Package ‘ssize.fdr’

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Description This package contains a set of functions that calculates appropriate sample sizes for one-sample t-tests, two-sample t-tests, and F-tests for microarray experiments based on desired power while controlling for false discovery rates. For all tests, the standard deviations (variances) among genes can be assumed fixed or random. This is also true for effect sizes among genes in one-sample and two sample experiments. Functions also output a chart of power versus sample size, a table of power at different sample sizes, and a table of critical test values at different sample sizes.
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Sample Size Calculations for Microarray Experiments

Description

This package calculates appropriate sample sizes for one-sample, two-sample, and multi-sample microarray experiments for a desired power of the test. Sample sizes are calculated under controlled false discovery rates and fixed proportions of non-differentially expressed genes. Outputs a graph of power versus sample size.

Details

Package: ssize.fdr
Type: Package
Version: 1.2
Date: 2015-02-21
License: GPL-3

For all functions, the user inputs the desired power, the false discovery rate to be controlled, the proportion(s) of non-differentially expressed genes, and the maximum possible sample size to be used in calculations. If the user inputs a vector of proportions of non-differentially expressed genes, sample size calculations are performed for each proportion. For the function ssize.twosamp, the user must additionally input the common difference in mean treatment expressions as well as the common standard deviation for all genes. This becomes the common effect size and common standard deviation for all genes when using the function ssize.onesamp. For the function ssize.twosampvary (ssize.onesampvary) the differences in mean treatment expressions (effect sizes) are assumed to follow a normal distribution and the variances among genes are assumed to follow an inverse gamma distribution, so parameters for these distributions must be entered. For the function ssize.F, the design matrix of the experiment, the parameter vector, and an optional coefficient matrix or vector of linear contrasts of interest must also be entered. The function ssize.Fvary allows the variances of the genes to follow an inverse gamma distribution, so the shape and scale parameters must be specified by the user.

Author(s)

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References


Examples
a<-0.05 #false discovery rate to be controlled
pwr<-0.8 #desired power
p0<-c(0.5,0.9,0.95) #proportions of non-differentially expressed genes
N<-20; N1<-35 #maximum sample size for calculations

##Example of function ssize.nonesamp
d<-1 #effect size
s<-0.5 #standard deviation
os$ssize<-ssize.nonesamp(delta=d,sigma=s,fdr=a,pwr,p0=maxN=N1,s=side="two-sided")
os$$size #first sample sizes to reach desired power
os$power #calculated power for each sample size
os$crit.vals #calculated critical value for each sample size

##Example of function ssize.nonesamp.vary
dm<-2; ds<-1 #the effect sizes of the genes follow a Normal(2,1) distribution
alph<-3; beta<-1 #the variances of the genes follow an Inverse Gamma(3,1) distribution.
osv$ssize<ssize.nonesamp.vary(delta=dm,deltaSE=ds,a=alph,b=beta,fdr=a,pwr,p0=maxN=N1,s=side="two-sided")
osv$$size #first sample sizes to reach desired power
osv$power #calculated power for each sample size
osv$crit.vals #calculated critical value for each sample size

##Example of function ssize.twosamp
##Calculates sample sizes for two-sample microarray experiments
##See Figure 1.(a) of Liu & Hwang (2007)
d1<-1 #difference in differentially expressed genes to be detected
s1<-0.5 #standard deviation
ts$ssize<-ssize.twosamp(d1=s1,delta=delta1,sigma=s1,fdr=a,pwr,p0=maxN=N1,s=side="two-sided")
ts$$size #first sample sizes to reach desired power
ts$power #calculated power for each sample size
ts$crit.vals #calculated critical value for each sample size

##Example of function ssize.twosamp.vary
##Calculates sample sizes for multi-sample microarray experiments in which both the differences
##in expressions between treatments and the standard deviations vary among genes.
##See Figure 3.(a) of Liu & Hwang (2007)
dm<-2 #mean parameter of normal distribution of differences between
treatments among genes
ds<-1 #standard deviation parameter of normal distribution of differences between
treatments among genes
alph<-3 #shape parameter of inverse gamma distribution followed by standard deviations
beta<-1 #scale parameter of inverse gamma distribution followed by standard deviations
tsv$ssize<ssize.twosamp.vary(d1=dm,deltaSE=ds,a=alph,b=beta,fdr=a,pwr,p0=maxN=N1,s=side="two-sided")
ts$power #calculated power for each sample size
ts$crit.vals #calculated critical value for each sample size
Sample Size Calculations for Multi-Sample Microarray Experiments

Description

This function calculates appropriate sample sizes for multi-sample microarray experiments for a desired power. Sample size calculations are performed at controlled false discovery rates and user-specified proportions of non-differentially expressed genes, design matrix, and standard deviation. A graph of power versus sample size is created.

