

Package ‘PDXpower’

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Type Package

Title Time to Event Outcome in Experimental Designs of Pre-Clinical Studies

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Description Conduct simulation-based customized power calculation for clustered time to event data in a mixed crossed/nested design, where a number of cell lines and a number of mice within each cell line are considered to achieve a desired statistical power, motivated by Eckel-Passow and colleagues (2021) <[doi:10.1093/neuonc/noab137](https://doi.org/10.1093/neuonc/noab137)> and Li and colleagues (2024) <[doi:10.48550/arXiv.2404.08927](https://doi.org/10.48550/arXiv.2404.08927)>. This package provides two commonly used models for powering a design, linear mixed effects and Cox frailty model. Both models account for within-subject (cell line) correlation while holding different distributional assumptions about the outcome. Alternatively, the counterparts of fixed effects model are also available, which produces similar estimates of statistical power.

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Encoding UTF-8

Depends R (>= 3.5.0),survival,stats,parallel

Imports nlme,frailtypack,ggplot2,ggpubr

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Suggests testthat (>= 3.0.0), spelling

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Contents

animals1	2
animals2	2
plotpower	3
PowANOVA	4
PowANOVADat	5
PowerTable	7
PowFrailty	9
PowFrailtyDat	11
print.PowerTable	12
SimPDXdata	13

Index	15
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animals1	<i>Simulated preliminary animals uncensored data</i>
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Description

The animals1 data frame has 18 rows and 3 columns, with all uncensored observations.

Usage

```
data(animals1)
```

Format

This data frame contains the following columns:

ID PDX line identifier.

Y time-to-event variable.

Tx treatment indicator. 0 denotes the placebo group and 1 the treatment group.

animals2	<i>Simulated preliminary animals censored data</i>
----------	--

Description

The animals2 data frame has 18 rows and 4 columns, with some censored observations.

Usage

```
data(animals2)
```

Format

This data frame contains the following columns:

ID PDX line identifier.

Y time-to-event variable.

Tx treatment indicator. 0 denotes the placebo group and 1 the treatment group.

status event status. 0 denotes right-censoring and 1 the event occurs.

plotpower	<i>A function to generate a four-panel power curve under specified number of PDX lines and number of individuals per PDX lines per treatment</i>
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Description

A function to generate a four-panel power curve under specified number of PDX lines and number of individuals per PDX lines per treatment

Usage

```
plotpower(
  object,
  ylim = c(0, 0.1),
  x.axis.n.breaks = 10,
  y.axis.n.breaks = 10,
  cut.off = 0.8,
  legend.position = "right"
)
```

Arguments

object	object of class 'PowerTable'.
ylim	limit of y axis.
x.axis.n.breaks	number of breaks of the x axis. Default is 10.
y.axis.n.breaks	number of breaks of the y axis. Default is 10.
cut.off	a number to indicate the cut-off for power analysis. Default is 0.8.
legend.position	the position of legends ("none", "left", "right", "bottom", "top", or two-element numeric vector).

Value

a figure generated by ggplot.

 PowANOVA

A function to obtain a power table with the combination of various number of PDX lines and number of individuals per PDX lines per treatment based on a prior knowledge of median survival

Description

A function to obtain a power table with the combination of various number of PDX lines and number of individuals per PDX lines per treatment based on a prior knowledge of median survival

Usage

```
PowANOVA(
  ctl.med.surv = 2.4,
  tx.med.surv = 4.8,
  tau2 = NULL,
  icc = 0.1,
  sigma2 = 1,
  n = NULL,
  m = NULL,
  sim = 100,
  two.sided = TRUE,
  alpha = 0.05,
  fixed.effect = FALSE,
  ncores = NULL
)
```

Arguments

ctl.med.surv	a numeric value of the hypothesized medial survival in the control arm. Default is 2.4.
tx.med.surv	a numeric value of the hypothesized medial survival in the treatment arm. Default is 4.8.
tau2	variance of PDX line specific random effect. Default is NULL. tau2 should be specified only when icc is set as NULL.
icc	intraclass correlation coefficient. Default is 0.1. If icc is specified, then tau2 will be calculated automatically. Otherwise, tau2 must be specified.
sigma2	variance of random error.
n	an integer number to specify the number of PDX lines.
m	an integer number to specify the number of individuals per PDX line per treatment.
sim	Number of Monte Carlo samples to be generated. Default is 100.
two.sided	A logical value to indicate if a two-sided hypothesis testing is conducted. Default is TRUE.

alpha significance level. Default is 0.05.
 fixed.effect logical value to indicate if a fixed effects only model is fitted. Default is FALSE.
 ncores number of cores for parallel computation.

