

# Package ‘mbQTL’

April 16, 2024

**Type** Package

**Title** mbQTL: A package for SNP-Taxa mGWAS analysis

**Version** 1.2.0

**Description** mbQTL is a statistical R package for simultaneous 16srRNA,16srDNA (microbial) and variant, SNP, SNV (host) relationship, correlation, regression studies.

We apply linear, logistic and correlation based statistics to identify the relationships of taxa, genus, species and variant, SNP, SNV in the infected host. We produce various statistical significance measures such as P values, FDR, BC and probability estimation to show significance of these relationships. Further we provide various visualization function for ease and clarification of the results of these analysis. The package is compatible with dataframe, MRexperiment and text formats.

**License** MIT + file LICENSE

**Encoding** UTF-8

**Depends** R (>= 4.3.0)

**DeploySubPath** mbQTL

**biocViews** SNP, Microbiome, WholeGenome, Metagenomics,  
StatisticalMethod, Regression

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metagenomeSeq, pheatmap, broom, graphics, stats, methods

**Suggests** knitr, rmarkdown, BiocStyle

**VignetteBuilder** knitr

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## R topics documented:

mbQTL-package	2
allToAllProduct	3
binarizeMicrobe	3
coringTaxa	4
CovFile	4
histPvalueLm	5
linearTaxaSnp	5
logitPlotSnpTaxa	6
logRegSnpsTaxa	7
mbQtlCorHeatmap	8
metagenomeSeqObj	9
metagenomeSeqToMbqtl	9
microbeAbund	10
prepareCorData	10
qqPlotLm	11
RegSnp	11
SnpFile	12
taxaSnpCor	12
<b>Index</b>	<b>14</b>

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mbQTL-package	<i>title mbQTL is a package for microbial QTL/GWAS Analysis</i>
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## Description

This package provides statistical methods for identifying significant relationships between microbial/taxa and genetic SNP signatures. We use three models 1) linear regression between all taxa-snp. Main function is `linearTaxaSnp()`. 2) Correlation analysis between taxa-snp across all taxa and snps. Main function is `taxaSnpCor()` and 3) Logistic regression analysis between each taxa and each snp simultaneously or for a specific cases. Main function is `logRegSnpsTaxa()`.

## Author(s)

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Authors:

- Steven Schiff
- Joseph N Paulson

**See Also**

The package vignette can be accessed with `vignette("mbQTL")`.

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allToAllProduct	<i>allToAllProduct creates a dataframe of snp and taxa correlations</i>
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---

**Description**

This internal function takes the original snp dataframe and returns a long parsed snp dataframe

**Usage**

```
allToAllProduct(SnpFile, microbeAbund, rsID = NULL)
```

**Arguments**

SnpFile	the snp file (rownames is sample number and colnames is the snps)
microbeAbund	the taxa abundance dataframe (rownames sample names and colnames taxa Genus/species/family)
rsID	Default is NULL and will run across the who dataset unless specific rsID/SNP/chr_region is specified

**Value**

A dataframe of correlations between snps and taxa

**Examples**

```
data(microbeAbund)
data(SnpFile)
x <- allToAllProduct(SnpFile, microbeAbund, "chr1.171282963_T")
```

---

binarizeMicrobe	<i>binarizeMicrobe binarizes microbe abundace file based on user's cutoff</i>
-----------------	---

---

**Description**

This function creates a dataframe output produces a formatted dataframe prepared.

**Usage**

```
binarizeMicrobe(microbeAbund, cutoff = NULL, selectmicrobe = NULL)
```

**Arguments**

microbeAbund the taxa abundance dataframe (rownames sample names and colnames taxa Genus/species/family)  
 cutoff cutoff at which the user chose to call taxa positive or negative across samples (should be a numeric value for normalized or count values).  
 selectmicrobe default is and all taxa are considered at the same time, if the user is interested in a specific pathogen use name of the pathogen for example "Haemophilus".

**Value**

A data frame of microbial abundance.

