

# Package ‘cobindR’

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**Title** Finding Co-occurring motifs of transcription factor binding sites

**Description** Finding and analysing co-occurring motifs of transcription factor binding sites in groups of genes

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---

cobindR-package	<i>An R package for analyzing co-occurring transcription factor binding sites</i>
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---

**Description**

Many transcription factors (TFs) regulate gene expression by binding to specific DNA motifs near genes. Often the regulation of gene expression is not only controlled by one TF, but by many TFs together, that can either interact in a cooperative manner or interfere with each other. In recent years high throughput methods, like ChIP-Seq, have become available to produce large amounts of data, that contain potential regulatory regions. In silico analysis of transcription factor binding sites can help to interpret these enormous datasets in a convenient and fast way or narrow down the results to the most significant regions for further experimental studies.

cobindR provides a complete set of methods to analyse and detect pairs of TFs, including support of diverse input formats and different background models for statistical testing. Several visualization tools are implemented to ease the interpretation of the results.

**Author(s)**

Yue-Hien Lee, Robert Lehmann, Stefan Kroeger, Manuela Benary

**See Also**

The core class in this package: [cobindr-class](#). The core function in this package: [find.pairs](#).

---

bg_binding_sites	<i>motif hits in the background sequences</i>
------------------	---

---

**Description**

motif hits in the background sequences

**Usage**

```
## S4 method for signature 'cobindr'
bg_binding_sites(x)
## S4 replacement method for signature 'cobindr,data.frame'
bg_binding_sites(x) <- value
```

**Arguments**

x	a cobindr object
value	data.frame holding the binding site hits in the background sequences

**Value**

motif hits in background sequences (data.frame)

**Author(s)**

Rob Lehmann <r.lehmann@biologie.hu-berlin.de>

**See Also**

[uid](#), [name](#), [sequences](#), [bg\\_sequences](#), [desc](#), [configuration](#), [binding\\_sites](#), [pfm](#), [bg\\_binding\\_sites](#), [pairs](#), [bg\\_pairs](#), [pair](#)

**Examples**

```
cfg <- cobindRConfiguration()
sequence_type(cfg) <- 'fasta'
sequence_source(cfg) <- system.file('extdata/sox_oct_example_vignette_seqs.fasta', package='cobindR')
sequence_origin(cfg) <- 'Mouse Embryonic Stem Cell Example CHIP-Seq Oct4 Peak bg_binding_sites'
cbr <- cobindr(cfg)
bg_binding_sites(cbr)
```

---

bg\_pairs

*motif hit pairs in the background sequences*

---

**Description**

motif hit pairs in the background sequences

**Usage**

```
## S4 method for signature 'cobindr'
bg_pairs(x)
## S4 replacement method for signature 'cobindr,data.frame'
bg_pairs(x) <- value
```

**Arguments**

x                    a cobindr object  
value                data.frame holding the binding site pairs in the background sequences

**Value**

background motif pairs (data.frame)

**Author(s)**

Rob Lehmann <r.lehmann@biologie.hu-berlin.de>

**See Also**

[uid](#),[name](#),[sequences](#),[bg\\_sequences](#),[desc](#),[configuration](#),[binding\\_sites](#),[bg\\_binding\\_sites](#),[pfm](#),[pairs](#),[bg\\_pairs](#),[pair](#)

**Examples**

```
cfg <- cobindRConfiguration()
sequence_type(cfg) <- 'fasta'
sequence_source(cfg) <- system.file('extdata/sox_oct_example_vignette_seqs.fasta', package='cobindR')
sequence_origin(cfg) <- 'Mouse Embryonic Stem Cell Example ChIP-Seq Oct4 Peak bg_pairs'
cbr <- cobindr(cfg)
bg_pairs(cbr)
```

---

bg_sequences	<i>list of background sequence</i>
--------------	------------------------------------

---

**Description**

list of background sequence

**Usage**

```
## S4 method for signature 'cobindr'
bg_sequences(x)
## S4 replacement method for signature 'cobindr,list'
bg_sequences(x) <- value
```

**Arguments**

x	a cobindr object
value	list of background sequence of type SeqObj

**Value**

list of background sequences (SeqObj)

**Author(s)**

Rob Lehmann <r.lehmann@biologie.hu-berlin.de>

**See Also**

[uid](#),[name](#),[bg\\_sequences](#),[bg\\_sequences](#),[desc](#),[configuration](#),[binding\\_sites](#),[bg\\_binding\\_sites](#),[pfm](#),[pairs](#),[bg\\_pairs](#),[p](#)

## Examples

```
cfg <- cobindRConfiguration()
sequence_type(cfg) <- 'fasta'
sequence_source(cfg) <- system.file('extdata/sox_oct_example_vignette_seqs.fasta', package='cobindR')
sequence_origin(cfg) <- 'Mouse Embryonic Stem Cell Example CHIP-Seq Oct4 Peak bg_sequences'
cbr <- cobindr(cfg)
length(bg_sequences(cbr))
```

---

bg\_sequence\_origin      *background sequence origin note*

---

## Description

background sequence origin note

## Usage

```
## S4 method for signature 'configuration'
bg_sequence_origin(x)
## S4 replacement method for signature 'configuration,character'
bg_sequence_origin(x) <- value
```

## Arguments

x	a cobindR configuration object
value	a character

## Value

background sequence origin (character)

## Author(s)

Rob Lehmann <r.lehmann@biologie.hu-berlin.de>

## See Also

[id](#), [experiment\\_description](#), [sequence\\_source](#), [sequence\\_origin](#), [sequence\\_type](#), [bg\\_sequence\\_source](#), [bg\\_sequence](#)

## Examples

```
cfg <- cobindRConfiguration()
bg_sequence_origin(cfg)
```

---

*bg\_sequence\_source*      *background sequence source note*

---

## **Description**

background sequence source note

## **Usage**

```
## S4 method for signature 'configuration'  
bg_sequence_source(x)  
## S4 replacement method for signature 'configuration,character'  
bg_sequence_source(x) <- value
```

## **Arguments**

x	a cobindR configuration object
value	a character

## **Value**

background sequence source (character)

## **Author(s)**

Rob Lehmann <r.lehmann@biologie.hu-berlin.de>

## **See Also**

[id](#), [experiment\\_description](#), [sequence\\_source](#), [sequence\\_origin](#), [sequence\\_type](#), [bg\\_sequence\\_source](#), [bg\\_sequence](#)

## **Examples**

```
cfg <- cobindRConfiguration()  
bg_sequence_source(cfg)
```

---

bg_sequence_type	<i>background sequence type note</i>
------------------	--------------------------------------

---

### Description

background sequence type note

### Usage

```
## S4 method for signature 'configuration'  
bg_sequence_type(x)  
## S4 replacement method for signature 'configuration,character'  
bg_sequence_type(x) <- value
```

### Arguments

x	a cobindR configuration object
value	a character

### Value

bg\_sequence\_type (character)

### Author(s)

Rob Lehmann <r.lehmann@biologie.hu-berlin.de>

### See Also

[id](#), [experiment\\_description](#), [sequence\\_source](#), [sequence\\_origin](#), [sequence\\_type](#), [bg\\_sequence\\_source](#), [bg\\_sequence](#)

### Examples

```
cfg <- cobindRConfiguration()  
bg_sequence_type(cfg)
```

---

binding_sites	<i>motif hits on the foreground sequences</i>
---------------	---

---

## Description

motif hits on the foreground sequences

## Usage

```
## S4 method for signature 'cobindr'  
binding_sites(x)  
## S4 replacement method for signature 'cobindr,data.frame'  
binding_sites(x) <- value
```

## Arguments

x	a cobindr object
value	data.frame holding the binding site hits in the foreground sequences

## Value

motif hits in foreground sequences as data.frame

## Author(s)

Rob Lehmann <r.lehmann@biologie.hu-berlin.de>

## See Also

[uid](#),[name](#),[sequences](#),[bg\\_sequences](#),[desc](#),[configuration](#),[binding\\_sites](#),[bg\\_binding\\_sites](#),[pfm](#),[pairs](#),[bg\\_pairs](#),[pair](#)

## Examples

```
cfg <- cobindRConfiguration()  
sequence_type(cfg) <- 'fasta'  
sequence_source(cfg) <- system.file('extdata/sox_oct_example_vignette_seqs.fasta',package='cobindR')  
sequence_origin(cfg) <- 'Mouse Embryonic Stem Cell Example ChIP-Seq Oct4 Peak binding_sites'  
cbr <- cobindr(cfg)  
binding_sites(cbr)
```

---

cobindr-class	Class "cobindr"
---------------	-----------------

---

### Description

Container for experiment run and its meta-data

### Objects from the Class

Objects can be created by calls of the form `new("cobindr", conf, name, desc)`.

