**Project 2: epistatic interactions in biological pathway diagrams**

Suited for: bachelor or master projects in technical domains (bioinformatics, applied mathematics/computer science, systems biology)

Background: to analyse modern day genomics data types, pathway analysis is one of the important approaches. In pathway analysis, we use dynamic representations of textbook pathway diagrams, on which real measurement can be mapped. These measurements can be of many types, for example gene expression changes (transcriptomics) or differences in epigenetic regulation. In addition to visualisation, the mapping of data can also be used to statistically determine the pathways in which the most changes have occurred, using so-called overrepresentation analysis. Considering the full complexity of biological regulation, pathway diagrams can be extended with interactions at different levels. For example, non-coding RNA regulations could be added, such as micro RNAs, or the effects of genetic variations, such as SNPs. However, adding all this information to pathways will clutter the diagrams and make them extremely difficult to visualise and interpret. Therefore, we need to make the diagrams more interactive, or choose which interactions are relevant in the condition of interest and only visualise those. In order to determine which genes have an influence on each other, we can use information on interactions based on the outcome of so-called genome-wide association studies (GWAS), which study the links between SNPs and phenotypic outcome(s) on a genome-wide scale. Given the huge amount of variants measured, the analyses of GWAS data is far from easy, and we have to take the effects of multiple testing into account, to avoid many false-positive findings. Being already complicated for single SNP effects, such analyses even get more difficult when studying epistatic, or gene-gene, interactions.

Kristel van Steen’s group at the Université de Liège has developed dedicated analysis methods for the study of epistatic interactions, called MB-MDR. These methods can even be applied to search for epistatic interactions on a genome-wide scale, which requires substantial computational power and sample size. When applied to *individual target pathways*, where we would have to look for pairwise interactions between a small subset of tens to maximum hundreds of genes only, the computational requirements are much lower.

Project: In this project we want to join efforts and combine pathway analysis tools (PathVisio, Wikipathways) developed at BiGCaT, UM with the computational tools for epistatic analysis developed at ULg. Data sets under study at BiGCaT and pathways selected from the curated Wikipathways collection will be used to apply the within-pathway interaction analysis to. Possibly, the project can be extended, to not only analyse pathways, but also Gene Sets or Gene Ontology classes. These both are groups of genes related to a similar function, but without an underlying pathway diagram. Depending on the project duration and your background, also visualisation options in pathways for those SNPs and genes for which we find epistatic interactions, can be studied. Supervision will be shared between both universities, with daily supervision at UM, and co-supervision from ULg. Your stand will be at Maastricht University, at BiGCaT.

Contact details: Lars Eijssen - [l.eijssen@maastrichtuniversity.nl](mailto:l.eijssen@maastrichtuniversity.nl); Kristel Van Steen – [kristel.vansteen@ulg.ac.be](mailto:kristel.vansteen@ulg.ac.be)

Keywords: Genetics, Bioinformatics, Pathway analysis, Epistasis, Genomics