Value

Object of PowANOVA with elements
 PowTab the estimates of statistical power across n and m.

Examples

```
require(PDXpower)
PowTab <- PowANOVA(ct1.med.surv = 2.4, tx.med.surv = 4.8, sim = 5, icc = 0.4,
n = 3, m = 2, ncores = 1)
PowTab
plotpower(PowTab, ylim = c(0, 1))
```

PowANOVADat	<i>A function to obtain a power table with the combination of various number of PDX lines and number of individuals per PDX lines per treatment based on a preliminary dataset</i>
-------------	--

Description

A function to obtain a power table with the combination of various number of PDX lines and number of individuals per PDX lines per treatment based on a preliminary dataset

Usage

```
PowANOVADat(
  data = NULL,
  formula = NULL,
  random = NULL,
  n = NULL,
  m = NULL,
  sim = 100,
  two.sided = TRUE,
  alpha = 0.05,
  fixed.effect = FALSE,
  digits = 4,
  ncores = NULL
)
```

Arguments

<code>data</code>	data.frame in which to interpret the variables named in the formula.
<code>formula</code>	a two-sided linear formula object describing the fixed-effects part of the model, with the response on the left of a <code>~</code> operator and the terms, separated by <code>+</code> operators, on the right.
<code>random</code>	an one-sided formula of the form <code>~ x1 + . . . + xn ID</code> .
<code>n</code>	an integer number to specify the number of PDX lines.
<code>m</code>	an integer number to specify the number of individuals per PDX line per treatment.
<code>sim</code>	Number of Monte Carlo samples to be generated. Default is 1000.
<code>two.sided</code>	a logical value to indicate if a two-sided hypothesis testing is conducted. Default is TRUE.
<code>alpha</code>	significance level. Default is 0.05.
<code>fixed.effect</code>	logical value to indicate if a fixed effects only model is fitted. Default is FALSE.
<code>digits</code>	digits the number of significant digits to use when printing.
<code>ncores</code>	number of cores for parallel computation.

Value

Object of PowANOVADat with elements

<code>beta</code>	the estimated treatment effect from the pilot data.
<code>tau2</code>	the estimated inter-PDX variance from the pilot data.
<code>sigma2</code>	the estimated random error variance from the pilot data.
<code>PowTab</code>	the estimates of statistical power across <code>n</code> and <code>m</code> .

Examples

```
require(PDXpower)
data(animals1)
PowTab <- PowANOVADat(data = animals1, formula = log(Y) ~ Tx, random = ~ 1|ID,
n = 3, m = 2, ncores = 1)
PowTab
plotpower(PowTab[[4]], ylim = c(0, 1))
```

PowerTable	<i>A function to obtain a power table with the combination of various number of PDX lines and number of individuals per PDX lines per treatment.</i>
------------	--

Description

A function to obtain a power table with the combination of various number of PDX lines and number of individuals per PDX lines per treatment.

Usage

```
PowerTable(  
  n,  
  m,  
  beta,  
  tau2 = 0.5,  
  alpha = 0.05,  
  lambda = 0.03,  
  nu = 2,  
  sigma2 = 1,  
  two.sided = TRUE,  
  distr = c("Weibull", "normal"),  
  Ct = 5,  
  censor = TRUE,  
  sim = 1000,  
  print = c("both", "ANOVA", "Cox-frailty"),  
  fixed.effect = FALSE,  
  ncores = NULL  
)
```

Arguments

n	an integer number to specify the number of PDX lines.
m	an integer number to specify the number of individuals per PDX line per treatment.
beta	Treatment effect for the treated group.
tau2	variance of PDX line specific random effect.
alpha	significance level. Default is 0.05.
lambda	Scale parameter of Weibull distribution for the baseline hazard.
nu	Shape parameter of Weibull distribution for the baseline hazard.
sigma2	Error variance of log survival time for both treatment groups.
two.sided	A logical value to indicate if a two-sided hypothesis testing is conducted. Default is TRUE.

distr	Distributional assumption of the simulated event time.
Ct	a fixed time point when a study is designed to end for generating type 1 censoring data.
censor	logical value of whether a censoring distribution is considered in a data generation setting. Default is TRUE.
sim	Number of Monte Carlo samples to be generated. Default is 1000.
print	a string to indicate which model result to be printed. If print = "both", then the power curves of both models will be printed. Otherwise, print a power curve from one of the two models by specifying either print = "ANOVA" or print = "Cox-frailty".
fixed.effect	logical value to indicate if a fixed effects only model is fitted. Default is FALSE.
ncores	number of cores for parallel computation.

