Package ‘CorrBin’

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Title  Nonparametrics with clustered binary data

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Depends  R (>= 2.10), boot

Suggests  geepack, lattice

Description  This package implements non-parametric analyses for clustered binary data. The elements of the cluster are assumed exchangeable, and identical joint distribution (also known as marginal compatibility, or reproducibility) is assumed for clusters of different sizes. A trend test based on stochastic ordering is implemented.

License  GPL (>= 2)

LazyLoad  yes

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Description

This package implements nonparametric methods for analysing exchangeable binary data with variable cluster sizes with emphasis on trend testing. The input should specify the treatment group, cluster-size, and the number of responses (i.e. the number of cluster elements with the outcome of interest) for each cluster.

Details

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<thead>
<tr>
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<tr>
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- The `CBData` and `read.CBData` functions create a ‘CBData’ object used by the analysis functions.
- `ran.CBData` can be used to generate random data with prespecified mean response and within-cluster correlation.
• \texttt{mc.test.chisq} tests the assumption of marginal compatibility underlying all the methods, while \texttt{mc.est} estimates the distribution of the number of responses under marginal compatibility.

• Finally, \texttt{trend.test} performs three different tests for trend along the treatment groups.

\textbf{Author(s)}

Aniko Szabo

Maintainer: Aniko Szabo <aszabo@mcw.edu>

\textbf{References}

Szabo A, George EO. (2009) On the Use of Stochastic Ordering to Test for Trend with Clustered Binary Data. \textit{Biometrika}


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\textbf{CBData}

Create a ‘CBdata’ object from a data frame.

\textbf{Description}

The \texttt{CBData} function creates an object of class \texttt{CBData} that is used in further analyses. It identifies the variables that define treatment group, clustersize and the number of responses.

\textbf{Usage}

\texttt{CBData(x, trt, clustersize, nresp, freq = NULL)}

\textbf{Arguments}

\begin{itemize}
  \item \texttt{x} \hspace{2cm} a data frame with one row representing a cluster or potentially a set of clusters of the same size and number of responses
  \item \texttt{trt} \hspace{2cm} the name of the variable that defines treatment group
  \item \texttt{clustersize} \hspace{2cm} the name of the variable that defines cluster size
  \item \texttt{nresp} \hspace{2cm} the name of the variable that defines the number of responses in the cluster
  \item \texttt{freq} \hspace{2cm} the name of the variable that defines the number of clusters represented by the data row. If \texttt{NULL}, then each row is assumed to correspond to one cluster.
\end{itemize}
Value

A data frame with each row representing all the clusters with the same trt/size/number of responses, and standardized variable names:

- **Trt**: factor, the treatment group
- **ClusterSize**: numeric, the cluster size
- **NResp**: numeric, the number of responses
- **Freq**: numeric, number of clusters with the same values

Author(s)

Aniko Szabo

See Also

- `read.CBData` for creating a CBData object directly from a file.

Examples

```r
data(shelltox)
sh <- CBData(shelltox, trt="Trt", clustersize="ClusterSize", nresp="NResp")
str(sh)
```

Description

The data set is based on a developmental toxicity experiment on the effect of ethylene glycol diethyl ether (EGDE) on fetal development of New Zealand white rabbits. In the study, four groups of pregnant does were randomly assigned to dose levels $0, 25, 50$, and $100$ milligrams per kilogram body weight of EGDE. For each litter and at each dose level, the adverse response used is the combined number of fetal malformation and fetal death.

Usage

```r
data(egde)
```

Format

A `CBData` object, that is a data frame with the following variables:

- **Trt**: factor giving treatment group
- **ClusterSize**: the size of the litter
- **NResp**: the number of affected fetuses
- **Freq**: the number of litters with the given ClusterSize/NResp combination
**Source**

**Examples**
```r
data(egde)
stripchart(I(NResp/ClusterSize)~Trt, cex=sqrt(egde$Freq), data=egde, pch=1, method="jitter", vertical=TRUE, ylab="Proportion affected")
```

---

**Description**
GEE.trend.test implements a GEE based test for linear increasing trend for correlated binary data.

**Usage**
```r
GEE.trend.test(cbdata, scale.method = c("fixed", "trend", "all"))
```

**Arguments**
- `cbdata` : a CBData object
- `scale.method` : character string specifying the assumption about the change in the overdispersion (scale) parameter across the treatment groups: "fixed" - constant scale parameter (default); "trend" - linear trend for the log of the scale parameter; "all" - separate scale parameter for each group.

