

Package ‘CopulaREMADA’

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

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Description The bivariate copula mixed model for meta-analysis of diagnostic test accuracy studies in Nikoloulopoulos (2015) <doi:10.1002/sim.6595>. The vine copula mixed model for meta-analysis of diagnostic test accuracy studies accounting for disease prevalence in Nikoloulopoulos (2017) <doi:10.1177/0962280215596769> and also accounting for non-evaluable subjects in Nikoloulopoulos (2020) <doi:10.1515/ijb-2019-0107>. The hybrid vine copula mixed model for meta-analysis of diagnostic test accuracy case-control and cohort studies in Nikoloulopoulos (2018) <doi:10.1177/0962280216682376>. The D-vine copula mixed model for meta-analysis and comparison of two diagnostic tests in Nikoloulopoulos (2019) <doi:10.1177/0962280218796685>. The multinomial quadrivariate D-vine copula mixed model for meta-analysis of diagnostic tests with non-evaluable subjects in Nikoloulopoulos (2020) <doi:10.1177/0962280220913898>. The one-factor copula mixed model for joint meta-analysis of multiple diagnostic tests (2022) <doi:10.1111/rssa.12838>.

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

Description

Fits copula mixed models for multivariate meta-analysis of diagnostic test accuracy studies proposed in Nikoloulopoulos (2015, 2017, 2018a, 2018b, 2019, 2020a, 2020b, 2022).

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, 2020a);
- The hybrid vine copula mixed model for meta-analysis of diagnostic test accuracy case-control and cohort studies (Nikoloulopoulos, 2018b);
- The D-vine copula mixed model for meta-analysis and comparison of two diagnostic tests (Nikoloulopoulos, 2019).
- The multinomial quadrivariate D-vine copula mixed model for diagnostic studies meta-analysis accounting for non-evaluable subjects (Nikoloulopoulos, 2020b).
- The one-factor copula mixed model for joint meta-analysis of multiple diagnostic tests (Nikoloulopoulos, 2022).

Author(s)

Aristidis K. Nikoloulopoulos.

References

- Nikoloulopoulos, A.K. (2015) A mixed effect model for bivariate meta-analysis of diagnostic test accuracy studies using a copula representation of the random effects distribution. *Statistics in Medicine*, **34**, 3842–3865. doi: [10.1002/sim.6595](https://doi.org/10.1002/sim.6595).
- Nikoloulopoulos, A.K. (2017) A vine copula mixed effect model for trivariate meta-analysis of diagnostic test accuracy studies accounting for disease prevalence. *Statistical Methods in Medical Research*, **26**, 2270–2286. doi: [10.1177/0962280215596769](https://doi.org/10.1177/0962280215596769).
- Nikoloulopoulos, A.K. (2018a) On composite likelihood in bivariate meta-analysis of diagnostic test accuracy studies. *AStA Advances in Statistical Analysis*, **102**, 211–227. doi: [10.1007/s10182-0170299y](https://doi.org/10.1007/s10182-0170299y).
- Nikoloulopoulos, A.K. (2018b) Hybrid copula mixed models for combining case-control and cohort studies in meta-analysis of diagnostic tests. *Statistical Methods in Medical Research*, **27**, 2540–2553. doi: [10.1177/0962280216682376](https://doi.org/10.1177/0962280216682376).
- Nikoloulopoulos, A.K. (2019) A D-vine copula mixed model for joint meta-analysis and comparison of diagnostic tests. *Statistical Methods in Medical Research*, 28(10-11):3286–3300. doi: [10.1177/0962280218796685](https://doi.org/10.1177/0962280218796685).
- Nikoloulopoulos, A.K. (2020a) An extended trivariate vine copula mixed model for meta-analysis of diagnostic studies in the presence of non-evaluable outcomes. *The International Journal of Biostatistics*, 16(2). doi: [10.1515/ijb20190107](https://doi.org/10.1515/ijb20190107).
- Nikoloulopoulos, A.K. (2020b) A multinomial quadrivariate D-vine copula mixed model for diagnostic studies meta-analysis in the presence of non-evaluable subjects. *Statistical Methods in Medical Research*, 29 (10), 2988–3005. doi: [10.1177/0962280220913898](https://doi.org/10.1177/0962280220913898).
- Nikoloulopoulos, A.K. (2022) An one-factor copula mixed model for joint meta-analysis of multiple diagnostic tests. *Journal of the Royal Statistical Society: Series A (Statistics in Society)*, 185 (3), 1398–1423. doi: [10.1111/rssa.12838](https://doi.org/10.1111/rssa.12838).