Usage

ssize.F(X, beta, L = NULL, dn, sigma, fdr = 0.05, power = 0.8, pi0 = 0.95, maxN = 20, cex.title=1.15, cex.legend=1)
**Arguments**

- **X**: design matrix of experiment
- **beta**: parameter vector
- **L**: coefficient matrix or vector for linear contrasts of interest
- **dn**: a function of the degrees of freedom based on the design of the experiment
- **sigma**: the standard deviation for all genes
- **fdr**: the false discovery rate to be controlled
- **power**: the desired power to be achieved
- **pi0**: a vector (or scalar) of proportions of non-differentially expressed genes
- **maxN**: the maximum sample size used for power calculations
- **cex.title**: controls size of chart titles
- **cex.legend**: controls size of chart legend

**Details**

Standard deviations are assumed to be identical for all genes. See the function `ssize.Fvary` for sample size calculations with varying standard deviations among genes.

If a vector is input for `pi0`, sample size calculations are performed for each proportion.

**Value**

- **ssize**: sample sizes (for each treatment) at which desired power is first reached
- **power**: power calculations with corresponding sample sizes
- **crit.vals**: critical value calculations with corresponding sample sizes

**Note**

Powers calculated to be 0 may be negligibly conservative.

Critical values calculated as ‘NA’ are values >100.

**Author(s)**

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**References**


**See Also**

`ssize.twoSampVary`, `ssize.oneSamp`, `ssize.oneSampVary`, `ssize.F`, `ssize.Fvary`
Examples

```r
# Sample size calculation for three-treatment loop design microarray experiment
# See Figure S2 of Liu & Hwang (2007)

des <- matrix(c(1, -1, 0, 0, 0, 1, 0), ncol = 2, byrow = FALSE) # design matrix of loop design experiment
b <- c(1, -0.5) # difference between first two treatments is 1 and second and  
                # third treatments is -0.5

df <- function(n) (3 * n - 2) # degrees of freedom for this design is 3n-2
s <- 1 # standard deviation
a <- 0.05 # false discovery rate to be controlled
power <- 0.8 # desired power
p0 <- c(0.5, 0.9, 0.95, 0.995) # proportions of non-differentially expressed genes

N1 <- 20 # maximum sample size for calculations

ft <- ssize.Fvary(X = des, beta = b, dn = df, sigma = s, fdr = a, power = power, pi0 = p0, maxN = N1)

ft$ssize # first sample sizes to reach desired power for each proportion of  
         # non-differentially expressed genes
ft$power # power for each sample size
ft$crit.vals # critical value for each sample size
```

### ssize.Fvary

**Sample Size Calculations for Multi-Sample Microarray Experiments with Differing Variances among Genes**

**Description**

This function calculates appropriate sample sizes for multi-sample microarray experiments in which standard deviations vary among genes. Sample sizes are determined based on a desired power, a controlled false discovery rate, and user-specified proportions of non-differentially expressed genes and design matrix. A graph of power versus sample size is created.

**Usage**

```r
ssize.Fvary(X, beta, L = NULL, dn, a, b, fdr = 0.05, power = 0.8, pi0 = 0.95,  
            maxN = 20, cex.title = 1.15, cex.legend = 1)
```

**Arguments**

- `X`: design matrix of experiment
- `beta`: parameter vector
- `L`: coefficient matrix or vector for linear contrasts of interest
- `dn`: a function of the degrees of freedom based on the design of the experiment
- `a`: shape parameter of inverse gamma distribution followed by variances of genes
- `b`: scale parameter of inverse gamma distribution followed by variances of genes
- `fdr`: the false discovery rate to be controlled
- `power`: the desired power to be achieved
pi0        a vector (or scalar) of proportions of non-differentially expressed genes
maxn      the maximum sample size used for power calculations
cex.title  controls size of chart titles
cex.legend  controls size of chart legend

Details
The variances among genes are assumed to follow an Inverse Gamma distribution with shape parameter a and scale parameter b.
If a vector is input for pi0, sample size calculations are performed for each proportion.

