Package ‘CFAcoop’

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Description Cellular cooperation compromises the plating efficiency-based analysis of clonogenic survival data. This tool provides functions that enable a robust analysis of colony formation assay (CFA) data in presence or absence of cellular cooperation.


Power regression for parameter estimation, calculation of survival fractions, uncertainty analysis and plotting functions are provided.

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analyze_survival analyze_survival

Description

wrapper function for robust analysis of clonogenic survival data from the colony formation assay according to Brix et al. (2020), Radiation Oncology. Mean values are calculated and used for power regression. Resulting coefficients are used for calculation of survival fractions and corresponding uncertainty analysis.

Usage

analyze_survival(RD, name = "no name", xtreat = NULL, C = 20)

Arguments

RD data.frame or matrix containing a table of experiment data
name optional: experiment name (e.g. name of cell line)
xtreat optional: treatment dose of the colonies counted in the corresponding columns of RD
C number of colonies counted for which the survival fraction is to be calculated (default = 20)

Value

list object containing several experiments and treatments organized for convenient plotting with plot_sf

Examples

seeded <- rep(10*(seq(1,5,0.5), each = 3)
df.1 <- data.frame(
  "seeded" = seeded,
  "counted1" = 0.4 * seeded^{1.1} * rnorm(n = length(seeded),1,0.05),
  "counted2" = 0.2 * seeded^{1.125} * rnorm(n = length(seeded),1,0.05),
  "counted3" = 0.05 * seeded^{1.25} * rnorm(n = length(seeded),1,0.05))
df.2 <- data.frame("seeded" = seeded,
```
calculate_sf

"counted1" = 0.5 * seeded^1.01 * rnorm(n = length(seeded),1,0.05),
"counted2" = 0.4 * seeded^1.0125 * rnorm(n = length(seeded),1,0.05),
"counted3" = 0.2 * seeded^1.025 * rnorm(n = length(seeded),1,0.05))
SF <- vector("list",2)
SF[[1]] <- analyze_survival(RD = df.1,
   name = "cell line a",
   xtreat = c(0,1,4),
   C = 20)
SF[[2]] <- analyze_survival(RD = df.2,
   name = "cell line b",
   xtreat = c(0,1,4))
```

## calculate_sf

### Description

calculates the survival fraction according to the procedure presented in Brix et al. (2020), which is robust against cellular cooperation.

### Usage

calculate.sf(par_ref, par_treat, C = 20)

### Arguments

- **par_ref**: summary.lm object or 2-column matrix for the treatment-free reference survival
- **par_treat**: summary.lm object or 2-column matrix for the clonogenic survival after treatment
- **C**: colony number for which the survival fraction is calculated (default = 20)

### Value

survival fractions. If par_ref and par_treat are summary.lm objects, a scalar is returned. If par_ref and par_treat are matrices, a vector of the same length as nrow(par_treat) is returned

### Examples

```r
seeded <- 10^seq(1, 5, 0.5)
counted.ref <- 0.4 * 10^seq(1, 5, 0.5) + rnorm(n = 9, 0, 0.1)^1.1
counted.treat <- 0.01 * 10^seq(1, 5, 0.5) + rnorm(n = 9, 0, 0.1)^1.2
fit_ref <- pwr_reg(seeded = seeded, counted = counted.ref)
fit_treat <- pwr_reg(seeded = seeded, counted = counted.treat)
calculate.sf(par_ref = fit_ref, par_treat = fit_treat)
```

```r
data("CFAdata")
D <- subset.data.frame(
   x = CFAdata,
   subset = cell.line == levels(CFAdata$cell.line)[1]
)
```
fit_ref <- pwr_reg(seeded = D$'Cells seeded', counted = D$'0 Gy')
fit_treat <- pwr_reg(seeded = D$'Cells seeded', counted = D$'4 Gy')
calculate_sf(par_ref = fit_ref, par_treat = fit_treat)

CFAdata

Colony Formation Assay data on cellular cooperation

Description
Clonogenic survival data from seven cell lines T47D, MDA-MB231, A549, HCC1806, SKBR3, SKLU1 and BT20 as presented in Figure 2 in Brix et al. (2020).

