

# Package ‘TTMap’

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**Type** Package

**Title** Two-Tier Mapper: a clustering tool based on topological data analysis

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## Description

TTMap is a clustering method that groups together samples with the same deviation in comparison to a control group. It is specially useful when the data is small. It is parameter free.

**License** GPL-2

**Suggests** BiocStyle, airway

**Depends** rgl, colorRamps

**Imports** grDevices,graphics,stats,utils, methods, SummarizedExperiment, Biobase

**biocViews** Software, Microarray, DifferentialExpression, MultipleComparison, Clustering, Classification

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TTMap-package	<i>Two-Tier Mapper: a clustering tool based on topological data analysis</i>
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**Description**

TTMap is a clustering method that groups together samples with the same deviation in comparison to a control group. It is specially useful when the data is small. It is parameter free.

**Details**

The DESCRIPTION file: TTMap/DESCRIPTION Version 1.0

**Author(s)**

Rachel Jeitziner Maintainer: Rachel Jeitziner <rachel.jeitziner@epfl.ch>

**References**

R. Jeitziner et al., TTMap, 2018, DOI:arXiv:1801.01841

**See Also**

rgl, colorRamps

**Examples**

```
#to be found in \code{\link[TTMap]{ttmap_sgn_genes}}
```

---

calcul_e	<i>Calculation of the value of epsilon</i>
----------	--

---

**Description**

Calculation of the value of epsilon

**Usage**

```
calcul_e(dd5, pvalcutoff = 0.95, tt1, alpha = 1, S =
colnames(tt1$Normal.mat))
calcul_e_single(dd5, pvalcutoff = 0.95, tt1, alpha = 1, S =
colnames(tt1$Normal.mat))
```

**Arguments**

dd5	distance matrix as created by generate_mismatch_distance
pvalcutoff	cutoff of 0.05 percent (default) or less
tt1	output of <a href="#">control_adjustment</a>
alpha	a cutoff value for the FC between the group of control and the disease group
S	subset of columns to be considered

**Value**

al number representing the cutoff to choose for the relatedness with dd5

**Author(s)**

Rachel Jeitziner

**See Also**

[control\\_adjustment](#), [hyperrectangle\\_deviation\\_assessment](#), [tmap\\_sgn\\_genes](#), [generate\\_mismatch\\_distance](#)

**Examples**

```
##--
library(airway)
data(airway)
airway <- airway[rowSums(assay(airway))>80,]
assay(airway) <- log(assay(airway)+1,2)
ALPHA <- 1
the_experiment <- TMap::make_matrices(airway,
seq_len(4), seq_len(4) + 4,
rownames(airway), rownames(airway))
TMAP_part1prime <-TMap::control_adjustment(
normal.pcl = the_experiment$CTRL,
tumor.pcl = the_experiment$TEST,
normalname = "The_healthy_controls",
dataname = "Effect_of_cancer",
org.directory = tempdir(), e = 0, P = 1.1, B = 0);
Kprime <- 4;
TMAP_part1_hda <-
TMap::hyperrectangle_deviation_assessment(x =
TMAP_part1prime,
k = Kprime,dataname = "Effect_of_cancer",
normalname = "The_healthy_controls");
annot <- c(paste(colnames(
the_experiment$TEST[-(seq_len(3))]), "Dis", sep = "."),
paste(colnames(the_experiment$CTRL[
-seq_len(3)]), "Dis", sep = "."))
dd5_sgn_only <-TMap::generate_mismatch_distance(
TMAP_part1_hda,
select=rownames(TMAP_part1_hda$Dc.Dmat), alpha = ALPHA)
e <- TMap::calcul_e(dd5_sgn_only, 0.95, TMAP_part1prime, 1)
```

---

control\_adjustment      *Calculates a corrected control group, discovers outliers in it.*

---

**Description**

[control\\_adjustment](#) function finds outliers in the control group and removes them

**Usage**

```
control_adjustment(normal.pcl, tumor.pcl, normalname, dataname,
org.directory = "", A = 1, e = 0, meth = 0, P = 1.1, B = 0)
```

**Arguments**

normal.pcl	the control matrix with annotation as obtained by \$CTRL from <a href="#">make_matrices</a>
tumor.pcl	the disease/test data matrix with annotation as obtained by \$TEST from <a href="#">make_matrices</a>
normalname	A name for the corrected control files
dataname	the name of the project
org.directory	where the outputs should be saved
A	integer if A=0 then the difference to the median is calculated otherwise the difference to the mean.
e	integer giving how far to the median an outlier is at least
meth	value or method that defines how to replace outliers, default is set to replace by the median
P	if more than P percent of features are outliers the feature is removed, by default all are kept
B	Batch vector a vector for normal and test samples with a same number corresponding to a same batch

**Details**

[control\\_adjustment](#) calculates a corrected control group, discovers outliers in it.

