*DAME*finder: A package to detect changes in allele-specific methylation

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Stands for

D

A

ME

Stands for

Differential

A

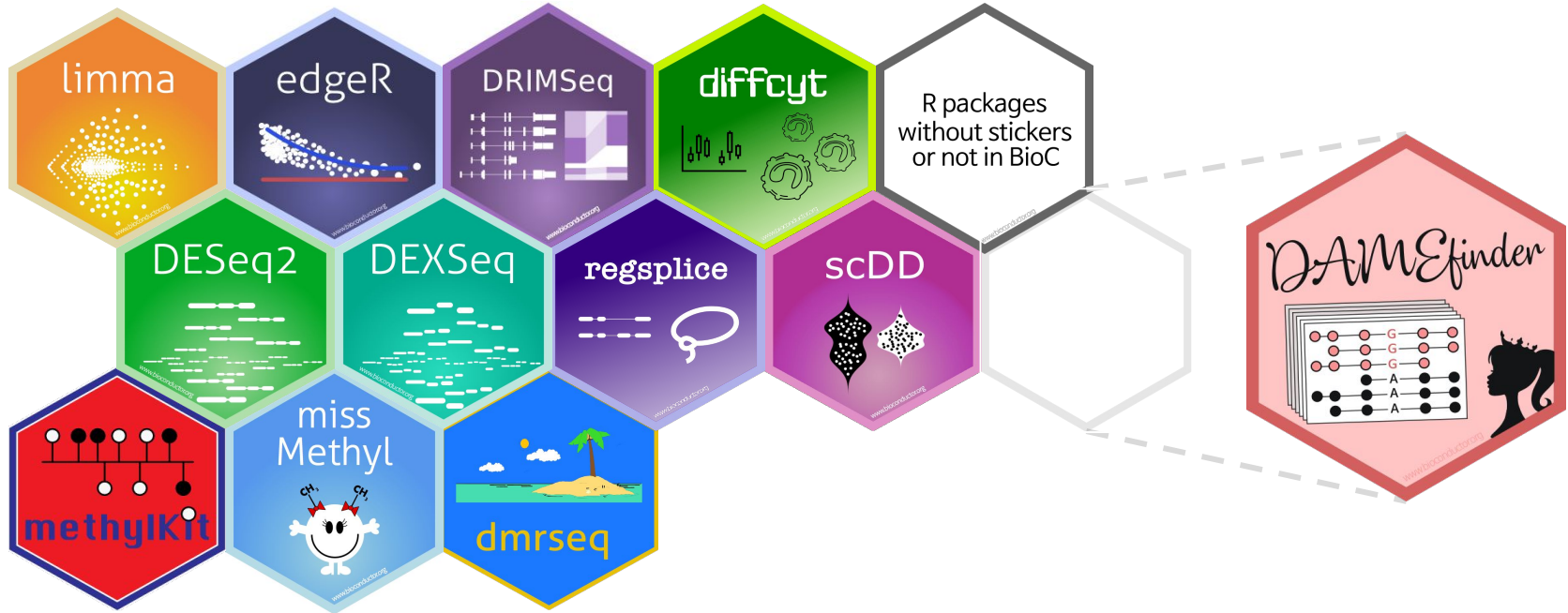ME

Stands for

Differential

Allele-specific

ME

Stands for
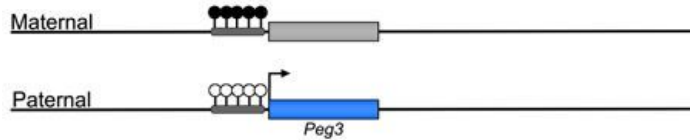
Differential

Allele-specific

MEthylated *region*
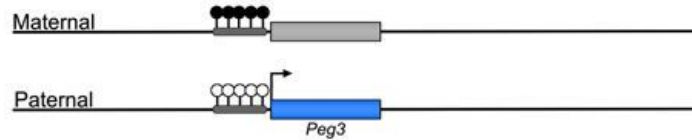
The world of *differential* Bioconductor

