Package 'T2EQ'

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Type Package

Title Functions for Applying the T^2-Test for Equivalence

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Description Contains functions for applying the T^2-test for equivalence.
The T^2-test for equivalence is a multivariate two-sample equivalence test.
Distance measure of the test is the Mahalanobis distance.
For multivariate normally distributed data the T^2-test for equivalence
is exact and UMPI.
The function T2EQ() implements the T^2-test for equivalence
according to Wellek (2010) <DOI:10.1201/ebk1439808184>.
The function T2EQ.dissolution.profiles.hoffelder() implements a variant
of the T^2-test for equivalence according to Hoffelder (2016)
<http://www.ecv.de/suse_item.php?suseId=Z|pi|8430> for the
equivalence comparison of highly variable dissolution profiles.

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Contents

T2EQ-package *Functions for Applying the T^2-Test for Equivalence*

Description

Contains functions for applying the T^2-test for equivalence. The T^2-test for equivalence is a multivariate two-sample equivalence test. Distance measure of the test is the Mahalanobis distance. For multivariate normally distributed data the T^2-test for equivalence is exact and UMPI. The function T2EQ() implements the T^2-test for equivalence according to Wellek (2010). The function T2EQ.dissolution.profiles.hoffelder() implements a variant of the T^2-test for equivalence according to Hoffelder (2016) for the equivalence comparison of highly variable dissolution profiles.

Details

Index of help topics:

```
T2EQ                        Function for applying the T^2-test for
                            equivalence
T2EQ-package                Functions for Applying the T^2-Test for
                            Equivalence
T2EQ.dissolution.profiles.hoffelder
                            The T^2-test for equivalence for dissolution
                            data
ex_data_JoBS                Example dataset from Hoffelder et al. (2015)
ex_data_pharmind            Example dataset from Hoffelder (2016)
```

Author(s)

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References

Wellek, S. (2010), *Testing Statistical Hypotheses of Equivalence and Noninferiority. Second edition.* Boca Raton: Chapman & Hall/CRC.

Hoffelder, T., Goessl, R., Wellek, S. (2015). Multivariate Equivalence Tests for Use in Pharmaceutical Development. *Journal of Biopharmaceutical Statistics*, 25:3, 417-437. URL: http://dx.doi.org/10.1080/10543406.2014.920344

Hoffelder, T. (2016). Highly Variable Dissolution Profiles: Comparison of T^2-Test for Equivalence and f_2 Based Methods. *pharmind*, 78:4, 587-592. URL: http://www.ecv.de/suse_item.php?suseId=Z|pi|8430

Tsong, Y., Hammerstrom, T., Sathe, P., Shah, V.P. (1996). Statistical Assessment of Mean Differences between two Dissolution Data Sets. *Drug Information Journal*, 30:4, 1105-1112. URL: http://dx.doi.org/10.1177/009286159603000427

EMA (2010). Guidance on the Investigation of Bioequivalence. URL: http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2010/01/WC500070039.pdf

Examples

```
## Not run: A recalculation of the example evaluation in Hoffelder et al. (2015)
can be done with the following code:
## End(Not run)

data(ex_data_JoBS)
REF_JoBS <- cbind(ex_data_JoBS[ which(ex_data_JoBS$Group=='REF'), ]
            [c("Diss_15_min","Diss_20_min","Diss_25_min")])
TEST_JoBS <- cbind(ex_data_JoBS[ which(ex_data_JoBS$Group=='TEST'), ]
            [c("Diss_15_min","Diss_20_min","Diss_25_min")])
equivalence_margin_JoBS <- 0.74^2
test_T2EQ_JoBS <- T2EQ(X=REF_JoBS,Y=TEST_JoBS,eq_margin = equivalence_margin_JoBS)

## Not run: A recalculation of the results underlying Figure 1 in Hoffelder (2016)
can be done with the following code:
## End(Not run)

data(ex_data_pharmind)
REF_pharmind <- cbind(ex_data_pharmind[ which(ex_data_pharmind$Group=='REF'), ]
                [c("Diss_10_min","Diss_20_min","Diss_30_min")])
TEST_pharmind <- cbind(ex_data_pharmind[ which(ex_data_pharmind$Group=='TEST'), ]
                [c("Diss_10_min","Diss_20_min","Diss_30_min")])
test_T2EQ.dissolution.profiles.hoffelder_pharmind <-
      T2EQ.dissolution.profiles.hoffelder(X=REF_pharmind,Y=TEST_pharmind)
```

