

# Package ‘Melissa’

September 25, 2024

**Type** Package

**Title** Bayesian clustering and imputation of single cell methylomes

**Version** 1.21.0

**Description** Melissa is a Bayesian probabilistic model for jointly clustering and imputing single cell methylomes. This is done by taking into account local correlations via a Generalised Linear Model approach and global similarities using a mixture modelling approach.

**Depends** R (>= 3.5.0), BPRMeth, GenomicRanges

**License** GPL-3 | file LICENSE

**Encoding** UTF-8

**LazyData** true

**RoxygenNote** 7.1.0

**Imports** data.table, parallel, ROCR, matrixcalc, mclust, ggplot2, doParallel, foreach, MCMCpack, cowplot, magrittr, mvtnorm, truncnorm, assertthat, BiocStyle, stats, utils

**Suggests** testthat, knitr, rmarkdown

**VignetteBuilder** knitr

**biocViews** ImmunoOncology, DNAMethylation, GeneExpression, GeneRegulation, Epigenetics, Genetics, Clustering, FeatureExtraction, Regression, RNASeq, Bayesian, KEGG, Sequencing, Coverage, SingleCell

**git\_url** <https://git.bioconductor.org/packages/Melissa>

**git\_branch** devel

**git\_last\_commit** b2edeb7

**git\_last\_commit\_date** 2024-04-30

**Repository** Bioconductor 3.20

**Date/Publication** 2024-09-24

**Author** C. A. Kapourani [aut, cre]

**Maintainer** C. A. Kapourani <kapouranis.andreas@gmail.com>

## Contents

binarise_files . . . . .	2
cluster_ari . . . . .	3
cluster_error . . . . .	4
create_melissa_data_obj . . . . .	4
eval_cluster_performance . . . . .	6
eval_imputation_performance . . . . .	7
extract_y . . . . .	8
filter_regions . . . . .	9
impute_met_files . . . . .	10
impute_test_met . . . . .	11
init_design_matrix . . . . .	12
log_sum_exp . . . . .	13
Melissa . . . . .	14
melissa . . . . .	14
melissa_encode_dt . . . . .	16
melissa_gibbs . . . . .	17
melissa_synth_dt . . . . .	19
partition_dataset . . . . .	19
plot_melissa_profiles . . . . .	20
<b>Index</b>	<b>22</b>

---

binarise_files	<i>Binarise CpG sites</i>
----------------	---------------------------

---

### Description

Script for binarising CpG sites and formatting the coverage file so it can be directly used from the BPRMeth package. The format of each file is the following: <chr> <start> <met\_level>, where met\_level can be either 0 or 1. To read compressed files, e.g ending in .gz or .bz2, the R.utils package needs to be installed.

### Usage

```
binarise_files(indir,outdir = NULL,format = 1,no_cores = NULL)
```

### Arguments

indir	Directory containing the coverage files, output from Bismark.
outdir	Directory to store the output files for each cell with exactly the same name. If NULL, then a directory called 'binarised' inside 'indir' will be create by default.
format	Integer, denoting the format of coverage file. When set to '1', the coverage file format is assumed to be: "<chr> <start> <end> <met_prg> <met_reads> <unmet_reads>". When set to '2', then the format is assumed to be: "<chr> <start> <met_prg> <met_reads> <unmet_reads>".
no_cores	Number of cores to use for parallel processing. If NULL, no parallel processing is used.

**Value**

No value is returned, the binarised data are stored in the outdir.

**Author(s)**

C.A.Kapourani <C.A.Kapourani@ed.ac.uk>

**See Also**

[create\\_melissa\\_data\\_obj](#), [melissa](#), [filter\\_regions](#)

**Examples**

```
## Not run:  
# Met directory  
met_dir <- "name_of_met_dir"  
  
binarise_files(met_dir)  
  
## End(Not run)
```

---

cluster\_ari

*Compute clustering ARI*

---

**Description**

cluster\_ari computes the clustering performance in terms of the Adjusted Rand Index (ARI) metric.

