# Package 'depower'

January 23, 2025

Title Power Analysis for Differential Expression Studies

Version 2025.1.20

**Description** Provides a convenient framework to simulate, test, power, and visualize data for differential expression studies with lognormal or negative binomial outcomes. Supported designs are two-sample comparisons of independent or dependent outcomes. Power may be summarized in the context of controlling the per-family error rate or family-wise error rate. Negative binomial methods are described in Yu, Fernandez, and Brock (2017) <doi:10.1186/s12859-017-1648-2> and Yu, Fernandez, and Brock (2020) <doi:10.1186/s12859-020-3541-7>.

```
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glmm\_bnb

GLMM for BNB ratio of means

#### **Description**

Generalized linear mixed model for bivariate negative binomial outcomes.

# Usage

```
glmm_bnb(data, test = "wald", ci_level = NULL, ...)
```

# **Arguments**

data (list)

A list whose first element is the vector of negative binomial values from sample 1 and the second element is the vector of negative binomial values from sample 2. Each vector must be sorted by the subject/item index and must be the same sample size. NAs are silently excluded. The default output from sim\_bnb().

test (String: "wald"; "c("wald", "lrt"))

The statistical method used for the test results. test = "wald" performs a Wald test and optionally the Wald confidence intervals. test = "lrt" performs a likelihood ratio test and optionally the profile likelihood confidence intervals (means and ratio). The Wald interval is always used for the dispersion and standard deviation of the item (subject) random intercept.

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```
ci_level (Scalar numeric: NULL; (0, 1))

If NULL, confidence intervals are set as NA. If in (0, 1), confidence intervals are calculated at the specified level. Profile likelihood intervals are computationally intensive, so intervals from test = "lrt" may be slow.

Optional arguments passed to glmmTMB::glmmTMB().
```

#### **Details**

```
Uses glmmTMB::glmmTMB() in the form
glmmTMB(
  formula = value ~ condition + (1 | item),
  data = data,
  dispformula = ~ 1,
  family = nbinom2
)
```

to model dependent negative binomial outcomes  $X_1, X_2 \sim \text{BNB}(\mu, r, \theta)$  where  $\mu$  is the mean of sample 1, r is the ratio of the means of sample 2 with respect to sample 1, and  $\theta$  is the dispersion parameter.

The hypotheses for the LRT and Wald test of r are

```
H_{null}: log(r) = 0

H_{alt}: log(r) \neq 0
```

where  $r = \frac{\bar{X}_2}{\bar{X}_1}$  is the population ratio of arithmetic means for sample 2 with respect to sample 1 and  $log(r_{null}) = 0$  assumes the population means are identical.

When simulating data from sim\_bnb(), the mean is a function of the item (subject) random effect which in turn is a function of the dispersion parameter. Thus, glmm\_bnb() has biased mean and dispersion estimates. The bias increases as the dispersion parameter gets smaller and decreases as the dispersion parameter gets larger. However, estimates of the ratio and standard deviation of the random intercept tend to be accurate. The p-value for glmm\_bnb() is generally overconservative compared to glmm\_poisson(), wald\_test\_bnb() and lrt\_bnb(). In summary, the negative binomial mixed-effects model fit by glmm\_bnb() is not recommended for the BNB data simulated by sim\_bnb(). Instead, wald\_test\_bnb() or lrt\_bnb() should typically be used instead.

#### Value

A list with the following elements:

Slot	Subslot	Name	Description
1		chisq	$\chi^2$ test statistic for the ratio of means.
2		df	Degrees of freedom.
3		р	p-value.
4		ratio	Estimated ratio of means (sample 2 / sample 1).
4	1	estimate	Point estimate.
4	2	lower	Confidence interval lower bound.

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4	3	upper	Confidence interval upper bound.
5		mean1	Estimated mean of sample 1.
5	1	estimate	Point estimate.
5	2	lower	Confidence interval lower bound.
5	3	upper	Confidence interval upper bound.
6		mean2	Estimated mean of sample 2.
6	1	estimate	Point estimate.
6	2	lower	Confidence interval lower bound.
6	3	upper	Confidence interval upper bound.
7		dispersion	Estimated dispersion.
7	1	estimate	Point estimate.
7	2	lower	Confidence interval lower bound.
7	3	upper	Confidence interval upper bound.
8		item_sd	Estimated standard deviation of the item (subject) random intercept.
8	1	estimate	Point estimate.
8	2	lower	Confidence interval lower bound.
8	3	upper	Confidence interval upper bound.
9		n1	Sample size of sample 1.
10		n2	Sample size of sample 2.
11		method	Method used for the results.
12		test	Type of hypothesis test.
13		alternative	The alternative hypothesis.
14		ci_level	Confidence level of the interval.
15		hessian	Information about the Hessian matrix.
16		convergence	Information about convergence.

# References

Hilbe JM (2011). *Negative Binomial Regression*, 2 edition. Cambridge University Press. ISBN 9780521198158 9780511973420, doi:10.1017/CBO9780511973420.

Hilbe JM (2014). *Modeling count data*. Cambridge University Press, New York, NY. ISBN 9781107028333 9781107611252, doi:10.1017/CBO9781139236065.

# See Also

```
glmmTMB::glmmTMB()
```

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```
)
lrt <- glmm_bnb(d, test = "lrt")</pre>
wald <- glmm_bnb(d, test = "wald", ci_level = 0.95)</pre>
wald
# Compare results to manual calculation of chi-square statistic
# Use the same data, but as a data frame instead of list
set.seed(1234)
d <- sim_bnb(</pre>
 n = 40,
 mean1 = 10,
 ratio = 1.2,
  dispersion = 2,
  return_type = "data.frame"
mod_alt <- glmmTMB::glmmTMB(</pre>
  formula = value ~ condition + (1 | item),
  data = d,
  dispformula = ~1,
  family = glmmTMB::nbinom2,
mod_null <- glmmTMB::glmmTMB(</pre>
  formula = value ~ 1 + (1 | item),
  data = d,
  dispformula = ~1,
  family = glmmTMB::nbinom2,
lrt_chisq <- as.numeric(-2 * (logLik(mod_null) - logLik(mod_alt)))</pre>
lrt_chisq
wald_chisq <- summary(mod_alt)$coefficients$cond["condition2", "z value"]^2</pre>
wald_chisq
anova(mod_null, mod_alt)
```

 ${\tt glmm\_poisson}$ 

GLMM for Poisson ratio of means

# **Description**

Generalized linear mixed model for two dependent Poisson outcomes.

glmm\_poisson

#### **Usage**

```
glmm_poisson(data, test = "wald", ci_level = NULL, ...)
```

#### **Arguments**

data (list)

A list whose first element is the vector of Poisson values from sample 1 and the second element is the vector of Poisson values from sample 2. Each vector must be sorted by the subject/item index and must be the same sample size. NAs are silently avaleded. The default output from a in back ()

silently excluded. The default output from sim\_bnb().

test (String: "wald"; "c("wald", "lrt"))

The statistical method used for the test results. test = "wald" performs a Wald test and optionally the Wald confidence intervals. test = "lrt" performs a likelihood ratio test and optionally the profile likelihood confidence intervals (means and ratio). The Wald interval is always used for the standard deviation of the

item (subject) random intercept.

ci\_level (Scalar numeric: NULL; (0, 1))

If NULL, confidence intervals are set as NA. If in (0, 1), confidence intervals are calculated at the specified level. Profile likelihood intervals are computationally

intensive, so intervals from test = "lrt" may be slow.

... Optional arguments passed to glmmTMB::glmmTMB().

#### **Details**

```
Uses glmmTMB::glmmTMB() in the form
```

```
glmmTMB(
  formula = value ~ condition + (1 | item),
  data = data,
  family = stats::poisson
)
```

to model dependent Poisson outcomes  $X_1 \sim \text{Poisson}(\mu)$  and  $X_2 \sim \text{Poisson}(r\mu)$  where  $\mu$  is the mean of sample 1 and r is the ratio of the means of sample 2 with respect to sample 1.

The hypotheses for the LRT and Wald test of r are

```
H_{null}: log(r) = 0

H_{alt}: log(r) \neq 0
```

where  $r = \frac{X_2}{X_1}$  is the population ratio of arithmetic means for sample 2 with respect to sample 1 and  $log(r_{null}) = 0$  assumes the population means are identical.

When simulating data from <code>sim\_bnb()</code>, the mean is a function of the item (subject) random effect which in turn is a function of the dispersion parameter. Thus, <code>glmm\_poisson()</code> has biased mean estimates. The bias increases as the dispersion parameter gets smaller and decreases as the dispersion parameter gets larger. However, estimates of the ratio and standard deviation of the random intercept tend to be accurate. In summary, the Poisson mixed-effects model fit by <code>glmm\_poisson()</code> is not recommended for the BNB data simulated by <code>sim\_bnb()</code>. Instead, <code>wald\_test\_bnb()</code> or <code>lrt\_bnb()</code> should typically be used instead.

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# Value

A list with the following elements:

Slot	Subslot	Name	Description
1		chisq	$\chi^2$ test statistic for the ratio of means.
2		df	Degrees of freedom.
3		р	p-value.
4		ratio	Estimated ratio of means (sample 2 / sample 1).
4	1	estimate	Point estimate.
4	2	lower	Confidence interval lower bound.
4	3	upper	Confidence interval upper bound.
5		mean1	Estimated mean of sample 1.
5	1	estimate	Point estimate.
5	2	lower	Confidence interval lower bound.
5	3	upper	Confidence interval upper bound.
6		mean2	Estimated mean of sample 2.
6	1	estimate	Point estimate.
6	2	lower	Confidence interval lower bound.
6	3	upper	Confidence interval upper bound.
7		item_sd	Estimated standard deviation of the item (subject) random intercept.
7	1	estimate	Point estimate.
7	2	lower	Confidence interval lower bound.
7	3	upper	Confidence interval upper bound.
8		n1	Sample size of sample 1.
9		n2	Sample size of sample 2.
10		method	Method used for the results.
11		test	Type of hypothesis test.
12		alternative	The alternative hypothesis.
13		ci_level	Confidence level of the interval.
14		hessian	Information about the Hessian matrix.
15		convergence	Information about convergence.

#### References

Hilbe JM (2011). *Negative Binomial Regression*, 2 edition. Cambridge University Press. ISBN 9780521198158 9780511973420, doi:10.1017/CBO9780511973420.

Hilbe JM (2014). *Modeling count data*. Cambridge University Press, New York, NY. ISBN 9781107028333 9781107611252, doi:10.1017/CBO9781139236065.

# See Also

```
glmmTMB::glmmTMB()
```

```
#------
# glmm_poisson() examples
#------
library(depower)
```

```
set.seed(1234)
d <- sim_bnb(</pre>
 n = 40,
 mean1 = 10,
 ratio = 1.2,
 dispersion = 2
lrt <- glmm_poisson(d, test = "lrt")</pre>
lrt
wald <- glmm_poisson(d, test = "wald", ci_level = 0.95)</pre>
# Compare results to manual calculation of chi-square statistic
#-----
# Use the same data, but as a data frame instead of list
set.seed(1234)
d <- sim_bnb(</pre>
 n = 40,
 mean1 = 10,
 ratio = 1.2,
 dispersion = 2,
 return_type = "data.frame"
mod_alt <- glmmTMB::glmmTMB(</pre>
 formula = value ~ condition + (1 | item),
 data = d,
 family = stats::poisson,
)
mod_null <- glmmTMB::glmmTMB(</pre>
 formula = value ~ 1 + (1 | item),
 data = d,
 family = stats::poisson,
)
lrt_chisq <- as.numeric(-2 * (logLik(mod_null) - logLik(mod_alt)))</pre>
1rt_chisq
wald_chisq <- summary(mod_alt)$coefficients$cond["condition2", "z value"]^2</pre>
wald_chisq
anova(mod_null, mod_alt)
```

#### **Description**

Generalized linear model for two independent negative binomial outcomes.

#### Usage

```
glm_nb(data, equal_dispersion = FALSE, test = "wald", ci_level = NULL, ...)
```

#### **Arguments**

data

A list whose first element is the vector of negative binomial values from group 1 and the second element is the vector of negative binomial values from group 2. NAs are silently excluded. The default output from sim\_nb().

equal\_dispersion

(Scalar logical: FALSE)

(list)

If TRUE, the model is fit assuming both groups have the same population dispersion parameter. If FALSE (default), the model is fit assuming different dispersions.

test (String: "wald"; "c("wald", "lrt"))

The statistical method used for the test results. test = "wald" performs a Wald test and optionally the Wald confidence intervals. test = "lrt" performs a likelihood ratio test and optionally the profile likelihood confidence intervals.

ci\_level (Scalar numeric: NULL; (0, 1))

If NULL, confidence intervals are set as NA. If in (0, 1), confidence intervals are calculated at the specified level. Profile likelihood intervals are computationally intensive, so intervals from test = "lrt" may be slow.

.. Optional arguments passed to glmmTMB::glmmTMB().

# Details

```
Uses glmmTMB::glmmTMB() in the form
```

```
glmmTMB(
  formula = value ~ condition,
  data = data,
  dispformula = ~ condition,
  family = nbinom2
)
```

to model independent negative binomial outcomes  $X_1 \sim \text{NB}(\mu, \theta_1)$  and  $X_2 \sim \text{NB}(r\mu, \theta_2)$  where  $\mu$  is the mean of group 1, r is the ratio of the means of group 2 with respect to group 1,  $\theta_1$  is the dispersion parameter of group 1, and  $\theta_2$  is the dispersion parameter of group 2.

The hypotheses for the LRT and Wald test of r are

