

# Package ‘LiquidAssociation’

July 27, 2025

**Type** Package

**Title** LiquidAssociation

**Version** 1.62.0

**Date** 2009-10-07

**Author** Yen-Yi Ho <yho@jhsp.h.edu>

**Maintainer** Yen-Yi Ho <yho@jhsp.h.edu>

**Description** The package contains functions for calculate direct and model-based estimators for liquid association. It also provides functions for testing the existence of liquid association given a gene triplet data.

**Depends** geepack, methods, yeastCC, org.Sc.sgd.db

**Imports** Biobase, graphics, grDevices, methods, stats

**License** GPL (>=3)

**LazyLoad** yes

**biocViews** Pathways, GeneExpression, CellBiology, Genetics, Network, TimeCourse

**git\_url** <https://git.bioconductor.org/packages/LiquidAssociation>

**git\_branch** RELEASE\_3\_21

**git\_last\_commit** a39c674

**git\_last\_commit\_date** 2025-04-15

**Repository** Bioconductor 3.21

**Date/Publication** 2025-07-27

## Contents

|                                     |   |
|-------------------------------------|---|
| LiquidAssociation-package . . . . . | 2 |
| CNM-class . . . . .                 | 3 |
| CNM.full-methods . . . . .          | 4 |
| CNM.simple-methods . . . . .        | 5 |
| getsGLA-methods . . . . .           | 6 |

|                                      |           |
|--------------------------------------|-----------|
| getsLA-methods . . . . .             | 8         |
| GLA-methods . . . . .                | 9         |
| LA-methods . . . . .                 | 10        |
| LiquidAssociation-internal . . . . . | 11        |
| plotGLA-methods . . . . .            | 12        |
| <b>Index</b>                         | <b>13</b> |

---

|                                   |
|-----------------------------------|
| LiquidAssociation-package         |
| <i>Liquid Association Package</i> |

---

**Description**

The LiquidAssociation package provide methods to examine a special kind of three-way interaction called liquid association. The term liquid association was first proposed by contains functions for calculate direct and model-based estimators for liquid associaiton. It also provides functions for testing the existence of liquid associaiton given a gene triplet data.

**Details**

|           |                        |
|-----------|------------------------|
| Package:  | LiquidAssociation      |
| Type:     | Package                |
| Version:  | 1.0.4                  |
| Date:     | 2009-10-05             |
| License:  | GPL version 2 or newer |
| LazyLoad: | yes                    |

GLA LA CNM.full CNM.simple getsGLA getsLA plotGLA

**Author(s)**

Yen-Yi Ho <yho@jhsph.edu>  
Maintainer: Yen-Yi Ho <yho@jhsph.edu>

**References**

Ker-Chau Li, Genome-wide coexpression dynamics: theory and application (2002). PNAS 99 (26): 16875-16880.

Yen-Yi Ho, Leslie Cope, Thomas A. Louis, and Giovanni Parmigiani, GENERALIZED LIQUID ASSOCIATION (April 2009). Johns Hopkins University, Dept. of Biostatistics Working Papers. Working Paper 183. <http://www.bepress.com/jhubiostat/paper183>

**Examples**

```
data<-matrix(rnorm(300), ncol=3)

colnames(data)<-c("Gene1", "Gene2", "Gene3")

FitCNM.full<-CNM.full(data)

FitCNM.full
```

CNM-class

*Class CNM***Description**

This is a class representation for CNM model fitting results.

**Objects from the Class**

Objects can be created by calls of the form `new("CNM", ...)` or the functions [CNM.full-methods](#) and [CNM.simple-methods](#)

**Slots**

**Model:** Object of class character representing the fitted CNM model.

**output:** Object of class matrix representing the parameter estimates from the fitted CNM model.

**Methods**

**print** signature(`x` = "CNM"): Display CNM model fitting result.

**show** signature(`object` = "CNM"): Display CNM model fitting result.

**Note**

The usage of this class is demonstrated in the vignette.

**Author(s)**

Yen-Yi Ho

**References**

Yen-Yi Ho, Leslie Cope, Thomas A. Louis, and Giovanni Parmigiani, GENERALIZED LIQUID ASSOCIATION (April 2009). Johns Hopkins University, Dept. of Biostatistics Working Papers. Working Paper 183. <http://www.bepress.com/jhubiostat/paper183>. Yen-Yi Ho, Leslie Cope, Thomas A. Louis, and Giovanni Parmigiani, GENERALIZED LIQUID ASSOCIATION (April 2009). Johns Hopkins University, Dept. of Biostatistics Working Papers. Working Paper 183. <http://www.bepress.com/jhubiostat/paper183>.