What is allele-specific methylation?
 (in humans at least)

Simplified biology:
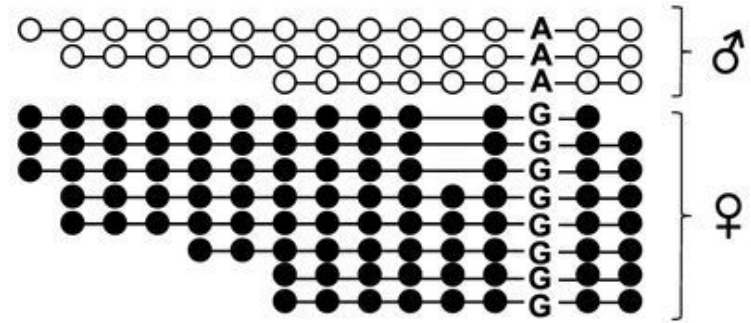

Maternal

Paternal

Peg3

What is allele-specific methylation?
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Simplified biology:

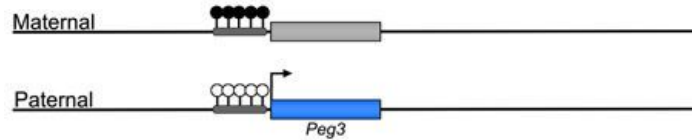In the reads (from Bisulfite-seq):
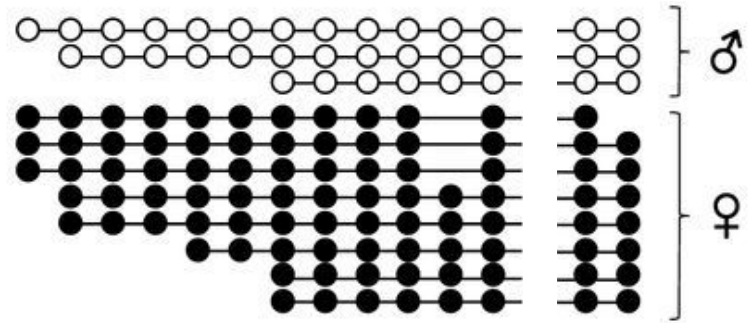

SNP = single nucleotide polymorphism

What is allele-specific methylation?
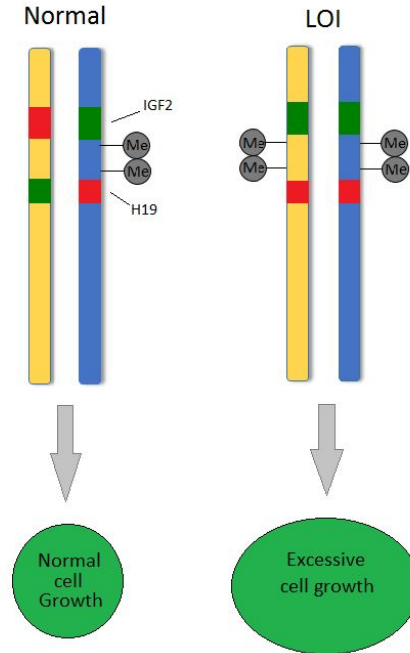 (in humans at least)

Simplified biology:

In the reads (from Bisulfite-seq):

When do changes in allele-specific methylation occur?

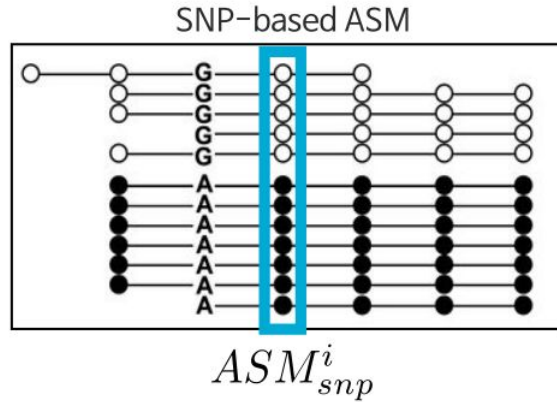# When do changes in allele-specific methylation occur?

