Package 'transformGamPoi'

November 3, 2025

```
Version 1.17.0
Description Variance-stabilizing transformations help with the analysis of
     heteroskedastic data (i.e., data where the variance is not constant, like count data).
     This package provide two types of variance stabilizing transformations: (1) methods based on the
     delta method (e.g., 'acosh', 'log(x+1)'), (2) model residual based (Pearson and randomized
     quantile residuals).
BugReports https://github.com/const-ae/transformGamPoi/issues
URL https://github.com/const-ae/transformGamPoi
License GPL-3
Encoding UTF-8
Imports glmGamPoi, DelayedArray, Matrix, MatrixGenerics,
     SummarizedExperiment, HDF5Array, methods, utils, Rcpp
Suggests testthat, TENxPBMCData, scran, knitr, rmarkdown, BiocStyle
Roxygen list(markdown = TRUE)
RoxygenNote 7.1.2
Config/testthat/edition 3
biocViews SingleCell, Normalization, Preprocessing, Regression
VignetteBuilder knitr
LinkingTo Rcpp
git_url https://git.bioconductor.org/packages/transformGamPoi
git branch devel
git_last_commit 7ddcbe2
git_last_commit_date 2025-10-29
Repository Bioconductor 3.23
Date/Publication 2025-11-02
Author Constantin Ahlmann-Eltze [aut, cre] (ORCID:
     <https://orcid.org/0000-0002-3762-068X>)
Maintainer Constantin Ahlmann-Eltze <artjom31415@googlemail.com>
```

Title Variance Stabilizing Transformation for Gamma-Poisson Models

Type Package

2 acosh_transform

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.handle_data_parameter

Take any kind of data and extract the matrix

Description

Adapted from glmGamPoi:::handle_data_parameter

Usage

```
.handle_data_parameter(data, on_disk, allow_sparse = TRUE)
```

Value

A matrix.

acosh_transform

Delta method-based variance stabilizing transformation

Description

Delta method-based variance stabilizing transformation

Usage

```
acosh_transform(
  data,
  overdispersion = 0.05,
  size_factors = TRUE,
    ...,
  on_disk = NULL,
  verbose = FALSE
)
shifted_log_transform(
  data,
  overdispersion = 0.05,
```

