# Package 'cold' 

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## Type Package <br> Title Count Longitudinal Data

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Author M. Helena Goncalves and M. Salome Cabral, apart from a set of Fortran-77 subroutines written by R. Piessens and E. de Doncker, belonging to the suite "Quadpack".
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Description Performs regression analysis for longitudinal count data, allowing for serial dependence among observations from a given individual and two dimensional random effects on the linear predictor. Estimation is via maximization of the exact likelihood of a suitably defined model. Missing values and unbalanced data are allowed. Details can be found in the accompanying scientific papers: Goncalves \& Cabral (2021, Journal of Statistical Software, [doi:10.18637/jss.v099.i03](doi:10.18637/jss.v099.i03)) and Goncalves et al. (2007, Computational Statistics \& Data Analysis, [doi:10.1016/j.csda.2007.03.002](doi:10.1016/j.csda.2007.03.002)).

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cold-package Count Longitudinal Data

## Description

Performs Poisson regression analysis for longitudinal count data, allowing for serial dependence among observations from a given individual and two random effects. Estimation is via maximization of the exact likelihood of a suitably defined model. Missing values and unbalanced data are allowed.

## Details

This package contains functions to perform the fit of parametric models via likelihood method for count longitudinal data using "S4" classes and methods as implemented in the methods package.

## Author(s)

M. Helena Gonçalves and M. Salomé Cabral

## References

Azzalini, A. (1994). Logistic regression and other discrete data models for serially correlated observations. J. Ital. Stat. Society, 3 (2), 169-179. doi: 10.1007/bf02589225.
Gonçalves, M. Helena (2002). Likelihood methods for discrete longitudinal data. PhD thesis, Faculty of Sciences, University of Lisbon.

Gonçalves, M. Helena, Cabral, M. Salomé, Ruiz de Villa, M. Carme, Escrich, Eduardo and Solanas, Montse. (2007). Likelihood approach for count data in longitudinal experiments. Computational Statistics and Data Analysis, 51, 12, 6511-6520. doi: 10.1016/j.csda.2007.03.002.
Gonçalves, M. Helena and Cabral, M. Salomé. (2021). cold: An R Package for the Analysis of Count Longitudinal Data. Journal of Statistical Software, 99, 3, 1-24. doi: 10.18637/jss.v099.i03.

See Also
cold-class, cold, Methods

## Description

Computes an analysis deviance table for two nested fitted model objects of class cold.

## Usage

\#\# S4 method for signature 'cold'
anova(object, ...)

## Arguments

object an object of class cold.
... an object of class cold.

## Warning

The comparison between two models by anova will only be valid if they are fitted to the same dataset.

## Methods

signature (object = "ANY"): Generic function.
signature(object="cold"): Anova for cold object.

## Note

It uses the naive solution of Pinheiro et al. (2000) to calculate the p-value when the difference between the models is the number of random effects.

## References

Pinheiro, J.C. and Bates, D.M. (2000). Mixed-Effects Models in S and S-PLUS. Springer-Verlag.

## Examples

```
##### data = seizure
seiz1 <- cold(y ~ lage + lbase + v4 + trt + trt:lbase, data = seizure,
start = NULL, dependence = "AR1")
seiz2 <-cold(y ~ lage + lbase + v4 + trt, data = seizure, start = NULL,
dependence = "AR1")
anova(seiz1, seiz2)
##### data = datacold
mod0 <- cold(z ~ Time * Treatment, data = datacold, time = "Time",
id = "Subject", dependence = "ind")
mod0R <- cold(z ~ Time * Treatment, random = ~ 1, data = datacold,
time = "Time", id = "Subject", dependence = "indR")
summary(mod0R)
anova(mod0, mod0R)
```

```
bolus Bolus data
```


## Description

The dataset has the number of requests per interval in 12 successive four-hourly intervals following abdominal surgery for 65 patients in a clinical trial to compare two groups (bolus/lock-out combinations).

## Usage

```
    data("bolus")
```


## Format

A data frame with 780 observations on the following 4 variables.
id identifies de number of the individual profile. This vector contains observations of 65 individual profiles.
group a factor with levels 1 mg and 2 mg .
time a numeric vector that identifies the number of the time points observed.
y a numeric vector with the number of analgesic doses taken by hospital patients in 12 successive four-hourly intervals.

## Details

The group 2 mg has 30 patients and the group 1 mg has 35 patients.