**Details**
The actual work is performed by the `geese` function of the geepack library. This function only provides a convenient wrapper to obtain the results in the same format as `RS.trend.test` and `SO.trend.test`.

The implementation aims for testing for increasing trend, and a one-sided p-value is reported. The test statistic is asymptotically normally distributed, and a two-sided p-value can be easily computed if needed.

**Value**
A list with components
- `statistic` : numeric, the value of the test statistic
- `p.val` : numeric, asymptotic one-sided p-value of the test
**Author(s)**
Aniko Szabo, aszabo@mcw.edu

**See Also**
- RS.trend.test, SO.trend.test for alternative tests; CBData for constructing a CBData object.

**Examples**
```r
data(shelltox)
GEE.trend.test(shelltox, "trend")
```

---

**mc.est**

*Distribution of the number of responses assuming marginal compatibility.*

**Description**
The `mc.est` function estimates the distribution of the number of responses in a cluster under the assumption of marginal compatibility: information from all cluster sizes is pooled. The estimation is performed independently for each treatment group.

**Usage**
```r
mc.est(cbdata)
```

**Arguments**
- `cbdata` a `CBData` object

**Details**
The EM algorithm given by Stefanescu and Turnbull (2003) is used.

**Value**
A data frame giving the estimated pdf for each treatment and clustersize. It has the following columns:

- `Prob` numeric, the probability of `NResp` responses in a cluster of size `ClusterSize` in group `Trt`
- `Trt` factor, the treatment group
- `ClusterSize` numeric, the cluster size
- `NResp` numeric, the number of responses
mc.test.chisq

Author(s)
Aniko Szabo

References

Examples
data(shelltox)
sh.mc <- mc.est(shelltox)

library(lattice)
xyplot(Prob~NResp|factor(ClusterSize), groups=Trt, data=sh.mc, subset=ClusterSize>0, type="l", as.table=TRUE, auto.key=list(columns=4, lines=TRUE, points=FALSE), xlab="Number of responses", ylab="Probability P(R=r|N=n)"

---

mc.test.chisq

Test the assumption of reproducibility

Description
mc.test.chisq tests whether the assumption of reproducibility is violated in the data.

Usage
mc.test.chisq(cbdata)

Arguments
cbdata a CBData object

Details
The assumption of marginal compatibility (AKA interpretability) implies that the marginal probability of response does not depend on cluster size. Stefanescu and Turnbull (2003), and Pang and Kuk (2007) developed a Cochran-Armitage type test for trend in the marginal probability of success as a function of the cluster size. mc.test.chisq implements a generalization of that test extending it to multiple treatment groups.

Value
A list with the following components:
overall.chi the test statistic; sum of the statistics for each group
overall.p p-value of the test
individual a list of the results of the test applied to each group separately:
NOSTASOT

- chi.sq the test statistic for the group
- p p-value for the group

Author(s)
Aniko Szabo

References

See Also
- CBData for constructing a CBData object, mc.est for estimating the distribution under marginal compatibility.

Examples

data(shelltox)
mctest.chisq(shelltox)

NOSTASOT Finding the NOSTASOT dose

Description
The NOSTASOT dose is the No-Statistical-Significance-Of-Trend dose – the largest dose at which no trend in the rate of response has been observed. It is often used to determine a safe dosage level for a potentially toxic compound.

Usage

NOSTASOT(cbdata, test = c("RS", "GEE", "GEEtrend", "GEEall", "SO"),
   exact = test == "SO", R = 100, sig.level = 0.05, control = soControl())

Arguments
cbdata a CBData object
test character string defining the desired test statistic. See trend.test for details.
extact logical, should an exact permutation test be performed. See trend.test for details.
R integer, number of permutations for the exact test
sig.level numeric between 0 and 1, significance level of the test
control an optional list of control settings for the stochastic order ("SO") test, usually a call to soControl. See there for the names of the settable control values and their effect.
Details

A series of hypotheses about the presence of an increasing trend overall, with all but the last group, all but the last two groups, etc. are tested. Since this set of hypotheses forms a closed family, one can test these hypotheses in a step-down manner with the same \texttt{sig.level} type I error rate at each step and still control the family-wise error rate.