---

coringTaxa	coringTaxa creates correlation dataframe for taxa
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---

**Description**

This function creates an output correlation data frame for all microbial taxa (or other organisms such as viral or parasitic taxa)

**Usage**

```
coringTaxa(microbeAbund)
```

**Arguments**

microbeAbund the taxa abundance dataframe (rownames sample names and colnames taxa Genus/species/family)

**Value**

A data frame of correlations between taxa

**Examples**

```
data(microbeAbund)
x <- coringTaxa(microbeAbund)
```

---

CovFile	mbQTL "CovFile"
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---

**Description**

The "CovFile" is the covariate file for linear regression option of taxa and snp association. The covariance file is generated randomly by assigning sex and site of collection to the samples.) rownames are covariate and colnames samples.

---

histPvalueLm	<i>histPvalueLm a histogram of Taxa and SNP linear regression analysis. This function creates a histogram object of all SNPs with all taxa Linear regression analysis p values.</i>
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---

### Description

histPvalueLm a histogram of Taxa and SNP linear regression analysis. This function creates a histogram object of all SNPs with all taxa Linear regression analysis p values.

### Usage

```
histPvalueLm(LinearAnalysisTaxaSNP)
```

### Arguments

LinearAnalysisTaxaSNP  
the data frame result created from the linearTaxaSnp() function.

### Value

A histogram object of p values observed from taxa and SNP Linear Regression analysis.

### Examples

```
data(microbeAbund)
data(microbeAbund)
data(SnpFile)
data(CovFile)
LinearAnalysisTaxaSNPFile <- linearTaxaSnp(microbeAbund, SnpFile, Covariate = CovFile)
x <- histPvalueLm(LinearAnalysisTaxaSNPFile)
```

---

linearTaxaSnp	<i>linearTaxaSnp Performs linear regression analysis between taxa and SNPs and returns concordance statistics</i>
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---

### Description

This function creates a dataframe output from the results all snps with all taxa linear regression analysis of all snps in the dataset. The result is a dataframe with P values and FDRs of all regressions. MatrixeQTL core functions are utilized to achieve this. Note the main functions used are Matrix\_eQTL\_engine() assuming linear regression with or without a covariate file.

### Usage

```
linearTaxaSnp(microbeAbund, SnpFile, Covariate = NULL)
```

**Arguments**

microbeAbund	the taxa abundance dataframe (rownames sample names and colnames taxa Genus/species/family)
SnpFile	the snp dataframe (values 0,1,2 indicating zygoty), rownames sample names and colnames snp names.
Covariate	default is NULL, hence assumed non-existent. If covariates are available they need to be formatted in the CovFile format, that is colnames are sample numbers matching samples in the microbe abundance and snp file and row names are the co-variates names (such as sex, disease etc).

**Value**

A data frame which is a result of Linear Regression of all snp, taxa relationships, with P values and P value corrected values.

**Examples**

```
data(microbeAbund)
data(SnpFile)
data(CovFile)
x <- linearTaxaSnp(microbeAbund, SnpFile, Covariate = CovFile)
```

---

logitPlotSnpTaxa	<i>logitPlotSnpTaxa produces bar plots for counts of ref vs alt vs het alleles for particular rsID taxa combinations</i>
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---

**Description**

This function creates a dataframe output produces a formatted dataframe prepared.

**Usage**

```
logitPlotSnpTaxa(
  microbeAbund,
  SnpFile,
  selectmicrobe = NULL,
  rsID,
  ref = NULL,
  alt = NULL,
  het = NULL,
  color = NULL,
  cutoff = NULL
)
```

**Arguments**

microbeAbund	original microbe abundance file (colnames microbe, rownames= sample IDs)
SnpsFile	original snp file with (0,1,2 values for ref, het, alt genotypes), colnames SNP names, rownames, sample IDs.
selectmicrobe	name of the microbe of interest (for example individual significant microbes associate with a snp).
rsID	name of the snp of interest (for example individual significant snps associated with a microbe)
ref	the name of reference genotype for example "GG"
alt	the name of snp (variant) genotype for example "AA"
het	the name of hetrozygote genotype for example "GA"
color	the default is NULL and the color is set to c("#ffaa1e", "#87365b").
cutoff	cutoff at which we call microbe present or absent