## Source

Weiss, Robert E. (2005). Modeling Longitudinal Data. Springer
https://robweiss.faculty.biostat.ucla.edu/book-data-sets

## References

Henderson, R. and Shimakura, S. (2003). A Serially Correlated Gamma Frailty Model for Longitudinal Count Data. Biometrika, vol. 90, No. 2, 355-366

## Examples

```
data(bolus)
## change the reference class
contrasts(bolus$group)
bolus$group<-relevel(factor(bolus$group), ref = "2mg")
contrasts(bolus$group)
## Weiss, Robert E. (2005) pp 353-356, compare with Table 11.2
bol0R <- cold(y ~ time + group, random = ~ 1, data = bolus,
dependence = "indR")
summary (bol0R)
## reparametrization of time
bolus$time1 <- bolus$time - 6
bol0R1 <- cold(y ~ time1 + group, random = ~ 1,data = bolus,
dependence = "indR")
summary (bol0R1)
bol1R1 <- cold(y ~ time1 + group, random = ~ 1, data = bolus,
time = "time1", dependence = "AR1R")
```

summary (bol1R1)
anova(bol0R1, bol1R1)
plot(bol1R1, which = 1, factor = group, ylab = "Bolus count")

## coeftest Extract summary statistics

## Description

Extract information from poisson regression model objects of class cold.

## Usage

coeftest (object)

## Arguments

object an object of class cold.

## Value

Extract a list of summary statistics from poisson regression model corresponding to the fixed effects coefficients.
coeftest-methods Methods for function coeftest

## Description

Extract information from poisson regression model objects of class cold.

## Usage

```
    ## S4 method for signature 'cold'
    coeftest(object)
```


## Arguments

object an object of class cold.

## Value

Extract a list of summary statistics from poisson regression model corresponding to the fixed effects coefficients.

## Methods

signature(object="cold"): list of summary statistics of fixed effects coefficients for cold object.

## Examples

```
##### data = seizure
seiz1M <- cold(y ~ lage + lbase + v4 + trt + trt:lbase, data = seizure,
start = NULL, dependence = "AR1")
coeftest(seiz1M)
```


## Description

Performs the fit of parametric models via likelihood method. Serial dependence and two random effects are allowed according to the stochastic model chosen. Missing values are automatically accounted for computing the likelihood function.

## Usage

cold(formula, random, data, id="id", time="time", subSET, dependence ="ind", start=NULL, method="BFGS", integration="QUADPACK", M="6000", control=coldControl(), integrate=coldIntegrate(), cublim=coldcublim(), trace=FALSE)

## Arguments

formula a description of the model to be fitted of the form response $\sim$ predictors.
random the predictos that includes random effects of the form response~predictors.
data a data frame containing the variables in the formula. NA values are allowed. If data is missing, an error message is produced. See "Details".
id a string that matches the name of the id variable in data, i.e., the subject identification variable. By default, the program expects a variable named id to be present in the data.frame, otherwise the name of the variable playing the role of id must be declared by assigning id here.

| time | a string that matches the name of the time variable in data. By default, the pro- <br> gram expects a variable named time to be present in the data. frame, otherwise <br> the name of the variable playing the role of time must be declared by assigning |
| :--- | :--- |
| time here. |  |
| an optional expression indicating the subset of the rows of data that should be |  |
| used in the fit. All observations are included by default. |  |
| expression stating which dependence structure should be used in the fit. The |  |
| default is "ind". According to the stochastic model chosen serial dependence |  |
| and random effects are allowed. There are six options: "ind" (independence), |  |
| "AR1" (first order autoregressive), "indR" (independence with random intercept), |  |
| dependence | "AR1R" (first order autoregressive with random intercept), "indR2" (indepen- |
| dence with two random effects) or "AR1R2" (first order autoregressive with two |  |
| random effects). |  |
| start | a vector of initial values for the nuisance parameters of the likelihood. The <br> dimension of the vector is according to the structure of the dependence model. |
| method | The method used in the optimization process: "BFGS", "CG", "L-BFGS-B" and <br> "SANN". The default is "BFGS". See optim for details. |
| integration | The integration code allows the user choose the integration method to solve <br> the integrals: "QUADPACK" (fortran routines, only for random intercept models), <br> "cubature" (uses cubature package to compute integrals when the dependence |
| structure includes one or two random effects), "MC" (uses Monte Carlo methods |  |
| to compute integrals when the dependence structure includes one or two random |  |
| effects). The default is "QUADPACK". |  |

## Details

data are contained in a data.frame. Each element of the data argument must be identifiable by a name. The simplest situation occurs when all subjects are observed at the same time points. If there are missing values in the response variable NA values must be inserted. The response variable represent the individual profiles of each subject, it is expected a variable in the data.frame that identifies the correspondence of each component of the response variable to the subject that it belongs, by default is named id variable. It is expected a variable named time to be present in the
data.frame. If the time component has been given a different name, this should be declared. The time variable should identify the time points that each individual profile has been observed.
subSET is an optional expression indicating the subset of data that should be used in the fit. This is a logical statement of the type variable $1==" a " \&$ variable $2>x$ which identifies the observations to be selected. All observations are included by default.

