# Package 'ludic' 

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ludic-package ludic

## Description

Linkage Using Diagnosis Codes

## Details

This package implements probabilistic record linkage methods that relies on the use of diagnosis codes only, in the absence of direct identifiers .

| Package: | ludic |
| :--- | :--- |
| Type: | Package |
| Version: | ludic 0.2 .0 |
| Date: | 2021-08-18 |
| License: | The "MIT License" (MIT) |

The main function of ludic is recordLink.

## Author(s)

Boris P. Hejblum, Tianxi Cai - Maintainer: Boris P. Hejblum

## References

Hejblum BP, Weber G, Liao KP, Palmer N, Churchill S, Szolovits P, Murphy S, Kohane I and Cai T, Probabilistic Record Linkage of De-Identified Research Datasets Using Diagnosis Codes, Scientific Data, 6:180298 (2019). doi: 10.1038/sdata.2018.298.

Zhang HG, Hejblum BP, Weber G, Palmer N, Churchill S, Szolovits P, Murphy S, Liao KP, Kohane I and Cai T, ATLAS: An automated association test using probabilistically linked health records with application to genetic studies, JAMIA, in press (2021). doi: 10.1101/2021.05.02.21256490.

```
agree_C Fast C++ implementation of agreement vector for the element-wise
comparison of 2 matrices
```


## Description

agree_C_sparse uses sparse matrices.

## Usage

```
agree_C(mat_A, mat_B)
    agree_C_sparse(mat_A, mat_B)
```


## Arguments

$$
\begin{array}{ll}
\text { mat_A } & \text { a nB } \times K \text { matrix of the observations to be matched. Must be integers. } \\
\text { mat_B } & \begin{array}{l}
\text { a nA } \times K \text { matrix of the database into which a match is looked for. Must be inte- } \\
\text { gers. }
\end{array}
\end{array}
$$

## Examples

```
mat1 <- matrix(round(rnorm(n=1000, sd=1.2)), ncol=10, nrow=100)
mat2 <- rbind(mat1[1:10, ],
    matrix(round(rnorm(n=900, sd=1.2)), ncol=10, nrow=90)
    )
rownames(mat1) <- paste0("A", 1:nrow(mat1))
rownames(mat1) <- paste0("B", 1:nrow(mat1))
mat1 <- 1*(mat1>1)
mat2 <- 1*(mat2>1)
```

atlas Association testing by combining several matching thresholds

## Description

Computes association test p -values from a generalized linear model for each considered threshold, and computes a p-value for the combination of all the envisioned thresholds through Fisher's method using perturbation resampling.

## Usage

```
    atlas(
        match_prob,
        \(y\),
        x ,
        covar = NULL,
        thresholds \(=\) seq(from \(=0.1\), to \(=0.9\), by \(=0.2\) ),
        nb_perturb = 200,
        dist_family = c("gaussian", "binomial"),
        impute_strategy = c("weighted average", "best")
    )
```


## Arguments

match_prob matching probabilities matrix (e.g. obtained through recordLink) of dimensions $\mathrm{n} 1 \times \mathrm{n} 2$.
$y \quad$ response variable of length $n 1$. Only binary phenotypes are supported at the moment.
$x \quad$ a matrix or a data.frame of predictors of dimensions $n 2 \times p$. An intercept is automatically added within the function.
covar a matrix or a data.frame of variables to be adjusted on in the test of dimensions $n 3 \times p$. Default is NULL in which case there is no adjustment.
thresholds a vector (possibly of length 1) containing the different threshold to use to call a match. Default is seq (from $=0.5$, to $=0.95$, by $=0.05$ ) .
nb_perturb the number of perturbation used for the p-value combination. Default is 200.
dist_family a character string indicating the distribution family for the glm. Currently, only 'gaussian' and 'binomial' are supported. Default is 'gaussian'.
impute_strategy
a character string indicating which strategy to use to impute x from the matching probabilities match_prob. Either "best" (in which case the highest probable match above the threshold is imputed) or "weighted average" (in which case weighted mean is imputed for each individual who has at least one match with a posterior probability above the threshold). Default is "weighted average".

