Package ‘katdetectr’

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Title Detection, Characterization and Visualization of Kataegis in Sequencing Data

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Description Kataegis refers to the occurrence of regional hypermutation and is a phenomenon observed in a wide range of malignancies. Using changepoint detection katdetectr aims to identify putative kataegis foci from common data-formats housing genomic variants. Katdetectr has shown to be a robust package for the detection, characterization and visualization of kataegis.

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BugReports https://github.com/ErasmusMC-CCBC/katdetectr/issues

Depends R (>= 4.2)

Imports Biobase (>= 2.54.0), BiocParallel (>= 1.26.2), BSgenome (>= 1.62.0), BSgenome.Hsapiens.UCSC.hg19 (>= 1.4.3), BSgenome.Hsapiens.UCSC.hg38 (>= 1.4.4), changepoint (>= 2.2.3), changepoint.np (>= 1.0.3), checkmate (>= 2.0.0), dplyr (>= 1.0.8), GenomeInfoDb (>= 1.28.4), GenomicRanges (>= 1.44.0), ggplot2 (>= 3.3.5), ggtext (>= 0.1.1), IRanges (>= 2.26.0), maftools (>= 2.10.5), methods (>= 4.1.3), plyranges (>= 1.17.0), Rdpack (>= 2.3.1), rlgl (>= 1.0.2), S4Vectors (>= 0.30.2), scales (>= 1.2.0), tibble (>= 3.1.6), tidyr (>= 1.2.0), tools, utils, VariantAnnotation (>= 1.38.0)

Suggests BiocStyle (>= 2.26.0), knitr (>= 1.37), rmarkdown (>= 2.13), stats, testthat (>= 3.0.0)

VignetteBuilder knitr

RdMacros Rdpack

biocViews WholeGenome, Software, SNP, Sequencing, Classification, VariantAnnotation

Config/testthat/edition 3
**constructKatdetect**

**Description**

Constructor function for a KatDetect object.

**Usage**

```r
constructKatdetect(  
  genomicVariants = VariantAnnotation::VRanges(),  
  segments = GenomicRanges::GRanges(),  
  kataegisFoci = GenomicRanges::GRanges(),  
  info = list()  
)
```
detectKataegis

Arguments

- genomicVariants
  - (VRanges)
- segments
  - (GRanges)
- kataegisFoci
  - (GRanges)
- info
  - (list)

Value

(KatDetect): Returns a KatDetect object.

Author(s)

Daan Hazelaar

Examples

constructKatdetect()

detectKataegis

detectKataegis

Description

Detection of kataegis foci using changepoint detection.

Changepoint detection is performed on the intermutation distance (IMD) of the variants using the changepoint (killick 2014) package.

Note that we recommend using the default parameters for the detection of kataegis.

Usage

detectKataegis(
  genomicVariants,
  refSeq = "hg19",
  minSizeKataegis = 6,
  IMDcutoff = 1000,
  test.stat = "Exponential",
  penalty = "BIC",
  pen.value = 0,
  method = "PELT",
  minseglen = 2,
  BPPARAM = BiocParallel::SerialParam(),
  aggregateRecords = FALSE
)
Arguments

**genomicVariants**

(\texttt{VRanges}, VCF or MAF): VRanges, or path to VCF or MAF file containing genomic variants.

**refSeq**

(character or data.frame): The used reference genome for variant calling. Choose: "hg19" or "hg38". For analysis of non standard sequences: provide a data.frame containing the length of the sequences.

**minSizeKataegis**

(integer): Minimal number of variants required within a segment for classification as a kataegis foci.

**IMDcutoff**

(numberic or function): When a numeric is supplied this represents the max mean IMD within a segment for classification as a kataegis foci. When a custom function is supplied by the user a IMD cutoff value is determined for each segment.

**test.stat**

(character): Distribution that is fitted to the data (Exponential or Empirical). See \texttt{cpt.meanvar}.

