FraseR: Find RAre Splicing Events in RNA-seq data

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Abstract

Whole exome sequencing and whole genome Sequencing is already a standard in the field of diagnostics of rare disorders. But due to the lack of biological knowledge and interpretation of the vast of variants RNA-seq is an important complementary tool to assess outliers and detect potentially disease causing splice variants.

If you use *FraseR* in published research, please cite:

Mertes C, Gagneur J, *et al.* **FraseR: Find RAre Splicing Events in RNA-seq data** *bioRxiv*

Contents

1 Quick guide to *FraseR*

To start quickly with *FraseR* just call this 4 functions to get a standard analysis on an example data set from the following publication [**?**].

```
# load FraseR package
library(FraseR)

# create sample annotation and settings
settings <- createTestFraseRSettings()

# run full standard analysis
fds <- FraseR(settings)
```

```
## Wed May 17 19:15:16 2017:  Start counting the split reads ...
## Wed May 17 19:15:16 2017:  Count split reads for sample:  sample1
## Wed May 17 19:15:17 2017:  Count split reads for sample:  sample2
## Wed May 17 19:15:17 2017:  Count split reads for sample:  sample3
## Wed May 17 19:15:17 2017:  Count split reads for sample:  sample4
## Wed May 17 19:15:17 2017:  Count split reads for sample:  sample5
## Wed May 17 19:15:17 2017:  Count split reads for sample:  sample6
## Wed May 17 19:15:17 2017:  Count split reads for sample:  sample7
## Wed May 17 19:15:17 2017:  Count split reads for sample:  sample8
## Wed May 17 19:15:17 2017:  Count split reads for sample:  sample9
## Wed May 17 19:15:17 2017:  Count split reads for sample:  sample10
## Wed May 17 19:15:17 2017:  Count split reads for sample:  sample11
## Wed May 17 19:15:17 2017:  Count split reads for sample:  sample12
## Wed May 17 19:15:17 2017 :  count ranges need to be merged ...
## Wed May 17 19:15:18 2017:  Preparing data for HDF5 conversion:  rawCountsJ
## Wed May 17 19:15:18 2017:  Writing data:  rawCountsJ to file:  /data/nasif12/home_if12/mertes/Fr
## Wed May 17 19:15:19 2017:  Create splice site indices ...
## Wed May 17 19:15:19 2017:  Start counting the non spliced reads ...
## Wed May 17 19:15:19 2017:  In total 94 splice junctions are found.
## Wed May 17 19:15:20 2017:  In total 111 splice sites (acceptor/donor)
will be counted ...
```

```
## Wed May 17 19:15:20 2017:  Count non spliced reads for sample:  sample1
## Wed May 17 19:15:20 2017:  Count non spliced reads for sample:  sample2
## Wed May 17 19:15:20 2017:  Count non spliced reads for sample:  sample3
## Wed May 17 19:15:20 2017:  Count non spliced reads for sample:  sample4
## Wed May 17 19:15:20 2017:  Count non spliced reads for sample:  sample5
## Wed May 17 19:15:20 2017:  Count non spliced reads for sample:  sample6
## Wed May 17 19:15:20 2017:  Count non spliced reads for sample:  sample7
## Wed May 17 19:15:20 2017:  Count non spliced reads for sample:  sample8
## Wed May 17 19:15:20 2017:  Count non spliced reads for sample:  sample9
## Wed May 17 19:15:20 2017:  Count non spliced reads for sample:  sample10
## Wed May 17 19:15:20 2017:  Count non spliced reads for sample:  sample11
## Wed May 17 19:15:21 2017:  Count non spliced reads for sample:  sample12
## Wed May 17 19:15:21 2017 :  Fast merging of counts ...
## Wed May 17 19:15:21 2017:  Preparing data for HDF5 conversion:  rawCountsSS
## Wed May 17 19:15:21 2017:  Writing data:  rawCountsSS to file:  /data/nasif12/home_if12/mertes/F
## Wed May 17 19:15:22 2017:  Writing final FraseR object ('/data/ouga/home/ag_gagneur/mertes/Frase
## Wed May 17 19:15:22 2017:  Calculate the PSI3 values ...
## Wed May 17 19:15:23 2017:  Preparing data for HDF5 conversion:  psi3
## Wed May 17 19:15:23 2017:  Writing data:  psi3 to file:  /data/nasif12/home_if12/mertes/FraseR/s
## Wed May 17 19:15:23 2017:  Preparing data for HDF5 conversion:  rawOtherCounts_psi3
## Wed May 17 19:15:23 2017:  Writing data:  rawOtherCounts_psi3 to file:
/data/nasif12/home_if12/mertes/FraseR/savedObjects/Data_Analysis/rawOtherCounts_psi3.h5
## Wed May 17 19:15:23 2017:  Calculate the PSI5 values ...
## Wed May 17 19:15:23 2017:  Preparing data for HDF5 conversion:  psi5
## Wed May 17 19:15:23 2017:  Writing data:  psi5 to file:  /data/nasif12/home_if12/mertes/FraseR/s
## Wed May 17 19:15:23 2017:  Preparing data for HDF5 conversion:  rawOtherCounts_psi5
## Wed May 17 19:15:23 2017:  Writing data:  rawOtherCounts_psi5 to file:
/data/nasif12/home_if12/mertes/FraseR/savedObjects/Data_Analysis/rawOtherCounts_psi5.h5
