Package ‘CopulaREMADA’

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CopulaREMADA-package

Copula Mixed Models for Multivariate Meta-Analysis of Diagnostic Test Accuracy Studies

Description


Details

This package contains R functions to implement:

- The copula mixed model for meta-analysis of diagnostic test accuracy studies and produce SROC curves and summary operating points (a pair of average sensitivity and specificity) with a confidence region and a predictive region (Nikoloulopoulos, 2015, 2018a). All the analyses presented in Section 7 of Nikoloulopoulos (2015) are given as code examples in the package;
- The vine copula mixed model for meta-analysis of diagnostic test accuracy studies accounting for disease prevalence and non-evaluable subjects (Nikoloulopoulos, 2017, 2018b);
- The hybrid vine copula mixed model for meta-analysis of diagnostic test accuracy case-control and cohort studies (Nikoloulopoulos, 2018c);

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- The D-vine copula mixed model for meta-analysis and comparison of two diagnostic tests (Nikoloulopoulos, 2018d).
- The multinomial quadivariate D-vine copula mixed model for diagnostic studies meta-analysis accounting for non-evaluable subjects (Nikoloulopoulos, 2018e).

**Author(s)**

Aristidis K. Nikoloulopoulos.

**References**


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**The rheumatoid arthritis data**

**Description**

Data obtained from a meta-analysis that aimed to determine whether anti-cyclic citrullinated peptide (anti-CCP) antibody identifies more accurately patients with rheumatoid arthritis than rheumatoid factor (RF) does. We include $N = 22$ studies that assessed both RF and anti-CCP2 antibody for diagnosing rheumatoid arthritis.
Format

A data frame with 22 observations on the following 8 variables.

- **TP1** the number of true positives for RF
- **FN1** the number of false negatives for RF
- **FP1** the number of false positives for RF
- **TN1** the number of true negatives for RF
- **TP2** the number of true positives for anti-CCP2
- **FN2** the number of false negatives for anti-CCP2
- **FP2** the number of false positives for anti-CCP2
- **TN2** the number of true negatives for anti-CCP2

References


---

`betaDG`  
*The beta-D-Glucan-data*

Description

Data on 8 cohort studies in the meta-analysis in Karageorgopoulos et al. (2011). The interest there is to assess beta-D-Glucan as a serum or plasma marker for the presence of invasive fungal infections.

Usage

data(betaDG)

Format

A data frame with 8 observations on the following 4 variables.

- **TP** the number of true positives
- **FN** the number of false negatives
- **FP** the number of false positives
- **TN** the number of true negatives

References

Description

For copula mixed models for diagnostic test accuracy studies numerical evaluation of the MLE is easily done with the following steps:

1. Calculate Gauss-Legendre quadrature points $gl\$nodes$ and weights $gl\$weights$.

2. Convert from independent uniform quadrature points to dependent uniform quadrature points that have distribution ‘cop’. The inverse of the conditional distribution $qcondcop$ corresponding to the copula ‘cop’ is used to achieve this.

3. Numerically evaluate the joint probability mass function with the bivariate integral in a double sum.

With Gauss-Legendre quadrature, the same nodes and weights are used for different functions; this helps in yielding smooth numerical derivatives for numerical optimization via quasi-Newton. Our comparisons show that $n_q = 15$ is adequate with good precision to at least at four decimal places.

Usage

CopulaREMADA.norm(TP, FN, FP, TN, gl, mgrid, qcond, tau2par)
CopulaREMADA.beta(TP, FN, FP, TN, gl, mgrid, qcond, tau2par)
countermonotonicCopulaREMADA.norm(TP, FN, FP, TN, gl, mgrid)
countermonotonicCopulaREMADA.beta(TP, FN, FP, TN, gl, mgrid)

Arguments

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>TP</td>
<td>the number of true positives</td>
</tr>
<tr>
<td>FN</td>
<td>the number of false negatives</td>
</tr>
<tr>
<td>FP</td>
<td>the number of false positives</td>
</tr>
<tr>
<td>TN</td>
<td>the number of true negatives</td>
</tr>
<tr>
<td>gl</td>
<td>a list containing the components of Gauss-Legendre nodes $gl$nodes$ and weights $gl$weights$</td>
</tr>
<tr>
<td>mgrid</td>
<td>a list containing two matrices with the rows of the output matrix $x$ are copies of the vector $gl$nodes$; columns of the output matrix $y$ are copies of the vector $gl$nodes$. For more details see also meshgrid</td>
</tr>
<tr>
<td>qcond</td>
<td>function for the inverse of conditional copula cdf</td>
</tr>
<tr>
<td>tau2par</td>
<td>function for mapping Kendall’s tau to copula parameter</td>
</tr>
</tbody>
</table>
Value

A list containing the following components:

- **minimum**: the value of the estimated minimum of the negative log-likelihood
- **estimate**: the MLE
- **gradient**: the gradient at the estimated minimum of the negative log-likelihood
- **hessian**: the hessian at the estimated minimum of the negative log-likelihood
- **code**: an integer indicating why the optimization process terminated
- **iterations**: the number of iterations performed

For more details see `nlm`

References


See Also

- `rcopularemada`

Examples

```r
nq=15
gl=gauss.quad.prob(nq,"uniform")
mgrid<- meshgrid(gl$n, gl$n)

data(LAG)
attach(LAG)
c27@est.b=CopulaREMADA.beta(TP, FN, FP, TN, gl, mgrid, qcondcln270, tau2par.cln270)
detach(LAG)

data(MRI)
attach(MRI)
c27@est.n=CopulaREMADA.norm(TP, FN, FP, TN, gl, mgrid, qcondcln270, tau2par.cln270)
detach(MRI)

data(CT)
attach(CT)
est.n=countermonotonicCopulaREMADA.norm(TP, FN, FP, TN, gl, mgrid)
est.b=countermonotonicCopulaREMADA.beta(TP, FN, FP, TN, gl, mgrid)
detach(CT)
```
**The coronary CT angiography data**

**Description**
Data on 26 studies from a systematic review for diagnostic accuracy studies of coronary computed tomography angiography for the detection of coronary artery disease.

