Package 'POD'

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Type Package

Title Probability of Detection for Qualitative PCR Methods

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Description This tool computes the probability of detection (POD) curve and the limit of detection (LOD), i.e. the number of copies of the target DNA sequence required to ensure a 95 % probability of detection (LOD95). Other quantiles of the LOD can be specified. This is a reimplementation of the mathematical-statistical modelling of the validation of qualitative polymerase chain reaction (PCR) methods within a single laboratory as provided by the commercial tool 'PROLab' <http://quodata.de/>. The modelling itself has been described by Uhlig et al. (2015) <doi:10.1007/s00769-015-1112-9>.

License GPL-3

Encoding UTF-8

LazyData true

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R topics documented:

`analyzeSingleLab` *Analyze Single Lab Qualitative PCR Outcomes*

Description

Compute the POD curve and the LOD value to validate a qualitative PCR method of a single laboratory.

Usage

```
analyzeSingleLab(x = NULL, X = NULL, S = NULL, N = NULL,
  qLOD = 95, b = 1)
```

Arguments

`x`	A matrix or dataframe with columns 'X', 'S' and 'N'.
`X`	Nominal DNA concentration.
`S`	Number of successfull PCR outcomes.
`N`	Total number of PCR experiments.
`qLOD`	The quantile(s) for the Limit Of Detection (LOD). Divided by 100 if greater than one.
`b`	Fixed value for the corrective parameter

Details

According to the suggestion of Uhlig et al. (2015), the corrective parameter b is set to 1 if it is close to 1 (simplified fit). However, if sensitivity is better than achievable according to the theoretical POD curve or average amplification probability is higher at higher dilution levels than at lower dilution levels, the b is estimated from the data (full fit). The value of b can be changed by the user. However, it is not recommended to do so.

Value

A list with following items

x Input data plus extra columns

b The parameter b, as provided by the user

fit.glm.simple Results for the simplified GLM

fit.glm.full Results for the full GLM

where "fit.glm.simple" and "fit.glm.full" are lists with the following parameters

b The parameter b (estimated from the model)

lambda The parameter λ (estimated from the model)

model The generalized linear model (GLM) fit to the data

lod A named vector of LOD values

lodci The 95% confidence interval of the LOD

warn A character vector containing warnings that appeared during GLM fit

References

Uhlig et al. Accred Qual Assur (2015) 20: 75. https://doi.org/10.1007/s00769-015-1112-9

Examples

```
x <- cbind(
 X=c(0.1,1,2,5,10,20),
 S=c( 0,5,6,6,6,6 ),
 N=c( 6,6,6,6,6,6 )
)
obj <- analyzeSingleLab(x=x)
```

`computePOD` *Compute the Probability Of Detection (POD)*

Description

Compute the Probability Of Detection (POD) in qualitative PCR experiments carried out by a single laboratory.

Usage

```
computePOD(x, lambda = 1, b = 1)
```

Arguments

`x`	Nominal DNA concentrations (numeric vector)
`lambda`	The fraction of detected DNA fragments (numeric scalar)
`b`	correction parameter (numeric scalar)

Value

The POD function as described in Uhlig et al., 2015

References

Uhlig et al. Accred Qual Assur (2015) 20: 75. https://doi.org/10.1007/s00769-015-1112-9

Examples

```
# the optimal POD
computePOD(exp(seq(1, 10, 1)), 1, 1)
# some other POD
computePOD(exp(seq(1, 10, 1)), 0.5, 1.29)
```

`foreign` *Support Other Platforms*

Description

Export formatted data or code for use by other platforms

Usage

```
exportQuodata(obj)

exportSAS(obj)

exportExcelMacro(dest)
```

Arguments

`obj`	A list returned by `analyzeSingleLab`.
`dest`	The path to write the excel macro to.

Details

The output of exportQuodata can be used on the QuoData website (http://quodata.de/content/validation-qualitative-pcr-methods-single-laboratory). Function `exportExcelMacro()` creates an Excel macro in the specified directory. Existing files will not be overwritten!

Value

Nothing is returned by `exportQuodata()` and `exportSAS()`. Function `exportExcelMacro()` returns a boolean, `FALSE` if a file with name 'pod.xlsm' already exists, `TRUE` otherwise.