**Usage**

```
cluster_ari(C_true, C_post)
```

**Arguments**

C\_true            True cluster assignemnts.  
C\_post            Posterior responsibilities of predicted cluster assignemnts.

**Value**

The clustering ARI.

**Author(s)**

C.A.Kapourani <C.A.Kapourani@ed.ac.uk>

---

`cluster_error`      *Compute clustering assignment error* `cluster_error` computes the clustering assignment error; i.e. the average number of incorrect cluster assignments:

$$OE = \sum_{n=1}^N (I(LT_n \neq LP_n)) / N$$


---

### Description

Compute clustering assignment error

`cluster_error` computes the clustering assignment error, i.e. the average number of incorrect cluster assignments:

$$OE = \sum_{n=1}^N (I(LT_n \neq LP_n)) / N$$

### Usage

`cluster_error(C_true, C_post)`

### Arguments

`C_true`            True cluster assignments.  
`C_post`            Posterior mean of predicted cluster assignments.

### Value

The clustering assignment error

### Author(s)

C.A.Kapourani <C.A.Kapourani@ed.ac.uk>

---

`create_melissa_data_obj`

*Create methylation regions for all cells*

---

### Description

Wrapper function for creating methylation regions for all cells, which is the input object for Melissa prior to filtering.

**Usage**

```

create_melissa_data_obj(
  met_dir,
  anno_file,
  chrom_size_file = NULL,
  chr_discarded = NULL,
  is_centre = FALSE,
  is_window = TRUE,
  upstream = -5000,
  downstream = 5000,
  cov = 5,
  sd_thresh = -1,
  no_cores = NULL
)

```

**Arguments**

met_dir	Directory of (binarised) methylation files, each file corresponds to a single cell.
anno_file	The annotation file with 'tab' delimited format: "chromosome", "start", "end", "strand", "id", "name" (optional). Read the 'BPRMeth' documentation for more details.
chrom_size_file	Optional file name to read genome chromosome sizes.
chr_discarded	Optional vector with chromosomes to be discarded.
is_centre	Logical, whether 'start' and 'end' locations are pre-centred. If TRUE, the mean of the locations will be chosen as centre. If FALSE, the 'start' will be chosen as the center; e.g. for genes the 'start' denotes the TSS and we use this as centre to obtain K-bp upstream and downstream of TSS.
is_window	Whether to consider a predefined window region around centre. If TRUE, then 'upstream' and 'downstream' parameters are used, otherwise we consider the whole region from start to end location.
upstream	Integer defining the length of bp upstream of 'centre' for creating the genomic region. If is_window = FALSE, this parameter is ignored.
downstream	Integer defining the length of bp downstream of 'centre' for creating the genomic region. If is_window = FALSE, this parameter is ignored.
cov	Integer defining the minimum coverage of CpGs that each region must contain.
sd_thresh	Optional numeric defining the minimum standard deviation of the methylation change in a region. This is used to filter regions with no methylation variability.
no_cores	Number of cores to be used for parallel processing of data.

**Value**

A melissa\_data\_obj object, with the following elements:

- met: A list of elements of length N, where N are the total number of cells. Each element in the list contains another list of length M, where M is the total number of genomic regions, e.g. promoters. Each element in the inner list is an I x 2 matrix, where I are the total number of observations. The first column contains the input observations x (i.e. CpG locations) and the 2nd column contains the corresponding methylation level.
- anno\_region: The annotation object.
- opts: A list with the parameters that were used for creating the object.

**Author(s)**

C.A.Kapourani <C.A.Kapourani@ed.ac.uk>

**See Also**

[binarise\\_files](#), [melissa](#), [filter\\_regions](#)

**Examples**

```
## Not run:
# Met directory
met_dir <- "name_of_met_dir"
# Annotation file name
anno_file <- "name_of_anno_file"

obj <- create_melissa_data_obj(met_dir, anno_file)

# Extract annotation regions
met <- obj$met

# Extract annotation regions
anno <- obj$anno_region

## End(Not run)
```

---

eval\_cluster\_performance

*Evaluate clustering performance*

---

**Description**

eval\_cluster\_performance is a wrapper function for computing clustering performance in terms of ARI and clustering assignment error.

