.

Vanbelle S. (2017). Comparing dependent kappa coefficients obtained on multilevel data. *Biometrical Journal* 59(5):1016-1034.

Examples

```
## Not run:
ccc_est_by_time(bdaw, "AUC", "SUBJ", "MET", "VNUM")
ccc_est_by_time(bpres, "SIS", "ID", "METODE", "NM", test=TRUE)

## End(Not run)
```

ccc_sim_data

Data simulation using fixed and random effects

Description

The fixed effects and standard deviations of random effects can be set to specific values or, alternatively, obtained from an object of class `lme`.

Usage

```
ccc_sim_data(
  n = 30,
  nrep = 1,
  nsim = 1,
  model = NULL,
  b = NULL,
  g = NULL,
  mu = 0,
  sa = 1,
  sab = 0,
  sag = 0,
  bg = NULL,
  se = 1,
  future_seed = TRUE,
  workers = 15,
  extra.info = TRUE,
  ...
)
```

Arguments

| | |
|-------------------|---|
| <code>n</code> | Integer. Number of subjects |
| <code>nrep</code> | Integer. Number of replicates |
| <code>nsim</code> | Integer. Number of data sets simulated. |

| | |
|-------------|--|
| model | Object of class lme. |
| b | Vector. Method fixed effects. |
| g | Vector. Time fixed effects. |
| mu | Integer. Overall mean. |
| sa | Integer. Standard deviation of subject's random effect. |
| sab | Integer. Standard deviation of subject-method interaction's random effect. |
| sag | Integer. Standard deviation of subject-time interaction's random effect. |
| bg | Vector. Method-time interaction's fixed effects. The vector of effects have to be ordered by method and time. |
| se | Integer. Standard deviation of random error effect. |
| future_seed | Logical/Integer. The seed to be used for parallelization. Further details in furr_options . |
| workers | Integer. Number of cores to be used for parallelization. Default is 15. Capped to number of available cores minus 1. |
| extra.info | Logical. Should the information about CCC/ICC and variance components simulated be shown? Default is set to TRUE. |
| ... | To pass further arguments. |

Details

Random effects are simulated as normal distributions with mean 0 and the correspondign standard deviations. The simulated data is obtained as the addition of the simulated values and the fixed effects. Parallel computation is used except if data is simulated from an object of class 'lme'. In this case. data is simulated using the [simulateY](#) function from nlmeU package.

Value

A data frame with the simulated data.

See Also

[ccc_vc](#)

Examples

```
# # Reliability data:
# 50 subjects, one method, one time, 2 replicates
# Overall mean: -0.25; Subjects standard deviation: 1.5, Random error standard deviation: 1
set.seed(101)
df <- ccc_sim_data(n=50, b = NULL, g = NULL, mu = -0.25, sa = 1.5, se = 1, nrep=2)

# Method comparison data (non-longitudinal)
# 50 subjects, two methods, 2 replicates
# Overall mean: -0.25; Subjects standard deviation: 1.5, Random error standard deviation: 1
# Difference of means between methods 2 and 1: 1
# Three data sets simulated
```

```

set.seed(202)
df <- ccc_sim_data(n=50, nsim=3, b = c(0,1), mu = -0.25, sa = 1.5, se = 1, nrep=2)

# Method comparison data (longitudinal)
# 50 subjects, two methods, 3 times, 1 replicate,
# Overall mean: -0.25; Subjects standard deviation: 1.5, Random error standard deviation: 1
# Difference of means between methods 2 and 1: 1
# Difference of means between times 3,2 and 1 respectively: 0.5 and 0.25.
# Subject-methods interaction standard deviation: 0.25
# Subject-times interaction standard deviation: 0.5
# Same difference of means at each time

set.seed(202)
df <- ccc_sim_data(n=50, b = c(0,1), g=c(0,0.25,0.5), mu = -0.25, sa = 1.5,
sab=0.25,sag=0.5,se = 1, nrep=2)

# Simulate data using the estimates of a linear mixed model
set.seed(2024)
df3 <- ccc_sim_data(n=50, b = c(0,1), g=c(0,0.25,0.5), mu = -0.25, sa = 1.5,
sab=0.25,sag=0.5,bg=c(0,0.5,0.75,0,1,1),se = 1, nrep=2)
mod3 <- lme_model(df3,"y","id","times","met",control.lme=nlme::lmeControl(opt = 'optim'))
ccc_sim_data(nsim=10,model=mod3)

```

ccc_vc

Concordance Correlation Coefficient estimation by variance components.