```
H_{null}: log(r) = 0

H_{alt}: log(r) \neq 0
```

where  $r=\frac{\bar{X}_2}{\bar{X}_1}$  is the population ratio of arithmetic means for group 2 with respect to group 1 and  $log(r_{null})=0$  assumes the population means are identical.

#### Value

A list with the following elements:

Slot	Subslot	Name	Description
1		chisq	$\chi^2$ test statistic for the ratio of means.
2		df	Degrees of freedom.
3		р	p-value.
4		ratio	Estimated ratio of means (group 2 / group 1).
4	1	estimate	Point estimate.
4	2	lower	Confidence interval lower bound.
4	3	upper	Confidence interval upper bound.
5		mean1	Estimated mean of group 1.
5	1	estimate	Point estimate.
5	2	lower	Confidence interval lower bound.
5	3	upper	Confidence interval upper bound.
6		mean2	Estimated mean of group 2.
6	1	estimate	Point estimate.
6	2	lower	Confidence interval lower bound.
6	3	upper	Confidence interval upper bound.
7		dispersion1	Estimated dispersion of group 1.
7	1	estimate	Point estimate.
7	2	lower	Confidence interval lower bound.
7	3	upper	Confidence interval upper bound.
8		dispersion2	Estimated dispersion of group 2.
8	1	estimate	Point estimate.
8	2	lower	Confidence interval lower bound.
8	3	upper	Confidence interval upper bound.
9		n1	Sample size of group 1.
10		n2	Sample size of group 2.
11		method	Method used for the results.
12		test	Type of hypothesis test.
13		alternative	The alternative hypothesis.
14		equal_dispersion	Whether or not equal dispersions were assumed.
15		ci_level	Confidence level of the intervals.
16		hessian	Information about the Hessian matrix.
17		convergence	Information about convergence.

# References

Hilbe JM (2011). *Negative Binomial Regression*, 2 edition. Cambridge University Press. ISBN 9780521198158 9780511973420, doi:10.1017/CBO9780511973420.

Hilbe JM (2014). *Modeling count data*. Cambridge University Press, New York, NY. ISBN 9781107028333 9781107611252, doi:10.1017/CBO9781139236065.

#### See Also

```
glmmTMB::glmmTMB()
```

```
#-----
# glm_nb() examples
#-----
library(depower)
set.seed(1234)
d <- sim_nb(</pre>
 n1 = 60,
 n2 = 40,
 mean1 = 10,
 ratio = 1.5,
 dispersion1 = 2,
 dispersion2 = 8
lrt <- glm_nb(d, equal_dispersion = FALSE, test = "lrt", ci_level = 0.95)</pre>
wald <- glm_nb(d, equal_dispersion = FALSE, test = "wald", ci_level = 0.95)</pre>
wald
#-----
# Compare results to manual calculation of chi-square statistic
# Use the same data, but as a data frame instead of list
set.seed(1234)
d <- sim_nb(</pre>
 n1 = 60,
 n2 = 40,
 mean1 = 10,
 ratio = 1.5,
 dispersion1 = 2,
 dispersion2 = 8,
 return_type = "data.frame"
mod_alt <- glmmTMB::glmmTMB(</pre>
 formula = value ~ condition,
 data = d,
 dispformula = ~ condition,
 family = glmmTMB::nbinom2,
mod_null <- glmmTMB::glmmTMB(</pre>
 formula = value ~ 1,
 data = d,
 dispformula = ~ condition,
 family = glmmTMB::nbinom2,
```

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```
lrt_chisq <- as.numeric(-2 * (logLik(mod_null) - logLik(mod_alt)))
lrt_chisq
wald_chisq <- summary(mod_alt)$coefficients$cond["condition2", "z value"]^2
wald_chisq
anova(mod_null, mod_alt)</pre>
```

1rt\_bnb

Likelihood ratio test for BNB ratio of means

#### **Description**

Likelihood ratio test for the ratio of means from bivariate negative binomial outcomes.

## Usage

```
lrt_bnb(data, ratio_null = 1, ...)
```

#### Arguments

data (list)

A list whose first element is the vector of negative binomial values from sample 1 and the second element is the vector of negative binomial values from sample 2. Each vector must be sorted by the subject/item index and must be the same sample size. NAs are silently excluded. The default output from sim\_bnb().

ratio\_null (Scalar numeric: 1; (0, Inf))

The ratio of means assumed under the null hypothesis (sample 2 / sample 1). Typically, ratio\_null = 1 (no difference). See 'Details' for additional infor-

mation.

... Optional arguments passed to the MLE function mle\_bnb().

#### **Details**

This function is primarily designed for speed in simulation. Missing values are silently excluded.

Suppose  $X_1 \mid G = g \sim \operatorname{Poisson}(\mu g)$  and  $X_2 \mid G = g \sim \operatorname{Poisson}(r\mu g)$  where  $G \sim \operatorname{Gamma}(\theta, \theta^{-1})$  is the random item (subject) effect. Then  $X_1, X_2 \sim \operatorname{BNB}(\mu, r, \theta)$  is the joint distribution where  $X_1$  and  $X_2$  are dependent (though conditionally independent),  $X_1$  is the count outcome for sample 1 of the items (subjects),  $X_2$  is the count outcome for sample 2 of the items (subjects),  $\mu$  is the conditional mean of sample 1, r is the ratio of the conditional means of sample 2 with respect to sample 1, and  $\theta$  is the gamma distribution shape parameter which controls the dispersion and the correlation between sample 1 and 2.

The hypotheses for the LRT of r are

lrt\_bnb

$$H_{null}: r = r_{null}$$
  
 $H_{alt}: r \neq r_{null}$ 

where  $r = \frac{\bar{X}_2}{\bar{X}_1}$  is the population ratio of arithmetic means for sample 2 with respect to sample 1 and  $r_{null}$  is a constant for the assumed null population ratio of means (typically  $r_{null} = 1$ ).

The LRT statistic is

$$\begin{split} \lambda &= -2 \ln \frac{\sup_{\Theta_{null}} L(r,\mu,\theta)}{\sup_{\Theta} L(r,\mu,\theta)} \\ &= -2 \left[ \ln \sup_{\Theta_{null}} L(r,\mu,\theta) - \ln \sup_{\Theta} L(r,\mu,\theta) \right] \\ &= -2 (l(r_{null},\hat{\mu},\tilde{\theta}) - l(\hat{r},\hat{\mu},\hat{\theta})) \end{split}$$

Under  $H_{null}$ , the LRT test statistic is asymptotically distributed as  $\chi_1^2$ . The approximate level  $\alpha$  test rejects  $H_{null}$  if  $\lambda \geq \chi_1^2(1-\alpha)$ . Note that the asymptotic critical value is known to underestimate the exact critical value. Hence, the nominal significance level may not be achieved for small sample sizes (possibly  $n \leq 10$  or  $n \leq 50$ ).

#### Value

A list with the following elements:

Slot	Subslot	Name	Description
1		chisq	$\chi^2$ test statistic for the ratio of means.
2		df	Degrees of freedom.
3		р	p-value.
4		ratio	Estimated ratio of means (sample 2 / sample 1).
5		alternative	Point estimates under the alternative hypothesis.
5	1	mean1	Estimated mean of sample 1.
5	2	mean2	Estimated mean of sample 2.
5	3	dispersion	Estimated dispersion.
6		null	Point estimates under the null hypothesis.
6	1	mean1	Estimated mean of sample 1.
6	2	mean2	Estimated mean of sample 2.
6	3	dispersion	Estimated dispersion.
7		n1	The sample size of sample 1.
8		n2	The sample size of sample 2.
9		method	Method used for the results.
10		ratio_null	Assumed population ratio of means.
11		mle_code	Integer indicating why the optimization process terminated.
12		mle_message	Information from the optimizer.

### References

Rettiganti M, Nagaraja HN (2012). "Power Analyses for Negative Binomial Models with Application to Multiple Sclerosis Clinical Trials." *Journal of Biopharmaceutical Statistics*, **22**(2), 237–259. ISSN 1054-3406, 1520-5711, doi:10.1080/10543406.2010.528105.

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Aban IB, Cutter GR, Mavinga N (2009). "Inferences and power analysis concerning two negative binomial distributions with an application to MRI lesion counts data." *Computational Statistics & Data Analysis*, **53**(3), 820–833. ISSN 01679473, doi:10.1016/j.csda.2008.07.034.

# **Examples**

```
#----
# lrt_bnb() examples
#-----
library(depower)

set.seed(1234)
sim_bnb(
    n = 40,
    mean1 = 10,
    ratio = 1.2,
    dispersion = 2
) |>
    lrt_bnb()
```

1rt\_nb

Likelihood ratio test for NB ratio of means

# Description

Likelihood ratio test for the ratio of means from two independent negative binomial outcomes.

# Usage

```
lrt_nb(data, equal_dispersion = FALSE, ratio_null = 1, ...)
```

# **Arguments**

data (list)

A list whose first element is the vector of negative binomial values from group 1 and the second element is the vector of negative binomial values from group 2. NAs are silently excluded. The default output from sim\_nb().

equal\_dispersion

(Scalar logical: FALSE)

If TRUE, the LRT is calculated assuming both groups have the same population dispersion parameter. If FALSE (default), the LRT is calculated assuming different dispersions.

ratio\_null (Scalar numeric: 1; (0, Inf))

The ratio of means assumed under the null hypothesis (group 2 / group 1). Typically ratio\_null = 1 (no difference). See 'Details' for additional information.

... Optional arguments passed to the MLE function mle\_nb().

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#### **Details**

This function is primarily designed for speed in simulation. Missing values are silently excluded.

Suppose  $X_1 \sim NB(\mu, \theta_1)$  and  $X_2 \sim NB(r\mu, \theta_2)$  where  $X_1$  and  $X_2$  are independent,  $X_1$  is the count outcome for items in group 1,  $X_2$  is the count outcome for items in group 2,  $\mu$  is the arithmetic mean count in group 1, r is the ratio of arithmetic means for group 2 with respect to group 1,  $\theta_1$  is the dispersion parameter of group 1, and  $\theta_2$  is the dispersion parameter of group 2.

The hypotheses for the LRT of r are

$$H_{null}: r = r_{null}$$
  
 $H_{alt}: r \neq r_{null}$ 

where  $r=\frac{\bar{X}_2}{\bar{X}_1}$  is the population ratio of arithmetic means for group 2 with respect to group 1 and  $r_{null}$  is a constant for the assumed null population ratio of means (typically  $r_{null}=1$ ).

The LRT statistic is

$$\begin{split} \lambda &= -2\ln\frac{\sup_{\Theta_{null}}L(r,\mu,\theta_1,\theta_2)}{\sup_{\Theta}L(r,\mu,\theta_1,\theta_2)} \\ &= -2\left[\ln\sup_{\Theta_{null}}L(r,\mu,\theta_1,\theta_2) - \ln\sup_{\Theta}L(r,\mu,\theta_1,\theta_2)\right] \\ &= -2(l(r_{null},\tilde{\mu},\tilde{\theta}_1,\tilde{\theta}_2) - l(\hat{r},\hat{\mu},\hat{\theta}_1,\hat{\theta}_2)) \end{split}$$

Under  $H_{null}$ , the LRT test statistic is asymptotically distributed as  $\chi_1^2$ . The approximate level  $\alpha$  test rejects  $H_{null}$  if  $\lambda \geq \chi_1^2(1-\alpha)$ . Note that the asymptotic critical value is known to underestimate the exact critical value. Hence, the nominal significance level may not be achieved for small sample sizes (possibly  $n \leq 10$  or  $n \leq 50$ ).

#### Value

A list with the following elements:

Slot	Subslot	Name	Description
1		chisq	$\chi^2$ test statistic for the ratio of means.
2		df	Degrees of freedom.
3		р	p-value.
4		ratio	Estimated ratio of means (group 2 / group 1).
5		alternative	Point estimates under the alternative hypothesis.
5	1	mean1	Estimated mean of group 1.
5	2	mean2	Estimated mean of group 2.
5	3	dispersion1	Estimated dispersion of group 1.
5	4	dispersion2	Estimated dispersion of group 2.
6		null	Point estimates under the null hypothesis.
6	1	mean1	Estimated mean of group 1.
6	2	mean2	Estimated mean of group 2.
6	3	dispersion1	Estimated dispersion of group 1.
6	4	dispersion2	Estimated dispersion of group 2.
7		n1	Sample size of group 1.
8		n2	Sample size of group 2.

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9	method	Method used for the results.
10	equal_dispersion	Whether or not equal dispersions were assumed.
11	ratio_null	Assumed population ratio of means.
12	mle_code	Integer indicating why the optimization process terminated.
13	mle_message	Information from the optimizer.

#### References

Rettiganti M, Nagaraja HN (2012). "Power Analyses for Negative Binomial Models with Application to Multiple Sclerosis Clinical Trials." *Journal of Biopharmaceutical Statistics*, **22**(2), 237–259. ISSN 1054-3406, 1520-5711, doi:10.1080/10543406.2010.528105.

Aban IB, Cutter GR, Mavinga N (2009). "Inferences and power analysis concerning two negative binomial distributions with an application to MRI lesion counts data." *Computational Statistics & Data Analysis*, **53**(3), 820–833. ISSN 01679473, doi:10.1016/j.csda.2008.07.034.

# **Examples**

mle\_bnb

MLE for BNB

### **Description**

Maximum likelihood estimates (MLE) for bivariate negative binomial outcomes.

### Usage

```
mle_bnb_null(data, ratio_null = 1, method = "nlm_constrained", ...)
mle_bnb_alt(data, method = "nlm_constrained", ...)
```

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## Arguments

data

(list)

A list whose first element is the vector of negative binomial values from sample 1 and the second element is the vector of negative binomial values from sample 2. Each vector must be sorted by the subject/item index and must be the same sample size. NAs are silently excluded. The default output from sim\_bnb().

ratio\_null

(Scalar numeric: 1; (0, Inf))

The ratio of means assumed under the null hypothesis (sample 2 / sample 1).

Typically ratio\_null = 1 (no difference).

method

(string: "nlm\_constrained")

The optimization method. Must choose one of "nlm", "nlm\_constrained", "optim", or "optim\_constrained". The default bounds for constrained optimization are [1e-03, 1e06].

Optional arguments passed to the optimization method.

#### **Details**

These functions are primarily designed for speed in simulation. Missing values are silently excluded.

Suppose  $X_1 \mid G = g \sim \operatorname{Poisson}(\mu g)$  and  $X_2 \mid G = g \sim \operatorname{Poisson}(r\mu g)$  where  $G \sim \operatorname{Gamma}(\theta, \theta^{-1})$  is the random item (subject) effect. Then  $X_1, X_2 \sim \operatorname{BNB}(\mu, r, \theta)$  is the joint distribution where  $X_1$  and  $X_2$  are dependent (though conditionally independent),  $X_1$  is the count outcome for sample 1 of the items (subjects),  $X_2$  is the count outcome for sample 2 of the items (subjects),  $\mu$  is the conditional mean of sample 1, r is the ratio of the conditional means of sample 2 with respect to sample 1, and  $\theta$  is the gamma distribution shape parameter which controls the dispersion and the correlation between sample 1 and 2.