**Usage**

```
eval_cluster_performance(obj, C_true)
```

**Arguments**

obj	Output of Melissa inference object.
C_true	True cluster assignemnts.

**Value**

The ‘melissa’ object, with an additional slot named ‘clustering’, containing the ARI and clustering assignment error performance.

**Author(s)**

C.A.Kapourani <C.A.Kapourani@ed.ac.uk>

**See Also**

[create\\_melissa\\_data\\_obj](#), [melissa](#), [filter\\_regions](#), [eval\\_imputation\\_performance](#), [eval\\_cluster\\_performa](#)

**Examples**

```
## Extract synthetic data
dt <- melissa_synth_dt

# Partition to train and test set
dt <- partition_dataset(dt)

# Create basis object from BPRMeth package
basis_obj <- BPRMeth::create_rbf_object(M = 3)

# Run Melissa
melissa_obj <- melissa(X = dt$met, K = 2, basis = basis_obj, vb_max_iter = 10,
  vb_init_nstart = 1, is_parallel = FALSE, is_verbose = FALSE)

# Compute cluster performance
melissa_obj <- eval_cluster_performance(melissa_obj, dt$opts$C_true)

cat("ARI: ", melissa_obj$clustering$ari)
```

---

eval\_imputation\_performance

*Evaluate imputation performance*

---

**Description**

eval\_imputation\_performance is a wrapper function for computing imputation/clustering performance in terms of different metrics, such as AUC and precision recall curves.

**Usage**

```
eval_imputation_performance(obj, imputation_obj)
```

**Arguments**

**obj** Output of Melissa inference object.

**imputation\_obj** List containing two vectors of equal length, corresponding to true methylation states and predicted/imputed methylation states.

**Value**

The 'melissa' object, with an additional slot named 'imputation', containing the AUC, F-measure, True Positive Rate (TPR) and False Positive Rate (FPR), and Precision Recall (PR) curves.

**Author(s)**

C.A.Kapourani <C.A.Kapourani@ed.ac.uk>

**See Also**

[create\\_melissa\\_data\\_obj](#), [melissa](#), [impute\\_test\\_met](#), [filter\\_regions](#), [eval\\_imputation\\_performance](#), [eval\\_cluster\\_performance](#)

**Examples**

```
# First take a subset of cells to efficiency
# Extract synthetic data
dt <- melissa_synth_dt

# Partition to train and test set
dt <- partition_dataset(dt)

# Create basis object from BPRMeth package
basis_obj <- BPRMeth::create_rbf_object(M = 3)

# Run Melissa
melissa_obj <- melissa(X = dt$met, K = 2, basis = basis_obj, vb_max_iter = 10,
  vb_init_nstart = 1, is_parallel = FALSE, is_verbose = FALSE)

imputation_obj <- impute_test_met(obj = melissa_obj, test = dt$met_test)

melissa_obj <- eval_imputation_performance(obj = melissa_obj,
  imputation_obj = imputation_obj)

cat("AUC: ", melissa_obj$imputation$auc)
```

---

extract\_y

*Extract responses y*

---

**Description**

Given a list of observations, extract responses y

**Usage**

```
extract_y(X, coverage_ind)
```

**Arguments**

X	Observations
coverage_ind	Which observations have coverage

**Value**

The design matrix H





```
# Run on synthetic data from Melissa package
filt_obj <- filter_by_variability(melissa_encode_dt, min_var = 0.1)
```

---

```
impute_met_files      Impute/predict methylation files
```

---

### Description

Make predictions of missing methylation states, i.e. perform imputation using Melissa. Each file in the directory will be used as input and a new file will be created in `outdir` with an additional column containing the predicted met state (value between 0 and 1). Note that predictions will be made only on annotation regions that were used for training Melissa. Check [impute\\_test\\_met](#), if you want to make predictions only on test data.