Description

Estimation of the concordance correlation coefficient for either non-repeated, non-longitudinal, or longitudinal repeated measurements using the variance components from a linear mixed model. The appropriate intraclass correlation coefficient is used as estimator of the concordance correlation coefficient.

Usage

```

ccc_vc(
  dataset,
  ry,
  rind,
  rmet = NULL,
  rtime = NULL,
  vecD = NULL,
  covar = NULL,
  int = F,
  rho = 0,
  cl = 0.95,

```

```

control.lme = list(),
transf = "F2",
boot = FALSE,
boot_param = FALSE,
boot_ci = "BCa",
nboot = 300,
parallel = FALSE,
future_seed = TRUE,
workers = 15,
sd_est = TRUE,
apVar = TRUE,
...
)

```

Arguments

| | |
|-------------|---|
| dataset | an object of class <code>data.frame</code> . |
| ry | Character string. Name of the outcome in the data set. |
| rind | Character string. Name of the subject variable in the data set. |
| rmet | Character string. Name of the method variable in the data set. |
| rtime | Character string. Name of the time variable in the data set. |
| vecD | Vector of weights. The length of the vector must be the same as the number of repeated measures. |
| covar | Character vector. Name of covariates to include in the linear mixed model as fixed effects. |
| int | Binary indicating if the subject-method interaction has to be included in the model when analyzing the non-longitudinal setting (defaults to <code>FALSE</code>). |
| rho | Within subject correlation structure. A value of 0 (default option) stands for compound symmetry and 1 is used for autoregressive of order 1 structure. |
| c1 | Confidence level. |
| control.lme | A list of control values for the estimation algorithm used in <code>lme</code> function. For further details see <code>lme</code> help. |
| transf | Character string. Whether to apply a transformation of the coefficient for inference. Valid options are: "F" for Fisher's Z-transformation; "F2" For Fisher's Z-transformation setting $m=2$ (default); "KG" Konishi-Gupta transformation; "None", no transformation is applied. See *Details* for further information. |
| boot | Logical. Whether to compute the CCC confidence interval by bootstrapping or asymptotic methods (defaults to <code>FALSE</code>). |
| boot_param | Logical. Whether to compute a parametric bootstrap or a non-parametric bootstrap (defaults to <code>FALSE</code>). |
| boot_ci | Character. Type of bootstrap confidence interval. Either "BCa" (which is the default) or "empirical". |
| nboot | Integer. Number of bootstrap resamples. Default is 300. |
| parallel | Logical. Whether the code is parallelized. The parallelization method is <code>multisession</code> . |

| | |
|-------------|--|
| future_seed | Logical/Integer. The seed to be used for parallelization. Further details in furr_options . |
| workers | Integer. Number of cores to be used for parallelization. Default is 15. Capped to number of available cores minus 1. |
| sd_est | Logical. Whether to estimate the asymptotic standard deviation (defaults to TRUE) or to only report the ccc/icc value. |
| apVar | Logical. Should the asymptotic variance-covariance matrix of the variance components be estimated in the linear mixed model? (Defaults to TRUE). |
| ... | To pass further arguments. |

Details

The concordance correlation coefficient is estimated using the appropriate intraclass correlation coefficient (see Carrasco and Jover, 2003; Carrasco et al., 2009; Carrasco et al, 2013).

The scenarios considered are: a) reliability assessment (several measurements taken with one method); b) methods comparison data with non-repeated measurements (only one measurement by subject and method); c) Methods comparison data with non-longitudinal repeated measurements, i.e. replicates (multiple measurements by subject and method); and d) Methods comparison data with longitudinal repeated measurements (multiple longitudinal measurements by subject and method).

The variance components estimates are obtained from a linear mixed model (LMM) estimated by restricted maximum likelihood. The function *lme* from package *nlme* (Pinheiro et al., 2021) is used to estimate the LMM.

The standard error of CCC and its confidence interval can be obtained: a) asymptotically, using Taylor's series expansion of 1st order (Ver Hoef, 2012); b) using balanced randomized cluster bootstrap approach (Davison and Hinkley, 1997; Field and Welsh, 2007); c) using parametric bootstrap (Davison and Hinkley, 1997).