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```
pseudo_count = 1/(4 * overdispersion),
  size_factors = TRUE,
 minimum_overdispersion = 0.001,
 on_disk = NULL,
  verbose = FALSE
)
```

Arguments

data

any matrix-like object (e.g. matrix, dgCMatrix, DelayedArray, HDF5Matrix) with one column per sample and row per gene. It can also be an object of type glmGamPoi, in which case it is directly used to calculate the variance-stabilized values.

overdispersion the simplest count model is the Poisson model. However, the Poisson model assumes that variance = mean. For many applications this is too rigid and the Gamma-Poisson allows a more flexible mean-variance relation (variance = $mean + mean^2 * overdispersion$).

overdispersion can either be

- a single boolean that indicates if an overdispersion is estimated for each
- a numeric vector of length nrow(data) fixing the overdispersion to those values.
- the string "global" to indicate that one dispersion is fit across all genes.

Note that overdispersion = 0 and overdispersion = FALSE are equivalent and both reduce the Gamma-Poisson to the classical Poisson model. Default: 0.05 which is roughly the overdispersion observed on ostensibly homogeneous cell lines.

size_factors

in large scale experiments, each sample is typically of different size (for example different sequencing depths). A size factor is an internal mechanism of GLMs to correct for this effect.

size_factors is either a numeric vector with positive entries that has the same lengths as columns in the data that specifies the size factors that are used. Or it can be a string that species the method that is used to estimate the size factors (one of c("normed_sum", "deconvolution", "poscounts")). Note that "normed_sum" and "poscounts" are fairly simple methods and can lead to suboptimal results. For the best performance, I recommend to use size_factors = "deconvolution" which calls scran::calculateSumFactors(). However, you need to separately install the scran package from Bioconductor for this method to work. Also note that size_factors = 1 and size_factors = FALSE are equivalent. If only a single gene is given, no size factor is estimated (ie. size_factors = 1). Default: "normed_sum".

additional parameters for glmGamPoi::glm_gp() which is called in case overdispersion = TRUE.

on_disk

a boolean that indicates if the dataset is loaded into memory or if it is kept on disk to reduce the memory usage. Processing in memory can be significantly 4 acosh_transform

faster than on disk. Default: NULL which means that the data is only processed in memory if data is an in-memory data structure.

verbose boolean that decides if information about the individual steps are printed. De-

fault: FALSE

pseudo_count instead of specifying the overdispersion, the shifted_log_transform is com-

monly parameterized with a pseudo-count (pseudo-count = 1/(4*overdispersion)).

If both the pseudo-count and overdispersion is specified, the overdispersion

is ignored. Default: 1/(4 * overdispersion)

minimum_overdispersion

the acosh_transform converges against 2*sqrt(x) for overdispersion == 0. However, the shifted_log_transform would just become 0, thus here we apply the minimum_overdispersion to avoid this behavior.

Value

a matrix (or a vector if the input is a vector) with the transformed values.

Functions

- acosh_transform: 1/sqrt(alpha) acosh(2 * alpha * x + 1)
- shifted_log_transform: 1/sqrt(alpha)log(4*alpha*x+1)

References

Ahlmann-Eltze, Constantin, and Wolfgang Huber. "Transformation and Preprocessing of Single-Cell RNA-Seq Data." bioRxiv (2021).

Ahlmann-Eltze, Constantin, and Wolfgang Huber. "glmGamPoi: Fitting Gamma-Poisson Generalized Linear Models on Single Cell Count Data." Bioinformatics (2020)

Dunn, Peter K., and Gordon K. Smyth. "Randomized quantile residuals." Journal of Computational and Graphical Statistics 5.3 (1996): 236-244.

Hafemeister, Christoph, and Rahul Satija. "Normalization and variance stabilization of single-cell RNA-seq data using regularized negative binomial regression." Genome biology 20.1 (2019): 1-15.

Hafemeister, Christoph, and Rahul Satija. "Analyzing scRNA-seq data with the sctransform and offset models." (2020)

Lause, Jan, Philipp Berens, and Dmitry Kobak. "Analytic Pearson residuals for normalization of single-cell RNA-seq UMI data." Genome Biology (2021).

See Also

```
acosh_transform, shifted_log_transform, and residual_transform
```

Examples

```
# Load a single cell dataset
sce <- TENxPBMCData::TENxPBMCData("pbmc4k")
# Reduce size for this example
set.seed(1)</pre>
```

estimate_size_factors 5

Description

Estimate the Size Factors

Usage

```
estimate_size_factors(Y, method, verbose = FALSE)
```

Arguments

```
Y any matrix-like object (base::matrix(), DelayedArray, HDF5Matrix, Matrix::Matrix(), etc.)
method one of c("normed_sum", "deconvolution", "poscounts")
```

Value

a vector with one size factor per column of Y

residual_transform Residual-based Variance Stabilizing Transformation

Description

Fit an intercept Gamma-Poisson model that corrects for sequencing depth and return the residuals as variance stabilized results for further downstream application, for which no proper count-based method exist or is performant enough (e.g., clustering, dimensionality reduction).

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Usage