**Value**

Several files are created

```
paste(org.directory, normalname, ".normMesh", sep = "")
```

The normal matrix with only common features with the test matrix. This file is only created if the two have different rows

```
paste(org.directory, dataname, ".normMesh", sep = "")
```

The test matrix with only common features with the normal matrix. This file is only created if the two have different rows.

```
mean_vs_variance.pdf
```

A pdf showing a plot of the mean (X axis) against the variances (Y axis) of each feature

```
mean_vs_variance_after_correction.pdf
```

A pdf showing a plot of the mean (X axis) against the variances (Y axis) of each feature after correction of the control group

```
na_numbers_per_row.txt
```

number of outliers per row

```
na_numbers_per_col.txt
```

number of outliers per column

And values of `tmap_part1_ctrl_adj`

```
e
```

Selected criteria for what is an outlier

```
tag.pcl
```

Annotation of features, ID of features and weight

```
Normal.mat
```

The control matrix without annotation and only with the common rows with Disease.mat

```
Disease.mat
```

The test/disease matrix without annotation and only with the common rows with Disease.mat

flat.Nmat	A list \$mat being the corrected control matrix \$m a record of the different numbers of removed genes per sample
record	numbers recording the number of columns in Disease.mat and Normal.mat
B	The batch vector B introduced in the beginning
U1	The different batches in Normal.mat
U2	The different batches in Disease.mat

**Author(s)**

Rachel Jeitziner

**See Also**

[hyperrectangle\\_deviation\\_assessment](#), [tmap](#) [tmap\\_sgn\\_genes](#)

**Examples**

```
##--
library(airway)
data(airway)
airway <- airway[rowSums(assay(airway))>80,]
assay(airway) <- log(assay(airway)+1,2)
ALPHA <- 1
the_experiment <- TMap::make_matrices(airway,
seq_len(4), seq_len(4) + 4,
rownames(airway), rownames(airway))
TMAP_part1prime <-TMap::control_adjustment(
normal.pcl = the_experiment$CTRL,
tumor.pcl = the_experiment$TEST,
normalname = "The_healthy_controls",
dataname = "Effect_of_cancer",
org.directory = tempdir(), e = 0, P = 1.1, B = 0);
```

---

generate\_correlation *Generates different distance matrices*

---

**Description**

Single cell complete mismatch distance, single cell complete mismatch distance with a parameter of cutoff, mismatch distance, correlation distance, p-value of correlation test distance and euclidean distance.

**Usage**

```
generate_single_cell_complete_mismatch(tmap_part1_hda,
select, alpha = 1)
generate_single_cell_mismatch_with_parameter(tmap_part1_hda,
select, alpha = 1)
generate_correlation(tmap_part1_hda, select)
generate_euclidean(tmap_part1_hda, select)
generate_mismatch_distance(tmap_part1_hda, select, alpha = 1)
generate_p_val_correlation(tmap_part1_hda, select)
```

**Arguments**

tmap_part1_hda	an object given back by <a href="#">hyperrectangle_deviation_assessment</a>
select	A sublist of rownames of tmap_part1_hda\$Dc.Dmat
alpha	A real number corresponding to a cutoff

**Details**

If one is interested only in clustering samples according to a list of genes belonging to a certain pathway, then this list is provided to the parameter select. Alpha is a cutoff for deviations that should be considered as noise, for gene expression data such as normalised RNA-seq or microarrays for instance a cutoff of 1, corresponding to a two fold change is being chosen.

