Package 'SLDAssay'

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Type Package

Title Software for Analyzing Limiting Dilution Assays

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Description Calculates maximum likelihood estimate, exact and asymptotic confidence intervals, and exact and asymptotic goodness of fit p-values for concentration of infectious units from serial limiting dilution assays. This package uses the likelihood equation, exact goodness of fit p-values, and exact confidence intervals described in Meyers et al. (1994) <http://jcm.asm.org/content/32/3/732.full.pdf>. This software is also implemented as a web application through the Shiny R package <https://iupm.shinyapps.io/sldassay/>.

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LazyData TRUE

Imports compiler

Depends R (>= 3.2.1)

RoxygenNote 5.0.1

NeedsCompilation no

Repository CRAN

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R topics documented:

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get.mle   *IUPM, PGOF, and CI*

Description

Calculates the maximum likelihood estimate of concentration of infectious units from a single serial limiting dilution (SLD) assay. Also calculates corresponding exact and asymptotic confidence intervals, and a goodness-of-fit p-value. While this package was developed with the purpose of estimating IUPM, it is applicable to SLD assays in general.

Usage

```
get.mle(pos, replicates, dilutions, monte = 15000, conf.level = 0.95,
  iupm = TRUE, na.rm = FALSE)
```

Arguments

pos	Vector of number of positive wells at each dilution level (outcome of SLD Assay)
replicates	Vector of number of replicates at each dilution level
dilutions	Vector of number of cells per well at each dilution level
monte	Number of Monte Carlo samples. Default is exact (no MC sampling), unless more than 15,000 possible positive well outcomes exist, in which case 15,000 MC samples are taken. Use monte=F for exact computation.
conf.level	Confidence level of the interval.
iupm	Boolean variable, indicates whether to return MLE as IUPM (TRUE) or probability a cell is infected (FALSE)
na.rm	Boolean variable, indicates whether dilution levels valued NA should be stripped before the computation proceeds (FALSE)

Value

MLE	Maximum likelihood estimate for the given outcome vector.
BC_MLE	Bias corrected maximum likelihood estimate for the given outcome vector.
Exact_PGOF	P value for goodness of fit. PGOF is the probability of an experimental result as rare as or rarer than that obtained, assuming that the model is correct. Low values of PGOF, (e.g. PGOF < 0.01), indicate rare or implausible experimental results. Samples with a very low PGOF might be considered for retesting.
Asymp_PGOF	P value calculated using an asymptotic Chi-Squared distribution with D-1 degrees of freedom, where D is the number of dilution levels in an SLD assay.
Exact_CI	Exact confidence interval, computed from the likelihood ratio test (recommended)
Asymp_CI	Wald asymptotic confidence interval, based on the normal approximation to the binomial distribution.

References

Myers, L. E., McQuay, L. J., & Hollinger, F. B. (1994). Dilution assay statistics. Journal of Clinical Microbiology, 32(3), 732-739. DOI:10.1.1.116.1568

Examples

```
# Duplicates row 4 of Table 4 from Myers, et. al.
# Myers et. al. divides IUPM space into discrete values. This package searches
# entire parameter space, yielding a slightly different and more accurate MLE.
row4 <- get.mle(pos=c(2,1,0,0,0,0),  # Number of positive wells per dilution level
                replicates=rep(2,6), # Number of replicates per dilution level
                dilutions=c(1e6,2e5,4e4,8e3,1600,320), # Cells per dilution level
                conf.level=0.95,   # Significance level
                iupm=TRUE,              # Display MLE in infected units per million
                )

# Duplicates row 21 of Table 4 from Myers, et. al.
# Low PGOF example
# Myers et. al. divides IUPM space into discrete values. This package searches
# entire parameter space, yielding a slightly different and more accurate MLE.
row21 <- get.mle(pos=c(2,2,2,0,1,0),
                replicates=rep(2,6),
                dilutions=c(1e6,2e5,4e4,8e3,1600,320),
                conf.level=0.95,
                iupm=TRUE)

# Example calculating IUs per cell for an assay with 1 DL.
 iu.example <- get.mle(pos=7, replicates=8, dilutions=25,
                       conf.level=0.95, iupm=FALSE)

# Monte Carlo example
# 67,081 total possible positive well outcomes, therefore
# Monte Carlo sampling is used to reduce computation time.
MC.example <- get.mle(pos=c(30,9,1,0),
                       replicates=c(36,36,6,6),
                       dilutions=c(2.5e6,5e5,1e5,2.5e4),
                       conf.level=0.95,
                       monte = 5000,
                       iupm=TRUE )
```

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