**Usage**
data(coronary)

**Format**
A data frame with 26 observations on the following 6 variables.

- **TP**  the number of true positives
- **FN**  the number of false negatives
- **FP**  the number of false positives
- **TN**  the number of true negatives
- **NEP** the number of non-evaluable positives
- **NEN** the number of non-evaluable negatives

**References**

---

**The computing tomography data**

**Description**
Data on 17 studies of computed tomography (CT) for the diagnosis of lymph node metastasis in women with cervical cancer, one of three imaging techniques in the meta-analysis in Scheidler et al. (1997). Diagnosis of metastatic disease by CT relies on nodal enlargement.

**Usage**
data(CT)
Format
A data frame with 17 observations on the following 4 variables.

TP  the number of true positives
FN  the number of false negatives
FP  the number of false positives
TN  the number of true negatives

References

---

Simulation from a trivariate C-vine copula

Description
Simulation from a trivariate C-vine copula

Usage
cvinesim(N, param, qcondcop12, qcondcop13, qcondcop23, tau2par12, tau2par13, tau2par23)

Arguments
N sample size
param Kendall's tau values for margins (1,2), (1,3), (23|1)
qcondcop12 function for the inverse of conditional copula cdf at the (1,2) bivariate margin
qcondcop13 function for the inverse of conditional copula cdf at the (1,3) bivariate margin
qcondcop23 function for the inverse of conditional copula cdf at the (2,3|1) bivariate margin
tau2par12 function for mapping Kendall's tau at the (1,2) bivariate margin to copula parameter
tau2par13 function for mapping Kendall's tau at the (1,3) bivariate margin to copula parameter
tau2par23 function for mapping Kendall's tau at the (2,3|1) bivariate margin to the conditional copula parameter

Details
Choices are 'cop' in rcop are bvn, frk, cln, cln90 (rotated by 90 degrees cln), cln180 (rotated by 180 degrees cln), cln270 (rotated by 270 degrees cln).
See help page for dcp for the abbreviations of the copula names.
dcop

Value

Nx3 matrix with values in (0,1)

References


See Also

qcondcop dcop rcop

dcop

Bivariate copula densities

Description

Bivariate copula densities for parametric families.

Usage

dbvn(u,v,cpar)
dfrk(u,v,cpar)
dcln(u,v,cpar)
dcln90(u,v,cpar)
dcln180(u,v,cpar)
dcln270(u,v,cpar)

Arguments

u value in interval 0,1; could be a vector
v value in interval 0,1; could be a vector
cpar copula parameter: scalar.

Details

Choices are ‘cop’ in dcop are bvn, frk, cln, cln90 (rotated by 90 degrees cln), cln180 (rotated by 180 degrees cln), cln270 (rotated by 270 degrees cln).

The copula names are abbreviations for:
bvn = bivariate normal or Gaussian
frk = Frank
cln = Clayton or Mardia-Takahasi-Cook-Johnson
**dvinesim**

**Value**

pdf value(s).

**References**


**See Also**

qcondcop rcop

---

**dvinesim**  
*Simulation from a (truncated) quadrivariate D-vine copula*

**Description**

Simulation from a (truncated) quadrivariate D-vine copula. Lower-order trees (if any) are composed with BVN copulas.

**Usage**

dvinesim(nsim, param, qcond1, pcond1, tau2par1, qcond2, pcond2, tau2par2)
dtrvinesim(nsim, trparam, qcond1, pcond1, tau2par1, qcond2, pcond2, tau2par2)

**Arguments**

- **nsim** sample size
- **param** Kendall’s tau values for margins (1,2), (2,3), (3,4), (1,3|2), (2,4|3), (1,4|23)
- **trparam** Kendall’s tau values for margins (1,2), (2,3), (3,4)
- **qcond1** function for the inverse conditional copula cdf at the (1,2) and (3,4) bivariate margins
- **pcond1** function for the conditional copula cdf at the (1,2) and (3,4) bivariate margins
- **tau2par1** function for mapping Kendall’s tau at the (1,2) and (3,4) bivariate margins to copula parameter
- **qcond2** function for the inverse conditional copula cdf at the (2,3) bivariate margin
- **pcond2** function for the conditional copula cdf at the (2,3) bivariate margin
- **tau2par2** function for mapping Kendall’s tau at the (2,3) bivariate margin to copula parameter
Details

Choices are `cop` in rcop are bvn, frk, cln, cln90 (rotated by 90 degrees cln), cln180 (rotated by 180 degrees cln), cln270 (rotated by 270 degrees cln).

See help page for dcop for the abbreviations of the copula names.

Value

Nx4 matrix with values in (0,1)

References


See Also

qcondcop dcop rcop

Description

The estimated parameters can be obtained by using a quasi-Newton method applied to the logarithm of the joint likelihood. This numerical method requires only the objective function, i.e., the logarithm of the joint likelihood, while the gradients are computed numerically and the Hessian matrix of the second order derivatives is updated in each iteration. The standard errors (SE) of the ML estimates can be also obtained via the gradients and the Hessian computed numerically during the maximization process.
Usage

```r
hybridCopulaREMADA.norm(TP, FN, FP, TN, type, perm, gl, mgrid1, mgrid2, qcondcop12, qcondcop13, tau2par12, tau2par13, qcond, tau2par)
hybridCopulaREMADA.beta(TP, FN, FP, TN, type, perm, gl, mgrid1, mgrid2, qcondcop12, qcondcop13, tau2par12, tau2par13, qcond, tau2par)
```