**Value**

Distance matrix

**Author(s)**

Rachel Jeitziner

**Examples**

```
tmap_part1_hda <- list()
tmap_part1_hda$Dc.Dmat <- matrix(c(-1, 2, 0, -4, 5, 6), nrow = 2)
rownames(tmap_part1_hda$Dc.Dmat) <- c("Gene1", "Gene2")
colnames(tmap_part1_hda$Dc.Dmat) <- c("A", "B", "C")
dd <- TMap::generate_mismatch_distance(tmap_part1_hda, select =
rownames(tmap_part1_hda$Dc.Dmat))
dd <- TMap::generate_euclidean(tmap_part1_hda, select =
rownames(tmap_part1_hda$Dc.Dmat))
```

---

hyperrectangle\_deviation\_assessment

*Calculation of deviation components*

---

**Description**

[hyperrectangle\\_deviation\\_assessment](#) function calculates the hyperrectangle deviation assessment (HDA) that calculates the deviation components using `normal_hda2` which calculates the normal component of the test sample and `deviation_hda2` which calculates the deviation component.

**Usage**

```
hyperrectangle_deviation_assessment(x,
k = dim(x$Normal.mat)[2], dataname,
normalname, Org.directory = getwd())
```

**Arguments**

x	output object given back by <a href="#">control_adjustment</a> , list
k	A factor if not all the lines in the control group should be kept
dataname	the name of the project
normalname	A name for the corrected control files
Org.directory	where the outputs should be saved

**Details**

The function performs the hyperrectangle deviation assessment (HDA)

**Value****Outputs**

Tdis.pcl	The matrix of the deviation components for each test sample
Tnorm.pcl	The matrix of the normal components for each test sample
NormalModel.pcl	The normal model used

**Values**

Dc.Dmat	the deviation component matrix composed of the deviation components of all the samples in the test group
m	the values of the filter function per sample in the test group

**Author(s)**

Rachel Jeitziner

**See Also**

[control\\_adjustment](#), [hyperrectangle\\_deviation\\_assessment](#), [tmap\\_sgn\\_genes](#)

**Examples**

```
##a full example can be found in tmap_sgn_genes
##--
library(airway)
data(airway)
airway <- airway[rowSums(assay(airway))>80,]
assay(airway) <- log(assay(airway)+1,2)
ALPHA <- 1
the_experiment <- TMap::make_matrices(airway,
seq_len(4), seq_len(4) + 4,
rownames(airway), rownames(airway))
TMAP_part1prime <- TMap::control_adjustment(
normal.pcl = the_experiment$CTRL,
tumor.pcl = the_experiment$TEST,
normalname = "The_healthy_controls",
dataname = "Effect_of_cancer",
org.directory = tempdir(), e = 0, P = 1.1, B = 0);
Kprime <- 4;
```

```

TMAP_part1_hda <-
TMap::hyperrectangle_deviation_assessment(x =
TMAP_part1prime,
k = Kprime, dataname = "Effect_of_cancer",
normalname = "The_healthy_controls");

```

---

make_matrices	<i>Prepares the matrices for <a href="#">control_adjustment</a></i>
---------------	---

---

## Description

[make\\_matrices](#) generates the control and the test matrix in the right format

## Usage

```

make_matrices(mat, col_ctrl, col_test, NAME, CLID,
GWEIGHT = rep(1, dim(mat)[1]), EWEIGHT = 0)

```

## Arguments

mat	the gene expressions can be <b>matrix</b> , <b>data.frame</b> , " <a href="#">RangedSummarizedExperiment</a> ", " <a href="#">ExpressionSet</a> " format
col_ctrl	the columns in the matrix "mat" of the control samples
col_test	the columns in the matrix "mat" of the test samples
NAME	Name of genes, or annotation, e.g. WNT4
CLID	Identities of genes, e.g. ENSMUSG00000000001
GWEIGHT	the weight for each gene
EWEIGHT	the weight for each experiment

## Details

[make\\_matrices](#) generates the test matrix and the control matrix in the format accepted by [control\\_adjustment](#) from a matrix object

## Value

junk                    A list containing \$CTRL and \$TEST the matrices to impute in [control\\_adjustment](#)

## Author(s)

Rachel Jeitziner

## See Also

[control\\_adjustment](#), [hyperrectangle\\_deviation\\_assessment](#), [tmap\\_sgn\\_genes](#), "[RangedSummarizedExperiment](#)"