Examples

```
x <- cbind(
 X=c( 0.1,1,2,5,10,20 ),
 S=c( 0,5,6,6,6,6 ),
 N=c( 6,6,6,6,6,6 )
)
obj <- analyzeSingleLab(x=x)
exportQuodata(obj)
```

plotPOD *Generate Plot to Analyze Single Lab PCR Outcomes*

Description

Show POD curve and LOD value to validate qualitative PCR methods of a single laboratory.

Usage

```
plotPOD(obj, model = c("auto", "simple", "full"), qLOD = 95,
  show.ci = TRUE, show.warnings = FALSE)
```

Arguments

obj	A list returned by analyzeSingleLab.
model	Simple or full model
qLOD	The quantile(s) for LOD to be shown in the plot. Multiplied by 100 if less than one.
show.ci	Show the confidence interval of the LOD in the plot.
show.warnings	Show the warning regarding significant deviation from 1 in the plot.

Details

The graph generated by this function gives the laboratory-specific rates of detection (RODs) as blue diamonds. The blue curve denotes the mean POD curve along with the corresponding 95% confidence range highlighted as the grey band. The POD curve under ideal conditions is displayed as the black dashed curve.

If model is set to "auto", a plausiblity test is applied to determine if the POD curve bases on the simplified or on full parameter estimation. If the corrective parameter determined from the full model significantly differs from 1, a message is shown in the plot. Testing for significant deviation is currently done by checking the condition $1 - b > 0.2$. The threshould 0.2 has been determined empirically to agree with the original webtool and might be changed in future versions of the package.

Three cases can be distinguished. First, the value for the slope parameter b is significantly less than 1. This means the average amplification probability is higher at higher dilution levels than at lower dilution levels. Such a situation can be related to: inhibitory matrix effects, a large variability in the amplification process from the one test to another under repeatability conditions, or accidental problems causing false positives if the number of copies of the target DNA sequence is less than 1. Second, the calculated POD curve indicates sensitivity better than achievable according to the theoretical POD curve. Third, the number of positive test results is significantly higher than expected at nominal copies of nominal DNA concentrations in $[0.5, 1.5]$. In this case check the correctness of the serial dilution.

Another warning appears if the LOD of interest exceeds the highest number of considered nominal copies.

Value

The passed list 'obj' is returned invisibly.

Examples

```
x <- cbind(
 X=c(0.1,1,2,5,10,20),
 S=c( 0,5,6,6,6,6 ),
 N=c( 6,6,6,6,6,6 )
)
obj <- analyzeSingleLab(x=x)
plotPOD(obj)
```

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print.pod *Summary of POD objects*

Description

Generate nicely formatted output of the POD object

Usage

```
## S3 method for class 'pod'
print(x, ...)
```

Arguments

x	An object of class 'pod'
...	Other parameters, not supported yet.

Value

Nothing is returned.

Examples

```
x <- cbind(
 X=c( 0.1,1,2,5,10,20 ),
 S=c( 0,5,6,6,6,6 ),
 N=c( 6,6,6,6,6,6 )
)
obj <- analyzeSingleLab(x=x)
print(obj)

obj <- analyzeSingleLab(x=x, qLOD=c(50, 70, 95))
print(obj)
```

testdata *Get Test Data*

Description

Some data to test the functionality of the package

Usage

```
grohmann2015collaborative(lab = NULL)

sas.logistic()
```

Arguments

lab	A numeric vector indicating from which laboratory the data should be taken.

Value

If a lab is not NULL, a data.frame with three columns ('X', 'S', 'N') is returned. If lab is NULL, these three columns are supplemented by a fourth column indicating the laboratory.

Data grohmann2015collaborative was generated by Grohmann et al. (2015) and has been used as exemplary data by Uhlig et al. (2015) to assess performance of their statistical approach to validate PCR results. Data sas.logistic was taken from the part of the SAS manual dealing with logistic regression (https://support.sas.com/documentation/onlinedoc/stat/ex_code/132/logiex14.html).

References

Grohmann et al. Accred Qual Assur (2015) 20: 85. https://doi.org/10.1007/s00769-015-1108-5
Uhlig et al. Accred Qual Assur (2015) 20: 75. https://doi.org/10.1007/s00769-015-1112-9

Examples

```
x.all <- grohmann2015collaborative()
x.5 <- grohmann2015collaborative(5)
sas <- sas.logistic()
```

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