

# Package ‘PAIRADISE’

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**Title** PAIRADISE: Paired analysis of differential isoform expression  
**Version** 1.28.0  
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**Description** This package implements the PAIRADISE procedure for detecting differential isoform expression between matched replicates in paired RNA-Seq data.  
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|            |                   |
|------------|-------------------|
| clean.data | <i>clean.data</i> |
|------------|-------------------|

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**Description**

Removes missing data and invalid pairs from the matched pair data to be analyzed by PAIRADISE.

**Usage**

clean.data(my.data)

**Arguments**

my.data                      Data frame containing grouped data to be analyzed.

**Details**

The data frame has 7 columns, arranged as follows: Column 1 contains the ID of the exons/events. Column 2 contains counts of isoform 1 corresponding to the first group. Column 3 contains counts of isoform 2 corresponding to the first group. Column 4 contains counts of isoform 1 corresponding to the second group. Column 5 contains counts of isoform 2 corresponding to the second group. Replicates in columns 2-5 should be separated by commas, e.g. 1623,432,6 for three replicates. Column 6 contains the effective length of isoform 1. Column 7 contains the effective length of isoform 2.

**Value**

The function clean.data returns a list containing the following entries:

- |          |                                              |
|----------|----------------------------------------------|
| I1       | Group 1 isoform 1 counts for each replicate. |
| S1       | Group 1 isoform 2 counts for each replicate. |
| I2       | Group 2 isoform 1 counts for each replicate. |
| S2       | Group 2 isoform 2 counts for each replicate. |
| length_I | Effective lengths of isoform 1.              |

|          |                                                            |
|----------|------------------------------------------------------------|
| length_S | Effective lengths of isoform 2.                            |
| exonList | IDs of the exons/events.                                   |
| nExon    | Number of exons/events.                                    |
| M        | Vector containing the number of replicates per exon/event. |

---

|        |                           |
|--------|---------------------------|
| counts | <i>PDseDataSet counts</i> |
|--------|---------------------------|

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**Description**

PDseDataSet counts

**Usage**

counts(object)

**Arguments**

object            A PDseDataSet object

**Value**

A counts matrix

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|           |                  |
|-----------|------------------|
| load.data | <i>load.data</i> |
|-----------|------------------|

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**Description**

Loads the matched pair data to be analyzed by PAIRADISE.

**Usage**

load.data(my.data)

**Arguments**

my.data            Data frame containing grouped data to be analyzed.

**Details**

The data frame has 7 columns, arranged as follows: Column 1 contains the ID of the exons/events. Column 2 contains counts of isoform 1 corresponding to the first group. Column 3 contains counts of isoform 2 corresponding to the first group. Column 4 contains counts of isoform 1 corresponding to the second group. Column 5 contains counts of isoform 2 corresponding to the second group. Replicates in columns 2-5 should be separated by commas, e.g. 1623,432,6 for three replicates. Column 6 contains the effective length of isoform 1. Column 7 contains the effective length of isoform 2.

**Value**

The function `load.data` returns a list containing the following entries:

|          |                                                            |
|----------|------------------------------------------------------------|
| I1       | Group 1 isoform 1 counts for each replicate.               |
| S1       | Group 1 isoform 2 counts for each replicate.               |
| I2       | Group 2 isoform 1 counts for each replicate.               |
| S2       | Group 2 isoform 2 counts for each replicate.               |
| length_I | Effective lengths of isoform 1.                            |
| length_S | Effective lengths of isoform 2.                            |
| exonList | IDs of the exons/events.                                   |
| nExon    | Number of exons/events.                                    |
| M        | Vector containing the number of replicates per exon/event. |

---

*logit*


---

*logit*


---

**Description**

Takes in a vector and applies the `logit` function elementwise to that vector

**Usage**

```
logit(x)
```

**Arguments**

`x` : numeric vector, whose entries should be strictly between 0 and 1

**Value**

```
logit(x)
```

---

|               |                      |
|---------------|----------------------|
| loglikelihood | <i>loglikelihood</i> |
|---------------|----------------------|

---

### Description

Used internally in PAIRADISE to compute the log-likelihood function

### Usage

```
loglikelihood(
  M,
  I1,
  S1,
  I2,
  S2,
  l.iI,
  l.iS,
  logit.psi1,
  logit.psi2,
  alpha,
  s1,
  s2,
  s,
  mu,
  delta
)
```

