

# Package ‘cfTools’

October 2, 2025

**Type** Package

**Title** Informatics Tools for Cell-Free DNA Study

**Version** 1.9.0

**Description** The cfTools R package provides methods for cell-free DNA (cfDNA) methylation data analysis to facilitate cfDNA-based studies. Given the methylation sequencing data of a cfDNA sample, for each cancer marker or tissue marker, we deconvolve the tumor-derived or tissue-specific reads from all reads falling in the marker region. Our read-based deconvolution algorithm exploits the pervasiveness of DNA methylation for signal enhancement, therefore can sensitively identify a trace amount of tumor-specific or tissue-specific cfDNA in plasma. cfTools provides functions for (1) cancer detection: sensitively detect tumor-derived cfDNA and estimate the tumor-derived cfDNA fraction (tumor burden); (2) tissue deconvolution: infer the tissue type composition and the cfDNA fraction of multiple tissue types for a plasma cfDNA sample. These functions can serve as foundations for more advanced cfDNA-based studies, including cancer diagnosis and disease monitoring.

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|             |                          |
|-------------|--------------------------|
| beta_matrix | <i>Beta value matrix</i> |
|-------------|--------------------------|

---

Description

A list of methylation levels (e.g., beta values), where each row is a sample and each column is a marker

**Usage**

```
data("beta_matrix")
```

**Format**

A tibble with 20 rows and 3 variables

**marker1** Beta values of marker1 for all samples

**marker2** Beta values of marker2 for all samples

**marker3** Beta values of marker3 for all samples

**Value**

A tibble with 20 rows and 3 variables

**Author(s)**

Ran Hu <huran@ucla.edu>

---

CancerDetector

*Cancer Detector*

---

**Description**

Detect tumor-derived cfDNA and estimate the tumor burden.

**Usage**

```
CancerDetector(  
  readsBinningFile,  
  tissueMarkersFile,  
  lambda = 0.5,  
  id = "sample"  
)
```

**Arguments**

**readsBinningFile** a file of the fragment-level methylation states of reads that mapped to the markers.

**tissueMarkersFile** a file of paired shape parameters of beta distributions for markers.

**lambda** a number controlling "confounding" markers' distance from average markers.

**id** the sample ID.

**Value**

a list containing the cfDNA tumor burden and the normal cfDNA fraction.

## Examples

```
## input files
demo.dir <- system.file("data", package="cfTools")
readsBinningFile <- file.path(demo.dir, "CancerDetector.reads.txt.gz")
tissueMarkersFile <- file.path(demo.dir, "CancerDetector.markers.txt.gz")
lambda <- 0.5
id <- "test"

CancerDetector(readsBinningFile, tissueMarkersFile, lambda, id)
```

---

CancerDetector.markers

*Cancer-specific marker parameter*

---

## Description

The paired shape parameters of beta distributions for cancer-specific markers

## Usage

```
data("CancerDetector.markers")
```

## Format

A tibble with 1266 rows and 3 variables

**markerName** Name of the marker

**tumor** Paired beta distribution shape parameters for tumor samples

**normalPlasma** Paired beta distribution shape parameters for normal plasma samples

## Value

A tibble with 1266 rows and 3 variables

## Author(s)

Ran Hu <huran@ucla.edu>

---

CancerDetector.reads    *Fragment-level methylation state for cancer detection*

---

### Description

The fragment-level methylation states of reads that mapped to the cancer-specific markers

### Usage

```
data("CancerDetector.reads")
```

### Format

A tibble with 9991 rows and 2 variables

**markerName** Name of the marker

**methState** Fragment-level methylation states, which are represented by a sequence of binary values (0 represents unmethylated CpG and 1 represents methylated CpG on the same fragment)

### Value

A tibble with 9991 rows and 2 variables

### Author(s)

Ran Hu <huran@ucla.edu>

---

cfDeconvolve    *cfDNA methylation read deconvolution*

---

### Description

Infer the tissue-type composition of plasma cfDNA.