When estimating asymptotically the standard error, the confidence intervals are built using the point estimate of the CCC/ICC, its standard error, and the appropriate quantile of the standard Normal distribution. However, the approximation to the asymptotic Normal distribution is improved if the CCC/ICC is transformed using the Fisher's Z-transformation (Fisher, 1925), or the Konishi-Gupta transformation (Konishi and Gupta, 1989). In case the number of replicates is equal to 2, both transformations give the same result.

Value

A ccc class object. Generic function `summary` show a summary of the results. The output is a list with the following components:

- `ccc`. CCC/ICC estimate
- `model`. nlme object with the fitted linear mixed model.
- `vc`. Variance components estimates.
- `sigma`. Variance components asymptotic covariance matrix.

References

- Carrasco, JL; Jover, L. (2003). Estimating the generalized concordance correlation coefficient through variance components. *Biometrics*, 59, 849-858.
- Carrasco, JL; King, TS; Chinchilli, VM. (2009). The concordance correlation coefficient for repeated measures estimated by variance components. *Journal of Biopharmaceutical Statistics*, 19, 90:105.
- Davison A.C., Hinkley D.V. (1997). *Bootstrap Methods and Their Application*. Cambridge: Cambridge University Press.
- Field, C.A., Welsh, A.H. (2007). Bootstrapping Clustered Data. *Journal of the Royal Statistical Society. Series B (Statistical Methodology)*. 69(3), 369-390.
- Fisher, R. A. (1925) *Statistical Methods for Research Workers*. Edinburgh: Oliver
- Konishi, S. and Gupta, A. K. (1989) Testing the equality of several intraclass correlation coefficients. *J Statist. Planng Inf.*, 21, 93-105.
- Pinheiro J, Bates D, DebRoy S, Sarkar D, R Core Team (2021). nlme: Linear and Nonlinear Mixed Effects Models. R package version 3.1-152, <https://CRAN.R-project.org/package=nlme>.
- Ver Hoef, J.M. (2012) Who Invented the Delta Method?, *The American Statistician*, 66:2, 124-127.

Examples

```
## Not run:
# Scenario 1. Reliability
newdat <- bpres |> dplyr::filter(METODE==1)
icc_rel<-ccc_vc(newdat,"DIA","ID")
icc_rel
summary(icc_rel)

# Confidence interval using non-parametric bootstrap

icc_rel_bt<-ccc_vc(newdat,"DIA","ID",boot=TRUE,sd_est=FALSE,
nboot=500,parallel=TRUE)
icc_rel_bt
summary(icc_rel_bt)

#' # Scenario 2. Non-longitudinal methods comparison.
# Only 1 measure by subject and method.
# No subjects-method interaction included in the model.

newdat <- bpres |> dplyr::filter(NM==1)
ccc_mc<-ccc_vc(newdat,"DIA","ID","METODE")
ccc_mc
summary(ccc_mc)

# Confidence interval using parametric bootstrap

ccc_mc_bt<-ccc_vc(newdat,"DIA","ID",boot=TRUE,boot_param=TRUE,
```

```

sd_est=FALSE,nboot=500,parallel=TRUE)
ccc_mc_bt
summary(ccc_mc_bt)

# Scenario 3. Non-longitudinal methods comparison.
# Two measures by subject and method.
# No subject-method interaction included in the model.

ccc_mc=ccc_vc(bpres,"DIA","ID","METODE")
ccc_mc
summary(ccc_mc)

# Scenario 4. Methods comparison in longitudinal repeated measures setting.
ccc_mc_lon<-ccc_vc(bdaw,"AUC","SUBJ","MET","VNUM")
ccc_mc_lon
summary(ccc_mc_lon)

# Scenario 5. Methods comparison in longitudinal repeated measures setting.
# More weight given to readings from first time.

ccc_mc_lonw<-ccc_vc(bfat,"BF","SUBJECT","MET","VISITNO",vecD=c(2,1,1))
ccc_mc_lonw
summary(ccc_mc_lonw)

## End(Not run)

```

lme_model

Fits a Linear Mixed Effects Model

Description

Fits a Linear Mixed Effects Model

Usage

```

lme_model(
  dataset,
  ry,
  rind,
  rtime = NULL,
  rmet = NULL,
  vecD = NULL,
  covar = NULL,
  rho = 0,
  int = FALSE,