**Value**

A bar ggplot comparing the counts of ref vs alt vs het genotype

**Examples**

```
data(microbeAbund)
data(SnpsFile)
x <- logitPlotSnpsTaxa(microbeAbund, SnpsFile,
  selectmicrobe = "Neisseria", rsID = "chr2.241072116_A",
  ref = NULL, alt = NULL, het = NULL, color = NULL, cutoff = NULL
)
```

---

logRegSnpsTaxa	logRegSnpsTaxa <i>Performs logistic regression analysis between taxa and SNPs and returns concordance statistics</i>
----------------	--

---

**Description**

This function creates a dataframe output from the results of either a unique taxa and all snps or all taxa and all snps in the dataset. The result is a dataframe with P values and FDRs of all regressions.

**Usage**

```
logRegSnpsTaxa(microbeAbund, SnpsFile, cutoff = NULL, selectmicrobe = NULL)
```

**Arguments**

microbeAbund	the taxa abundance dataframe (rownames sample names and colnames taxa Genus/species/family)
SnpFile	the snp dataframe (values 0,1,2 indicating zygosity), rownames sample names and colnames snp names.
cutoff	default is NULL, hence anything above cutoff is considered positive, the cut-off at which the specific or all taxa are considered positive for the pathogen (1 indicates positive and 0 negative).
selectmicrobe	default is and all taxa are considered at the same time, if the user is interested in a specific pathogen use name of the pathogen for example "Haemophilus".

**Value**

A data frame which is a result of Logistic regression products of individual snp, taxa relationships, with P values and P value corrected values (FDR, Bonferroni).

**Examples**

```
data(microbeAbund)
data(SnpFile)
x <- logRegSnpsTaxa(microbeAbund, SnpFile, selectmicrobe = c("Haemophilus"))
```

---

mbQtlCorHeatmap	<i>mbQtlCorHeatmap for making heatmap for snp, taxa rho values</i>
-----------------	--

---

**Description**

This function produces a log heatmap +1 of the correlation rho values across snp, taxa datasets

**Usage**

```
mbQtlCorHeatmap(final_var_long, labels_col = NULL, ...)
```

**Arguments**

final_var_long	the long data frame of rho values created by the taxaSnpCor() function.
labels_col	set to NULL as default if TRUE, labels will appear on the heatmap.
...	all other parameters for pheatmap.

**Value**

A data frame of correlations between taxa



**Examples**

```

data(microbeAbund)
data(SnpFile)
for_all_rsids <- allToAllProduct(SnpFile, microbeAbund)
correlationMicrobes <- coringTaxa(microbeAbund)
taxaSnpCor(for_all_rsids, correlationMicrobes)
final_var_long <- taxaSnpCor(for_all_rsids, correlationMicrobes, probs = c(0.0001, 0.9999))
x <- mbQtlCorHeatmap(final_var_long)

```

---

```

metagenomeSeqObj      mbQTL      "metagenomeSeqObj"      "MetagenomSeqObj"      is      an
                        MRexperiment object format of the "microbeAbund" file.

```

---

**Description**

```

mbQTL "metagenomeSeqObj"
"MetagenomSeqObj" is an MRexperiment object format of the "microbeAbund" file.

```

---

```

metagenomeSeqToMbqtl  %

```

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**January 2023**

*metagenomeSeqToMbqtl* Converts *metagenomeSeq* obj to compatible *taxa* dataframe

---

**Description**

This function takes and MRexperiment class object transforms it and makes the result dataframe compatible with mbQTL taxa input file

**Usage**

```

metagenomeSeqToMbqtl(meta_glom, norm, log, aggregate_taxa = NULL)

```

**Arguments**

```

meta_glom      MRexperiment class obj from metagenomeSeq package.
norm           A logical indicating whether or not to return normalized counts.
log           TRUE/FALSE whether or not to log2 transform scale.
aggregate_taxa it is recommended that the normalization occurs at taxa level (default NULL)
              however, if the user chooses to aggregate on the phyla/family/Genus or Species
              level before normalization they have the option.

