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>. 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, ggrepur

RoxygenNote 7.2.3

Suggests testthat (>= 3.0.0), spelling

Language en-US

LazyData true

NeedsCompilation no

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Description

The `mice1` data frame has 18 rows and 3 columns, with all uncensored observations.

Usage

```r
data(mice1)
```

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.
mice2  

Description

The `mice2` data frame has 18 rows and 4 columns, with some censored observations.

Usage

data(mice2)

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

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

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), n.breaks = NULL)

Arguments

- **object**: object of class 'PowerTable'.
- **ylim**: limit of y axis.
- **n.breaks**: number of breaks of the x axis. Default is NULL.

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

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**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**

```r
PowANOVA(
  ctl.med.surv = 2.4,
  tx.med.surv = 4.8,
  tau2 = 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 0.1.
- `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 1000.
- `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

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

PowANOVADat  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

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

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

Arguments

data  data.frame in which to interpret the variables named in the formula.

formula  a two-sided linear formula object describing the fixed-effects part of the model, with the response on the left of a ~ operator and the terms, separated by + operators, on the right.

random  an one-sided formula of the form ~ x1 + . . . + xn | ID.
PowerTable

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.

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.

$n$ 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.

$\text{sim}$ Number of Monte Carlo samples to be generated. Default is 1000.

$\text{two.sided}$ a logical value to indicate if a two-sided hypothesis testing is conducted. Default is TRUE.

$\text{alpha}$ significance level. Default is 0.05.

$\text{fixed.effect}$ logical value to indicate if a fixed effects only model is fitted. Default is FALSE.

$n\text{cores}$ number of cores for parallel computation.

Value

Object of PowANOVADat with elements

$\text{beta}$ the estimated treatment effect from the pilot data.

$\text{tau2}$ the estimated inter-PDX variance from the pilot data.

$\text{sigma2}$ the estimated random error variance from the pilot data.

$\text{PowTab}$ the estimates of statistical power across $n$ and $m$.

Examples

```
require(PDXpower)
data(mice1)
PowTab <- PowANOVADat(data = mice1, formula = log(Y) ~ Tx, random = ~ 1|ID, 
n = 3, m = 2, ncores = 1)
PowTab
plotpower(PowTab[[4]], ylim = c(0, 1))
```
**PowerTable**

**Usage**

```r
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 $n$.
- **NofMice**: the number of mice 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

```r
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)
```
PowFrailty

```r
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**

```r
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**

- `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.
- `nu` shape parameter of Weibull distribution for the baseline hazard. Default is 1, i.e., constant failure rate.
- `tau2` variance of PDX line specific random effect. Default is 0.1.
- `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.

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 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 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

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,
\begin{verbatim}
Ct = 5, 
two.sided = TRUE, 
alpha = 0.05, 
fixed.effect = FALSE, 
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.
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 PowFrailtyDat with elements

lambda: the estimated scale parameter of Weibull baseline hazard from the pilot data.
u: the estimated shape parameter of Weibull baseline hazard from the pilot data.
beta: the estimated treatment effect from the pilot data.
tau2: the estimated inter-PDX variance from the pilot data.
sigma2: the estimated random error variance from the pilot data.
PowTab: the estimates of statistical power across n and m.
\end{verbatim}
Examples

```r
require(PDXpower)
data(mice2)
PowTab <- PowFrailtyDat(data = mice2, formula = Surv(Y,status) ~ Tx + cluster(ID),
n = 3, m = 2, ncores = 1)
PowTab
plotpower(PowTab[[5]], ylim = c(0, 1))
```

---

print.PowANOVADat  

Print PowANOVADat

Description

Print PowANOVADat

Usage

```r
## S3 method for class 'PowANOVADat'
print(x, digits = 4, ...)
```

Arguments

- `x` object of class 'PowANOVADat'.
- `digits` the number of significant digits to use when printing.
- `...` Further arguments passed to or from other methods.

Value

a summary of power analysis including parameter estimates and statistical power.

Author(s)

Shanpeng Li <lishanpeng0913@ucla.edu>

See Also

PowANOVADat
### Description
Print PowerTable

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

### Arguments
- `x`: object of class 'PowerTable'.
- `digits`: the number of significant digits to use when printing.
- `...`: 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)
Shanpeng Li <lishanpeng0913@ucla.edu>

### See Also
- `PowerTable`

---

### Description
Print PowFrailtyDat

### Usage
```r
## S3 method for class 'PowFrailtyDat'
print(x, digits = 4, ...)
```

### See Also
- `PowFrailtyDat`
SimPDXdata

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.

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

  x  object of class 'PowFrailtyDat'.
  digits  the number of significant digits to use when printing.
  ...  Further arguments passed to or from other methods.

Value

  a summary of power analysis including parameter estimates and statistical power.

Author(s)

  Shanpeng Li <lishanpeng0913@ucla.edu>

See Also

  PowFrailtyDat
**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**

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