Value

Object of class PowerTable with elements

NofLine	the number of PDX line n.
NofAnimals	the number of animals per arm per PDX line m.
ANOVARandom	the proportion of rejecting null treatment effect by fitting a ANOVA mixed effects model.
Coxrandom	the proportion of rejecting null treatment effect by fitting a Cox frailty model.
ANOVAfix	the proportion of rejecting null treatment effect by fitting a ANOVA fixed effects model if fixed.effects = TRUE.
Coxfix	the proportion of rejecting null treatment effect by fitting a Cox fixed effects model if fixed.effects = TRUE.
censoringrate	the average censoring rate across all Monte Carlo replicates.
beta	the pre-determined treatment effect.
lambda	the pre-determined scale parameter of baseline hazard for the Cox frailty model.
nu	the pre-determined shape parameter of baseline hazard for the Cox frailty model.
tau2	the pre-determined inter-PDX variance.
Ct	the pre-determined fixed time point to indicate the end of a study for type I censoring.
nsim	total number of Monte Carlo replicates.
sigma2	the pre-determined error variance for the ANOVA mixed effects model.
censor	a logical value to indicate whether type I censoring mechanism is considered for simulation.
print	a string to indicate which model is considered for simulation.
fixed.effect	a logical value to indicate whether a fixed effects model is considered for simulation.
call	match call.

See Also[plotpower](#)**Examples**

```

n <- 3
m <- 2
beta <- 0.8
lambda <- 0.3
nu <- 1
tau2 <- 0.1

fit <- PowerTable(n = n, m = m, beta = beta, lambda = lambda, nu = nu,
                 tau2 = tau2, distr = "Weibull", sim = 5,
                 censor = FALSE,
                 print = "both", ncores = 1)
plotpower(fit, ylim = c(0, 1))

```

PowFrailty

A function to obtain a power table with the combination of various number of PDX lines and number of individuals per PDX lines per treatment based on a prior knowledge of median survival

Description

A function to obtain a power table with the combination of various number of PDX lines and number of individuals per PDX lines per treatment based on a prior knowledge of median survival

Usage

```

PowFrailty(
  ctl.med.surv = 2.4,
  tx.med.surv = 4.8,
  nu = 1,
  tau2 = 0.1,
  n = NULL,
  m = NULL,
  sim = 1000,
  censor = FALSE,
  Ct = 5,
  two.sided = TRUE,
  alpha = 0.05,
  fixed.effect = FALSE,
  ncores = NULL
)

```

Arguments

<code>ctl.med.surv</code>	a numeric value of the hypothesized medial survival in the control arm. Default is 2.4.
<code>tx.med.surv</code>	a numeric value of the hypothesized medial survival in the treatment arm. Default is 4.8.
<code>nu</code>	shape parameter of Weibull distribution for the baseline hazard. Default is 1, i.e., constant failure rate.
<code>tau2</code>	variance of PDX line specific random effect. Default is 0.1.
<code>n</code>	an integer number to specify the number of PDX lines.
<code>m</code>	an integer number to specify the number of individuals per PDX line per treatment.
<code>sim</code>	Number of Monte Carlo samples to be generated. Default is 1000.
<code>censor</code>	logical value of whether a censoring distribution is considered in a data generation setting. Default is FALSE.
<code>Ct</code>	a fixed time point when a study is designed to end for generating type 1 censoring data.
<code>two.sided</code>	A logical value to indicate if a two-sided hypothesis testing is conducted. Default is TRUE.
<code>alpha</code>	significance level. Default is 0.05.
<code>fixed.effect</code>	logical value to indicate if a fixed effects only model is fitted. Default is FALSE.
<code>ncores</code>	number of cores for parallel computation.

Value

Object of `PowFrailty` with elements

`PowTab` the estimates of statistical power across `n` and `m`.

Examples

```
require(PDXpower)
PowTab <- PowFrailty(ctl.med.surv = 2.4, tx.med.surv = 4.8, sim = 100,
n = 3, m = 2, ncores = 1)
PowTab
plotpower(PowTab, ylim = c(0, 1))
```

PowFrailtyDat	<i>A function to obtain a power table with the combination of various number of PDX lines and number of individuals per PDX lines per treatment based on a preliminary dataset</i>
---------------	--

Description

A function to obtain a power table with the combination of various number of PDX lines and number of individuals per PDX lines per treatment based on a preliminary dataset

Usage

```
PowFrailtyDat(
  data = NULL,
  formula = NULL,
  maxit = 50,
  hazard = "Weibull",
  n = NULL,
  m = NULL,
  sim = 1000,
  censor = FALSE,
  Ct = 5,
  two.sided = TRUE,
  alpha = 0.05,
  fixed.effect = FALSE,
  digits = 4,
  ncores = NULL
)
```