### Usage

```
impute_met_files(
  met_dir,
  outdir = NULL,
  obj,
  anno_region,
  basis = NULL,
  is_predictive = TRUE,
  no_cores = NULL
)
```

### Arguments

<code>met_dir</code>	Directory of methylation files, each file corresponds to a single cell. It should contain three columns <code>&lt;chr&gt;</code> <code>&lt;pos&gt;</code> <code>&lt;met_state&gt;</code> (similar to the input required by <a href="#">create_melissa_data_obj</a> ), where <code>met_state</code> can be any value that denotes missing CpG information, e.g. -1. Note that files can contain also CpGs for which we have coverage information, and we can check the predictions made by Melissa, hence the value can also be 0 (unmet) or (1) met. Predictions made by Melissa, will not change the <code>&lt;met_state&gt;</code> column. Melissa will just add an additional column named <code>&lt;predicted&gt;</code> .
<code>outdir</code>	Directory to store the output files for each cell with exactly the same name. If NULL, then a directory called 'imputed' inside 'met_dir' will be created by default.
<code>obj</code>	Output of Melissa inference object.
<code>anno_region</code>	Annotation region object. This will be the output of <a href="#">create_melissa_data_obj</a> function, e.g. <code>melissa_data\$anno_region</code> . This is required to select those regions that were used to train Melissa.
<code>basis</code>	Basis object, if NULL we perform imputation using Melissa, otherwise using BPRMeth (then <code>obj</code> should be BPRMeth output).
<code>is_predictive</code>	Logical, use predictive distribution for imputation, or choose the cluster label with the highest responsibility.
<code>no_cores</code>	Number of cores to be used for parallel processing of data.

**Value**

A new directory `outdir` containing files (cells) with predicted / imputed methylation states per CpG location.

**Author(s)**

C.A.Kapourani <C.A.Kapourani@ed.ac.uk>

**See Also**

[create\\_melissa\\_data\\_obj](#), [melissa](#), [filter\\_regions](#)

**Examples**

```
## Not run:
# Met directory
met_dir <- "name_of_met_dir"
# Annotation file name
anno_file <- "name_of_anno_file"
# Create data object
melissa_data <- create_melissa_data_obj(met_dir, anno_file)
# Run Melissa
melissa_obj <- melissa(X = melissa_data$met, K = 2)
# Annotation object
anno_region <- melissa_data$anno_region

# Perform imputation
impute_met_dir <- "name_of_met_dir_for_imputing_cells"
out <- impute_met_files(met_dir = impute_met_dir, obj = melissa_obj,
                       anno_region = anno_region)

## End(Not run)
```

---

impute\_test\_met

*Impute/predict test methylation states*

---

**Description**

Make predictions of missing methylation states, i.e. perform imputation using Melissa. This requires keeping a subset of data as a held out test set during Melissa inference. If you want to impute a whole directory containing cells (files) with missing methylation levels, see [impute\\_met\\_files](#).

**Usage**

```
impute_test_met(
  obj,
  test,
  basis = NULL,
  is_predictive = TRUE,
  return_test = FALSE
)
```

**Arguments**

obj	Output of Melissa inference object.
test	Test data to evaluate performance.
basis	Basis object, if NULL we perform imputation using Melissa, otherwise using BPRMeth.
is_predictive	Logical, use predictive distribution for imputation, or choose the cluster label with the highest responsibility.
return_test	Whether or not to return a list with the predictions.

**Value**

A list containing two vectors, the true methylation state and the predicted/imputed methylation states.

**Author(s)**

C.A.Kapourani <C.A.Kapourani@ed.ac.uk>

**See Also**

[create\\_melissa\\_data\\_obj](#), [melissa](#), [filter\\_regions](#), [eval\\_imputation\\_performance](#), [eval\\_cluster\\_performance](#)

**Examples**

```
# Extract synthetic data
dt <- melissa_synth_dt

# Partition to train and test set
dt <- partition_dataset(dt)

# Create basis object from BPRMeth package
basis_obj <- BPRMeth::create_rbf_object(M = 3)

# Run Melissa
melissa_obj <- melissa(X = dt$met, K = 2, basis = basis_obj, vb_max_iter=10,
  vb_init_nstart = 1, is_parallel = FALSE, is_verbose = FALSE)

imputation_obj <- impute_test_met(obj = melissa_obj,
  test = dt$met_test)
```

---

init\_design\_matrix     *Initialise design matrices*

---

**Description**

Given a list of observations, initialise design matrices H for computational efficiency.