 arthritis

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

Nishimura, K., Sugiyama, D., Kogata, Y., et al. (2007) Meta-analysis: Diagnostic accuracy of anti-cyclic citrullinated peptide antibody and rheumatoid factor for rheumatoid arthritis. *Annals of Internal Medicine*, **146**(11), 797–808.

Dimou, N.L., Adam, M. and Bagos, P.G. (2016) A multivariate method for meta-analysis and comparison of diagnostic tests. *Statistics in Medicine*, **35**(20), 3509–3523.

 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

Karageorgopoulos, D.E., Vouloumanou, E.K., Ntziora, F., et al. (2011) *beta*-D-Glucan assay for the diagnosis of invasive fungal infections: a meta-analysis. *Clinical Infectious Diseases*, **52**(6), 750–770.

CopulaREMADA

Maximum likelihood estimation for copula mixed models for diagnostic test accuracy studies

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

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 <code>gl\$nodes</code> and weights <code>gl\$weights</code>
mgrid	a list containing two matrices with the rows of the output matrix <code>x</code> are copies of the vector <code>gl\$nodes</code> ; columns of the output matrix <code>y</code> are copies of the vector <code>gl\$nodes</code> . For more details see also meshgrid
qcond	function for the inverse of conditional copula cdf
tau2par	function for mapping Kendall's tau 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 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

Nikoloulopoulos, A.K. (2015) A mixed effect model for bivariate meta-analysis of diagnostic test accuracy studies using a copula representation of the random effects distribution. *Statistics in Medicine*, **34**, 3842–3865. doi: [10.1002/sim.6595](https://doi.org/10.1002/sim.6595).

See Also

[rCopulaREMADA](#)

Examples

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

data(LAG)
attach(LAG)
c270est.b=CopulaREMADA.beta(TP, FN, FP, TN, gl, mgrid, qcondc1n270, tau2par.c1n270)
detach(LAG)
```

```
data(MRI)
attach(MRI)
c270est.n=CopulaREMADA.norm(TP, FN, FP, TN, gl, mgrid, qcondln270, 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)
```

coronary

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

Schuetz, G. M., Schlattmann, P., and Dewey, M. (2012). Use of 3x2 tables with an intention to diagnose approach to assess clinical performance of diagnostic tests: Meta-analytical evaluation of coronary CT angiography studies. *BMJ* (Online), **345**:e6717.

CT

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

Scheidler, J., H. Hricak, K. K. Yu, L. Subak, and M. R. Segal. (1997) Radiological evaluation of lymph node metastases in patients with cervical cancer: A meta-analysis. *Journal of the American Medical Association*, **278**, 1096–1101.

cvinesim

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 [dcop](#) for the abbreviations of the copula names.

Value

Nx3 matrix with values in (0,1)

References

Joe H (2011) Dependence comparisons of vine copulae with four or more variables. In: Kurowicka D, Joe H, editors. *Dependence Modeling: Handbook on Vine Copulae*. Singapore: World Scientific; 2011. p. 139–164

Joe H (2014) *Dependence Modeling with Copulas*. Chapman & Hall/CRC.

Joe H (2014) *CopulaModel: Dependence Modeling with Copulas*. Software for book: *Dependence Modeling with Copulas*, Chapman & Hall/CRC, 2014.

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)
dc1n(u, v, cpar)
dc1n90(u, v, cpar)
dc1n270(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

Value

pdf value(s).

References

Joe H (1997) *Multivariate Models and Dependence Concepts*. Chapman & Hall

Joe H (2014) *Dependence Modeling with Copulas*. Chapman & Hall/CRC.

Joe H (2014) *CopulaModel: Dependence Modeling with Copulas*. Software for book: *Dependence Modeling with Copulas*, Chapman & Hall/CRC, 2014.

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

- Joe H (2011) Dependence comparisons of vine copulae with four or more variables. In: Kurowicka D, Joe H, editors. *Dependence Modeling: Handbook on Vine Copulae*. Singapore: World Scientific; 2011. p. 139–164
- Joe H (2014) *Dependence Modeling with Copulas*. Chapman & Hall/CRC.
- Joe H (2014) *CopulaModel: Dependence Modeling with Copulas*. Software for book: *Dependence Modeling with Copulas*, Chapman & Hall/CRC, 2014.
- Nikoloulopoulos, A.K. (2018) A D-vine copula mixed model for joint meta-analysis and comparison of diagnostic tests. *Statistical Methods in Medical Research*, in press. doi: [10.1177/0962280218796685](https://doi.org/10.1177/0962280218796685).
- Nikoloulopoulos, A.K. (2018) A multinomial quadrivariate D-vine copula mixed model for diagnostic studies meta-analysis accounting for non-evaluable subjects. *ArXiv e-prints*, arXiv:1812.05915. <https://arxiv.org/abs/1812.05915>.

See Also

[qcondcop](#) [dcop](#) [rcop](#)

FactorCopulaREMADA	<i>Maximum likelihood estimation of 1-factor copula mixed models for joint meta-analysis of T diagnostic tests</i>
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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