## Wed May 17 19:15:24 2017:  Calculate the PSI site values ...
## Wed May 17 19:15:24 2017:  Preparing data for HDF5 conversion:  psiSite
## Wed May 17 19:15:24 2017:  Writing data:  psiSite to file:  /data/nasif12/home_if12/mertes/Frase
```

```
## Wed May 17 19:15:24 2017:  Preparing data for HDF5 conversion:  rawOtherCounts_psiSite

## Wed May 17 19:15:24 2017:  Writing data:  rawOtherCounts_psiSite to file:
/data/nasif12/home_if12/mertes/FraseR/savedObjects/Data_Analysis/rawOtherCounts_psiSite.h5

## Wed May 17 19:15:24 2017:  Calculate the Zscore for psi3 values ...

## Wed May 17 19:15:24 2017:  Preparing data for HDF5 conversion:  zscore_psi3

## Wed May 17 19:15:24 2017:  Writing data:  zscore_psi3 to file:  /data/nasif12/home_if12/mertes/F

## Wed May 17 19:15:25 2017:  Calculate the Zscore for psi5 values ...

## Wed May 17 19:15:25 2017:  Preparing data for HDF5 conversion:  zscore_psi5

## Wed May 17 19:15:25 2017:  Writing data:  zscore_psi5 to file:  /data/nasif12/home_if12/mertes/F

## Wed May 17 19:15:25 2017:  Calculate the Zscore for psiSite values ...

## Wed May 17 19:15:25 2017:  Preparing data for HDF5 conversion:  zscore_psiSite

## Wed May 17 19:15:25 2017:  Writing data:  zscore_psiSite to file:  /data/nasif12/home_if12/merte

## Wed May 17 19:15:25 2017:  Calculate P-values for the psi3 splice type
...

## Wed May 17 19:15:25 2017:  Sites to test:  80

## Wed May 17 19:15:35 2017:  Warnings in VGLM code while computing pvalues:
## 63 x xxx diagonal elements of the working weights variable 'wz' have been
replaced by 1.819e-12
## 13650 x value out of range in 'lgamma'

## Wed May 17 19:15:35 2017:  Errors in VGLM code while computing pvalues:
## 35 x could not obtain valid initial values.  Try using 'etastart', 'coefstart'
or 'mustart', else family-specific arguments such as 'imethod'.

## Wed May 17 19:15:35 2017:  Preparing data for HDF5 conversion:  pvalue_psi3

## Wed May 17 19:15:35 2017:  Writing data:  pvalue_psi3 to file:  /data/nasif12/home_if12/mertes/F

## Wed May 17 19:15:35 2017:  Writing final FraseR object ('/data/ouga/home/ag_gagneur/mertes/Frase

## Wed May 17 19:15:35 2017:  Calculate P-values for the psi5 splice type
...

## Wed May 17 19:15:35 2017:  Sites to test:  80

## Wed May 17 19:15:45 2017:  Warnings in VGLM code while computing pvalues:
## 10 x xxx diagonal elements of the working weights variable 'wz' have been
replaced by 1.819e-12
## 13400 x value out of range in 'lgamma'
```

```
## Wed May 17 19:15:45 2017:  Errors in VGLM code while computing pvalues:
## 30 x could not obtain valid initial values.  Try using 'etastart', 'coefstart'
or 'mustart', else family-specific arguments such as 'imethod'.

## Wed May 17 19:15:45 2017:  Preparing data for HDF5 conversion:  pvalue_psi5

## Wed May 17 19:15:45 2017:  Writing data:  pvalue_psi5 to file:  /data/nasif12/home_if12/mertes/F

## Wed May 17 19:15:46 2017:  Writing final FraseR object ('/data/ouga/home/ag_gagneur/mertes/Frase

## Wed May 17 19:15:46 2017:  Calculate P-values for the psiSite splice type
...

## Wed May 17 19:15:46 2017:  Sites to test:  96

## Wed May 17 19:15:57 2017:  Warnings in VGLM code while computing pvalues:
## 1 x iterations terminated because half-step sizes are very small
## 1 x some quantities such as z, residuals, SEs may be inaccurate due to
convergence at a half-step
## 94 x xxx diagonal elements of the working weights variable 'wz' have been
replaced by 1.819e-12
## 17600 x value out of range in 'lgamma'

## Wed May 17 19:15:57 2017:  Errors in VGLM code while computing pvalues:
## 1 x NA/NaN/Inf in 'y'
## 34 x could not obtain valid initial values.  Try using 'etastart', 'coefstart'
or 'mustart', else family-specific arguments such as 'imethod'.

## Wed May 17 19:15:57 2017:  Preparing data for HDF5 conversion:  pvalue_psiSite

## Wed May 17 19:15:57 2017:  Writing data:  pvalue_psiSite to file:  /data/nasif12/home_if12/merte

## Wed May 17 19:15:57 2017:  Writing final FraseR object ('/data/ouga/home/ag_gagneur/mertes/Frase

# annotate junctions and splice sites
# TODO
# fds <- annotateRanges(fds)

# visualize results
# TODO
# plotSampleResults(fds, "sample1")
```

