Package ‘populationPDXdesign’

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Type Package

Title Designing Population PDX Studies

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Description Run simulations to assess the impact of various designs features and the underlying biological behaviour on the outcome of a Patient Derived Xenograft (PDX) population study. This project can either be deployed to a server as a 'shiny' app or installed locally as a package and run the app using the command 'populationPDXdesignApp()'.

License GPL (>= 3)

Depends R (>= 3.0.0)

Imports devtools, ggplot2, plyr, roxygen2, shiny, shinyCSSloaders

Suggests testthat

ROxygenNote 6.0.1

NeedsCompilation no

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**callsInSingleExperiment**

*Simulation of a single population PDX experiment*

**Description**

This is an internal function. Please use cautiously if calling directly. Samples some animals and classify as responders or non-responders based on number of models studied (PDXn), number of mice measured per model (PDXr), the classification accuracy (C_Acc) and the underlying biological response rate (Biol_RR). Example usage: `callsInSingleExperiment(PDXn=8, PDXr=3, C_Acc=0.95, Biol_RR=30)`

**Usage**

`callsInSingleExperiment(PDXn, PDXr, C_Acc, Biol_RR)`

**Arguments**

- **PDXn**: number of PDX models studied
- **PDXr**: number of mice measured per PDX model
- **C_Acc**: classification accuracy
- **Biol_RR**: underlying biological response rate for this treatment

**Value**

Dataframe with three columns:
- **PDXModel**: a string that indicates the model id
- **PDXclassification**: a numeric value that indicates the true biological classification of that PDX - 0 equal non-responder and 1 equal responder
- **StudyResult**: a numeric value that indicates the classification of the PDX model after sampling - 0 equal non-responder and 1 equal responder

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getMode

Function to return the mode of a vector of values

Description
This is an internal function. Please use cautiously if calling directly. Returns the mode from numeric vector. Example usage: `getMode(c(0,1,1))`

Usage
```r
getMode(v)
```

Arguments
- `v` vector of numeric values

Value
- a numeric value

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noFalseCalls

Function to calculate the number of false calls for a design for a go-no go threshold

Description
This is an internal function. Please use cautiously if calling directly. Returns the number of false calls from a simulation study exploring the impact of varying PDXn and PDXr for an underlying Biol_RR for a particularly go-no go threshold. A false call can only arise in the situation where the underlying Biol_RR is below the go-no go threshold. Example usage: `noFalseCalls(impactvarying_pdxn_pdxr_Brr, gonogothreshold=SPI)`

Usage
```r
noFalseCalls(dataset, gonogothreshold)
```

Arguments
- `dataset` dataset obtained as output from the `varying_PDXn_PDXr` function
- `gonogothreshold` go-no go threshold
Value

vector with three elements:
- numeric value indicating the number of experiments simulated
- numeric value indicating the number of experiments which were above the go-no go threshold
- numeric value indicating the FPR

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nomissedcalls
Function to calculate the number of missed calls for a design for a go-no go threshold

Description

This is an internal function. Please use cautiously if calling directly. Returns the number of missed calls from a simulation study exploring the impact of varying PDXn and PDXr for an underlying Biol_RR for a particularly go-no go threshold. A missed call can only arise in the situation where the underlying Biol_RR exceeds the go-no go threshold. Example usage: nomissedCalls(ImpactVarying_PDXn_PDXr_BRR, GoNoGoThreshold)

Usage

nomissedCalls(dataset, GoNoGoThreshold)

Arguments

dataset dataset obtained as output from the 'varying_PDXn_PDXr' function
GoNoGoThreshold go-no go threshold

Value

vector with three elements:
- numeric value indicating the number of experiments simulated
- numeric value indicating the number of experiments which were below the go-no go threshold
- numeric value indicating the percent of missed calls

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outcomeInSingleExperiment

Function to summarise the results for a single simulation representing one experiment