Arguments

- **TP**: the number of true positives
- **FN**: the number of false negatives
- **FP**: the number of false positives
- **TN**: the number of true negatives
- **type**: a scalar indicating the study type: 1: Cohort study; 2: Case-control study.
- **perm**: a scalar indicating the selected permutation of indices:
  - 1: Pilot variable is the number of TP. The bivariate margins are 12, 13, 23|1;
  - 2: Pilot variable is the number of TN. The bivariate margins are 23, 12, 13|2;
  - 3: Pilot variable is the TP+FN. The bivariate margins are 13, 23, 12|3;
- **gl**: a list containing the components of Gauss-Legendre nodes `gl$nodes` and weights `gl$weights`
- **mgrid1**: a list containing three-dimensional arrays. For more details see `meshgrid`
- **mgrid2**: a list containing two matrices with the rows of the output matrix `x` are copies of the vector `gl$nodes`; columns of the output matrix `y` are copies of the vector `gl$nodes`. For more details see also `meshgrid`
- **qcondcop12**: function for the inverse of conditional copula cdf at the (1,2) bivariate margin of the vine
- **qcondcop13**: function for the inverse of conditional copula cdf at the (1,3) bivariate margin of the vine
- **tau2par12**: function for mapping Kendall’s tau at the (1,2) bivariate margin of the vine to copula parameter
- **tau2par13**: function for mapping Kendall’s tau at the (1,3) bivariate margin of the vine to copula parameter
- **qcond**: function for the inverse of conditional copula cdf
- **tau2par**: function for mapping Kendall’s tau to the bivariate copula parameter

Value

A list containing the following components:

- **minimum**: the value of the estimated minimum of the negative log-likelihood
estimate the MLE

gradient the gradient at the estimated minimum of the negative log-likelihood

hessian the hessian at the estimated minimum of the negative log-likelihood

code an integer indicating why the optimization process terminated

iterations the number of iterations performed

For more details see nlm

References


See Also

*VineCopulaREMADA, CopulaREMADA*

Examples

```r
# simulate the data from N=25 cohort studies
N=25
p=c(0.8,0.7,0.4)
g=c(0.1,.01,0.05)
taus=c(-0.5,-0.3,-0.0001)
qcondcop12=qcondcop13=qcondcop13=qcondcln90
tau2par12=tau2par23=tau2par13=tau2par.cln90
simdat1=rvineCopulaREMADA.beta(N,p,g,taus,0,0,
qcondcop12,qcondcop13,qcondcop23,tau2par12,tau2par13,tau2par23)
# simulate data from the N=25 case-control studies
tau=.5
p=p[-3]
g=g[-3]
simdat2=rcopulaREMADA.beta(N,p,g,tau,rcln,tau2par.cln)
# combine the data
TP=c(simdat1$TP,simdat2$TP)
TN=c(simdat1$TN,simdat2$TN)
FP=c(simdat1$FP,simdat2$FP)
FN=c(simdat1$FN,simdat2$FN)
type=rep(c(1,2),each=N)

# fit the hybrid copula mixed model
nq=21
gl=gauss.quad.prob(nq,"uniform")
mgrid1<- meshgrid(gl$n,gl$n,gl$n,nargout=3)
mgrid2<- meshgrid(gl$n,gl$n)
perm=1
qcond=qcondcln
tau2par=tau2par.cln
# est=hybridCopulaREMADA.beta(TP,FP,TN,type,perm,gl,mgrid1,mgrid2,
```
The lymphangiography data

Description

Data on 17 studies of lymphangiography (LAG) for the diagnosis of lymph node metastasis in women with cervical cancer, one of three imaging techniques in the meta-analysis in Scheidler et al. (1997). Diagnosis of metastatic disease by LAG is based on the presence of nodal-filling defects.

Usage

data(LAG)

Format

A data frame with 17 observations on the following 4 variables.

- **TP** the number of true positives
- **FN** the number of false negatives
- **FP** the number of false positives
- **TN** the number of true negatives

References


A list containing four-dimensional arrays

Description

A list containing four-dimensional arrays. Replicates of the quadrature points that produce an 4-dimensional full grid.
Examples

data(mgrid15)

dim(mgrid15$X)

dim(mgrid15$Y)

dim(mgrid15$Z)

dim(mgrid15$W)

data(mgrid30)

dim(mgrid30$X)

dim(mgrid30$Y)

dim(mgrid30$Z)

dim(mgrid30$W)

data(mgrid50)

dim(mgrid50$X)

dim(mgrid50$Y)

dim(mgrid50$Z)

dim(mgrid50$W)

The coronary CT angiography data in Menke and Kowalski (2016).

Description

Data on 30 studies from a systematic review for diagnostic accuracy studies of coronary computed tomography angiography for the detection of coronary artery disease.

Usage

data(MK2016)

Format

A data frame with 30 observations on the following 6 variables.

TP the number of true positives
FN the number of false negatives
FP the number of false positives
TN the number of true negatives
NEP the number of non-evaluable positives
NEN the number of non-evaluable negatives

References

The magnetic resonance imaging data

Description

Data on 10 studies of magnetic resonance imaging (MRI) for the diagnosis of lymph node metastasis in women with cervical cancer, the last imaging technique in the meta-analysis in Scheidler et al. (1997). Diagnosis of metastatic disease by MRI relies on nodal enlargement.

Usage

data(MRI)

Format

A data frame with 10 observations on the following 4 variables.

TP the number of true positives
FN the number of false negatives
FP the number of false positives
TN the number of true negatives

References


Maximum likelihood estimation for multinomial quadrivariate (truncated) D-vine copula mixed models for diagnostic test accuracy studies accounting for non-evaluable outcomes

Description

The estimated parameters can be obtained by using a quasi-Newton method applied to the logarithm of the joint likelihood. This numerical method requires only the objective function, i.e., the logarithm of the joint likelihood, while the gradients are computed numerically and the Hessian matrix of the second order derivatives is updated in each iteration. The standard errors (SE) of the ML estimates can be also obtained via the gradients and the Hessian computed numerically during the maximization process.
Usage

```
multinomVineCopulaREMADA.norm(TP, FN, FP, TN, NEP, NEN, 
    gl, mgrid, qcond1, pcond1, tau2par1, 
    qcond2, pcond2, tau2par2)
multinomVineCopulaREMADA.beta(TP, FN, FP, TN, NEP, NEN, 
    gl, mgrid, qcond1, pcond1, tau2par1, 
    qcond2, pcond2, tau2par2)
tmultinomVineCopulaREMADA.norm(TP, FN, FP, TN, NEP, NEN, 
    gl, mgrid, 
    qcond1, pcond1, tau2par1, 
    qcond2, pcond2, tau2par2)
tmultinomVineCopulaREMADA.beta(TP, FN, FP, TN, NEP, NEN, 
    gl, mgrid, 
    qcond1, pcond1, tau2par1, 
    qcond2, pcond2, tau2par2)
```