The result html will be discussed in the corresponding section **??**

2 Standard workflow

The standard workflow for detecting rare abarrent splicing events in RNA-seq data can be divided into five steps.

1. Data preparation 2.1
2. Counting reads 2.2
3. Calculate PSI- and Zscore-values 2.3
4. Calculate P-values 2.4
5. Visualize results 2.5

Step 2-5 is wrapped up in one function `FraseR`, but each step can be called individually and parametrizied. A detailed explanaition of each step is given in the following subsections.

2.1 Data preparation

To start a RNA-seq data analysis with *FraseR* some preparation steps are needed. First of all we need a table with basic informations which then can be transformed into a *FraseRSettings* object. The minimum of information per sample is an unique sample name, the path to the aligned bam file. Additionally groups can be specified for the P-value calculations later. If a **NA** is asigned no P-values will be calculated. An example sample table is given within the package:

```
library(data.table)
head(fread(system.file(
    "extdata", "sampleTable.tsv", package="FraseR", mustWork=TRUE
)))
```

```
##    sampleID                bamFile group    gene
## 1:  sample1 extdata/bam/sample1.bam     1 TIMMDC1
## 2:  sample2 extdata/bam/sample2.bam     1 TIMMDC1
## 3:  sample3 extdata/bam/sample3.bam     2  MCOLN1
## 4:  sample4 extdata/bam/sample4.bam     3    CLPP
## 5:  sample5 extdata/bam/sample5.bam    NA    NHDF
## 6:  sample6 extdata/bam/sample6.bam    NA    NHDF
```

The RNA-seq data should be aligned with a splice-aware aligner like STAR[**?**] or GEM[**?**]. To gain better results the samples should be processed with the same protocol and origin from the same tissue.

To gain better results at least 20 samples should be sequenced.

To create a settings object for *FraseR* the constructor `FraseRSettings` should be called with at least a sampleData table. For an example have a look into the `createTestFraseRSettings`. In addition to the sampleData you can specify further parameters.

