



Lheuristic. A Shiny app to select genes potentially regulated by methylation

Sánchez-Pla, Alex^{1,3}, Castellano, Pol¹, Miró, Berta², Carmona, Francesc¹

¹ Departament de Genètica Microbiologia i Estadística, Universitat de Barcelona

² International Rice Research Institute, (IRRI), Philippines

³ Statistic and Bioinformatics Unit. Vall d'Hebron Research Institute. (VHIR). Barcelona

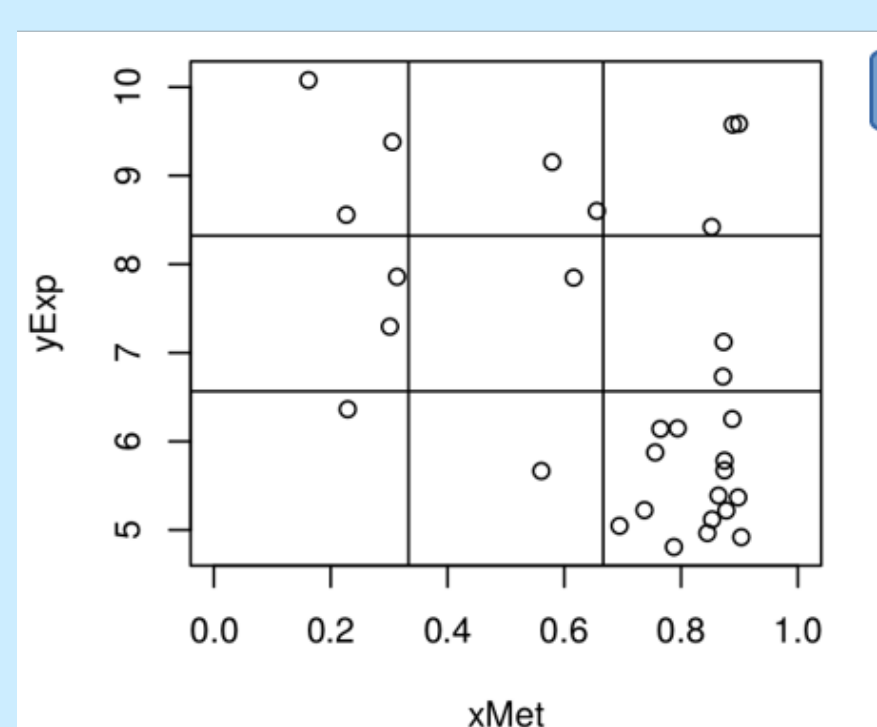


1 Background

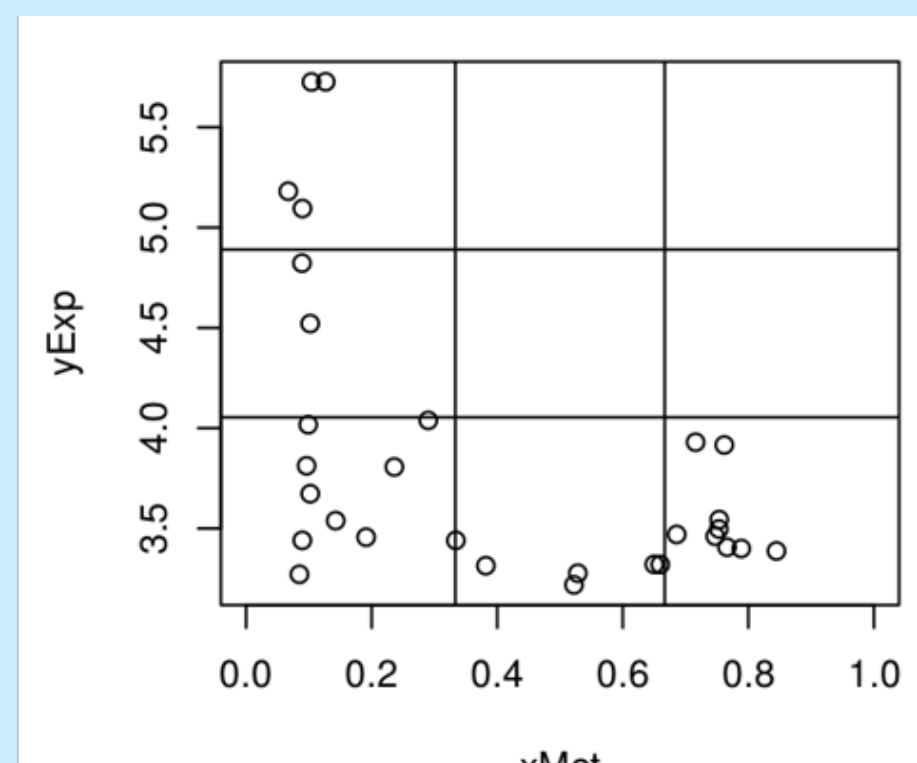
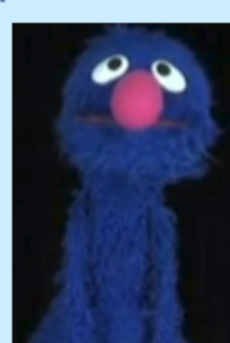
- Methylation of genes involved in the oncogenic process is a key process contributing to tumor initiation and/or progression [4].
- Finding *Genes Regulated by Methylation* (GRM) can lead to a better understanding and be a guide to finding new drug targets.
- In cancer-related genes it is common to observe a decrease in gene expression associated with hypermethylation.