```

```

    cl = 0.95,
    control.lme = list(),
    apVar = TRUE,
    ...
)

```

Arguments

| | |
|-------------|---|
| dataset | an object of class <code>data.frame</code> . |
| ry | Character string. Name of the outcome in the data set. |
| rind | Character string. Name of the subject variable in the data set. |
| rtime | Character string. Name of the time variable in the data set. |
| rmet | Character string. Name of the method variable in the data set. |
| vecD | Vector of weights. The length of the vector must be the same as the number of repeated measures. |
| covar | Character vector. Name of covariates to include in the linear mixed model as fixed effects. |
| rho | Within subject correlation structure. A value of 0 (default option) stands for compound symmetry and 1 is used for autoregressive of order 1 structure. |
| int | Boolean indicating if the subject-method interaction has to be included in the model. |
| cl | Confidence level. |
| control.lme | A list of control values for the estimation algorithm used in <code>lme</code> function. For further details see <code>lme</code> help. |
| apVar | Logical. Should the asymptotic variance-covariance matrix of the variance components be estimated in the linear mixed model? (Defaults to TRUE). |
| ... | To pass further arguments. |

Value

an object of class `lme`.

Examples

```

# Reliability ICC
set.seed(2024)
df <- ccc_sim_data(b = NULL, g = NULL, mu = -0.25, sa = 1.5, se = 1)
mod1 <- lme_model(df, "y", "id")
mod1

#Non-longitudinal Methods comparison data
set.seed(2024)
df2 <- ccc_sim_data(n=50, b = c(0,1), mu = -0.25, sa = 1.5, se = 1, nrep=2)
mod2 <- lme_model(df2, "y", "id", rmet="met")
mod2

```

```
# Longitudinal Methods comparison data
set.seed(2024)
df3 <- ccc_sim_data(n=50, b = c(0,1), g=c(0,0.25,0.5), mu = -0.25, sa = 1.5,
                  sab=0.25,sag=0.5,bg=c(0,0.5,0.75,0,1,1),se = 1, nrep=2)

mod3 <- lme_model(df3,"y","id","times","met",control.lme=nlme::lmeControl(opt = 'optim'))
mod3
```

 sim_power_ccc

Power and confidence interval range

Description

Power and confidence interval range obtained by simulation

Usage

```
sim_power_ccc(
  n = 30,
  nrep = 2,
  nsim = 300,
  r0 = 0,
  alpha = 0.05,
  model = NULL,
  b = NULL,
  g = NULL,
  mu = 0,
  sa = 1,
  sab = 0,
  sag = 0,
  bg = NULL,
  se = 1,
  extra.info = TRUE,
  vecD = NULL,
  covar = NULL,
  int = FALSE,
  rho = 0,
  cl = 0.95,
  control.lme = list(),
  transf = "F2",
  future_seed = TRUE,
  workers = 15
)
```

Arguments

| | |
|-------------|---|
| n | Integer. Number of subjects |
| nrep | Integer. Number of replicates |
| nsim | Integer. Number of data sets simulated. |
| r0 | Integer. Null hypothesis value. |
| alpha | Type-I error rate. |
| model | object of class lme. |
| b | Vector. Method fixed effects. |
| g | Vector. Time fixed effects. |
| mu | Integer. Overall mean. |
| sa | Integer. Standard deviation of subject's random effect. |
| sab | Integer. Standard deviation of subject-method interaction's random effect. |
| sag | Integer. Standard deviation of subject-time interaction's random effect. |
| bg | Vector. Method-time interaction's fixed effects |
| se | Integer. Standard deviation of random error effect. |
| extra.info | Logical. Should the information about CCC and variance components simulated be shown? Default is set to TRUE. |
| vecD | Vector of weights. The length of the vector must be the same as the number of repeated measures. |
| covar | Character vector. Name of covariates to include in the linear mixed model as fixed effects. |
| int | Binary indicating if the subject-method interaction has to be included in the model when analyzing the non-longitudinal setting (defaults to FALSE). |
| rho | Within subject correlation structure. A value of 0 (default option) stands for compound symmetry and 1 is used for autoregressive of order 1 structure. |
| cl | Confidence level. |
| control.lme | A list of control values for the estimation algorithm used in lme function. For further details see lme help. |
| transf | Character string. Whether to apply a transformation of the coefficient for inference. Valid options are: "F" for Fisher's Z-transformation; "F2" For Fisher's Z-transformation setting m=2 (default); "KG" Konishi-Gupta transformasion; "None", no transformation is applied. See *Details* for further information. |
| future_seed | Logical/Integer. The seed to be used for parallellization. Further details in furr_options. |
| workers | Integer. Number of cores to be used for parallellization. Default is 15. Capped to number of available cores minus 1. |

Details

The power and the range of the confidence interval are computed using the approach suggested in Choudhary and Nagaraja (2018). Data sets are simulated by setting the fixed effects values and the standard deviation of the random effects. The CCC and its standard error are estimated in each data set, along with its 95% confidence interval and the Wald test [Ztest](#).