**Usage**

```
init_design_matrix(basis, X, coverage_ind)
```

**Arguments**

basis	Basis object.
X	Observations
coverage_ind	Which observations have coverage

**Value**

The design matrix H

---

log_sum_exp	<i>Compute stable log-sum-exp</i>
-------------	-----------------------------------

---

**Description**

log\_sum\_exp computes the log sum exp trick for avoiding numeric underflow and have numeric stability in computations of small numbers.

**Usage**

```
log_sum_exp(x)
```

**Arguments**

x	A vector of observations
---	--------------------------

**Value**

The logs-sum-exp value

**Author(s)**

C.A.Kapourani <C.A.Kapourani@ed.ac.uk>

**References**

<https://hips.seas.harvard.edu/blog/2013/01/09/computing-log-sum-exp/>

---

Melissa	Melissa: <i>Bayesian clustering and imputation of single cell methylomes</i>
---------	--

---

**Description**

Bayesian clustering and imputation of single cell methylomes

**Usage**

```
.datatable.aware
```

**Format**

An object of class `logical` of length 1.

**Value**

Melissa main package documentation.

**Author(s)**

C.A.Kapourani <kapouranis.andreas@gmail.com>

**See Also**

[melissa](#), [create\\_melissa\\_data\\_obj](#), [partition\\_dataset](#), [plot\\_melissa\\_profiles](#), [filter\\_regions](#)

---

melissa	<i>Cluster and impute single cell methylomes using VB</i>
---------	---

---

**Description**

`melissa` clusters and imputes single cells based on their methylome landscape on specific genomic regions, e.g. promoters, using the Variational Bayes (VB) EM-like algorithm.

**Usage**

```
melissa(  
  X,  
  K = 3,  
  basis = NULL,  
  delta_0 = NULL,  
  w = NULL,  
  alpha_0 = 0.5,  
  beta_0 = NULL,  
  vb_max_iter = 300,  
  epsilon_conv = 1e-05,  
  is_kmeans = TRUE,  
  vb_init_nstart = 10,
```

```

    vb_init_max_iter = 20,
    is_parallel = FALSE,
    no_cores = 3,
    is_verbose = TRUE
)

```

## Arguments

X	The input data, which has to be a <a href="#">list</a> of elements of length N, where N are the total number of cells. Each element in the list contains another list of length M, where M is the total number of genomic regions, e.g. promoters. Each element in the inner list is an I X 2 matrix, where I are the total number of observations. The first column contains the input observations x (i.e. CpG locations) and the 2nd columns contains the corresponding methylation level.
K	Integer denoting the total number of clusters K.
basis	A 'basis' object. E.g. see <code>create_basis</code> function from BPRMeth package. If NULL, will an RBF object with 3 basis functions will be created.
delta_0	Parameter vector of the Dirichlet prior on the mixing proportions pi.
w	Optional, an Mx(D)xK array of the initial parameters, where first dimension are the genomic regions M, 2nd the number of covariates D (i.e. basis functions), and 3rd are the clusters K. If NULL, will be assigned with default values.
alpha_0	Hyperparameter: shape parameter for Gamma distribution. A Gamma distribution is used as prior for the precision parameter tau.
beta_0	Hyperparameter: rate parameter for Gamma distribution. A Gamma distribution is used as prior for the precision parameter tau.
vb_max_iter	Integer denoting the maximum number of VB iterations.
epsilon_conv	Numeric denoting the convergence threshold for VB.
is_kmeans	Logical, use Kmeans for initialization of model parameters.
vb_init_nstart	Number of VB random starts for finding better initialization.
vb_init_max_iter	Maximum number of mini-VB iterations.
is_parallel	Logical, indicating if code should be run in parallel.
no_cores	Number of cores to be used, default is <code>max_no_cores - 1</code> .
is_verbose	Logical, print results during VB iterations.