The MLEs of r and  $\mu$  are  $\hat{r}=\frac{\bar{x}_2}{\bar{x}_1}$  and  $\hat{\mu}=\bar{x}_1$ . The MLE of  $\theta$  is found by maximizing the profile log-likelihood  $l(\hat{r},\hat{\mu},\theta)$  with respect to  $\theta$ . When  $r=r_{null}$  is known, the MLE of  $\mu$  is  $\tilde{\mu}=\frac{\bar{x}_1+\bar{x}_2}{1+r_{null}}$  and  $\tilde{\theta}$  is obtained by maximizing the profile log-likelihood  $l(r_{null},\tilde{\mu},\theta)$  with respect to  $\theta$ .

The backend method for numerical optimization is controlled by argument method which refers to stats::nlm(), stats::nlminb(), or stats::optim(). If you would like to see warnings from the optimizer, include argument warnings = TRUE.

# Value

• For mle\_bnb\_alt, a list with the following elements:

Slot	Name	Description
1	mean1	MLE for mean of sample 1.
2	mean2	MLE for mean of sample 2.
3	ratio	MLE for ratio of means.
4	dispersion	MLE for BNB dispersion.
5	nll	Minimum of negative log-likelihood.
6	nparams	Number of estimated parameters.
7	n1	Sample size of sample 1.
8	n2	Sample size of sample 2.

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9	method	Method used for the results.
10	mle_method	Method used for optimization.
11	mle_code	Integer indicating why the optimization process terminated.
12	mle_message	Additional information from the optimizer.

• For mle\_bnb\_null, a list with the following elements:

Slot	Name	Description
1	mean1	MLE for mean of sample 1.
2	mean2	MLE for mean of sample 2.
3	ratio_null	Population ratio of means assumed for null hypothesis. mean2 = mean1 * ratio_null.
4	dispersion	MLE for BNB dispersion.
5	nll	Minimum of negative log-likelihood.
6	nparams	Number of estimated parameters.
7	n1	Sample size of sample 1.
8	n2	Sample size of sample 2.
9	method	Method used for the results.
10	mle_method	Method used for optimization.
11	mle_code	Integer indicating why the optimization process terminated.
12	mle_message	Additional information from the optimizer.

#### References

Rettiganti M, Nagaraja HN (2012). "Power Analyses for Negative Binomial Models with Application to Multiple Sclerosis Clinical Trials." *Journal of Biopharmaceutical Statistics*, **22**(2), 237–259. ISSN 1054-3406, 1520-5711, doi:10.1080/10543406.2010.528105.

Aban IB, Cutter GR, Mavinga N (2009). "Inferences and power analysis concerning two negative binomial distributions with an application to MRI lesion counts data." *Computational Statistics & Data Analysis*, **53**(3), 820–833. ISSN 01679473, doi:10.1016/j.csda.2008.07.034.

## See Also

```
sim_bnb(), nll_bnb
```

```
#-----
# mle_bnb() examples
#------
library(depower)

set.seed(1234)
d <- sim_bnb(
    n = 40,
    mean1 = 10,
    ratio = 1.2,
    dispersion = 2
)

mle_alt <- d |>
```

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```
mle_bnb_alt()
mle_null <- d |>
  mle_bnb_null()
mle_alt
mle_null
```

mle\_nb

MLE for NB

#### **Description**

Maximum likelihood estimates (MLE) for two independent negative binomial outcomes.

#### Usage

```
mle_nb_null(
  data,
  equal_dispersion = FALSE,
  ratio_null = 1,
 method = "nlm_constrained",
)
mle_nb_alt(data, equal_dispersion = FALSE, method = "nlm_constrained", ...)
```

# **Arguments**

data

(list)

A list whose first element is the vector of negative binomial values from group 1 and the second element is the vector of negative binomial values from group 2. NAs are silently excluded. The default output from sim\_nb().

equal\_dispersion

(Scalar logical: FALSE)

If TRUE, the MLEs are calculated assuming both groups have the same population dispersion parameter. If FALSE (default), the MLEs are calculated assuming

different dispersions.

ratio\_null (Scalar numeric: 1; (0, Inf))

The ratio of means assumed under the null hypothesis (group 2 / group 1). Typ-

ically ratio\_null = 1 (no difference).

method (string: "nlm\_constrained")

> The optimization method. Must choose one of "nlm", "nlm\_constrained", "optim", or "optim\_constrained". The default bounds for constrained opti-

mization are [1e-03, 1e06].

Optional arguments passed to the optimization method.

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#### **Details**

These functions are primarily designed for speed in simulation. Missing values are silently excluded.

Suppose  $X_1 \sim \text{NB}(\mu, \theta_1)$  and  $X_2 \sim \text{NB}(r\mu, \theta_2)$ , where  $X_1$  and  $X_2$  are independent,  $X_1$  is the count outcome for items in group 1,  $X_2$  is the count outcome for items in group 2,  $\mu$  is the arithmetic mean count in group 1, r is the ratio of arithmetic means for group 2 with respect to group 1,  $\theta_1$  is the dispersion parameter of group 1, and  $\theta_2$  is the dispersion parameter of group 2.

The MLEs of r and  $\mu$  are  $\hat{r} = \frac{\bar{x}_2}{\bar{x}_1}$  and  $\hat{\mu} = \bar{x}_1$ . The MLEs of  $\theta_1$  and  $\theta_2$  are found by maximizing the profile log-likelihood  $l(\hat{r}, \hat{\mu}, \theta_1, \theta_2)$  with respect to  $\theta_1$  and  $\theta_2$ . When  $r = r_{null}$  is known, the MLE of  $\mu$  is  $\tilde{\mu} = \frac{n_1\bar{x}_1 + n_2\bar{x}_2}{n_1 + n_2}$  and  $\tilde{\theta}_1$  and  $\tilde{\theta}_2$  are obtained by maximizing the profile log-likelihood  $l(r_{null}, \tilde{\mu}, \theta_1, \theta_2)$ .

The backend method for numerical optimization is controlled by argument method which refers to stats::nlm(), stats::nlminb(), or stats::optim(). If you would like to see warnings from the optimizer, include argument warnings = TRUE.

#### Value

• For mle\_nb\_alt(), a list with the following elements:

Slot	Name	Description
1	mean1	MLE for mean of group 1.
2	mean2	MLE for mean of group 2.
3	ratio	MLE for ratio of means.
4	dispersion1	MLE for dispersion of group 1.
5	dispersion2	MLE for dispersion of group 2.
6	equal_dispersion	Were equal dispersions assumed.
7	n1	Sample size of group 1.
8	n2	Sample size of group 2.
9	nll	Minimum of negative log-likelihood.
10	nparams	Number of estimated parameters.
11	method	Method used for the results.
12	mle_method	Method used for optimization.
13	mle_code	Integer indicating why the optimization process terminated.
14	mle_message	Additional information from the optimizer.

• For mle\_nb\_null(), a list with the following elements:

Slot	Name	Description
1	mean1	MLE for mean of group 1.
2	mean2	MLE for mean of group 2.
3	ratio_null	Population ratio of means assumed for null hypothesis. mean2 = mean1 * ratio_null.
4	dispersion1	MLE for dispersion of group 1.
5	dispersion2	MLE for dispersion of group 2.
6	equal_dispersion	Were equal dispersions assumed.
7	n1	Sample size of group 1.
8	n2	Sample size of group 2.
9	nll	Minimum of negative log-likelihood.

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10	nparams	Number of estimated parameters.
11	method	Method used for the results.
12	mle_method	Method used for optimization.
13	mle_code	Integer indicating why the optimization process terminated.
14	mle_message	Additional information from the optimizer.

#### References

Rettiganti M, Nagaraja HN (2012). "Power Analyses for Negative Binomial Models with Application to Multiple Sclerosis Clinical Trials." *Journal of Biopharmaceutical Statistics*, **22**(2), 237–259. ISSN 1054-3406, 1520-5711, doi:10.1080/10543406.2010.528105.

Aban IB, Cutter GR, Mavinga N (2009). "Inferences and power analysis concerning two negative binomial distributions with an application to MRI lesion counts data." *Computational Statistics & Data Analysis*, **53**(3), 820–833. ISSN 01679473, doi:10.1016/j.csda.2008.07.034.

## See Also

```
sim_nb(), nll_nb
```

```
# mle_nb() examples
library(depower)
d <- sim_nb(</pre>
  n1 = 60,
  n2 = 40,
  mean1 = 10,
  ratio = 1.5,
  dispersion1 = 2,
  dispersion2 = 8
)
mle_alt <- d |>
  mle_nb_alt()
mle_null <- d |>
  mle_nb_null()
mle_alt
mle_null
```

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nll\_bnb

Negative log-likelihood for BNB

#### **Description**

The negative log-likelihood for bivariate negative binomial outcomes.

# Usage

```
nll_bnb_null(param, value1, value2, ratio_null)
nll_bnb_alt(param, value1, value2)
```

# **Arguments**

param (numeric)

The vector of initial values for BNB parameters. Must be in the following order

for each scenario:

• Null: c(mean1, dispersion)

• Alternative: c(mean1, mean2, dispersion)

for samples 1 and 2.

value1 (numeric)

The vector of BNB values from sample 1. Must be sorted by the subject/item

index. Must not contain NAs.

value2 (numeric)

The vector of BNB values from sample 2. Must be sorted by the subject/item

index. Must not contain NAs.

ratio\_null (Scalar numeric: (0, Inf))

The ratio of means assumed under the null hypothesis (sample 2 / sample 1).

Typically ratio\_null = 1 (no difference).

#### **Details**

These functions are primarily designed for speed in simulation. Arguments are not checked.

Suppose  $X_1 \mid G = g \sim \operatorname{Poisson}(\mu g)$  and  $X_2 \mid G = g \sim \operatorname{Poisson}(r\mu g)$  where  $G \sim \operatorname{Gamma}(\theta, \theta^{-1})$  is the random item (subject) effect. Then  $X_1, X_2 \sim \operatorname{BNB}(\mu, r, \theta)$  is the joint distribution where  $X_1$  and  $X_2$  are dependent (though conditionally independent),  $X_1$  is the count outcome for sample 1 of the items (subjects),  $X_2$  is the count outcome for sample 2 of the items (subjects),  $\mu$  is the conditional mean of sample 1, r is the ratio of the conditional means of sample 2 with respect to sample 1, and  $\theta$  is the gamma distribution shape parameter which controls the dispersion and the correlation between sample 1 and 2.

The likelihood is

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$$\begin{split} L(r,\mu,\theta \mid X_{1},X_{2}) = & \left(\frac{\theta^{\theta}}{\Gamma(\theta)}\right)^{n} \times \\ & \frac{\mu^{\sum x_{1i} + \sum x_{2i}}}{\prod_{i=1}^{n} x_{1i}!} \frac{r^{\sum x_{2i}}}{\prod_{i=1}^{n} x_{2i}!} \times \\ & \frac{\prod_{i=1}^{n} \Gamma(x_{1i} + x_{2i} + \theta)}{(\mu + r\mu + \theta)^{\sum x_{1i} + x_{2i} + \theta}} \end{split}$$

and the parameter space is  $\Theta=\{(r,\mu,\theta):r,\mu,\theta>0\}$  . The log-likelihood is

$$l(r, \mu, \theta) = n \left[ \theta \ln \theta - \ln \Gamma(\theta) \right] + n(\bar{x}_1 + \bar{x}_2) \ln(\mu) + n\bar{x}_2 \ln r + \sum_{i=1}^{n} \ln \Gamma(x_{1i} + x_{2i} + \theta) - n(\bar{x}_1 + \bar{x}_2 + \theta) \ln(\mu + r\mu + \theta) - \sum_{i=1}^{n} \ln x_{1i}! - \sum_{i=1}^{n} \ln x_{2i}!$$

#### Value

Scalar numeric negative log-likelihood.

## References

Rettiganti M, Nagaraja HN (2012). "Power Analyses for Negative Binomial Models with Application to Multiple Sclerosis Clinical Trials." *Journal of Biopharmaceutical Statistics*, **22**(2), 237–259. ISSN 1054-3406, 1520-5711, doi:10.1080/10543406.2010.528105.

Aban IB, Cutter GR, Mavinga N (2009). "Inferences and power analysis concerning two negative binomial distributions with an application to MRI lesion counts data." *Computational Statistics & Data Analysis*, **53**(3), 820–833. ISSN 01679473, doi:10.1016/j.csda.2008.07.034.

#### See Also

```
sim_nb(), stats::nlminb(), stats::nlm(), stats::optim()
```

```
#-----
# nll_bnb*() examples
#------
library(depower)

set.seed(1234)
d <- sim_bnb(
    n = 40,
    mean1 = 10,
    ratio = 1.2,</pre>
```

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```
dispersion = 2
)

nll_bnb_alt(
   param = c(mean1 = 10, mean2 = 12, dispersion = 2),
   value1 = d[[1L]],
   value2 = d[[2L]]
)

nll_bnb_null(
   param = c(mean = 10, dispersion = 2),
   value1 = d[[1L]],
   value2 = d[[2L]],
   ratio_null = 1
)
```

nll\_nb

Negative log-likelihood for NB

# Description

The negative log-likelihood for two independent samples of negative binomial distributions.

# Usage

```
nll_nb_null(param, value1, value2, equal_dispersion, ratio_null)
nll_nb_alt(param, value1, value2, equal_dispersion)
```

# Arguments

param (numeric)

The vector of initial values for NB parameters. Must be in the following order for each scenario:

- Null and unequal dispersion: c(mean1, dispersion1, dispersion2)
- Alternative and unequal dispersion: c(mean1, mean2, dispersion1, dispersion2)
- Null and equal dispersion: c(mean1, dispersion)
- Alternative and equal dispersion: c(mean1, mean2, dispersion)

for groups 1 and 2.

value1 (numeric)

The vector of NB values from group 1. Must not contain NAs.

value2 (numeric

The vector of NB values from group 2. Must not contain NAs.

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equal\_dispersion

(Scalar logical)

If TRUE, the log-likelihood is calculated assuming both groups have the same population dispersion parameter. If FALSE (default), the log-likelihood is calculated assuming different dispersions.

ratio\_null (Scalar numeric: (0, Inf))

> The ratio of means assumed under the null hypothesis (group 2 / group 1). Typically ratio\_null = 1 (no difference).

#### **Details**

These functions are primarily designed for speed in simulation. Arguments are not checked.

Suppose  $X_1 \sim NB(\mu, \theta_1)$  and  $X_2 \sim NB(r\mu, \theta_2)$  where  $X_1$  and  $X_2$  are independent,  $X_1$  is the count outcome for items in group 1,  $X_2$  is the count outcome for items in group 2,  $\mu$  is the arithmetic mean count in group 1, r is the ratio of arithmetic means for group 2 with respect to group 1,  $\theta_1$  is the dispersion parameter of group 1, and  $\theta_2$  is the dispersion parameter of group 2.