### Usage

```
cfDeconvolve(
  readsBinningFile,
  tissueMarkersFile,
  numTissues,
  emAlgorithmType = "em.global.unknown",
  likelihoodRatioThreshold = 2,
  emMaxIterations = 100,
  randomSeed = 0,
  id = "sample"
)
```

**Arguments**

|                          |                                                                                                                                      |
|--------------------------|--------------------------------------------------------------------------------------------------------------------------------------|
| readsBinningFile         | a file of the fragment-level methylation states of reads that mapped to the markers. Either in plain text or compressed form.        |
| tissueMarkersFile        | a file of paired shape parameters of beta distributions for markers.                                                                 |
| numTissues               | a number of tissue types.                                                                                                            |
| emAlgorithmType          | a read-based tissue deconvolution EM algorithm type: em.global.unknown (default), em.global.known, em.local.unknown, em.local.known. |
| likelihoodRatioThreshold | a positive float number. Default is 2.                                                                                               |
| emMaxIterations          | a number of EM algorithm maximum iteration. Default is 100.                                                                          |
| randomSeed               | a random seed that initialize the EM algorithm. Default is 0.                                                                        |
| id                       | the sample ID.                                                                                                                       |

**Value**

a list containing the cfDNA fractions of different tissue types and an unknown class.

**Examples**

```
## input files
demo.dir <- system.file("data", package="cfTools")
readsBinningFile <- file.path(demo.dir, "cfDeconvolve.reads.txt.gz")
tissueMarkersFile <- file.path(demo.dir, "cfDeconvolve.markers.txt.gz")
numTissues <- 7
emAlgorithmType <- "em.global.unknown"
likelihoodRatioThreshold <- 2
emMaxIterations <- 100
randomSeed <- 0
id <- "test"

cfDeconvolve(readsBinningFile, tissueMarkersFile, numTissues,
emAlgorithmType, likelihoodRatioThreshold, emMaxIterations, randomSeed, id)
```

---

cfDeconvolve.markers    *Tissue-specific marker parameter*

---

**Description**

The paired shape parameters of beta distributions for tissue-specific markers

**Usage**

```
data("cfDeconvolve.markers")
```

**Format**

A tibble with 10 rows and 8 variables

**markerName** Name of the marker

**tissue1** Paired beta distribution shape parameters for tissue1 samples

**tissue2** Paired beta distribution shape parameters for tissue2 samples

**tissue3** Paired beta distribution shape parameters for tissue3 samples

**tissue4** Paired beta distribution shape parameters for tissue4 samples

**tissue5** Paired beta distribution shape parameters for tissue5 samples

**tissue6** Paired beta distribution shape parameters for tissue6 samples

**tissue7** Paired beta distribution shape parameters for tissue7 samples

**Value**

A tibble with 10 rows and 8 variables

**Author(s)**

Ran Hu <huran@ucla.edu>

---

|                    |                                                                  |
|--------------------|------------------------------------------------------------------|
| cfDeconvolve.reads | <i>Fragment-level methylation state for tissue deconvolution</i> |
|--------------------|------------------------------------------------------------------|

---

**Description**

The fragment-level methylation states of reads that mapped to the tissue-specific markers

**Usage**

```
data("cfDeconvolve.reads")
```

**Format**

A tibble with 942 rows and 2 variables

**markerName** Name of the marker

**methState** Fragment-level methylation states, which are represented by a sequence of binary values (0 represents unmethylated CpG and 1 represents methylated CpG on the same fragment)

**Value**

A tibble with 942 rows and 2 variables

**Author(s)**

Ran Hu <huran@ucla.edu>

---

|        |                                     |
|--------|-------------------------------------|
| cfSort | <i>cfSort: tissue deconvolution</i> |
|--------|-------------------------------------|

---

### Description

Tissue deconvolution in cfDNA using DNN models.