An example in colorectal cancer

"...loss of the normal parent of origin dependent gene silencing..."

Cui et. al., Cancer Research. 2002

What does the package do?

1. Detect ASM for each sample

SNP-based ASM

$$ASM^i_{snp}$$

OR

tuple-based ASM

$$ASM^i_{tuple}$$
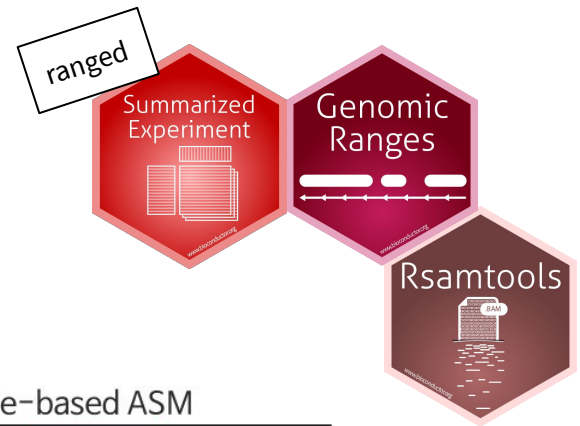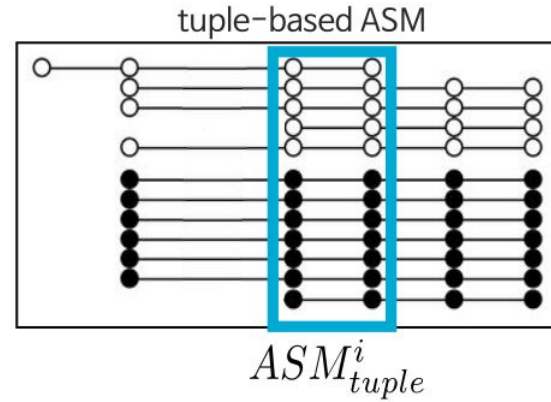
```
calc_asm(sampleList, beta = 0.5, a = 0.2, transform = modulus_sqrt,
    coverage = 5, verbose = TRUE)
```