Description

This is an internal function. Please use cautiously if calling directly. From a simulation of a single experiment, the estimated response rate is determined and captured with the meta data (e.g. PDXn, PDXr) for that experiment. Example usage: outcomeInSingleExperiment(df=outcomeInSingleExperiment_1, PDXn=8, PDXr=3, C_Acc=0.95, Biol_RR=SPI)

Usage

outcomeInSingleExperiment(df, PDXn, PDXr, C_Acc, Biol_RR)

Arguments

df data frame from callsInSingleExperiment
PDXn PDXn
PDXr PDXr
C_Acc the classification accuracy (numeric value between 0 and 1)
Biol_RR Biol_RR

Value

a vector with 8 values that captures the input design and the estimated response rate for that design from a single simulation

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outcomeMultipleExperiments

Function to run simulations to mimic population PDX studies for a defined scenario

Description

This is an internal function. Please use cautiously if calling directly. Simulations are used to mimic population PDX studies for specified values of PDXn, PDXr, Biol_RR and C_Acc. Example usage: outcomeMultipleExperiments(PDXn=8, PDXr=3, C_Acc=0.95, Biol_RR=30, iterations=500)
plotFalsepositive

Usage

outcomeMultipleExperiments(PDXn, PDFx, C_Acc, Biol_RR, iterations)

Arguments

- PDXn: PDXn
- PDFx: PDFx
- C_Acc: the classification accuracy (numeric value between 0 and 1)
- Biol_RR: Biol_RR
- iterations: no of experiments to simulated

Value

a dataframe where each row represents the results from a simulation mimicking an individual experiment for a particular design with meta data returned to describe the experimental design

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plotFalsepositive

- A function to visualise the false positive rate as a function of PDXn and PDFx

Description

This is an internal function. Please use cautiously if calling directly. A visualisation of the false positive rate behaviour from the simulations

Usage

plotFalsepositive(data)

Arguments

- data: data frame with four columns which indicate the PDXn, PDFx, Biol_RR and the FPR for a specified go-no go threshold

Value

a graphic visualisation

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plotSensitivity

A function to visualise the sensitivity as a function of PDXn and PDXr

Description
This is an internal function. Please use cautiously if calling directly. A visualisation of the sensitivity from the simulations

Usage
plotSensitivity(data)

Arguments
data       data frame with four columns which indicate the PDXn, PDXr, Biol_RR and the MissedCalls for a specified go-no go threshold

Value
a graphic visualisation

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populationPDXdesignApp

Function populationPDXdesignApp

Description
Runs the 'shiny' app.

Usage
populationPDXdesignApp()

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Examples

```r
if (interactive()) {
  populationPDXdesignApp()
}
```

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**server**

*shiny* app server function

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**Description**

This is an internal function. Please use cautiously if calling directly.

**Usage**

```r
server(input, output, session)
```

**Arguments**

- `input`
- `output`
- `session`

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**ui**

*shiny* app user interface function

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**Description**

This is an internal function. Please use cautiously if calling directly.

**Usage**

```r
ui()
```

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varyingPDXnPDXrBiolRR  

Function to run simulations to mimic population PDX studies for variety of experimental and biological scenarios

Description

This is an internal function. Please use cautiously if calling directly. Simulations are used to mimic population PDX studies by inputing a variety of experimental factors (PDXn and PDXr) and biological factors (Biol_RR and C_Acc). Example usage: varyingPDXnPDXrBiolRR(PDXn_range=c(8,10,12), PDXr_range=c(1,5), Biol_rr_range=c(5,15), c_acc=PN95, iterations=5)

Usage

varyingPDXnPDXrBiolRR(PDXn_range, PDXr_range, Biol_rr_range, C_acc, iterations)

Arguments

- PDXn_range  
  a vector of PDXn values to study
- PDXr_range  
  a vector of PDXr values to study
- Biol_RR_range  
  a vector of values between 0 and 100 to indicate the Biol_RR to study
- C_Acc  
  the classification accuracy (numeric value between 0 and 1)
- iterations  
  iterations

Value

a dataframe where each row represents the results from a simulation mimicking an individual experiment for a particular design with meta data returned to describe the experimental design

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