**penalty**

(character): Penalty used to guard against overfitting (BIC or Manual). See \texttt{cpt.meanvar}.

**pen.value**

(integer): Only needed for manual penalty. See \texttt{cpt.meanvar}.

**method**

(character): The search method used in changepoint analysis. Choice of: "PELT", "AMOC", "SegNeigh" or "BinSeg".

**minseglen**

(integer): Min. size of segments (no. of variants).

**BPPARAM**

(\texttt{BiocParallelParam}): Can be used for parallelization purposes.

**aggregateRecords**

(logical): Aggregate multiple samples and treat as-if all records originate from a single sample.

Value

(KatDetect): Returns a KatDetect object including putative kataegis foci.

Author(s)

Daan Hazelaar

Job van Riet

References


Examples

\begin{verbatim}
syntheticData <- generateSyntheticData()
kd <- detectKataegis(syntheticData)
\end{verbatim}
generateSyntheticData

Generate genomic variants with pre-defined kataegis foci.

Description

This function generates a synthetic dataset (VRanges) containing background genomic variants and a no. of desired interjected kataegis foci.

Usage

```r
generateSyntheticData(
  genome = BSgenome.Hsapiens.UCSC.hg19::BSgenome.Hsapiens.UCSC.hg19,
  nBackgroundVariants = 100,
  seqnames = NULL,
  probMutationType = c(0.8, 0.1, 0.1),
  nKataegisFoci = 5,
  nKataegisVariants = 20,
  expectedIMD = 100,
  sampleName = "syntheticData",
  removeValidationColumns = TRUE
)
```

Arguments

- `genome` (*BSgenome*): The genome (DNA) which will be sampled for genomic variants.
- `nBackgroundVariants` (integer): The no. of generated background genomic variants.
- `seqnames` (character): The sequences on which genomic variants will be sampled. If NULL, then all human autosomes and sex chromosomes will be used.
- `probMutationType` (numeric): The probability of a generated variant being an SNV, MNV, Deletion or Insertion, respectively.
- `nKataegisFoci` (integer): The no. of generated and interjected kataegis foci.
- `nKataegisVariants` (integer): The no. of genomic variants within each kataegis foci.
- `expectedIMD` (integer): The expected mean intermutational distance (IMD) of the generated kataegis foci.
- `sampleName` (character): The name of the sample.
- `removeValidationColumns` (logical): Include columns with extra information regarding mutation sampling?

Value

- *(VRanges)*: VRanges containing background genomic variants and pre-defined kataegis foci.
getGenomicVariants

Author(s)
Daan Hazelaar
Job van Riet

Examples
syntheticData1 <- generateSyntheticData()

syntheticData2 <- generateSyntheticData(
genome = BSgenome.Hsapiens.UCSC.hg38::BSgenome.Hsapiens.UCSC.hg38,
nBackgroundVariants = 75,
seqnames = c("chr1", "chrX"),
nKataegisFoci = 1,
nKataegisVariants = 25,
sampleName = "testSample",
removeValidationColumns = FALSE)

getGenomicVariants
Retrieve genomic variants from KatDetect object.

Description
Retrieve genomic variants from KatDetect object.

Usage
getGenomicVariants(x)

## S4 method for signature 'KatDetect'
getGenomicVariants(x)

Arguments
x (KatDetect): KatDetect object.

Value
(VRanges): Returns a VRanges with annotated genomic variants.

Examples
kd <- constructKatdetect()
getGenomicVariants(kd)
getInfo

`getInfo` Retrieve model parameters from a `KatDetect` object.

**Description**
Retrieve model parameters from a `KatDetect` object.

**Usage**
```r
getInfo(x)
```

## S4 method for signature 'KatDetect'
```r
getInfo(x)
```

**Arguments**
- `x` (KatDetect): `KatDetect` object.

**Value**
(list): Returns a list with all model parameters used for kataegis detection.

**Examples**
```r
kd <- constructKatdetect()
getInfo(kd)
```

getKataegisFoci

`getKataegisFoci` Retrieve kataegis foci from a `KatDetect` object.