### Usage

```
cfSort(readsBinningFile, id = "sample")
```

### Arguments

|                  |                                                                                                                 |
|------------------|-----------------------------------------------------------------------------------------------------------------|
| readsBinningFile | a file of the fragment-level methylation states of reads that mapped to the cfSort markers. In compressed form. |
| id               | the sample ID.                                                                                                  |

### Value

the tissue composition of the cfDNA sample.

### Examples

```
## input files
demo.dir <- system.file("data", package="cfTools")
readsBinningFile <- file.path(demo.dir, "cfSort_reads.txt.gz")
id <- "test"

cfSort(readsBinningFile, id)
```

---

|                |                       |
|----------------|-----------------------|
| cfSort_markers | <i>cfSort markers</i> |
|----------------|-----------------------|

---

### Description

Marker information for the cfSort function, where each row is the information about a marker

### Usage

```
data("cfSort_markers")
```

### Format

A tibble with 51035 rows and 4 variables

**marker\_index** The marker index used in cfSort method

**alpha\_threshold** The alpha threshold for each marker

**pair** The pair of tissues used for identifying the marker

**group** The group number for each marker



**Value**

A tibble with 51035 rows and 4 variables

**Author(s)**

Ran Hu <huran@ucla.edu>

---

|              |                                                                         |
|--------------|-------------------------------------------------------------------------|
| cfSort_reads | <i>Fragment-level methylation state for cfSort tissue deconvolution</i> |
|--------------|-------------------------------------------------------------------------|

---

**Description**

The fragment-level methylation states of reads that mapped to the cfSort markers

**Usage**

```
data("cfSort_reads")
```

**Format**

A tibble with 99999 rows and 2 variables

**markerName** Name of the cfSort marker

**methState** Fragment-level methylation states, which are represented by a sequence of binary values (0 represents unmethylated CpG and 1 represents methylated CpG on the same fragment)

**Value**

A tibble with 99999 rows and 2 variables

**Author(s)**

Ran Hu <huran@ucla.edu>

---

|         |                                                                      |
|---------|----------------------------------------------------------------------|
| cfTools | <i>cfTools: a versatile package for analyzing cell-free DNA data</i> |
|---------|----------------------------------------------------------------------|

---

**Description**

Given the methylation sequencing data of a cell-free DNA (cfDNA) sample, for each cancer marker or tissue marker, we deconvolve the tumor-derived or tissue-specific reads from all reads falling in the marker region. Our read-based deconvolution algorithm exploits the pervasiveness of DNA methylation for signal enhancement, therefore can sensitively identify a trace amount of tumor-specific or tissue-specific cfDNA in plasma.

**Details**

Specifically, cfTools can deconvolve different sources of cfDNA fragments (or reads) in two contexts:

1. Cancer detection: separate cfDNA fragments into tumor-derived fragments and background normal fragments (2 classes), and estimate the tumor-derived cfDNA fraction.
2. Tissue deconvolution: separate cfDNA fragments from different tissues (> 2 classes), and estimate the cfDNA fraction of different tissue types (including an unknown type) for a plasma cfDNA sample.

These functions can serve as foundations for more advanced cfDNA-based studies, including cancer diagnosis and disease monitoring.

For an overview of the functionality provided by the package, please see the vignette: `vignette(package="cfTools")`

**Author(s)**

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**See Also**

[CancerDetector](#), [cfDeconvolve](#), [cfSort](#), [MergeCpGs](#), [MergePereads](#), [GenerateFragMeth](#), [GenerateMarkerParam](#), [PlotFractionPie](#)

---

CpG\_OB\_demo

*Methylation information for CpG on the original bottom strand (OB)*

---

**Description**

Methylation information for CpG on the original bottom strand (OB), which is one of the outputs from 'bismark methylation extractor'