## Value

An object of class `melissa` with the following elements:

- `W`: An (M+1) X K matrix with the optimized parameter values for each cluster, M are the number of basis functions. Each column of the matrix corresponds a different cluster k.
- `W_Sigma`: A list with the covariance matrices of the posterior parameter W for each cluster k.
- `r_nk`: An (N X K) responsibility matrix of each observations being explained by a specific cluster.
- `delta`: Optimized Dirichlet parameter for the mixing proportions.
- `alpha`: Optimized shape parameter of Gamma distribution.
- `beta`: Optimized rate parameter of the Gamma distribution

- basis: The basis object.
- lb: The lower bound vector.
- labels: Cluster assignment labels.
- pi\_k: Expected value of mixing proportions.

### Details

The modelling and mathematical details for clustering profiles using mean-field variational inference are explained here: <http://rpubs.com/cakapourani/>. More specifically:

- For Binomial/Bernoulli observation model check: <http://rpubs.com/cakapourani/vb-mixture-bpr>
- For Gaussian observation model check: <http://rpubs.com/cakapourani/vb-mixture-lr>

### Author(s)

C.A.Kapourani <C.A.Kapourani@ed.ac.uk>

### See Also

[create\\_melissa\\_data\\_obj](#), [partition\\_dataset](#), [plot\\_melissa\\_profiles](#), [impute\\_test\\_met](#), [impute\\_met\\_files](#), [filter\\_regions](#)

### Examples

```
# Example of running Melissa on synthetic data

# Create RBF basis object with 4 RBFs
basis_obj <- BPRMeth::create_rbf_object(M = 4)

set.seed(15)
# Run Melissa
melissa_obj <- melissa(X = melissa_synth_dt$met, K = 2, basis = basis_obj,
  vb_max_iter = 10, vb_init_nstart = 1, vb_init_max_iter = 5,
  is_parallel = FALSE, is_verbose = FALSE)

# Extract mixing proportions
print(melissa_obj$pi_k)
```

---

melissa\_encode\_dt

*Synthetic ENCODE single cell methylation data*

---

### Description

Small synthetic ENCODE data generated by inferring methylation profiles from bulk ENCODE data, and subsequently generating single cells. It consists of  $N = 200$  cells and  $M = 100$  genomic regions. The data are in the required format for directly running Melissa and are used as a case study for the vignette.

### Usage

melissa\_encode\_dt



**Format**

A list object containing methylation regions, annotation data and the options used for creating the data. This in general would be the output of the `create_melissa_data_obj` function. It has the following three objects:

- `met`: A list containing the methylation data, each element of the list is a different cell.
- `anno_region`: Corresponding annotation data for each genomic region.
- `opts`: Parameters/options used to generate the data.

**Value**

Synthetic ENCODE methylation data

**See Also**

[create\\_melissa\\_data\\_obj](#)

---

melissa\_gibbs

*Gibbs sampling algorithm for Melissa model*

---

**Description**

`melissa_gibbs` implements the Gibbs sampling algorithm for performing clustering of single cells based on their DNA methylation profiles, where the observation model is the Bernoulli distributed Probit Regression likelihood. NOTE: that Gibbs sampling is really slow and we recommend using the VB implementation: [melissa](#).

**Usage**

```
melissa_gibbs(  
  X,  
  K = 2,  
  pi_k = rep(1/K, K),  
  w = NULL,  
  basis = NULL,  
  w_0_mean = NULL,  
  w_0_cov = NULL,  
  dir_a = rep(1, K),  
  lambda = 1/2,  
  gibbs_nsim = 1000,  
  gibbs_burn_in = 200,  
  inner_gibbs = FALSE,  
  gibbs_inner_nsim = 50,  
  is_parallel = TRUE,  
  no_cores = NULL,  
  is_verbose = FALSE  
)
```