---

ex_data_JoBS *Example dataset from Hoffelder et al. (2015)*

Description

Multivariate example dataset of dissolution profiles. Dataset consists of two three-dimensional samples. The names of the three variables are "Diss_15_min","Diss_20_min" and "Diss_25_min". Variable "Group" discriminates between first sample (`Group == "REF"`) and second sample (`Group == "Test"`). Sample size is 12 per group.

Usage

```
data("ex_data_JoBS")
```

Format

A data frame with 24 observations on the following 4 variables.

`Group` a factor with levels `REF` `TEST`

`Diss_15_min` a numeric vector

`Diss_20_min` a numeric vector

`Diss_25_min` a numeric vector

Details

Example dataset from Hoffelder et al. (2015).

Source

Hoffelder, T., Goessl, R., Wellek, S. (2015), "Multivariate Equivalence Tests for Use in Pharmaceutical Development", *Journal of Biopharmaceutical Statistics*, 25:3, 417-437.

References

URL: http://dx.doi.org/10.1080/10543406.2014.920344

Examples

```
data(ex_data_JoBS)
```

---

ex_data_pharmind *Example dataset from Hoffelder (2016)*

Description

Multivariate example dataset of dissolution profiles. Dataset consists of two three-dimensional samples. The names of the three variables are "Diss_10_min","Diss_20_min" and "Diss_30_min". Variable "Group" discriminates between first sample (`Group == "REF"`) and second sample (`Group == "Test"`). Sample size is 12 per group.

Usage

```
data("ex_data_pharmind")
```

Format

A data frame with 24 observations on the following 4 variables.

`Diss_10_min` a numeric vector

`Diss_20_min` a numeric vector

`Diss_30_min` a numeric vector

`Group` a character vector

Details

Example dataset underlying Figure 1 in Hoffelder (2016).

Source

Hoffelder, T. (2016), "Highly Variable Dissolution Profiles: Comparison of T^2-Test for Equivalence and f_2 Based Methods", *pharmind*, 78:4, 587-592.

References

URL: http://www.ecv.de/suse_item.php?suseId=Z|pi|8430

Examples

```
data(ex_data_pharmind)
```

T2EQ *Function for applying the T^2-test for equivalence*

Description

The function T2EQ() implements the T^2-test for equivalence (see Wellek,2010 or Hoffelder et al., 2015). The T^2-test for equivalence is a multivariate two-sample equivalence test. Distance measure of the test is the Mahalanobis distance.

Usage

```
T2EQ(X, Y, eq_margin, alpha = 0.05, print.results = TRUE)
```

Arguments

X	numeric data matrix of the first sample. The rows of X contain the individual observations of the sample, the columns contain the variables/components of the multivariate sample.
Y	numeric data matrix of the second sample. The rows of X contain the individual observations of the sample, the columns contain the variables/components of the multivariate sample.
eq_margin	numeric (>0). The equivalence margin of the test.
alpha	numeric (0<alpha<1). The significance level of the T^2-test for equivalence. Usually set to 0.05 which is the default.
print.results	logical; if TRUE (default) summary statistics and test results are printed in the output. If NO no output is created

Details

For multivariate normally distributed data the T^2-test for equivalence is exact and UMPI.

Value

a data frame; three columns containing the results of the test

p.value	numeric; the p-value of the T^2-test for equivalence
testresult.num	numeric; 0 (null hypothesis of nonequivalence not rejected) or 1 (null hypothesis of nonequivalence rejected, decision in favor of equivalence)
testresult.text	character; test result of the T^2-test for equivalence in text mode

Author(s)

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References

Wellek, S. (2010), *Testing Statistical Hypotheses of Equivalence and Noninferiority. Second edition.* Boca Raton: Chapman & Hall/CRC.