2. Summarize ASM change with a moderated t-stat
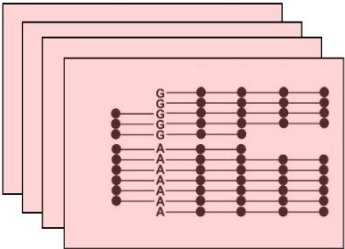
Group A

Group B

2. Summarize ASM change with a moderated t-stat

Group A

Group B

t-statistic
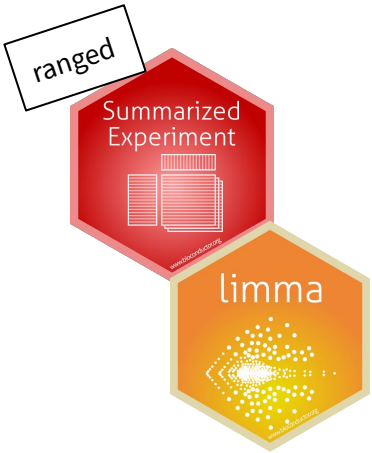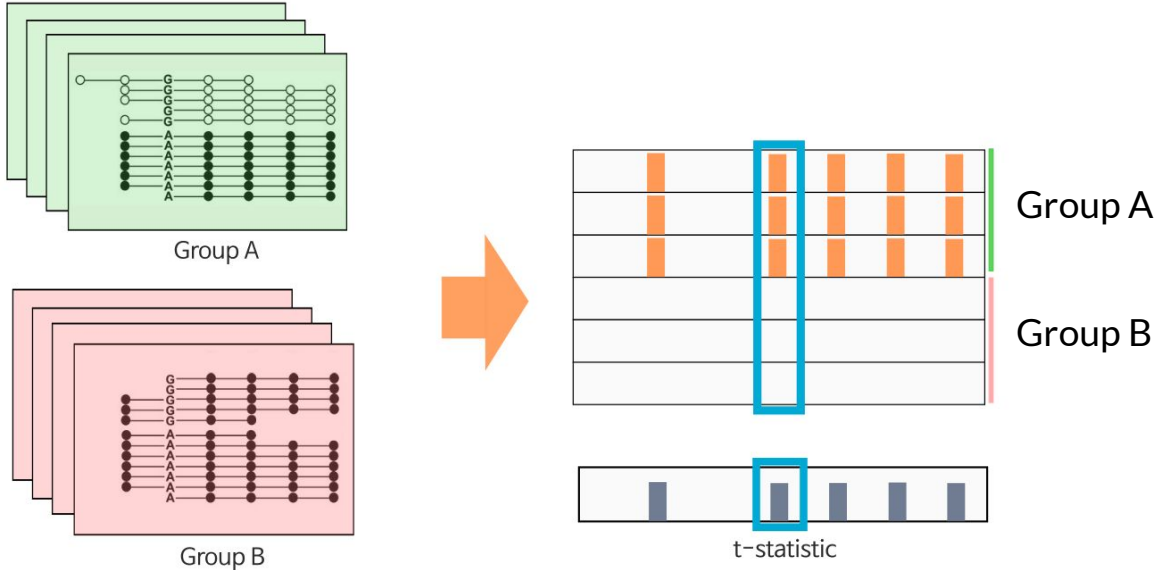
3. Scan for regions of consistent change
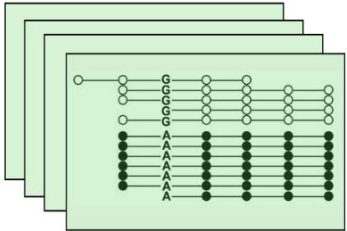
bumphunter
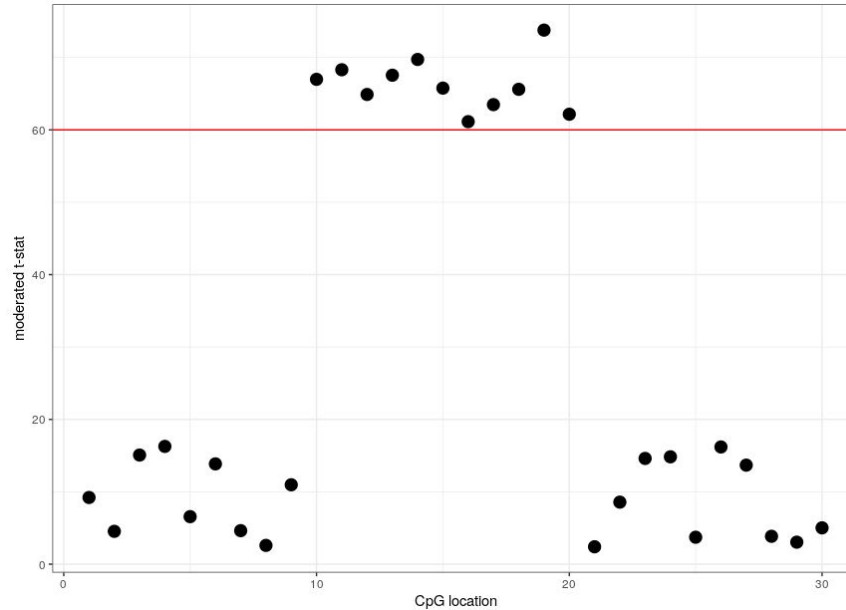

```
find_dames (SumExp, design, coef = 2, contrast = NULL, smooth = TRUE,
           Q = 0.5, pvalAssign = "simes", maxGap = 20, verbose = TRUE,
           maxPerms = 10, method = "ls", trend = FALSE, ...)
```