1. The parallel backend (a *BiocParallelParam* object)
2. The read filtering (a *ScanBamParam* object)

3. The name of the statistical method to be used
4. An output folder for the resulting figures and the cache
5. If the data is strand specific or not. (Not implemented yet)

The following shows how to create a test setting object. This object will be used throughout the whole vignette.

```
library(FraseR)
settings <- createTestFraseRSettings()
settings
```

```
## ------------------- Sample data table ----------------
##     sampleID                      bamFile condition    gene
##  1:  sample1  .../extdata/bam/sample1.bam         1 TIMMDC1
##  2:  sample2  .../extdata/bam/sample2.bam         1 TIMMDC1
##  3:  sample3  .../extdata/bam/sample3.bam         2  MCOLN1
##  4:  sample4  .../extdata/bam/sample4.bam         3    CLPP
##  5:  sample5  .../extdata/bam/sample5.bam        NA    NHDF
##  6:  sample6  .../extdata/bam/sample6.bam        NA    NHDF
##  7:  sample7  .../extdata/bam/sample7.bam        NA    NHDF
##  8:  sample8  .../extdata/bam/sample8.bam        NA    NHDF
##  9:  sample9  .../extdata/bam/sample9.bam        NA    NHDF
## 10: sample10 .../extdata/bam/sample10.bam        NA    NHDF
## 11: sample11 .../extdata/bam/sample11.bam        NA    NHDF
## 12: sample12 .../extdata/bam/sample12.bam        NA    NHDF
##
##
## ---------------------- Settings ----------------------
## Analysis name:               Data Analysis
## Statistical method:          betaBin
## Analysis is strand specific: FALSE
## Working directory:           '/data/ouga/home/ag_gagneur/mertes/FraseR'
##
##
## ------------------- Parallel backend -----------------
## class: SerialParam
##   bpisup: TRUE; bpnworkers: 1; bptasks: 0; bpjobname: BPJOB
##   bplog: FALSE; bpthreshold: INFO; bpstopOnError: TRUE
##   bptimeout: 2592000; bpprogressbar: FALSE
##   bplogdir: NA
##
##
## ------------------- BAM parameters -------------------
## class: ScanBamParam
## bamFlag (NA unless specified):
## bamSimpleCigar: FALSE
```

```
## bamReverseComplement: FALSE
## bamTag:
## bamTagFilter:
## bamWhich: 0 ranges
## bamWhat:
## bamMapqFilter: 10
```