Hoffelder, T., Goessl, R., Wellek, S. (2015). Multivariate Equivalence Tests for Use in Pharmaceutical Development. *Journal of Biopharmaceutical Statistics*, 25:3, 417-437. URL: http://dx.doi.org/10.1080/10543406.2014.920344

Examples

```
## Not run: A recalculation of the example evaluation in Hoffelder et al. (2015)
can be done with the following code:
## End(Not run)

data(ex_data_JoBS)
REF_JoBS <- cbind(ex_data_JoBS[ which(ex_data_JoBS$Group=='REF'), ]
            [c("Diss_15_min","Diss_20_min","Diss_25_min")])
TEST_JoBS <- cbind(ex_data_JoBS[ which(ex_data_JoBS$Group=='TEST'), ]
            [c("Diss_15_min","Diss_20_min","Diss_25_min")])
equivalence_margin_JoBS <- 0.74^2
test_T2EQ_JoBS <- T2EQ(X=REF_JoBS,Y=TEST_JoBS,eq_margin = equivalence_margin_JoBS)
```

T2EQ.dissolution.profiles.hoffelder

The T^2-test for equivalence for dissolution data

Description

The function `T2EQ.dissolution.profiles.hoffelder()` implements a variant of the T^2-test for equivalence analyses of highly variable dissolution profiles (see Hoffelder,2016). It is a multivariate two-sample equivalence procedure. Distance measure of the test is the Mahalanobis distance.

Usage

```
T2EQ.dissolution.profiles.hoffelder(X, Y, alpha = 0.05, print.results = TRUE)
```

Arguments

`X`	numeric data matrix of the first sample (REF). The rows of `X` contain the individual observations of the REF sample, the columns contain the variables/components of the multivariate sample. More precisely, the variables are the measured dissolution time points and the rows contain the individual dissolution profiles.

Y	numeric data matrix of the second sample (TEST). The rows of Y contain the individual observations of the TEST sample, the columns contain the variables/components of the multivariate sample. More precisely, the variables are the measured dissolution time points and the rows contain the individual dissolution profiles.
alpha	numeric (0<alpha<1). The significance level of the test. Usually set to 0.05 which is the default.
print.results	logical; if TRUE (default) summary statistics and test results are printed in the output. If NO no output is created

Details

This function implements a variant of the T^2-test for equivalence suggested in Hoffelder (2016): The equivalence margin of the test is a compromise between the suggestions of Tsong et al. (1996) and EMA (2010) requirements. See Hoffelder (2016) for a discussion on that equivalence margin.

Value

a data frame; three columns containing the results of the test

p.value	numeric; the p-value of the equivalence test according to Hoffelder (2016)
testresult.num	numeric; 0 (null hypothesis of nonequivalence not rejected) or 1 (null hypothesis of nonequivalence rejected, decision in favor of equivalence)
testresult.text	character; test result of the test in text mode

Author(s)

Thomas Hoffelder <thomas.hoffelder at boehringer-ingelheim.com>

References

Hoffelder, T. (2016). Highly Variable Dissolution Profiles: Comparison of T^2-Test for Equivalence and f_2 Based Methods. *pharmind*, 78:4, 587-592. URL: http://www.ecv.de/suse_item.php?suseId=Z|pi|8430

Wellek, S. (2010), *Testing Statistical Hypotheses of Equivalence and Noninferiority. Second edition.* Boca Raton: Chapman & Hall/CRC.

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EMA (2010). Guidance on the Investigation of Bioequivalence. URL: http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2010/01/WC500070039.pdf

Examples

```
## Not run: A recalculation of the results underlying Figure 1 in Hoffelder (2016)
can be done with the following code:
## End(Not run)
```

```
data(ex_data_pharmind)
REF_pharmind <- cbind(ex_data_pharmind[ which(ex_data_pharmind$Group=='REF'), ]
                  [c("Diss_10_min","Diss_20_min","Diss_30_min")])
TEST_pharmind <- cbind(ex_data_pharmind[ which(ex_data_pharmind$Group=='TEST'), ]
                  [c("Diss_10_min","Diss_20_min","Diss_30_min")])
test_T2EQ.dissolution.profiles.hoffelder_pharmind <-
      T2EQ.dissolution.profiles.hoffelder(X=REF_pharmind,Y=TEST_pharmind)
```

Index