Arguments

- **TP**: the number of true positives
- **FN**: the number of false negatives
- **FP**: the number of false positives
- **TN**: the number of true negatives
- **NEP**: the number of non-evaluable positives in the presence of non-evaluable subjects
- **NEN**: the number of non-evaluable negatives in the presence of non-evaluable subjects
- **gl**: a list containing the components of Gauss-Legendre nodes `gl$nodes` and weights `gl$weights`
- **mgrid**: a list containing 4-dimensional arrays.
- **qcond1**: function for the inverse conditional copula cdf at the (1,2) and (3,4) bivariate margin
- **pcond1**: function for the conditional copula cdf at the (1,2) and (3,4) bivariate margin
- **tau2par1**: function for mapping Kendall’s tau at the (1,2) and (3,4) bivariate margin to copula parameter
- **qcond2**: function for the inverse conditional copula cdf at the (2,3) bivariate margin
- **pcond2**: function for the conditional copula cdf at the (2,3) bivariate margin
- **tau2par2**: function for mapping Kendall’s tau at the (2,3) bivariate margin to copula parameter

Value

A list containing the following components:

- **minimum**: the value of the estimated minimum of the negative log-likelihood
- **estimate**: the MLE
- **gradient**: the gradient at the estimated minimum of the negative log-likelihood
hessian  the hessian at the estimated minimum of the negative log-likelihood
code     an integer indicating why the optimization process terminated
iterations the number of iterations performed

For more details see nlm

References


See Also

rmultinomVineCopulaREMADA

Examples

nq=15
gl=gauss.quad.prob(nq,"uniform")
data(mgrid15)

data(MK2016)
attach(MK2016)

#out=tmultinomVineCopulaREMADA.beta(TP,FN,FP,TN,NEP,NEN,
#gl,mgrid15,qcondcln180,pcondcln180,tau2par.cln180,
#qcondcln90,pcondcln90,tau2par.cln90)
detach(MK2016)

OGT  
The orale glucose tolerance data

Description

Data on 10 studies of the oral glucose tolerance test for the diagnosis of diabetes mellitus in patients during acute coronary syndrome hospitalization in Ye et al. (2012).

Usage

data(OGT)
Format
A data frame with 10 observations on the following 4 variables.

TP  the number of true positives
FN  the number of false negatives
FP  the number of false positives
TN  the number of true negatives

References

\[ \text{pcondcop} \]

**Bivariate copula conditional distribution functions**

**Description**
Bivariate copula conditional distribution functions

**Usage**
\[
\begin{align*}
pcondbvn(v, u, cpar) \\
pcondfrk(v, u, cpar) \\
pcondcln(v, u, cpar) \\
pcondcln90(v, u, cpar) \\
pcondcln180(v, u, cpar) \\
pcondcln270(v, u, cpar)
\end{align*}
\]

**Arguments**
\[
\begin{align*}
v & \quad \text{conditioning value in interval 0,1; could be a vector} \\
u & \quad \text{value in interval 0,1; could be a vector} \\
cpar & \quad \text{copula parameter: scalar.}
\end{align*}
\]

**Details**
Choices appending ‘cop’ are bvn, frk, cln, cln90 (rotated by 90 degrees cln), cln180 (rotated by 180 degrees cln), cln270 (rotated by 270 degrees cln).
See help page for *dcop* for the abbreviations of the copula names.

**Value**
inverse conditional cdf value(s)
References


See Also
dcop rcop

---

qcondcop  
*Bivariate copula conditional quantile functions*

Description

Bivariate copula conditional quantile functions

Usage

qcondbvn(p, u, cpar)  
qcondfrk(p, u, cpar)  
qcondcln(p, u, cpar)  
qcondcln90(p, u, cpar)  
qcondcln180(p, u, cpar)  
qcondcln270(p, u, cpar)

Arguments

- **u**: conditioning value in interval 0,1; could be a vector
- **p**: quantile in interval 0,1; could be a vector
- **cpar**: copula parameter: scalar.

Details

Choices appending ’cop’ are bvn, frk, cln, cln90 (rotated by 90 degrees cln), cln180 (rotated by 180 degrees cln), cln270 (rotated by 270 degrees cln).

See help page for *dcop* for the abbreviations of the copula names.

Value

inverse conditional cdf value(s)

References

quadVineCopulaREMADA  Maximum likelihood estimation for quadrivariate D-vine copula mixed models for joint meta-analysis and comparison of two diagnostic tests

Description

The estimated parameters can be obtained by using a quasi-Newton method applied to the logarithm of the joint likelihood. This numerical method requires only the objective function, i.e., the logarithm of the joint likelihood, while the gradients are computed numerically and the Hessian matrix of the second order derivatives is updated in each iteration. The standard errors (SE) of the ML estimates can be also obtained via the gradients and the Hessian computed numerically during the maximization process.

Usage

quadVineCopulaREMADA.norm(tp1, fn1, fp1, tn1, tp2, fn2, fp2, tn2, gl, mgrid, qcond1, pcond1, tau2par1, qcond2, pcond2, tau2par2)
quadVineCopulaREMADA.beta(tp1, fn1, fp1, tn1, tp2, fn2, fp2, tn2, gl, mgrid, qcond1, pcond1, tau2par1, qcond2, pcond2, tau2par2)
quadVineCopulaREMADA.norm.beta(tp1, fn1, fp1, tn1, tp2, fn2, fp2, tn2, gl, mgrid, qcond1, pcond1, tau2par1, qcond2, pcond2, tau2par2)