### Slots

**uid:** Object of class "character" ~~ unique id for internal representation

**name:** Object of class "character" ~~ name of the experiment

**sequences:** Object of class "list" ~~ list of sequence objects to be analyzed

**bg\_sequences:** Object of class "list" ~~list of background sequences for statistical analyses

**desc:** Object of class "character" ~~ verbal experiment description

**configuration:** Object of class "configuration" ~~the configuration object used to describe the experiment

**pfm:** Object of class "list" ~~list of pfms to be used

**binding\_sites:** Object of class "data.frame" ~~ data frame for predicted binding sites. Data frame structure: uid:integer, seqObj\_uid:integer, pfm:factor, start:integer, end:integer, score:double, seq:character, strand:factor, source:factor.

**bg\_binding\_sites:** Object of class "data.frame" ~~ data frame for predicted binding sites in the background sequences. Data frame structure: uid:integer, seqObj\_uid:integer, pfm:factor, start:integer, end:integer, score:double, seq:character, strand:factor, source:factor.

**pairs:** Object of class "data.frame" ~~ data frame for predicted pairs of transcription factors. Data frame structure: uid:integer, seqObj\_uid:integer, pair:factor, bs\_uid1:integer, bs\_uid2:integer, distance\_start:integer.

**bg\_pairs:** Object of class "data.frame" ~~ data frame for predicted pairs of transcription factors in the background sequences. Data frame structure: uid:integer, seqObj\_uid:integer, pair:factor, bs\_uid1:integer, bs\_uid2:integer, distance\_start:integer.

**pairs\_of\_interest:** Object of class "factor" ~~ contains pairs for search

### Methods

**detrending** signature(object = "cobindr"): ...

**find.pairs** signature(object = "cobindr"): ...

**generate.background** signature(object = "cobindr"): ...

**get.bindingsite.ranges** signature(object = "cobindr"): ...

**get.pairs** signature(object = "cobindr"): ...

**get.significant.pairs** signature(object = "cobindr"): ...  
**initialize** signature(.Object = "cobindr"): ...  
**input.pwm** signature(object = "cobindr"): ...  
**plot.detrending** signature(object = "cobindr"): ...  
**plot.gc** signature(object = "cobindr"): ...  
**plot.pairedistance** signature(object = "cobindr"): ...  
**plot.pairedistribution** signature(object = "cobindr"): ...  
**plot.positionprofile** signature(object = "cobindr"): ...  
**plot.positions.simple** signature(object = "cobindr"): ...  
**plot.positions** signature(object = "cobindr"): ...  
**plot.tfbs.heatmap** signature(object = "cobindr"): ...  
**plot.tfbs.venndiagram** signature(object = "cobindr"): ...  
**plot.tfbslogo** signature(object = "cobindr"): ...  
**predicted2pwm** signature(object = "cobindr"): ...  
**rtfbs** signature(object = "cobindr"): ...  
**search.gadem** signature(object = "cobindr"): ...  
**search.pwm** signature(object = "cobindr"): ...  
**testCpG** signature(object = "cobindr"): ...  
**write.bindingsites.table** signature(object = "cobindr"): ...  
**write.bindingsites** signature(object = "cobindr"): ...  
**write.sequences** signature(object = "cobindr"): ...  
**write** signature(x = "cobindr", file = "character"): ...

### Author(s)

Manuela Benary <manuela.benary@cms.hu-berlin.de>

### See Also

[SeqObj configuration](#)

### Examples

```
showClass("cobindr")
```

---

cobindRConfiguration    *cobindR configuration object constructor*

---

**Description**

cobindR configuration object constructor

**Usage**

```
## S4 method for signature 'character'  
cobindRConfiguration(x)
```

**Arguments**

x                    path to configuration file. NULL by default

**Value**

cobindR configuration object

**Author(s)**

Rob Lehmann <r.lehmann@biologie.hu-berlin.de>

**See Also**

[seqObj](#)

**Examples**

```
cfg <- cobindRConfiguration()
```

---

comment                    *comment of cobindR SeqObj object*

---

**Description**

comment of cobindR SeqObj object

**Usage**

```
## S4 method for signature 'SeqObj'  
comment(x)  
## S4 replacement method for signature 'SeqObj,character'  
comment(x) <- value
```

**Arguments**

x                    a cobindR seqObj object  
value                comment to the sequence (character)

**Value**

comment (character)

**Author(s)**

Rob Lehmann <r.lehmann@biologie.hu-berlin.de>

**See Also**

[uid,name,species,comment,location,sequence](#)

**Examples**

```
library(Biostrings)
so <- seqObj(DNAString('A'), id='', name='', species='',comment='',location='')
comment(so)
```

---

configuration

*configuration of cobindr object*

---

**Description**

configuration of cobindr object

**Usage**

```
## S4 method for signature 'cobindr'
configuration(x)
## S4 replacement method for signature 'cobindr,configuration'
configuration(x) <- value
```

**Arguments**

x                    a cobindr object  
value                returns the configuration object used in this cobindR object

**Value**

cobindR configuration object

**Author(s)**

Rob Lehmann <r.lehmann@biologie.hu-berlin.de>

**See Also**

[uid](#), [name](#), [sequences](#), [bg\\_sequences](#), [desc](#), [configuration](#), [binding\\_sites](#), [bg\\_binding\\_sites](#), [pfm](#), [pairs](#), [bg\\_pairs](#), [pair](#)

**Examples**

```
cfg <- cobindRConfiguration()
sequence_type(cfg) <- 'fasta'
sequence_source(cfg) <- system.file('extdata/sox_oct_example_vignette_seqs.fasta', package='cobindR')
sequence_origin(cfg) <- 'Mouse Embryonic Stem Cell Example ChIP-Seq Oct4 Peak configuration'
cbr <- cobindr(cfg)
configuration(cbr)
```

---

```
configuration-class  Class "configuration"
```

---

**Description**

Container for experiment description.

**Objects from the Class**

Objects can be created by calls of the form `new("configuration", fname)`.

**Slots**

**id:** Object of class "character" ~~ unique id for internal representation  
**experiment\_description:** Object of class "character" ~~ verbal experiment description  
**sequence\_source:** Object of class "character" ~~ file path or list of paths  
**sequence\_origin:** Object of class "character" ~~ source of sequence data, e.g. ensembl  
**sequence\_type:** Object of class "character" ~~ either ChipSeq or Fasta or BED are available  
**bg\_sequence\_source:** Object of class "character" ~~ file path or list of paths  
**bg\_sequence\_origin:** Object of class "character" ~~ how the background is obtained - either simulated or from fasta files or from gene ids  
**bg\_sequence\_type:** Object of class "character" ~~ determines the generation of the background sequences. Possible values: simulated, fasta and geneid  
**species:** Object of class "character" ~~ reference species  
**downstream:** Object of class "numeric" ~~ length of sequence downstream of reference point, e.g. transcription start site  
**upstream:** Object of class "numeric" ~~ length of sequence upstream of reference point, e.g. transcription start site  
**max\_distance:** Object of class "numeric" ~~ maximal distance allowed between cooccurring transcription factor binding sites  
**pairs:** Object of class "character" ~~ list of pairs of interesting transcription factors

**pfm\_path:** Object of class "character" ~~ path to pfm matrix file  
**threshold:** Object of class "numeric" ~~ threshold for transcription factor binding site prediction  
**fdrThreshold:** Object of class "numeric" ~~ false discovery rate for filtering results (used in rtfbs)  
**date:** Object of class "character" ~~ data of experiment run  
**path:** Object of class "character" ~~ path of configuration file  
**mart:** Object of class "character" ~~ optional mirror for biomaRt  
**pseudocount:** Object of class "numeric" ~~ sets the pseudocount for the detrending analysis  
**pValue:** Object of class "numeric" ~~ optional p-Value for search with RGADEM

## Methods

**initialize** signature(.Object = "configuration"): ...  
**read.background.fasta** signature(object = "configuration"): ...  
**read.pfm** signature(object = "configuration"): ...  
**read.sequences** signature(object = "configuration"): ...  
**write** signature(x = "configuration", file = "character"): ...

