Topics in genetic epidemiology

Assignment and Organization

Select one of the provided papers (cfr. class - http://bio3.giga.ulg.ac.be/index.php/education/courses-at-ulg/) and discuss it following the layout of "critical evaluation of a paper" (see class materials). Consider the series of questions (questions series I OR questions series II) that best matches the paper of your choice. Provide a written reflection of your work via a comprehensive slides presentation or modest report, in which you have woven in the guiding questions, following a logical story. This (slides) report will contribute to your "written exam".

Take 3 questions from your series of questions, and address these in depth, also via a slides presentation. Name the file "Genetic Epidemiology Assignment _your name" and submit it to Prof Van Steen (kristel.vansteen@uliege.be) with the subject title "Genetic Epidemiology Assignment", by April 22. During the class of April 24 you are expected to present your slides in ~20 minutes (depending on the total number of presentations). During ~10 minutes, your presentation will be taken as a starting point for Q&A and a discussion to clarify unknown concepts, while making links to the course materials and the latest developments in the field.

All classes are organized as online sessions via a GoToMeeting virtual room.

Questions Series I: Guiding questions related to genome-wide association studies

1. Describe the biological/research question(s) and put them in context.
2. What is the design of the study? (markers, subjects). Is it different from the designs seen in class? If so, what was the motivation to select a different design?
3. Which quality control procedures have been put in place? Are they in line with the Travemünde criteria? If not, was there a motivation given in the paper for adopting a different criterium, or can you come up with a motivation yourself? Be critical.
4. How did one make use of the concept of LD (linkage disequilibrium)? Was it used to reduce the number of tests? Was it used after the analysis to identify causal variants? Other uses?
5. What type of association test was carried out? Single locus at the time? Haplotype-analysis was considered as well? What is the possible advantage of performing a haplotype analysis? What are the drawbacks?
6. Was there a need to correct for population stratification? What is population stratification? How did one correct for it? Are there other ways?
7. Were the genetic association results supported by a replication analysis or a validation analysis? If so, what did it involve? What are the factors causing a non-replication? May it also be the existence of gene-gene interactions?
8. What are the final conclusions of the study and how much trust can be given to them (when looking at the replication/validation results)?
9. What type of follow-up analyses do the authors advocate? Do these analyses involve multi-omics data? Why or why not?
10. Can you situate the study in the context of (modern) "genetic epidemiology"? What does modern genetic epidemiology stand for? What is the link with bioinformatics?

Questions Series II: Guiding questions related to systems medicine

(Adapt the questions to the "systems medicine" concept covered by your paper. Each question starts with the main theme of the question, which is relevant to different aspects of systems medicine.)

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-environment interaction study be different (more complex? less complex?) than a gene-gene interaction study?
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"?

Evaluation criteria - presentation

Criterium	Key words
Clarity	Logical flows, slides content, slides composition, clear explanations with references
Illustrations on slides	Adequate number of illustrations; not only copy and paste from course but be creative and insert novel illustrations from the www; supportive illustrations
Presentation	Eager beaver (a person who is very enthusiastic about doing something)
Understanding	Presentation content as presented is understood or evidence is given that sufficient efforts were made towards understanding presented concepts; adequate replies to questions and comments (incl. those from fellow students)

Evaluation criteria – (slides) report

Criterium	Key words
Clarity	Logical content flow; story around replies to questions
Illustrations	Adequate number of illustrations
Content	Correct (flawless)
Critical reading	Components of "critical reading" are visible (e.g., adequate report structure, discussion/conclusion section summarizes the results of a critical reflection)

Proposed scoring (to be discussed in class):

HW (presentation – 3 questions)	Exam (report – 10 questions)
6/20	14/20