For the models with random intercept indR and AR1R, by default cold compute integrals based on a Fortran-77 subroutine package QUADPACK. For some data sets, when the dependence structure has a random intercept term, the user could have the need to do a specification of the integrate argument list changing the integration limits in the coldIntegrate function. The coldIntegrate is an auxiliary function for controlling cold fitting. There are more two options to fit models with a random intercept by setting integration="cubature" or integration="MC". For the models with two random effects indR2 and AR1R2, the user has two define the integration method by setting integration="cubature" or integration="MC". The second random effect is considered to be included in the time argument that plays the role of the time variable in the data.frame. For the two random effects models we have a random intercept and a random slope.

## Value

An object of class cold.

## Background

Assume that each subject of a given set has been observed at number of successive time points. For each subject and for each time point, a count response variable, and a set of covariates are recorded.
Individual random effects, $b_{0}$, can be incorporated in the form of a random intercept term of the linear predictor of the logarithmic regression, assuming a normal distribution of mean 0 and variance $\sigma^{2}$, parameterized as $\omega=\log \left(\sigma^{2}\right)$. The combination of serial Markov dependence with a random intercept corresponds here to the dependence structures indR, AR1R.
Two dimensional randoms effects can also be incorporated the linear predictor of the logarithmic regression. Consider a two-dimensional vector of random effects $b=\left(b_{0}, b_{1}\right)$ where we assumed to be a random sample from the bivariate normal distribution, $b \sim N(0, D)$ with $\operatorname{var}\left(b_{0}\right)=\sigma_{b_{0}}^{2}$, $\operatorname{var}\left(b_{1}\right)=\sigma_{b_{1}}^{2}$ and $\operatorname{cov}\left(b_{0}, b_{1}\right)=0$.
The combination of serial Markov dependence with two random effects corresponds here to the dependence structures indR2, AR1R2.
Original sources of the above formulation are given by Azzalini (1994), as for the AR1, and by Gonçalves (2002) and Gonçalves and Azzalini (2008) for the its extensions.

## Author(s)

M. Helena Gonçalves and M. Salomé Cabral

## References

Azzalini, A. (1994). Logistic regression and other discrete data models for serially correlated observations. J. Ital. Stat. Society, 3 (2), 169-179. doi: 10.1007/bf02589225.
Gonçalves, M. Helena (2002). Likelihood methods for discrete longitudinal data. PhD thesis, Faculty of Sciences, University of Lisbon.

Gonçalves, M. Helena, Cabral, M. Salomé, Ruiz de Villa, M. Carme, Escrich, Eduardo and Solanas, Montse. (2007). Likelihood approach for count data in longitudinal experiments. Computational statistics and Data Analysis, 51, 12, 6511-6520. doi: 10.1016/j.csda.2007.03.002.
Gonçalves, M. Helena and Cabral, M. Salomé. (2021). cold: An R Package for the Analysis of Count Longitudinal Data. Journal of Statistical Software, 99, 3, 1-24. doi: 10.18637/jss.v099.i03.

## See Also

cold-class, coldControl, coldIntegrate, optim

## Examples

```
##### data = seizure
str(seizure)
### AR1
seiz1M <- cold(y ~ lage + lbase + v4 + trt + trt:lbase, data = seizure,
start = NULL, dependence = "AR1")
summary(seiz1M)
getAIC(seiz1M)
getLogLik(seiz1M)
### independence
seiz0M <- cold(y ~ lage + lbase + v4 + trt + trt:lbase, data = seizure,
start = NULL, dependence = "ind")
summary(seiz0M)
getAIC(seiz0M)
getLogLik(seiz0M)
##### data= datacold
str(datacold)
### AR1R with the default integration method
mod1R <- cold(z ~ Time * Treatment, random = ~ 1, data = datacold,
time = "Time", id = "Subject", dependence = "AR1R")
summary (mod1R)
vareff(mod1R)
randeff(mod1R)
### AR1R with integration="cubature"
mod1R.c <- cold(z ~ Time*Treatment, random = ~ 1, data = datacold,
time = "Time", id = "Subject", dependence = "AR1R", integration = "cubature")
summary (mod1R.c)
```

```
cold-class Class cold of a maximum likelihood estimation
```


## Description

This class encapsulates results of a maximum likelihood procedure.

## Objects from the Class

Objects can be created by calls of the form new ("cold", . . .), but most often as the result of a call to cold.