## Author(s)

Manuela Benary <manuela.benary@cms.hu-berlin.de>

## See Also

[SeqObj cobindr](#)

## Examples

```
showClass("configuration")
```

---

downstream

*downstream range [bp] used in experiment*

---

## Description

downstream range [bp] used in experiment

## Usage

```

## S4 method for signature 'configuration'
downstream(x)
## S4 replacement method for signature 'configuration,numeric'
downstream(x) <- value
  
```

**Arguments**

x                    a cobindR configuration object  
value                downstream distance [bp] of feature to be included (numeric)

**Value**

considered downstream range [bp]

**Author(s)**

Rob Lehmann <r.lehmann@biologie.hu-berlin.de>

**See Also**

[id](#), [experiment\\_description](#), [sequence\\_source](#), [sequence\\_origin](#), [sequence\\_type](#), [bg\\_sequence\\_source](#), [bg\\_sequence](#)

**Examples**

```
cfg <- cobindRConfiguration()  
downstream(cfg)
```

---

experiment\_description

*description of cobindR or configuration object*

---

**Description**

description of cobindR or configuration object

**Usage**

```
## S4 method for signature 'configuration'  
experiment_description(x)  
## S4 replacement method for signature 'configuration,character'  
experiment_description(x) <- value  
## S4 method for signature 'cobindr'  
experiment_description(x)  
## S4 replacement method for signature 'cobindr,character'  
experiment_description(x) <- value
```

**Arguments**

x                    a cobindR or configuration object  
value                description

**Value**

experiment description (character)

**Author(s)**

Rob Lehmann <r.lehmann@biologie.hu-berlin.de>

**See Also**

[id](#), [experiment\\_description](#), [sequence\\_source](#), [sequence\\_origin](#), [sequence\\_type](#), [bg\\_sequence\\_source](#), [bg\\_sequence](#)

**Examples**

```
cfg <- cobindRConfiguration()

experiment_description(cfg)

sequence_type(cfg) <- 'fasta'
sequence_source(cfg) <- system.file('extdata/sox_oct_example_vignette_seqs.fasta', package='cobindR')
sequence_origin(cfg) <- 'Mouse Embryonic Stem Cell Example ChIP-Seq Oct4 Peak desc'
cbr <- cobindr(cfg)

experiment_description(cbr)
```

---

fdrThreshold

*fdrThreshold of cobindR configuration object*

---

**Description**

fdrThreshold of cobindR configuration object.

**Usage**

```
## S4 method for signature 'configuration'
fdrThreshold(x)
## S4 replacement method for signature 'configuration,numeric'
fdrThreshold(x) <- value
```

**Arguments**

x                    a cobindR configuration object  
value                the false discovery rate threshold to be used for hit search

**Value**

fdrThreshold (numeric)

**Author(s)**

Rob Lehmann <r.lehmann@biologie.hu-berlin.de>

**See Also**

[id](#),[experiment\\_description](#),[sequence\\_source](#),[sequence\\_origin](#),[sequence\\_type](#),[bg\\_sequence\\_source](#),[bg\\_sequence](#)

**Examples**

```
cfg <- cobindRConfiguration()
fdrThreshold(cfg)
```

---

find.pairs	<i>function to find pairs of binding sites for every sequence in a given object of class "cobindr"</i>
------------	--

---

**Description**

find.pairs creates a data frame with all pairs in all sequences within the given distance.

**Usage**

```
find.pairs(x, background_scan = FALSE, n.cpu = NA)
```

**Arguments**

x	an object of the class "cobindr", which will hold all necessary information about the sequences and the hits.
background_scan	logical flag, if background_scan = TRUE the pairs for the background sequences will be found.
n.cpu	number of CPUs to be used for parallelization. Default value is 'NA' in which case the number of available CPUs is checked and than used.

**Value**

runObj	an object of the class "cobindr" including the pairs of transcription factor binding sites
--------	--

**Author(s)**

Yue-Hien Lee <>

**See Also**

[plot.detrending](#)

---

```
get.bindingsite.ranges
```

*convenience function to convert predicted binding sites to GRanges object.*

---

## Description

Function converts predicted binding sites into a GRanges object (package: GenomicFeatures). This allows for easy interaction with other tools as well as output of different formats (bed, gff).

## Usage

```
get.bindingsite.ranges(x, ...)
```

## Arguments

x	An object of the class "cobindr", which will hold the predicted binding site locations.
...	optional additional parameters

## Value

A GRanges object holding the positions of all predicted transcription factor binding sites relative to the input sequence.

## Author(s)

Robert Lehmann <r.lehmann@biologie.hu-berlin.de>

## See Also

get.pairs write.bindingsites write.bindingsites.table

## Examples

```
# export(get.bindingsite.ranges(runObj), "tfbs_hits.gff3")
```

---

`get.pairs`                      *function to get output of findPairs*

---

### **Description**

Function returns the results of `findPairs()` as a data frame. The data.frame consists of 6 columns, namely

- a unique id for each pair,
- the unique id of the sequence, where the pair was found,
- the names of the corresponding PFMs,
- the unique id for each PFM, and
- the distance window in which the pair occurs.

### **Usage**

```
## S4 method for signature 'cobindr'  
get.pairs(x, background = FALSE)
```

### **Arguments**

`x`                      an object of the class "cobindr", which holds all necessary information about the sequences and the predicted binding sites.

`background`            logical flag. If background is 'TRUE' the pairs found in the background sequences are used.

### **Author(s)**

Stefan Kroeger <kroeger@informatik.hu-berlin.de>

### **See Also**

[get.significant.pairs](#), [write.bindingsites](#), [write.sequences](#), [write](#)

---

`get.significant.pairs`    *function to returns the results of detrending as a data.frame*

---

### **Description**

`get.significant.pairs` returns a data.frame of observed distances between the specified pair of PWMs in the foreground set of the sequences as well as the background set of sequences. The distance distribution for the pair in the background is used for detrending.

**Usage**

```
## S4 method for signature 'cobindr'
get.significant.pairs(x, pwm1, pwm2, bin_length=20, z_value=3, overlap=0, abs.distance=FALSE)
```

**Arguments**

x	an object of the class "cobindr", which will hold all necessary information about the sequences and the hits.
pwm1	name of the first PWM
pwm2	name of the second PWM
bin_length	defines size of bins for distance analysis, default value is 20nucleotides
z_value	level of significance
overlap	number of nucleotides which are allowed for an overlap
abs.distance	logical flag

**Author(s)**

Stefan Kroeger <kroeger@informatik.hu-berlin.de>

**See Also**

[plot.detrening](#), [get.pairs](#), [find.pairs](#)

---

id	<i>id of cobindR configuration object</i>
----	---

---

**Description**

id of cobindR configuration object.

**Usage**

```
## S4 method for signature 'configuration'
id(x)
## S4 replacement method for signature 'configuration,character'
id(x) <- value
```

**Arguments**

x	a cobindR configuration object
value	the identifier of the configuration object

**Value**

id (character)

**Author(s)**

Rob Lehmann <r.lehmann@biologie.hu-berlin.de>

**See Also**

[id](#), [experiment\\_description](#), [sequence\\_source](#), [sequence\\_origin](#), [sequence\\_type](#), [bg\\_sequence\\_source](#), [bg\\_sequence](#)

**Examples**

```
cfg <- cobindRConfiguration()
id(cfg)
```

---

location	<i>location of cobindR SeqObj object</i>
----------	--

---

**Description**

location of cobindR seqObj object (e.g. chr1)

**Usage**

```
## S4 method for signature 'SeqObj'
location(x)
## S4 replacement method for signature 'SeqObj,character'
location(x) <- value
```

**Arguments**

x	a cobindR seqObj object
value	the location description of the sequence

**Value**

returns location (character)

**Author(s)**

Rob Lehmann <r.lehmann@biologie.hu-berlin.de>

**See Also**

[uid](#), [name](#), [species](#), [location](#), [comment](#), [sequence](#)

**Examples**

```
library(Biostrings)
so <- seqObj(DNAString('A'), id='', name='', species='', comment='', location='')
location(so)
```

---

mart	<i>biomart of cobindR configuration object</i>
------	--

---

### Description

biomart of cobindR configuration object. Set to "ensembl" as default

### Usage

```
## S4 method for signature 'configuration'  
mart(x)  
## S4 replacement method for signature 'configuration,character'  
mart(x) <- value
```

### Arguments

x	a cobindR configuration object
value	name of biomart to retrieve sequence data

### Value

mart (character)

### Author(s)

Rob Lehmann <r.lehmann@biologie.hu-berlin.de>

### See Also

[id](#), [experiment\\_description](#), [sequence\\_source](#), [sequence\\_origin](#), [sequence\\_type](#), [bg\\_sequence\\_source](#), [bg\\_sequence](#)

### Examples

```
cfg <- cobindRConfiguration()  
mart(cfg)
```

---

max_distance	<i>max_distance of cobindR configuration object</i>
--------------	---

---

### Description

max\_distance of cobindR configuration object.

### Usage

```
## S4 method for signature 'configuration'  
max_distance(x)  
## S4 replacement method for signature 'configuration,numeric'  
max_distance(x) <- value
```

### Arguments

x	a cobindR configuration object
value	the maximal distance of two hits to be considered a pair

### Value

max\_distance (character)

### Author(s)

Rob Lehmann <r.lehmann@biologie.hu-berlin.de>

### See Also

[id](#),[experiment\\_description](#),[sequence\\_source](#),[sequence\\_origin](#),[sequence\\_type](#),[bg\\_sequence\\_source](#),[bg\\_sequence](#)

### Examples

```
cfg <- cobindRConfiguration()  
max_distance(cfg)
```

---

name	<i>name of cobindR SeqObj object</i>
------	--------------------------------------

---

### Description

name of cobindR seqObj object.