```
residual_transform(
  data,
  residual_type = c("randomized_quantile", "pearson", "analytic_pearson"),
  clipping = FALSE,
  overdispersion = 0.05,
  size_factors = TRUE,
  offset_model = TRUE,
  overdispersion_shrinkage = TRUE,
  ridge_penalty = 2,
  on_disk = NULL,
  return_fit = FALSE,
  verbose = FALSE,
  ...
)
```

Arguments

data

any matrix-like object (e.g. matrix, dgCMatrix, DelayedArray, HDF5Matrix) with one column per sample and row per gene. It can also be an object of type glmGamPoi, in which case it is directly used to calculate the variance-stabilized values.

residual_type

a string that specifies what kind of residual is returned as variance stabilizedvalue.

"randomized_quantile" The discrete nature of count distribution stops simple transformations from obtaining a truly standard normal residuals. The trick of of quantile randomized residuals is to match the cumulative density function of the Gamma-Poisson and the Normal distribution. Due to the discrete nature of Gamma-Poisson distribution, a count does not correspond to a single quantile of the Normal distribution, but to a range of possible value. This is resolved by randomly choosing one of the mapping values from the Normal distribution as the residual. This ensures perfectly normal distributed residuals, for the cost of introducing randomness. More details are available in the documentation of statmod::qresiduals() and the corresponding publication by Dunn and Smyth (1996).

"pearson" The Pearson residuals are defined as $res = (y-m)/sqrt(m+m^2*theta)$.

"analytic_pearson" Similar to the method above, however, instead of estimating m using a GLM model fit, m is approximated by $m_i j = (\sum_j y_{ij})(\sum_i y_{ij})/(\sum_{i,j} y_{ij})$. For all details, see Lause et al. (2021). Note that overdispersion_shrinkage and ridge_penalty are ignored when fitting analytic Pearson residuals.

The two above options are the most common choices, however you can use any residual_type supported by glmGamPoi::residuals.glmGamPoi(). Default: "randomized_quantile"

clipping

a single boolean or numeric value specifying that all residuals are in the range [-clipping, +clipping]. If clipping = TRUE, we use the default of clipping

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> = sqrt(ncol(data)) which is the default behavior for sctransform. Default: FALSE, which means no clipping is applied.

overdispersion the simplest count model is the Poisson model. However, the Poisson model assumes that variance = mean. For many applications this is too rigid and the Gamma-Poisson allows a more flexible mean-variance relation (variance = $mean + mean^2 * overdispersion$).

overdispersion can either be

- a single boolean that indicates if an overdispersion is estimated for each
- a numeric vector of length nrow(data) fixing the overdispersion to those values.
- the string "global" to indicate that one dispersion is fit across all genes.

Note that overdispersion = 0 and overdispersion = FALSE are equivalent and both reduce the Gamma-Poisson to the classical Poisson model. Default: 0.05 which is roughly the overdispersion observed on ostensibly homogeneous cell lines.

offset_model

boolean to decide if β_1 in $y = \beta_0 + \beta_1 log(sf)$, is set to 1 (i.e., treating the log of the size factors as an offset) or is estimated per gene. From a theoretical point, it should be fine to treat β_1 as an offset, because a cell that is twice as big, should have twice as many counts per gene (without any gene-specific effects). However, sctransform suggested that it would be advantageous to nonetheless estimate β_0 as it may counter data artifacts. On the other side, Lause et al. (2020) demonstrated that the estimating β_0 and β_1 together can be difficult. If you still want to fit sctransform's model, you can set the ridge_penalty argument to a non-zero value, which shrinks β_1 towards 1 and resolves the degeneracy. Default: TRUE.

overdispersion_shrinkage, size_factors

arguments that are passed to the underlying call to glmGamPoi::glm_gp(). Default for each: TRUE.

another argument that is passed to glmGamPoi::glm_gp(). It is ignored if ridge_penalty offset_model = TRUE. Default: 2.

> a boolean that indicates if the dataset is loaded into memory or if it is kept on disk to reduce the memory usage. Processing in memory can be significantly faster than on disk. Default: NULL which means that the data is only processed

in memory if data is an in-memory data structure.

return_fit boolean to decide if the matrix of residuals is returned directly (return_fit

= FALSE) or if in addition the glmGamPoi-fit is returned (return_fit = TRUE).

Default: FALSE.

verbose boolean that decides if information about the individual steps are printed. De-

fault: FALSE

additional parameters passed to glmGamPoi::glm_gp().

Details

on_disk

Internally, this method uses the glmGamPoi package. The function goes through the following steps

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- 1. fit model using glmGamPoi::glm_gp()
- 2. plug in the trended overdispersion estimates
- 3. call glmGamPoi::residuals.glmGamPoi() to calculate the residuals.

Value

a matrix (or a vector if the input is a vector) with the transformed values. If return_fit = TRUE, a list is returned with two elements: fit and Residuals.

References

Ahlmann-Eltze, Constantin, and Wolfgang Huber. "glmGamPoi: Fitting Gamma-Poisson Generalized Linear Models on Single Cell Count Data." Bioinformatics (2020)

Dunn, Peter K., and Gordon K. Smyth. "Randomized quantile residuals." Journal of Computational and Graphical Statistics 5.3 (1996): 236-244.

Hafemeister, Christoph, and Rahul Satija. "Normalization and variance stabilization of single-cell RNA-seq data using regularized negative binomial regression." Genome biology 20.1 (2019): 1-15.

Hafemeister, Christoph, and Rahul Satija. "Analyzing scRNA-seq data with the sctransform and offset models." (2020)

Lause, Jan, Philipp Berens, and Dmitry Kobak. "Analytic Pearson residuals for normalization of single-cell RNA-seq UMI data." Genome Biology (2021).

See Also