Value
ssize      sample sizes (for each treatment) at which desired power is first reached
power        power calculations with corresponding sample sizes
crit.vals      critical value calculations with corresponding sample sizes

Note
Numerical integration used in calculations performed by the function integrate, which uses adaptive quadrature of functions.
Powers calculated to be 0 may be negligibly conservative.
Critical values calculated as ‘NA’ are values >100.

Author(s)
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References

See Also
ssize.twoSamp, ssize.twoSampVary, ssize.oneSamp, ssize.oneSampVary, ssize.F

Examples
```r
## Sample size calculation for three-treatment loop design microarray experiment
# Design matrix of loop design experiment
b <- c(1, 0, 0.5)  # difference between first two treatments is 1 and second and third
# treatments is -0.5
# Design matrix of loop design experiment
# degrees of freedom for this design is 3n-2
# variances among genes follow an Inverse Gamma(3,1)
# fdr to be fixed
```

Sample Size Calculations for One-Sample Microarray Experiments

Description

This function calculates appropriate sample sizes for one-sample microarray experiments for a desired power. Sample size calculations are performed at controlled false discovery rates and user-specified proportions of non-differentially expressed genes, effect size, and standard deviation. A graph of power versus sample size is created.

Usage

\[
\text{ssize.oneSamp}(\delta, \sigma, \text{fdr} = 0.05, \text{power} = 0.8, \pi_0 = 0.95, \text{maxN} = 35, \text{side} = \text{"two-sided"}, \text{cex.title}=1.15, \text{cex.legend}=1) \]

Arguments

- **delta**: the common effect size for all genes
- **sigma**: the standard deviation for all genes
- **fdr**: the false discovery rate to be controlled
- **power**: the desired power to be achieved
- **pi0**: a vector (or scalar) of proportions of non-differentially expressed genes
- **maxN**: the maximum sample size used for power calculations
- **side**: options are "two-sided", "upper", or "lower"
- **cex.title**: controls size of chart titles
- **cex.legend**: controls size of chart legend

Details

Effect sizes and standard deviations are assumed to be identical for all genes. See the function `ssize.oneSampVary` for sample size calculations with varying effects sizes and standard deviations among genes.

If a vector is input for pi0, sample size calculations are performed for each proportion.
ssize.oneSamp

Value

ssize          sample sizes at which desired power is first reached
power          power calculations with corresponding sample sizes
crit.vals      critical value calculations with corresponding sample sizes

Note

Powers calculated to be 0 may be negligibly conservative.
Critical values calculated as ‘NA’ are values >20.
Running this function with the side option of “lower” will possibly result in multiple warnings.
Calculating the probability that an observation is less than the negative critical value under a t-
distribution with non-centrality parameter $delta/sigma$ (see argument section above) and the appro-
priate degrees of freedom is a calculation that is performed many times while the function runs.
When the difference between the critical value and $delta/sigma$ is large, this probability is virtually
zero. This happens repeatedly while the function optimize finds the appropriate critical value for
each sample size. Because of this, the function pt outputs a value <1e-8 in addition to a warning
of “full precision not achieved”. This has no impact on the accuracy of the resulting calculations of
sample size.

Author(s)

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References

Liu, Peng and J. T. Gene Hwang. 2007. Quick calculation for sample size while controlling false

See Also

ssize.twoSampVary, ssize.oneSamp, ssize.oneSampVary, ssize.F, ssize.Fvary

Examples

d<-2  ##effect size
s<-1   ##standard deviation
a<-0.05 ##false discovery rate to be controlled
pwr<-0.8 ##desired power
p0<-c(0.5,0.9,0.95) #proportions of non-differentially expressed genes
N<-20   ##maximum sample size for calculations
os<-ssize.oneSamp(delta=d, sigma=s, fdr=a, power=pwr, pi0=p0, maxN=N, side="two-sided")
osssize ##first sample sizes to reach desired power
os$power  ##calculated power for each sample size
os$crit.vals ##calculated critical value for each sample size
Description

This function calculates appropriate sample sizes for two-sample microarray experiments in which effect sizes as well as variances vary among genes. Sample sizes are determined based on a desired power, a controlled false discovery rate, and user-specified proportions of non-differentially expressed genes. Outputs a graph of power versus sample size. A graph of power versus sample size is created.