**Description**
Retrieve kataegis foci from a `KatDetect` object.

**Usage**
```r
getKataegisFoci(x)
```

## S4 method for signature 'KatDetect'
```r
getKataegisFoci(x)
```

**Arguments**
- `x` (KatDetect): `KatDetect` object.
getSegments

Value

(GRanges): Returns a GRanges with annotated kataegis foci.

Examples

kd <- constructKatdetect()
getKataegisFoci(kd)

gtSegments

Retrieve segments from KatDetect a object.

Description

Retrieve segments from KatDetect a object.

Usage

getSegments(x)

## S4 method for signature 'KatDetect'
getSegments(x)

Arguments

x (KatDetect): KatDetect object.

Value

(GRanges): Returns a GRanges with annotated segments.

Examples

kd <- constructKatdetect()
getSegments(kd)
KatDetect-class

Description

The katdetectr package introduces a new S4 object which stores all relevant information regarding kataegis detection.

Value

(KatDetect) KatDetect object.

Slots

- kataegisFoci (GRanges): Contains all annotated putative kataegis foci.
- genomicVariants (VRanges): Contains all processed and annotated genomic variants.
- segments (GRanges): Contains all segments detected after changepoint genomic analysis.
- info (list): Contains some general information and model parameters used for kataegis detection.

Author(s)

Daan Hazelaar
Job van Riet

Examples

```r
syntheticData <- generateSyntheticData()
kd <- detectKataegis(syntheticData)

getKataegisFoci(kd)
genomicVariants(kd)
segments(kd)
info(kd)
```

katdetectr

Katdetectr: A package for kataegis detection, characterization and visualization

Description

The katdetectr package provides three main functions: detectKataegis(), rainfallPlot() and generateSyntheticData()

Details

See the vignette for more details, a step by step explanation of these function, and the general katdetectr workflow.
Description

Visualize the IMD, segments and putative kataegis foci using a rainfall plot.
Y-axis represents the 5' intermutation distance (IMD) of each genomic variant in a log10-scale.
X-axis represent variant ID.
Variants within kataegis foci are bold with the kataegis foci shown in a blue rectangle (if showKataegis = TRUE). Color represent the mutation type whilst horizontal lines represent the mean IMD of a segments and Vertical lines depict the detected changepoints (if showSegmentation = TRUE).

Usage

```
rainfallPlot(  
  kd,  
  showSequence = "All",  
  showKataegis = TRUE,  
  showSegmentation = FALSE  
)
```

Arguments

kd $(\text{KatDetect})$: KatDetect object.
showSequence (character): Which sequence(s) should be visualized? Choice of: 'All', 'Kataegis', c('seqname1', 'seqname2').
showKataegis (logical): Highlight putative kataegis foci and underlying genomic variants?
showSegmentation (logical): Show changepoints and mean IMD of each segment?

Value

$(\text{ggplot})$: Returns rainfall plot.

Author(s)

Daan Hazelaar
Job van Riet

Examples

```
syntheticData <- generateSyntheticData(nBackgroundVariants = 200)
kd <- detectKataegis(syntheticData)

# Visualize the IMD of the genomic variants by constructing a rainfall plot
ekadetctr::rainfallPlot(kd)
```
`rainfallPlot`

```r
# Show the chromosomes which contain one or more kataegis foci
kadetector::rainfallPlot(kd, showSequence = "Kataegis")

# Show only chromosome 1 and 2
kadetector::rainfallPlot(kd = kd, showSequence = c("chr1", "chr2"))

# Display changepoints and mean IMD per segment
kadetector::rainfallPlot(kd = kd, showSequence = c("chr1", "chr2"), showSegmentation = TRUE)
```
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