2.2 Counting reads

Counting of the reads are straight forward and is done through the `countRNAData` function. The only required parameter is the FraseRSettings object. First all split reads are extracted from each individuel sample and cached if enabled. Then a dataset wide junction map is created (all visible junctions over all samples). After that for each sample the non-spliced reads at each given donor and acceptor site is counted. The resulting *FraseRDataSet* object contains two *SummarizedExperiment* objects for each the junctions and the splice sites.

```
fds <- countRNAData(settings)
```

```
## Wed May 17 19:15:58 2017:  Start counting the split reads ...
## Wed May 17 19:15:58 2017:  Count split reads for sample:  sample1
## Wed May 17 19:15:58 2017:  Count split reads for sample:  sample2
## Wed May 17 19:15:58 2017:  Count split reads for sample:  sample3
## Wed May 17 19:15:58 2017:  Count split reads for sample:  sample4
## Wed May 17 19:15:59 2017:  Count split reads for sample:  sample5
## Wed May 17 19:15:59 2017:  Count split reads for sample:  sample6
## Wed May 17 19:15:59 2017:  Count split reads for sample:  sample7
## Wed May 17 19:15:59 2017:  Count split reads for sample:  sample8
## Wed May 17 19:15:59 2017:  Count split reads for sample:  sample9
## Wed May 17 19:15:59 2017:  Count split reads for sample:  sample10
## Wed May 17 19:15:59 2017:  Count split reads for sample:  sample11
## Wed May 17 19:15:59 2017:  Count split reads for sample:  sample12
## Wed May 17 19:15:59 2017 :  count ranges need to be merged ...
## Wed May 17 19:15:59 2017:  Preparing data for HDF5 conversion:  rawCountsJ
## Wed May 17 19:15:59 2017:  Writing data:  rawCountsJ to file:  /data/nasif12/home_if12/mertes/Fr
## Wed May 17 19:15:59 2017:  Create splice site indices ...
```

```
## Wed May 17 19:16:00 2017:  Start counting the non spliced reads ...

## Wed May 17 19:16:00 2017:  In total 94 splice junctions are found.

## Wed May 17 19:16:00 2017:  In total 111 splice sites (acceptor/donor)
will be counted ...

## Wed May 17 19:16:00 2017:  Count non spliced reads for sample:  sample1

## Wed May 17 19:16:00 2017:  Count non spliced reads for sample:  sample2

## Wed May 17 19:16:00 2017:  Count non spliced reads for sample:  sample3

## Wed May 17 19:16:00 2017:  Count non spliced reads for sample:  sample4

## Wed May 17 19:16:00 2017:  Count non spliced reads for sample:  sample5

## Wed May 17 19:16:00 2017:  Count non spliced reads for sample:  sample6

## Wed May 17 19:16:00 2017:  Count non spliced reads for sample:  sample7

## Wed May 17 19:16:00 2017:  Count non spliced reads for sample:  sample8

## Wed May 17 19:16:00 2017:  Count non spliced reads for sample:  sample9

## Wed May 17 19:16:01 2017:  Count non spliced reads for sample:  sample10

## Wed May 17 19:16:01 2017:  Count non spliced reads for sample:  sample11

## Wed May 17 19:16:01 2017:  Count non spliced reads for sample:  sample12

## Wed May 17 19:16:01 2017 :  Fast merging of counts ...

## Wed May 17 19:16:01 2017:  Preparing data for HDF5 conversion:  rawCountsSS

## Wed May 17 19:16:01 2017:  Writing data:  rawCountsSS to file:  /data/nasif12/home_if12/mertes/F

## Wed May 17 19:16:02 2017:  Writing final FraseR object ('/data/ouga/home/ag_gagneur/mertes/Frase

fds

## -------------------- Sample data table -----------------
##     sampleID                       bamFile condition    gene
##  1:  sample1  .../extdata/bam/sample1.bam         1 TIMMDC1
##  2:  sample2  .../extdata/bam/sample2.bam         1 TIMMDC1
##  3:  sample3  .../extdata/bam/sample3.bam         2  MCOLN1
##  4:  sample4  .../extdata/bam/sample4.bam         3    CLPP
##  5:  sample5  .../extdata/bam/sample5.bam        NA    NHDF
##  6:  sample6  .../extdata/bam/sample6.bam        NA    NHDF
##  7:  sample7  .../extdata/bam/sample7.bam        NA    NHDF
##  8:  sample8  .../extdata/bam/sample8.bam        NA    NHDF
##  9:  sample9  .../extdata/bam/sample9.bam        NA    NHDF
## 10: sample10 .../extdata/bam/sample10.bam        NA    NHDF
## 11: sample11 .../extdata/bam/sample11.bam        NA    NHDF
## 12: sample12 .../extdata/bam/sample12.bam        NA    NHDF
```

```
##
##
## Number of samples:      12
## Number of junctions:    94
## Number of splice sites: 111
## assays(2): rawCountsJ rawCountsSS
##
##
## ---------------------- Settings ----------------------
## Analysis name:               Data Analysis
## Statistical method:          betaBin
## Analysis is strand specific: FALSE
## Working directory:           '/data/ouga/home/ag_gagneur/mertes/FraseR'
##
##
## ------------------- Parallel backend -----------------
## class: SerialParam
##   bpisup: TRUE; bpnworkers: 1; bptasks: 0; bpjobname: BPJOB
##   bplog: FALSE; bpthreshold: INFO; bpstopOnError: TRUE
##   bptimeout: 2592000; bpprogressbar: FALSE
##   bplogdir: NA
##
##
## ------------------- BAM parameters -------------------
## class: ScanBamParam
## bamFlag (NA unless specified):
## bamSimpleCigar: FALSE
## bamReverseComplement: FALSE
## bamTag:
## bamTagFilter:
## bamWhich: 0 ranges
## bamWhat:
## bamMapqFilter: 10
```

To understand the parallelizing option will be discussed in the parallel section **??**.