Usage

ssizeNonesampvary(deltaMean, deltaSE, a, b, fdr = 0.05, power = 0.8, pi0 = 0.95, maxN = 35, side = "two-sided", cex.title=1.15, cex.legend=1)

Arguments

deltaMean  mean of normal distribution followed by effect sizes among genes
deltaSE  standard deviation of normal distribution followed by effect sizes among genes
a  shape parameter of inverse gamma distribution followed by variances of genes
b  scale parameter of inverse gamma distribution followed by variances of genes
fdr  the false discovery rate to be controlled
power  the desired power to be achieved
pi0  a vector (or scalar) of proportions of non-differentially expressed genes
maxN  the maximum sample size used for power calculations
side  options are "two-sided", "upper", or "lower"
cex.title  controls size of chart titles
cex.legend  controls size of chart legend

Details

The effect sizes among genes are assumed to follow a Normal distribution with mean specified by deltaMean and standard deviation specified by deltaSE. The variances among genes are assumed to follow an Inverse Gamma distribution with shape parameter a and scale parameter b.

If a vector is input for pi0, sample size calculations are performed for each proportion.

Value

ssize  sample sizes (for each treatment) at which desired power is first reached
power  power calculations with corresponding sample sizes
crit.vals  critical value calculations with corresponding sample sizes
Note

Numerical integration used in calculations performed by the function integrate, which uses adaptive quadrature of functions.

Powers calculated to be 0 may be negligibly conservative.

Critical values calculated as ‘NA’ are values >20.

Running this function may result in many warnings. Probabilities under different t-distributions with non-zero non-centrality parameters are calculated many times while the function runs. If these probabilities are virtually zero, the function pt outputs a value <1e-8 and outputs a warning of “full precision not achieved”. These values have no impact on the accuracy of the resulting calculations.

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References


See Also

ssize.twosampVary, ssize.onesamp, ssize.onesampVary, ssize.F, ssize.Fvary

Examples

dm<-2; ds<-1 ##the effect sizes of the genes follow a Normal(2,1) distribution
alph<-3; beta<-1 ##the variances of the genes follow an Inverse Gamma (3,1) distribution.
a2<-0.05 ##false discovery rate to be controlled
pwr2<-0.8 ##desired power
p0<-c(0.90,0.95,0.995) ##proportions of non-differentially expressed genes
N1<-35 ##maximum sample size to be used in calculations

osv<-ssize.onesampVary(deltaMean=dm,deltaSE=ds,a=alph,b=beta,fdr=a2,power=pwr2,pi0=p0,
maxN=N1,sdir=“two-sided”)
osv$s$size ##first sample sizes to reach desired power
osv$power ##calculated power for each sample size
osv$crit.vals ##calculated critical value for each sample size

Description

This function calculates appropriate sample sizes for two-sample microarray experiments for a desired power. Sample size calculations are performed at controlled false discovery rates, user-specified proportions of non-differentially expressed genes, effect size, and standard deviation. A graph of power versus sample size is created.
Usage

```r
ssize.twoSamp(delta, sigma, fdr = 0.05, power = 0.8, pi0 = 0.95, maxN = 35,
               side = "two-sided", cex.title=1.15, cex.legend=1)
```

Arguments

- `delta`: the common difference in mean expressions between the two samples for all genes
- `sigma`: the common standard deviation of expressions for all genes
- `fdr`: the false discovery rate to be controlled
- `power`: the desired power to be achieved
- `pi0`: a vector (or scalar) of proportions of non-differentially expressed genes
- `maxN`: the maximum sample size used for power calculations
- `side`: options are "two-sided", "upper", or "lower"
- `cex.title`: controls size of chart titles
- `cex.legend`: controls size of chart legend

Details

The true difference between mean expressions of the two samples as well as the standard deviations of expressions are assumed identical for all genes. See the function `ssize.twoSampVary` for sample size calculations with varying differences between sample mean expressions and standard deviations among genes.

If a vector is input for `pi0`, sample size calculations are performed for each proportion.

Value

- `ssize`: sample sizes (for each treatment) at which desired power is first reached
- `power`: power calculations with corresponding sample sizes
- `crit.vals`: critical value calculations of two-sample t-test with corresponding sample sizes

Note

Powers calculated to be 0 may be negligibly conservative.

Critical values calculated as ‘NA’ are values >20.