## Slots

coefficients: Object of class "matrix". Estimated parameters.
se: Object of class "matrix". Standard errors of estimated parameters.
covariance: Object of class "matrix". Covariance of estimated parameters.
correlation: Object of class "matrix". Correlation of estimated parameters.
log.likelihood: Object of class "numeric". The value of the log likelihood.
message: Object of class "integer". A character string giving any additional information returned by the optimizer, or NULL. See optim for details.
n. cases: Object of class "numeric". Number of individual profiles used in the optimization procedure.
ni.cases: Object of class "numeric". Number of individual profiles in the dataset.
aic: Object of class "numeric". The Akaike information criterion for a fitted model object.
Fitted: Object of class "numeric". The fitted values for the estimated parameters.
bi.estimate: Object of class "numeric". The estimated values for the individual random effects.
Fitted.av: Object of class "numeric".
Time: Object of class "numeric". Vector of time points.
model.matrix: Object of class "matrix". The model matrix.
$y$.matrix: Object of class "matrix". The matrix of response values.
random.matrix: Object of class "matrix". The model matrix of random effects.
subset.data: Object of class "data.frame". The data subset if considered.
final.data: Object of class "data.frame". The data set considered.
$y . a v:$ Object of class "numeric". The average of the response value over an individual profile.
data.id: Object of class "numeric". Vector of individual observations.
call: Object of class "language". The call to "cold".

## Methods

anova signature(object="cold"): Anova table.
coeftest signature (object="cold"): A list of summary statistics of the fixed effects coefficients.
fitted signature(object="cold"): The fitted values of a fitted model.
fixeff signature(object="cold"): The values corresponding to the fixed effects of a fitted model.
getAIC signature(object="cold"): A numeric value corresponding to the AIC of the fitted model.
getcoef signature(object="cold"): The values corresponding to the coefficient estimates of the fitted model.
getLogLik signature(object="cold"): A numeric value corresponding to the log-Likelihood of the fitted model.
getvcov signature(object="cold"): The variance-covariance matrix of the fitted model.
model.mat signature(object="cold"): The fixed effects model matrix of the fitted model.
plot signature ( $x=$ "cold", $y=" m i s s i n g "$ ): Plots three type of plots.
randeff signature(object="cold"): A data frame corresponding to the conditional random effects of the fitted model.
show signature(object="cold"): Display object briefly.
summary signature(object="cold"): Generate object summary.
vareff signature(object="cold"): Numeric value(s) corresponding to the estimated random effect(s) variance of the fitted model.

```
cold-internal Internal functions
```


## Description

Functions for internal usage only.

```
coldControl Auxiliary for controlling "cold" fitting
```


## Description

Auxiliary function as user interface for cold fitting.

## Usage

coldControl(maxit=100, abstol=-Inf,reltol=sqrt(.Machine\$double.eps))

## Arguments

| maxit | maximum number of iterations. |
| :--- | :--- |
| abstol | absolute convergence tolerance. |
| reltol | relative convergence tolerance. |

## Details

See R documentation of optim for details of standard default values for the remaining options not considered in coldControl.

## Value

A list with the arguments as components.

## See Also

cold-class, optim

```
coldcublim Auxiliary for controlling "cold" fitting
```


## Description

Auxiliary function as user interface for cold fitting.

## Usage

coldcublim ( $11 \mathrm{i}=-4,12 \mathrm{i}=-4,11 \mathrm{~s}=4,12 \mathrm{~s}=4$, tol=1e-4, maxEval=100)

## Arguments

11s upper limit of integration for the log-likelihood.

12s upper limit of integration for the log-likelihood.

11i

12i
tol
maxEval
lower limit of integration for the log-likelihood.

2i lower limit of integration for the log-likelihood.
maxEval The maximum number of function evaluations needed.

## Value

A list with the arguments as components.

## Description

Auxiliary function as user interface for cold fitting.

## Usage

coldIntegrate(li=-4,ls=4, epsabs=.Machine\$double.eps^.25,
epsrel=.Machine\$double.eps^. 25 ,limit=100, key=6,lig=-4,lsg=4)

## Arguments

li
ls upper limit of integration for the log-likelihood.
epsabs absolute accuracy requested.
epsrel relative accuracy requested.
key integer from 1 to 6 for choice of local integration rule for number of GaussKronrod quadrature points. A gauss-kronrod pair is used with:
$7-15$ points if key $=1$,
10-21 points if key $=2$,
$15-31$ points if key $=3$,
$20-41$ points if key $=4$,
25-51 points if key $=5$ and
30-61 points if key $=6$.
limit integer that gives an upperbound on the number of subintervals in the partition of (li,ls), limit.ge.1.
lig lower limit of integration for the gradient.
lsg upper limit of integration for the gradient.

