Systems Medicine

Assignment and Organization

Select a paper and discuss it following the layout of "critical evaluation of a paper" (see class materials). If you would like to discuss another paper than one from the list below, please first have your selection verified by the tutor! Discuss amongst yourself so as to have selected a different "topic" per person.

Provide a written reflection of your work via a comprehensive slides deck, in which you have woven in guiding questions/themes that match the paper of your choice. The "guiding questions" assume having selected a genome-wide interaction paper but the corresponding "themes" can be extrapolated to any type of "large-scale interaction" study (f.i. host-microbiome interactions, gene-environment interactions, edgetics, directionality in gene expression interation studies using genomic profiles, …).

Select a portion of your slides, addressing 3 series of questions in greater depth (more details in class), and name it "Bioinformatics Applications Assignment _ your name". Submit your work to Prof Van Steen (kristel.vansteen@uliege.be) with the subject title "Bioinformatics Applications Assignment", by 1st April. During the class of April 4, you are expected to present your slides in ~15 minutes (~5 minutes per Q). Thereafter, your presentation will be taken as a starting point to Q&As and a group discussion, maximizing the learning experience, while making links to latest developments in the field. The slides deck covering all Qs will need to be submitted prior to the day of the exam; this work will be integrated in the exam.

Papers

Example case studies via:

Gene-environment - https://pubmed.ncbi.nlm.nih.gov/27901618/

Edgetics: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3902775/

Omics-based Subnetwork discovery:

https://www.nature.com/articles/s41540-019-0099-y

Integrative analysis to explore genetic stability of gut microbiome:

https://pubmed.ncbi.nlm.nih.gov/33838112/

Gene-gene and implications for risk score development:
https://alzres.biomedcentral.com/articles/10.1186/s13195-021-00794-8

10 series of "guiding" questions

Each series of questions starts with the main theme, which is relevant to different aspects of systems medicine.

Adapt according to the particular "systems medicine" concept(s) covered by your selected paper.

1. Setting: Describe the biological question(s) and the set-up of the study. Highlight specific differences with a classical genome-wide association study where the aim is to find genetic predispositions to disease.
2. Definition: Give an epidemiology oriented definition of "interactions/epistasis". Is it different from effect modification? Give and discuss different definitions of "interactions/epistasis", in different contexts. Is there a difference between statistical and genetic epistasis? Is it easy to translate statistical epistasis into biological epistasis? How can this translation be facilitated?
3. Adding levels of complexity: In what ways will a gene-gene or gene-environment interaction study be different (more complex? less complex?) than a GWAS?
4. Computational efficiency: What is meant by an exhaustive search? Is this feasible in the context of a genome-wide setting?
5. Networks: Does it make sense to investigate higher-order interactions?
6. Simplistic versus more elaborate, sophisticated methods: What are the criticisms to traditional regression-based approaches in the context of genome-wide interaction studies (GxG or GxE) and can you give alternative methods to deal with the abundance of complex data patterns?
7. One popular method/approach singled out: What is multifactor dimensionality reduction? What are its advantages and limitations? What are some advantages and limitations of machine learning / deep learning methods?
8. Replication: Replication and validation are important components of any genetic association study. What would replication of a genome-wide interaction study involve?
9. Experimental validation: What is the state of the art? What are the problems when trying to experimentally validate findings from big Omics (integrative) studies?
10. Personalized medicine: Can you highlight the differences between "genomics for personalized medicine" and "public health genomics"?