### Usage

```
## S4 method for signature 'SeqObj'  
name(x)  
## S4 method for signature 'cobindr'  
name(x)  
## S4 replacement method for signature 'SeqObj,character'  
name(x) <- value  
## S4 replacement method for signature 'cobindr,character'  
name(x) <- value
```

### Arguments

x	a cobindR seqObj object
value	the name describing the sequence object

### Value

name (character)

### Author(s)

Rob Lehmann <r.lehmann@biologie.hu-berlin.de>

### See Also

[uid,name,species,location,comment,sequence](#)

### Examples

```
library(Biostrings)  
so <- seqObj(DNAString('A'), id='', name='', species='',comment='',location='')  
name(so)
```

---

pairs *motif hit pairs in the foreground sequences*

---

### Description

motif hit pairs in the foreground sequences

### Usage

```
## S4 method for signature 'configuration'
pairs(x)
## S4 replacement method for signature 'configuration,character'
pairs(x) <- value
## S4 method for signature 'cobindr'
pairs(x)
## S4 replacement method for signature 'cobindr,data.frame'
pairs(x) <- value
```

### Arguments

x	a cobindr configuration object
value	for a configuration object, pairs is a character specifying the motif pairs which should be considered. for a cobindr object, pairs is a data.frame holding the detected motif pairs.

### Value

pairs (character)

### Author(s)

Rob Lehmann <r.lehmann@biologie.hu-berlin.de>

### See Also

[id](#), [experiment\\_description](#), [sequence\\_source](#), [sequence\\_origin](#), [sequence\\_type](#), [bg\\_sequence\\_source](#), [bg\\_sequence](#)

### Examples

```
cfg <- cobindrConfiguration()
pairs(cfg)
```

---

pairs\_of\_interest      *pairs\_of\_interest of cobindr object*

---

## Description

pairs\_of\_interest of cobindr object.

## Usage

```
## S4 method for signature 'cobindr'  
pairs_of_interest(x)  
## S4 replacement method for signature 'cobindr,factor'  
pairs_of_interest(x) <- value
```

## Arguments

x	a cobindr object
value	factors specifying the motif pairs that are to be evaluated

## Value

pairs\_of\_interest (factor)

## Author(s)

Rob Lehmann <r.lehmann@biologie.hu-berlin.de>

## See Also

[uid](#),[name](#),[sequences](#),[bg\\_sequences](#),[desc](#),[configuration](#),[binding\\_sites](#),[bg\\_binding\\_sites](#),[pfm](#),[pairs](#),[bg\\_pairs](#),[pair](#)

## Examples

```
cfg <- cobindRConfiguration()  
sequence_type(cfg) <- 'fasta'  
sequence_source(cfg) <- system.file('extdata/sox_oct_example_vignette_seqs.fasta', package='cobindR')  
sequence_origin(cfg) <- 'Mouse Embryonic Stem Cell Example ChIP-Seq Oct4 Peak pairs_of_interest'  
cbr <- cobindr(cfg)  
pairs_of_interest(cbr)
```

---

path	<i>path of cobindR configuration object</i>
------	---

---

**Description**

path of cobindR configuration object.

**Usage**

```
## S4 method for signature 'configuration'  
path(x)  
## S4 replacement method for signature 'configuration,character'  
path(x) <- value
```

**Arguments**

x	a cobindR configuration object
value	the path of the loaded configuration file

**Value**

path (character)

**Author(s)**

Rob Lehmann <r.lehmann@biologie.hu-berlin.de>

**See Also**

[id](#), [experiment\\_description](#), [sequence\\_source](#), [sequence\\_origin](#), [sequence\\_type](#), [bg\\_sequence\\_source](#), [bg\\_sequence](#)

**Examples**

```
cfg <- cobindRConfiguration()  
path(cfg)
```

---

pfm	<i>pfm list used in experiment</i>
-----	------------------------------------

---

## Description

pfm list used in experiment

## Usage

```
## S4 method for signature 'cobindr'  
pfm(x)  
## S4 replacement method for signature 'cobindr,list'  
pfm(x) <- value
```

## Arguments

x	a cobindr object
value	a list of motif matrices

## Value

pfm (list of motif matrices)

## Author(s)

Rob Lehmann <r.lehmann@biologie.hu-berlin.de>

## See Also

[uid](#),[name](#),[sequences](#),[bg\\_sequences](#),[desc](#),[configuration](#),[binding\\_sites](#),[bg\\_binding\\_sites](#),[pfm](#),[pairs](#),[bg\\_pairs](#),[pair](#)

## Examples

```
cfg <- cobindRConfiguration()  
sequence_type(cfg) <- 'fasta'  
sequence_source(cfg) <- system.file('extdata/sox_oct_example_vignette_seqs.fasta', package='cobindR')  
sequence_origin(cfg) <- 'Mouse Embryonic Stem Cell Example ChIP-Seq Oct4 Peak pfm'  
cbr <- cobindr(cfg)  
pfm(cbr)
```

---

pfm_path	<i>path to pfms to be used</i>
----------	--------------------------------

---

### Description

path to pfms to be used

### Usage

```
## S4 method for signature 'configuration'  
pfm_path(x)  
## S4 replacement method for signature 'configuration,character'  
pfm_path(x) <- value
```

### Arguments

x	a cobindR configuration object
value	the path to the folder containing the motif matrices to be used

### Value

pfm\_path (character)

### Author(s)

Rob Lehmann <r.lehmann@biologie.hu-berlin.de>

### See Also

[id](#),[experiment\\_description](#),[sequence\\_source](#),[sequence\\_origin](#),[sequence\\_type](#),[bg\\_sequence\\_source](#),[bg\\_sequence](#)

### Examples

```
cfg <- cobindRConfiguration()  
pfm_path(cfg)
```

---

plot.detrending      *function to plot distances between a pair of PWMs*

---

### Description

plot.detrending plots a histograms of observed distances between the specified pair of PWMs in the foreground set of the sequences as well as the background set of sequences. The distance distribution for the pair in the background is used for detrending.

### Usage

```
## S4 method for signature 'cobindr'  
plot.detrending(x, pwm1, pwm2, bin_length=20, z_value=3, overlap=0,  
abs.distance=FALSE)
```

### Arguments

x	an object of the class "cobindr", which will hold all necessary information about the sequences and the hits.
pwm1	name of the first PWM
pwm2	name of the second PWM
bin_length	defines size of bins for distance analysis, default value is 20 nucleotides
z_value	level of significance
overlap	number of nucleotides which are allowed for an overlap
abs.distance	logical flag

### Author(s)

Yue-Hien Lee

### See Also

[plot.pairdistribution](#), [plot.pairdistance](#)

---

plot.gc      *function to visualize GC content or CpG content of input sequences*

---

### Description

plot.gc calculates the GC (or CpG) content based on a window size for each sequence and plots the content for all sequences as a heatmap over position and sequence.

**Usage**

```
## S4 method for signature 'cobindr'
plot.gc(x, seq.ids, cpg = F, wind.size = 50,
sig.test = F, hm.margin = c(4, 10), frac = 10, n.cpu = NA)
```

**Arguments**

x	an object of the class "cobindr", which will hold all necessary information about the sequences.
seq.ids	list of sequence identifiers, for which the GC (or CpG) content will be plotted.
cpg	logical flag, if cpg=TRUE the CpG content rather than the GC content will be calculated and plotted.
wind.size	integer describing the window size for GC content calculation
sig.test	logical flag, if sig.test=TRUE wilcoxon.test is performed per individual window against all windows in other sequence at the same position. The significance test might be slow for large number of sequences
hm.margin	optional argument providing the margin widths for the heatmap (if sig.test=FALSE)
frac	determines the overlap between consecutive windows as fraction wind.size/frac
n.cpu	number of CPUs to be used for parallelization. Default value is 'NA' in which case the number of available CPUs is checked and then used.