The NOSTASOT dose is the largest dose at which the trend is not statistically significant. If the trend test is not significant with all the groups included, the largest dose is the NOSTASOT dose. If the testing sequence goes down all the way to two groups, and a significant trend is still detected, the lowest dose is the NOSTASOT dose. This assumes that the lowest dose is a control group, and this convention might not be meaningful otherwise.

Value

a list with two components

\begin{itemize}
\item \texttt{NOSTASOT} character string identifying the NOSTASOT dose.
\item \texttt{p} numeric vector of the p-values of the tests actually performed. The last element corresponds to all doses included, and will not be missing. p-values for tests that were not actually performed due to the procedure stopping are set to NA.
\end{itemize}

Author(s)

Aniko Szabo, aszabo@mcw.edu

References


See Also

trend.test for details about the available trend tests.

Examples

data(shelltox)
NOSTASOT(shelltox, test="RS")

Description

\texttt{qpower.pdf} and \texttt{betabin.pdf} calculate the probability distribution function for the number of responses in a cluster of the q-power and beta-binomial distributions, respectively.
Usage

qpower.pdf(p, rho, n)
betabin.pdf(p, rho, n)

Arguments

p numeric, the probability of success.
rho numeric between 0 and 1 inclusive, the within-cluster correlation.
n integer, cluster size.

Details

The pdf of the q-power distribution is

\[ P(X = x) = \binom{n}{x} \sum_{k=0}^{x} (-1)^k \binom{x}{k} q^{(n-x+k)\gamma}, \]

where \( q = 1 - p \), and the intra-cluster correlation

\[ \rho = \frac{q^\gamma - q^2}{q(1-q)}. \]

The pdf of the beta-binomial distribution is

\[ P(X = x) = \binom{n}{x} \frac{B(\alpha + x, n + \beta - x)}{B(\alpha, \beta)}, \]

where \( \alpha = p \frac{1-\rho}{\rho} \), and \( \alpha = (1-p) \frac{1-\rho}{\rho} \).

Value

a numeric vector of length \( n + 1 \) giving the value of \( P(X = x) \) for \( x = 0, \ldots, n \).

Author(s)

Aniko Szabo, aszabo@mcw.edu

References


See Also

ran.CBData for generating an entire dataset using these functions
Examples

```r
#the distributions have quite different shapes
#with q-power assigning more weight to the "all affected" event than other distributions
plot(0:10, betabin.pdf(0.3, 0.4, 10), type="o", ylim=c(0,0.34),
     ylab="Density", xlab="Number of responses out of 10")
lines(0:10, qpower.pdf(0.3, 0.4, 10), type="o", col="red")
```

---

**ran.CBData**

*Generate random correlated binary data*

---

**Description**

*ran.mc.CBData* generates a random *CBData* object from a given two-parameter distribution.

*p.gen.fun* and *rho.gen.fun* are functions that generate the parameter values for each treatment group; *pdf.fun* is a function generating the pdf of the number of responses given the two parameters *p* and *rho*, and the cluster size *n*.

**Usage**

```r
ran.CBData(sample.sizes, p.gen.fun = function(g) 0.3,
            rho.gen.fun = function(g) 0.2, pdf.fun = qpower.pdf)
```

**Arguments**

- `sample.sizes`: a dataset with variables Trt, ClusterSize and Freq giving the number of clusters to be generated for each Trt/ClusterSize combination.
- `p.gen.fun`: a function of one parameter that generates the value of the first parameter of *pdf.fun* (*p*) given the group number.
- `rho.gen.fun`: a function of one parameter that generates the value of the second parameter of *pdf.fun* (*rho*) given the group number.
- `pdf.fun`: a function of three parameters (*p*, *rho*, *n*) giving the PDF of the number of responses in a cluster given the two parameters (*p*, *rho*), and the cluster size (*n*). Functions implementing two common distributions: the beta-binomial (*betabin.pdf*) and q-power (*qpower.pdf*) are provided in the package.

**Details**

*p.gen.fun* and *rho.gen.fun* expect the parameter value of 1 to represent the first group, 2 - the second group, etc.