Arguments

TP1  the number of true positives for test 1
FN1  the number of false negatives for test 1
FP1  the number of false positives for test 1
TN1  the number of true negatives for test 1
TP2  the number of true positives for test 2
FN2  the number of false negatives for test 2
FP2  the number of false positives for test 2
TN2  the number of true negatives for test 2
gl  a list containing the components of Gauss-Legendre nodes gl$nodes and weights gl$weights
mgrid a list containing 4-dimensional arrays.
qcond1 function for the inverse conditional copula cdf at the (1,2) bivariate margin
quadVineCopulaREMADA

pcond1  function for the conditional copula cdf at the (1,2) bivariate margin

tauRpar1  function for mapping Kendall’s tau at the (1,2) bivariate margin to copula parameter

qcond2  function for the inverse conditional copula cdf at the (3,4) bivariate margin

pcond2  function for the conditional copula cdf at the (3,4) bivariate margin

tau2par2  function for mapping Kendall’s tau at the (3,4) bivariate margin to copula parameter

Value

A list containing the following components:

- **minimum**: the value of the estimated minimum of the negative log-likelihood
- **estimate**: the MLE
- **gradient**: the gradient at the estimated minimum of the negative log-likelihood
- **hessian**: the hessian at the estimated minimum of the negative log-likelihood
- **code**: an integer indicating why the optimization process terminated
- **iterations**: the number of iterations performed

For more details see `nlm`

References


Examples

```r
nq=15
g1=gauss.quad.prob(nq,"uniform")
data(mgrid15)
data(arthritis)
attach(arthritis)

qcond1=qcondc1n270
pcond1=pcondc1n270
tau2par1=tau2par.c1n270

qcond2=qcondfrk
pcond2=pcondfrk
tau2par2=tau2par.frk

# out<-quadVineCopulaREMADA.norm(TP1,FN1,FP1,TN1,TP2,FN2,FP2,TN2,
# g1,mgrid15,qcond1,pcond1,tau2par1,qcond2,pcond2,tau2par2)
detach(arthritis)
```
Simulation from parametric bivariate copula families

**Description**

Simulation from parametric bivariate copula families

**Usage**

rbvn(N, cpar)
rfrk(N, cpar)
rcln(N, cpar)
rcln90(N, cpar)
rcln180(N, cpar)
rcln270(N, cpar)

**Arguments**

- **N**: sample size
- **cpar**: copula parameter: scalar

**Details**

Choices are 'cop' in rcop are bvn, frk, cln, cln90 (rotated by 90 degrees cln), cln180 (rotated by 180 degrees cln), cln270 (rotated by 270 degrees cln).

See help page for dcop for the abbreviations of the copula names.

**Value**

nx2 matrix with values in (0,1)

**References**


**See Also**

qcondcop dcop
Description

To simulate the data we have used the following steps:

1. Simulate the study size $n$ from a shifted gamma distribution with parameters $\alpha = 1.2, \beta = 0.01, \log = 30$ and round off to the nearest integer.
2. Simulate $(u_1, u_2)$ from a parametric family of copulas ‘cop’.
3. Convert to beta realizations or normal realizations.
4. Draw the number of diseased $n_1$ from a $B(n, 0.43)$ distribution.
5. Set $n_2 = n - n_1, y_j = n_j x_j$ and then round $y_j$ for $j = 1, 2$.

Usage

```
rcopularemada.norm(N, p, si, tau = rcop, tau2par)
rcopularemada.beta(N, p, g, tau = rcop, tau2par)
```

Arguments

- `N`: sample size
- `p`: Pair $(\pi_1, \pi_2)$ of sensitivity/specificity
- `si`: Pair $(\sigma_1, \sigma_2)$ of variability; normal margins
- `g`: Pair $(\gamma_1, \gamma_2)$ of variability; beta margins
- `tau`: Kendall’s tau value
- `rcop`: function for copula generation
- `tau2par`: function for mapping from Kendall’s tau to copula parameter

Value

A list containing the following simulated components:

- `TP`: the number of true positives
- `FN`: the number of false negatives
- `FP`: the number of false positives
- `TN`: the number of true negatives

References

Simulation from multinomial quadrivariate (truncated) D-vine copula mixed models for diagnostic test accuracy studies accounting for non-evaluable outcomes

Usage

```r
rmultinomVineCopulaREMADA.norm(N, p, si, taus, qcond1, pcond1, tau2par1, qcond2, pcond2, tau2par2)
```

```r
rmultinomVineCopulaREMADA.beta(N, p, g, taus, qcond1, pcond1, tau2par1, qcond2, pcond2, tau2par2)
```

Description

Simulation from for multinomial quadrivariate (truncated) D-vine copula mixed models for diagnostic test accuracy studies accounting for non-evaluable outcomes

Examples

```r
nq = 15
gl = gauss.quad.prob(nq, "uniform")
mgrid <- meshgrid(gl$n, gl$n)

N = 20
tau = c(0.5, 0.5)
p = c(0.7, 0.9)
g = c(0.2, 0.1)
simDat = rCopulaREMADA.norm(N, p, g, tau, ncln270, tau2par.cl270)

TP = simDat$TP
TN = simDat$TN
FP = simDat$FP
FN = simDat$FN

c270est.b = rCopulaREMADA.beta(TP, FN, FP, TN, gl, mgrid, qcondcln, tau2par.cl270)

si = c(2, 1)
tau = 0.5
simDat = rCopulaREMADA.norm(N, p, si, tau, ncln, tau2par.cln)

TP = simDat$TP
TN = simDat$TN
FP = simDat$FP
FN = simDat$FN

c.est.n = rCopulaREMADA.norm(TP, FN, FP, TN, gl, mgrid, qcondcln, tau2par.cln)
```
Arguments

N sample size
p Vector \((\pi_1, \pi_2, \pi_3)\) of sensitivity/specificity/prevalence
si Vector \((\sigma_1, \sigma_2, \sigma_3)\) of variability; normal margins
g Vector \((\gamma_1, \gamma_2, \gamma_3)\) of variability; beta margins
taus Kendall’s tau values
qcond1 function for the inverse conditional copula cdf at the (1,2) and (3,4) bivariate margin
pcond1 function for the conditional copula cdf at the (1,2) and (3,4) bivariate margin
tau2par1 function for mapping Kendall’s tau at the (1,2) and (3,4) bivariate margin to copula parameter
qcond2 function for the inverse conditional copula cdf at the (2,3) bivariate margin
pcond2 function for the conditional copula cdf at the (2,3) bivariate margin
tau2par2 function for mapping Kendall’s tau at the (2,3) bivariate margin to copula parameter

Value

Simulated data with 6 columns and \(N\) rows.