## Value

a list containing the following:

- influencefn_pvals p-values obtained from influence function perturbations with the covariates as columns and the thresholds as rows, with an additional row at the top for the combination
- wald_pvals a matrix containing the p-values obtained from the Wald test with the covariates as columns and the thresholds as rows
- ptbed_pvals a list containing, for each covariates, a matrix with the nb_perturb perturbed $p$-values with the different thresholds as rows
- theta_impute a matrix of the estimated coefficients from the glm when imputing the weighted average for covariates (as columns) with the thresholds as rows
- sd_theta a matrix of the estimated SD (from the influence function) of the coefficients from the glm when imputing the weighted average for covariates (as columns), with the thresholds as rows
- ptbed_theta_impute a list containing, for each covariates, a matrix with the nb_perturb perturbed estimated coefficients from the glm when imputing the weighted average for covariates, with the different thresholds as rows
- impute_strategy a character string indicating which impute strategy was used (either "weighted average" or "best")


## References

Zhang HG, Hejblum BP, Weber G, Palmer N, Churchill S, Szolovits P, Murphy S, Liao KP, Kohane I and Cai T, ATLAS: An automated association test using probabilistically linked health records with application to genetic studies, JAMIA, in press (2021). doi: 10.1101/2021.05.02.21256490.

## Examples

```
#rm(list=ls())
n_sims <- 1#5000
mysim <- function(i){
    x <- matrix(ncol=2, nrow=99, stats::rnorm(n=99*2))
    #plot(density(rbeta(n=1000, 1,2)))
    match_prob <- matrix(rbeta(n=103*99, 1, 2), nrow=103, ncol=99)
    #y <- rnorm(n=103, mean = 1, sd = 0.5)
    #return(atlas(match_prob, y, x, dist_family="gaussian")$influencefn_pvals)
    y <- rbinom(n=103, size = 1, prob=0.5)
    return(atlas(match_prob, y, x, dist_family="binomial")$influencefn_pvals)
}
#res <- pbapply::pblapply(1:n_sims, mysim, cl = parallel::detectCores()-1)
res <- lapply(1:n_sims, mysim)
size <- sapply(1:(ncol(res[[1]])-2),
                    FUN = function(i){
            rowMeans(sapply(res, function(m){m[, i]<0.05}), na.rm = TRUE)
            }
)
rownames(size) <- rownames(res[[1]])
colnames(size) <- colnames(res[[1]])[-(-1:0 + ncol(res[[1]]))]
size
```

```
comb_pvals Fisher's rule for combining several p-values
```


## Description

Compute the negative of the log-sum for a vector of p -values.

## Usage

comb_pvals(pv)

## Arguments

pv the vector of p-values to be combined together

## Details

According to Fisher's rule, if the p-values are correlated, then this does not follow a simple chisquare mixture under the null.

## Value

the Fisher combination of the p-values. See Details.

```
em_winkler
Implementation of Winkler's EM algorithm for Fellegi-Sunter matching method
```


## Description

em_winkler_big implements the same method when the data are too big to compute the agreement matrix. Agreement is then recomputed on the fly each time it is needed. The EM steps are completely done in C++. This decreases the RAM usage (still important though), at the cost of increasing computational time.

## Usage

em_winkler $($
data1,
data2,
tol = 0.001,
maxit = 500,
do_plot = TRUE,
oneone = FALSE,
verbose = FALSE
)

```
em_winkler_big(
    data1,
    data2,
    tol = 0.001,
    maxit = 500,
    do_plot = TRUE,
    oneone = FALSE,
    verbose = FALSE
)
```