**See Also**

related methods [print](#), [show](#).

**Examples**

```
showClass("CNM")
```

---

CNM.full-methods

*The function fits a full conditional normal model (CNM)*

---

**Description**

'CNM.full' is used to fit the full (means, variance, and correlation) conditional normal model using GEE.

**Arguments**

|         |  |
|---------|--|
| object  | An numerical matrix object with three columns or an object of ExpressionSet class with three features.           |
| geneMap | A character vector with three elements representing the mapping between gene names and feature names (optional). |
| dim     | An index of the column for the gene to be treated as the third controller variable. The default value is dim=3.  |

**Details**

The input object can be a numerical matrix with three columns with row representing observations and column representing three variables. It can also be an ExpressionSet object with three features. If input a matrix class data, all three columns of the object representing the variables should have column names. Each variable in the object will be standardized with mean 0 and variance 1 in the function. In addition, the third variable will be quantile normalized within the function. More detail example about the usage of geneMap is demonstrated in the vignette.

**Value**

'CNM.full' returns a object of CNM class with two Slots. The first slot describes the fitted model. The second slot is a matrix contains the CNM model fitting results. The row of this matrix represents the parameters in the CNM model. The first column, estimates, is the estimated value of the corresponding parameters. The second column, san.se, is the value of sandwich standard error estimator for the estimates. The third column, wald, is the wald test statistic as described in Ho et al (2009). The corresponding p value for the wald test statistic is represented in the fourth column. A more detailed interpretation of these values is illustrated in the vignette.

**Author(s)**

Yen-Yi Ho

## References

Yen-Yi Ho, Leslie Cope, Thomas A. Louis, and Giovanni Parmigiani, GENERALIZED LIQUID ASSOCIATION (April 2009). Johns Hopkins University, Dept. of Biostatistics Working Papers. Working Paper 183. <http://www.bepress.com/jhubiostat/paper183>.

Jun Yan and Jason Fine. Estimating equations for association structures Statistics in Medicine. 23(6): 859–74; discussion 875–7,879–80. <http://dx.doi.org/10.1002/sim.1650>

## See Also

[CNM.simple-methods](#), [CNM-class](#)

## Examples

```
data<-matrix(rnorm(300), ncol=3)

colnames(data)<-c("Gene1", "Gene2", "Gene3")

FitCNM.full<-CNM.full(data)

FitCNM.full
```

---

|                    |   |
|--------------------|---|
| CNM.simple-methods | <i>The function fits a reduced conditional normal model (CNM)</i> |
|--------------------|---|

---

## Description

'CNM.simple' is used to fit the reduced (correlation only) conditional normal model using GEE.

## Arguments

|         |  |
|---------|--|
| object  | An numerical matrix object with three columns or an object of ExpressionSet class with three features.           |
| geneMap | A character vector with three elements representing the mapping between gene names and feature names (optional). |
| dim     | An index of the column for the gene to be treated as the third controller variable. The default value is dim=3.  |

## Details

The input object can be a numerical matrix with three columns with row representing observations and column representing three variables. It can also be an ExpressionSet object with three features. If input a matrix class data, all three columns of the object representing the variables should have column names. Each variable in the object will be standardized with mean 0 and variance 1 in the function. In addition, the third variable will be quantile normalized within the function. More detail example about the usage of geneMap is demonstrated in the vignette.

**Value**

'CNM.full' returns a object of CNM class with two Slots. The first slot describes the fitted model. The second slot is a matrix contains the CNM model fitting results. The row of this matrix represents the parameters in the CNM model. The first column, estimates, is the estimated value of the corresponding parameters. The second column, san.se, is the value of sandwich standard error estimator for the estimates. The third column, wald, is the wald test statistic as described in Ho et al (2009). The corresponding p value for the wald test statistic is represented in the fourth column. A more detailed interpretation of these values is illustrated in the vignette.