```

**Value**

A data frame of normalized/not normalized counts compatible with mbQTL.

**Examples**

```
data(metagenomeSeqObj)
x <- metagenomeSeqToMbqtl(metagenomeSeqObj, norm = TRUE, log = TRUE, aggregate_taxa = NULL)
```

---

microbeAbund	mbQTL " <i>microbiomeAbund</i> " File
--------------	---------------------------------------

---

**Description**

This is the microbial Abundance file generated from 16s it is either this file or the "metaGenomeSeqObj". The "microbiomeAbund" file is a randomly generated file format for total microbe presence (number of reads)(parasite/viral transcripts) for specific species. This could be generated from select taxa results from biom() or MRexperiment objects as long as the samples are colnames and taxa are rownames.

---

prepareCorData	prepareCorData <i>prepares and joins snp-taxa and taxa-taxa correlation file.</i>
----------------	---

---

**Description**

This function creates a dataframe output produces a formatted dataframe prepared.

**Usage**

```
prepareCorData(microbeAbund, SnpFile, cutoff = NULL, selectmicrobe = NULL)
```

**Arguments**

microbeAbund	the taxa abundance dataframe (rownames sample names and colnames taxa Genus/species/family)
SnpFile	the snp dataframe (values 0,1,2 indicating zygosity), rownames sample names and colnames snp names.
cutoff	default is NULL, hence anything above cutoff is considered positive, the cutoff at which the specific or all taxa are considered positive for the pathogen (1 indicates positive and 0 negative).
selectmicrobe	default is and all taxa are considered at the same time, if the user is interested in a specific pathogen use name of the pathogen for example "Haemophilus".

**Value**

A data frame which is a result of Logistic regression products of individual snp, taxa relationships, with P values and P value corrected values.

---

qqPlotLm	<i>qqPlotLm creates QQ-Plot of all SNPs with all taxa Linear regression analysis This function creates QQ-Plot object of all SNPs with all taxa Linear regression analysis of expected versus observed P values</i>
----------	---

---

### Description

qqPlotLm creates QQ-Plot of all SNPs with all taxa Linear regression analysis This function creates QQ-Plot object of all SNPs with all taxa Linear regression analysis of expected versus observed P values

### Usage

```
qqPlotLm(microbeAbund, SnpFile, Covariate = NULL)
```

### Arguments

microbeAbund	the taxa abundance dataframe (rownames sample names and colnames taxa Genus/species/family)
SnpFile	the snp dataframe (values 0,1,2 indicating zygoty), rownames sample names and colnames snp names.
Covariate	default is NULL, hence assumed non-existent. If covariates are available they need to be formatted in the CovFile format, that is colnames are sample numbers matching samples in the microbe abundance and snp file and row names are the covariates names (such as sex, disease etc).

### Value

A QQplot object of expected versus obsesrved taxa and SNP Linear Regression analysis

### Examples

```
data(microbeAbund)
data(SnpFile)
data(CovFile)
x <- qqPlotLm(microbeAbund, SnpFile, Covariate = CovFile)
```

---

RegSnp	<i>RegSnp creates a dataframe of parsed long snp files</i>
--------	--

---

### Description

This internal function takes the original snp dataframe and retruns a long parsed snp dataframe

**Usage**

```
RegSnp(SnpFile, microbeAbund)
```

**Arguments**

SnpFile            the snp file (rownames is sample number and colnames is the snps)  
microbeAbund      the microbial abundance file (rownames is sample number and colnames is the microbe)

**Value**

A long parsed dataframe of snps

---

SnpFile	mbQTL " <i>SnpFile</i> "
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---

**Description**

The "SnpFile" is randomly generated from GATK (Van der Auwera GA & O'Connor BD. (2020). Genomics in the Cloud: Using Docker, GATK, and WDL in Terra (1st Edition). O'Reilly Media) snp calls followed by plink (Purcell S, et al. (2007) PLINK: a toolset for whole-genome association and population-based linkage analysis. American Journal of Human Genetics) processing and it needs to be in (0,1,2) format representing the zygosity of the snps.