### Arguments

|            |                                                              |
|------------|--------------------------------------------------------------|
| M          | Number of replicates for the current exon. Positive integer. |
| I1         | Exon inclusion counts for group 1. Positive integers.        |
| S1         | Exon skipping counts for group 1. Positive integers.         |
| I2         | Exon inclusion counts for group 2. Positive integers.        |
| S2         | Exon skipping counts for group 2. Positive integers.         |
| l.iI       | Effective length of inclusion isoform. Positive integer.     |
| l.iS       | Effective length of skipping isoform. Positive integer.      |
| logit.psi1 | Numeric vector with values of logit psi1.                    |
| logit.psi2 | Numeric vector with values of logit psi2.                    |
| alpha      | Numeric vector with values of alpha.                         |
| s1         | Group 1 standard deviation. Positive number.                 |
| s2         | Group 2 standard deviation. Positive number.                 |
| s          | Overall standard deviation. Positive number.                 |
| mu         | Parameter mu.                                                |
| delta      | Parameter delta.                                             |

**Value**

log likelihood value at input.

---

optimize1

*optimize1*

---

**Description**

Used internally in PAIRADISE to compute the MLEs of delta, mu, sigma1, sigma2, sigma

**Usage**

```
optimize1(
  x,
  M,
  I1,
  S1,
  I2,
  S2,
  l.iI,
  l.iS,
  logit.psi1,
  logit.psi2,
  alpha,
  equal.variance = FALSE
)
```

**Arguments**

|                |                                                                                                                                                                                                                                                                                                                                        |
|----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| x              | Numeric vector such that $x = (\text{sigma1}, \text{sigma2}, \text{sigma}, \text{mu}, \text{delta})$ if <code>equal.variance = FALSE</code> , and $x = (\text{sigma1}, \text{sigma}, \text{mu}, \text{delta})$ if <code>equal.variance = TRUE</code> . <code>sigma1</code> , <code>sigma2</code> , <code>sigma</code> must be positive |
| M              | Number of replicates for the current exon.                                                                                                                                                                                                                                                                                             |
| I1             | Exon inclusion counts for group 1. Positive integers.                                                                                                                                                                                                                                                                                  |
| S1             | Exon skipping counts for group 1. Positive integers.                                                                                                                                                                                                                                                                                   |
| I2             | Exon inclusion counts for group 2. Positive integers.                                                                                                                                                                                                                                                                                  |
| S2             | Exon skipping counts for group 2. Positive integers.                                                                                                                                                                                                                                                                                   |
| l.iI           | Effective length of inclusion isoform. Positive integer.                                                                                                                                                                                                                                                                               |
| l.iS           | Effective length of skipping isoform. Positive integer.                                                                                                                                                                                                                                                                                |
| logit.psi1     | Numeric vector with values of logit psi1.                                                                                                                                                                                                                                                                                              |
| logit.psi2     | Numeric vector with values of logit psi2.                                                                                                                                                                                                                                                                                              |
| alpha          | Numeric vector with values of alpha.                                                                                                                                                                                                                                                                                                   |
| equal.variance | Are the group variances assumed equal? Default value is FALSE.                                                                                                                                                                                                                                                                         |

**Value**

The MLEs.

---

|           |                  |
|-----------|------------------|
| optimize2 | <i>optimize2</i> |
|-----------|------------------|

---

**Description**

Used internally in PAIRADISE to compute the MLEs of  $\text{logit}(\psi_1)$ ,  $\text{logit}(\psi_2)$ ,  $\alpha$

**Usage**

optimize2(x, k, I1, S1, I2, S2, l.iI, l.iS, delta, mu, s1, s2, s)

**Arguments**

|       |                                                                                     |
|-------|-------------------------------------------------------------------------------------|
| x     | Numeric vector such that $x = (\text{logit}(\psi_1), \text{logit}(\psi_2), \alpha)$ |
| k     | Index representing current replicate number.                                        |
| I1    | Exon inclusion counts for group 1. Positive integers.                               |
| S1    | Exon skipping counts for group 1. Positive integers.                                |
| I2    | Exon inclusion counts for group 2. Positive integers.                               |
| S2    | Exon skipping counts for group 2. Positive integers.                                |
| l.iI  | Effective length of inclusion isoform. Positive integer.                            |
| l.iS  | Effective length of skipping isoform. Positive integer.                             |
| delta | Parameter delta.                                                                    |
| mu    | Parameter mu.                                                                       |
| s1    | Group 1 standard deviation. Positive number.                                        |
| s2    | Group 2 standard deviation. Positive number.                                        |
| s     | Overall standard deviation. Positive number.                                        |

**Value**

The MLEs.