#### **Unequal dispersion parameters:**

When the dispersion parameters are not equal, the likelihood is

$$L(r, \mu, \theta_1, \theta_2 \mid X_1, X_2) = \left(\frac{\theta_1^{\theta_1}}{\Gamma(\theta_1)}\right)^{n_1} \frac{\mu^{\sum x_{1i}}}{(\mu + \theta_1)^{\sum x_{1i} + n_1 \theta_1}} \times \left(\frac{\theta_2^{\theta_2}}{\Gamma(\theta_2)}\right)^{n_2} \frac{(r\mu)^{\sum x_{2j}}}{(r\mu + \theta_2)^{\sum x_{2j} + n_2 \theta_2}} \times \prod_{i=1}^{n_1} \frac{\Gamma(x_{1i} + \theta_1)}{x_{1i}!} \prod_{j=1}^{n_2} \frac{\Gamma(x_{2j} + \theta_2)}{x_{2j}!}$$

and the parameter space is  $\Theta = \{(r, \mu, \theta_1, \theta_2) : r, \mu, \theta_1, \theta_2 > 0\}$ . The log-likelihood is

$$\begin{split} l(r,\mu,\theta_1,\theta_2) &= n_1 \left[ \theta_1 \ln \theta_1 - \ln \Gamma(\theta_1) \right] + \\ &\quad n_2 \left[ \theta_2 \ln \theta_2 - \ln \Gamma(\theta_2) \right] + \\ &\quad (n_1 \bar{x}_1 + n_2 \bar{x}_2) \ln(\mu) - n_1 (\bar{x}_1 + \theta_1) \ln(\mu + \theta_1) + \\ &\quad n_2 \bar{x}_2 \ln(r) - n_2 (\bar{x}_2 + \theta_2) \ln(r\mu + \theta_2) + \\ &\quad \sum_{i=1}^{n_1} \left( \ln \Gamma(y_{1i} + \theta_1) - \ln(y_{1i}!) \right) + \\ &\quad \sum_{j=1}^{n_2} \left( \ln \Gamma(y_{2j} + \theta_2) - \ln(y_{2j}!) \right) \end{split}$$

## **Equal dispersion parameters:**

When the dispersion parameters are equal, the likelihood is

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$$L(r, \mu, \theta \mid X_1, X_2) = \left(\frac{\theta^{\theta}}{\Gamma(\theta)}\right)^{n_1 + n_2} \times \frac{\mu^{\sum x_{1i}}}{(\mu + \theta)^{\sum x_{1i} + n_1 \theta}} \frac{(r\mu)^{\sum x_{2j}}}{(r\mu + \theta)^{\sum x_{2j} + n_2 \theta}} \times \prod_{i=1}^{n_1} \frac{\Gamma(x_{1i} + \theta)}{x_{1i}!} \prod_{j=1}^{n_2} \frac{\Gamma(x_{2j} + \theta)}{x_{2j}!}$$

and the parameter space is  $\Theta = \{(r, \mu, \theta) : r, \mu, \theta > 0\}$ . The log-likelihood is

$$l(r, \mu, \theta) = (n_1 + n_2) \left[ \theta \ln \theta - \ln \Gamma(\theta) \right] +$$

$$(n_1 \bar{x}_1 + n_2 \bar{x}_2) \ln(\mu) - n_1 (\bar{x}_1 + \theta) \ln(\mu + \theta) +$$

$$n_2 \bar{x}_2 \ln(r) - n_2 (\bar{x}_2 + \theta) \ln(r\mu + \theta) +$$

$$\sum_{i=1}^{n_1} (\ln \Gamma(y_{1i} + \theta) - \ln(y_{1i}!)) +$$

$$\sum_{j=1}^{n_2} (\ln \Gamma(y_{2j} + \theta) - \ln(y_{2j}!))$$

#### Value

Scalar numeric negative log-likelihood.

#### References

Rettiganti M, Nagaraja HN (2012). "Power Analyses for Negative Binomial Models with Application to Multiple Sclerosis Clinical Trials." *Journal of Biopharmaceutical Statistics*, **22**(2), 237–259. ISSN 1054-3406, 1520-5711, doi:10.1080/10543406.2010.528105.

Aban IB, Cutter GR, Mavinga N (2009). "Inferences and power analysis concerning two negative binomial distributions with an application to MRI lesion counts data." *Computational Statistics & Data Analysis*, **53**(3), 820–833. ISSN 01679473, doi:10.1016/j.csda.2008.07.034.

#### See Also

```
sim_nb(), stats::nlminb(), stats::nlm(), stats::optim()
```

```
ratio = 1.5,
  dispersion1 = 2,
  dispersion2 = 8
)
nll_nb_alt(
  param = c(mean1 = 10, mean2 = 15, dispersion = 2, dispersion2 = 8),
  value1 = d[[1L]],
  value2 = d[[2L]],
  equal_dispersion = FALSE
)
nll_nb_null(
  param = c(mean = 10, dispersion = 2, dispersion2 = 8),
  value1 = d[[1L]],
  value2 = d[[2L]],
  equal_dispersion = FALSE,
  ratio_null = 1
)
```

plot.depower

Plot power objects

# **Description**

An automatic plot method for objects returned by power().

# Usage

```
## S3 method for class 'depower'
plot(
    x,
    x_axis = NULL,
    y_axis = NULL,
    color = NULL,
    facet_row = NULL,
    facet_col = NULL,
    hline = NULL,
    caption = TRUE,
    caption_width = 70L,
    ...
)
```

## **Arguments**

x (depower)

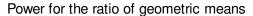
The data frame returned by power().

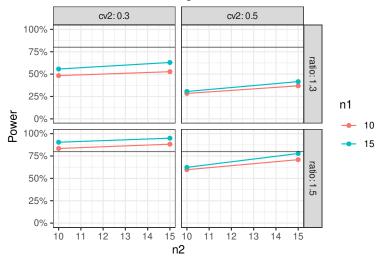
x_axis	(string: NULL; names(x)) The name of the column to be used for the x-axis. Automatically chosen if NULL.
y_axis	(string: NULL; names(x)) The name of the column to be used for the y-axis. Automatically chosen if NULL. Generally, "power" (default) should be used for the y-axis.
color	(string: NULL; names(x)) The name of the column to be used for the ggplot2::aes() color aesthetic. Automatically chosen if NULL. Use NA to turn off.
facet_row	(string: NULL; names(x)) The name of the column to be used for the ggplot2::facet_grid() row. Automatically chosen if NULL. Use NA to turn off.
facet_col	(string: NULL; names(x)) The name of the column to be used for the ggplot2::facet_grid() column. Automatically chosen if NULL. Use NA to turn off.
hline	(numeric: NULL; (0, 1)) The y-intercept at which to draw a horizontal line.
caption	(Scalar logical: TRUE) If TRUE (default), a caption is added to the plot. The caption includes information on parameter values that were conditioned on to generate the plot. If FALSE, the caption is not included.
caption_width	(Scalar integer: 70L) The target column number for wrapping the caption text.
	Unused additional arguments.

#### **Details**

If you are limited by the output from plot.depower(), keep in mind that the object returned by power() is a standard data frame. This allows you to easily plot all results with standard plotting functions. In addition, because plot.depower() uses ggplot2, you can modify the plot as you normally would. For example:

```
set.seed(1234)
sim_log_lognormal(
    n1 = c(10, 15),
    n2 = c(10, 15),
    ratio = c(1.3, 1.5),
    cv1 = c(0.3),
    cv2 = c(0.3, 0.5),
    nsims = 1000
) |>
    power(alpha = 0.05) |>
    plot(hline = 0.8, caption_width = 60) +
    ggplot2::theme_bw() +
    ggplot2::theme(plot.caption = ggplot2::element_text(hjust = 0)) +
    ggplot2::labs(title = "Power for the ratio of geometric means")
```





Conditioned on: CV1=0.3, Correlation=0, Alpha=0.05, Test=Welch's t-Test, and N Simulations=1000.

#### Value

A ggplot2::ggplot() object.

# See Also

power()

```
sim_log_lognormal(
  n1 = c(10, 15),
 n2 = c(10, 15),
  ratio = c(1.3, 1.5),
  cv1 = c(0.3, 0.5),
  cv2 = c(0.3, 0.5),
  cor = c(0.3),
  nsims = 500
) |>
  power(alpha = 0.01) |>
  plot()
# Power for two-sample independent AND two-sample dependent t-test
set.seed(1234)
sim_log_lognormal(
  n1 = c(10, 15),
 n2 = c(10, 15),
  ratio = c(1.3, 1.5),
  cv1 = c(0.3),
  cv2 = c(0.3),
  cor = c(0, 0.3, 0.6),
  nsims = 500
) |>
  power(alpha = c(0.05, 0.01)) |>
  plot(facet_row = "cor", color = "test")
# Power for one-sample t-test
set.seed(1234)
sim_log_lognormal(
 n1 = c(10, 15),
  ratio = c(1.2, 1.4),
  cv1 = c(0.3, 0.5),
  nsims = 500
  power(alpha = c(0.05, 0.01)) |>
  plot()
# Power for independent two-sample NB test
set.seed(1234)
sim_nb(
  n1 = c(10, 15),
  mean1 = 10,
  ratio = c(1.8, 2),
  dispersion1 = 10,
  dispersion2 = 3,
  nsims = 100
) |>
  power(alpha = 0.01) \mid >
  plot()
# Power for BNB test
set.seed(1234)
```

```
sim_bnb(
  n = c(10, 12),
  mean1 = 10,
  ratio = c(1.3, 1.5),
  dispersion = 5,
  nsims = 100
) |>
  power(alpha = 0.01) |>
  plot()
```

power

Simulated power

## **Description**

A method to calculate power for objects returned by sim\_log\_lognormal(), sim\_nb(), and sim\_bnb().

# Usage

```
power(data, ..., alpha = 0.05, list_column = FALSE, ncores = 1L)
```

#### **Arguments**

data	(depower)
------	-----------

The simulated data returned by sim\_log\_lognormal(), sim\_nb(), or sim\_bnb().

... (functions)

The function(s) used to perform the test. If empty, a default test function will be selected based on class(data). Names are used for labeling and should be unique. If names are empty, the call coerced to character will be used for name value pairs. See 'Detaile'

name-value pairs. See 'Details'.

alpha (numeric: 0.05; (0,1))

The expected probability of rejecting a single null hypothesis when it is actually

true. See 'Details'.

list\_column (Scalar logical: FALSE)

If TRUE, the data and result list-columns are included in the returned data frame. If FALSE (default), the data and result list-columns are not included in

the returned data frame.

ncores (Scalar integer: 1L; [1, Inf))

The number of cores (number of worker processes) to use. Do not set greater than the value returned by parallel::detectCores(). May be helpful when

the number of parameter combinations is large and nsims is large.

#### **Details**

Power is calculated as the proportion of hypothesis tests which result in a p-value less than or equal to alpha. e.g.

```
sum(p <= alpha, na.rm = TRUE) / nsims</pre>
```

Power is defined as the expected probability of rejecting the null hypothesis for a chosen value of the unknown effect. In a multiple comparisons scenario, power is defined as the marginal power, which is the expected power of the test for each individual null hypothesis assumed to be false.

Other forms of power under the multiple comparisons scenario include disjunctive or conjunctive power. Disjunctive power is defined as the expected probability of correctly rejecting one or more null hypotheses. Conjunctive power is defined as the expected probability of correctly rejecting all null hypotheses. In the simplest case, and where all hypotheses are independent, if the marginal power is defined as  $\pi$  and m is the number of null hypotheses assumed to be false, then disjunctive power may be calculated as  $1-(1-\pi)^m$  and conjunctive power may be calculated as  $\pi^m$ . Disjunctive power tends to decrease with increasingly correlated hypotheses and conjunctive power tends to increase with increasingly correlated hypotheses.

#### Argument . . .:

... are the name-value pairs for the functions used to perform the tests. If not named, the functions coerced to character will be used for the name-value pairs. Typical in non-standard evaluation, ... accepts bare functions and converts them to a list of expressions. Each element in this list will be validated as a call and then evaluated on the simulated data. A base::call() is simply an unevaluated function. Below are some examples of specifying ... in power().

```
# Examples of specifying ... in power()
data <- sim_nb(</pre>
  n1 = 10,
  mean1 = 10,
  ratio = c(1.6, 2),
  dispersion1 = 2,
  dispersion2 = 2,
  nsims = 200
)
# ... is empty, so a an appropriate default function will be provided
power(data)
# This is equivalent to leaving ... empty
power(data, "NB Wald test" = wald_test_nb())
# If not named, "wald_test_nb()" will be used to label the function
power(data, wald_test_nb())
# You can specify any parameters in the call. The data argument
# will automatically be inserted or overwritten.
  power("NB Wald test" = wald_test_nb(equal_dispersion=TRUE, link="log"))
```

```
# Multiple functions may be used.
data |>
   power(
    wald_test_nb(link='log'),
    wald_test_nb(link='sqrt'),
    wald_test_nb(link='squared'),
    wald_test_nb(link='identity')
)

# Just like functions in a pipe, the parentheses are required.
# This will error because wald_test_nb is missing parentheses.
try(power(data, wald_test_nb))
```

In most cases\*, any user created test function may be utilized in ... if the following conditions are satisfied:

- 1. The function contains argument data which is defined as a list with the first and second elements for simulated data.
- 2. The return object is a list with element p for the p-value of the hypothesis test.

Validate with test cases beforehand.

\*Simulated data of class log\_lognormal\_mixed\_two\_sample has both independent and dependent data. To ensure the appropriate test function is used, power.log\_lognormal\_mixed\_two\_sample() allows only t\_test\_welch() and t\_test\_paired() in .... Each will be evaluated on the simulated data according to column data\$cor. If one or both of these functions are not included in ..., the corresponding default function will be used automatically. If any other test function is included, an error will be returned.

#### **Argument** alpha:

 $\alpha$  is known as the type I assertion probability and is defined as the expected probability of rejecting a null hypothesis when it was actually true.  $\alpha$  is compared with the p-value and used as the decision boundary for rejecting or not rejecting the null hypothesis.