4. Visualization
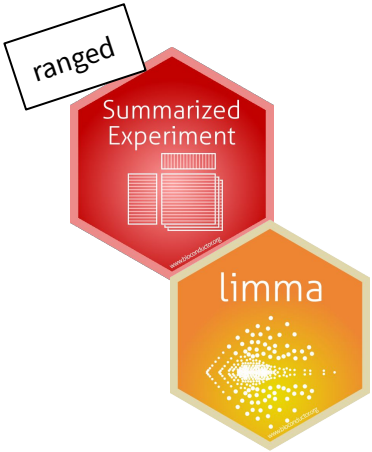
Plot reads overlapping a SNP (all or a random subset of the reads)
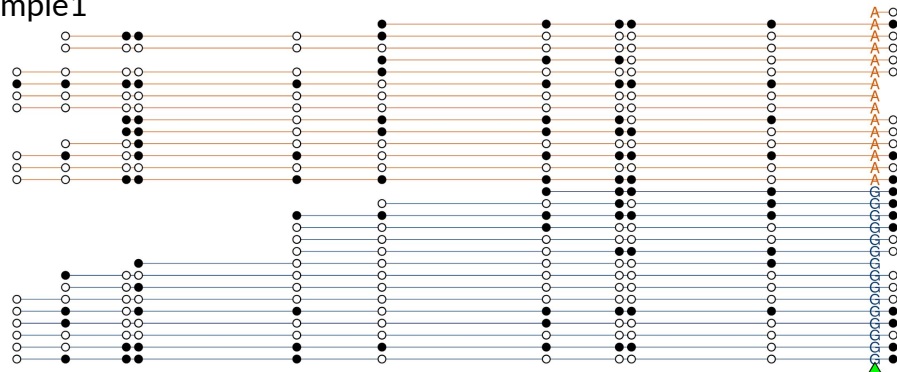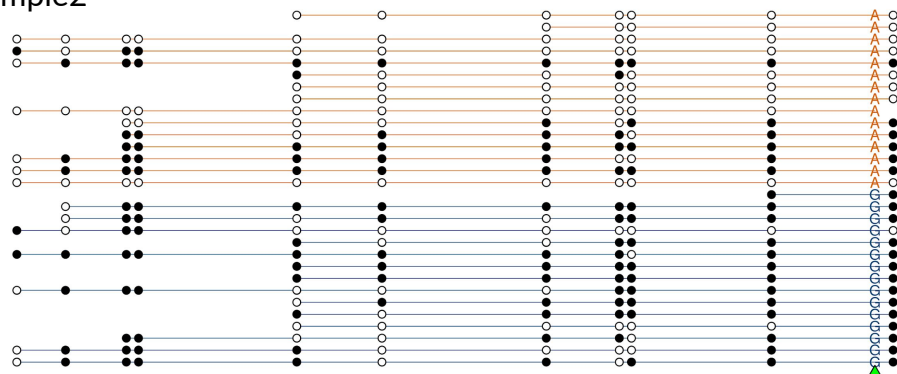

```
methyl_circle_plot (snp, vcfFile, bamFile,
                    refFile,
                    dame = NULL,
                    letterSize = 2.5,
                    pointSize = 3,
                    sampleReads = FALSE,
                    numReads = 20)
```