Running this function with the `side` option of "lower" will possibly result in multiple warnings. Calculating the probability that an observation is less than the negative critical value under a t-distribution with non-centrality parameter `delta/sigma` (see argument section above) and the appropriate degrees of freedom is a calculation that is performed many times while the function runs. When the difference between the critical value and `delta/sigma` is large, this probability is virtually zero. This happens repeatedly while the function `optimize` finds the appropriate critical value for each sample size. Because of this, the function `pt` outputs a value <1e-8 in addition to a warning of “full precision not achieved”. This has no impact on the accuracy of the resulting calculations of sample size.
ssize.twoSampVary

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References


See Also

ssize.twoSampVary, ssize.oneSamp, ssize.oneSampVary, ssize.F, ssize.Fvary

Examples

```r
##See Figure 1.(a) of Liu & Hwang (2007)
d<-1 ##difference in differentially expressed genes to be detected
s<-0.5 ##standard deviation
a<-0.05 ##false discovery rate to be controlled
pwr<0.8 ##desired power
p0<.c(0.5,0.9,0.95) ##proportions of non-differentially expressed genes
N<20 ##maximum sample size for calculations

t$ssize##first sample sizes to reach desired power for each proportion of 
non-differentially expressed genes
t$power ##calculated power for each sample size
t$crit.vals##calculated critical value for each sample size
```

ssize.twoSampVary

Sample Size Calculations for Two-Sample Microarray Experiments with Differing Mean Expressions and Standard Deviations Among Genes

Description

This function calculates appropriate sample sizes for two-sample microarray experiments in which the differences between mean treatment expression levels (delta.g for gene g) as well as standard deviations vary among genes. Sample sizes are determined based on a desired power, a controlled false discovery rate, and user-specified proportions of non-differentially expressed genes. A graph of power versus sample size is created.

Usage

```r
ssize.twoSampVary(deltaMean, deltaSE, a, b, fdr = 0.05, power = 0.8, pi0 = 0.95, 
maxN = 35, side = "two-sided", cex.title=1.15, cex.legend=1)
```
Arguments

deltaMean: location (mean) parameter of normal distribution followed by each \textit{delta.g}
deltaSE: scale (standard deviation) parameter of normal distribution followed by each \textit{delta.g}
a: shape parameter of inverse gamma distribution followed by variances of genes
b: scale parameter of inverse gamma distribution followed by variances of genes
fdr: the false discovery rate to be controlled
power: the desired power to be achieved
pi0: a vector (or scalar) of proportions of non-differentially expressed genes
maxN: the maximum sample size used for power calculations
side: options are "two-sided", "upper", or "lower"
cex.title: controls size of chart titles
cex.legend: controls size of chart legend

Details

Each \textit{delta.g} is assumed to follow a Normal distribution with mean specified by \textit{deltaMean} and standard deviation specified by \textit{deltaSE}. The variances among genes are assumed to follow an Inverse Gamma distribution with shape parameter \textit{a} and scale parameter \textit{b}.

If a vector is input for \textit{pi0}, sample size calculations are performed for each proportion.

Value

ssize: sample sizes (for each treatment) at which desired power is first reached
power: power calculations with corresponding sample sizes
crit.vals: critical value calculations with corresponding sample sizes

Note

Numerical integration used in calculations performed by the function \texttt{integrate}, which uses adaptive quadrature of functions.

Powers calculated to be 0 may be negligibly conservative.

Critical values calculated as ‘NA’ are values >20.

Running this function may result in many warnings. Probabilities under different t-distributions with non-zero non-centrality parameters are calculated many times while the function runs. If these probabilities are virtually zero, the function \texttt{pt} outputs a value <1e-8 and outputs a warning of “full precision not achieved”. These values have no impact on the accuracy of the resulting calculations.

Author(s)

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References


See Also

ssize.twoSampVary, ssize.oneSamp, ssize.oneSampVary, ssize.F, ssize.Fvary

Examples

```r
# See Figure 3.(a) of Liu & Hwang (2007)
dm<-2; ds<-1  # the delta.g's follow a Normal(2,1) distribution
alph<-3; beta<-1  # the variances of genes follow an Inverse Gamma(a,b) distribution
a2<-0.05  # false discovery rate to be controlled
pwr2<-0.8  # desired power
p0<-c(0.90,0.95,0.995)  # proportions of non-differentially expressed genes
N1<-35  # maximum sample size to be used in calculations

sv<-ssize.twoSampVary(deltaMean=dm,deltaSE=ds,a=alph,b=beta,fdr=a2,power=pwr2,pi0=p0,
maxN=N1,sidetwo-sided)
sv$ssize  # first sample size(s) to reach desired power
sv$power  # calculated power for each sample size
sv$crit.vals  # calculated critical value for each sample size
```
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