**Author(s)**

Yen-Yi Ho

**References**

Yen-Yi Ho, Leslie Cope, Thomas A. Louis, and Giovanni Parmigiani, GENERALIZED LIQUID ASSOCIATION (April 2009). Johns Hopkins University, Dept. of Biostatistics Working Papers. Working Paper 183. <http://www.bepress.com/jhubiostat/paper183>.

Jun Yan and Jason Fine. Estimating equations for association structures Statistics in Medicine. 23(6): 859–74; discussion 875-7,879-80. <http://dx.doi.org/10.1002/sim.1650>

**See Also**

[CNM.full-methods](#), [CNM-class](#)

**Examples**

```
data<-matrix(rnorm(300), ncol=3)

colnames(data)<-c("Gene1", "Gene2", "Gene3")

FitCNM.simple<-CNM.simple(data)

FitCNM.simple
```

---

getsGLA-methods

*Function to calculate the sGLA test statistic for a given triplet data*

---

**Description**

'getsGLA' is used to calculate the sGLA test statistic and corresponding p value.

**Arguments**

|         |  |
|---------|--|
| object  | An numerical matrix object with three columns or an object of ExpressionSet class with three features.                     |
| boots   | The number of bootstrap iterations for estimating the bootstrap standard error of sGLA. Default value is boots=30.         |
| perm    | The number of permutation iterations for generating the null distribution of the sGLA test statistic. Default is perm=100. |
| cut     | cut==M +1. M is the number of grip points pre-specified over the third variable.   |
| dim     | An index of the column for the gene to be treated as the third controller variable. Default is dim=3                       |
| geneMap | A character vector with three elements representing the mapping between gene names and feature names (optional).           |

**Details**

The input object can be a numerical matrix with three columns with row representing observations and column representing three variables. It can also be an ExpressionSet object with three features. If input a matrix class data, all three columns of the object representing the variables should have column names. Each variable in the object will be standardized with mean 0 and variance 1 in the function. In addition, the third variable will be quantile normalized within the function. More detail example about the usage of geneMap is demonstrated in the vignette.

**Value**

'getsGLA' returns a vector with two elements. The first element is the value of test statistic and second element is the corresponding p value. A more detailed interpretation of these values is illustrated in the vignette.

**References**

Yen-Yi Ho, Leslie Cope, Thomas A. Louis, and Giovanni Parmigiani, GENERALIZED LIQUID ASSOCIATION (April 2009). Johns Hopkins University, Dept. of Biostatistics Working Papers. Working Paper 183. <http://www.bepress.com/jhubiostat/paper183>.

**See Also**

[GLA-methods](#), [getsLA-methods](#)

**Examples**

```
data<-matrix(rnorm(300), ncol=3)

colnames(data)<-c("Gene1", "Gene2", "Gene3")

sGLAest<-getsGLA(data, boots=20, perm=100, cut=4, dim=3)

sGLAest
```

---

getsLA-methods

*Function to calculate the sLA test statistic for a given triplet data*


---

## Description

'getsLA' is used to calculate the sLA test statistic and corresponding p value.

## Arguments

|         |  |
|---------|--|
| object  | An numerical matrix object with three columns or an object of ExpressionSet class with three features.                     |
| boots   | The number of bootstrap iterations for estimating the bootstrap standard error of sGLA. Default value is boots=30.         |
| perm    | The number of permutation iterations for generating the null distribution of the sGLA test statistic. Default is perm=100. |
| dim     | An index of the column for the gene to be treated as the third controller variable. Default is dim=3                       |
| geneMap | A character vector with three elements representing the mapping between gene names and feature names (optional).           |

## Details

The input object can be a numerical matrix with three columns with row representing observations and column representing three variables. It can also be an ExpressionSet object with three features. If input a matrix class data, all three columns of the object representing the variables should have column names. Each variable in the object will be standardized with mean 0 and variance 1 in the function. In addition, the third variable will be quantile normalized within the function. More detail example about the usage of geneMap is demonstrated in the vignette.

## Value

'getsLA' returns a vector with two elements. The first element is the value of test statistic and second element is the corresponding p value. A more detailed interpretation of these values is illustrated in the vignette.

## See Also

LA, getsGLA

## Examples

```
data<-matrix(rnorm(300), ncol=3)

colnames(data)<-c("Gene1", "Gene2", "Gene3")

sLAest<-getsLA(data, boots=20, perm=100)
```



sLAest

GLA-methods

*Function to calculate GLA estimate***Description**

'GLA' is used to calculate the GLA estimate for a gene triplet data.