The family-wise error rate is the expected probability of making one or more type I assertions among a family of hypotheses. Using Bonferroni's method,  $\alpha$  is chosen for the family of hypotheses then divided by the number of tests performed (m). Each individual hypothesis is tested at  $\frac{\alpha}{m}$ . For example, if you plan to conduct 30 hypothesis tests and want to control the family-wise error rate to no greater than  $\alpha=0.05$ , you would set alpha = 0.05/30.

The per-family error rate is the expected number of type I assertions among a family of hypotheses. If you calculate power for the scenario where you perform 1,000 hypotheses and want to control the per-family error rate to no greater than 10 type I assertions, you would choose alpha = 10/1000. This implicitly assumes all 1,000 hypotheses are truly null. Alternatively, if you assume 800 of these hypotheses are truly null and 200 are not, alpha = 10/1000 would control the per-family error rate to no greater than 8 type I assertions. If it is acceptable to keep the per-family error rate as 10, setting alpha = 10/800 would provide greater marginal power than the previous scenario.

These two methods assume that the distribution of p-values for the truly null hypotheses are uniform(0,1), but remain valid under various other testing scenarios (such as dependent tests). Other multiple comparison methods, such as FDR control, are common in practice but don't directly fit into this power simulation framework.

#### Column nsims:

The final number of valid simulations per unique set of simulation parameters may be less than the original number requested. This may occur when the test results in a missing p-value. For wald\_test\_bnb(), pathological MLE estimates, generally from small sample sizes and very small dispersions, may result in a negative estimated standard deviation of the ratio. Thus the test statistic and p-value would not be calculated. Note that simulated data from sim\_nb() and sim\_bnb() may also reduce nsims during the data simulation phase.

The nsims column in the return data frame is the effective number of simulations for power results.

#### Value

A data frame with the following columns appended to the data object:

```
Column Name Description
alpha Type I assertion probability.
test Name-value pair of the function and statistical test: c(as.character(...) = names(...).
data List-column of simulated data.
result List-column of test results.
power Power of the test for corresponding parameters.
```

For power(list\_column = FALSE), columns data, and result are excluded from the data frame.

#### References

Yu L, Fernandez S, Brock G (2017). "Power analysis for RNA-Seq differential expression studies." *BMC Bioinformatics*, **18**(1), 234. ISSN 1471-2105, doi:10.1186/s1285901716482.

Yu L, Fernandez S, Brock G (2020). "Power analysis for RNA-Seq differential expression studies using generalized linear mixed effects models." *BMC Bioinformatics*, **21**(1), 198. ISSN 1471-2105, doi:10.1186/s1285902035417.

Rettiganti M, Nagaraja HN (2012). "Power Analyses for Negative Binomial Models with Application to Multiple Sclerosis Clinical Trials." *Journal of Biopharmaceutical Statistics*, **22**(2), 237–259. ISSN 1054-3406, 1520-5711, doi:10.1080/10543406.2010.528105.

Aban IB, Cutter GR, Mavinga N (2009). "Inferences and power analysis concerning two negative binomial distributions with an application to MRI lesion counts data." *Computational Statistics & Data Analysis*, **53**(3), 820–833. ISSN 01679473, doi:10.1016/j.csda.2008.07.034.

Julious SA (2004). "Sample sizes for clinical trials with Normal data." *Statistics in Medicine*, **23**(12), 1921–1986. doi:10.1002/sim.1783.

Vickerstaff V, Omar RZ, Ambler G (2019). "Methods to adjust for multiple comparisons in the analysis and sample size calculation of randomised controlled trials with multiple primary outcomes." *BMC Medical Research Methodology*, **19**(1), 129. ISSN 1471-2288, doi:10.1186/s1287401907544.

#### See Also

```
plot.depower()
```

```
#-----
# power() examples
library(depower)
# Power for independent two-sample t-Test
set.seed(1234)
data <- sim_log_lognormal(</pre>
 n1 = 20,
 n2 = 20,
 ratio = c(1.2, 1.4),
 cv1 = 0.4,
 cv2 = 0.4,
 cor = 0,
 nsims = 1000
# Welch's t-test is used by default
power(data)
# But you can specify anything else that is needed
power(
 data = data,
 "Welch's t-Test" = t_test_welch(alternative = "greater"),
 alpha = 0.01
)
# Power for dependent two-sample t-Test
set.seed(1234)
sim_log_lognormal(
 n1 = 20,
 n2 = 20,
 ratio = c(1.2, 1.4),
 cv1 = 0.4,
 cv2 = 0.4,
 cor = 0.5,
 nsims = 1000
) |>
 power()
# Power for mixed-type two-sample t-Test
set.seed(1234)
sim_log_lognormal(
 n1 = 20,
 n2 = 20,
 ratio = c(1.2, 1.4),
 cv1 = 0.4,
 cv2 = 0.4,
 cor = c(0, 0.5),
 nsims = 1000
) |>
```

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```
power()
# Power for one-sample t-Test
set.seed(1234)
sim_log_lognormal(
 n1 = 20,
 ratio = c(1.2, 1.4),
 cv1 = 0.4,
 nsims = 1000
) |>
 power()
# Power for independent two-sample NB test
set.seed(1234)
sim_nb(
 n1 = 10,
 mean1 = 10,
 ratio = c(1.6, 2),
 dispersion1 = 2,
 dispersion2 = 2,
 nsims = 200
) |>
 power()
# Power for BNB test
set.seed(1234)
sim_bnb(
 n = 10,
 mean1 = 10,
 ratio = c(1.4, 1.6),
 dispersion = 10,
 nsims = 200
) |>
 power()
```

sim\_bnb

Simulate data from a BNB distribution

## Description

Simulate data from the bivariate negative binomial (BNB) distribution. The BNB distribution is used to simulate count data where the event counts are jointly dependent (correlated). For independent data, see sim\_nb().

# Usage

```
sim_bnb(
  n,
  mean1,
```

```
mean2,
  ratio,
  dispersion,
  nsims = 1L,
  return_type = "list",
 max\_zeros = 0.99,
  ncores = 1L
)
```

### Arguments

(integer: [2, Inf)) n

The number(s) of paired observations.

(numeric: (0, Inf)) mean1

The mean(s) of sample 1  $(\mu_1)$ .

(numeric: (0, Inf)) mean2, ratio

Only specify one of these arguments.

• mean2: The mean(s) of sample  $2 (\mu_2)$ .

• ratio: The ratio(s) of means for sample 2 with respect to sample 1  $\left(r = \frac{\mu_2}{\mu_1}\right)$ .

mean2 = ratio \* mean1

dispersion (numeric: (0, Inf))

The gamma distribution shape parameter(s)  $(\theta)$  which control the dispersion and

the correlation between sample 1 and 2. See 'Details' and 'Examples'.

nsims (Scalar integer: 1L; [1, Inf))

The expected number of simulated data sets. If nsims > 1, the data is returned

in a list-column of a depower simulation data frame. nsims may be reduced

depending on max\_zeros.

(string: "list"; c("list", "data.frame")) return\_type

> The data structure of the simulated data. If "list" (default), a list object is returned. If "data.frame" a data frame in tall format is returned. The list object provides computational efficiency and the data frame object is convenient

for formulas. See 'Value'.

(Scalar numeric: 0.99; [0, 1]) max\_zeros

> The maximum proportion of zeros each group in a simulated dataset is allowed to have. If the proportion of zeros is greater than this value, the corresponding data is excluded from the set of simulations. This is most likely to occur when

the sample size is small and the dispersion parameter is small.

ncores (Scalar integer: 1L; [1, Inf))

> The number of cores (number of worker processes) to use. Do not set greater than the value returned by parallel::detectCores(). May be helpful when

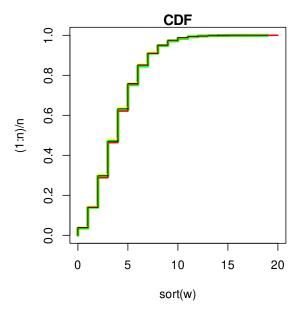
the number of parameter combinations is large and nsims is large.

### **Details**

The negative binomial distribution may be defined using a gamma-Poisson mixture distribution. In this case, the Poisson parameter  $\lambda$  is a random variable with gamma distribution. Equivalence between different parameterizations are demonstrated below:

```
# Define constants and their relationships
n <- 10000
dispersion <- 8
mu <- 4
p <- dispersion / (dispersion + mu)</pre>
q <- mu / (mu + dispersion)</pre>
variance <- mu + (mu^2 / dispersion)</pre>
rate <- p / (1 - p)
scale <- (1 - p) / p
# alternative formula for mu
mu_alt <- (dispersion * (1 - p)) / p
stopifnot(isTRUE(all.equal(mu, mu_alt)))
set.seed(20240321)
# Using built-in rnbinom with dispersion and mean
w <- rnbinom(n = n, size = dispersion, mu = mu)</pre>
# Using gamma-Poisson mixture with gamma rate parameter
x <- rpois(</pre>
  n = n,
  lambda = rgamma(n = n, shape = dispersion, rate = rate)
)
# Using gamma-Poisson mixture with gamma scale parameter
y <- rpois(
 n = n,
 lambda = rgamma(n = n, shape = dispersion, scale = scale)
# Using gamma-Poisson mixture with multiplicative mean and
# gamma scale parameter
z <- rpois(</pre>
 n = n,
 lambda = mu * rgamma(n = n, shape = dispersion, scale = 1/dispersion)
# Compare CDFs
par(mar=c(4,4,1,1))
plot(
 x = sort(w),
  y = (1:n)/n,
  xlim = range(c(w,x,y,z)),
 ylim = c(0,1),
  col = 'green',
  lwd = 4,
  type = '1',
```

```
main = 'CDF'
)
lines(x = sort(x), y = (1:n)/n, col = 'red', lwd = 2)
lines(x = sort(y), y = (1:n)/n, col = 'yellow', lwd = 1.5)
lines(x = sort(z), y = (1:n)/n, col = 'black')
```



The BNB distribution is implemented by compounding two conditionally independent Poisson random variables  $X_1 \mid G = g \sim \text{Poisson}(\mu g)$  and  $X_2 \mid G = g \sim \text{Poisson}(r \mu g)$  with a gamma random variable  $G \sim \text{Gamma}(\theta, \theta^{-1})$ . The probability mass function for the joint distribution of  $X_1, X_2$  is

$$P(X_1 = x_1, X_2 = x_2) = \frac{\Gamma(x_1 + x_2 + \theta)}{(\mu + r\mu + \theta)^{x_1 + x_2 + \theta}} \frac{\mu^{x_1}}{x_1!} \frac{(r\mu)^{x_2}}{x_2!} \frac{\theta^{\theta}}{\Gamma(\theta)}$$

where  $x_1, x_2 \in \mathbb{N}^{\geq 0}$  are specific values of the count outcomes,  $\theta \in \mathbb{R}^{>0}$  is the dispersion parameter which controls the dispersion and level of correlation between the two samples (otherwise known as the shape parameter of the gamma distribution),  $\mu \in \mathbb{R}^{>0}$  is the mean parameter, and  $r = \frac{\mu_2}{\mu_1} \in \mathbb{R}^{>0}$  is the ratio parameter representing the multiplicative change in the mean of the second sample relative to the first sample. G denotes the random subject effect and the gamma distribution scale parameter is assumed to be the inverse of the dispersion parameter  $(\theta^{-1})$  for identifiability.

Correlation decreases from 1 to 0 as the dispersion parameter increases from 0 to infinity. For a given dispersion, increasing means also increases the correlation. See 'Examples' for a demonstration.

See 'Details' in sim\_nb() for additional information on the negative binomial distribution.

#### Value

If nsims = 1 and the number of unique parameter combinations is one, the following objects are returned:

• If return\_type = "list", a list:

Slot	Name	Description
1		Simulated counts from sample 1.
2		Simulated counts from sample 2.

• If return\_type = "data.frame", a data frame:

Column	Name	Description
1	item	Subject/item indicator.
2	condition	Sample/condition indicator.
3	value	Simulated counts.

If nsims > 1 or the number of unique parameter combinations is greater than one, each object described above is returned in a list-column named data in a depower simulation data frame:

Column	Name	Description
1	n1	Sample size of sample 1.
2	n2	Sample size of sample 2.
3	mean1	Mean for sample 1.
4	mean2	Mean for sample 2.
5	ratio	Ratio of means (sample 2 / sample 1).
6	dispersion	Gamma distribution shape parameter (dispersion).
7	nsims	Number of valid simulation iterations.
8	distribution	Distribution sampled from.
9	data	List-column of simulated data.

# References

Yu L, Fernandez S, Brock G (2020). "Power analysis for RNA-Seq differential expression studies using generalized linear mixed effects models." *BMC Bioinformatics*, **21**(1), 198. ISSN 1471-2105, doi:10.1186/s1285902035417.

Rettiganti M, Nagaraja HN (2012). "Power Analyses for Negative Binomial Models with Application to Multiple Sclerosis Clinical Trials." *Journal of Biopharmaceutical Statistics*, **22**(2), 237–259. ISSN 1054-3406, 1520-5711, doi:10.1080/10543406.2010.528105.

Aban IB, Cutter GR, Mavinga N (2009). "Inferences and power analysis concerning two negative binomial distributions with an application to MRI lesion counts data." *Computational Statistics & Data Analysis*, **53**(3), 820–833. ISSN 01679473, doi:10.1016/j.csda.2008.07.034.

### See Also

```
sim_nb(), stats::rpois(), stats::rgamma(), stats::rnbinom()
```

# Examples

```
#-----#
# sim_bnb() examples
#-------
library(depower)
```

```
# Paired two-sample data returned in a data frame
sim_bnb(
  n = 10,
 mean1 = 10,
  ratio = 1.6,
  dispersion = 3,
  nsims = 1,
  return_type = "data.frame"
)
# Paired two-sample data returned in a list
sim_bnb(
  n = 10,
  mean1 = 10,
  ratio = 1.6,
  dispersion = 3,
  nsims = 1,
  return_type = "list"
# Two simulations of paired two-sample data
# returned as a list of data frames
sim_bnb(
 n = 10,
  mean1 = 10,
  ratio = 1.6,
  dispersion = 3,
  nsims = 2,
  return_type = "data.frame"
)
# Two simulations of Paired two-sample data
# returned as a list of lists
sim_bnb(
  n = 10,
  mean1 = 10,
  ratio = 1.6,
  dispersion = 3,
  nsims = 2,
  return_type = "list"
)
# Visualization of the BNB distribution as dispersion varies.
set.seed(1234)
data <- lapply(</pre>
  X = c(1, 10, 100, 1000),
  FUN = function(x) {
    d <- sim_bnb(</pre>
      n = 1000,
      mean1 = 10,
```

