MethylAid-summarized data for Illumina 450k (N=2800) and EPIC (N=2620) arrays

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1 Introduction

MethylAidData contains MethylAid-summarized data on 2800 Illumina 450k array samples and 2620 Illumina EPIC/850k array that can be used as reference when processing newly generated methylation array data using MethylAid.

The data on 450k arrays is based on a subset from a large-scale multiple omics study conducted by several Dutch Biobanks; the BIOS consortium (http://www.bbmri.nl/engb/activities/rainbow-projects/bios) [1]. The raw Illumina 450k array data, idat-files, are available through the EGA archive (https://ega-archive.org/dacs/EGAC00001000277).

MethylAid-summarized data for EPIC methylation arrays stems from studies led by the University of Southampton (N=1434) [2] and the University of Essex (N=1186).

The summarization performed by *MethylAid* entails the following for each sample:

- 1. calculation of the median Methylated and Unmethylated intensities
- 2. extraction of all quality control probe intensities

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- 3. construction of quality control metrics e.g. sample-dependent, sample-independent and detection p-values
- 4. storing everything efficiently to allow fast rendering of the various quality control plots provided by *MethylAid*,

see van Iterson et al.[3] for detailed description of MethylAid.

2 Preparation of the data

Using raw idat-files (e.g. EGA accession number EGAC00001000277 after approval by Data Access Committee). Once the raw idat-files have been downloaded and a targets file is constructed, *MethylAid* can be used to summarize the data and perform quality control using the interactive *shiny* [4] application.

Data sets of this size are preferably summarized in parallel and batches to overcome long run times or memory issues. *MethylAid* provides several options to do this using the *BiocParallel*-package[5]. For example, if multiple cores are available these could be used like this:

```
library(MethylAid)
targets ##constructed from EGA
BPPARAM <- MulticoreParam(workers = 8, verbose=TRUE)
summarize(targets, batchSize = 100, BPPARAM = BPPARAM, file="exampleDataLarge")</pre>
```

Another option would be thus use a cluster, see the vignette of *MethylAid* how to set this up.

3 Using MethylAidData

The summarized data contained in *MethylAidData* can be used in two ways, 1) to explore a large data set using *MethylAid* and 2) use this data as a background data set on top of own data. Since version 1.1.4, *MethylAid* has the functionality to show as background data set in the filter control plots. As such it can be used as a reference data set and can give guidance to when removing outlying samples. Furthermore, the data gives confirmation of the default thresholds used to determine outlying samples.

Additionally, since MethylAid(1.1.4) functionality is added to construct your own background data and several summarizedData-objects can be merged to give one larger summarizedData-object to use as your own reference or to determine filter thresholds, for example for hydroxymethylation data for which there are currently no thresholds available.

MethylAid-summarized data

References

- [1] M. J. et al Bonder. Disease variants alter transcription factor levels and methylation of their binding sites. *Nat. Genet.*, 49(1):131–138, Jan 2017.
- [2] P. G. Burney, C. Luczynska, S. Chinn, and D. Jarvis. The European Community Respiratory Health Survey. *Eur. Respir. J.*, 7(5):954–960, May 1994.
- [3] M. van Iterson, E. W. Tobi, R. C. Slieker, W. den Hollander, R. Luijk, P. E. Slagboom, and B. T. Heijmans. MethylAid: visual and interactive quality control of large Illumina 450k datasets. *Bioinformatics*, 30(23):3435–3437, 2014.
- [4] RStudio and Inc. *shiny: Web Application Framework for R*, 2014. R package version 0.9.1. URL: http://CRAN.R-project.org/package=shiny.
- [5] Martin Morgan, Michel Lang, and Ryan Thompson. *BiocParallel: Bioconductor facilities for parallel evaluation*. R package version 1.0.3.