**Arguments**

|         |  |
|---------|--|
| object  | An numerical matrix object with three columns or an object of ExpressionSet class with three features.           |
| cut     | cut==M +1. M is the number of grip points pre-specified over the third variable.                                 |
| dim     | An index of the column for the gene to be treated as the third controller variable. Default is dim=3             |
| geneMap | A character vector with three elements representing the mapping between gene names and feature names (optional). |

**Details**

The input object can be a numerical matrix with three columns with row representing observations and column representing three variables. It can also be an ExpressionSet object with three features. If input a matrix class data, all three columns of the object representing the variables should have column names. Each variable in the object will be standardized with mean 0 and variance 1 in the function. In addition, the third variable will be quantile normalized within the function. More detail example about the usage of geneMap is demonstrated in the vignette.

**Value**

'GLA' returns a numerical value representing the estimated value. A more detailed interpretation of the value is illustrated in the vignette.

**Author(s)**

Yen-Yi Ho

**References**

Yen-Yi Ho, Leslie Cope, Thomas A. Louis, and Giovanni Parmigiani, GENERALIZED LIQUID ASSOCIATION (April 2009). Johns Hopkins University, Dept. of Biostatistics Working Papers. Working Paper 183. <http://www.bepress.com/jhubiostat/paper183>

**See Also**

[LA-methods](#), [getsGLA-methods](#)

**Examples**

```
data<-matrix(rnorm(300), ncol=3)

colnames(data)<-c("Gene1", "Gene2", "Gene3")

GLAest<-GLA(data, cut=4, dim=3)

GLAest
```

LA-methods

*Function to calculate LA estimate***Description**

'LA' is used to calculate the LA estimate for a gene triplet data.

**Arguments**

|         |  |
|---------|--|
| object  | An numerical matrix object with three columns or an object of ExpressionSet class with three features.           |
| dim     | An index of the column for the gene to be treated as the third controller variable. Default is dim=3             |
| geneMap | A character vector with three elements representing the mapping between gene names and feature names (optional). |

**Details**

The input object can be a numerical matrix with three columns with row representing observations and column representing three variables. It can also be an ExpressionSet object with three features. If input a matrix class data, all three columns of the object representing the variables should have column names. Each variable in the object will be standardized with mean 0 and variance 1 in the function. In addition, the third variable will be quantile normalized within the function. More detail example about the usage of geneMap is demonstrated in the vignette.

**Value**

'LA' returns a numerical value representing the estimated value. A more detailed explanation of the value is illustrated in the vignette.

**Author(s)**

Yen-Yi Ho

## References

Ker-Chau Li, Genome-wide coexpression dynamics: theory and application (2002). PNAS 99 (26): 16875-16880.

Yen-Yi Ho, Leslie Cope, Thomas A. Louis, and Giovanni Parmigiani, GENERALIZED LIQUID ASSOCIATION (April 2009). Johns Hopkins University, Dept. of Biostatistics Working Papers. Working Paper 183. <http://www.bepress.com/jhubiostat/paper183>

## See Also

[GLA-methods](#), [getsLA-methods](#)

## Examples

```
data<-matrix(rnorm(300), ncol=3)

colnames(data)<-c("Gene1", "Gene2", "Gene3")

LAest<-LA(data)

LAest
```

---

LiquidAssociation-internal

*Internal LiquidAssociation Functions*

---

## Description

```
stand(object, ...)
qqnorm2(object, ...)
form(object, ...)
boots.se(object, ...)
permute3.se(object, ...)
boots.gla.se2(object, ...)
```

## Note

These are not to be called by the user (or in some cases are just waiting for proper documentation to be written).

---

|                 |   |
|-----------------|---|
| plotGLA-methods | <i>The function plots scatter plots of two variables conditioning on the value of a third variable.</i> |
|-----------------|---|

---

### Description

'plotGLA' is a function to plot the scatter plots of two variables conditioning on the value of a third variable.