```
FactorCopulaREMADA.norm(TP, FN, FP, TN, gl, mgrid, qcond1, tau2par1, qcond2, tau2par2)
```

```
FactorCopulaREMADA.beta(TP, FN, FP, TN, gl, mgrid, qcond1, tau2par1, qcond2, tau2par2)
```

Arguments

- | | |
|----|--|
| TP | an $n \times T$ matrix where n is the number of studies. Column j has the number of true positives for test j for $j = 1 \dots T$ |
| FN | an $n \times T$ matrix where n is the number of studies. Column j has the number of false negatives Column j has the number of true positives for test j for $j = 1 \dots T$ |

FP	an $n \times T$ matrix where n is the number of studies. Column j has the number of false positives Column j has the number of true positives for test j for $j = 1 \dots T$
TN	an $n \times T$ matrix where n is the number of studies. Column j has the number of true negatives Column j has the number of true positives for test j for $j = 1 \dots T$
gl	a list containing the components of Gauss-Legendre nodes <code>gl\$nodes</code> and weights <code>gl\$weights</code>
mgrid	a list containing two matrices with the rows of the output matrix <code>x</code> are copies of the vector <code>gl\$nodes</code> ; columns of the output matrix <code>y</code> are copies of the vector <code>gl\$nodes</code> . For more details see also meshgrid
qcond1	function for the inverse conditional copula cdfs that link the factor with the latent sensitivities
tau2par1	function for mapping Kendall's tau to copula parameter at the copulas that link the factor with the latent sensitivities
qcond2	function for the inverse conditional copula cdfs that link the factor with the latent specificities
tau2par2	function for mapping Kendall's tau to copula parameter at the copulas that link the factor with the latent specificities

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 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

Nikoloulopoulos, A.K. (2022) An one-factor copula mixed model for joint meta-analysis of multiple diagnostic tests. *Journal of the Royal Statistical Society: Series A (Statistics in Society)*, 185 (3), 1398–1423. doi: [10.1111/rssa.12838](https://doi.org/10.1111/rssa.12838).

Examples

```
data(arthritis)
attach(arthritis)
TP=cbind(TP1,TP2)
TN=cbind(TN1,TN2)
```

```

FP=cbind(FP1,FP2)
FN=cbind(FN1,FN2)

nq=25
gl=gauss.quad.prob(nq,"uniform")
mgrid=meshgrid(gl$n,gl$n)
qcond1=qcondc1n
qcond2=qcondc1n270
tau2par1=tau2par.c1n
tau2par2=tau2par.c1n270

out=FactorCopulaREMADA.norm(TP,FN,FP,TN,gl,mgrid,qcond1,tau2par1,qcond2,tau2par2)
se=sqrt(diag(solve(out$hessian)))

detach(arthritis)

```

hybridCopulaREMADA	<i>Maximum likelihood estimation for hybrid copula mixed models for combining case-control and cohort studies in meta-analysis of diagnostic tests</i>
--------------------	--

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

```

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

gl	a list containing the components of Gauss-Legendre nodes <code>gl\$nodes</code> and weights <code>gl\$weights</code>
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 <code>x</code> are copies of the vector <code>gl\$nodes</code> ; columns of the output matrix <code>y</code> are copies of the vector <code>gl\$nodes</code> . 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 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

Nikoloulopoulos, A.K. (2018) Hybrid copula mixed models for combining case-control and cohort studies in meta-analysis of diagnostic tests. *Statistical Methods in Medical Research*, **27**, 2540–2553. doi: [10.1177/0962280216682376](https://doi.org/10.1177/0962280216682376).