---

|           |                                                                                                    |
|-----------|----------------------------------------------------------------------------------------------------|
| PAIRADISE | <i>PAIRADISE Detecting allele-specific alternative splicing from population-scale RNA-seq data</i> |
|-----------|----------------------------------------------------------------------------------------------------|

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## Description

We introduce PAIRADISE (PAIred Replicate analysis of Allelic Differential Splicing Events), a method for detecting allele-specific alternative splicing (ASAS) from RNA-seq data. PAIRADISE uses a statistical model that aggregates ASAS signals across multiple individuals in a population. It formulates ASAS detection as a statistical problem for identifying differential alternative splicing from RNA-seq data with paired replicates. The PAIRADISE statistical model is applicable to many forms of allele-specific isoform variation (e.g. RNA editing), and can be used as a generic statistical model for RNA-seq studies involving paired replicates.

## See Also

[pairadise](#)

---

|           |                  |
|-----------|------------------|
| pairadise | <i>pairadise</i> |
|-----------|------------------|

---

## Description

Primary function of the PAIRADISE package. Analyzes matched pairs for differences in isoform expression. Uses parallel processing to speed up computation.

## Usage

```
pairadise(
  pdat,
  nIter = 100,
  tol = 10^(-2),
  pseudocount = 0,
  seed = 12321,
  equal.variance = FALSE,
  numCluster = 2,
  BPPARAM = MulticoreParam(numCluster)
)
```

## Arguments

|       |                                                                                                                            |
|-------|----------------------------------------------------------------------------------------------------------------------------|
| pdat  | A PDseDataSet object                                                                                                       |
| nIter | Positive integer. Specifies the maximum number of iterations of the optimization algorithm allowed. Default is nIter = 100 |

|                |                                                                                                                                                                                                     |
|----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| tol            | Positive number. Specifies the tolerance level for terminating the optimization algorithm, defined as the difference in log-likelihood ratios between iterations. Default is $\text{tol} = 10^{-2}$ |
| pseudocount    | Positive number. Specifies a value for a pseudocount added to each count at the beginning of the analysis. Default is $\text{pseudocount} = 0$                                                      |
| seed           | An integer to set seed.                                                                                                                                                                             |
| equal.variance | Are the group variances assumed equal? Default value is FALSE.                                                                                                                                      |
| numCluster     | Number of clusters to use for parallel computing.                                                                                                                                                   |
| BPPARAM        | parallel parameters from package BiocParallel.                                                                                                                                                      |

### Details

This is the primary function of the PAIRADISE package that implements the PAIRADISE algorithm.

### Value

A PDseDataSet object contains outputs from PAIRADISE algorithm.

### Examples

```
#####
## Example: Simulated data ##
#####

set.seed(12345)
data("sample_dataset")
pdat <- PDseDataSetFromMat(sample_dataset)
pdat <- pairadise(pdat, numCluster = 4)
results(pdat)
```

---

PDseDataSet-class

*PDseDataSet object and constructor*


---

### Description

‘PDseDataSet’ is a subclass of ‘SummarizedExperiment’. It can be used to store inclusion and skipping splicing counts for pair designed samples.

### Usage

```
PDseDataSet(counts, design, lengths)
```

**Arguments**

|         |                                                                                                           |
|---------|-----------------------------------------------------------------------------------------------------------|
| counts  | The counts of splicing events, including inclusion and skipping counts in 3 dimensions for each sample.   |
| design  | The paired design data.frame, including sample column for sample ids and group column for design factors. |
| lengths | Two columns iLen and sLen for the effective lengths of inclusion and skipping isoforms.                   |

**Value**

A PDseDataSet object

**Examples**

```
icount <- matrix(1:4, 1)
scount <- matrix(5:8, 1)
account <- abind::abind(icount, scount, along = 3)
design <- data.frame(sample = rep(c("s1", "s2"), 2),
  group = rep(c("T", "N"), each = 2))
lens <- data.frame(sLen=1L, iLen=2L)
PDseDataSet(account, design, lens)
```

---

PDseDataSetFromMat

*PDseDataSet from rMATs/PAIRADISE Mat format*


---

**Description**

The Mat format should have 7 columns, arranged as follows: Column 1 contains the ID of the alternative splicing events. Column 2 contains counts of isoform 1 corresponding to the first group. Column 3 contains counts of isoform 2 corresponding to the first group. Column 4 contains counts of isoform 1 corresponding to the second group. Column 5 contains counts of isoform 2 corresponding to the second group. Column 6 contains the effective length of isoform 1. Column 7 contains the effective length of isoform 2. Replicates in columns 2-5 should be separated by commas, e.g. "1623,432,6" for three replicates and the replicate order should be consistent for each column to ensure pairs are matched correctly.

