

An R pipeline using the "targets" package for Multi-Omics Integrative Analyses





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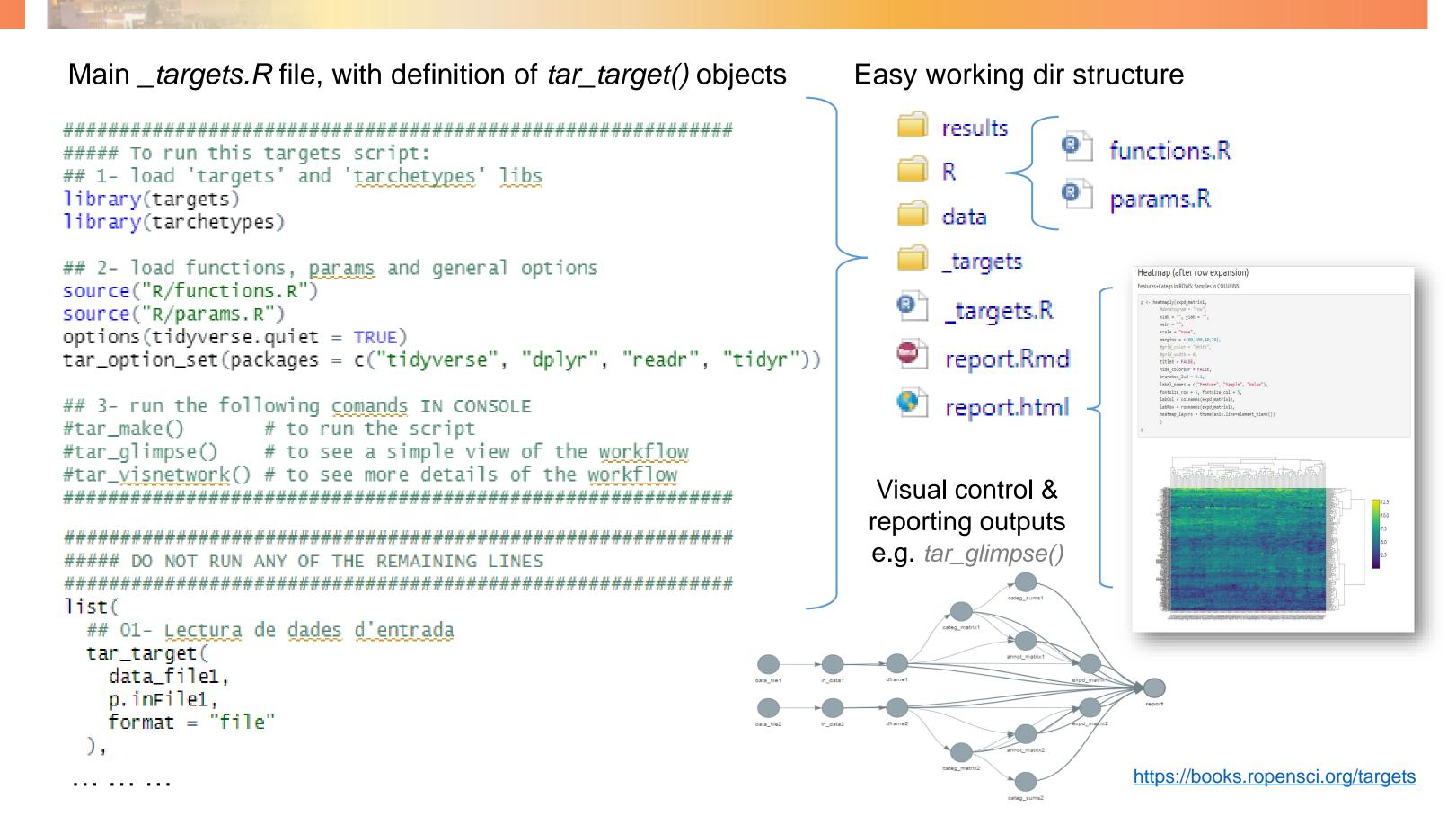


