Package: CFAcoop (via r-universe)

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Type Package

Title Colony Formation Assay: Taking into Account Cellular Cooperation

Version 1.0.0

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Depends R (>= 3.5.0)

URL `https://github.com/ZytoHMGU/CFAcoop`

BugReports `https://github.com/ZytoHMGU/CFAcoop/issues`

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. The implemented method has been described in Brix et al. (2020). (Brix, N., Samaga, D., Hennel, R. et al. ``The clonogenic assay: robustness of plating efficiency-based analysis is strongly compromised by cellular cooperation.'' Radiat Oncol 15, 248 (2020). <doi:10.1186/s13014-020-01697-y>) Power regression for parameter estimation, calculation of survival fractions, uncertainty analysis and plotting functions are provided.

License GPL-3

Encoding UTF-8

LazyData true

RoxygenNote 7.1.1

Imports Hmisc

Suggests knitr, rmarkdown, testthat

VignetteBuilder knitr

Repository https://zytohmgu.r-universe.dev

RemoteUrl https://github.com/zytohmgu/cfacoop

RemoteRef HEAD

RemoteSha 39bb6d02387d0f00f2cad4f03e38901c078d4cc4

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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,
```

```
  "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` *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

```
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)
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

Brix, N., Samaga, D., Hennel, R. et al. "The clonogenic assay: robustness of plating efficiency-based analysis is strongly compromised by cellular cooperation." Radiat Oncol 15, 248 (2020). <doi:10.1186/s13014-020-01697-y>

Examples

```
data(CFAdata)
head(CFAdata)
cll <- levels(CFAdata$cell.line)
```

`export_sf` *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("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)
  )
}
export_sf(SF)
```

`plot_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)
```

`pwr_reg` *pwr_reg*

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

```
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)
)
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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