 - When methylation is low (“off”) the gene can express normally and its expression may be any value, low or high,
 - when methylation is medium or high (“on”), the expression of the gene will be *repressed* and its values will tend to be low .
- As a consequence relation plots depicting methylation and expression may show L-shape patterns so the strategy adopted will be to mine such plots and select those that have such a shape.

2 Results

- We developed a heuristic method based on imitating the visual selection of L-shapes by overimposing a 3×3 grid on the scatterplot ([5]).



Non L-shape



L-shape

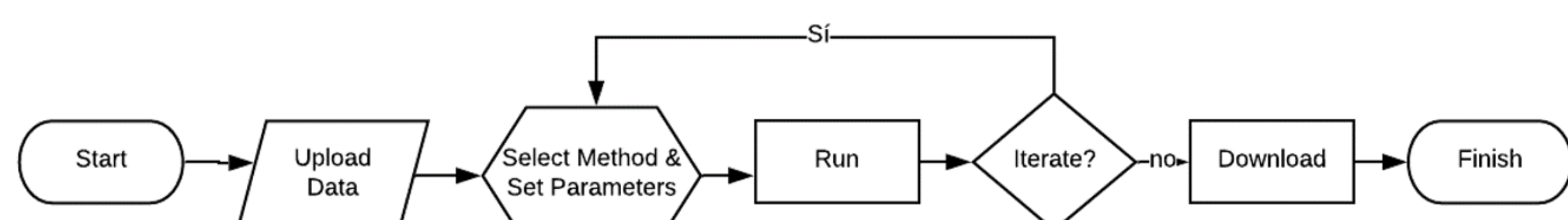


- The algorithm has been implemented in R (package ready-to-be-submitted to Bioconductor).
- A Shiny application has been created to select genes potentially regulated by methylation using a combination of the *Lheuristic* method and a *naïve* approach (negative correlation).