**Examples**

```

##--
##--
Aa = 6
B1 = 3
B2 = 3
C0 = 100
D0 = 10000
a0 = 4
b0 = 0.1
a1 = 6
b1 = 0.1
a2 = 2
b2 = 0.5
ALPHA = 1
E = 1
Pw = 1.1
Bw = 0
RA <- matrix(rep(0, Aa * D0), nrow = D0)
RB1 <- matrix(rep(0, B1 * D0), nrow = D0)
RB2 <- matrix(rep(0, B2 * D0), nrow = D0)
RA <- lapply(seq_len(D0 - C0), function(i) rnorm(Aa,
mean = a0, sd = sqrt(b0)))
RA<-do.call(rbind, RA)
RB1<- lapply(seq_len(D0 - C0), function(i) rnorm(B1,
mean = a0, sd = sqrt(b0)))
RB1 <- do.call(rbind, RB1)
RB2 <- lapply(seq_len(D0 - C0), function(i) rnorm(B2,
mean = a0, sd = sqrt(b0)))
RB2 <- do.call(rbind, RB2)
RA_c <- lapply(seq_len(C0), function(i) rnorm(Aa,
mean = a0, sd = sqrt(b0)))
RA_c <- do.call(rbind, RA_c)
RB1_c <- lapply(seq_len(C0), function(i) rnorm(B1,
mean = a1, sd = sqrt(b1)))
RB1_c <- do.call(rbind, RB1_c)
RB2_c <- lapply(seq_len(C0), function(i) rnorm(B2,
mean = a2, sd = sqrt(b2)))
RB2_c <- do.call(rbind, RB2_c)
norm1 <- rbind(RA, RA_c)
dis <- cbind(rbind(RB1, RB1_c), rbind(RB2, RB2_c))
colnames(norm1) <- paste("N", seq_len(Aa), sep = "")
rownames(norm1) <- c(paste("norm", seq_len(D0 - C0), sep = ""),
paste("diff", seq_len(C0), sep = ""))
colnames(dis) <- c(paste("B1", seq_len(B1), sep=""),
paste("B2", seq_len(B2), sep = ""))
rownames(dis)<-c(paste("norm",
seq_len(D0 - C0), sep = ""),
paste("diff", seq_len(C0), sep = ""))
the_experiment <- TMap::make_matrices(cbind(norm1, dis),
col_ctrl = colnames(norm1),
col_test = colnames(dis), NAME = rownames(norm1),
CLID = rownames(norm1))
###other example using SummarizedExperiment
library(airway)
data(airway)

```

```
airway <- airway[rowSums(assay(airway))>80,]
assay(airway) <- log(assay(airway)+1,2)
the_experiment <- TMap::make_matrices(airway,
seq_len(4), seq_len(4) + 4,
rownames(airway), rownames(airway))
```

---

make\_matrices-methods *Prepares the matrices for [control\\_adjustment](#)*

---

### Description

make\_matrices generates the control (output \$CTRL) and the test (output \$TEST) matrix in the right format for [control\\_adjustment](#)

### Methods

signature(mat = "data.frame") Method make\_matrice for data.frame object.

signature(mat = "matrix") Method make\_matrice for matrix object.

signature(mat = "SummarizedExperiment") Method make\_matrice for SummarizedExperiment object.

signature(mat = "RangedSummarizedExperiment") Method make\_matrice for RangedSummarizedExperiment object.

signature(mat = "ExpressionSet") Method make\_matrice for ExpressionSet object.

---

tmap

*Visualisation of the clustering*

---

### Description

Enables a quick view on the groups in the dataset (globally) and how locally they differ.

### Usage

```
tmap(tmap_part1_hda, m1,
select = row.names(tmap_part1_hda$Dc.Dmat),
ddd, e, filename = "TEST", n = 3, ad = 0, bd = 0, piq = 1,
dd = generate_mismatch_distance(tmap_part1_hda = tmap_part1_hda,
select = select), mean_value_m1 = "N", ni = 2)
```