## Details

coldIntegrate returns a list of constants that are used to compute integrals based on a Fortran-77 subroutine dqage from a Fortran-77 subroutine package QUADPACK for the numerical computation of definite one-dimensional integrals. The subroutine dqage is a simple globally adaptive integrator in which it is possible to choose between 6 pairs of Gauss-Kronrod quadrature formulae for the rule evaluation component. The source code dqage was modified and re-named dqager, the change was the introduction of an extra variable that allow, in our Fortran- 77 subroutines when have a call to dqager, to control for which parameter the integral is computed.
For given values of li and ls , the above-described numerical integration is performed over the interval $\left(\mathrm{li}^{*} \sigma, \mathrm{ls} * \sigma\right)$, where $\sigma=\exp (\omega) / 2$ is associated to the current parameter value $\omega$ examined by the optim function. In some cases, this integration may generate an error, and the user must
suitably adjust the values of 1 i and ls . In case different choices of these quantities all lead to a successful run, it is recommended to retain the one with largest value of the log-likelihood. Integration of the gradient is regulated similarly by lig and lsg.
For datasets where the individual profiles have a high number of observed time points (say, more than 30), use coldIntegrate function to set the integration limits for the likelihood and for the gradient to small values than the default ones.
When the fitting procedure is complete but the computation of the information matrix produces NaNs, changing in coldIntegrate function the default values for the gradient integration limits (lig and lsg) might solve this problem.

## Value

A list with the arguments as components.

## See Also

cold-class

## Examples

```
##### data= seizure
    Integ <- coldIntegrate(li = -3.5, ls = 3.5, lig = -3.5, lsg = 3.5)
    ### AR1R without patient 207
    seizure207 <- seizure[seizure$id != 207, ]
    seiz1R1.207 <- cold(y~ lage + lbase + v4 + trt + trt:lbase,
    random = ~ 1, data = seizure207, dependence = "AR1R", integrate = Integ)
    summary (seiz1R1.207)
```

    datacold Data
    
## Description

This example is an artificial data.

## Usage

data(datacold)

## Format

A data frame with 390 observations on the following 4 variables.
Subject identifies de number of the individual profile. This vector contains observations of 30 individual profiles.

Treatment a factor with levels 0 and 1.
Time a numeric vector that identifies the number of the time points observed.
$z$ a numeric vector representing the response variable.

## Examples

```
data(datacold)
mod0<- cold(z~Time*Treatment, data=datacold, time="Time",
id="Subject", dependence="ind")
summary (mod0)
modI<- cold(z~Time*Treatment, data=datacold, time="Time",
id="Subject", dependence="AR1")
summary (modI)
anova(mod0,modI)
plot(modI, which=1,factor=Treatment, xlab="Time (weeks)",
ylab="Count", main="Model AR1")
### independent with random intercept
mod0R <- cold(z ~ Time * Treatment, random = ~ 1, data = datacold,
time = "Time", id = "Subject", dependence = "indR")
summary(mod0R)
### independent with random intercept (dependence="indR")
### using cubature (integration = "cubature")
mod0R.C <- cold(z ~ Time * Treatment, random = ~ 1, data = datacold,
time = "Time", id = "Subject", dependence = "indR", integration = "cubature")
summary(mod0R.C)
randeff(mod0R.C)
```

\#\#\# dependence="indR2"
\#\# It takes a long time to run
\#\# Using Monte Carlo method (integration = "MC")
mod0R2MC <- cold(z ~ Time * Treatment, ~ 1 + Time, datacold, time = "Time",
id = "Subject", dependence = "indR2", integration = "MC")

```
summary (mod0R2MC)
randeff(mod0R2MC)
## Using cubature (integration = "cubature")
mod0R2C<-cold(z ~ Time * Treatment, random = ~ 1 + Time, data = datacold,
time = "Time", id = "Subject", dependence = "indR2", integration = "cubature")
summary (mod0R2C)
```

datacoldM Data with missing values

## Description

This example is an artificial data with missing values.

## Usage

data("datacoldM")

## Format

A data frame with 390 observations on the following 4 variables.
Subject identifies de number of the individual profile. This vector contains observations of 30 individual profiles.

Treatment a factor with levels 0 and 1.
Time a numeric vector that identifies the number of the time points observed.
$z$ a numeric vector representing the response variable.

## Examples

```
data(datacoldM)
    str(datacoldM)
mod0.M<- cold(z~Time*Treatment, data=datacoldM, time="Time",
id="Subject", dependence="ind")
summary (mod0.M)
mod1.M<- cold(z~Time*Treatment, data=datacoldM, time="Time",
id="Subject", dependence="AR1")
summary (mod1.M)
anova(mod0.M,mod1.M)
```


## Description

Methods for function fitted extracting fitted values of a fitted model object from class cold.

## Usage

\#\# S4 method for signature 'cold'
fitted(object)

## Arguments

object an object of class cold.

## Methods

signature(object="cold"): fitted for cold object.

## Examples

```
##### data = seizure
seiz1M<-cold(y ~ lage + lbase + v4 + trt + trt:lbase, data = seizure,
start = NULL, dependence = "AR1")
fitted(seiz1M)[1:16]
```

    fixeff Extract fixed effects estimates
    
## Description

Methods for function fixeff extracting fixed effects estimates of a fitted model object from class cold.

## Usage

fixeff(object)

## Arguments

object an object of class cold.

## Value

Extract fixed effects estimates.

```
fixeff-methods Methods for function fixeff
```


## Description

Methods for function fixeff extracting fixed effects estimates of a fitted model object from class cold.