**Usage**

```
data("CpG_OB_demo")
```

**Format**

A tibble with 2224 rows and 5 variables

**sequence ID** ID of the sequence

**methylation state** Methylated or unmethylated CpG site

**chromosome name** Chromosome name

**chromosome start** Chromosome start position

**methylation call** Methylation call

**Value**

A tibble with 2224 rows and 5 variables

**Author(s)**

Ran Hu <huran@ucla.edu>

---

`CpG_OT_demo`*Methylation information for CpG on the original top strand (OT)*

---

**Description**

Methylation information for CpG on the original top strand (OT), which is one of the outputs from 'bismark methylation extractor'

**Usage**

```
data("CpG_OT_demo")
```

**Format**

A tibble with 2556 rows and 5 variables

**sequence ID** ID of the sequence

**methylation state** Methylated or unmethylated CpG site

**chromosome name** Chromosome name

**chromosome start** Chromosome start position

**methylation call** Methylation call

**Value**

A tibble with 2556 rows and 5 variables

**Author(s)**

Ran Hu <huran@ucla.edu>

---

`demo.fragment_level.meth.bed`*Fragment-level methylation information*

---

**Description**

A BED file of fragment-level methylation information

**Usage**

```
data("demo.fragment_level.meth.bed")
```

**Format**

A tibble with 552 rows and 9 variables

**chr** Chromosome

**start** Chromosome start

**end** Chromosome end

**name** ID of the sequence

**fragmentLength** Fragment length

**strand** Strand

**cpgNumber** Number of CpG sites on the fragment

**cpgPosition** Postions of CpG sites on the fragment

**methState** A string of methylation states of CpG sites on the fragment

**Value**

A tibble with 552 rows and 9 variables

**Author(s)**

Ran Hu <huran@ucla.edu>

---

|                    |                                   |
|--------------------|-----------------------------------|
| demo.refo_frag.bed | <i>Fragment-level information</i> |
|--------------------|-----------------------------------|

---

**Description**

A BED file of fragment-level information

**Usage**

```
data("demo.refo_frag.bed")
```

**Format**

A tibble with 559 rows and 6 variables

**chr** Chromosome

**start** Chromosome start

**end** Chromosome end

**fragmentLength** Fragment length

**strand** Strand

**name** ID of the sequence

**Value**

A tibble with 559 rows and 6 variables

**Author(s)**

Ran Hu <huran@ucla.edu>

---

|                    |                                             |
|--------------------|---------------------------------------------|
| demo.refo_meth.bed | <i>Methylation information on fragments</i> |
|--------------------|---------------------------------------------|

---

**Description**

A BED file of methylation information on fragments

**Usage**

```
data("demo.refo_meth.bed")
```

**Format**

A tibble with 552 rows and 8 variables

**chr** Chromosome

**cpgStart** Start position of first CpG on the fragment

**cpgEnd** End position of first CpG on the fragment

**strand** Strand

**cpgNumber** Number of CpG sites on the fragment

**cpgPosition** Positions of CpG sites on the fragment

**methState** A string of methylation states of CpG sites on the fragment

**name** ID of the sequence

**Value**

A tibble with 552 rows and 8 variables

**Author(s)**

Ran Hu <huran@ucla.edu>

---

|                 |                                    |
|-----------------|------------------------------------|
| demo.sorted.bed | <i>Paired-end sequencing reads</i> |
|-----------------|------------------------------------|

---

**Description**

Paired-end sequencing reads information

**Usage**

```
data("demo.sorted.bed")
```

**Format**

A tibble with 1117 rows and 6 variables

**chr** Chromosome name

**start** Chromosome start

**end** Chromosome end

**name** Sequence ID

**score** Mapping quality score

**strand** Strand

**Value**

A tibble with 1117 rows and 6 variables

**Author(s)**

Ran Hu <huran@ucla.edu>

---

GenerateFragMeth

*Generate fragment-level information about methylation states*

---

**Description**

Join two lists containing the fragment information and the methylation states on each fragment into one list.