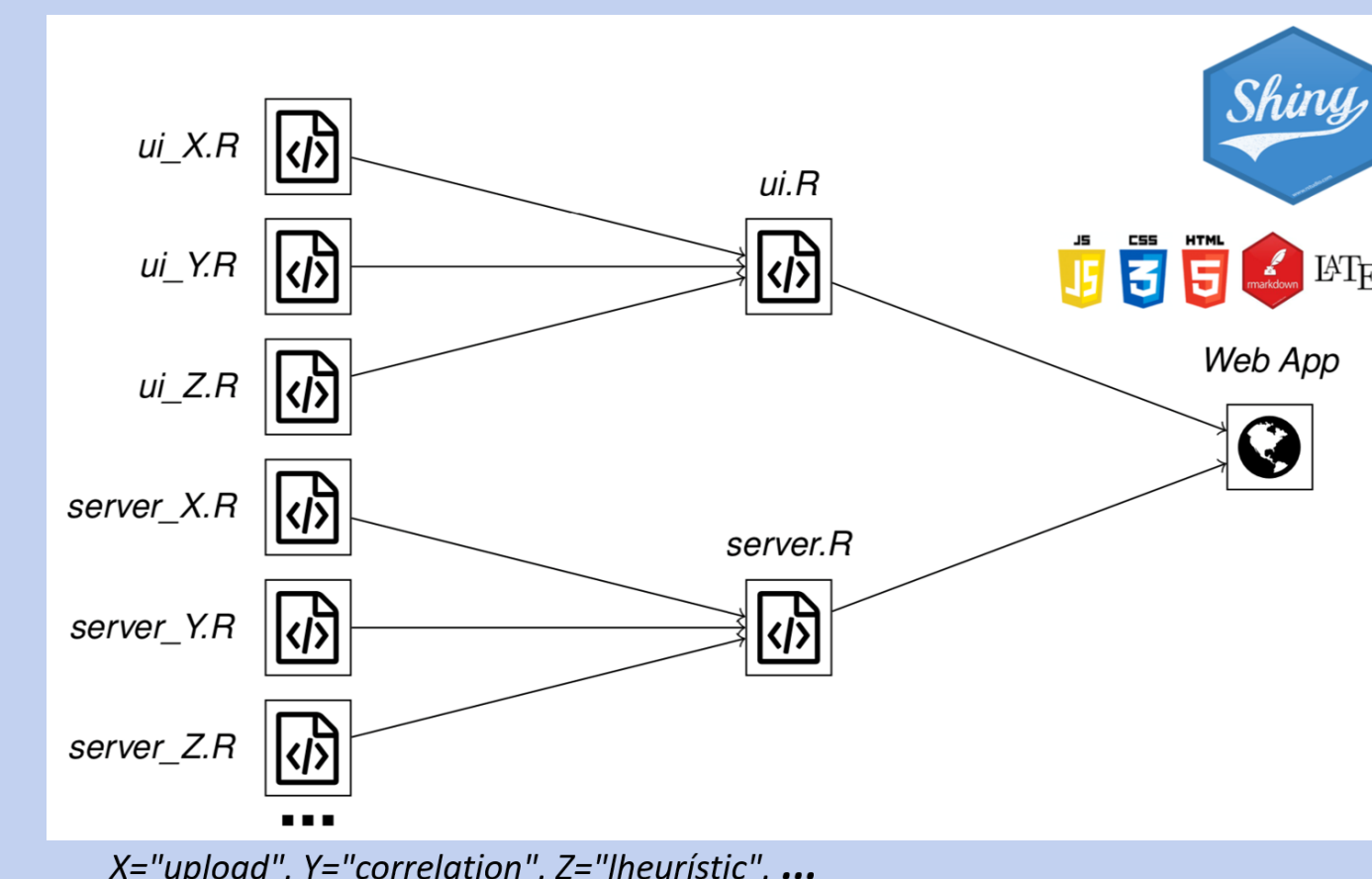
2.1 Availability

- Code is available in github:
<https://github.com/pcastellanoescuder/Lheuristic>
- The application is available in:
<http://cinna.upc.edu:3838/alex/lheuristic>