**Arguments**

<code>X</code>	A list of length <code>I</code> , where <code>I</code> are the total number of cells. Each element of the list contains another list of length <code>N</code> , where <code>N</code> is the total number of genomic regions. Each element of the inner list is an <code>L x 2</code> matrix of observations, where 1st column contains the locations and the 2nd column contains the methylation level of the corresponding CpGs.
<code>K</code>	Integer denoting the number of clusters <code>K</code> .
<code>pi_k</code>	Vector of length <code>K</code> , denoting the mixing proportions.
<code>w</code>	A <code>N x M x K</code> array, where each column contains the basis function coefficients for the corresponding cluster.
<code>basis</code>	A 'basis' object. E.g. see <code>create_rbf_object</code> from <code>BPRMeth</code> package
<code>w_0_mean</code>	The prior mean hyperparameter for <code>w</code>
<code>w_0_cov</code>	The prior covariance hyperparameter for <code>w</code>
<code>dir_a</code>	The Dirichlet concentration parameter, prior over <code>pi_k</code>
<code>lambda</code>	The complexity penalty coefficient for penalized regression.
<code>gibbs_nsim</code>	Argument giving the number of simulations of the Gibbs sampler.
<code>gibbs_burn_in</code>	Argument giving the burn in period of the Gibbs sampler.
<code>inner_gibbs</code>	Logical, indicating if we should perform Gibbs sampling to sample from the augmented BPR model.
<code>gibbs_inner_nsim</code>	Number of inner Gibbs simulations.
<code>is_parallel</code>	Logical, indicating if code should be run in parallel.
<code>no_cores</code>	Number of cores to be used, default is <code>max_no_cores - 1</code> .
<code>is_verbose</code>	Logical, print results during EM iterations

**Value**

An object of class `melissa_gibbs`.

**Author(s)**

C.A.Kapourani <C.A.Kapourani@ed.ac.uk>

**See Also**

[melissa](#), [create\\_melissa\\_data\\_obj](#), [partition\\_dataset](#), [filter\\_regions](#)

**Examples**

```
# Example of running Melissa Gibbs on synthetic data

# Create RBF basis object with 4 RBFs
basis_obj <- BPRMeth::create_rbf_object(M = 4)

set.seed(15)
# Run Melissa Gibbs
melissa_obj <- melissa_gibbs(X = melissa_synth_dt$met, K = 2, basis = basis_obj,
  gibbs_nsim = 10, gibbs_burn_in = 5, is_parallel = FALSE, is_verbose = FALSE)
```

```
# Extract mixing proportions
print(melissa_obj$pi_k)
```

---

melissa_synth_dt	<i>Synthetic single cell methylation data</i>
------------------	---

---

### Description

Small synthetic data for quick analysis. It consists of  $N = 50$  cells and  $M = 50$  genomic regions.

### Usage

```
melissa_synth_dt
```

### Format

A list object containing methylation regions, annotation data and the options used for creating the data. This in general would be the output of the [create\\_melissa\\_data\\_obj](#) function. It has the following three objects:

- met: A list containing the methylation data, each element of the list is a different cell.
- anno\_region: Corresponding annotation data for each genomic region.
- opts: Parameters/options used to generate the data.

### Value

Synthetic methylation data

### See Also

[create\\_melissa\\_data\\_obj](#)

---

partition_dataset	<i>Partition synthetic dataset to training and test set</i>
-------------------	---

---

### Description

Partition synthetic dataset to training and test set

### Usage

```
partition_dataset(
  dt_obj,
  data_train_prcg = 0.5,
  region_train_prcg = 0.95,
  cpG_train_prcg = 0.5,
  is_synth = FALSE
)
```

**Arguments**

dt\_obj            Melissa data object  
data\_train\_prcg    Percentage of genomic regions that will be fully used for training, i.e. across the whole region we will have no CpGs missing.  
region\_train\_prcg    Fraction of genomic regions to keep for training set, i.e. some genomic regions will have no coverage at all during training.  
cpg\_train\_prcg    Fraction of CpGs in each genomic region to keep for training set.  
is\_synth           Logical, whether we have synthetic data or not.