**Usage**

```
PDseDataSetFromMat(dat)
```

**Arguments**

|     |                           |
|-----|---------------------------|
| dat | The Mat format dataframe. |
|-----|---------------------------|

**Value**

A PDseDataSet object

**Examples**

```
data("sample_dataset")
pdat <- PDseDataSetFromMat(sample_dataset)
```

---

|         |                                               |
|---------|-----------------------------------------------|
| results | <i>Extract results for pairadise analysis</i> |
|---------|-----------------------------------------------|

---

**Description**

Extract results for pairadise analysis

**Usage**

```
results(pdat, p.adj = "BH", sig.level = 0.01, details = FALSE)
```

**Arguments**

|           |                                              |
|-----------|----------------------------------------------|
| pdat      | A PDseDataSet object from pairadise analysis |
| p.adj     | The p ajustment method.                      |
| sig.level | The cutoff of significant results            |
| details   | Whether to list detailed results.            |

**Value**

The function return a results DataFrame.

|           |                                                |
|-----------|------------------------------------------------|
| testStats | Vector of test statistics for paired analysis. |
| p.value   | Vector of pvalues for each exon/event.         |
| p.adj     | The adjusted p values                          |

If details is TRUE, more detailed parameter estimates for constrained and unconstrained model will return.

**Examples**

```
data("sample_dataset")
pdat <- PDseDataSetFromMat(sample_dataset)
pdat <- pairadise(pdat)
results(pdat)
```

---

|                |                       |
|----------------|-----------------------|
| sample_dataset | <i>sample_dataset</i> |
|----------------|-----------------------|

---

## Description

The CEU dataset was generated by analyzing the allele-specific alternative splicing events in the GEUVADIS CEU data. Allele-specific reads were mapped onto alternative splicing events using rPGA (version 2.0.0). Then the allele-specific bam files mapped onto the two haplotypes are merged together to detect alternative splicing events using rMATS (version 3.2.5)<sup>16</sup>.

The LUSC dataset was generated by analyzing the tumor versus adjacent control samples from TCGA LUSC RNA-seq data.

## Usage

```
data(sample_dataset)
```

```
data(sample_dataset_CEU)
```

```
data(sample_dataset_LUSC)
```

## Format

The dataset has 7 columns, arranged as follows:

**ExonID** Column 1 contains the ID of the alternative splicing events.

**I1** Column 2 contains counts of isoform 1 corresponding to the first group.

**S1** Column 3 contains counts of isoform 2 corresponding to the first group.

**I2** Column 4 contains counts of isoform 1 corresponding to the second group.

**S2** Column 5 contains counts of isoform 2 corresponding to the second group.

**I\_len** Column 6 contains the effective length of isoform 1.

**S\_len** Column 7 contains the effective length of isoform 2.

The dataset has 7 columns, arranged as follows:

**ExonID** Column 1 contains the ID of the alternative splicing events.

**I1** Column 2 contains counts of isoform 1 corresponding to the first group.

**S1** Column 3 contains counts of isoform 2 corresponding to the first group.

**I2** Column 4 contains counts of isoform 1 corresponding to the second group.

**S2** Column 5 contains counts of isoform 2 corresponding to the second group.

**I\_len** Column 6 contains the effective length of isoform 1.

**S\_len** Column 7 contains the effective length of isoform 2.

The dataset has 7 columns, arranged as follows:

**ExonID** Column 1 contains the ID of the alternative splicing events.

- I1** Column 2 contains counts of isoform 1 corresponding to the first group.
- S1** Column 3 contains counts of isoform 2 corresponding to the first group.
- I2** Column 4 contains counts of isoform 1 corresponding to the second group.
- S2** Column 5 contains counts of isoform 2 corresponding to the second group.
- I\_len** Column 6 contains the effective length of isoform 1.
- S\_len** Column 7 contains the effective length of isoform 2.

---

|         |                |
|---------|----------------|
| sigmoid | <i>sigmoid</i> |
|---------|----------------|

---

**Description**

Takes in a vector and applies the sigmoid function elementwise to that vector

**Usage**

sigmoid(x)

**Arguments**

x : numeric vector

**Value**

sigmoid(x)

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