See Also

[VineCopulaREMADA](#), [CopulaREMADA](#)

Examples

```

# simulate the data from N=25 cohort studies
N=25
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=qcondc1n90
tau2par12=tau2par23=tau2par13=tau2par.c1n90
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=0.5
p=p[-3]
g=g[-3]
simdat2=rCopulaREMADA.beta(N,p,g,tau,rcln,tau2par.c1n)
# 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)

qcond=qcondc1n
tau2par=tau2par.c1n
est=hybridCopulaREMADA.beta(TP,FN,FP,TN,type,gl,mgrid1,mgrid2,
qcondcop12,qcondcop13,tau2par12,tau2par13,qcond,tau2par)

```

LAG

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

Scheidler, J., H. Hricak, K. K. Yu, L. Subak, and M. R. Segal. (1997) Radiological evaluation of lymph node metastases in patients with cervical cancer: A meta-analysis. *Journal of the American Medical Association*, **278**, 1096–1101.

mgrid

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)
```

MK2016

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

Menke, J. and Kowalski, J. (2016). Diagnostic accuracy and utility of coronary ct angiography with consideration of unevaluable results: A systematic review and multivariate bayesian random-effects meta-analysis with intention to diagnose. *European Radiology*, **26**(2):451–458.

MRI

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)

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 <code>gl\$nodes</code> and weights <code>gl\$weights</code>
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 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

Nikoloulopoulos, A.K. (2020) A multinomial quadrivariate D-vine copula mixed model for diagnostic studies meta-analysis in the presence of non-evaluable subjects. *Statistical Methods in Medical Research*, 29 (10), 2988–3005. doi: [10.1177/0962280220913898](https://doi.org/10.1177/0962280220913898).

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, qcondc1n180, pcondc1n180, tau2par.c1n180,
qcondc1n90, pcondc1n90, tau2par.c1n90)

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

Ye, Y., Xie, H., Zhao, X., Zhang, S. (2012) The oral glucose tolerance test for the diagnosis of diabetes mellitus in patients during acute coronary syndrome hospitalization: a meta-analysis of diagnostic test accuracy. *Cardiovascular Diabetology*, **11**(5):155.

pcondcop

Bivariate copula conditional distribution functions

Description

Bivariate copula conditional distribution functions

Usage

```
pcondbvn(v, u, cpar)
pcondfrk(v, u, cpar)
pcondcln(v, u, cpar)
pcondcln90(v, u, cpar)
pcondcln270(v, u, cpar)
```

Arguments

v	conditioning value in interval 0,1; could be a vector
u	value 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

Joe H (1997) *Multivariate Models and Dependence Concepts*. Chapman & Hall

Joe H (2014) *Dependence Modeling with Copulas*. Chapman & Hall/CRC.

Joe H (2014) *CopulaModel: Dependence Modeling with Copulas*. Software for book: *Dependence Modeling with Copulas*, Chapman & Hall/CRC, 2014.

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)
qcondcln270(p, u, cpar)
```

Arguments

<code>u</code>	conditioning value in interval 0,1; could be a vector
<code>p</code>	quantile in interval 0,1; could be a vector
<code>cpar</code>	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

Joe H (1997) *Multivariate Models and Dependence Concepts*. Chapman & Hall

Joe H (2014) *Dependence Modeling with Copulas*. Chapman & Hall/CRC.

Joe H (2014) *CopulaModel: Dependence Modeling with Copulas*. Software for book: *Dependence Modeling with Copulas*, Chapman & Hall/CRC, 2014.