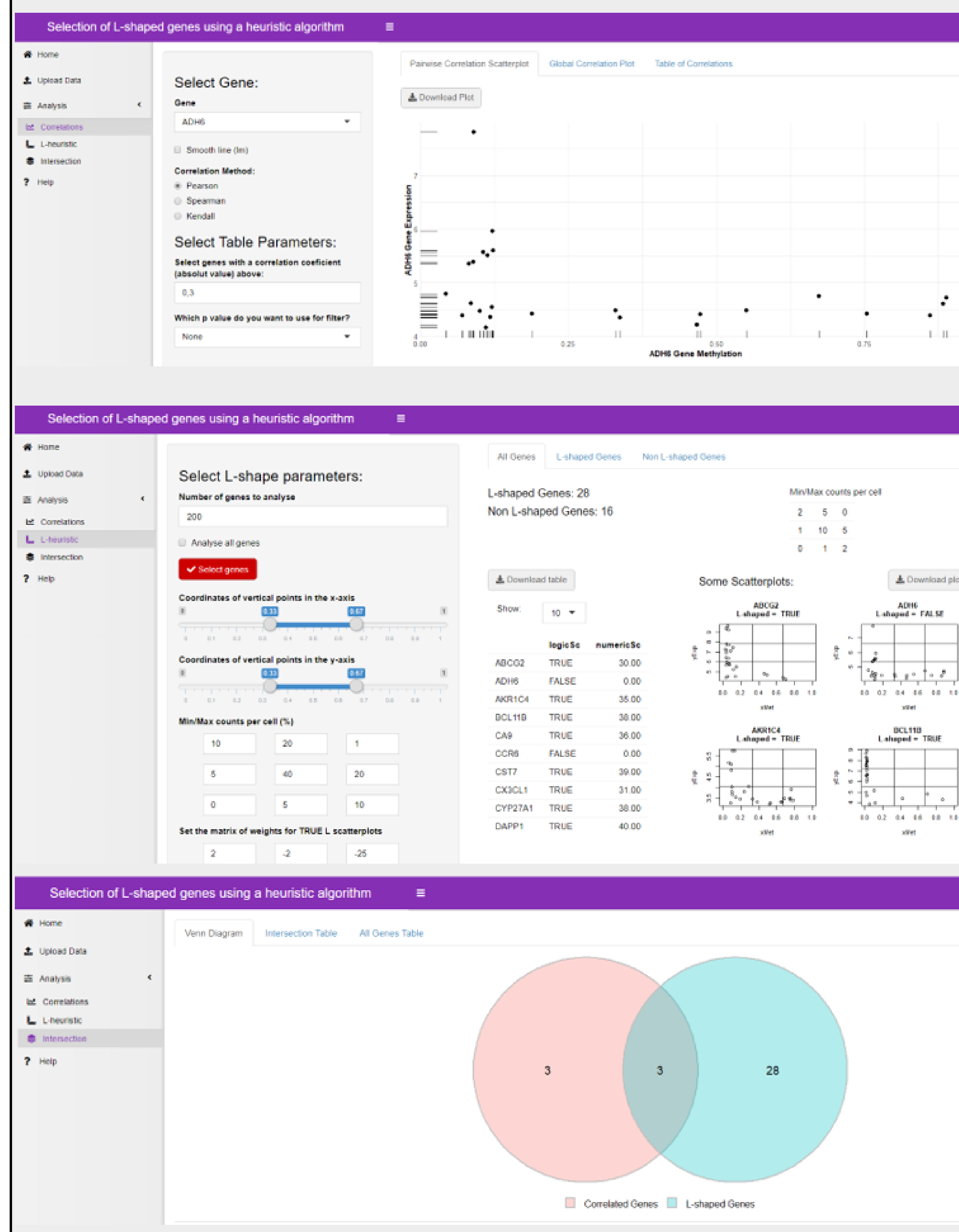
3 App Usage



4 App architecture



5 Interface



- [1] Sarah Bazzocco, Hafid Alazzouzi, M. Carne Ruiz de Villa, Alex Sanchez-Pla, John M. Mariadason, Diego Arango (2013) *Genome-Wide Analysis of DNA Methylation in Colorectal Cancer*. Submitted.
- [2] Yihua Liu and Peng Qiu. (2012) *Integrative analysis of methylation and gene expression data in TCGA* IEEE International Workshop on Genomic Signal Processing and Statistics (GENSIPS)
- [3] Jeffrey Racine. (2012) A primer on regression splines.
http://cran.r-project.org/web/packages/crs/vignettes/spline_primer.pdf
- [4] B Sadikovic, K Al-Romaih, J.A Squire, and M Zielenska. Cause and Consequences of Genetic and Epigenetic Alterations in Human Cancer. *Current Genomics*, 9(6):394–408, September 2008.
- [5] Sanchez-Pla, A., Miró B., Carmona, F. et al. *A heuristic algorithm to select genes potentially regulated by methylation* [version 1; not peer reviewed]. F1000Research 2019, 8:1017 (slides) (doi: 10.7490/f1000research.1116986.1)