## Methods

signature(object="cold"): fixed effects estimates of a fitted model object.

## Examples

```
##### data = seizure
### AR1
seiz1M <- cold(y ~ lage + lbase + v4 + trt + trt:lbase, data = seizure,
start = NULL, dependence = "AR1")
fixeff(seiz1M)
### indR
seiz0R<-cold(y ~ lage + lbase + trt + trt:lbase + v4, random = ~ 1,
    data = seizure, dependence = "indR")
fixeff(seiz0R)
```

    getAIC Extract the Akaike Information Criterion
    
## Description

Methods for function getAIC extracting the Akaike information criterion of the fitted model object from class cold.

## Usage

getAIC(object)

## Arguments

object an object of class cold.

## Value

Returns a numeric value corresponding to the AIC of the fitted model.

```
getAIC-methods Methods for function getAIC
```


## Description

Methods for function getAIC extracting the Akaike information criterion of the fitted model object from class cold.

## Usage

\#\# S4 method for signature 'cold' getAIC(object)

## Arguments

object an object of class cold.

## Value

Returns a numeric value corresponding to the AIC of the fitted model.

## Methods

getAIC signature(object="cold"): Returns a numeric value corresponding to the AIC of the fitted model.

## Examples

```
##### data = seizure
### AR1
seiz1M <- cold(y ~ lage + lbase + v4 + trt + trt:lbase, data = seizure,
start = NULL, dependence = "AR1")
getAIC(seiz1M)
### indR
seiz0R <- cold(y ~ lage + lbase + trt + trt:lbase + v4, random = ~ 1,
        data = seizure, dependence = "indR")
getAIC(seiz0R)
```

```
getcoef Extract the coefficient estimates
```


## Description

Methods for function getcoef extracting the coefficient estimates of the fitted model object from class cold.

## Usage

getcoef(object)

## Arguments

object an object of class cold.

## Value

Returns the coefficient estimates of the fitted model.

```
getcoef-methods Methods for function getcoef
```


## Description

Methods for function getcoef extracting the coefficient estimates of the fitted model object from class cold.

## Methods

signature(object="cold"): Returns the coefficient estimates of the fitted model.

## Examples

```
##### data = seizure
### AR1
seiz1M <- cold(y ~ lage + lbase + v4 + trt + trt:lbase, data = seizure,
start = NULL, dependence = "AR1")
getcoef(seiz1M)
### indR
seiz0R <- cold(y ~ lage + lbase + trt + trt:lbase + v4, random = ~ 1,
        data = seizure, dependence = "indR")
getcoef(seiz0R)
```

```
    getLogLik Extract Log-Likelihood
```


## Description

Extract the Log-Likelihood of a fitted model object from class cold.

## Usage <br> getLogLik(object)

## Arguments

object an object of class cold.

## Value

Returns a numeric value corresponding to the log-Likelihood of the fitted model.

```
getLogLik-methods Methods for function getLogLik
```


## Description

Extract the Log-Likelihood of a fitted model object from class cold.

## Usage

\#\# S4 method for signature 'cold'
getLogLik(object)

## Arguments

object an object of class cold.

## Value

Returns a numeric value corresponding to the log-Likelihood of the fitted model.

## Methods

signature(object="cold"): Returns a numeric value corresponding to the log-Likelihood of the fitted model.

## Examples

```
##### data = seizure
### AR1R
seiz1M<-cold(y~lage+lbase+v4+trt+trt:lbase, data=seizure, start=NULL,
dependence="AR1")
getLogLik(seiz1M)
### indR
seiz0R<-cold(y ~ lage + lbase + trt + trt:lbase + v4, random = ~ 1,
    data = seizure, dependence = "indR")
getLogLik(seiz0R)
```

    getvcov Extract variance-covariance matrix
    
## Description

Extract the variance-covariance matrix of a fitted model object from class cold.

## Usage

getvcov(object)

## Arguments

object an object of class cold.

## Value

Returns a numeric value corresponding to the variance-covariance matrix.

```
getvcov-methods Methods for function getvcov
```


## Description

Extract the variance-covariance matrix of a fitted model object from class cold.

## Methods

signature(object="cold"): Returns a numeric value corresponding to the variance-covariance matrix of the fixed effect estimates.

## Examples

```
##### data = seizure
### AR1
seiz1M <- cold(y ~ lage + lbase + v4 + trt + trt:lbase, data = seizure,
start = NULL, dependence = "AR1")
getvcov(seiz1M)
```

model.mat Extract the fixed effects model matrix

## Description

Methods for function model. mat extracting the fixed effects model matrix for a fitted model object from class cold.

## Usage

model.mat (object)

## Arguments

object an object of class cold.