### Arguments

tmap\_part1\_hda

list output of [hyperrectangle\\_deviation\\_assessment](#)

m1

either a user imputed vector whose names are the names of the samples with addition of .Dis. or by default it is the amount of deviation

select

Should all the features (default) or only a sublist be considered to calculate the distance

ddd	Annotation matrix with rownames the different sample names with addition of .Dis. There can be as many columns as wanted, but only the column n will be selected to annotated the clusters
e	integer parameter defining under which value two samples are considered to be close
filename	Name for the description file annotating the clusters
n	The column to be considered to annotate the clusters
ad	if ad!=0 then the clusters on the output picture will not be annotated
bd	if different than 0 (default), the output will be without outliers of the test data set (clusters composed of only "piq" element)
piq	parameter used to determine what small clusters are, see bd
dd	the distance matrix to be used
mean_value_m1	if == "N" the average of the values in m1 divided by the number of the samples are put into the legend (by default represents the average of the samples in a cluster of the mean-deviation of the features) otherwise it will show the average value of the values in m1 (is useful for instance if m1 represents the age of the samples)
ni	The column to consider to annotate the samples (is put into parenthesis) for the description file

### Details

Is the Two-tiers Mapper function. The output is an interactive image of the clusters in the different layers.

### Value

all	the clusters in the overall group
low	the clusters in the lower quartile group
mid1	the clusters in the first middle quartile group
mid2	the clusters in the second middle quartile group
high	the clusters in the higher quartile group

### Author(s)

Rachel Jeitziner

### See Also

[control\\_adjustment](#), [hyperrectangle\\_deviation\\_assessment](#), [tmap\\_sgn\\_genes](#)

### Examples

```
##--
library(airway)
data(airway)
airway <- airway[rowSums(assay(airway))>80,]
assay(airway) <- log(assay(airway)+1,2)
ALPHA <- 1
the_experiment <- TMap::make_matrices(airway,
```

```

seq_len(4), seq_len(4) + 4,
rownames(airway), rownames(airway))
TMAP_part1prime <-TMAP::control_adjustment(
normal.pcl = the_experiment$CTRL,
tumor.pcl = the_experiment$TEST,
normalname = "The_healthy_controls",
dataname = "Effect_of_cancer",
org.directory = tempdir(), e = 0, P = 1.1, B = 0);
Kprime <- 4;
TMAP_part1_hda <-
TMAP::hyperrectangle_deviation_assessment(x =
TMAP_part1prime,
k = Kprime,dataname = "Effect_of_cancer",
normalname = "The_healthy_controls");
annot <- c(paste(colnames(
the_experiment$TEST[,-(seq_len(3))]),"Dis", sep = "."),
paste(colnames(the_experiment$CTRL[
-seq_len(3)]), "Dis", sep = "."))
annot <- cbind(annot, annot)
rownames(annot)<-annot[, 1]
dd5_sgn_only <-TMAP::generate_mismatch_distance(
TMAP_part1_hda,
select=rownames(TMAP_part1_hda$Dc.Dmat), alpha = ALPHA)
TMAP_part2 <-
TMAP::tmap(TMAP_part1_hda, TMAP_part1_hda$m,
select = rownames(TMAP_part1_hda$Dc.Dmat), annot,
e = TMAP::calcul_e(dd5_sgn_only, 0.95, TMAP_part1prime, 1),
filename = "first_comparison", n = 1, dd = dd5_sgn_only)

```

---

tmap_sgn_genes	<i>Gives a list of associated genes per cluster</i>
----------------	---

---

## Description

[tmap\\_sgn\\_genes](#) function

## Usage

```

tmap_sgn_genes(tmap_part2_gtlmap, tmap_part1_hda,
tmap_part1_ctrl_adj, c, n = 2, a = 0,
filename = "TEST2", annot = tmap_part1_ctrl_adj$tag.pcl,
col = "NAME", path = getwd(), Relaxed = 1)
tmap_sgn_genes_inter2(q, tmap_part1_hda, alpha = 0)
tmap_sgn_genes_inter(q, tmap_part1_hda, alpha = 0)

```

## Arguments

tmap\_part2\_gtlmap  
output of [tmap](#)

tmap\_part1\_hda  
output of [hyperrectangle\\_deviation\\_assessment](#)

tmap\_part1\_ctrl\_adj  
output of [control\\_adjustment](#)

c	annotation file of the samples
n	column to give the name to the cluster
a	cutoff to be considered different than noise
filename	Name of the files
annot	annotation file
col	which column should be considered to annotate the features
path	where to put the output files
Relaxed	If Relaxed then one allows sample to be as the control and for all the others in one cluster to be going in the same direction (more than alpha) otherwise all the features must be deviating to be considered a significant feature
q	The sample in one cluster
alpha	cutoff to be considered different than noise inherited by a