See Also

[dcop](#) [rcop](#)

quadVineCopulaREMADA *Maximum likelihood estimation of 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 <code>gl\$nodes</code> and weights <code>gl\$weights</code>
mgrid	a list containing 4-dimensional arrays.
qcond1	function for the inverse conditional copula cdf at the (1,2) bivariate margin
pcond1	function for the conditional copula cdf at the (1,2) bivariate margin
tau2par1	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

Nikoloulopoulos, A.K. (2019) A D-vine copula mixed model for joint meta-analysis and comparison of diagnostic tests. *Statistical Methods in Medical Research*, 28(10-11):3286–3300. doi: [10.1177/0962280218796685](https://doi.org/10.1177/0962280218796685).

Examples

```
nq=15
gl=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,
gl, mgrid15, qcond1, pcond1, tau2par1, qcond2, pcond2, tau2par2)

detach(arthritis)
```

`rcop`*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)
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

Joe H (1997) *Multivariate Models and Dependence Concepts*. Chapman & Hall

Joe H (2014) *Dependence Modeling with Copulas*. Chapman & Hall/CRC.

Joe H (2014) *CopulaModel: Dependence Modeling with Copulas*. Software for book: *Dependence Modeling with Copulas*, Chapman & Hall/CRC, 2014.

See Also

[qcondcop](#) [dcop](#)

rCopulaREMADA	<i>Simulation from copula mixed models for diagnostic test accuracy studies</i>
---------------	---

Description

To simulate the data we have used the following steps:

1. Simulate the study size n from a shifted gamma distribution with parameters $\alpha = 1.2, \beta = 0.01, lag = 30$ 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 (π_1, π_2) of sensitivity/specificity
si	Pair (σ_1, σ_2) of variability; normal margins
g	Pair (γ_1, γ_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

Nikoloulopoulos, A.K. (2015) A mixed effect model for bivariate meta-analysis of diagnostic test accuracy studies using a copula representation of the random effects distribution. *Statistics in Medicine*, **34**, 3842–3865. doi: [10.1002/sim.6595](https://doi.org/10.1002/sim.6595).

See Also

[CopulaREMADA rcop](#)

Examples

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

N=20
tau=-0.5
p=c(0.7,0.9)
g=c(0.2,0.1)
simDat=rCopulaREMADA.beta(N,p,g,tau,rcln270,tau2par.cln270)
TP=simDat$TP
TN=simDat$TN
FP=simDat$FP
FN=simDat$FN
c270est.b=CopulaREMADA.beta(TP,FN,FP,TN,gl,mgrid,qcondcln270,tau2par.cln270)

si=c(2,1)
tau=0.5
simDat=rCopulaREMADA.norm(N,p,si,tau,rcln,tau2par.cln)
TP=simDat$TP
TN=simDat$TN
FP=simDat$FP
FN=simDat$FN
cest.n=CopulaREMADA.norm(TP,FN,FP,TN,gl,mgrid,qcondcln,tau2par.cln)
```

rFactorCopulaREMADA *Simulation from 1-factor copula mixed models for joint meta-analysis of T diagnostic tests*

Description

Simulation from 1-factor copula mixed models for joint meta-analysis of T diagnostic tests

Usage

```
rFactorCopulaREMADA.norm(N,p,si,taus,qcond1,tau2par1,qcond2,tau2par2)
rFactorCopulaREMADA.beta(N,p,g,taus,qcond1,tau2par1,qcond2,tau2par2)
```

Arguments

N	number of studies
p	vector of sensitivities and specificities
si	vector of variabilities; normal margins
g	vector of variabilities; beta margins

taus	Kendall's tau values
qcond1	function for the inverse conditional copula cdfs that link the factor with the latent sensitivities
tau2par1	function for mapping Kendall's tau to copula parameter at the copulas that link the factor with the latent sensitivities
qcond2	function for the inverse conditional copula cdfs that link the factor with the latent specificities
tau2par2	function for mapping Kendall's tau to copula parameter at the copulas that link the factor with the latent specificities

Value

A list with the simulated data in matrices with T 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

References

Nikoloulopoulos, A.K. (2022) An one-factor copula mixed model for joint meta-analysis of multiple diagnostic tests. *Journal of the Royal Statistical Society: Series A (Statistics in Society)*, 185 (3), 1398–1423. doi: [10.1111/rssa.12838](https://doi.org/10.1111/rssa.12838).

Examples