Plot (random subset of) reads in a region
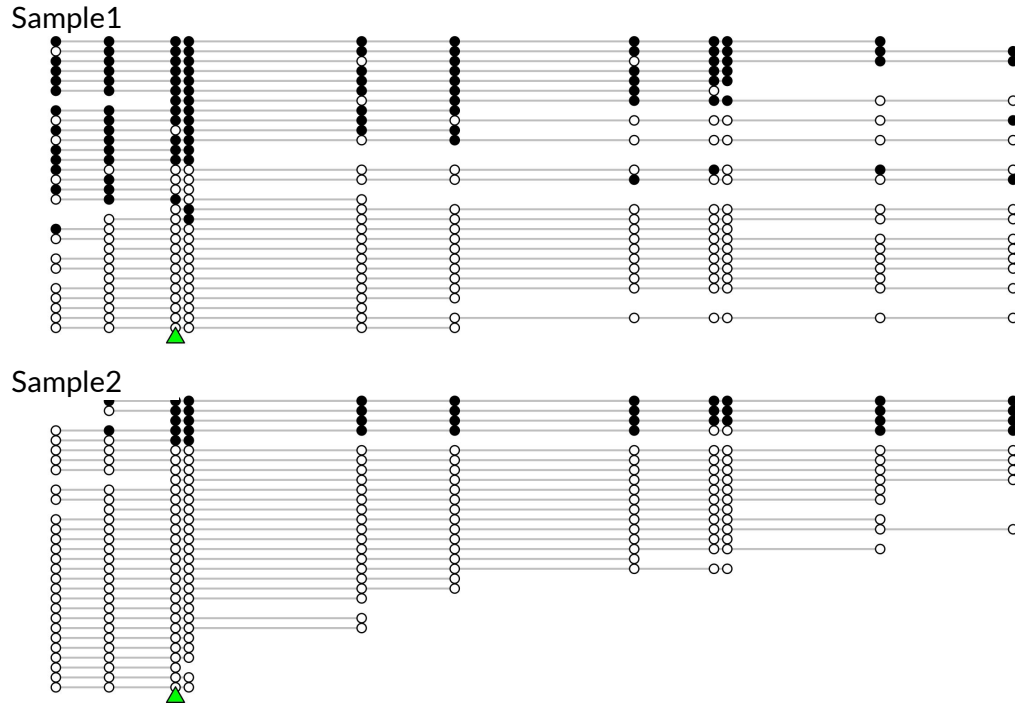
Sample1


```
methyl_circle_plotCpG (cpgsite, bamFile,
                       refFile,
                       pointSize = 3,
                       dame = NULL,
                       order = FALSE,
                       sampleReads = FALSE,
                       numReads = 20)
```