## Arguments

| data1 | either a binary (1 or 0 values only) matrix or binary data frame of dimension n1 <br>  <br> x K whose rownames are the observation identifiers. |
| :--- | :--- |
| data2 | either a binary (1 or 0 values only) matrix or a binary data frame of dimension <br> $\mathrm{n} 2 \times \mathrm{K}$ whose rownames are the observation identifiers. |
| tol | tolerance for the EM algorithm convergence. |
| maxit | maximum number of iterations for the EM algorithm. |
| do_plot | a logical flag indicating whether a plot should be drawn for the EM convergence. <br> Default is TRUE. |
| oneone | a logical flag indicating whether 1-1 matching should be enforced. If TRUE, then <br> returned matchingScores are only kept for the maximum score per column <br> while lower scores are replace by threshold-1. Default is FALSE in which case <br> original matchingScores are returned. |
| verbose | a logical flag indicating whether intermediate values from the EM algorithm <br> should be printed. Useful for debugging. Default is FALSE. |

## Value

a list containing:

- matchingScore a matrix of size $\mathrm{n} 1 \times \mathrm{n} 2$ with the matching score for each $\mathrm{n} 1 * \mathrm{n} 2$ pair.
- threshold_ms threshold value for the matching scores above which pairs are considered true matches.
- estim_nbmatch an estimation of the number of true matches ( N pairs considered multiplied by p the estimated proportion of true matches from the EM algorithm)
- convergence_status a logical flag indicating whether the EM algorithm converged


## References

Winkler WE. Using the EM Algorithm for Weight Computation in the Fellegi-Sunter Model of Record Linkage. Proc Sect Surv Res Methods, Am Stat Assoc 1988: 667-71.
Grannis SJ, Overhage JM, Hui S, et al. Analysis of a probabilistic record linkage technique without human review. AMIA 2003 Symp Proc 2003: 259-63.

## Examples

```
mat1 <- matrix(round(rnorm(n=1000, sd=1.2)), ncol=10, nrow=100)
mat2 <- rbind(mat1[1:10, ],
    matrix(round(rnorm(n=900, sd=1.2)), ncol=10, nrow=90)
    )
rownames(mat1) <- paste0("A", 1:nrow(mat1))
rownames(mat1) <- paste0("B", 1:nrow(mat1))
mat1 <- 1*(mat1>1)
mat2 <- 1*(mat2>1)
em_winkler(mat1, mat2)
```

loglikC_bin C++ implementation of the pseudo-likelihood computation

## Description

loglikC_bin implements an even faster C++ implementation of the pseudo-likelihood computation for binary variables
loglikC_bin_wDates implements a C++ implementation of the pseudo-likelihood computation for binary variables with dates

## Usage

loglikC_bin(Bmat, Amat, eps_p, eps_n, piA, piB)
loglikC_bin_wDates(Bmat, Amat, Bdates, Adates, eps_p, eps_n, piA, piB)
loglikratioC_diff_arbitrary(Bmat, Amat, d_max, cost)

## Arguments

Bmat $\quad \mathrm{K} \times \mathrm{nB}$ matrix of the observations to be matched.
Amat $\quad n A \times K$ matrix the database into which a match is looked for.
eps_p a vector of length $K$ giving the prior discrepancy rate expected from $A$ to $B$ for the positives, for each variable.
eps_n a vector of length $K$ giving the prior discrepancy rate expected from A to $B$ for the negatives, for each variable.
piA a vector of length $K$ giving the prior probabilities of observing each variable in A.
a vector of length $K$ giving the prior probabilities of observing each variable in B.

Bdates $\quad n B \times K$ matrix of the dates for each observations to be matched.
Adates $\quad n A \times K$ matrix of the dates for database into which a match is looked for.

```
d_max a numeric vector of length K giving the minimum difference from which it is
    considered a discrepancy.
cost a numeric vector of length K giving the arbitrary cost of discrepancy.
```

$\begin{array}{ll}\text { matchingScore_C } & \text { Fast } C++ \text { computation of the final posterior probabilities in the E-M } \\ \text { Winkler's method }\end{array}$

## Description

matchingScore_C_sparse_big implements a version using sparse matrices. It has a better management of memory but is a little bit slower (indicated for big matrices)

## Usage

matchingScore_C(agreemat, m, u, nA, nB)
matchingScore_C_sparse_big(mat_A, mat_B, m, u)