**Author(s)**

Robert Lehmann <r.lehmann@biologie.hu-berlin.de>

**See Also**

[testCpG](#)

**Examples**

```
library(Biostrings)

n <- 50 # number of input sequences
l <- 100 # length of sequences
bases <- c("A","C","G","T") # alphabet
# generate random input sequences with two groups with differing GC content
seqs <- sapply(1:(3*n/4), function(x) paste(sample(bases, l, replace=TRUE,
prob=c(.3,.22,.2,.28)), collapse=""))
seqs <- append(seqs, sapply(1:(n/4), function(x) paste(sample(bases, l,
replace=TRUE, prob=c(.25,.25,.25,.25)), collapse="")))
#save sample sequences in fasta file
tmp.file <- tempfile(pattern = "cobindr_sample_seq", tmpdir = tempdir(),
fileext = ".fasta")
writeXStringSet(DNAStringSet(seqs), tmp.file)

cfg <- new('configuration')
slot(cfg, 'sequence_type') <- 'fasta'
```

```
slot(cfg, 'sequence_source') <- tmp.file
# avoid complaint of validation mechanism
slot(cfg, 'pfm_path') <- system.file('extdata/pfms', package='cobindr')
slot(cfg, 'pairs') <- ''

runObj <- new('cobindr', cfg, 'test')

plot.gc(runObj, cpG = TRUE)

unlink(tmp.file)
```

---

plot.pairdistance      *function to plot the distance of the pairs in the sequences*

---

### Description

For a specified pair of PWMs the function creates histogram plot of distances between pairs of TFs as specified by pwm1 and pwm2

### Usage

```
## S4 method for signature 'cobindr'
plot.pairdistance(x, pwm1, pwm2, breaks=50, main=NA, xlab=NA, ylab=NA, background=FALSE)
```

### Arguments

x	an object of the class "cobindr", which will hold all necessary information about the sequences and the hits.
pwm1	name of the first PWM
pwm2	name of the second PWM
breaks	number of breaks to separate the distance distribution into
main	figure title
xlab	label for the x-axis of the figure
ylab	label for the y-axis of the figure
background	flag allowing to plot foreground or background distance distribution

### Author(s)

Manuela Benary <manuela.benary@cms.hu-berlin.de>

### See Also

[plot.pairdistribution](#)

---

`plot.pairdistribution` *function to plot the distribution of the number of pairs in the sequences*

---

### Description

For a specified pair of PWMs the function visualizes in how many sequences how many of the pairs can be found.

### Usage

```
## S4 method for signature 'cobindr'  
plot.pairdistribution(x, pwm1, pwm2)
```

### Arguments

<code>x</code>	an object of the class "cobindr", which will hold all necessary information about the sequences and the hits.
<code>pwm1</code>	name of the first PWM
<code>pwm2</code>	name of the second PWM

### Author(s)

Manuela Benary <manuela.benary@cms.hu-berlin.de>

### See Also

[plot.detrening](#), [plot.pairdistance](#)

---

`plot.positionprofile` *function to plot a profile over the total number of predicted transcription factor binding sites for each PWM.*

---

### Description

`plot.positionprofile` provides position-wise profile plot over total number of predicted TFBS for each PWM over all input sequences. Windowing is used to provide a smoother appearance, the window size can be adjusted with the window parameter.

### Usage

```
## S4 method for signature 'cobindr'  
plot.positionprofile(x, wind.len = 50)
```

**Arguments**

x	an object of the class "cobindr", which will hold all necessary information about the sequences and the hits.
wind.len	integer, defining the length of the window for counting the hits.

**Author(s)**

Robert Lehmann <r.lehmann@biologie.hu-berlin.de>

**See Also**

[plot.positions](#)

---

plot.positions	<i>function to plot hits for each PWM on the individual sequence</i>
----------------	--

---

**Description**

plot.positions plots hits for each PWM on the individual sequence. Which sequences to plot can be specified by providing a list of sequence identifiers seq.ids. Which PWMs to plot can be specified as list of PWMs. The total height of the plot can be adjusted via argument height.

**Usage**

```
## S4 method for signature 'cobindr'
plot.positions(x, seq.ids, pwms, main, order.seq = FALSE, wind.size = 400, frac = 10)
```

**Arguments**

x	an object of the class "cobindr", which will hold all necessary information about the sequences and the hits.
seq.ids	list of sequence identifiers, for which the positions of TFBS will be plotted.
pwms	list of PWMs, for which the positions will be visualized. If no list is given, all PWMs in runObj are used.
main	title for the plot, if no title is given than 'predicted TFBS positions per sequence' will be used
order.seq	logical flag, if TRUE similar patterns of TFBS are shown together. This is computationally expensive for large numbers of sequences.
wind.size	integer describing the windows which will be used to enhance clustering of TFBS patterns. Necessary if order.seq=TRUE
frac	integer

**Author(s)**

Robert Lehmann <r.lehmann@biologie.hu-berlin.de>

---

plot.positions.simple *function to plot hits for each PWM on the individual sequence*

---

### Description

plot.positions plots hits for each PWM on the individual sequence. Which sequences to plot can be specified by providing a list of sequence identifiers seq.ids. Which PWMs to plot can be specified as list of PWMs. The total height of the plot can be adjusted via argument height.

### Usage

```
## S4 method for signature 'cobindr'
plot.positions.simple(x, seq.ids, pwms, main)
```

### Arguments

x	an object of the class "cobindr", which will hold all necessary information about the sequences and the hits.
seq.ids	list of sequence identifiers, for which the positions of TFBS will be plotted.
pwms	list of PWMs, for which the positions will be visualized. If no list is given, all PWMs in runObj are used.
main	title for the plot, if no title is given than 'predicted TFBS positions per sequence' will be used

### Author(s)

Robert Lehmann <r.lehmann@biologie.hu-berlin.de

### See Also

[plot.positionprofile](#)

---

plot.tfbs.heatmap *function to do plot a heatmap of overlaps between all specified PWMs*

---

### Description

plot.tfbs.heatmap plots a heatmap of overlaps between all specified PWMs. For each overlap, the significance is determined based on the hypergeometric test. If a file path is specified in pdf.name, the diagram will be written into the specified file.

### Usage

```
## S4 method for signature 'cobindr'
plot.tfbs.heatmap(x, pwms, include.empty.seqs = FALSE)
```

## Arguments

x	an object of the class "cobindr", which will hold all necessary information about the sequences and the hits.
pwms	list of PWMs, for which the overlap will be visualized. If no list is given, all PWMs in runObj are used.
include.empty.seqs	logical flag, if include.empty.seqs == TRUE, sequences without hits of the specified PWMs are also included in the diagram.

## Details

In this plot for each pair of PWMs the overlap of sequences with hits of the given PWMs is calculated. The number of sequences in each overlap are color-coded in the heatmap. For each overlap the significance is calculated using the hypergeometric test. If the significance is below 0.05 (or below 0.01), the corresponding field is marked with one (or two) \*.

## Warning

- unknown identifier if the list of PWMs contains unknown PWM identifiers a warning is given and the method stops
- no hits if no hits are found in the object, the method gives a warning and stops

## Author(s)

Manuela Benary <manuela.benary@cms.hu-berlin.de>

## See Also

[plot.tfbs.venndiagram](#)

---

plot.tfbs.venndiagram *function visualize the overlaps of PWM hits over the sequences.*

---

## Description

The distribution of PWM hits over the sequences is visualized as Venn diagram. If a list of PWM names is provided, only these PWMs are included in the Venn diagram. If include.empty.seqs == TRUE, sequences without hits of the specified PWMs are also included in the diagram. If a file path is specified in pdf.name, the diagram will be written into the specified file.

## Usage

```
## S4 method for signature 'cobindr'  
plot.tfbs.venndiagram(x, pwms, include.empty.seqs = FALSE)
```

**Arguments**

x	an object of the class "cobindr", which will hold all necessary information about the sequences and the hits.
pwms	list of PWMs, which shall be visualized in the Venn-Diagram. If no list is given, all PWMs in the runObj are used. The package "VennDiagram" only allows Venn plots with up to 4 elements.
include.empty.seqs	logical flag, if include.empty.seqs == TRUE, sequences without hits of the specified PWMs are also included in the diagram.

**Warning**

- unknown identifier: if the list of PWMs contains unknown PWM identifiers a warning is given and the method stops
- too many PWMs: if more than 4 PWMs are listed a warning is given and the method stops
- no hits: if no hits are found in the object, the method gives a warning and stops

**Author(s)**

Manuela Benary <manuela.benary@cms.hu-berlin.de>

**References**

using the package "VennDiagram" (<http://www.biomedcentral.com/1471-2105/12/35/>)

**See Also**

[plot.tfbs.heatmap](#)

---

plot.tfbslogo      *function to plot sequence logos based on hits of tools*

---

**Description**

plot.tfbslogo produces a sequence logo based on all hits per position weight matrix. If a file path is specified in pdf.name, sequences logos will be written into the specified file.

**Usage**

```
## S4 method for signature 'cobindr'
plot.tfbslogo(x, pwms)
```

**Arguments**

x	Object
pwms	vector of names of position weight matrices used for searching the sequences. For each pwm a new sequence logo based on the hits is produced.

**Author(s)**

Robert Lehmann <r.lehmann@biologie.hu-berlin.de>

---

predicted2pwm                    *function to convert predicted TFBS hits into a PWM*

---

**Description**

function converts for each input PWM the predicted TFBS hits into a PWM. Function is intended to be used together with the sequence logo creation function 'plot.tfbslogo'.

**Usage**

```
## S4 method for signature 'cobindr'  
predicted2pwm(x, as.pfm=FALSE)
```

**Arguments**

x	object of class "cobindr" describing the sequences and the predicted TFBS.
as.pfm	logical flag, to indicate whether the function should return a PFM (TRUE) or a PWM (FALSE)

**Value**

predPwm	positional frequency matrix based on consensus matrix
---------	---

**Author(s)**

Robert Lehmann <r.lehmann@biologie.hu-berlin.de>

**See Also**

[plot.tfbslogo](#)

---

pseudocount	<i>pseudocount of cobindR configuration object</i>
-------------	--

---

## Description

pseudocount of cobindR configuration object. Set to 10 as default

## Usage

```
## S4 method for signature 'configuration'  
pseudocount(x)  
## S4 replacement method for signature 'configuration,character'  
pseudocount(x) <- value
```

## Arguments

x	a cobindR configuration object
value	pseudocount for detrending analysis, i.e. the default number in each distance bin.