Sample2

Sorted by methylation

Plot summary of scores

```
dame_track(dame, window = 0,
           derASM = snpASM,
           ASM = tupleASM,
           colvec = color,
           plotSNP = TRUE)
```
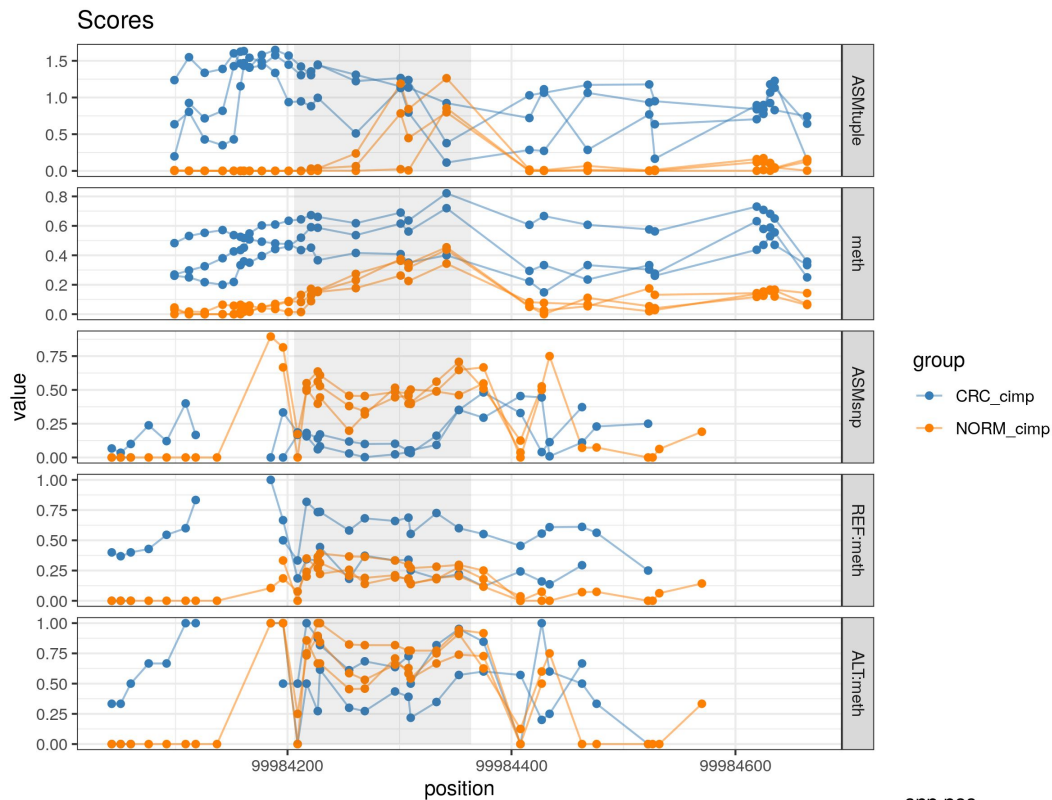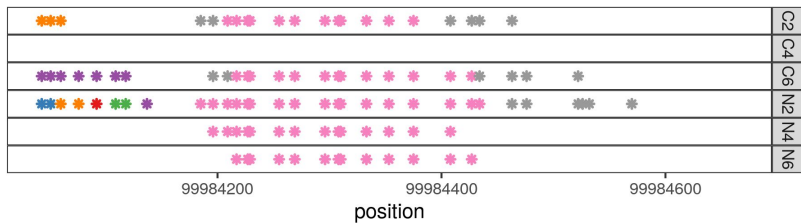
To summarize

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1. DAMEfinder detects allele-specific methylation from BS-seq data
2. Allele-specific methylation can be SNP-based, or not
3. The package screens for regions of change in allele-specificity
4. It makes region-wise plots

https://github.com/markrobinsonuzh/DAMEfinder

DAMEfinder

DAMEfinder (**D**ifferential **A**llele-specific **ME**thylation **finder**) is an R-package that detects allele-specific methylation (ASM) in a cohort of samples, and detects regions of differential ASM within groups of interest, based on **Bisulfite-sequencing** files.

DAMEfinder runs in two modes: **SNP-based** (exhaustive-mode) and **tuple-based** (fast-mode), which converge when calculating differential methylation.
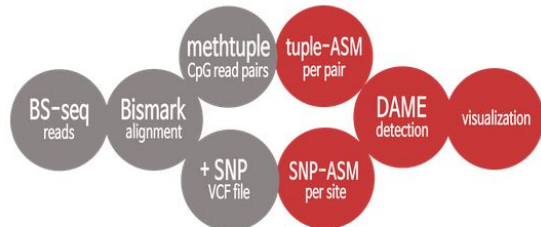
Please refer to the vignette for more details on running the pipeline. Preprint out!

DAMEfinder: A method to detect differential allele-specific methylation

Stephany Orjuela, Dania Machlab, Mirco Menigatti, Giancarlo Marra, Mark D. Robinson
doi: https://doi.org/10.1101/800383

Abstract | Full Text | Info/History | Metrics | Preview PDF

Abstract

DNA methylation is a highly studied epigenetic signature that is associated with regulation of gene expression, whereby genes with high levels of promoter methylation are generally repressed. Genomic imprinting occurs when one of the parental alleles is methylated, i.e, when there is inherited allele-specific methylation (ASM). A special case of imprinting occurs during X chromosome inactivation in females, where one of the two X chromosomes is silenced, in order to achieve dosage compensation between the sexes. Another more widespread form of ASM is sequence dependent (SD-ASM), where ASM is linked to a nearby heterozygous single nucleotide polymorphism (SNP).

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