```
N=50
```

```
qcond1=qcondc1n
tau2par1=tau2par.c1n
qcond2=qcondc1n270
tau2par2=tau2par.c1n270
```

```
p=c(0.8,0.7,0.8,0.7,0.8,0.7)
mu=log(p/(1-p))
si=rep(1,6)
taus=c(0.6,0.7,0.5,-0.3,-0.4,-0.2)
```

```
out=rFactorCopulaREMADA.norm(N,p,si,taus,qcond1,tau2par1,qcond2,tau2par2)
```

```
TP=out$TP
FN=out$FN
TN=out$TN
FP=out$FP
```

rmultinomVineCopulaREMADA

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

Description

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

Usage

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

Arguments

N	sample size
p	Vector (π_1, π_2, π_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

Nikoloulopoulos, A.K. (2020) A multinomial quadrivariate D-vine copula mixed model for diagnostic studies meta-analysis in the presence of non-evaluable subjects. *Statistical Methods in Medical Research*, 29 (10), 2988–3005. doi: [10.1177/0962280220913898](https://doi.org/10.1177/0962280220913898).

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( 0.82050793,-0.51867629,0.26457961)

qcond1=qcondc1n180
pcond1=pcondc1n180
tau2par1=tau2par.c1n180

qcond2=qcondc1n90
pcond2=pcondc1n90
tau2par2=tau2par.c1n90

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

TP=out[,1]
NEP=out[,2]
FN=out[,3]
TN=out[,4]
NEN=out[,5]
FP=out[,6]
```

rVineCopulaREMADA	<i>Simulation from trivariate vine copula mixed models for diagnostic test accuracy studies accounting for disease prevalence and non-evaluable results</i>
-------------------	---

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 (π_1, π_2, π_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

Simuated 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

Nikoloulopoulos, A.K. (2017) A vine copula mixed effect model for trivariate meta-analysis of diagnostic test accuracy studies accounting for disease prevalence. *Statistical Methods in Medical Research*, **26**, 2270–2286. doi: [10.1177/0962280215596769](https://doi.org/10.1177/0962280215596769).

Nikoloulopoulos, A.K. (2018) A vine copula mixed model for trivariate meta-analysis of diagnostic studies accounting for disease prevalence and non-evaluable subjects. *ArXiv e-prints*, arXiv:1812.03685. <https://arxiv.org/abs/1812.03685>.

See Also

[rCopulaREMADA rcop cvinesim](#)

Examples

```
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.cln90
# 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 <code>SROC.norm</code> and <code>SROC.beta</code>)
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

Nikoloulopoulos, A.K. (2015) A mixed effect model for bivariate meta-analysis of diagnostic test accuracy studies using a copula representation of the random effects distribution. *Statistics in Medicine*, **34**, 3842–3865. doi: [10.1002/sim.6595](https://doi.org/10.1002/sim.6595).

See Also

[CopulaREMADA](#) [rCopulaREMADA](#)

Examples

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

data(telomerase)
attach(telomerase)
est.n=countermonotonicCopulaREMADA.norm(TP, FN, FP, TN, gl, mgrid)
est.b=countermonotonicCopulaREMADA.beta(TP, FN, FP, TN, gl, mgrid)
SROC(est.b$e, est.n$e, TP, FN, FP, TN)
detach(telomerase)
```

```

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

data(MRI)
attach(MRI)
c270est.n=CopulaREMADA.norm(TP, FN, FP, TN, gl, mgrid, qcondcln270, tau2par.cln270)
SROC.norm(c270est.n$e, dcln270, qcondcln270, tau2par.cln270, TP, FN, FP, TN)
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, FP, TN, points=TRUE, curves=TRUE, NEP, NEN)
detach(MK2016)

```

tau2par

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

Joe H (1997) *Multivariate Models and Dependence Concepts*. Chapman & Hall

Joe H (2014) *Dependence Modeling with Copulas*. Chapman & Hall/CRC.

Joe H (2014) *CopulaModel: Dependence Modeling with Copulas*. Software for book: *Dependence Modeling with Copulas*, Chapman & Hall/CRC, 2014.