Motivation and Main Idea

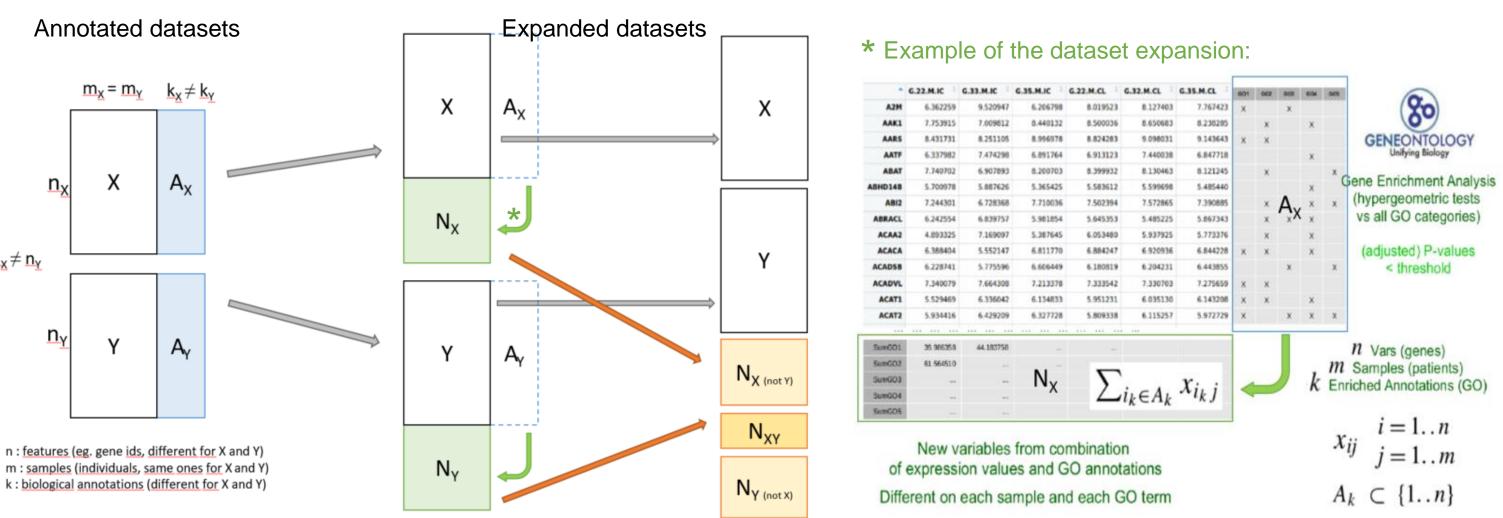
One common approach to multi-omics integration is using Dimension Reduction techniques, which are also helpful for data visualization^{1,2}. There is however some space for improvement: One point that may be improved is the difficulty in interpreting results from the biological point of view. Another is the lack of pipelines covering the whole integration process, which may be simpler to use than usual bioinformatic pipelines^{3,4}, such as those based on Galaxy⁵ and NextFlow⁶, which require a certain level of technical knowledge to be configured. Our proposal addresses these two points, by

- 1. Adding biological annotations (GO⁷, GSEA⁸...) to the original datasets (X, Y) **before** the joint analysis, thus creating the **expanded datasets** $(N_x, N_y...)$ with new annotation-derived features,
- 2. Performing the analysis of the original and expanded datasets with contrasted Multi-**Block Dimension Reduction methods** (such as RGCCA⁹, MFA¹⁰),
- 3. Implementing a pipeline with the targets package¹¹ that allows data scientists and researchers to work entirely within R, in a reproducible and easy-to-use workflow.

The targets Package



Expanding Data with Biological Annotations



 $N_X = rac{1}{r_X}(X imes A_X'),$

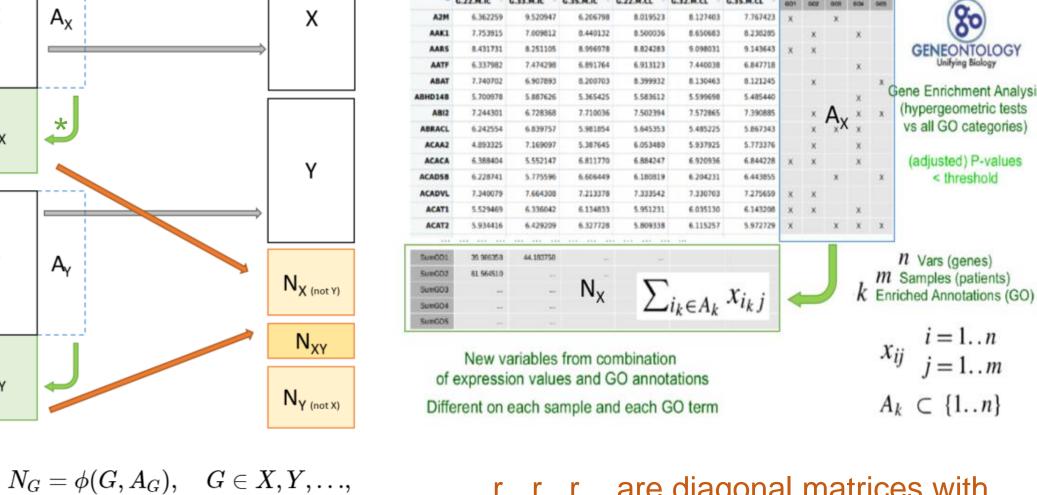
 $N_Y = rac{1}{r_Y}(Y imes A_Y'),$

 $N_{XY} = rac{w_X}{r_{XY}}(X imes A'_{XY}) + rac{w_Y}{r_{XY}}(Y imes A'_{XY}),$

Biological annotations performed with enrichment methods based on gene over-representation or gene list enrichment analysis