2.3 PSI- and Zscore-value calculation

After counting the user needs to compute the PSI-values and Z-scores for each site. Since this is just a

```
fds <- calculatePSIValues(fds)

## Wed May 17 19:16:03 2017:  Calculate the PSI3 values ...
```

```
## Wed May 17 19:16:03 2017:  Preparing data for HDF5 conversion:  psi3

## Wed May 17 19:16:03 2017:  Writing data:  psi3 to file:  /data/nasif12/home_if12/mertes/FraseR/s

## Wed May 17 19:16:04 2017:  Preparing data for HDF5 conversion:  rawOtherCounts_psi3

## Wed May 17 19:16:04 2017:  Writing data:  rawOtherCounts_psi3 to file:
/data/nasif12/home_if12/mertes/FraseR/savedObjects/Data_Analysis/rawOtherCounts_psi3.h5

## Wed May 17 19:16:04 2017:  Calculate the PSI5 values ...

## Wed May 17 19:16:04 2017:  Preparing data for HDF5 conversion:  psi5

## Wed May 17 19:16:04 2017:  Writing data:  psi5 to file:  /data/nasif12/home_if12/mertes/FraseR/s

## Wed May 17 19:16:04 2017:  Preparing data for HDF5 conversion:  rawOtherCounts_psi5

## Wed May 17 19:16:04 2017:  Writing data:  rawOtherCounts_psi5 to file:
/data/nasif12/home_if12/mertes/FraseR/savedObjects/Data_Analysis/rawOtherCounts_psi5.h5

## Wed May 17 19:16:04 2017:  Calculate the PSI site values ...

## Wed May 17 19:16:05 2017:  Preparing data for HDF5 conversion:  psiSite

## Wed May 17 19:16:05 2017:  Writing data:  psiSite to file:  /data/nasif12/home_if12/mertes/Frase

## Wed May 17 19:16:05 2017:  Preparing data for HDF5 conversion:  rawOtherCounts_psiSite

## Wed May 17 19:16:05 2017:  Writing data:  rawOtherCounts_psiSite to file:
/data/nasif12/home_if12/mertes/FraseR/savedObjects/Data_Analysis/rawOtherCounts_psiSite.h5

fds <- calculateZScores(fds)

## Wed May 17 19:16:06 2017:  Calculate the Zscore for psi3 values ...

## Wed May 17 19:16:06 2017:  Preparing data for HDF5 conversion:  zscore_psi3

## Wed May 17 19:16:06 2017:  Writing data:  zscore_psi3 to file:  /data/nasif12/home_if12/mertes/F

## Wed May 17 19:16:06 2017:  Calculate the Zscore for psi5 values ...

## Wed May 17 19:16:06 2017:  Preparing data for HDF5 conversion:  zscore_psi5

## Wed May 17 19:16:06 2017:  Writing data:  zscore_psi5 to file:  /data/nasif12/home_if12/mertes/F

## Wed May 17 19:16:06 2017:  Calculate the Zscore for psiSite values ...

## Wed May 17 19:16:06 2017:  Preparing data for HDF5 conversion:  zscore_psiSite

## Wed May 17 19:16:06 2017:  Writing data:  zscore_psiSite to file:  /data/nasif12/home_if12/merte

fds

## ------------------- Sample data table -----------------
##     sampleID                      bamFile condition    gene
##  1:  sample1  .../extdata/bam/sample1.bam         1 TIMMDC1
##  2:  sample2  .../extdata/bam/sample2.bam         1 TIMMDC1
```

```
##  3:  sample3  .../extdata/bam/sample3.bam         2  MCOLN1
##  4:  sample4  .../extdata/bam/sample4.bam         3    CLPP
##  5:  sample5  .../extdata/bam/sample5.bam        NA    NHDF
##  6:  sample6  .../extdata/bam/sample6.bam        NA    NHDF
##  7:  sample7  .../extdata/bam/sample7.bam        NA    NHDF
##  8:  sample8  .../extdata/bam/sample8.bam        NA    NHDF
##  9:  sample9  .../extdata/bam/sample9.bam        NA    NHDF
## 10: sample10 .../extdata/bam/sample10.bam        NA    NHDF
## 11: sample11 .../extdata/bam/sample11.bam        NA    NHDF
## 12: sample12 .../extdata/bam/sample12.bam        NA    NHDF
##
##
## Number of samples:      12
## Number of junctions:    94
## Number of splice sites: 111
## assays(11): rawCountsJ psi3 ... rawOtherCounts_psiSite
##   zscore_psiSite
##
##
## ---------------------- Settings ----------------------
## Analysis name:               Data Analysis
## Statistical method:          betaBin
## Analysis is strand specific: FALSE
## Working directory:           '/data/ouga/home/ag_gagneur/mertes/FraseR'
##
##
## ------------------- Parallel backend -----------------
## class: SerialParam
##   bpisup: TRUE; bpnworkers: 1; bptasks: 0; bpjobname: BPJOB
##   bplog: FALSE; bpthreshold: INFO; bpstopOnError: TRUE
##   bptimeout: 2592000; bpprogressbar: FALSE
##   bplogdir: NA
##
##
## ------------------- BAM parameters -------------------
## class: ScanBamParam
## bamFlag (NA unless specified):
## bamSimpleCigar: FALSE
## bamReverseComplement: FALSE
## bamTag:
## bamTagFilter:
## bamWhich: 0 ranges
## bamWhat:
## bamMapqFilter: 10
```

