Virtual BSC RS/Life Session: A Multi-Objective Genetic Algorithm to Find Active Modules in Multiplex Biological Networks (MOGAMUN) and Sex differences in genetic architecture in UK Biobank

Objectives

Title: A Multi-Objective Genetic Algorithm to Find Active Modules in Multiplex Biological Networks

Abstract: One of the most challenging tasks in computational biology is the integration of complementary biological data produced from different experimental sources. Our goal here is to combine expression data and biological networks to identify “active modules”, i.e. subnetworks of interacting genes/proteins associated with expression changes in different biological contexts. We developed MOGAMUN, a multi-objective genetic algorithm that finds dense subnetworks with an overall deregulation. We compared the performance of MOGAMUN with 3 state-of-the-art methods (jActiveModules [3],COSINE [4] and PinnacleZ [5]), on simulated expression datasets, where MOGAMUN showed the best performances. We also applied MOGAMUN to identify active modules for a rare monogenic disease, Facioscapulohumeral muscular dystrophy (FSHD). We found active modules that represent both known and new cellular processes associated with the hallmarks of the FSHD disorder. MOGAMUN is available as a Bioconductor package.

References

[1] Deb, K. et al. (2002). A fast and elitist multiobjective genetic algorithm: NSGA-II. IEEE transactions on evolutionary computation, 6, 182-197. [2] Valdeolivas et al. (2018). Random walk with restart on multiplex and heterogeneous biological networks. Bioinformatics, 35(3), 497-505. [3] Ideker, T., Ozier, O., Schwikowski, B., & Siegel, A. F. (2002). Discovering regulatory and signalling circuits in molecular interaction networks. Bioinformatics,18(suppl_1), S233-S240. [4] Ma, H., Schadt, E. E., Kaplan, L. M., & Zhao, H. (2011). COSINE: COndition-SpecIfic sub-NEtwork identification using a global optimization method. Bioinformatics,27(9), 1290-1298. [5] Chuang, H. Y., Lee, E., Liu, Y. T., Lee, D., & Ideker, T. (2007). Network based classification of breast cancer ? metastasis. Molecular systems biology,3(1)

Engineer in Computer Science, with a Master's Degree in Artificial Intelligence, and a PhD in Bioinformatics. She won the State Award for early research in 2008, and the Art, Science and Light award, to the best receptional thesis of the University of Veracruz in 2015. She started working in the systems biology field in 2017, where she dealt with omics data, in particular, transcriptomics and, more recently, metabolomics. Elva is currently doing a postdoc at the INRAE. Her main interests are applications of Artificial Intelligence to solve real-world problems, in particular, those related to health and/or biology.

Title: Sex differences in genetic architecture in UK Biobank

Abstract: Sex is arguably the most important differentiating characteristic in most mammalian species, separating populations into different groups, with varying behaviors, morphologies, and physiologies based on their complement of sex chromosomes, amongst other factors. In humans, despite males and females sharing nearly identical genomes, there are differences between the sexes in complex traits and in the risk of a wide array of diseases. Gene by sex interactions (GxS) are thought to account for some of these differences. However, the extent and basis of these interactions are poorly understood.

Here we provide insights into both the scope and mechanism of GxS across the genome of circa 450,000 individuals of European ancestry and 530 complex traits in the UK Biobank. We found small yet widespread differences in genetic architecture across traits through the calculation of sex-specific heritability, genetic correlations, and sex-stratified genome-wide association studies (GWAS). We also found that, in some cases, sex-agnostic GWAS efforts might be missing loci of interest, and looked into possible improvements in the prediction of high-level phenotypes. Finally, we studied the potential functional role of the differences observed through sex-biased eQTL and gene-level analyses.

This study marks a broad examination of the genetics of sex differences. Our findings parallel previous reports, suggesting the presence of sex genetic heterogeneity across complex traits of generally modest magnitude. Our results suggest the need to consider sex-stratified analyses for future studies to shed light into possible sex-specific molecular mechanisms.

undergraduate degree in Biotechnology from 2012 to 2016 at the Polytechnic University of Valencia (Spain). She undertook her undergrad thesis regarding multi-omics integration under the supervision of Dr Sonia Tarazona and Dr Ana Conesa. In 2016 she moved to the UK to pursue a Master's in Bioinformatics at the University of Edinburgh, having been awarded a La Caixa Scholarship. She completed her master's thesis on transcriptomics of immunotherapy under the supervision of Dr Nizar Batada. Starting in 2017, she has been working towards her PhD in Genetics and Genomics at the Roslin Institute, under the supervision of Professor Albert Tenesa and Dr James Prendergast, focusing on gene by sex interactions in the UK Biobank.

Speakers

Elva Novoa, Postdoc at Toxalim (Research Centre in Food Toxicology), Université de Toulouse, INRAE, ENVT, INP-Purpan, UPS, 31300 Toulouse, France and **Elena Bernabéu**, PhD student at The Roslin Institute, University of Edinburgh

Barcelona Supercomputing Center - Centro Nacional de Supercomputación

---