- Gene Ontology (GO)
- Gene Sets (MSigBD-GSEA) Pathways (KEGG, Reactome)

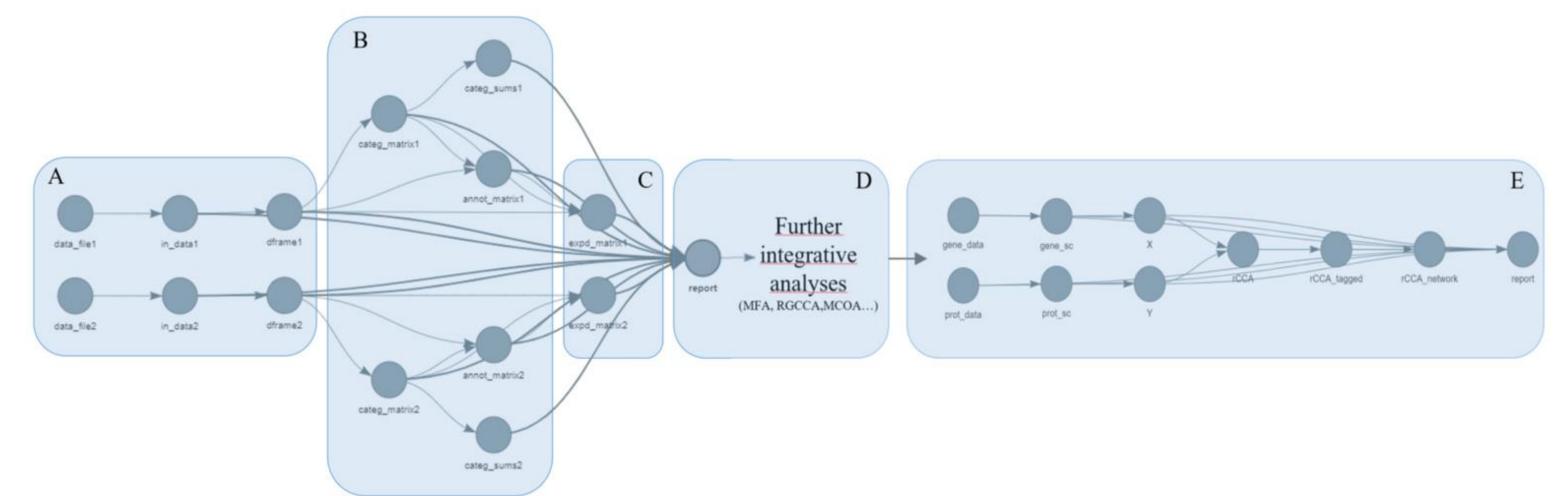
Custom annotations also allowed



r_x, r_y, r_{xy}, are diagonal matrices with the number of features annotated to each biological category