Value

A data frame with the following components:

- n Number of subjects
- reps Number of replicates
- CCC. Median of the CCC estimates.
- Power. Empirical power computed as proportion of times the null hypothesis is rejected using a type-I error rate of alpha.
- SEICC. Average of CCC standard errors.
- SEZ. Average of transformed CCC standard errors.
- Range IC95. Average of CCC confidence interval widths.

References

Choudhary, P.K. and Nagaraja, H.N. (2018). Measuring Agreement-Models, Methods, and Applications. John Wiley & Sons

Examples

```
# Power to test the CCC is above 0.8 with 35 subjects and 4 replicates.
# Two methods, three times. Simulated CCC=0.87.
sim_pw<-sim_power_ccc(n = 35, nrep=4, nsim=500, r0=0.8, b = c(-0.5,0.5),
g=c(-0.25,0,0.25), mu = -0.25, sa = 4,sab=0.5,sag=1,
bg=c(-0.5,-0.25,0.25,-0.5,0.25,0.75),se = 1)
```

Ztest

Wald's test on the Concordance Correlation Coefficient

Description

Wald's test is applied to assess whether the CCC (ICC) is greater than a reference value. Additionally, Wald's test is also used to compare two independent CCC (ICC).

Usage

```
Ztest(cccfit, cccfit2 = NULL, r0 = 0, info = TRUE)
```

Arguments

| | |
|---------|---|
| cccfit | An object of class ccc. |
| cccfit2 | An object of class ccc. |
| r0 | Integer. Null hypothesis value. |
| info | Logical. Should information about the transformation used be printed? |

Details

If only one ccc is provided, the function runs a one sided test to the null hypothesis value

$$z = \frac{\hat{\theta} - \rho_0}{SE(\hat{\theta})}$$

where

$$\hat{\theta}$$

stands for the CCC estimate and

$$SE(\hat{\theta})$$

its standard error. If a second CCC is provided, the function runs a two-sided test to the null hypothesis of equality of CCCs.

$$z = \frac{\hat{\theta}_1 - \hat{\theta}_2}{\sqrt{Var(\hat{\theta}_1) + Var(\hat{\theta}_2)}}$$

. In both cases, the p-value is computed as

$$P(X > z)$$

where X follows a standard Normal distribution. The test uses the transformation indicated when the ccc object was generated.

Value

A data frame with two columns: Z, the statistical test value; and the P-value associated.

Examples

```
# Testing the CCC is above 0.8
ccc_mc=ccc_vc(bpres,"DIA","ID","METODE")
ccc_mc
Ztest(ccc_mc,r0=0.8)

# Comparing two CCC

bpres_Male <- bpres |> dplyr::filter(SEX0==1)
bpres_Female <- bpres |> dplyr::filter(SEX0==2)

ccc_DIA_Male=ccc_vc(bpres_Male,"DIA","ID","METODE")
ccc_DIA_Female=ccc_vc(bpres_Female,"DIA","ID","METODE")
Ztest(ccc_DIA_Male,ccc_DIA_Female)
```

Index

* datasets

- bdaw, [2](#)
- bfat, [2](#)
- bpres, [3](#)

bdaw, [2](#)
bfat, [2](#)
bpres, [3](#)

ccc_est_by_time, [8](#)
ccc_sim_data, [10](#)
ccc_vc, [4](#), [5](#), [8](#), [11](#), [12](#)
ccclon, [4](#)
ccclonw, [5](#)
cccUst, [6](#)
cccvc, [7](#)

furrr_options, [9](#), [11](#), [14](#)

lme_model, [16](#)

p.adjust, [9](#)

sim_power_ccc, [18](#)
simulateY, [11](#)

Ztest, [19](#), [20](#)