## Value

pseudocount (numeric)

## Author(s)

Rob Lehmann <r.lehmann@biologie.hu-berlin.de>

## See Also

[id](#), [experiment\\_description](#), [sequence\\_source](#), [sequence\\_origin](#), [sequence\\_type](#), [bg\\_sequence\\_source](#), [bg\\_sequence](#)

## Examples

```
cfg <- cobindRConfiguration()  
pseudocount(cfg)
```

---

pValue	<i>pValue threshold used for motif hit finding</i>
--------	--

---

**Description**

pValue threshold used for motif hit finding

**Usage**

```
## S4 method for signature 'configuration'  
pValue(x)  
## S4 replacement method for signature 'configuration,numeric'  
pValue(x) <- value
```

**Arguments**

x	a cobindR configuration object
value	the p-value threshold used for hit searching

**Value**

pValue threshold (numeric)

**Author(s)**

Rob Lehmann <r.lehmann@biologie.hu-berlin.de>

**See Also**

[id](#),[experiment\\_description](#),[sequence\\_source](#),[sequence\\_origin](#),[sequence\\_type](#),[bg\\_sequence\\_source](#),[bg\\_sequence](#)

**Examples**

```
cfg <- cobindRConfiguration()  
pValue(cfg)
```

---

`rtfbs`*function performs TFBS prediction using the package rtfbs*

---

**Description**

function performs TFBS prediction using the package rtfbs

**Usage**

```
## S4 method for signature 'cobindr'  
rtfbs(x, append = F, background_scan = FALSE, n.cpu = NA)
```

**Arguments**

<code>x</code>	an object of the class "cobindr", which will hold all necessary information about the sequences and the hits.
<code>append</code>	logical flag, if <code>append=TRUE</code> the binding sites will be appended to already existing results
<code>background_scan</code>	logical flag, if <code>background_scan=TRUE</code> the background sequences will be searched for transcription factor binding sites
<code>n.cpu</code>	number of CPUs to be used for parallelization. Default value is 'NA' in which case the number of available CPUs is checked and than used.

**Value**

<code>x</code>	an object of the class "cobindr" including the predicted transcription factor binding sites
----------------	---

**Author(s)**

Yue-Hien Lee <>

**References**

uses the package "rtfbs" (<http://cran.r-project.org/web/packages/rtfbs/index.html>)

**See Also**

[search.pwm](#), [search.gadem](#)

## Examples

```
#####
# use simulated sequences
library(Biostrings)

n <- 400 # number of input sequences
l <- 500 # length of sequences
n.hits <- 250 # number of 'true' binding sites
bases <- c("A","C","G","T") # alphabet
# generate random input sequences with two groups with differing GC content
seqs <- sapply(1:(3*n/4), function(x) paste(sample(bases, l, replace=TRUE,
prob=c(.3,.22,.2,.28)), collapse=""))
seqs <- append(seqs, sapply(1:(n/4), function(x) paste(sample(bases, l,
replace=TRUE, prob=c(.25,.25,.25,.25)), collapse="")))
path <- system.file('extdata/pfms/myod.tfpfm',package='cobindr')
motif <- read.transfac.pfm(path)[[1]] # get PFM of binding site
# add binding sites with distance specificity
for(position in c(110, 150)) {
hits <- apply(apply(motif, 2, function(x) sample(x=bases, size=n.hits,
prob=x, replace=TRUE)), 1, paste, collapse='')
pos.hits <- round(rnorm(n.hits, mean=position, sd=8))
names(pos.hits) <- sample(1:n, n.hits)
for(i in 1:n.hits) substr(seqs[as.integer(names(pos.hits)[i])],
start=pos.hits[i], stop=pos.hits[i]+ncol(motif)) <- hits[i]
}
#save sample sequences in fasta file
tmp.file <- tempfile(pattern = "cobindr_sample_seq", tmpdir = tempdir(), fileext = ".fasta")
writeXStringSet(DNAStringSet(seqs), tmp.file)
#run cobindr
cfg <- cobindrConfiguration()
sequence_type(cfg) <- 'fasta'
sequence_source(cfg) <- tmp.file
sequence_origin(cfg) <- 'artificial sequences'
pfm_path(cfg) <- system.file('extdata/pfms',package='cobindr')
pairs(cfg) <- 'V$MYOD_01 V$MYOD_01'
fdrThreshold(cfg) <- 0
runObj <- cobindr(cfg, name='cobindr test using sampled sequences')
# perform tfbs prediction using rtfbs
runObj.bs <- rtfbs(runObj)
# show results
plot.positionprofile(runObj.bs)

#clean up
unlink(tmp.file)
```

**Description**

function performs TFBS prediction denovo or based on transfac / jaspar matrices pwms using rGADEM. If append=T, predicted hits are appended to the hits in the input object.

**Usage**

```
## S4 method for signature 'cobindr'
search.gadem(x, deNovo = FALSE, append = F, background_scan = FALSE)
```

**Arguments**

x	an object of the class "cobindr", which will hold all necessary information about the sequences and the hits.
deNovo	logical flag, if deNOVO=TRUE a denovo search is startet. Otherwise the given PFMs are used as seed.
append	logical flag, if append=TRUE the binding sites will be appended to already existing results
background_scan	logical flag, if background_scan=TRUE the function will search for binding sites in the set of background sequences

**Value**

x	an object of the class "cobindr" including the predicted transcription factor binding sites
---	---

**Author(s)**

Robert Lehmann <r.lehmann@biologie.hu-berlin.de>

**References**

uses package "rGADEM" (<http://www.bioconductor.org/packages/release/bioc/html/rGADEM.html>)

**See Also**

[rtfbs](#), [search.pwm](#)

**Examples**

```
#####
# use simulated sequences
library(Biostrings)

n <- 600 # number of input sequences
l <- 150 # length of sequences
n.hits <- 600 # number of 'true' binding sites
bases <- c("A","C","G","T") # alphabet
# generate random input sequences with two groups with differing GC content
```

```

seqs <- sapply(1:(3*n/4), function(x) paste(sample(bases, 1, replace=TRUE,
prob=c(.3,.22,.2,.28)), collapse=""))
seqs <- append(seqs, sapply(1:(n/4), function(x) paste(sample(bases, 1,
replace=TRUE, prob=c(.25,.25,.25,.25)), collapse="")))
path <- system.file('extdata/pfms/myod.tfpfm',package='cobindR')
motif <- read.transfac.pfm(path)[[1]] # get PFM of binding site
# add binding sites with distance specificity
for(position in c(70, 90)) {
hits <- apply(apply(motif, 2, function(x) sample(x=bases, size=n.hits,
prob=x, replace=TRUE)), 1, paste, collapse='')
pos.hits <- round(rnorm(n.hits, mean=position, sd=8))
names(pos.hits) <- sample(1:n, n.hits)
for(i in 1:n.hits) substr(seqs[as.integer(names(pos.hits)[i])], start=pos.hits[i],
stop=pos.hits[i]+ncol(motif)) <- hits[i]
}
#save sample sequences in fasta file
tmp.file <- tempfile(pattern = "cobindr_sample_seq", tmpdir = tempdir(), fileext = ".fasta")
writeXStringSet(DNAStringSet(seqs), tmp.file)
#run cobindr
cfg <- cobindRConfiguration()
sequence_type(cfg) <- 'fasta'
sequence_source(cfg) <- tmp.file
sequence_origin(cfg) <- 'artificial sequences'
pfm_path(cfg) <- system.file('extdata/pfms',package='cobindR')
pairs(cfg) <- 'V$MYOD_01 V$MYOD_01'
runObj <-cobindr(cfg, name='cobindr test using sampled sequences')

# perform tfbs prediction using rGADEM - commented out due to long time required
# runObj.bs <- search.gadem(runObj)
# show results
# plot.positions(runObj.bs)

#clean up
unlink(tmp.file)

```

---

search.pwm

*function to predict transcription factor binding sites using the method  
matchPWM from package Biostrings*


---

### Description

function to predict transcription factor binding sites using the method matchPWM from package Biostrings

### Usage

```

## S4 method for signature 'cobindr'
search.pwm(x, min.score = "80%", append = FALSE, background_scan =
FALSE, n.cpu = NA)

```

**Arguments**

x	an object of the class "cobindr", which will hold all necessary information about the sequences and the hits.
min.score	minimal score to define threshold for hits (default = .8)
append	logical flag, if append=TRUE the binding sites will be appended to already existing results
background_scan	logical flag, if background_scan=TRUE the background sequences will be searched for transcription factor binding sites
n.cpu	number of CPUs to be used for parallelization. Default value is 'NA' in which case the number of available CPUs is checked and then used.