 w_x , w_y , can be equal (e.g. 1) or distinct weights applied to each dataset

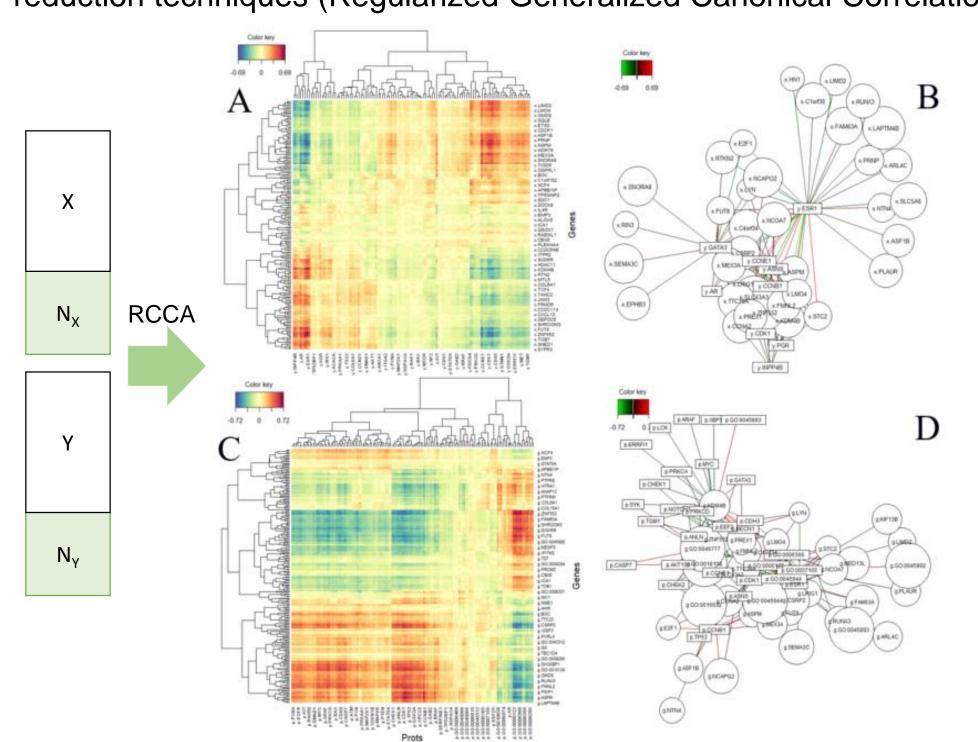
The Analysis Pipeline



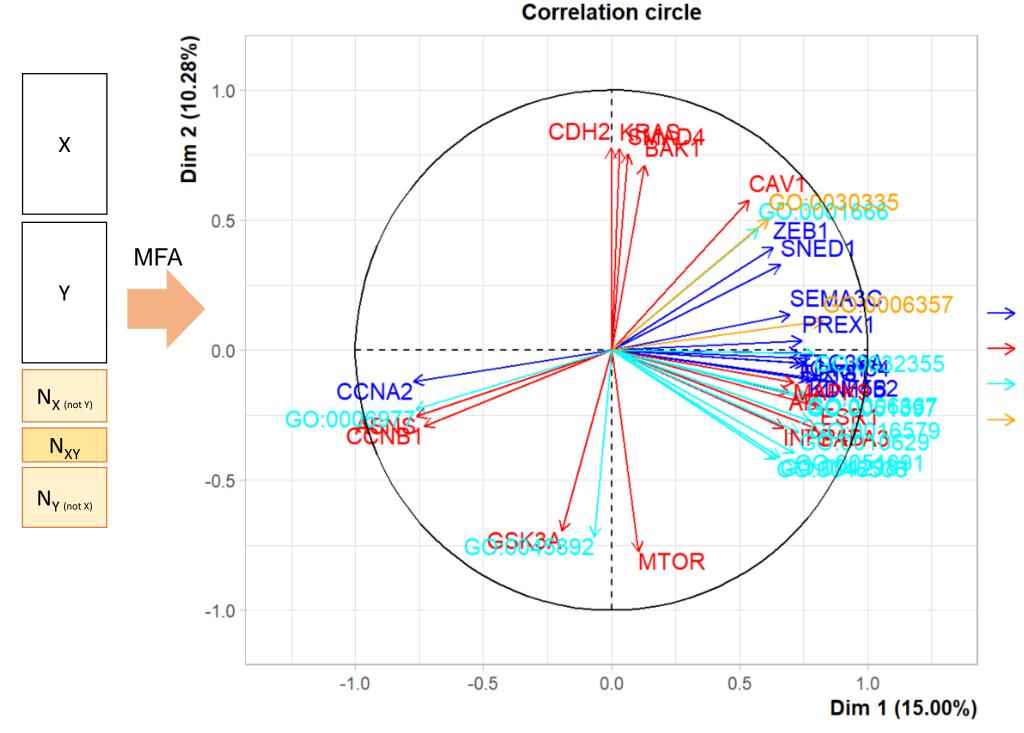
- A) Two 'omics-derived input data sets are loaded and converted to R data frames.
- B) Annotations are created, or loaded if custom annotation file provided, as additional objects, one for each given input matrix, and used to expand these original data, to end up with
- C) A pair of data frames containing the starting values plus the average expression/abundance values of the features related to each annotation as new variables. Then, a first R markdown report is rendered to show steps and main results of the annotate-and-expand process, and
- This output is used for further integrative analyses (MFA, or RGCCA in the depicted example: E).