## Arguments

agreemat binary sparse matrix of dimensions $N \times K$ containing the agreement rows for each pair of potential matches.
$m \quad$ vector of length $K$ containing the agreement weights.
$u \quad$ vector of length $K$ containing the disagreement weights.
nA integer indicating the number of observations to be matched.
$\mathrm{nB} \quad$ integer indicating the number of observations to be matched with.
mat_A a nB $\times$ K matrix of the observations to be matched.
mat_B a nA $\times \mathrm{K}$ matrix of the database into which a match is looked for.

```
matchProbs_rank_full_C
```

Compute the matching probabilities for each pair of observations

## Description

$C++$ version: for each observations in (1:n), all the matching probabilities are computed for the $p$ possible pairs.

## Usage

matchProbs_rank_full_C(computed_dist, prop_match)

## Arguments

computed_dist anxp matrix of computed distances used for ranking.
prop_match a priori proportion of matches ("rho_1")

## Value

an $\mathrm{n} p$ matrix containing the matching probabilities for each pair

```
pval_zscore
Compute p-values for a Z-score
```


## Description

Compute p-values for a Z-score assuming normal distribution of the z -score under the null Hypothesis H0

## Usage

pval_zscore(beta, sigma)

## Arguments

| beta | the estimate |
| :--- | :--- |
| sigma | estimate's estimated variance |

## Value

the p -value

## Description

An anonymized version of the binarized diagnosis code data from the RA1 and RA2 datasets, over both 6-year and 11-year time span.

## Usage

data(RA)

## Format

5 objects

- RA1_6y: an integer matrix of 0 s and 1 s containing 4,936 renamed diagnosis codes for 26,681 patients from the dataset RA1 recorded over a 6-year time span.
- RA2_6y: an integer matrix of 0 s and 1 s containing 4,936 renamed diagnosis codes for 5,707 patients from the dataset RA2 recorded over a 6-year time span.
- RA1_11y: an integer matrix of 0 s and 1 s containing 5,593 renamed diagnosis codes for 26,687 patients from the dataset RA1 recorded over a 11-year time span.
- RA2_11y: an integer matrix of 0 s and 1s containing 5,593 renamed diagnosis codes for 6,394 patients from the dataset RA2 recorded over a 11-year time span.
- silverstandard_truematches: a character matrix with two columns containing the identifiers of the 3,831 pairs of silver-standard matches.


## Details

The ICD-9 diagnosis codes have also been masked and randomly reordered, replaced by meaningless names. Finally, the silver-standard matching pairs are also provided to allow the benchmarking of methods for probabilistic record linkage using diagnosis codes.

## References

Hejblum BP, Weber G, Liao KP, Palmer N, Churchill S, Szolovits P, Murphy S, Kohane I and Cai T, Probabilistic Record Linkage of De-Identified Research Datasets Using Diagnosis Codes, Scientific Data, 6:180298 (2019). doi: 10.1038/sdata.2018.298.
Liao, K. P. et al. Electronic medical records for discovery research in rheumatoid arthritis. Arthritis Care \& Research 62, 1120-1127 (2010). doi: 10.1002/acr. 20184
Liao, K. P. et al. Methods to Develop an Electronic Medical Record Phenotype Algorithm to Compare the Risk of Coronary Artery Disease across 3 Chronic Disease Cohorts. PLoS ONE 10, e0136651 (2015). doi: 10.1371/journal.pone. 0136651