See Also

[dcop](#)

telomerase

The telomerase 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

```
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

Glas A.S., Roos D., Deutekom M., Zwinderman A.H., Bossuyt P.M., Kurth K.H. (2003) Tumor markers in the diagnosis of primary bladder cancer. A systematic review. *Journal of Urology*, **169**(6), 1975–82.

vine.vuong	<i>Vuong's test for the comparison of non-nested vine copula mixed models for diagnostic test accuracy studies</i>
------------	--

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.

Usage

```
vine.vuong.beta(qcondcop12,qcondcop13,qcondcop23,
tau2par12,tau2par13,tau2par23,param1,param2,TP,FN,FP,TN,gl,mgrid,NEP,NEN)
vine.vuong.norm(qcondcop12,qcondcop13,qcondcop23,
tau2par12,tau2par13,tau2par23,param1,param2,TP,FN,FP,TN,gl,mgrid,NEP,NEN)
tvine.vuong.beta(qcondcop12,qcondcop13,
tau2par12,tau2par13,param1,param2,TP,FN,FP,TN,gl,mgrid,NEP,NEN)
tvine.vuong.norm(qcondcop12,qcondcop13,
tau2par12,tau2par13,param1,param2,TP,FN,FP,TN,gl,mgrid,NEP,NEN)
tvine2.vuong.beta(qcondcop12,qcondcop13,
tau2par12,tau2par13,param1,param2,TP,FN,FP,TN,gl,mgrid,NEP,NEN)
tvine2.vuong.norm(qcondcop12,qcondcop13,
tau2par12,tau2par13,param1,param2,TP,FN,FP,TN,gl,mgrid,NEP,NEN)
```

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
gl	a list containing the components of Gauss-Legendre nodes <code>gl\$nodes</code> and weights <code>gl\$weights</code>
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

Nikoloulopoulos, A.K. (2017) A vine copula mixed effect model for trivariate meta-analysis of diagnostic test accuracy studies accounting for disease prevalence. *Statistical Methods in Medical Research*, **26**, 2270–2286. doi: [10.1177/0962280215596769](https://doi.org/10.1177/0962280215596769).

Nikoloulopoulos, A.K. (2020) An extended trivariate vine copula mixed model for meta-analysis of diagnostic studies in the presence of non-evaluable outcomes. *The International Journal of Biostatistics*, **16**(2). doi: [10.1515/ijb20190107](https://doi.org/10.1515/ijb20190107).

Vuong Q.H. (1989) Likelihood ratio tests for model selection and non-nested hypotheses. *Econometrica*, **57**, 307–333.

See Also

[CopulaREMADA](#)

Examples

```
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, gl, mgrid,
#qcondbvn, qcondbvn, qcondbvn,
#tau2par.bvn, tau2par.bvn, tau2par.bvn)
nest.n2.est= #nest.n2$e
c(0.87186926, 0.13696066, 0.70614956, 0.69152133,
0.51780203, 0.70883558, -0.41354870, 0.07701287, -0.12111253)
#c090est.b2=VineCopulaREMADA.beta(TP, FN, FP, TN, gl, mgrid,
#qcondcln90, qcondcln, qcondcln90, tau2par.cln90, tau2par.cln, tau2par.cln90)
c090est.b2.est= #c090est.b2$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(qcondcln90,qcondcln,qcondcln90,
tau2par.cln90,tau2par.cln,tau2par.cln90,
nest.n2.est,c090est.b2.est,TP,FN,FP,TN,g1,mgrid)
c090vuong.b2
detach(betaDG)

```

VineCopulaREMADA	<i>Maximum likelihood estimation for (truncated) vine copula mixed models for diagnostic test accuracy studies accounting for disease prevalence and non-evaluable outcomes</i>
------------------	---

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