### Arguments

|         |  |
|---------|--|
| object  | An numerical matrix object with three columns or an object of ExpressionSet class with three features..          |
| cut     | cut==M +1. M is the number of grip points pre-specified over the third variable .                                |
| dim     | An index of the column for the gene to be treated as the third controller variable.                              |
| filen   | The file name for the output graph can be specified when save=TRUE   |
| save    | If save=TRUE then output graphs will be save as PDF files with file name as specified by filen.                  |
| geneMap | A character vector with three elements representing the mapping between gene names and feature names (optional). |
| ...     | Other graphical parameters can be passed to function plot.   |

### Details

The input object can be a numerical matrix with three columns with row representing observations and column representing three variables. It can also be an ExpressionSet object with three features. More detail example about the usage of geneMap is demonstrated in the vignette.

### Author(s)

Yen-Yi Ho

### References

Yen-Yi Ho, Leslie Cope, Thomas A. Louis, and Giovanni Parmigiani, GENERALIZED LIQUID ASSOCIATION (April 2009). Johns Hopkins University, Dept. of Biostatistics Working Papers. Working Paper 183. <http://www.bepress.com/jhubiostat/paper183>

### Examples

```
data<-matrix(rnorm(300), ncol=3)

colnames(data)<-c("Gene1", "Gene2", "Gene3")

plotGLA(data, cut=3, dim=3, pch=16, filen="GLAplot", save=FALSE)
```

# Index

- \* **classes**
  - CNM-class, [3](#)
- \* **htest**
  - getsGLA-methods, [6](#)
  - getsLA-methods, [8](#)
- \* **internal**
  - LiquidAssociation-internal, [11](#)
- \* **methods**
  - CNM.full-methods, [4](#)
  - CNM.simple-methods, [5](#)
  - getsGLA-methods, [6](#)
  - getsLA-methods, [8](#)
  - GLA-methods, [9](#)
  - LA-methods, [10](#)
  - plotGLA-methods, [12](#)
- \* **models**
  - CNM.full-methods, [4](#)
  - CNM.simple-methods, [5](#)
- \* **package**
  - LiquidAssociation-package, [2](#)

boots.gla.se2  
(LiquidAssociation-internal),  
[11](#)

boots.se (LiquidAssociation-internal),  
[11](#)

CNM-class, [3](#)

CNM.full (CNM.full-methods), [4](#)

CNM.full, eSet-method  
(CNM.full-methods), [4](#)

CNM.full, matrix-method  
(CNM.full-methods), [4](#)

CNM.full-methods, [4](#)

CNM.simple (CNM.simple-methods), [5](#)

CNM.simple, eSet-method  
(CNM.simple-methods), [5](#)

CNM.simple, matrix-method  
(CNM.simple-methods), [5](#)

CNM.simple-methods, [5](#)

est.table (LiquidAssociation-internal),  
[11](#)

est.table1  
(LiquidAssociation-internal),  
[11](#)

form (LiquidAssociation-internal), [11](#)

getsGLA (getsGLA-methods), [6](#)

getsGLA, eSet-method (getsGLA-methods), [6](#)

getsGLA, matrix-method  
(getsGLA-methods), [6](#)

getsGLA-methods, [6](#)

getsLA (getsLA-methods), [8](#)

getsLA, eSet-method (getsLA-methods), [8](#)

getsLA, matrix-method (getsLA-methods), [8](#)

getsLA-methods, [8](#)

GLA (GLA-methods), [9](#)

GLA, eSet-method (GLA-methods), [9](#)

GLA, matrix-method (GLA-methods), [9](#)

GLA-methods, [9](#)

LA (LA-methods), [10](#)

LA, eSet-method (LA-methods), [10](#)

LA, matrix-method (LA-methods), [10](#)

LA-methods, [10](#)

LiquidAssociation  
(LiquidAssociation-package), [2](#)

LiquidAssociation-internal, [11](#)

LiquidAssociation-package, [2](#)

permute3.se  
(LiquidAssociation-internal),  
[11](#)

plotGLA (plotGLA-methods), [12](#)

plotGLA, eSet-method (plotGLA-methods),  
[12](#)

plotGLA, matrix-method  
(plotGLA-methods), [12](#)

plotGLA-methods, [12](#)

`print`, [4](#)  
`print`, CNM-method (CNM-class), [3](#)  
`product` (LiquidAssociation-internal), [11](#)  
  
`qqnorm2` (LiquidAssociation-internal), [11](#)  
  
`show`, [4](#)  
`show`, CNM-method (CNM-class), [3](#)  
`stand` (LiquidAssociation-internal), [11](#)