## Examples

```
if(interactive()){
rm(list=ls())
library(ludic)
data(RA)
res_match_6y <- recordLink(data1 = RA1_6y, data2 = RA2_6y,
    eps_plus = 0.01, eps_minus = 0.01,
    aggreg_2ways ="mean",
    min_prev = 0,
    use_diff = FALSE)
res_match_11y <- recordLink(data1 = RA1_11y, data2 = RA2_11y,
            eps_plus = 0.01, eps_minus = 0.01,
            aggreg_2ways ="mean",
            min_prev = 0,
```

```
use_diff = FALSE)
```

```
print.res_matching <- function(res, threshold=0.9, ref=silverstandard_truematches){
    have_match_row <- rowSums(res>threshold)
    have_match_col <- colSums(res>threshold)
    bestmatched_pairs_all <- cbind.data.frame(
        "D1"=rownames(res)[apply(res[,which(have_match_col>0), drop=FALSE], 2, which.max)],
        "D2"=names(have_match_col)[which(have_match_col>0)]
    )
    nTM_all <- nrow(ref)
    nP_all <- nrow(bestmatched_pairs_all)
    TPR_all <- sum(apply(bestmatched_pairs_all, 1, paste0, collapse="")
                %in% apply(ref, 1, paste0, collapse=""))/nTM_all
    PPV_all <- sum(apply(bestmatched_pairs_all, 1, paste0, collapse="")
                %in% apply(ref, 1, paste0, collapse=""))/nP_all
    cat("threshold: ", threshold,
        "\nnb matched: ", nP_all,"; nb true matches: ", nTM_all,
        "\nTPR: ", TPR_all, "; PPV: ", PPV_all, "\n\n", sep="")
}
print.res_matching(res_match_6y)
print.res_matching(res_match_11y)
}
```

    recordLink
        Probabilistic Patient Record Linkage
    
## Description

Probabilistic Patient Record Linkage

## Usage

```
recordLink(
        data1,
        data2,
        dates1 = NULL,
        dates2 = NULL,
        eps_plus,
        eps_minus,
        aggreg_2ways = "mean",
        min_prev = 0.01,
    data1_cont2diff = NULL,
    data2_cont2diff = NULL,
    d_max,
    use_diff = TRUE
)
```


## Arguments

| data1 | either a binary (1 or 0 values only) matrix or binary data frame of dimension n1 <br> x K whose rownames are the observation identifiers. <br> either a binary (1 or 0 values only) matrix or a binary data frame of dimension <br> n2 x K whose rownames are the observation identifiers. Columns should be in <br> the same order as in data1. |
| :--- | :--- |
| data2 |  |
| matrix or dataframe of dimension n1 x K including the concatenated dates inter- |  |
| vals for each corresponding diagnosis codes in data1. Default is NULL in which |  |
| case dates are not used. |  |

## Details

Dates: the use of dates1 and dates 2 requires that at least one date interval matches across dates 1 and dates 2 for claiming an agreement on a diagnosis code between data1 and data2, in addition of having that very same code recorded in both.

## Value

a matrix of size $n 1 \times n 2$ with the posterior probability of matching for each $n 1 * n 2$ pair

## References

Hejblum BP, Weber G, Liao KP, Palmer N, Churchill S, Szolovits P, Murphy S, Kohane I and Cai T, Probabilistic Record Linkage of De-Identified Research Datasets Using Diagnosis Codes, Scientific Data, 6:180298 (2019). doi: 10.1038/sdata.2018.298.

## Examples

```
set.seed(123)
ncodes <- 500
npat <- 200
incid <- abs(rnorm(n=ncodes, 0.15, 0.07))
bin_codes <- rbinom(n=npat*ncodes, size=1, prob=rep(incid, npat))
bin_codes_mat <- matrix(bin_codes, ncol=ncodes, byrow = TRUE)
data1_ex <- bin_codes_mat[1:(npat/2+npat/10),]
data2_ex <- bin_codes_mat[c(1:(npat/10), (npat/2+npat/10 + 1):npat), ]
rownames(data1_ex) <- paste0("ID", 1:(npat/2+npat/10), "_data1")
rownames(data2_ex) <- paste0("ID", c(1:(npat/10), (npat/2+npat/10 + 1):npat), "_data2")
if(interactive()){
res <- recordLink(data1 = data1_ex, data2 = data2_ex,
    use_diff = FALSE, eps_minus = 0.01, eps_plus = 0.01)
round(res[c(1:3, 19:23), c(1:3, 19:23)], 3)
}
```

test_han2018

Association testing using Han \& Lahiri estimating equations and jackknife approach