### Details

Is giving per cluster the features that vary in the same direction

### Value

generates a file per cluster of significant features with an annotation

### Author(s)

Rachel Jeitziner

### Examples

```
##--
library(airway)
data(airway)
airway <- airway[rowSums(assay(airway))>80,]
assay(airway) <- log(assay(airway)+1,2)
ALPHA <- 1
the_experiment <- TMap::make_matrices(airway,
seq_len(4), seq_len(4) + 4,
rownames(airway), rownames(airway))
TTMAP_part1prime <-TMap::control_adjustment(
normal.pcl = the_experiment$CTRL,
tumor.pcl = the_experiment$TEST,
normalname = "The_healthy_controls",
dataname = "Effect_of_cancer",
org.directory = tempdir(), e = 0, P = 1.1, B = 0);
Kprime <- 4;
TTMAP_part1_hda <-
TMap::hyperrectangle_deviation_assessment(x =
TTMAP_part1prime,
k = Kprime,dataname = "Effect_of_cancer",
normalname = "The_healthy_controls");
annot <- c(paste(colnames(
the_experiment$TEST[,-(seq_len(3))]),"Dis", sep = "."),
paste(colnames(the_experiment$CTRL[,-seq_len(3)]), "Dis", sep = "."))
annot <- cbind(annot, annot)
```

```

rownames(annot)<-annot[, 1]
dd5_sgn_only <-TMap::generate_mismatch_distance(
TMAP_part1_hda,
select=rownames(TMAP_part1_hda$Dc.Dmat), alpha = ALPHA)
TMAP_part2 <-
TMap::tmap(TMAP_part1_hda, TMAP_part1_hda$m,
select = rownames(TMAP_part1_hda$Dc.Dmat), annot,
e = TMap::calcul_e(dd5_sgn_only, 0.95, TMAP_part1prime, 1),
filename = "first_comparison", n = 1, dd = dd5_sgn_only)
TMap::tmap_sgn_genes(TMAP_part2, TMAP_part1_hda,
TMAP_part1prime, annot,
n = 2, a = 1, filename = "first_list_of_genes",
annot = TMAP_part1prime$tag.pcl, col = "NAME",
path = getwd(), Relaxed = 1)

```

---

write\_pcl

*Reading, writing and annotation files*


---

## Description

Reading ([read\\_pcl](#)), writing ([write\\_pcl](#)) files and annotating matrices (mat2pcl)

## Usage

```

mat2pcl(mat, tag)
write_pcl(df, dataname, fileaddress = "")
read_pcl(filename, na.type = "", Nrows = -1,
Comment.char = "", ...)

```

## Arguments

df	PCL object to be saved
dataname	Name of the file
fileaddress	Where to save the file
filename	File name to be loaded on R
na.type	feels the parameter na.strings of read.table
Nrows	Number of rows to be ignored (nrows of read.table)
Comment.char	comment.char of read.table
...	other read.table arguments
mat	matrix to be changed in annotated
tag	annotation

## Details

The file (called filename) MUST contain 3 columns before the actual values, which are called CLID, NAME and GWEIGHT, described bellow. The first row must be the header of the columns (starting with CLID,NAME and GWEIGHT) and the second row must be EWEIGHT. Representing how much weight each column has: if some columns are n replicates they can have each a weight of 1/n.

**Value**

Data frame composed of

CLID	Column called CLID which is the ID of the features, which will then be the rownames of the dataframe
NAME	A possibly longer name, more meaningfull than CLID, text format
GWEIGHT	A weight for each gene or feature. If some genes are less important than others or only a pathway should be selected than the file (called filename) should have this information
Matrix	The matrix with numbers of the different observations

**Author(s)**

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**See Also**

[control\\_adjustment](#)

**Examples**

```
library(airway)
data(airway)
airway <- airway[rowSums(assay(airway))>80,]
assay(airway) <- log(assay(airway)+1,2)
ALPHA <- 1
to_be_saved <- TMap::make_matrices(airway,
seq_len(4), seq_len(4) + 4,
rownames(airway), rownames(airway))
TMap::write_pcl(to_be_saved, "tempfile()", getwd())
```

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