```

VineCopulaREMADA.norm(TP,FN,FP,TN,g1,mgrid,
                      qcondcop12,qcondcop13,qcondcop23,
                      tau2par12,tau2par13,tau2par23,
                      NEP,NEN)
VineCopulaREMADA.beta(TP,FN,FP,TN,g1,mgrid,
                      qcondcop12,qcondcop13,qcondcop23,
                      tau2par12,tau2par13,tau2par23,
                      NEP,NEN)
tVineCopulaREMADA.norm(TP,FN,FP,TN,g1,mgrid,
                      qcondcop12,qcondcop13,
                      tau2par12,tau2par13,
                      NEP,NEN)
tVineCopulaREMADA.beta(TP,FN,FP,TN,g1,mgrid,
                      qcondcop12,qcondcop13,
                      tau2par12,tau2par13,
                      NEP,NEN)

```

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

<code>gl</code>	a list containing the components of Gauss-Legendre nodes <code>gl\$nodes</code> and weights <code>gl\$weights</code>
<code>mgrid</code>	a list containing three-dimensional arrays. For more details see meshgrid
<code>qcondcop12</code>	function for the inverse of conditional copula cdf at the (1,2) bivariate margin
<code>qcondcop13</code>	function for the inverse of conditional copula cdf at the (1,3) bivariate margin
<code>qcondcop23</code>	function for the inverse of conditional copula cdf at the (2,3 1) bivariate margin
<code>tau2par12</code>	function for mapping Kendall's tau at the (1,2) bivariate margin to copula parameter
<code>tau2par13</code>	function for mapping Kendall's tau at the (1,3) bivariate margin to copula parameter
<code>tau2par23</code>	function for mapping Kendall's tau at the (2,3 1) bivariate margin to the conditional copula parameter
<code>NEP</code>	the number of non-evaluable positives in the presence of non-evaluable subjects
<code>NEN</code>	the number of non-evaluable negatives in the presence of non-evaluable subjects

Value

A list containing the following components:

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

For more details see [nlm](#)

References

Nikoloulopoulos, A.K. (2017) A vine copula mixed effect model for trivariate meta-analysis of diagnostic test accuracy studies accounting for disease prevalence. *Statistical Methods in Medical Research*, **26**, 2270–2286. doi: [10.1177/0962280215596769](https://doi.org/10.1177/0962280215596769).

Nikoloulopoulos, A.K. (2020) An extended trivariate vine copula mixed model for meta-analysis of diagnostic studies in the presence of non-evaluable outcomes. *The International Journal of Biostatistics*, **16**(2). doi: [10.1515/ijb20190107](https://doi.org/10.1515/ijb20190107).

See Also

[rVineCopulaREMADA](#)

Examples

```

nq=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, gl, mgrid,
qcondbvn, qcondbvn, tau2par.bvn, tau2par.bvn)
detach(OGT)
#####
# In the precence of non-evaluable results #
data(coronary)
attach(coronary)
out=tVineCopulaREMADA.norm(TP, FN, FP, TN, 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 accurarcy studies*

Description

Vuong (1989)'s test for the comparison of non-nested copula mixed models for diagnostic test accurarcy 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)
vuong.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 maping 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 <code>gl\$nodes</code> and weights <code>gl\$weights</code>
mgrid	a list containing two matrices with the rows of the output matrix <code>X</code> are copies of the vector <code>gl\$nodes</code> ; columns of the output matrix <code>Y</code> are copies of the vector <code>gl\$nodes</code> . For more details see meshgrid

Value

A list containing the following components:

z	the test statistic
p-value	the p -value

References

Nikoloulopoulos, A.K. (2015) A mixed effect model for bivariate meta-analysis of diagnostic test accuracy studies using a copula representation of the random effects distribution. *Statistics in Medicine*, **34**, 3842–3865. doi: [10.1002/sim.6595](https://doi.org/10.1002/sim.6595).

Vuong Q.H. (1989) Likelihood ratio tests for model selection and non-nested hypotheses. *Econometrica*, **57**:307–333.

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, FN, FP, TN, gl, mgrid, qcondc1n270, tau2par.c1n270)
nest.n=CopulaREMADA.norm(TP, FN, FP, TN, gl, mgrid, qcondbvn, tau2par.bvn)
c90est.n=CopulaREMADA.norm(TP, FN, FP, TN, gl, mgrid, qcondc1n90, tau2par.c1n90)
vuong.beta(qcondc1n270, tau2par.c1n270, nest.n, c270est.b, TP, FN, FP, TN, gl, mgrid)
vuong.norm(qcondc1n90, tau2par.c1n90, nest.n, c90est.n, TP, FN, FP, TN, gl, mgrid)
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)
countermonotonicity.vuong(est.n, est.b, TP, FN, FP, TN, gl, mgrid)
detach(CT)
```

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