## Description

Association testing using Han \& Lahiri estimating equations and jackknife approach

## Usage

```
test_han2018(
    match_prob,
    y,
    x,
    covar_y = NULL,
    covar_x = NULL,
    jackknife_nrep = 100,
    jackknife_blocksize = max(floor(min(length(y), nrow(x))/jackknife_nrep), 1),
    methods = c("F", "M", "M2"),
    dist_family = c("gaussian", "binomial")
)
```


## Arguments

match_prob matching probabilities matrix (e.g. obtained through recordLink) of dimensions $\mathrm{n} 1 \times \mathrm{n} 2$.
y response variable of length n1. Only binary or gaussian phenotypes are supported at the moment.
a matrix or a data.frame of predictors of dimensions $\mathrm{n} 2 \times \mathrm{p}$. An intercept is automatically added within the function.
covar_y a matrix or a data.frame of predictors of dimensions $n 1 \times q 1$. An intercept is automatically added within the function.
covar_x a matrix or a data.frame of predictors of dimensions n 2 xq 2 . An intercept is automatically added within the function.
jackknife_nrep the number of jackknife repetitions. Default is 100 (from Han et al.).
jackknife_blocksize
the number of observations to remove in each jackknife.
methods a character vector which must be a subset of ("F", "M", "M2") indicating which estimator from Han et al. 2018 should be computed. Default is all 3.
dist_family a character string indicating the distribution family for the glm. Currently, only 'gaussian' and 'binomial' are supported. Default is 'gaussian'.

## Value

a list containing the following for each estimator in methods:

- beta a vector containing the p estimated coefficients
- varcov the $p \times p$ variance-covariance matrix of the beta coefficients
- zscores a vector containing the p Z -scores
- pval the corresponding Gaussian assumption p-values


## References

Han, Y., and Lahiri, P. (2019) Statistical Analysis with Linked Data. International Statistical Review, 87: S139-S157. doi: 10.1111/insr. 12295.

## Examples

```
# rm(list=ls())
# n_sims <- 500
# res <- pbapply::pblapply(1:n_sims, function(n){
# nx <- 99
# ny <- 103
# x <- matrix(ncol=2, nrow=ny, stats::rnorm(n=ny*2))
#
# #plot(density(rbeta(n=1000, 1,2)))
# match_prob <- diag(ny)[, 1:nx]#matrix(rbeta(n=ny*nx, 1, 2), nrow=ny, ncol=99)
#
# covar_y <- matrix(rnorm(n=ny, 1, 0.5), ncol=1)
# covar_x <- matrix(ncol=3, nrow=ny, stats::rnorm(n=ny*3))
#
# #y <- rnorm(n=ny, mean = x %*% c(2,-3) + covar_x %*% rep(0.2, ncol(covar_x)) + 0.5*covar_y, 0.5)
# y <- rbinom(n=ny, 1, prob=expit(x %*% c(2,-3) + covar_x %*%
# rep(0.2, ncol(covar_x)) + 0.5*covar_y))
# #glm(y~0+x+covar_y+covar_x, family = "binomial")
# return(
```

```
# #test_han2018(match_prob, y, x, jackknife_blocksize = 10, covar_x = NULL, covar_y = NULL)
# test_han2018(match_prob, y[1:ny], x[1:nx, ], dist_family = "binomial",
        jackknife_blocksize = 10, covar_x = covar_x[1:nx, ],
        covar_y = covar_y[1:ny, , drop=FALSE])
# )
# }, cl=parallel::detectCores()-1)
# pvals_F <- sapply(lapply(res, "[[", "F"), "[[", "beta")
# pvals_M <- sapply(lapply(res, "[[", "M"), "[[", "beta")
# pvals_M2 <- sapply(lapply(res, "[[", "M2"), "[[", "beta")
# quantile(pvals_F)
# quantile(pvals_M)
# quantile(pvals_M2)
# rowMeans(pvals_F<0.05)
# rowMeans(pvals_M<0.05)
# rowMeans(pvals_M2<0.05)
```


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