Integrative Analyses with Dimension Reduction Techniques

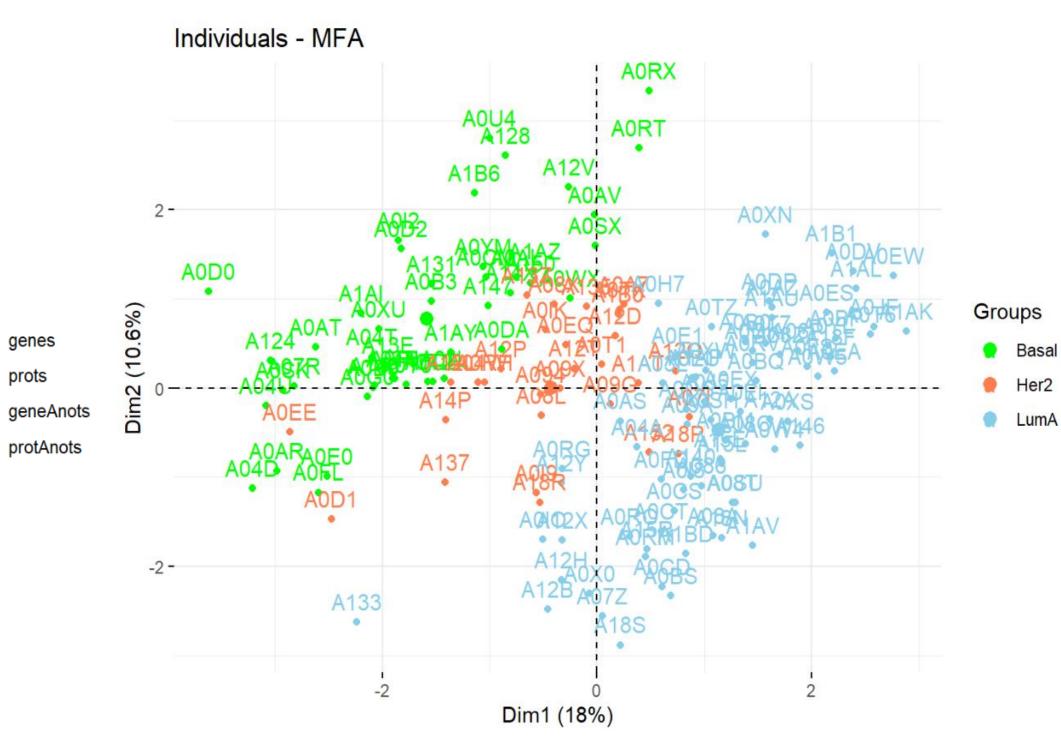
Integrative multi-omics analysis, combining protein and gene expression from 150 breast cancer samples (data from TCGA, available in miXomics¹²), expanded using GO categories, and applying distinct dimension reduction techniques (Regularized Generalized Canonical Correlation Analysis and Multiple Factor Analysis) implemented with packages miXomics or FactoMineR¹³ & factoextra¹⁴, respectively.



Heat maps (A, C) and association networks (B, D) resulting from the integration using RGCCA with miXomics R package. Performed with the original data sets (A, B) or using data expanded with enriched GO categories (C, D), where outputs contain higher level of information (higher density in both type of plots).



Correlation circle of the MFA analysis including N_x (geneAnots), N_Y (protAnots) and also N_{XY} (not shown), as supplementary data.



Plot of individual samples of the MFA analysis including X, Y and N_{xy} (new features from common annotations) as principal data.

References

- 1) Cavill C. et al. Briefings in Bioinformatics, 2016
- 2) Meng C. et al. Briefings in Bioinformatics, 2016
- 4) Wratten L. et al. Nature Methods, 2021

3) Leipzig J. Briefings in Bioinformatics, 2017

- 5) Galaxy Project: https://usegalaxy.org/
- 6) NextFlow: www.nextflow.io 7) GO Consortium, Nucleic Acids Res., 2017
- 8) Subramanian, A. et al. PNAS, 2005
- 9) Lé Cao, K-A. et al. Bioinformatics, 2009
- 10) de Tayrac, M. BMC Genomics, 2009.
- 11) targets: https://books.ropensci.org/targets/
- 12) miXomics <u>www.mixomics.org</u>
- 13) FactoMineR: http://factominer.free.fr/

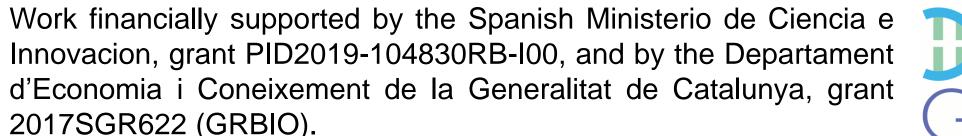
14) factoextra: https://rpkgs.datanovia.com/factoextra

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