TP the number of true positives
FN the number of false negatives
FP the number of false positives
TN the number of true negatives
NEP the number of non-evaluable positives
NEN the number of non-evaluable negatives

References


See Also
dvinesim

Examples

```
N=30
p=c(0.898745016, 0.766105342, 0.059168715, 0.109217888)
g=c(0.090270947, 0.079469009, 0.367463579, 0.154976269)
taus=c( 0.82058793, -0.51867629, 0.26457961)
qcond1=qcondcln180
```
Simulation from trivariate vine copula mixed models for diagnostic test accuracy studies accounting for disease prevalence and non-evaluable results

Description
Simulation from trivariate vine copula mixed models for diagnostic test accuracy studies accounting for disease prevalence and non-evaluable results

Usage
rvinecopularemada.beta(N, p, g, taus, omega1, omega0, qcondcop12, qcondcop13, qcondcop23, tau2par12, tau2par13, tau2par23)
rvinecopularemada.norm(N, p, si, taus, omega1, omega0, qcondcop12, qcondcop13, qcondcop23, tau2par12, tau2par13, tau2par23)

Arguments
N sample size
p Vector \((\pi_1, \pi_2, \pi_3)\) of sensitivity/specificity/prevalence
si Vector \((\sigma_1, \sigma_2, \sigma_3)\) of variability; normal margins
g Vector \((\gamma_1, \gamma_2, \gamma_3)\) of variability; beta margins
taus Kendall’s tau values
omega1 the probability for non-evaluable positives
omega0 the probability for non-evaluable negatives
qcondcop12 function for the inverse of conditional copula cdf at the (1,2) bivariate margin
qcondcop13 function for the inverse of conditional copula cdf at the (1,3) bivariate margin
qcondcop23 function for the inverse of conditional copula cdf at the (2,3|1) bivariate margin
tau2par12 function for mapping Kendall’s tau at the (1,2) bivariate margin to copula parameter

tau2par13 function for mapping Kendall’s tau at the (1,3) bivariate margin to copula parameter

tau2par23 function for mapping Kendall’s tau at the (2,3|1) bivariate margin to the conditional copula parameter

Value

Simulated data with 6 columns and \( N \) rows.

TP the number of true positives

FN the number of false negatives

FP the number of false positives

TN the number of true negatives

NEP the number of non-evaluable positives

NEN the number of non-evaluable negatives

References


See Also

rcopularemada rcop cvinesim

Examples

```r
p=c(0.8,0.7,0.4)
g=c(0.1,0.1,0.05)
taus=c(-0.5,-0.3,-0.0001)
qcondcop12=qcondcop23=qcondcop13=qcondcln90
tau2par12=tau2par23=tau2par13=tau2par.clin90
# in the absence of non-evaluable results
omega1=0
omega0=0
rVineCopulaREMADA.beta(50,p,g,taus,omega1,omega0,
qcondcop12,qcondcop13,qcondcop23,tau2par12,
tau2par13,tau2par23)
# in the presence of non-evaluable results
omega1=0.1
omega0=0.2
rVineCopulaREMADA.beta(50,p,g,taus,omega1,omega0,
qcondcop12,qcondcop13,qcondcop23,tau2par12,
tau2par13,tau2par23)
```
SROC

*Summary receiver operating characteristic curves for copula mixed effect models for bivariate meta-analysis of diagnostic test accuracy studies*

**Description**

Summary receiver operating characteristic (SROC) curves are demonstrated for the proposed models through quantile regression techniques and different characterizations of the estimated bivariate random effects distribution.

**Usage**

```
SROC.norm(param, dcop, qcondcop, tau2par, TP, FN, FP, TN,
           points=TRUE, curves=TRUE,
           NEP=rep(0, length(TP)), NEN=rep(0, length(TP)))
SROC.beta(param, dcop, qcondcop, tau2par, TP, FN, FP, TN,
           points=TRUE, curves=TRUE,
           NEP=rep(0, length(TP)), NEN=rep(0, length(TP)))
SROC(param.beta, param.normal, TP, FN, FP, TN,
      NEP=rep(0, length(TP)), NEN=rep(0, length(TP)))
```

**Arguments**

- `param`: A vector with the sensitivities, specificities, variabilities and Kendall’s tau value (the latter only for `SROC.norm` and `SROC.beta`)
- `param.beta`: A vector with the sensitivity, specificity and variabilities of the countermonotonic CopulaREMADA with beta margins
- `param.normal`: A vector with the sensitivity, specificity and variabilities of the countermonotonic CopulaREMADA with normal margins
- `dcop`: function for copula density
- `qcondcop`: function for the inverse of conditional copula cdf
- `tau2par`: function for mapping Kendall’s tau to copula parameter
- `TP`: the number of true positives
- `FN`: the number of false negatives
- `FP`: the number of false positives
- `TN`: the number of true negatives
- `points`: logical: print individual studies
- `curves`: logical: print quantile regression curves
- `NEP`: the number of non-evaluable positives in the presence of non-evaluable subjects
- `NEN`: the number of non-evaluable negatives in the presence of non-evaluable subjects
Value