**Value**

A *CBData* object with randomly generated number of responses with sample sizes specified in the call.
Author(s)

Aniko Szabo, aszabo@mcw.edu

See Also

betabin.pdf and qpower.pdf

Examples

```r
set.seed(3486)
ss <- expand.grid(Trt=0:3, ClusterSize=5, Freq=4)
#Trt is converted to a factor
rd <- ran.CBData(ss, p.gen.fun=function(g)2+0.1*g)
rd
```

---

**read.CBData**

Read data from external file into a CBData object

Description

A convinience function to read data from specially structured file directly into a CBData object.

Usage

```r
read.CBData(file, with.freq = TRUE, ...)
```

Arguments

- `file` name of file with data. The first column should contain the treatment group, the second the size of the cluster, the third the number of responses in the cluster. Optionally, a fourth column could give the number of times the given combination occurs in the data.
- `with.freq` logical indicator of whether a frequency variable is present in the file
- `...` additional arguments passed to `read.table`

Value

a CBData object

Author(s)

Aniko Szabo

See Also

CBData
RS.trend.test

Rao-Scott trend test

Description

RS.trend.test implements the Rao-Scott adjusted Cochran-Armitage test for linear increasing trend with correlated data.

Usage

RS.trend.test(cbdata)

Arguments

cbdata a CBData object

Details

The test is based on calculating a design effect for each cluster by dividing the observed variability by the one expected under independence. The number of responses and the cluster size are then divided by the design effect, and a Cochran-Armitage type test statistic is computed based on these adjusted values.

The implementation aims for testing for increasing trend, and a one-sided p-value is reported. The test statistic is asymptotically normally distributed, and a two-sided p-value can be easily computed if needed.

Value

A list with components

statistic numeric, the value of the test statistic
p.val numeric, asymptotic one-sided p-value of the test

Author(s)

Aniko Szabo, aszabo@mcw.edu

References


See Also

SO.trend.test, GEE.trend.test for alternative tests; CBData for constructing a CBData object.
Examples

data(shelltox)
RS.trend.test(shelltox)

shelltox  
*Shell Toxicology data*

Description

This is a classical developmental toxicology data set. Pregnant banded Dutch rabbits were treated with one of four levels of a chemical. The actual doses are not known, instead the groups are designated as Control, Low, Medium, and High. Before term the animals were sacrificed, and the total number of fetuses, as well as the number affected by the treatment was recorded.

Usage

data(shelltox)

Format

A 'CBData' object, that is a data frame with the following variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trt</td>
<td>factor giving treatment group</td>
</tr>
<tr>
<td>ClusterSize</td>
<td>the size of the litter</td>
</tr>
<tr>
<td>NResp</td>
<td>the number of affected fetuses</td>
</tr>
<tr>
<td>Freq</td>
<td>the number of litters with the given ClusterSize/NResp combination</td>
</tr>
</tbody>
</table>

Source


This data set has been analyzed (and listed) in numerous papers, including


Examples

data(shelltox)
stripchart(I(NResp/ClusterSize)-Trt, cex=sqrt(shelltox$Freq), data=shelltox, pch=1, method="jitter", vertical=TRUE, ylab="Proportion affected")
SO.LRT

Likelihood-ratio test statistic

Description

SO.LRT computes the likelihood ratio test statistic for stochastic ordering against equality assuming marginal compatibility for both alternatives. Note that this statistic does not have a $\chi^2$ distribution, so the p-value computation is not straightforward. The SO.trend.test function implements a permutation-based evaluation of the p-value for the likelihood-ratio test.

Usage

SO.LRT(cbdata, control = soControl())

Arguments

cbdata a CBData object

control an optional list of control settings, usually a call to soControl. See there for the names of the settable control values and their effect.

Value

The value of the likelihood ratio test statistic is returned with two attributes:

110 the log-likelihood under $H_0$ (equality)

111 the log-likelihood under $H_a$ (stochastic order)

Author(s)

Aniko Szabo

See Also

SO.trend.test, soControl

Examples

data(shelltox)
LRT <- SO.LRT(shelltox, control=soControl(max.iter = 100, max.directions = 50))
LRT
SO.mc.est computes the nonparametric maximum likelihood estimate of the distribution of the number of responses in a cluster $P(R = r|n)$ under a stochastic ordering constraint. Umbrella ordering can be specified using the turn parameter.