## Value

Returns a numeric value corresponding to the fixed effects model matrix.
model.mat-methods Methods for function model.mat

## Description

Methods for function model . mat extracting the fixed effects model matrix for a fitted model object from class cold.

## Methods

signature(object="cold"): Returns the fixed effects model matrix of the fitted model.

## Examples

```
\#\#\#\#\# data \(=\) seizure
\#\#\# AR1
seiz1M <- cold(y ~ lage + lbase + v4 + trt + trt:lbase, data = seizure,
start \(=\) NULL, dependence \(=\) "AR1")
model.mat(seiz1M)[1:20,]
```


## Description

Three plots (selectable by which) are currently available: a plot for the fitted model (which=1), a plot for the individual mean profile (which=2) and a plot for the observed data and the corresponded mean profile (which=3).

## Usage

```
## S4 method for signature 'cold,missing'
plot(x,which=c(1:3),xlab=NULL,ylab=NULL,
main=NULL,factor, subSET,ident=FALSE,
caption=c("Individual mean profiles"),cex.caption=1)
```


## Arguments

x
which
xlab label to plots.
ylab label to plots.
factor identify the factor for which=1.
cex.caption
main title to plots in addition to the caption.
subSET logical expression indicating elements to keep in individual mean profile plots: missing values are taken as FALSE for which=2.
ident logical expression indicating whether or not to add the number of the subject to individual mean profile plots. The ident argument is for option which=2.
caption captions to appear above the plots.
an object of class cold.
if a subset of the plots is required, specify a subset of the numbers 1:3. Default is (which=1).
controls the size of caption.

## Methods

signature ( $x=$ "ANY", $y=$ "ANY"): Generic function.
signature( $x=$ "cold", $y=$ "missing"): Plot diagnostics for cold object.

## Examples

```
##### data= datacold
### AR1R
mod1R <- cold(z ~ Time * Treatment, data = datacold, time = "Time",
id = "Subject", dependence = "AR1R")
plot(mod1R, which = 1, xlab = "Time(weeks)", ylab = "Count",
factor = Treatment, main = "Model AR1R")
plot(mod1R, which = 2, xlab = "Time(weeks)", ylab = "Count",
main = "Model AR1R")
par(mfrow = c(1, 2))
plot(mod1R, which = 2, ident = TRUE, subSET = Treatment == "0",
ylab = "Count", main = "0")
plot(mod1R, which = 2, ident = TRUE, subSET = Treatment == "1",
ylab = "Count", main = "1")
par(mfrow = c(1, 1))
par(mfrow = c(2, 2))
plot(mod1R, which = 3, subSET = (id == c(2)), xlab = "Time (weeks)",
ylab = "count", main = "0_Subject2")
plot(mod1R, which = 3, subSET = (id == c(10)), xlab = "Time (weeks)",
ylab = "Count", main = "0_Subject10")
plot(mod1R, which = 3, subSET = (id == c(26)), xlab = "Time (weeks)",
ylab = "Count", main = "1_Subject26")
plot(mod1R, which=3, subSET=(id == c(30)), xlab = "Time (weeks)",
ylab = "Count", main = "1_Subject32")
par(mfrow = c(1, 1))
```

randeff Extract conditional random effects

## Description

Methods for function randeff extracting conditional random effects of a fitted model object from class cold.

## Usage

randeff(object)

## Arguments

object an object of class cold.

## Value

Returns a data.frame corresponding to the conditional random effects of the fitted model.

```
randeff-methods Methods for function randeff
```


## Description

Methods for function randeff extracting conditional random effects of a fitted model object from class cold.

## Methods

signature(object="cold"): randeff for cold object.

## Examples

```
##### data = seizure
### indR
seiz0R <- cold(y ~ lage + lbase + trt + trt:lbase + v4, random = ~ 1,
        data = seizure, dependence = "indR")
randeff(seiz0R)
```


## Description

Methods for function resid extracting residual values of a fitted model object from class cold.

## Usage

```
## S4 method for signature 'cold'
resid(object, type = c( "pearson","response","null"),...)
```


## Arguments

object an object of class cold.
type
an optional character string specifying the type of residuals to be used. Two types are allowed: pearson and response. Defaults to "pearson".
... other arguments.

## Methods

signature(object="cold"): residuals for cold object.

## Examples

```
##### data = seizure
seiz1M <- cold(y ~ lage + lbase + v4 + trt + trt:lbase, data = seizure,
start = NULL, dependence = "AR1")
resid(seiz1M)[1:16]
```

seizure Epileptic Seizure

## Description

The dataset has the number of epileptic seizures in each of four two-week intervals, and in a baseline eight-week interval, for treatment and control groups with a total of 59 individuals.