**Value**

x	an object of the class "cobindr" including the predicted transcription factor binding sites
---	---

**Author(s)**

Robert Lehmann <r.lehmann@biologie.hu-berlin.de

**References**

uses matchPWM from package "Biostrings" (<http://www.bioconductor.org/packages/release/bioc/html/Biostrings.html>)

**See Also**

[rtfbs](#), [search.gadem](#)

**Examples**

```
#####
# use simulated sequences
library(Biostrings)

n <- 400 # number of input sequences
l <- 500 # length of sequences
n.hits <- 250 # number of 'true' binding sites
bases <- c("A","C","G","T") # alphabet
# generate random input sequences with two groups with differing GC content
seqs <- sapply(1:(3*n/4), function(x) paste(sample(bases, l, replace=TRUE,
prob=c(.3,.22,.2,.28)), collapse=""))
seqs <- append(seqs, sapply(1:(n/4), function(x) paste(sample(bases, l, replace=TRUE,
prob=c(.25,.25,.25,.25)), collapse="")))
path <- system.file('extdata/pfms/myod.tfpfm',package='cobindr')
motif <- read.transfac.pfm(path)[[1]] # get PFM of binding site
# add binding sites with distance specificity
for(position in c(110, 150)) {
hits <- apply(apply(motif, 2, function(x) sample(x=bases, size=n.hits, prob=x,
```

```

replace=TRUE)), 1, paste, collapse='')
pos.hits <- round(rnorm(n.hits, mean=position, sd=8))
names(pos.hits) <- sample(1:n, n.hits)
for(i in 1:n.hits) substr(seqs[as.integer(names(pos.hits)[i])], start=pos.hits[i],
stop=pos.hits[i]+ncol(motif)) <- hits[i]
}
#save sample sequences in fasta file
tmp.file <- tempfile(pattern = "cobindr_sample_seq", tmpdir = tempdir(), fileext = ".fasta")
writeXStringSet(DNAStringSet(seqs), tmp.file)
#run cobindr
cfg <- cobindrConfiguration()
sequence_type(cfg) <- 'fasta'
sequence_source(cfg) <- tmp.file
sequence_origin(cfg) <- 'artificial sequences'
pfm_path(cfg) <- system.file('extdata/pfms', package='cobindr')
pairs(cfg) <- 'V$MYOD_01 V$MYOD_01'
runObj <- cobindr(cfg, name='cobindr test using sampled sequences')
# perform tfbs prediction using matchPWM
runObj.bs <- search.pwm(runObj, min.score = '90')
# show results
plot.positionprofile(runObj.bs)
# clean up
unlink(tmp.file)

```

---

seqObj

*cobindr SeqObj object constructor*


---

## Description

cobindr SeqObj object constructor

## Usage

```

## S4 method for signature
## 'DNAString,character,character,character,character,character'
seqObj(seq,id,name,species,comment,location)

```

## Arguments

seq	DNAString object holding the sequence
id	id (character)
name	id (character)
species	id (character)
comment	id (character)
location	id (character)

**Value**

cobindR SeqObj object

**Author(s)**

Rob Lehmann <r.lehmann@biologie.hu-berlin.de>

**See Also**

[cobindRConfiguration](#)

**Examples**

```
library(Biostrings)
so <- seqObj(DNAString('A'), id='', name='', species='',comment='',location='')
sequence(so)
```

---

SeqObj-class

*Class "SeqObj"*

---

**Description**

Container for DNA sequence and its meta-data.

**Objects from the Class**

Objects can be created by calls of the form `new("SeqObj", seq, id, species, name, comment, location)`.

**Slots**

**uid:** Object of class "character" ~~ unique id for internal representation  
**name:** Object of class "character" ~~ biological reference name, if available  
**species:** Object of class "character" ~~ reference species  
**location:** Object of class "character" ~~ location on the reference genome  
**comment:** Object of class "character" ~~ comments and notes  
**sequence:** Object of class "DNAString" ~~ the sequence

**Methods**

**initialize** signature(.Object = "SeqObj"): ...  
**rtfbs.intern** signature(object = "SeqObj"): ...  
**write.fasta** signature(sequences = "SeqObj"): ...

**Author(s)**

Manuela Benary <manuela.benary@cms.hu-berlin.de>

**See Also**

[cobindr configuration](#)

**Examples**

```
showClass("SeqObj")
```

---

sequence	<i>returns sequence of cobindr SeqObj object</i>
----------	--

---

**Description**

returns sequence of cobindr seqObj object.

**Usage**

```
## S4 method for signature 'SeqObj'  
sequence(x)  
## S4 replacement method for signature 'SeqObj,DNAString'  
sequence(x) <- value
```

**Arguments**

x	a cobindr seqObj object
value	DNAString of the actual DNA sequence in this SeqObj

**Value**

sequence (DNAString)

**Author(s)**

Rob Lehmann <r.lehmann@biologie.hu-berlin.de>

**See Also**

[uid,name,species,location,comment,sequence](#)

**Examples**

```
library(Biostrings)  
so <- seqObj(DNAString('A'), id='', name='', species='',comment='',location='')  
sequence(so)
```

---

sequences	<i>sequences of cobindr object</i>
-----------	------------------------------------

---

### Description

sequences of cobindr object.

### Usage

```
## S4 method for signature 'cobindr'  
sequences(x)  
## S4 replacement method for signature 'cobindr,list'  
sequences(x) <- value
```

### Arguments

x	a cobindr object
value	the list of input sequences of type SeqObj

### Value

sequences (character)

### Author(s)

Rob Lehmann <r.lehmann@biologie.hu-berlin.de>

### See Also

[uid](#),[name](#),[sequences](#),[bg\\_sequences](#),[desc](#),[configuration](#),[binding\\_sites](#),[bg\\_binding\\_sites](#),[pfm](#),[pairs](#),[bg\\_pairs](#),[pair](#)

### Examples

```
cfg <- cobindRConfiguration()  
sequence_type(cfg) <- 'fasta'  
sequence_source(cfg) <- system.file('extdata/sox_oct_example_vignette_seqs.fasta', package='cobindR')  
sequence_origin(cfg) <- 'Mouse Embryonic Stem Cell Example CHIP-Seq Oct4 Peak Sequences'  
cbr <- cobindr(cfg)  
length(sequences(cbr))
```

---

sequence_origin	<i>returns sequence_origin of cobindR configuration object</i>
-----------------	--

---

### Description

returns sequence\_origin of cobindR configuration object.

### Usage

```
## S4 method for signature 'configuration'  
sequence_origin(x)  
## S4 replacement method for signature 'configuration,character'  
sequence_origin(x) <- value
```

### Arguments

x	a cobindR configuration object
value	the origin of the sequence

### Value

sequence\_origin (character)

### Author(s)

Rob Lehmann <r.lehmann@biologie.hu-berlin.de>

### See Also

[id](#), [experiment\\_description](#), [sequence\\_source](#), [sequence\\_origin](#), [sequence\\_type](#), [bg\\_sequence\\_source](#), [bg\\_sequence](#)

### Examples

```
cfg <- cobindRConfiguration()  
sequence_origin(cfg)
```

---

sequence_source	<i>returns sequence_source of cobindR configuration object</i>
-----------------	--

---

### Description

returns sequence\_source of cobindR configuration object.

### Usage

```
## S4 method for signature 'configuration'  
sequence_source(x)  
## S4 replacement method for signature 'configuration,character'  
sequence_source(x) <- value
```

### Arguments

x	a cobindR configuration object
value	the source of which the sequence is retrieved

### Value

sequence\_source (character)

### Author(s)

Rob Lehmann <r.lehmann@biologie.hu-berlin.de>

### See Also

[id](#), [experiment\\_description](#), [sequence\\_source](#), [sequence\\_origin](#), [sequence\\_type](#), [bg\\_sequence\\_source](#), [bg\\_sequence](#)

### Examples

```
cfg <- cobindRConfiguration()  
sequence_source(cfg)
```

---

sequence_type	<i>sequence type of cobindR configuration object</i>
---------------	--

---

**Description**

sequence type of cobindR configuration object

**Usage**

```
## S4 method for signature 'configuration'  
sequence_type(x)  
## S4 replacement method for signature 'configuration,character'  
sequence_type(x) <- value
```

**Arguments**

x	a cobindR configuration object
value	the type of the sequence used in this experiment (e.g. promotor)

**Value**

sequence\_type (character)

**Author(s)**

Rob Lehmann <r.lehmann@biologie.hu-berlin.de>

**See Also**

[id](#),[experiment\\_description](#),[sequence\\_source](#),[sequence\\_origin](#),[sequence\\_type](#),[bg\\_sequence\\_source](#),[bg\\_sequence](#)

**Examples**

```
cfg <- cobindRConfiguration()  
sequence_type(cfg)
```

---

species	<i>species of cobindR configuration or SeqObj</i>
---------	---

---

### Description

species of cobindR configuration or SeqObj

### Usage

```
## S4 method for signature 'configuration'  
species(object)  
## S4 replacement method for signature 'configuration'  
species(object) <- value  
## S4 method for signature 'SeqObj'  
species(object)  
## S4 replacement method for signature 'SeqObj'  
species(object) <- value
```

### Arguments

object	a cobindR configuration object
value	name of species in this experiment or SeqObj

### Value

sequence / experiment species (character)

### Author(s)

Rob Lehmann <r.lehmann@biologie.hu-berlin.de>

### See Also

[id](#), [experiment\\_description](#), [sequence\\_source](#), [sequence\\_origin](#), [sequence\\_type](#), [bg\\_sequence\\_source](#), [bg\\_sequence](#)

### Examples

```
cfg <- cobindRConfiguration()  
species(cfg)
```

---

testCpG	<i>function to cluster sequences based on their CpG and GC content</i>
---------	--

---

**Description**

diagnostical function - GC content and CpG content are clustered using 2D gaussian models (Mclust). FALSE is returned if > max.clust (default=1) subgroups are found using the bayesian information criterion (BIC). If do.plot=TRUE, the results are visualized.