```
ratio = 1.5,
      dispersion = x,
      nsims = 1,
      return_type = "data.frame"
    )
    cor <- cor(</pre>
      x = d[d\$condition == "1", ]\$value,
      y = d[d$condition == "2", ]$value
    cbind(dispersion = x, correlation = cor, d)
)
data <- do.call(what = "rbind", args = data)</pre>
ggplot2::ggplot(
  data = data,
  mapping = ggplot2::aes(x = value, fill = condition)
) +
  ggplot2::facet_wrap(
    facets = ggplot2::vars(.data$dispersion),
    ncol = 2,
    labeller = ggplot2::labeller(.rows = ggplot2::label_both)
  ) +
  ggplot2::geom\_density(alpha = 0.3) +
  ggplot2::coord\_cartesian(xlim = c(0, 60)) +
  ggplot2::geom_text(
    mapping = ggplot2::aes(
      x = 30,
      y = 0.12,
      label = paste0("Correlation: ", round(correlation, 2))
    ),
    check_overlap = TRUE
  ) +
  ggplot2::labs(
    x = "Value",
    y = "Density",
    fill = "Condition",
    caption = "Mean1=10, Mean2=15, ratio=1.5"
```

sim\_log\_lognormal

Simulate data from a normal distribution

# **Description**

Simulate data from the log transformed lognormal distribution (i.e. a normal distribution). This function handles all three cases:

1. One-sample data

- 2. Dependent two-sample data
- 3. Independent two-sample data

### Usage

```
sim_log_lognormal(
    n1,
    n2 = NULL,
    ratio,
    cv1,
    cv2 = NULL,
    cor = 0,
    nsims = 1L,
    return_type = "list",
    ncores = 1L,
    messages = TRUE
)
```

### **Arguments**

ratio

n1 (integer: [2, Inf))

The sample size(s) of sample 1.

n2 (integer: NULL; [2, Inf))

The sample size(s) of sample 2. Set as NULL if you want to simulate for the one-sample case.

(numeric: (0, Inf))

The assumed population fold change(s) of sample 2 with respect to sample 1.

- For one-sample data, ratio is defined as the geometric mean (GM) of the original lognormal population distribution.
- For dependent two-sample data, ratio is defined by GM(sample 2 / sample 1) of the original lognormal population distributions.
  - e.g. ratio = 2 assumes that the geometric mean of all paired ratios (sample 2 / sample 1) is 2.
- For independent two-sample data, the ratio is defined by GM(group 2) / GM(group 1) of the original lognormal population distributions.
  - e.g. ratio = 2 assumes that the geometric mean of sample 2 is 2 times larger than the geometric mean of sample 1.

See 'Details' for additional information.

cv1 (numeric: (0, Inf))

The coefficient of variation(s) of sample 1 in the original lognormal data.

cv2 (numeric: NULL; (0, Inf))

The coefficient of variation(s) of sample 2 in the original lognormal data. Set as NULL if you want to simulate for the one-sample case.

cor (numeric: 0; [-1, 1])

The correlation(s) between sample 1 and sample 2 in the original lognormal data. Not used for the one-sample case.

nsims (Scalar integer: 1L; [1, Inf))

The number of simulated data sets. If nsims > 1, the data is returned in a list-

column of a depower simulation data frame.

return\_type (string: "list"; c("list", "data.frame"))

The data structure of the simulated data. If "list" (default), a list object is returned. If "data.frame" a data frame in tall format is returned. The list object provides computational efficiency and the data frame object is convenient

for formulas. See 'Value'.

ncores (Scalar integer: 1L; [1, Inf))

The number of cores (number of worker processes) to use. Do not set greater than the value returned by parallel::detectCores(). May be helpful when

the number of parameter combinations is large and nsims is large.

messages (Scalar logical: TRUE)

Whether or not to display messages for pathological simulation cases.

#### **Details**

Based on assumed characteristics of the original lognormal distribution, data is simulated from the corresponding log-transformed (normal) distribution. This simulated data is suitable for assessing power of a hypothesis for the geometric mean or ratio of geometric means from the original lognormal data.

This method can also be useful for other population distributions which are positive and where it makes sense to describe the ratio of geometric means. However, the lognormal distribution is theoretically correct in the sense that you can log transform to a normal distribution, compute the summary statistic, then apply the inverse transformation to summarize on the original lognormal scale.

Let  $GM(\cdot)$  be the geometric mean and  $AM(\cdot)$  be the arithmetic mean. For independent lognormal samples  $X_1$  and  $X_2$ 

$$\operatorname{Fold} \operatorname{Change} = \frac{GM(X_2)}{GM(X_1)}$$

For dependent lognormal samples  $X_1$  and  $X_2$ 

Fold Change = 
$$GM\left(\frac{X_2}{X_1}\right)$$

Unlike ratios and the arithmetic mean, for equal sample sizes of  $X_1$  and  $X_2$  it follows that  $\frac{GM(X_2)}{GM(X_1)} = GM\left(\frac{X_2}{X_1}\right) = e^{AM(\ln X_2) - AM(\ln X_1)} = e^{AM(\ln X_2 - \ln X_1)}$ .

The coefficient of variation (CV) for X is defined as

$$CV = \frac{SD(X)}{AM(X)}$$

The relationship between sample statistics for the original lognormal data (X) and the natural logged data  $(\ln X)$  are

$$\begin{split} AM(X) &= e^{AM(\ln X) + \frac{Var(\ln X)}{2}} \\ GM(X) &= e^{AM(\ln X)} \\ Var(X) &= AM(X)^2 \left( e^{Var(\ln X)} - 1 \right) \\ CV(X) &= \frac{\sqrt{AM(X)^2 \left( e^{Var(\ln X)} - 1 \right)}}{AM(X)} \\ &= \sqrt{e^{Var(\ln X)} - 1} \end{split}$$

and

$$AM(\ln X) = \ln \left( \frac{AM(X)}{\sqrt{CV(X)^2 + 1}} \right)$$

$$Var(\ln X) = \ln(CV(X)^2 + 1)$$

$$Cor(\ln X_1, \ln X_2) = \frac{\ln (Cor(X_1, X_2)CV(X_1)CV(X_2) + 1)}{SD(\ln X_1)SD(\ln X_2)}$$

Based on the properties of correlation and variance,

$$Var(X_2 - X_1) = Var(X_1) + Var(X_2) - 2Cov(X_1, X_2)$$

$$= Var(X_1) + Var(X_2) - 2Cor(X_1, X_2)SD(X_1)SD(X_2)$$

$$SD(X_2 - X_1) = \sqrt{Var(X_2 - X_1)}$$

The standard deviation of the differences gets smaller the more positive the correlation and conversely gets larger the more negative the correlation. For the special case where the two samples are uncorrelated and each has the same variance, it follows that

$$Var(X_2 - X_1) = \sigma^2 + \sigma^2$$
$$SD(X_2 - X_1) = \sqrt{2}\sigma$$

### Value

If nsims = 1 and the number of unique parameter combinations is one, the following objects are returned:

• If one-sample data with return\_type = "list", a list:

Slot Name Description
1 One sample of simulated normal values.

• If one-sample data with return\_type = "data.frame", a data frame:

Column	Name	Description
1	item	Pair/subject/item indicator.
2.	value	Simulated normal values

• If two-sample data with return\_type = "list", a list:

Slot	Name	Description
1		Simulated normal values from sample 1.
2		Simulated normal values from sample 2

• If two-sample data with return\_type = "data.frame", a data frame:

Column	Name	Description
1	item	Pair/subject/item indicator.
2	condition	Time/group/condition indicator.
3	value	Simulated normal values.

If nsims > 1 or the number of unique parameter combinations is greater than one, each object described above is returned in data frame, located in a list-column named data.

• If one-sample data, a data frame:

Column	Name	Description
1	n1	The sample size.
2	ratio	Geometric mean [GM(sample 1)].
3	cv1	Coefficient of variation for sample 1.
4	nsims	Number of data simulations.
5	distribution	Distribution sampled from.
6	data	List-column of simulated data.

• If two-sample data, a data frame:

Column	Name	Description
1	n1	Sample size of sample 1.
2	n2	Sample size of sample 2.
3	ratio	Ratio of geometric means [GM(sample 2) / GM(sample 1)] or geometric mean ratio [GM(sample
4	cv1	Coefficient of variation for sample 1.
5	cv2	Coefficient of variation for sample 2.
6	cor	Correlation between samples.
7	nsims	Number of data simulations.
8	distribution	Distribution sampled from.
Q	data	List-column of simulated data

### References

Julious SA (2004). "Sample sizes for clinical trials with Normal data." *Statistics in Medicine*, **23**(12), 1921–1986. doi:10.1002/sim.1783.

Hauschke D, Steinijans VW, Diletti E, Burke M (1992). "Sample size determination for bioequivalence assessment using a multiplicative model." *Journal of Pharmacokinetics and Biopharmaceutics*, **20**(5), 557–561. ISSN 0090-466X, doi:10.1007/BF01061471.

Johnson NL, Kotz S, Balakrishnan N (1994). *Continuous univariate distributions*, Wiley series in probability and mathematical statistics, 2nd ed edition. Wiley, New York. ISBN 9780471584957 9780471584940.

### See Also

```
stats::rnorm(), mvnfast::rmvn()
```

# **Examples**

cv1 = 0.35,

```
#-----
# sim_log_lognormal() examples
#-----
library(depower)
# Independent two-sample data returned in a data frame
sim_log_lognormal(
 n1 = 10,
 n2 = 10,
 ratio = 1.3,
 cv1 = 0.35,
 cv2 = 0.35,
 cor = 0,
 nsims = 1,
 return_type = "data.frame"
)
# Independent two-sample data returned in a list
sim_log_lognormal(
 n1 = 10,
 n2 = 10,
 ratio = 1.3,
 cv1 = 0.35,
 cv2 = 0.35.
 cor = 0,
 nsims = 1,
 return_type = "list"
)
# Dependent two-sample data returned in a data frame
sim_log_lognormal(
 n1 = 10,
 n2 = 10,
 ratio = 1.3,
 cv1 = 0.35,
 cv2 = 0.35,
 cor = 0.4,
 nsims = 1,
 return_type = "data.frame"
)
# Dependent two-sample data returned in a list
sim_log_lognormal(
 n1 = 10,
 n2 = 10,
 ratio = 1.3,
```

```
cv2 = 0.35,
  cor = 0.4,
 nsims = 1,
  return_type = "list"
)
# One-sample data returned in a data frame
sim_log_lognormal(
 n1 = 10,
  ratio = 1.3,
  cv1 = 0.35,
  nsims = 1,
  return_type = "data.frame"
# One-sample data returned in a list
sim_log_lognormal(
  n1 = 10,
  ratio = 1.3,
  cv1 = 0.35,
 nsims = 1,
  return_type = "list"
)
# Independent two-sample data: two simulations for four parameter combinations.
# Returned as a list-column of lists within a data frame
sim_log_lognormal(
  n1 = c(10, 20),
 n2 = c(10, 20),
  ratio = 1.3,
  cv1 = 0.35,
  cv2 = 0.35,
  cor = 0,
  nsims = 2,
  return_type = "list"
)
# Dependent two-sample data: two simulations for two parameter combinations.
# Returned as a list-column of lists within a data frame
sim_log_lognormal(
  n1 = c(10, 20),
 n2 = c(10, 20),
  ratio = 1.3,
 cv1 = 0.35,
  cv2 = 0.35,
  cor = 0.4,
  nsims = 2,
  return_type = "list"
)
# One-sample data: two simulations for two parameter combinations
# Returned as a list-column of lists within a data frame
sim_log_lognormal(
```

```
n1 = c(10, 20),
ratio = 1.3,
cv1 = 0.35,
nsims = 2,
return_type = "list"
)
```

 $sim\_nb$ 

Simulate data from a NB distribution

# **Description**

Simulate data from two independent negative binomial (NB) distributions. For paired data, see sim\_bnb().

# Usage