## Usage

data(seizure)

## Format

A data frame with 236 observations on the following 9 variables.
id identifies de number of the individual profile. This vector contains observations of 59 individual profiles.
$y$ a numeric vector with the number of epileptic seizures in the four two-weeks intervals observed.
v4 a numeric vector indicating the fourth visit.
time a numeric vector that identifies the number of the time points observed.
trt a numeric vector indicator of treatment, whether the patient is treated with placebo ( $\operatorname{tr} t=0$ ) or progabide ( $\mathrm{tr} \mathrm{t}=1$ ).
base the number of epileptic seizures in a baseline 8 -week interval.
age a numeric vector of subject age.
lbase recode the variable base by $\log ($ base/4).
lage recode the variable age by $\log (a g e)$.

## Source

Thall, P.F., and Vail, S.C. (1990). Some covariance models for longitudinal count data with overdispersion. Biometrics, 46, 657-671.

## References

Diggle, P.J., Heagerty, P., Liang, K.Y., and Zeger, S.L. (2002). Analysis of Longitudinal Data. 2nd edition. Oxford University Press.

## Examples

```
##### data = seizure
str(seizure)
### independence
seiz0M <- cold(y ~ lage + lbase + v4 + trt + trt:lbase, data = seizure,
dependence = "ind")
summary(seiz0M)
### AR1
seiz1M <- cold(y ~ lage + lbase + v4 + trt + trt:lbase, data = seizure,
dependence = "AR1")
summary(seiz1M)
anova(seiz0M, seiz1M)
```

show-methods Methods for function show

## Description

Show objects of class cold and summary. cold.

## Methods

signature(object = "cold") Print simple summary of a cold object, just the call, the number of profiles in the fit, the number of coefficients, the value of the log-likelihood and a message giving additional information returned by the optimizer.
signature (object = "summary.cold") Shows call, the number of profiles in the fit, table of coefficients, standard errors and p-values, the log-likelihood, the AIC coefficient, and a message giving additional information returned by the optimizer.

## Description

Summarize objects.

## Usage

\#\# S4 method for signature 'cold'
summary (object, cov=FALSE, cor=FALSE)

## Arguments

object an object of class cold.
cov if set to TRUE prints the matrix of covariances between parameters estimates. The default is FALSE.
cor if set to TRUE prints the matrix of correlations between parameters estimates. The default is FALSE.

## Details

Computes and returns a list of summary statistics of the fitted model given a cold object, using the components (list elements) "call" and "terms" from its argument, plus depending on the structure of the dependence model chosen. In the table for coefficient estimates will appear rho if the dependence structure of the process corresponds to an AR1, AR1R or AR1R2. If the structure of the dependence model chosen includes the random intercept (models "indR" and "AR1R"), the variance estimate for random intercept is given. If the structure of the dependence model chosen includes two random effects (models "indR2" and "AR1R2") the variance estimates for random intercept and for the slope (time) are given.

## Methods

signature (object = "ANY"): Generic function.
signature (object = "cold"): Prints a summary as an object of class summary.cold, containing information about the matched call to cold, the number of profiles in the data, the number of profiles used in the fit, the log-likelihood, the AIC, a table with estimates, asymptotic SE, t -values and p -values, the estimated correlation and variance-covariance matrix for the estimated parameters if the user wishes, and a message giving additional information returned by the optimizer.

```
summary.cold-class Class summary.cold, summary of cold objects
```


## Description

Extract of cold object.

## Objects from the class

Objects can be created by calls of the form new("summary.cold", ...), but most often by invoking summary on an cold object. They contain values meant for printing by show.

## Slots

coefficients: Object of class "matrix". Estimated parameters.
se: Object of class "matrix". Standard errors of estimated parameters.
covariance: Object of class "matrix". Covariance of estimated parameters.
correlation: Object of class "matrix". Correlation of estimated parameters.
log.likelihood: Object of class "numeric". The value of the log likelihood.
message: Object of class "integer". A character string giving any additional information returned by the optimizer, or NULL. See optim for details.
n. cases: Object of class "numeric". Number of individual profiles used in the optimization procedure.
ni.cases: Object of class "numeric". Number of individual profiles in the dataset.
aic: Object of class "numeric". The Akaike information criterion for a fitted model object.
call: Object of class "language". The call that generated cold object.

## Extends

Class "cold", directly.

## Methods

show signature (object = "summary.cold"): Pretty-prints object.

## See Also

cold, cold-class

## Description

Methods for function vareff extracting the variance of random effects of a fitted model object.

## Usage

vareff(object)

## Arguments

object an object of class cold.

## Value

Returns the variance estimates of random effects of a fitted model.
vareff-methods Methods for function vareff

## Description

Methods for function vareff extracting the variance estimates of random effects of a fitted model object.

## Methods

```
signature(object="cold"): vareff for cold object.
```


## Examples

```
##### data = seizure
### indR
seiz0R <- cold(y ~ lage + lbase + trt + trt:lbase + v4, random = ~ 1,
        data = seizure, dependence = "indR")
vareff(seiz0R)
```


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