**Usage**

```
## S4 method for signature 'cobindr'  
testCpG(x, max.clust = 4, do.plot = F, n.cpu = NA)
```

**Arguments**

x	an object of the class "cobindr", which will hold all necessary information about the sequences and the hits.
max.clust	integer describing the maximal number of clusters which are used for separating the data.
do.plot	logical flag, if do.plot=TRUE a scatterplot for the GC and CpG content for each sequence is produced and the clusters are color coded.
n.cpu	number of CPUs to be used for parallelization. Default value is 'NA' in which case the number of available CPUs is checked and than used.

**Value**

result	logical flag, FALSE is returned if more than one subgroups are found using the bayesian information criterion (BIC)
gc	matrix with rows corresponding to sequences and columns corresponding to GC and CpG content

**Author(s)**

Robert Lehmann <r.lehmann@biologie.hu-berlin.de>

**References**

the method uses clustering functions from the package "mclust" (<http://www.stat.washington.edu/mclust/>)

**See Also**

[plot.gc](#)

**Examples**

```

cfg <- cobindRConfiguration()
sequence_type(cfg) <- 'fasta'
sequence_source(cfg) <- system.file('extdata/example.fasta', package='cobindR')
# avoid complaint of validation mechanism
pfm_path(cfg) <- system.file('extdata/pfms', package='cobindR')
pairs(cfg) <- ''
runObj <- cobindr( cfg)
testCpG(runObj, max.clust = 2, do.plot = TRUE)

```

---

threshold	<i>threshold used in motif hit finding</i>
-----------	--

---

**Description**

threshold used in motif hit finding

**Usage**

```

## S4 method for signature 'configuration'
threshold(x)
## S4 replacement method for signature 'configuration,numeric'
threshold(x) <- value

```

**Arguments**

x	a cobindR configuration object
value	the hit threshold

**Value**

threshold (numeric)

**Author(s)**

Rob Lehmann <r.lehmann@biologie.hu-berlin.de>

**See Also**

[id](#), [experiment\\_description](#), [sequence\\_source](#), [sequence\\_origin](#), [sequence\\_type](#), [bg\\_sequence\\_source](#), [bg\\_sequence](#)

**Examples**

```

cfg <- cobindRConfiguration()
threshold(cfg)

```

---

uid	<i>uid of cobindR SeqObj object</i>
-----	-------------------------------------

---

**Description**

uid of cobindR seqObj object.

**Usage**

```
## S4 method for signature 'SeqObj'  
uid(x)  
## S4 method for signature 'cobindr'  
uid(x)  
## S4 replacement method for signature 'SeqObj,character'  
uid(x) <- value  
## S4 replacement method for signature 'cobindr,character'  
uid(x) <- value
```

**Arguments**

x	a cobindR seqObj object
value	the unique id of the sequence or cobindr object

**Value**

uid (character)

**Author(s)**

Rob Lehmann <r.lehmann@biologie.hu-berlin.de>

**See Also**

[uid,name,species,location,comment,sequence](#)

**Examples**

```
library(Biostrings)  
so <- seqObj(DNAString('A'), id='', name='', species='',comment='',location='')  
uid(so)
```

---

upstream	<i>upstream range [bp] used in experiment</i>
----------	---

---

**Description**

upstream range [bp] used in experiment

**Usage**

```
## S4 method for signature 'configuration'  
upstream(x)  
## S4 replacement method for signature 'configuration,numeric'  
upstream(x) <- value
```

**Arguments**

x	a cobindR configuration object
value	upstream distance [bp] of feature to be included (numeric)

**Value**

considered upstream range [bp]

**Author(s)**

Rob Lehmann <r.lehmann@biologie.hu-berlin.de>

**See Also**

[id](#), [experiment\\_description](#), [sequence\\_source](#), [sequence\\_origin](#), [sequence\\_type](#), [bg\\_sequence\\_source](#), [bg\\_sequence](#)

**Examples**

```
cfg <- cobindRConfiguration()  
upstream(cfg)
```

---

write.bindingsites     *writes predicted binding sites as a BED file.*

---

**Description**

writes predicted binding sites as a BED file.

**Usage**

```
## S4 method for signature 'cobindr'  
write.bindingsites(x, file = NULL, background = FALSE)
```

**Arguments**

x	an object of the class "cobindr", which holds all necessary information about the sequences and the predicted binding sites.
file	path to file. If filename is 'NULL' a filename is generated based on the name of the object of class "cobindr".
background	logical flag. If background is 'TRUE' the binding sites found in the background sequences are used.

**Note**

At the moment write.bindingsites() only works for sequences based on gene ids. Otherwise please use write.bindingsites.table().

**Author(s)**

Stefan Kroeger <kroeger@informatik.hu-berlin.de>

**See Also**

[write.bindingsites.table](#), [write.pairs](#), [write.sequences](#), [write](#)

---

write.bindingsites.table  
*function to write predicted TFBS into a tab-separated file.*

---

**Description**

function to write predicted TFBS into a tab-separated file.

**Usage**

```
## S4 method for signature 'cobindr'  
write.bindingsites.table(x, file = NULL)
```

**Arguments**

x	an object of the class "cobindr", which will hold all necessary information about the sequences and the predicted binding sites.
file	path to file. If filename is 'NULL' a filename is generated based on the name of the object of class "cobindr".

**Author(s)**

Stefan Kroeger <kroeger@informatik.hu-berlin.de>

**See Also**

[write.pairs](#), [write.bindingsites](#), [write.sequences](#), [write](#)

---

write.pairs

*function to write output of findPairs into file*

---

**Description**

Function writes the results of findPairs() as a tab-separated file. The file consists of 6 columns, namely

- a unique id for each pair,
- the unique id of the sequence, where the pair was found,
- the names of the corresponding PFMs,
- the unique id for each PFM, and
- the distance window in which the pair occurs.

**Usage**

```
## S4 method for signature 'cobindr'
write.pairs(x, file = NULL, background = FALSE)
```

**Arguments**

x	an object of the class "cobindr", which holds all necessary information about the sequences and the predicted binding sites.
file	path to file. If filename is 'NULL' a filename is generated based on the name of the object of class "cobindr".
background	logical flag. If background is 'TRUE' the pairs found in the background sequences are used.

**Author(s)**

Stefan Kroeger <kroeger@informatik.hu-berlin.de>

**See Also**

[write.bindingsites.table](#), [write.bindingsites](#), [write.sequences](#), [write](#)

---

write.sequences	<i>writes the sequences of a cobindr-object into a fasta file.</i>
-----------------	--

---

**Description**

writes the sequences of a cobindr-object into a fasta file.

**Usage**

```
## S4 method for signature 'cobindr'  
write.sequences(x, slotname = "sequences", file = NULL)
```

**Arguments**

x	an object of the class "cobindr", which will hold all necessary information about the sequences.
slotname	string, describing whether to use foreground sequences (default) or background sequences
file	path to file. If filename is 'NULL' a filename is generated based on the name of the object of class "cobindr".

**Author(s)**

Stefan Kroeger <kroeger@informatik.hu-berlin.de>

**See Also**

[write.bindingsites.table](#), [write.bindingsites](#), [write.pairs](#), [write](#)

**Examples**

```
cfg <- cobindRConfiguration()  
sequence_type(cfg) <- 'fasta'  
sequence_source(cfg) <- system.file('extdata/example.fasta', package='cobindR')  
# avoid complaint of validation mechanism  
pfm_path(cfg) <- system.file('extdata/pfms', package='cobindR')  
pairs(cfg) <- ''  
runObj <- cobindr(cfg)  
write.sequences(runObj, file = file.path(tempfile("example.txt", tempdir()))) )
```

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