```
glmGamPoi::glm\_gp(), glmGamPoi::residuals.glmGamPoi(), sctransform::vst(), statmod::qresiduals()
```

Examples

```
# Load a single cell dataset
sce <- TENxPBMCData::TENxPBMCData("pbmc4k")</pre>
# Reduce size for this example
set.seed(1)
sce_red <- sce[sample(which(rowSums2(counts(sce)) > 0), 1000),
                sample(ncol(sce), 200)]
counts(sce_red) <- as.matrix(counts(sce_red))</pre>
# Residual Based Variance Stabilizing Transformation
rq <- residual_transform(sce_red, residual_type = "randomized_quantile",</pre>
                          verbose = TRUE)
pearson <- residual_transform(sce_red, residual_type = "pearson", verbose = TRUE)</pre>
# Plot first two principal components
pearson_pca <- prcomp(t(pearson), rank. = 2)</pre>
rq_pca \leftarrow prcomp(t(rq), rank. = 2)
plot(rq_pca$x, asp = 1)
points(pearson_pca$x, col = "red")
```

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transformGamPoi

Variance Stabilizing Transformation for Gamma Poisson Data

Description

Variance Stabilizing Transformation for Gamma Poisson Data

Usage

```
transformGamPoi(
  data,
  transformation = c("acosh", "shifted_log", "randomized_quantile_residuals",
    "pearson_residuals", "analytic_pearson_residuals"),
  overdispersion = 0.05,
  size_factors = TRUE,
 on_disk = NULL,
  verbose = FALSE
)
```

Arguments

data

any matrix-like object (e.g. matrix, dgCMatrix, DelayedArray, HDF5Matrix) with one column per sample and row per gene. It can also be an object of type glmGamPoi, in which case it is directly used to calculate the variance-stabilized values.

transformation one of c("acosh", "shifted_log", "randomized_quantile_residuals", "pearson_residuals", "analytic_pearson_residuals"). See acosh_transform, shifted_log_transform, or residual_transform for more information.

overdispersion the simplest count model is the Poisson model. However, the Poisson model assumes that variance = mean. For many applications this is too rigid and the Gamma-Poisson allows a more flexible mean-variance relation (variance = $mean + mean^2 * overdispersion$).

overdispersion can either be

- a single boolean that indicates if an overdispersion is estimated for each
- a numeric vector of length nrow(data) fixing the overdispersion to those
- the string "global" to indicate that one dispersion is fit across all genes.

Note that overdispersion = 0 and overdispersion = FALSE are equivalent and both reduce the Gamma-Poisson to the classical Poisson model. Default: 0.05 which is roughly the overdispersion observed on ostensibly homogeneous cell lines.

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size_factors

in large scale experiments, each sample is typically of different size (for example different sequencing depths). A size factor is an internal mechanism of GLMs to correct for this effect.

size_factors is either a numeric vector with positive entries that has the same lengths as columns in the data that specifies the size factors that are used. Or it can be a string that species the method that is used to estimate the size factors (one of c("normed_sum", "deconvolution", "poscounts")). Note that "normed_sum" and "poscounts" are fairly simple methods and can lead to suboptimal results. For the best performance, I recommend to use size_factors = "deconvolution" which calls scran::calculateSumFactors(). However, you need to separately install the scran package from Bioconductor for this method to work. Also note that size_factors = 1 and size_factors = FALSE are equivalent. If only a single gene is given, no size factor is estimated (ie. size_factors = 1). Default: "normed_sum".