Summary receiver operating characteristic curves

References


See Also

CopulaREMADA rCopulaREMADA

Examples

```r
nq=15
gl=gauss.quad.prob(nq,"uniform")
mgrid<- meshgrid(gl$n,gl$n)
data(telomerase)
attach(telomerase)
est.n=countermonotonicCopulaREMADA.norm(TP, FN, TP, FN, gl, mgrid)
est.b=countermonotonicCopulaREMADA.beta(TP, FN, TP, FN, gl, mgrid)
SROC(est.b$e, est.n$e, TP, FN, TP, FN)
detach(telomerase)

data(LAG)
attach(LAG)
c180est.b=CopulaREMADA.beta(TP, FN, TP, FN, gl, mgrid, qcondcln180, tau2par.cln180)
SROC.beta(c180est.b$e, dcln180, qcondcln180, tau2par.cln180, TP, FN, FN, TP)
detach(LAG)

data(MRI)
attach(MRI)
c270est.n=CopulaREMADA.norm(TP, FN, TP, FN, gl, mgrid, qcondcln270, tau2par.cln270)
SROC.norm(c270est.n$e, dcln270, qcondcln270, tau2par.cln270, TP, FN, FN, TP)
detach(MRI)

data(MK2016)
attach(MK2016)
p=c(0.898745016, 0.766105342, 0.059168715, 0.109217888)
g=c(0.090270947, 0.079469009, 0.367463579, 0.154976269)
taus=c(0.82050793, -0.51867629, 0.26457961)
SROC.beta(c[p[1:2],g[1:2],taus[1]],
dcln180, qcondcln180, tau2par.cln180,
TP, FN, FN, TP, points=TRUE, curves=TRUE, NEN)
detach(MK2016)
```
Mapping of Kendall's tau and copula parameter

Description

Bivariate copulas: mapping of Kendall's tau and copula parameter.

Usage

tau2par.bvn(tau)
tau2par.frk(tau)
tau2par.cln(tau)
tau2par.cln90(tau)
tau2par.cln180(tau)
tau2par.cln270(tau)

Arguments

tau Kendall's tau for the copula

Details

For abbreviations of names of copula families (after the dot in function names), see dcop help page.

Value

copula parameter

References


See Also

dcop
**telomerasetelomerase data**

**Description**

In Glas et al. (2003) the telomerase marker for the diagnosis of bladder cancer is evaluated using 10 studies. The interest was to define if this non-invasive and cheap marker could replace the standard of cystoscopy or histopathology.

**Usage**

```r
data(telomerase)
```

**Format**

A data frame with 10 observations on the following 4 variables.

- **TP** the number of true positives
- **FN** the number of false negatives
- **FP** the number of false positives
- **TN** the number of true negatives

**References**


---

**vine.vuong**

**Vuong’s test for the comparison of non-nested vine copula mixed models for diagnostic test accuracy studies**

**Description**

Vuong (1989)’s test for the comparison of non-nested vine copula mixed models for diagnostic test accuracy studies. It shows if a vine copula mixed model provides better fit than the standard GLMM. We compute the Vuong’s test with Model 1 being the vine copula mixed model with BVN copula and normal margins, i.e., the standard GLMM.
Arguments

qcondcop12  function for the inverse of conditional copula cdf at the (1,2) bivariate margin for Model 2
qcondcop13  function for the inverse of conditional copula cdf at the (1,3) bivariate margin for Model 2
qcondcop23  function for the inverse of conditional copula cdf at the (2,3|1) bivariate margin for Model 2
tau2par12   function for mapping Kendall’s tau at the (1,2) bivariate margin to copula parameter for Model 2
tau2par13   function for mapping Kendall’s tau at the (1,3) bivariate margin to copula parameter for Model 2
tau2par23   function for mapping Kendall’s tau at the (2,3|1) bivariate margin to the conditional copula parameter for Model 2
param1      parameters for the Model 1. i.e., the GLMM
param2      parameters for the Model 2
TP          the number of true positives
FN          the number of false negatives
FP          the number of false positives
TN          the number of true negatives
perm        a scalar indicating the selected permutation of indices:
            1: Pilot variable is the number of TP. The bivariate margins are 12, 13, 23|1;
            2: Pilot variable is the number of TN. The bivariate margins are 23, 12, 13|2;
            3: Pilot variable is the TP+FN. The bivariate margins are 13, 23, 12|3;
            1:TP, 2:TN, 3:TP+FN
gl          a list containing the components of Gauss-Legendre nodes gl$nodes and weights gl$weights
mgrid       a list containing three-dimensional arrays. For more details see meshgrid
NEP         the number of non-evaluable positives in the presence of non-evaluable subjects
NEN         the number of non-evaluable negatives in the presence of non-evaluable subjects
Value

A list containing the following components:

- `z` the test statistic
- `p-value` the p-value

References


See Also

CopulaREMADA

Examples

```r
nq=15
gl=gauss.quad.prob(nq,"uniform")
mgrid=meshgrid(gl$n,gl$n,gl$n,nargout=3)

data(betadg)
attach(betadg)
#nest.n2=VineCopulaREMADA.norm(TP,FN,FP,TN,2,gl,mgrid,
#qcondbvn,qcondbvn,qcondbvn,
#tau2par.bvn,tau2par.bvn,tau2par.bvn)

nest.n2.est= #nest.n2$e

c(0.87186926, 0.13696066, 0.70614956, 0.69152133,
0.51780203, 0.70883558, -0.41354870, 0.07701287, -0.12111253)

c090est.b2=VineCopulaREMADA.beta(TP,FN,FP,TN,2,gl,mgrid,
#qcondc1n90,qcondc1n,qcondc1n90,tau2par.cln90,tau2par.cln,tau2par.cln90)
c090est.b2.est= #c090est.b2$e

c(0.85528463, 0.14667571, 0.68321231, 0.04897466,
0.02776290, 0.08561436, -0.34639172, 0.04621924, -0.21627977)
c090vuong.b2=vine.vuong.beta(qcondc1n90,qcondc1n,qcondc1n90,
tau2par.cln90,tau2par.cln,tau2par.cln90,
nest.n2.est,c090est.b2.est,TP,FN,FP,TN,2,gl,mgrid)
c090vuong.b2
detach(betadg)
```
Maximum likelihood estimation for (truncated) vine copula mixed models for diagnostic test accuracy studies accounting for disease prevalence and non-evaluable outcomes

Description

The estimated parameters can be obtained by using a quasi-Newton method applied to the logarithm of the joint likelihood. This numerical method requires only the objective function, i.e., the logarithm of the joint likelihood, while the gradients are computed numerically and the Hessian matrix of the second order derivatives is updated in each iteration. The standard errors (SE) of the ML estimates can be also obtained via the gradients and the Hessian computed numerically during the maximization process.