**Usage**

```
GenerateFragMeth(frag_bed, meth_bed, output.dir = "", id = "")
```

**Arguments**

|                         |                                                                                                               |
|-------------------------|---------------------------------------------------------------------------------------------------------------|
| <code>frag_bed</code>   | a BED file containing information for every fragment, which is the output of <code>MergePEReads()</code> .    |
| <code>meth_bed</code>   | a BED file containing methylation states on every fragment, which is the output of <code>MergeCpGs()</code> . |
| <code>output.dir</code> | a path to the output directory. Default is "", which means the output will not be written into a file.        |
| <code>id</code>         | an ID name for the input data. Default is "", which means the output will not be written into a file.         |

**Value**

a list in BED file format and/or written to an output BED file.

**Examples**

```
## input files
demo.dir <- system.file("data", package="cfTools")
frag_bed <- read.delim(file.path(demo.dir, "demo.refo_frag.bed.txt.gz"),
  colClasses = "character")
meth_bed <- read.delim(file.path(demo.dir, "demo.refo_meth.bed.txt.gz"),
  colClasses = "character")

output <- GenerateFragMeth(frag_bed, meth_bed)
```

---

|                     |                                                    |
|---------------------|----------------------------------------------------|
| GenerateMarkerParam | <i>Generate the methylation pattern of markers</i> |
|---------------------|----------------------------------------------------|

---

**Description**

Output paired shape parameters of beta distributions for methylation markers.

**Usage**

```
GenerateMarkerParam(x, sample.types, marker.names, output.file = "")
```

**Arguments**

|              |                                                                                                                   |
|--------------|-------------------------------------------------------------------------------------------------------------------|
| x            | a list of methylation levels (e.g., beta values), where each row is a sample and each column is a marker.         |
| sample.types | a vector of sample types (e.g., tumor or normal, tissue types) corresponding to the rows of the list.             |
| marker.names | a vector of marker names corresponding to the columns of the list.                                                |
| output.file  | a character string naming the output file. Default is "", which means the output will not be written into a file. |

**Value**

a list containing the paired shape parameters of beta distributions for markers and/or written to an output file.

**Examples**

```
## input files
demo.dir <- system.file("data", package="cfTools")
methLevel <- read.table(file.path(demo.dir, "beta_matrix.txt.gz"),
  row.names=1, header = TRUE)
sampleTypes <- read.table(file.path(demo.dir, "sample_type.txt.gz"),
  row.names=1, header = TRUE)$sampleType
markerNames <- read.table(file.path(demo.dir, "marker_index.txt.gz"),
  row.names=1, header = TRUE)$markerIndex

output <- GenerateMarkerParam(methLevel, sampleTypes, markerNames)
```

---

|             |                                    |
|-------------|------------------------------------|
| markers.bed | <i>Genomic postions of markers</i> |
|-------------|------------------------------------|

---

**Description**

A BED file of genomic regions of markers

**Usage**

```
data("markers.bed")
```

**Format**

A tibble with 3 rows and 4 variables

**chr** Chromosome

**start** Chromosome start

**end** Chromosome end

**markerName** Marker name

**Value**

A tibble with 3 rows and 4 variables

**Author(s)**

Ran Hu <huran@ucla.edu>

---

|              |                    |
|--------------|--------------------|
| marker_index | <i>Marker name</i> |
|--------------|--------------------|

---

**Description**

A vector of marker names corresponding to the columns of the list of methylation levels.

**Usage**

```
data("marker_index")
```

**Format**

A tibble with 3 rows and 1 variables

**markerIndex** Marker name

**Value**

A tibble with 3 rows and 1 variables

**Author(s)**

Ran Hu <huran@ucla.edu>



MergeCpGs

*Generate fragment-level methylation states of CpGs***Description**

Merge the methylation states of all CpGs corresponding to the same fragment onto one line in output.