**Value**

The Melissa object with the following changes. The 'met' element will now contain only the 'training' data. An additional element called 'met\_test' will store the data that will be used during testing to evaluate the imputation performance. These data will not be seen from Melissa during inference.

**Author(s)**

C.A.Kapourani <C.A.Kapourani@ed.ac.uk>

**See Also**

[create\\_melissa\\_data\\_obj](#), [melissa](#), [filter\\_regions](#)

**Examples**

```
# Partition the synthetic data from Melissa package
dt <- partition_dataset(melissa_encode_dt)
```

---

plot\_melissa\_profiles *Plot predictive methylation profiles*

---

**Description**

This function plots the predictive distribution of the methylation profiles inferred using the Melissa model. Each colour corresponds to a different cluster.

**Usage**

```
plot_melissa_profiles(
  melissa_obj,
  region = 1,
  title = "Melissa profiles",
  x_axis = "genomic region",
  y_axis = "met level",
  x_labels = c("Upstream", "", "Centre", "", "Downstream"),
  ...
)
```

**Arguments**

<code>melissa_obj</code>	Clustered cell subtypes using Melissa inference functions.
<code>region</code>	Genomic region number.
<code>title</code>	Plot title
<code>x_axis</code>	x axis label
<code>y_axis</code>	x axis label
<code>x_labels</code>	x axis ticks labels
<code>...</code>	Additional parameters

**Value**

A ggplot2 object.

**Author(s)**

C.A.Kapourani <C.A.Kapourani@ed.ac.uk>

**See Also**

[create\\_melissa\\_data\\_obj](#), [melissa](#), [filter\\_regions](#), [eval\\_imputation\\_performance](#), [eval\\_cluster\\_performance](#)

**Examples**

```
# Extract synthetic data
dt <- melissa_synth_dt

# Create basis object from BPRMeth package
basis_obj <- BPRMeth::create_rbf_object(M = 3)

# Run Melissa
melissa_obj <- melissa(X = dt$met, K = 2, basis = basis_obj, vb_max_iter = 10,
  vb_init_nstart = 1, is_parallel = FALSE, is_verbose = FALSE)

gg <- plot_melissa_profiles(melissa_obj, region = 10)
```

# Index

## \* datasets

- Melissa, [14](#)
- melissa\_encode\_dt, [16](#)
- melissa\_synth\_dt, [19](#)
- .datatable.aware (Melissa), [14](#)
  
- binarise\_files, [2, 6](#)
  
- cluster\_ari, [3](#)
- cluster\_error, [4](#)
- create\_melissa\_data\_obj, [3, 4, 7–12, 14, 16–21](#)
  
- eval\_cluster\_performance, [6, 7, 8, 12, 21](#)
- eval\_imputation\_performance, [7, 7, 8, 12, 21](#)
  
- extract\_y, [8](#)
  
- filter\_by\_coverage\_across\_cells  
(filter\_regions), [9](#)
- filter\_by\_cpg\_coverage  
(filter\_regions), [9](#)
- filter\_by\_variability (filter\_regions),  
[9](#)
- filter\_cpgs, (filter\_regions), [9](#)
- filter\_regions, [3, 6–8, 9, 11, 12, 14, 16, 18, 20, 21](#)
  
- impute\_met\_files, [10, 11, 16](#)
- impute\_test\_met, [8, 10, 11, 16](#)
- init\_design\_matrix, [12](#)
  
- list, [15](#)
- log\_sum\_exp, [13](#)
  
- Melissa, [14](#)
- melissa, [3, 6–9, 11, 12, 14, 14, 17, 18, 20, 21](#)
- melissa\_cluster, (melissa), [14](#)
- melissa\_encode\_dt, [16](#)
- melissa\_filter (filter\_regions), [9](#)
- melissa\_gibbs, [17](#)
- melissa\_impute, (melissa), [14](#)
- melissa\_synth\_dt, [19](#)
- melissa\_vb (melissa), [14](#)
  
- partition\_dataset, [14, 16, 18, 19](#)
- plot\_melissa\_profiles, [14, 16, 20](#)