Usage

\[
\begin{align*}
\text{VineCopulaREMADA} & .\text{norm}(\text{TP}, \text{FN}, \text{FP}, \text{TN}, \text{perm}, \text{gl}, \text{mgrid}, \text{qcondcop12}, \text{qcondcop13}, \text{qcondcop23}, \text{tau2par12}, \text{tau2par13}, \text{tau2par23}, \text{NEP}, \text{NEN}) \\
\text{VineCopulaREMADA} & .\text{beta}(\text{TP}, \text{FN}, \text{FP}, \text{TN}, \text{perm}, \text{gl}, \text{mgrid}, \text{qcondcop12}, \text{qcondcop13}, \text{qcondcop23}, \text{tau2par12}, \text{tau2par13}, \text{tau2par23}, \text{NEP}, \text{NEN}) \\
\text{tVineCopulaREMADA} & .\text{norm}(\text{TP}, \text{FN}, \text{FP}, \text{TN}, \text{perm}, \text{gl}, \text{mgrid}, \text{qcondcop12}, \text{qcondcop13}, \text{tau2par12}, \text{tau2par13}, \text{NEP}, \text{NEN}) \\
\text{tVineCopulaREMADA} & .\text{beta}(\text{TP}, \text{FN}, \text{FP}, \text{TN}, \text{perm}, \text{gl}, \text{mgrid}, \text{qcondcop12}, \text{qcondcop13}, \text{tau2par12}, \text{tau2par13}, \text{NEP}, \text{NEN})
\end{align*}
\]

Arguments

- **TP**: the number of true positives
- **FN**: the number of false negatives
- **FP**: the number of false positives
- **TN**: the number of true negatives
- **perm**: a scalar indicating the selected permutation of indices:
  1: Pilot variable is the number of TP. The bivariate margins are 12, 13, 23|1;
  2: Pilot variable is the number of TN. The bivariate margins are 23, 12, 13|2;
  3: Pilot variable is the TP+FN. The bivariate margins are 13, 23, 12|3;
  1:TP, 2:TN, 3:TP+FN
gl

A list containing the following components:

- `minimum`: the value of the estimated minimum of the negative log-likelihood
- `estimate`: the MLE
- `gradient`: the gradient at the estimated minimum of the negative log-likelihood
- `hessian`: the hessian at the estimated minimum of the negative log-likelihood
- `code`: an integer indicating why the optimization process terminated
- `iterations`: the number of iterations performed

For more details see `nlm`

References


See Also

`rVineCopulaREMADA`
vuong

Examples

```
mq=15
gl=gauss.quad.prob(nq, "uniform")
mgrid=meshgrid(gl$n, gl$n, gl$n, nargout=3)

data(OGT)
attach(OGT)
# out=tVineCopulaREMADA.norm(TP, FN, FP, TN, 1, gl, mgrid,
# qcondbvn, qcondbvn, tau2par.bvn, tau2par.bvn)
detach(OGT)

# In the presence of non-evaluable results #
data(coronary)
attach(coronary)
# out=tVineCopulaREMADA.norm(TP, FN, FP, TN, 2, gl, mgrid,
# qcondbvn, qcondbvn, tau2par.bvn, tau2par.bvn, NEP, NEN)
detach(coronary)
```

vuong

Vuong’s test for the comparison of non-nested copula mixed models for diagnostic test accuracy studies

Description

Vuong (1989)’s test for the comparison of non-nested copula mixed models for diagnostic test accuracy studies. It shows if a copula mixed model provides better fit than the standard GLMM. We compute the Vuong’s test with Model 1 being the copula mixed model with BVN copula and normal margins, i.e., the standard GLMM.

Usage

```
vuong.norm(qcond, tau2par, param1, param2, TP, FN, FP, TN, gl, mgrid)
vyuong.beta(qcond, tau2par, param1, param2, TP, FN, FP, TN, gl, mgrid)
countermonotonicity.vuong(param1, param2, TP, FN, FP, TN, gl, mgrid)
```

Arguments

- `qcond`: function for conditional copula cdf for Model 2
- `tau2par`: function for mapping Kendall’s tau to copula parameter for Model 2
- `param1`: parameters for the Model 1, i.e., the GLMM
- `param2`: parameters for the Model 2
- `TP`: the number of true positives
- `FN`: the number of false negatives
- `FP`: the number of false positives
- `TN`: the number of true negatives
gl a list containing the components of Gauss-Legendre nodes gl$nodes and weights gl$weights

mgrid a list containing two matrices with the rows of the output matrix X are copies of the vector gl$nodes; columns of the output matrix Y are copies of the vector gl$nodes. For more details see meshgrid

Value

A list containing the following components:

- z the test statistic
- p-value the p-value

References


See Also

CopulaREMADA

Examples

nq=15
  gl=gauss.quad.prob(nq,"uniform")
  mgrid<- meshgrid(gl$n,gl$n)

  data(MRI)
  attach(MRI)
  c270est.b=CopulaREMADA.beta(TP,FP,TN,gl,mgrid,qcondcln270,tau2par.cln270)
  nest.n=CopulaREMADA.norm(TP,FP,TN,gl,mgrid,qcondbnv,tau2par.bvn)
  c90est.n=CopulaREMADA.norm(TP,FP,TN,gl,mgrid,qcondcln90,tau2par.cln90)
  vuong.beta(qcondcln270,tau2par.cln270,nest.n$e,c270est.b$e,TP,FP,TN,gl,mgrid)
  vuong.norm(qcondcln90,tau2par.cln90,nest.n$e,c90est.n$e,TP,FP,TN,gl,mgrid)

  detach(MRI)

  data(CT)
  attach(CT)
  est.n=countermonotonicCopulaREMADA.norm(TP,FP,TN,gl,mgrid)
  est.b=countermonotonicCopulaREMADA.beta(TP,FP,TN,gl,mgrid)
  countermonotonicity.vuong(est.n$e,est.b$e,TP,FP,TN,gl,mgrid)
  detach(CT)
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