Package ‘SimDissolution’

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Type Package

Title Modeling and Assessing Similarity of Drug Dissolutions Profiles

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Description Implementation of a model-based bootstrap approach for testing whether two formulations are similar. The package provides a function for fitting a pharmacokinetic model to time-concentration data and comparing the results for all five candidate models regarding the Residual Sum of Squares (RSS). The candidate set contains a First order, Hixson-Crowell, Higuchi, Weibull and a logistic model. The assessment of similarity implemented in this package is performed regarding the maximum deviation of the profiles. See Moellenhoff et al. (2018) <doi:10.1002/sim.7689> for details.

License GPL (>= 2)

Encoding UTF-8

LazyData true

Depends dplyr, alabama, mvtnorm, graphics

RoxygenNote 6.1.1

NeedsCompilation no

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**example_data**

*Time-Concentration data for two formulas*

**Description**

(Artificial) Concentration data for 2 formulas, each including 12 tablets. Concentrations are measured at six points in time.

**Usage**

```r
data(example_data)
```

**Format**

A data frame with 24 rows and 8 variables including tablet, group and measurements at six points in time.

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**f2**

*Function for computing the f2*

**Description**

Function for computing the f2, time points have to be identical. Validity criteria of the f2 have to be checked in advance. See Moellenhoff et al. (2018) <doi:10.1002/sim.7689>

**Usage**

```r
f2(conc1, conc2)
```

**Arguments**

- `conc1, conc2` data frames containing the concentrations obtained for each of the two formulations

**Value**

a single value for the f2

**References**


**Examples**

```r
data(example_data)
conc1<-select(filter(example_data,Group=="1"),-Tablet,-Group)
conc2<-select(filter(example_data,Group=="2"),-Tablet,-Group)
f2(conc1=conc1,conc2=conc2)
```
fit_pharm_mod

Fitting a pharmacokinetic model to concentration data

Description

This function fits a pharmacokinetic model (dissolution profile) to time-concentration data using non-linear least squares regression. The model can be chosen from a candidate set containing a First order, Hixson-Crowell, Higuchi, Weibull and a logistic model. See Moellenhoff et al. (2018) <doi:10.1002/sim.7689> for details.

Usage

```r
fit_pharm_mod(time, conc, m, plot = TRUE)
```

Arguments

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>time</td>
<td>a vector containing the time points of measurements</td>
</tr>
<tr>
<td>conc</td>
<td>data frame or matrix containing the concentrations (see the example)</td>
</tr>
<tr>
<td>m</td>
<td>model type. Built-in models are &quot;firstorder&quot;, &quot;hixson&quot;, &quot;higuchi&quot;, &quot;weibull&quot; and &quot;logistic&quot;</td>
</tr>
<tr>
<td>plot</td>
<td>plot of the model, default is TRUE.</td>
</tr>
</tbody>
</table>

Value

A list containing the model type and the obtained parameters, further the RSS for all possible models. Furthermore a plot is given.

References


Examples

```r
data(example_data)
conc1 <- select(filter(example_data, Group=="1"),-Tablet,-Group)
time <- c(10,15,20,30,45,60)
fit_pharm_mod(time,conc1,m="logistic")
```
**sim_test**

*Bootstrap test for the assessment of similarity of drug dissolutions profiles via maximum deviation*

**Description**

Function for testing whether two dissolution profiles are similar concerning the hypotheses $H_0 : \max_{t \in T} |m_1(t, \beta_1) - m_2(t, \beta_2)| \geq \epsilon$ vs. $H_1 : \max_{t \in T} |m_1(t, \beta_1) - m_2(t, \beta_2)| < \epsilon$.

$m_1$ and $m_2$ are pharmacokinetic models chosen from a candidate set containing a First order, Hixson-Crowell, Higuchi, Weibull and a logistic model.


**Usage**

```
sim_test(time1, time2 = time1, conc1, conc2, m1, m2, epsilon = 10, B = 1000, plot = FALSE)
```

**Arguments**

- `time1, time2` vectors containing the time points of measurements for each of the two formulations; if not further specified the time points are identical in both groups
- `conc1, conc2` data frames or matrices containing the concentrations obtained for each of the two formulations (see the example)
- `m1, m2` model types. Built-in models are "firstorder", "hixson", "higuchi", "weibull" and "logistic"
- `epsilon` positive argument specifying the equivalence threshold (in %), default is 10% corresponding to an f2 of 50 according to current guidelines
- `B` number of bootstrap replications. If missing, default value of B is 1000
- `plot` if TRUE, a plot of the absolute difference curve of the two estimated models will be given. The default is FALSE.

**Value**

A list containing the p.value, the types of models, the f2, the maximum absolute difference of the models, the estimated model parameters, the number of bootstrap replications and a summary of the bootstrap test statistic. Furthermore plots of the two models are given.

**References**

Examples

data(example_data)
conc1 <- select(filter(example_data,Group=="1"),-Tablet,-Group)
conc2 <- select(filter(example_data,Group=="2"),-Tablet,-Group)
time <- c(10,15,20,30,45,60)
sim_test(time1=time,time2=time,conc1=conc1,conc2=conc2,m1="logistic",m2="logistic",B=500,plot=TRUE)
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