

Package: tumgr (via r-universe)

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Type Package

Title Tumor Growth Rate Analysis

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<https://github.com/wilkersj/tumgr>

Depends R (>= 3.1.0), minpack.lm

Description A tool to obtain tumor growth rates from clinical trial patient data. Output includes individual and summary data for tumor growth rate estimates as well as optional plots of the observed and predicted tumor quantity over time.

LazyData true

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Suggests testthat

Repository <https://wilkersj.r-universe.dev>

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Description

Function to obtain tumor growth rates from clinical trial patient data. Output includes individual and summary data for tumor growth (g), decay (d) and phi (ϕ) estimates as well as optional plots of the observed and predicted tumor quantity over time. Tumor growth rates can be used to compare treatment efficacy and help predict overall survival in clinical trial datasets.

Usage

```
gdrate(input, pval, plots)
```

Arguments

input	A data frame containing patient tumor measurement data to be analyzed. This data frame should consist of the following three columns (with respective column names): "name" which contains a numeric value that uniquely identifies the patient for the respective row data, "date" which contains a numeric value for the day of evaluation for the respective row data, and "size" which contains the numeric value for the tumor quantity measurement (i.e., CT scan, PSA, CTN, CEA, etc.) for the respective row data. Each row of data for a patient should have a unique day of evaluation (i.e., if there are multiple lesions with measurements for a patient on a given day, then the sum of those measurements should be used as the value of tumor quantity in the "size" column for that day of evaluation).
pval	A numerical value indicating the p-value level desired for analysis (e.g., 0.05 or 0.10).
plots	A logical value for plot generation of the observed and predicted tumor quantity over time (use TRUE to generate plots).

Details

The regression-growth models used to generate growth rates are based on the assumption that change in tumor quantity during therapy results from two independent component processes: an exponential decrease or regression, d , and an exponential growth or regrowth of the tumor, g . The model for this is displayed below (labeled as gd) where $f(t)$ is the tumor quantity at time t in days, normalized to the tumor quantity at time 0, d is the rate of decay, and g is the rate of growth.

$$f(t) = e^{-dt} + e^{gt} - 1$$

For data showing continuous decrease from the start of treatment, g is eliminated as shown below (labeled as dx).

$$f(t) = e^{-dt}$$

Similarly, d is eliminated when data show a continuous growth from the start of treatment as shown below (labeled as gx).

$$f(t) = e^{gt}$$

The fourth model (below) contains an additional parameter, ϕ , which represents the proportion of tumor cells that undergo cell death due to therapy (labeled as $gdphi$).

$$f(t) = (\phi)e^{-dt} + (1 - \phi)e^{gt}$$

The Levenberg-Marquardt algorithm is used to solve these 4 non-linear least squares problems (using package **minpack.lm**) and among models where all parameters are significant predictors (given user supplied `pval`), the model which minimizes the AIC is the selected model for a given patient from which tumor growth rates are obtained (this output is contained in `results`). The port algorithm is attempted where the *gdphi* model does not converge.

Patients with insufficient or missing data, or patients with sufficient data where no model converged are excluded and noted individually in `results` and summarized in `models` with one of the following explanations: no data (cases with all missing data), only 1 or 2 data points (where the latter has less than 20 percent difference in tumor measurements), error data (where only one unique measurement value for a patient that is repeated 3 or more times, and/or where both the initial and final measurement value is zero), or not fit. Patient data that does not fall into one of the categories listed above are labeled as included. Plots can be generated for all included cases (cases fit by models) by setting the `plot` argument to `TRUE`, where the observed and predicted values from the selected model (labeled in plot legend) are depicted.

Value

<code>models</code>	Data frame summarizing included (by model type selected), and excluded (by reason for exclusion) cases. Columns are described below: - Group = indicator of included or excluded status - Analyzed = indicator of whether group was analyzed - Type = either selected model or reason for exclusion - N = number of cases - Percentage = percentage of cases
<code>sumstats</code>	Data frame containing descriptive statistics of growth rate results (N, median, IQR, mean and SD). Columns are described below: - Parameter = parameter for the row data - N = the number cases with parameter - Median = median of parameter - IQR = interquartile range of parameter - Mean = mean of parameter
<code>results</code>	Data frame containing growth rate results (<i>g,d,phi</i>), an indicator of included or excluded status, and the number of evaluations for individual patients. Columns are described below:

- name = the patient identifier
- nobs = the number of data points analyzed
- type = included or excluded status
- selectedFit = model selected for patient
- g = growth rate estimate
- d = regression rate estimate
- phi = phi estimate (proportion of tumor killed by treatment)

allest Data frame containing estimates (with respective SE, T value, and p-value) from all models that converged for each patient. Columns are described below:

- name = the patient identifier
- type = included or excluded status
- selectedFit = model selected for patient
- fit = model for the row data
- parameter = parameter from the fit model
- Estimate = estimated parameter value
- StdError = standard error of the estimate
- t.value = T value for the estimated value
- p.value = p-value for the estimated value
- N = number of data points analyzed

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Examples

```
# example data
data(sampleData)

# generate plots and results
par(mfrow=c(3, 2))
out <- gdrate(sampleData, 0.05, TRUE)
par(mfrow=c(1, 1))

# summary of cases
out$models
```

```
# descriptive statistics
out$sumstats

# plot g and d distributions
res <- out$results
par(mfrow=c(2,1))
hist(res$g, col='blue', main=paste('Median g=', round(median(na.omit(res$g)), digits=6)), xlab="g")
hist(res$d, col='blue', main=paste('Median d=', round(median(na.omit(res$d)), digits=6)), xlab="d")
par(mfrow=c(1,1))
```

sampleData

Example Patient Tumor Data

Description

Sample of control arm data for package examples from a phase 3, randomized, open-label study evaluating DN-101 in combination with Docetaxel in androgen-independent prostate cancer (AIPC) (ASCENT-2). The data was obtained from Project Data Sphere (sponsor Novacea, Inc).

Usage

```
data("sampleData")
```

Format

A data frame with 1250 observations on the following 3 variables.

name a numeric vector uniquely identifying patient

date a numeric vector for the date of measurement

size a numeric vector for the measurement

Source

Project Data Sphere (sponsor Novacea, Inc). <https://www.projectdatasphere.org/projectdatasphere/html/content/89>

Examples

```
data(sampleData)
str(sampleData)
```

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