```
sim_nb(
   n1,
   n2 = n1,
   mean1,
   mean2,
   ratio,
   dispersion1,
   dispersion2 = dispersion1,
   nsims = 1L,
   return_type = "list",
   max_zeros = 0.99,
   ncores = 1L
)
```

# **Arguments**

dispersion1 (numeric: (0, Inf))

The dispersion parameter(s) of group 1 ( $\theta_1$ ). See 'Details' and 'Examples'.

(numeric: dispersion1; (0, Inf)) dispersion2

The dispersion parameter(s) of group 2 ( $\theta_2$ ). See 'Details' and 'Examples'.

nsims (Scalar integer: 1L; [1, Inf))

> The expected number of simulated data sets. If nsims > 1, the data is returned in a list-column of a depower simulation data frame. nsims may be reduced

depending on max\_zeros.

(string: "list"; c("list", "data.frame")) return\_type

> The data structure of the simulated data. If "list" (default), a list object is returned. If "data.frame" a data frame in tall format is returned. The list object provides computational efficiency and the data frame object is convenient

for formulas. See 'Value'.

(Scalar numeric: 0.99; [0, 1]) max\_zeros

> The maximum proportion of zeros each group in a simulated dataset is allowed to have. If the proportion of zeros is greater than this value, the corresponding data is excluded from the set of simulations. This is most likely to occur when

the sample size is small and the dispersion parameter is small.

(Scalar integer: 1L; [1, Inf)) ncores

> The number of cores (number of worker processes) to use. Do not set greater than the value returned by parallel::detectCores(). May be helpful when

the number of parameter combinations is large and nsims is large.

### **Details**

The negative binomial distribution has many parameterizations. In the regression modeling context, it is common to specify the distribution in terms of its mean and dispersion. We use the following probability mass function:

$$P(X = x) = {x + \theta - 1 \choose x} \left(\frac{\theta}{\theta + \mu}\right)^{\theta} \left(\frac{\mu}{\mu + \theta}\right)^{x}$$
$$= \frac{\Gamma(x + \theta)}{x!\Gamma(\theta)} \left(\frac{\theta}{\theta + \mu}\right)^{\theta} \left(\frac{\mu}{\mu + \theta}\right)^{x}$$
$$= \frac{\Gamma(x + \theta)}{(\theta + \mu)^{\theta + x}} \frac{\theta^{\theta}}{\Gamma(\theta)} \frac{\mu^{x}}{x!}$$

where  $x \in \mathbb{N}^{\geq 0}$ ,  $\theta \in \mathbb{R}^{>0}$  is the dispersion parameter, and  $\mu \in \mathbb{R}^{>0}$  is the mean. This is analogous to the typical formulation where X is counting x failures given  $\theta$  successes and  $p = \frac{\theta}{\theta + \mu}$  is the probability of success on each trial. It follows that  $E(X) = \mu$  and  $Var(X) = \mu + \frac{\mu^2}{\theta}$ . The  $\theta$ parameter describes the 'dispersion' among observations. Smaller values of  $\theta$  lead to overdispersion and larger values of  $\theta$  decrease the overdispersion, eventually converging to the Poisson distribution.

Described above is the 'indirect quadratic parameterization' of the negative binomial distribution, which is commonly found in the R ecosystem. However, it is somewhat counterintuitive because the smaller  $\theta$  gets, the larger the overdispersion. The 'direct quadratic parameterization' of the negative binomial distribution may be found in some R packages and other languages such as SAS

and Stata. The direct parameterization is defined by substituting  $\alpha = \frac{1}{\theta}$  ( $\alpha > 0$ ) which results in  $Var(X) = \mu + \alpha \mu^2$ . In this case, the larger  $\alpha$  gets the larger the overdispersion, and the Poisson distribution is a special case of the negative binomial distribution where  $\alpha = 0$ .

A general class of negative binomial models may be defined with mean  $\mu$  and variance  $\mu + \alpha \mu^p$ . The 'linear parameterization' is then found by setting p=1, resulting in  $Var(X)=\mu+\alpha\mu$ . It's common to label the linear parameterization as 'NB1' and the direct quadratic parameterization as 'NB2'.

See 'Details' in sim\_bnb() for additional information on the gamma-Poisson mixture formulation of the negative binomial distribution.

### Value

If nsims = 1 and the number of unique parameter combinations is one, the following objects are returned:

• If return\_type = "list", a list:

Slot	Name	Description
1		Simulated counts from group 1.
2		Simulated counts from group 2.

• If return\_type = "data.frame", a data frame:

Column	Name	Description
1	item	Subject/item indicator.
2	condition	Group/condition indicator.
3	value	Simulated counts.

If nsims > 1 or the number of unique parameter combinations is greater than one, each object described above is returned in a list-column named data in a depower simulation data frame:

Column	Name	Description
1	n1	Sample size of group 1.
2	n2	Sample size of group 2.
3	mean1	Mean for group 1.
4	mean2	Mean for group 2.
5	ratio	Ratio of means (group 2 / group 1).
6	dispersion1	Dispersion parameter for group 1.
7	dispersion2	Dispersion parameter for group 2.
8	nsims	Number of valid simulation iterations.
9	distribution	Distribution sampled from.
10	data	List-column of simulated data.

### References

Yu L, Fernandez S, Brock G (2017). "Power analysis for RNA-Seq differential expression studies." *BMC Bioinformatics*, **18**(1), 234. ISSN 1471-2105, doi:10.1186/s1285901716482.

Rettiganti M, Nagaraja HN (2012). "Power Analyses for Negative Binomial Models with Application to Multiple Sclerosis Clinical Trials." *Journal of Biopharmaceutical Statistics*, **22**(2), 237–259. ISSN 1054-3406, 1520-5711, doi:10.1080/10543406.2010.528105.

Aban IB, Cutter GR, Mavinga N (2009). "Inferences and power analysis concerning two negative binomial distributions with an application to MRI lesion counts data." *Computational Statistics & Data Analysis*, **53**(3), 820–833. ISSN 01679473, doi:10.1016/j.csda.2008.07.034.

Hilbe JM (2011). *Negative Binomial Regression*, 2 edition. Cambridge University Press. ISBN 9780521198158 9780511973420, doi:10.1017/CBO9780511973420.

Hilbe JM (2014). *Modeling count data*. Cambridge University Press, New York, NY. ISBN 9781107028333 9781107611252, doi:10.1017/CBO9781139236065.

Cameron AC, Trivedi PK (2013). *Regression Analysis of Count Data*, Econometric Society Monographs, 2 edition. Cambridge University Press. doi:10.1017/CBO9781139013567.

#### See Also

```
sim_bnb(), stats::rnbinom()
```

### **Examples**

```
# sim_nb() examples
library(depower)
# Independent two-sample NB data returned in a data frame
sim_nb(
 n1 = 10,
 mean1 = 5,
 ratio = 1.6,
 dispersion1 = 0.5,
 dispersion2 = 0.5,
 nsims = 1,
 return_type = "data.frame"
# Independent two-sample NB data returned in a list
sim_nb(
 n1 = 10,
 mean1 = 5,
 ratio = 1.6,
 dispersion1 = 0.5,
 dispersion2 = 0.5,
 nsims = 1,
 return_type = "list"
# Two simulations of independent two-sample data
# returned as a list of data frames
sim_nb(
 n1 = 10,
```

```
mean1 = 5,
 ratio = 1.6,
 dispersion1 = 0.5,
 dispersion2 = 0.5,
 nsims = 2,
 return_type = "data.frame"
)
# Two simulations of independent two-sample data
# returned as a list of lists
sim_nb(
 n1 = 10,
 mean1 = 5,
 ratio = 1.6,
 dispersion1 = 0.5,
 dispersion2 = 0.5,
 nsims = 2,
 return_type = "list"
)
                ______
# Visualization of the NB distribution as dispersion varies between groups.
disp <- expand.grid(c(1, 10, 100), c(1, 10, 100))
set.seed(1234)
data <- mapply(</pre>
 FUN = function(disp1, disp2) {
   d <- sim_nb(</pre>
     n1 = 1000,
     mean1 = 10,
     ratio = 1.5,
     dispersion1 = disp1,
     dispersion2 = disp2,
     nsims = 1,
     return_type = "data.frame"
   cbind(dispersion1 = disp1, dispersion2 = disp2, d)
 disp1 = disp[[1]],
 disp2 = disp[[2]],
 SIMPLIFY = FALSE
)
data <- do.call(what = "rbind", args = data)</pre>
ggplot2::ggplot(
 data = data,
 mapping = ggplot2::aes(x = value, fill = condition)
) +
 ggplot2::facet_grid(
   rows = ggplot2::vars(.data$dispersion2),
   cols = ggplot2::vars(.data$dispersion1),
   labeller = ggplot2::labeller(
```

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```
.rows = ggplot2::label_both,
   .cols = ggplot2::label_both
)
) +
ggplot2::geom_density(alpha = 0.3) +
ggplot2::coord_cartesian(xlim = c(0, 50)) +
ggplot2::labs(
   x = "Value",
   y = "Density",
   fill = "Condition",
   caption = "Mean1=10, Mean2=15, ratio=1.5"
)
```

t\_test\_paired

Paired and one-sample t-Tests

### **Description**

Performs paired and one-sample t-Tests.

### Usage

```
t_test_paired(data, alternative = "two.sided", ci_level = NULL, mean_null = 0)
```

# Arguments

data (list)

A list whose first element is the vector of normal values from sample 1 and the second element is the vector of normal values from sample 2. Both vectors must be the same sample size and sorted by the subject/item index. If length(data) == 1L, the one-sample test is used. NAs are silently excluded. The default output from sim\_log\_lognormal().

alternative (string: "two.sided")

The alternative hypothesis. Must be one of "two.sided", "greater", or "less".

See 'Details' for additional information.

ci\_level (Scalar numeric: NULL; (0, 1))

If NULL, confidence intervals are set as NA. If in (0, 1), confidence intervals are

calculated at the specified level.

mean\_null (Scalar numeric: 0; (-Inf, Inf))

The mean or mean difference assumed under the null hypothesis. See 'Details'

for additional information.

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### **Details**

This function is primarily designed for speed in simulation. Missing values are silently excluded.

The one-sample test is used for both the true one-sample scenario and for the paired differences from a dependent two-sample scenario. Below we use paired difference language as that is the most common case. The hypotheses for the paired t-test are

$$H_{null}: \mu_{diff} = \mu_{null}$$
  $H_{alt}: egin{cases} \mu_{diff} 
eq \mu_{null} & ext{two-sided} \\ \mu_{diff} 
eq \mu_{null} & ext{greater than} \\ \mu_{diff} 
eq \mu_{null} & ext{less than} \end{cases}$ 

where  $\mu_{diff} = AM(X_2 - X_1)$  is the arithmetic mean of the paired differences (sample 2 - sample 1) and  $\mu_{null}$  is a constant for the assumed population mean difference (usually  $\mu_{null} = 0$ ).

The test statistic is

$$T = \frac{\bar{x}_{diff} - \mu_{null}}{\sqrt{\frac{s^2}{n}}}$$

where  $\bar{x}_{diff}$  is the sample mean of the differences,  $\mu_{null}$  is the population mean difference assumed under the null hypothesis, n is the sample size of the differences, and  $s^2$  is the sample variance.

The critical value of the test statistic has degrees of freedom

$$df = n - 1$$

and the p-value is calculated as

$$p = \begin{cases} 2 \min\{P(T \geq t_{n-1} \mid H_{null}), P(T \leq t_{n-1} \mid H_{null})\} & \text{two-sided} \\ P(T \geq t_{n-1} \mid H_{null}) & \text{greater than} \\ P(T \leq t_{n-1} \mid H_{null}) & \text{less than} \end{cases}$$

Let  $GM(\cdot)$  be the geometric mean and  $AM(\cdot)$  be the arithmetic mean. For dependent lognormal samples  $X_1$  and  $X_2$  it follows that  $\ln X_1$  and  $\ln X_2$  are dependent normally distributed variables. Setting  $\mu_{diff} = AM(\ln X_2 - \ln X_1)$  we have

$$e^{\mu_{diff}} = GM\left(\frac{X_2}{X_1}\right)$$

This forms the basis for making inference about the geometric mean ratio of the original lognormal data using the mean difference of the log transformed normal data.

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### Value

A list with the following elements:

Slot	Subslot	Name	Description
1		t	Value of the t-statistic.
2		df	Degrees of freedom for the t-statistic.
3		р	p-value.
4		mean_diff	Estimated mean or mean of the differences (sample 2 – sample 1).
4	1	estimate	Point estimate.
4	2	lower	Confidence interval lower bound.
4	3	upper	Confidence interval upper bound.
5		n	Number of paired observations.
6		method	Method used for the results.
7		alternative	The alternative hypothesis.
8		ci_level	The confidence level.
9		mean_null	Assumed population mean of the differences under the null hypothesis.

### References

Julious SA (2004). "Sample sizes for clinical trials with Normal data." *Statistics in Medicine*, **23**(12), 1921–1986. doi:10.1002/sim.1783.

Hauschke D, Steinijans VW, Diletti E, Burke M (1992). "Sample size determination for bioequivalence assessment using a multiplicative model." *Journal of Pharmacokinetics and Biopharmaceutics*, **20**(5), 557–561. ISSN 0090-466X, doi:10.1007/BF01061471.

Johnson NL, Kotz S, Balakrishnan N (1994). *Continuous univariate distributions*, Wiley series in probability and mathematical statistics, 2nd ed edition. Wiley, New York. ISBN 9780471584957 9780471584940.

### See Also

```
stats::t.test()
```

# Examples

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```
# Paired t-test using two dependent samples
set.seed(1234)
t_test2 <- sim_log_lognormal(
    n1 = 40,
    n2 = 40,
    ratio = 1.5,
    cv1 = 0.4,
    cv2 = 0.2,
    cor = 0.3
) |>
    t_test_paired(ci_level = 0.95)
```

t\_test\_welch

Welch's t-Test

# **Description**

Performs Welch's independent two-sample t-test.

### Usage

```
t_test_welch(data, alternative = "two.sided", ci_level = NULL, mean_null = 0)
```

### **Arguments**

data (list)

A list whose first element is the vector of normal values from group 1 and the second element is the vector of normal values from group 2. NAs are silently excluded. The default output from simplex legenerates.

excluded. The default output from sim\_log\_lognormal().

alternative (string: "two.sided")

The alternative hypothesis. Must be one of "two.sided", "greater", or "less".

See 'Details' for additional information.

ci\_level (Scalar numeric: NULL; (0, 1))

If NULL, confidence intervals are set as NA. If in (0, 1), confidence intervals are

calculated at the specified level.

mean\_null (Scalar numeric: 0; (-Inf, Inf))

The difference of means assumed under the null hypothesis. See 'Details' for

additional information.

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### **Details**

This function is primarily designed for speed in simulation. Missing values are silently excluded. The hypotheses for Welch's independent two-sample t-test are

$$H_{null}: \mu_2 - \mu_1 = \mu_{null}$$

$$H_{alt}: \begin{cases} \mu_2 - \mu_1 \neq \mu_{null} & \text{two-sided} \\ \mu_2 - \mu_1 > \mu_{null} & \text{greater than} \\ \mu_2 - \mu_1 < \mu_{null} & \text{less than} \end{cases}$$

where  $\mu_1$  is the population mean of group 1,  $\mu_2$  is the population mean of group 2, and  $\mu_{null}$  is a constant for the assumed difference of population means (usually  $\mu_{null} = 0$ ).

The test statistic is

$$T = \frac{(\bar{x}_2 - \bar{x}_1) - \mu_{null}}{\sqrt{\frac{s_1^2}{n_1} + \frac{s_2^2}{n_2}}}$$

where  $\bar{x}_1$  and  $\bar{x}_2$  are the sample means,  $\mu_{null}$  is the difference of population means assumed under the null hypothesis,  $n_1$  and  $n_2$  are the sample sizes, and  $s_1^2$  and  $s_2^2$  are the sample variances.

The critical value of the test statistic uses the Welch-Satterthwaite degrees of freedom

$$v = \frac{\left(\frac{s_1^2}{n_1} + \frac{s_2^2}{n_2}\right)^2}{(N_1 - 1)^{-1} \left(\frac{s_1^2}{n_1}\right)^2 + (N_2 - 1)^{-1} \left(\frac{s_2^2}{n_2}\right)^2}$$

and the p-value is calculated as

$$p = \begin{cases} 2\min\{P(T \geq t_v \mid H_{null}), P(T \leq t_v \mid H_{null})\} & \text{two-sided} \\ P(T \geq t_v \mid H_{null}) & \text{greater than} \\ P(T \leq t_v \mid H_{null}) & \text{less than} \end{cases}$$

Let  $GM(\cdot)$  be the geometric mean and  $AM(\cdot)$  be the arithmetic mean. For independent lognormal variables  $X_1$  and  $X_2$  it follows that  $\ln X_1$  and  $\ln X_2$  are independent normally distributed variables. Defining  $\mu_{X_2} - \mu_{X_1} = AM(\ln X_2) - AM(\ln X_1)$  we have

$$e^{\mu_{X_2} - \mu_{X_1}} = \frac{GM(X_2)}{GM(X_1)}$$

This forms the basis for making inference about the ratio of geometric means of the original lognormal data using the difference of means of the log transformed normal data. t\_test\_welch 59

### Value

A list with the following elements:

Slot	Subslot	Name	Description
1		t	Value of the t-statistic.
2		df	Degrees of freedom for the t-statistic.
3		р	p-value.
4		diff_mean	Estimated difference of means (group 2 – group 1).
4	1	estimate	Point estimate.
4	2	lower	Confidence interval lower bound.
4	3	upper	Confidence interval upper bound.
5		mean1	Estimated mean of group 1.
6		mean2	Estimated mean of group 2.
7		n1	Sample size of group 1.
8		n2	Sample size of group 2.
9		method	Method used for the results.
10		alternative	The alternative hypothesis.
11		ci_level	The confidence level.
12		mean_null	Assumed population difference of the means under the null hypothesis.

# References

Julious SA (2004). "Sample sizes for clinical trials with Normal data." *Statistics in Medicine*, **23**(12), 1921–1986. doi:10.1002/sim.1783.

Hauschke D, Steinijans VW, Diletti E, Burke M (1992). "Sample size determination for bioequivalence assessment using a multiplicative model." *Journal of Pharmacokinetics and Biopharmaceutics*, **20**(5), 557–561. ISSN 0090-466X, doi:10.1007/BF01061471.

Johnson NL, Kotz S, Balakrishnan N (1994). *Continuous univariate distributions*, Wiley series in probability and mathematical statistics, 2nd ed edition. Wiley, New York. ISBN 9780471584957 9780471584940.

### See Also