Usage

`SO.mc.est(cbdata, turn = 1, control = soControl())`

Arguments

cbdata an object of class `CBData`

turn integer specifying the peak of the umbrella ordering (see Details). The default corresponds to a non-decreasing order.

control an optional list of control settings, usually a call to `soControl`. See there for the names of the settable control values and their effect.

Details

Two different algorithms: EM and ISDM are implemented. In general, ISDM (the default) should be faster, though its performance depends on the tuning parameter max.directions: values that are too low or too high slow the algorithm down.

SO.mc.est allows extension to an umbrella ordering: $D_1 \geq_{st} \cdots \geq_{st} D_k \leq_{st} \cdots \leq_{st} D_n$ by specifying the value of $k$ as the turn parameter. This is an experimental feature, and at this point none of the other functions can handle umbrella orderings.

Value

A list with components:

- `MLest` data frame with the maximum likelihood estimates of $P(R = r|n)$
- `Q` numeric matrix; estimated weights for the mixing distribution
- `D` numeric matrix; directional derivative of the log-likelihood
- `loglik` the achieved value of the log-likelihood
- `converge` a 2-element vector with the achieved relative error and the performed number of iterations

Components Q and D are unlikely to be needed by the user.

Author(s)

Aniko Szabo, aszabo@mcw.edu
SO.trend.test

References

Szabo A, George EO. (2009) On the Use of Stochastic Ordering to Test for Trend with Clustered Binary Data. *Biometrika*

See Also

soControl

Examples

data(shelltox)
ml <- SO.mc.est(shelltox, control=soControl(eps=0.01, method="ISDM"))
attr(ml, "converge")

require(lattice)
panel.cumsum <- function(x,y,...){
x.ord <- order(x)
xord <- x[x.ord]
yord <- cumsum(y[x.ord])
panel.xyplot(xord, yord, ...)
}

xyplot(Prob~NResp|factor(ClusterSize), groups=Trt, data=ml, type="s",
panel=panel.superpose, panel.groups=panel.cumsum,
as.table=TRUE, auto.key=list(columns=4, lines=TRUE, points=FALSE),
ylab="Cumulative Probability R(R>r|N=n)",
ylim=c(0,1.1), main="Stochastically ordered estimates with marginal compatibility")

---

**SO.trend.test**  
*Likelihood ratio test of stochastic ordering*

**Description**

Performs a likelihood ratio test of stochastic ordering versus equality using permutations to estimate the null-distribution and the p-value. If only the value of the test statistic is needed, use *SO.LRT* instead.

**Usage**

`SO.trend.test(cbdata, R = 100, control = soControl())`

**Arguments**

- `cbdata` a `CBData` object.
- `R` an integer – the number of random permutations for estimating the null distribution.
- `control` an optional list of control settings, usually a call to `soControl`. See there for the names of the settable control values and their effect.
Details

The test is valid only under the assumption that the cluster-size distribution does not depend on group. During the estimation of the null-distribution the group assignments of the clusters are permuted keeping the group sizes constant; the within-group distribution of the cluster-sizes will vary randomly during the permutation test.

The default value of \( R \) is probably too low for the final data analysis, and should be increased.

Value

A list with the following components

- **LRT**: the value of the likelihood ratio test statistic. It has two attributes: 110 and 111 - the values of the log-likelihood under \( H_0 \) and \( H_a \) respectively.
- **p.val**: the estimated one-sided p-value.
- **boot.res**: an object of class "boot" with the detailed results of the permutations. See `boot` for details.

Author(s)

Aniko Szabo, aszabo@mcw.edu

References

Szabo A, George EO. (2009) On the Use of Stochastic Ordering to Test for Trend with Clustered Binary Data.

See Also

- `SO.LRT` for calculating only the test statistic, `soControl`

Examples

data(shelltox)
set.seed(45742)
sh.test <- SO.trend.test(shelltox, R=1/zero.noslash, control=soControl(eps=/zero.noslash.1, max.directions=25))
sh.test

# a plot of the resampled LRT values
# would look better with a reasonable value of R
null.vals <- sh.test$boot.res$t[,1]
hist(null.vals, breaks=10, freq=FALSE, xlab="Test statistic", ylab="Density", main="Simulated null-distribution", xlim=range(c(0,20,null.vals)))
points(sh.test$LRT, 0, pch="x", col="red", cex=3)
soControl

Control values for order-constrained fit

Description

The values supplied in the function call replace the defaults and a list with all possible arguments is returned. The returned list is used as the control argument to the mc.est, SO.LRT, and SO.trend.test functions.