Arguments

data	data.frame in which to interpret the variables named in the formula.
formula	a formula object, with the response on the left of a ~ operator, and the terms on the right. The response must be a survival object as returned by the Surv function.
maxit	maximum number of iterations needed for model fitting. Default is 50.
hazard	distributional assumption of the baseline hazard. Default is Weibull.
n	an integer number to specify the number of PDX lines.
m	an integer number to specify the number of individuals per PDX line per treatment.
sim	Number of Monte Carlo samples to be generated. Default is 1000.
censor	logical value of whether a censoring distribution is considered in a data generation setting. Default is FALSE.
Ct	a fixed time point when a study is designed to end for generating type 1 censoring data.

<code>two.sided</code>	A logical value to indicate if a two-sided hypothesis testing is conducted. Default is TRUE.
<code>alpha</code>	significance level. Default is 0.05.
<code>fixed.effect</code>	logical value to indicate if a fixed effects only model is fitted. Default is FALSE.
<code>digits</code>	digits the number of significant digits to use when printing.
<code>ncores</code>	number of cores for parallel computation.

Value

Object of `PowFrailtyDat` with elements

<code>lambda</code>	the estimated scale parameter of Weibull baseline hazard from the pilot data.
<code>nu</code>	the estimated shape parameter of Weibull baseline hazard from the pilot data.
<code>beta</code>	the estimated treatment effect from the pilot data.
<code>tau2</code>	the estimated inter-PDX variance from the pilot data.
<code>sigma2</code>	the estimated random error variance from the pilot data.
<code>PowTab</code>	the estimates of statistical power across <code>n</code> and <code>m</code> .

Examples

```
require(PDXpower)
data(animals2)
PowTab <- PowFrailtyDat(data = animals2, formula = Surv(Y,status) ~ Tx + cluster(ID),
n = 3, m = 2, ncores = 1)
PowTab
plotpower(PowTab[[5]], ylim = c(0, 1))
```

<code>print.PowerTable</code>	<i>Print PowerTable</i>
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Description

Print PowerTable

Usage

```
## S3 method for class 'PowerTable'
print(x, digits = 2, ...)
```

Arguments

<code>x</code>	object of class 'PowerTable'.
<code>digits</code>	the number of significant digits to use when printing.
<code>...</code>	Further arguments passed to or from other methods.

Value

Object of print.PowerTable with elements

data a data frame of estimated power across all combinations and n and m.

Author(s)

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See Also

[PowerTable](#)

SimPDXdata	<i>A function to calculate the power under pre-specified effect size, variance, and correlation using Monte Carlo sampling scheme by fitting ANOVA fixed effects model, ANOVA random effects model, Cox model, and frailty model.</i>
------------	---

Description

A function to calculate the power under pre-specified effect size, variance, and correlation using Monte Carlo sampling scheme

Usage

```
SimPDXdata(
  seed = 1000,
  n,
  m,
  beta,
  tau2,
  lambda = 0.03,
  nu = 2,
  sigma2 = 1,
  distr = c("Weibull", "normal"),
  two.sided = TRUE,
  Ct = 5,
  censor = TRUE
)
```

Arguments

seed	an integer random seed number.
n	an integer number to specify the number of PDX lines.
m	an integer number to specify the number of individuals per PDX line per treatment.

beta	Treatment effect for the treated group.
tau2	Error variance of random effect.
lambda	Scale parameter of Weibull distribution for the baseline hazard.
nu	Shape parameter of Weibull distribution for the baseline hazard.
sigma2	Error variance of log survival time for both treatment groups.
distr	distributional assumption of survival time.
two.sided	a logical value to indicate if a two-sided test is performed. Default is TRUE.
Ct	a fixed time point when a study is designed to end for generating type 1 censoring data.
censor	logical value of whether a censoring distribution is considered in a data generation setting. Default is TRUE.

Value

Object of SimPDXdata with elements

Data a simulated data.

Examples

```
require(PDXpower)
data <- SimPDXdata(n = 5, m = 3, beta = 0.8, sigma2 = 1, tau2 = 0.1,
                  distr = "normal", censor = FALSE)
```

Index

* datasets

animals1, [2](#)

animals2, [2](#)

animals1, [2](#)

animals2, [2](#)

plotpower, [3](#), [9](#)

PowANOVA, [4](#)

PowANOVADat, [5](#)

PowerTable, [7](#), [13](#)

PowFrailty, [9](#)

PowFrailtyDat, [11](#)

print.PowerTable, [12](#)

SimPDXdata, [13](#)