```
stats::t.test()
```

# **Examples**

```
#-----
# t_test_welch() examples
#------
library(depower)

# Welch's t-test
set.seed(1234)
sim_log_lognormal(
    n1 = 40,
    n2 = 40,
    ratio = 1.5,
    cv1 = 0.4,
```

```
cv2 = 0.4
) |>
  t_test_welch(ci_level = 0.95)
```

wald\_test\_bnb

Wald test for BNB ratio of means

### **Description**

Wald test for the ratio of means from bivariate negative binomial outcomes.

# Usage

```
wald_test_bnb(data, ci_level = NULL, link = "log", ratio_null = 1, ...)
```

# **Arguments**

data (list)

A list whose first element is the vector of negative binomial values from sample 1 and the second element is the vector of negative binomial values from sample 2. Each vector must be sorted by the subject/item index and must be the same sample size. NAs are silently excluded. The default output from sim\_bnb().

ci\_level (Scalar numeric: NULL; (0, 1))

If NULL, confidence intervals are set as NA. If in (0, 1), confidence intervals are

calculated at the specified level.

link (Scalar string: "log")

The one-to-one link function for transformation of the ratio in the test hypotheses. Must be one of "log" (default) "sgnt" "sguared" or "identity". See

ses. Must be one of "log" (default), "sqrt", "squared", or "identity". See

'Details' for additional information.

ratio\_null (Scalar numeric: 1; (0, Inf))

The (pre-transformation) ratio of means assumed under the null hypothesis (sample 2 / sample 1). Typically ratio\_null = 1 (no difference). See 'Details' for

additional information.

... Optional arguments passed to the MLE function mle\_bnb().

#### **Details**

This function is primarily designed for speed in simulation. Missing values are silently excluded.

Suppose  $X_1 \mid G = g \sim \operatorname{Poisson}(\mu g)$  and  $X_2 \mid G = g \sim \operatorname{Poisson}(r\mu g)$  where  $G \sim \operatorname{Gamma}(\theta, \theta^{-1})$  is the random item (subject) effect. Then  $X_1, X_2 \sim \operatorname{BNB}(\mu, r, \theta)$  is the joint distribution where  $X_1$  and  $X_2$  are dependent (though conditionally independent),  $X_1$  is the count outcome for sample 1 of the items (subjects),  $X_2$  is the count outcome for sample 2 of the items (subjects),  $\mu$  is the conditional mean of sample 1, r is the ratio of the conditional means of sample 2 with respect to sample 1, and  $\theta$  is the gamma distribution shape parameter which controls the dispersion and the correlation between sample 1 and 2.

The hypotheses for the Wald test of r are

$$H_{null}: f(r) = f(r_{null})$$
  
 $H_{alt}: f(r) \neq f(r_{null})$ 

where  $f(\cdot)$  is a one-to-one link function with nonzero derivative,  $r=\frac{\bar{X}_2}{\bar{X}_1}$  is the population ratio of arithmetic means for sample 2 with respect to sample 1, and  $r_{null}$  is a constant for the assumed null population ratio of means (typically  $r_{null}=1$ ).

Rettiganti and Nagaraja (2012) found that  $f(r)=r^2$ , f(r)=r, and  $f(r)=r^{0.5}$  had greatest power when r<1. However, when r>1,  $f(r)=\ln r$ , the likelihood ratio test, and  $f(r)=r^{0.5}$  had greatest power.  $f(r)=r^2$  was biased when r>1. Both  $f(r)=\ln r$  and  $f(r)=r^{0.5}$  produced acceptable results for any r value. These results depend on the use of asymptotic vs. exact critical values.

The Wald test statistic is

$$W(f(\hat{r})) = \left(\frac{f\left(\frac{\bar{x}_2}{\bar{x}_1}\right) - f(r_{null})}{f'(\hat{r})\hat{\sigma}_{\hat{r}}}\right)^2$$

where

$$\hat{\sigma}_{\hat{r}}^2 = \frac{\hat{r}(1+\hat{r})(\hat{\mu}+\hat{r}\hat{\mu}+\hat{\theta})}{n\left[\hat{\mu}(1+\hat{r})(\hat{\mu}+\hat{\theta})-\hat{\theta}\hat{r}\right]}$$

Under  $H_{null}$ , the Wald test statistic is asymptotically distributed as  $\chi_1^2$ . The approximate level  $\alpha$  test rejects  $H_{null}$  if  $W(f(\hat{r})) \geq \chi_1^2(1-\alpha)$ . Note that the asymptotic critical value is known to underestimate the exact critical value. Hence, the nominal significance level may not be achieved for small sample sizes (possibly  $n \leq 10$  or  $n \leq 50$ ). The level of significance inflation also depends on  $f(\cdot)$  and is most severe for  $f(r) = r^2$ , where only the exact critical value is recommended.

# Value

A list with the following elements:

Subslot	Name	Description
	chisq	$\chi^2$ test statistic for the ratio of means.
	df	Degrees of freedom.
	р	p-value.
	ratio	Estimated ratio of means (group 2 / group 1).
1	estimate	Point estimate.
2	lower	Confidence interval lower bound.
3	upper	Confidence interval upper bound.
	mean1	Estimated mean of sample 1.
	mean2	Estimated mean of sample 2.
	dispersion	Estimated dispersion.
	n1	The sample size of sample 1.
	n2	The sample size of sample 2.
	1 2	chisq df p ratio 1 estimate 2 lower 3 upper mean1 mean2 dispersion n1

10	method	Method used for the results.
11	ci_level	The confidence level.
12	link	Link function used to transform the ratio of means in the test hypotheses.
13	ratio_null	Assumed ratio of means under the null hypothesis.
14	mle_code	Integer indicating why the optimization process terminated.
15	mle_message	Information from the optimizer.

### References

Rettiganti M, Nagaraja HN (2012). "Power Analyses for Negative Binomial Models with Application to Multiple Sclerosis Clinical Trials." *Journal of Biopharmaceutical Statistics*, **22**(2), 237–259. ISSN 1054-3406, 1520-5711, doi:10.1080/10543406.2010.528105.

Aban IB, Cutter GR, Mavinga N (2009). "Inferences and power analysis concerning two negative binomial distributions with an application to MRI lesion counts data." *Computational Statistics & Data Analysis*, **53**(3), 820–833. ISSN 01679473, doi:10.1016/j.csda.2008.07.034.

# **Examples**

```
#----
# wald_test_bnb() examples
#-----
library(depower)

set.seed(1234)
sim_bnb(
    n = 40,
    mean1 = 10,
    ratio = 1.2,
    dispersion = 2
) |>
    wald_test_bnb()
```

wald\_test\_nb

Wald test for NB ratio of means

# Description

Wald test for the ratio of means from two independent negative binomial outcomes.

# Usage

```
wald_test_nb(
  data,
  equal_dispersion = FALSE,
  ci_level = NULL,
  link = "log",
  ratio_null = 1,
  ...
)
```

### Arguments

data (list)

A list whose first element is the vector of negative binomial values from group 1 and the second element is the vector of negative binomial values from group 2. NAs are silently excluded. The default output from sim\_nb().

equal\_dispersion

(Scalar logical: FALSE)

If TRUE, the Wald test is calculated assuming both groups have the same population dispersion parameter. If FALSE (default), the Wald test is calculated assuming different dispersions.

ci\_level (Scalar numeric: NULL; (0, 1))

If NULL, confidence intervals are set as NA. If in (0, 1), confidence intervals are

calculated at the specified level.

link (Scalar string: "log")

The one-to-one link function for transformation of the ratio in the test hypotheses. Must be one of "log" (default), "sqrt", "squared", or "identity".

ratio\_null (Scalar numeric: 1; (0, Inf))

The (pre-transformation) ratio of means assumed under the null hypothesis (group 2 / group 1). Typically ratio\_null = 1 (no difference). See 'Details' for addi-

tional information.

... Optional arguments passed to the MLE function mle\_nb().

### **Details**

This function is primarily designed for speed in simulation. Missing values are silently excluded.

Suppose  $X_1 \sim NB(\mu, \theta_1)$  and  $X_2 \sim NB(r\mu, \theta_2)$  where  $X_1$  and  $X_2$  are independent,  $X_1$  is the count outcome for items in group 1,  $X_2$  is the count outcome for items in group 2,  $\mu$  is the arithmetic mean count in group 1, r is the ratio of arithmetic means for group 2 with respect to group 1,  $\theta_1$  is the dispersion parameter of group 1, and  $\theta_2$  is the dispersion parameter of group 2.

The hypotheses for the Wald test of r are

$$H_{null}: f(r) = f(r_{null})$$
  
 $H_{alt}: f(r) \neq f(r_{null})$ 

where  $f(\cdot)$  is a one-to-one link function with nonzero derivative,  $r = \frac{\bar{X}_2}{\bar{X}_1}$  is the population ratio of arithmetic means for group 2 with respect to group 1, and  $r_{null}$  is a constant for the assumed null population ratio of means (typically  $r_{null} = 1$ ).

Rettiganti and Nagaraja (2012) found that  $f(r)=r^2$  and f(r)=r had greatest power when r<1. However, when r>1,  $f(r)=\ln r$ , the likelihood ratio test, and the Rao score test have greatest power. Note that  $f(r)=\ln r$ , LRT, and RST were unbiased tests while the f(r)=r and  $f(r)=r^2$  tests were biased when r>1. The  $f(r)=\ln r$ , LRT, and RST produced acceptable results for any r value. These results depend on the use of asymptotic vs. exact critical values.

The Wald test statistic is

$$W(f(\hat{r})) = \left(\frac{f\left(\frac{\bar{x}_2}{\bar{x}_1}\right) - f(r_{null})}{f'(\hat{r})\hat{\sigma}_{\hat{r}}}\right)^2$$

where

$$\hat{\sigma}_{\hat{r}}^{2} = \frac{\hat{r} \left[ n_{1} \hat{\theta}_{1} (\hat{r} \hat{\mu} + \hat{\theta}_{2}) + n_{2} \hat{\theta}_{2} \hat{r} (\hat{\mu} + \hat{\theta}_{1}) \right]}{n_{1} n_{2} \hat{\theta}_{1} \hat{\theta}_{2} \hat{\mu}}$$

Under  $H_{null}$ , the Wald test statistic is asymptotically distributed as  $\chi_1^2$ . The approximate level  $\alpha$  test rejects  $H_{null}$  if  $W(f(\hat{r})) \geq \chi_1^2(1-\alpha)$ . Note that the asymptotic critical value is known to underestimate the exact critical value. Hence, the nominal significance level may not be achieved for small sample sizes (possibly  $n \leq 10$  or  $n \leq 50$ ). The level of significance inflation also depends on  $f(\cdot)$  and is most severe for  $f(r) = r^2$ , where only the exact critical value is recommended.

### Value

A list with the following elements:

Slot	Subslot	Name	Description
1		chisq	$\chi^2$ test statistic for the ratio of means.
2		df	Degrees of freedom.
3		р	p-value.
4		ratio	Estimated ratio of means (group 2 / group 1).
4	1	estimate	Point estimate.
4	2	lower	Confidence interval lower bound.
4	3	upper	Confidence interval upper bound.
5		mean1	Estimated mean of group 1.
6		mean2	Estimated mean of group 2.
7		dispersion1	Estimated dispersion of group 1.
8		dispersion2	Estimated dispersion of group 2.
9		n1	Sample size of group 1.
10		n2	Sample size of group 2.
11		method	Method used for the results.
12		ci_level	The confidence level.
13		equal_dispersion	Whether or not equal dispersions were assumed.
14		link	Link function used to transform the ratio of means in the test hypotheses.
15		ratio_null	Assumed ratio of means under the null hypothesis.
16		mle_code	Integer indicating why the optimization process terminated.
17		mle_message	Information from the optimizer.

# References

Rettiganti M, Nagaraja HN (2012). "Power Analyses for Negative Binomial Models with Application to Multiple Sclerosis Clinical Trials." *Journal of Biopharmaceutical Statistics*, **22**(2), 237–259. ISSN 1054-3406, 1520-5711, doi:10.1080/10543406.2010.528105.

Aban IB, Cutter GR, Mavinga N (2009). "Inferences and power analysis concerning two negative binomial distributions with an application to MRI lesion counts data." *Computational Statistics & Data Analysis*, **53**(3), 820–833. ISSN 01679473, doi:10.1016/j.csda.2008.07.034.

# **Examples**

```
#------
# wald_test_nb() examples
#------
library(depower)

set.seed(1234)
sim_nb(
    n1 = 60,
    n2 = 40,
    mean1 = 10,
    ratio = 1.5,
    dispersion1 = 2,
    dispersion2 = 8
) |>
    wald_test_nb()
```

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