Usage

soControl(method = c("ISDM", "EM"), eps = 0.005, max.iter = 5000, max.directions = 0, start = ifelse(method == "ISDM", "H0", "uniform"), verbose = FALSE)

Arguments

- **method**: a string specifying the maximization method
- **eps**: a numeric value giving the maximum absolute error in the log-likelihood
- **max.iter**: an integer specifying the maximal number of iterations
- **max.directions**: an integer giving the maximal number of directions considered at one step of the ISDM method. If zero or negative, it is set to the number of non-empty cells. A value of 1 corresponds to the VDM algorithm.
- **start**: a string specifying the starting setup of the mixing distribution; "H0" puts weight only on constant vectors (corresponding to the null hypothesis of no change), "uniform" puts equal weight on all elements. Only a "uniform" start can be used for the "EM" algorithm.
- **verbose**: a logical value; if TRUE details of the optimization are shown.

Value

A list with components for each of the possible arguments.

Author(s)

Aniko Szabo aszabo@mcw.edu

See Also

mc.est, SO.LRT, SO.trend.test

Examples

# decrease the maximum number iterations and
# request the "EM" algorithm
soControl(method="EM", max.iter=100)
trend.test  

Test for increasing trend with correlated binary data

Description

The `trend.test` function provides a common interface to the trend tests implemented in this package: `SO.trend.test`, `RS.trend.test`, and `GEE.trend.test`. The details of each test can be found on their help page.

Usage

```r
trend.test(cbdata, test = c("RS", "GEE", "GEEtrend", "GEEall", "SO"),
            exact = test == "SO", R = 100, control = soControl())
```

Arguments

- `cbdata`: a `CBData` object
- `test`: character string defining the desired test statistic. "RS" performs the Rao-Scott test (`RS.trend.test`), "SO" performs the stochastic ordering test (`SO.trend.test`), "GEE", "GEEtrend", "GEEall" perform the GEE-based test (`GEE.trend.test`) with constant, linearly modeled, and freely varying scale parameters, respectively.
- `exact`: logical, should an exact permutation test be performed. Only an exact test can be performed for "SO". The default is to use the asymptotic p-values except for "SO".
- `R`: integer, number of permutations for the exact test
- `control`: an optional list of control settings for the stochastic order ("SO") test, usually a call to `soControl`. See there for the names of the settable control values and their effect.

Value

A list with two components and an optional "boot" attribute that contains the detailed results of the permutation test as an object of class `boot` if an exact test was performed.

- `statistic`: numeric, the value of the test statistic
- `p.val`: numeric, asymptotic one-sided p-value of the test

Author(s)

Aniko Szabo, aszabo@mcw.edu

See Also

- `SO.trend.test`, `RS.trend.test`, and `GEE.trend.test` for details about the available tests.
unwrap.CBData

Examples

```r
data(shelltox)
trend.test(shelltox, test="RS")
set.seed(5724)
#R=50 is too low to get a good estimate of the p-value
trend.test(shelltox, test="RS", R=50, exact=TRUE)
```

unwrap.CBData  | Unwrap a CBData object

Description

unwrap.CBData is a utility function that reformats a CBData object so that each row is one observation (instead of one or more clusters). A new ‘ID’ variable is added to indicate clusters. This form can be useful for setting up the data for a different package.

Usage

```r
unwrap.CBData(cbdata)
```

Arguments

- `cbdata` | a CBData object

Value

A data frame with one row for each cluster element (having a binary outcome) with the following standardized column names

- Trt | factor, the treatment group
- ClusterSize | numeric, the cluster size
- ID | factor, each level representing a different cluster
- Resp | numeric with 0/1 values, giving the response of the cluster element

Author(s)

Aniko Szabo

Examples

```r
data(shelltox)
ush <- unwrap.CBData(shelltox)
head(ush)
```
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