Usage
data(CFAdata)

Format
data.frame

References

Examples
data(CFAdata)
head(CFAdata)
c1l <- levels(CFAdata$cell.line)

export_sf

Description
export table with results of clonogenic survival analysis from the colony formation assay considering cellular cooperation

Usage
export_sf(SF)

Arguments
SF list build of objects returned by analyze_survival
Value
data.frame containing all estimated coefficients and effects from all experiments contained in SF

Examples

seeded <- rep(10^(seq(1, 5, 0.5)), each = 3)
df.1 <- data.frame(
  "seeded" = seeded,
  "counted1" = 0.4 * seeded^1.1 * rnorm(n = length(seeded), 1, 0.05),
  "counted2" = 0.2 * seeded^1.125 * rnorm(n = length(seeded), 1, 0.05),
  "counted3" = 0.05 * seeded^1.25 * rnorm(n = length(seeded), 1, 0.05)
)
df.2 <- data.frame(
  "seeded" = seeded,
  "counted1" = 0.5 * seeded^1.01 * rnorm(n = length(seeded), 1, 0.05),
  "counted2" = 0.4 * seeded^1.0125 * rnorm(n = length(seeded), 1, 0.05),
  "counted3" = 0.2 * seeded^1.025 * rnorm(n = length(seeded), 1, 0.05)
)
SF <- vector("list", 2)
SF[[1]] <- analyze_survival(
  RD = df.1, name = "cell line a",
  xtreat = c(0, 1, 4)
)
SF[[2]] <- analyze_survival(
  RD = df.2, name = "cell line b",
  xtreat = c(0, 1, 4)
)
export_sf(SF)
data("CFAdataset")
SF <- vector("list", 4)
ll <- levels(CFAdataset$cell.line)[c(1, 3, 5, 7)]
for (i in seq_along(ll)) {
  cdat <- subset.data.frame(
    x = CFAdataset,
    subset = CFAdataset$cell.line == ll[i]
  )
  SF[[i]] <- analyze_survival(
    RD = cdat[, -1],
    name = ll[i],
    xtreat = c(0, 1, 2, 4, 6, 8)
  )
}
export_sf(SF)

plot_sf

Description
plot cellular cooperativity and clonogenic survival for colony formation assay data
Usage

plot_sf(SF, showUncertainty = TRUE)

Arguments

SF
list build of objects returned by analyze_survival
showUncertainty
logical, switches on/off uncertainty bands for sf-values.

Value

none

Examples

seeded <- rep(10^(seq(1, 5, 0.5)), each = 3)
df.1 <- data.frame(
  "seeded" = seeded,
  "counted1" = 0.4 * seeded^1.1 * rnorm(n = length(seeded), 1, 0.05),
  "counted2" = 0.2 * seeded^1.125 * rnorm(n = length(seeded), 1, 0.05),
  "counted3" = 0.05 * seeded^1.25 * rnorm(n = length(seeded), 1, 0.05)
)
df.2 <- data.frame(
  "seeded" = seeded,
  "counted1" = 0.5 * seeded^1.01 * rnorm(n = length(seeded), 1, 0.05),
  "counted2" = 0.4 * seeded^1.0125 * rnorm(n = length(seeded), 1, 0.05),
  "counted3" = 0.2 * seeded^1.025 * rnorm(n = length(seeded), 1, 0.05)
)
SF <- vector("list", 2)
SF[[1]] <- analyze_survival(
  RD = df.1, name = "cell line a",
  xtreat = c(0, 1, 4)
)
SF[[2]] <- analyze_survival(
  RD = df.2, name = "cell line b",
  xtreat = c(0, 1, 4)
)
plot_sf(SF)
data("CFAdata")
SF <- vector("list", 4)
ll <- levels(CFAdata$cell.line)[c(1, 3, 5, 7)]
for (i in seq_along(ll)) {
  cdat <- subset.data.frame(
    x = CFAdata,
    subset = CFAData$cell.line == ll[i]
  )
  SF[[i]] <- analyze_survival(
    RD = cdat[, -1],
    name = ll[i],
    xtreat = c(0, 1, 2, 4, 6, 8)
  )
plot_sf(SF)
Description

`pwr_reg` performs a power regression (log(C) = log(a) + b * log(S) + e)) for clonogenic assay data of experiments examining the cellular cooperation.

Usage

`pwr_reg(seeded, counted)`

Arguments

- `seeded` numeric vector with number of cells seeded (S)
- `counted` numeric vector with number of colonies counted (C, same length as `seeded`)

Value

summary.lm object as returned by `summary`

Examples

```r
pwr_reg(
  seeded = 10^(seq(1, 5, 0.5)),
  counted = 0.4 * (10^seq(1, 5, 0.5))^1.25 * rnorm(n = 9, 1, 0.05)
)
```

```r
data(CFAdata)
D <- subset.data.frame(
  x = CFAdata,
  subset = cell.line == levels(CFAdata$cell.line)[1]
)
pwr_reg(seeded = D$`Cells seeded`, counted = D$`0 Gy`)
```
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