**Usage**

```
MergeCpGs(CpG_OT, CpG_OB, output.dir = "", id = "")
```

**Arguments**

|            |                                                                                                                                                 |
|------------|-------------------------------------------------------------------------------------------------------------------------------------------------|
| CpG_OT     | a file of methylation information for CpG on the original top strand (OT), which is one of the outputs from ‘bismark methylation extractor’.    |
| CpG_OB     | a file of methylation information for CpG on the original bottom strand (OB), which is one of the outputs from ‘bismark methylation extractor’. |
| output.dir | a path to the output directory. Default is "", which means the output will not be written into a file.                                          |
| id         | an ID name for the input data. Default is "", which means the output will not be written into a file.                                           |

**Value**

a list in BED file format and/or written to an output BED file.

**Examples**

```
## input files
demo.dir <- system.file("data", package="cfTools")
CpG_OT <- file.path(demo.dir, "CpG_OT_demo.txt.gz")
CpG_OB <- file.path(demo.dir, "CpG_OB_demo.txt.gz")

output <- MergeCpGs(CpG_OT, CpG_OB)
```

MergePEReads

*Generate fragment-level information for paired-end sequencing reads***Description**

Merge BED file (the output of ‘bedtools bamtobed’) to fragment-level for paired-end sequencing reads.

**Usage**

```
MergePEReads(bed_file, output.dir = "", id = "")
```

**Arguments**

|                         |                                                                                                        |
|-------------------------|--------------------------------------------------------------------------------------------------------|
| <code>bed_file</code>   | a (sorted) BED file of paired-end reads.                                                               |
| <code>output.dir</code> | a path to the output directory. Default is "", which means the output will not be written into a file. |
| <code>id</code>         | an ID name for the input data. Default is "", which means the output will not be written into a file.  |

**Value**

a list in BED file format and/or written to an output BED file.

**Examples**

```
## input files
demo.dir <- system.file("data", package="cfTools")
PEReads <- file.path(demo.dir, "demo.sorted.bed.txt.gz")

output <- MergePEReads(PEReads)
```

---

|                 |                       |
|-----------------|-----------------------|
| PlotFractionPie | <i>Plot Pie Chart</i> |
|-----------------|-----------------------|

---

**Description**

Generate a pie chart for a vector of class fractions (e.g., tissue composition or cfDNA fractions). Automatically filters small values into an "Other" group, and allows for custom colors and font size control.

**Usage**

```
PlotFractionPie(
  fraction_vector,
  title = "Composition",
  threshold = 0.01,
  class_colors = NULL,
  font_size = 1
)
```

**Arguments**

|                              |                                                                                                             |
|------------------------------|-------------------------------------------------------------------------------------------------------------|
| <code>fraction_vector</code> | a named numeric vector or one-row data.frame, where each value represents a class proportion.               |
| <code>title</code>           | the title of the plot.                                                                                      |
| <code>threshold</code>       | a numeric value. Classes with fraction values below this threshold will be grouped into "Other".            |
| <code>class_colors</code>    | a named character vector assigning colors to specific class names (e.g., <code>c("tumor" = "red")</code> ). |
| <code>font_size</code>       | numeric, font scaling factor (default is 1.0).                                                              |

**Value**

A pie chart is plotted to the current device.

**Examples**

```
df <- data.frame(  
  WBC = 0.93,  
  Liver = 0.04,  
  Lung = 0.02,  
  Muscle = 1.2345e-4,  
  Stomach = 9.87655e-03  
)  
PlotFractionPie(df, title = "cfDNA Composition", font_size = 1.2)
```

---

| sample_type | <i>Sample type</i> |
|-------------|--------------------|
|-------------|--------------------|

---

**Description**

A vector of sample types (e.g., tumor or normal, tissue types) corresponding to the rows of the list of methylation levels.

**Usage**

```
data("sample_type")
```

**Format**

A tibble with 20 rows and 1 variables

**sampleType** Sample type

**Value**

A tibble with 20 rows and 1 variables

**Author(s)**

Ran Hu <huran@ucla.edu>

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