---

taxaSnpCor	taxaSnpCor <i>for estimation of the rho value between snp, taxa correlations across datasets</i>
------------	--

---

**Description**

This function produces a log heatmap +1 of the correlation rho values across snp, taxa dataframe.

**Usage**

```
taxaSnpCor(for_all_rsids, correlationMicrobes, probs = NULL)
```

**Arguments**

for\_all\_rsids    A dataframe result of correlation analysis between the snps and taxa dataframe, an output of allToAllProduct() function.  
correlationMicrobes    A dataframe of correlation between coringTaxa() function.  
probs            Default is NULL if other that all rho values are wanted the value can be subseted using c(x,y).

**Value**

A data frame of correlations between taxa

**Examples**

```
data(microbeAbund)
data(SnpFile)
```

```
for_all_rsids <- allToAllProduct(SnpFile, microbeAbund)
correlationMicrobes <- coringTaxa(microbeAbund)
x <- taxaSnpCor(for_all_rsids, correlationMicrobes)
```

# Index

- \* **Correlation**
  - allToAllProduct, 3
- \* **LR**
  - linearTaxaSnp, 5
- \* **MRexperiment**
  - metagenomeSeqToMbqtl, 9
- \* **barplot**
  - logitPlotSnpTaxa, 6
- \* **correlation**
  - coringTaxa, 4
- \* **data**
  - CovFile, 4
  - metagenomeSeqObj, 9
  - microbeAbund, 10
  - SnpFile, 12
- \* **estimation**
  - taxaSnpCor, 12
- \* **heatmap**
  - mbQtlCorHeatmap, 8
- \* **histogram**
  - histPvalueLm, 5
- \* **linear\_regression**
  - histPvalueLm, 5
  - qqPlotLm, 11
- \* **linear**
  - linearTaxaSnp, 5
- \* **logistic\_regression**
  - logRegSnpsTaxa, 7
- \* **logitParsing**
  - binarizeMicrobe, 3
- \* **logitPlotDataframe**
  - binarizeMicrobe, 3
  - prepareCorData, 10
- \* **logitplot**
  - logitPlotSnpTaxa, 6
- \* **logit**
  - logRegSnpsTaxa, 7
- \* **long**
  - RegSnp, 11
- \* **metagenomeSeq**
  - metagenomeSeqToMbqtl, 9
- \* **normalization**
  - metagenomeSeqToMbqtl, 9
- \* **parsed**
  - RegSnp, 11
- \* **plot**
  - histPvalueLm, 5
  - qqPlotLm, 11
- \* **regression**
  - linearTaxaSnp, 5
- \* **rho**
  - mbQtlCorHeatmap, 8
  - taxaSnpCor, 12
- \* **snptaxa**
  - allToAllProduct, 3
- \* **snp**
  - histPvalueLm, 5
  - linearTaxaSnp, 5
  - logRegSnpsTaxa, 7
  - qqPlotLm, 11
  - RegSnp, 11
- \* **taxa**
  - coringTaxa, 4
  - histPvalueLm, 5
  - linearTaxaSnp, 5
  - logRegSnpsTaxa, 7
  - qqPlotLm, 11
- allToAllProduct, 3
- binarizeMicrobe, 3
- coringTaxa, 4
- CovFile, 4
- histPvalueLm, 5
- linearTaxaSnp, 5
- logitPlotSnpTaxa, 6
- logRegSnpsTaxa, 7

mbQTL (mbQTL-package), [2](#)  
mbQTL-package, [2](#)  
mbQtlCorHeatmap, [8](#)  
metagenomeSeqObj, [9](#)  
metagenomeSeqToMbqtl, [9](#)  
microbeAbund, [10](#)

prepareCorData, [10](#)

qqPlotLm, [11](#)

RegSnp, [11](#)

SnpFile, [12](#)

taxaSnpCor, [12](#)