... additional parameters passed to acosh_transform, shifted_log_transform,

or residual_transform

on_disk a boolean that indicates if the dataset is loaded into memory or if it is kept on

disk to reduce the memory usage. Processing in memory can be significantly faster than on disk. Default: NULL which means that the data is only processed

in memory if data is an in-memory data structure.

verbose boolean that decides if information about the individual steps are printed. De-

fault: FALSE

Value

a matrix (or a vector if the input is a vector) with the transformed values.

References

Ahlmann-Eltze, Constantin, and Wolfgang Huber. "Transformation and Preprocessing of Single-Cell RNA-Seq Data." bioRxiv (2021).

Ahlmann-Eltze, Constantin, and Wolfgang Huber. "glmGamPoi: Fitting Gamma-Poisson Generalized Linear Models on Single Cell Count Data." Bioinformatics (2020)

Dunn, Peter K., and Gordon K. Smyth. "Randomized quantile residuals." Journal of Computational and Graphical Statistics 5.3 (1996): 236-244.

Hafemeister, Christoph, and Rahul Satija. "Normalization and variance stabilization of single-cell RNA-seq data using regularized negative binomial regression." Genome biology 20.1 (2019): 1-15.

Hafemeister, Christoph, and Rahul Satija. "Analyzing scRNA-seq data with the sctransform and offset models." (2020)

Lause, Jan, Philipp Berens, and Dmitry Kobak. "Analytic Pearson residuals for normalization of single-cell RNA-seq UMI data." Genome Biology (2021).

See Also

acosh_transform, shifted_log_transform, and residual_transform

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Examples

```
# Load a single cell dataset
sce <- TENxPBMCData::TENxPBMCData("pbmc4k")</pre>
# Reduce size for this example
set.seed(1)
sce_red <- sce[sample(which(rowSums2(counts(sce)) > 0), 1000),
                sample(ncol(sce), 200)]
assay(sce_red, "acosh") <- transformGamPoi(sce_red, "acosh")</pre>
assay(sce_red, "shifted_log") <- transformGamPoi(sce_red, "shifted_log")</pre>
# Residual Based Variance Stabilizing Transformation
rq <- transformGamPoi(sce_red, transformation = "randomized_quantile", on_disk = FALSE,
                       verbose = TRUE)
pearson <- transformGamPoi(sce_red, transformation = "pearson", on_disk = FALSE, verbose = TRUE)</pre>
plot(rowMeans2(counts(sce_red)), rowVars(assay(sce_red, "acosh")), log = "x")
points(rowMeans2(counts(sce_red)), rowVars(assay(sce_red, "shifted_log")), col = "red")
points(rowMeans2(counts(sce_red)), rowVars(rq), col = "blue")
# Plot first two principal components
acosh_pca <- prcomp(t(assay(sce_red, "acosh")), rank. = 2)</pre>
rq_pca <- prcomp(t(rq), rank. = 2)
pearson_pca <- prcomp(t(pearson), rank. = 2)</pre>
plot(acosh_pca$x, asp = 1)
points(rq_pca$x, col = "blue")
points(pearson_pca$x, col = "green")
```

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