2.4 P-value calculation

2.5 Result visualisation

3 Acknowledgments

We thank Daniel Bader and Martin Morgan for input in the development of *FraseR*.

4 Session Info

- R Under development (unstable) (2017-05-02 r72649), `x86_64-pc-linux-gnu`
- Locale: `LC_CTYPE=en_US.UTF-8`, `LC_NUMERIC=C`, `LC_TIME=en_US.UTF-8`, `LC_COLLATE=en_US.UTF-8`, `LC_MONETARY=en_US.UTF-8`, `LC_MESSAGES=en_US.UTF-8`, `LC_PAPER=en_US.UTF-8`, `LC_NAME=C`, `LC_ADDRESS=C`, `LC_TELEPHONE=C`, `LC_MEASUREMENT=en_US.UTF-8`, `LC_IDENTIFICATION=C`
- Running under: `Scientific Linux 7.3 (Nitrogen)`
- Matrix products: default
- BLAS: `/data/nasif12/modules_if12/SL7/i12g/R/000-bioc6-devel/lib64/R/lib/libRblas.so`
- LAPACK: `/data/nasif12/modules_if12/SL7/i12g/R/000-bioc6-devel/lib64/R/lib/libRlapack.so`
- Base packages: base, datasets, graphics, grDevices, methods, parallel, splines, stats, stats4, utils
- Other packages: Biobase 2.37.2, BiocGenerics 0.23.0, BiocParallel 1.11.1, biomaRt 2.33.1, Biostrings 2.45.1, data.table 1.10.4, DelayedArray 0.3.5, FraseR 0.99.0, GenomeInfoDb 1.13.1, GenomicAlignments 1.13.2, GenomicRanges 1.29.4, ggplot2 2.2.1, htmlwidgets 0.8, IRanges 2.11.2, knitr 1.15.1, matrixStats 0.52.2, plotly 4.6.0, Rsamtools 1.29.0, S4Vectors 0.15.2, SummarizedExperiment 1.7.2, tidyr 0.6.3, VGAM 1.0-3, XVector 0.17.0
- Loaded via a namespace (and not attached): AnnotationDbi 1.39.0, assertthat 0.2.0, backports 1.0.5, BBmisc 1.11, BiocStyle 2.5.0, bitops 1.0-6, checkmate 1.8.2, codetools 0.2-15, colorspace 1.3-2, compiler 3.5.0, DBI 0.6-1, digest 0.6.12, dplyr 0.5.0, evaluate 0.10, GenomeInfoDbData 0.99.0, grid 3.5.0, gtable 0.2.0, HDF5Array 1.5.3, highr 0.6, htmltools 0.3.6, httr 1.2.1, jsonlite 1.4, lattice 0.20-35, lazyeval 0.2.0, magrittr 1.5, Matrix 1.2-10, memoise 1.1.0, munsell 0.4.3, plyr 1.8.4, prettyunits 1.0.2, progress 1.1.2, purrr 0.2.2.2, R.methodsS3 1.7.1,

R.oo 1.21.0, R.utils 2.5.0, R6 2.2.1, Rcpp 0.12.10, RCurl 1.95-4.8,
rhdf5 2.21.1, rmarkdown 1.5, rprojroot 1.2, RSQLite 1.1-2, Rsubread 1.27.2,
scales 0.4.1, stringi 1.1.5, stringr 1.2.0, tibble 1.3.0, tools 3.5.0,
viridisLite 0.2.0, XML 3.98-1.7, yaml 2.1.14, zlibbioc 1.23.0