Mode of Inheritance (MOI) Detection Task

14.4/10/19



As you may already know, each gene has a mode of inheritance. Several basic modes of inheritance exist for single-gene disorders. These include autosomal dominant, autosomal recessive, X-linked dominant, and X-linked recessive. However, not all genetic conditions will follow these patterns, and there are other rare forms of inheritance, such as mitochondrial inheritance.

For simplicity, the provided VCF (Variant Call Format) file contains genomic variants of a real, anonymous patient. It only includes variants in Chr17, so please do not consider X or Y-linked cases. Each variant may fall within one or multiple gene domains. We want to document the inheritance of each gene in a separate column labeled 'MOI.'

Each gene may have more than one mode of inheritance, depending on the associated disease. In these scenarios, maintain both possibilities, like 'AD/AR.' Accepted values should be either 'AD,' 'AR,' or 'AD/AR.'

Requirements

It's required that you check genomics databases that contain gene-phenotype relationships, and inheritance data as well. A list of these datasets includes OMIM, CGD, ClinGen Disease Validity, gene2Phenotype, and GenCC. You need to download these databases and preprocess them in a way that can be used in VCF annotation. Keep in mind that the order of these databases matters. If a gene is AD in OMIM but AR in CGD, consider OMIM as true.

Bonus

If a gene is not present in any of the mentioned databases, there is a machine learning method that predicts the inheritance of a gene, named Domino. Use this tool to predict the P(AD) for all the remaining genes.

Submission

- A .csv file containing 'ID', 'SYMBOL', 'MOI', and 'P_AD' for all variants in the input VCF.
- Scripts and documentation for data preprocess for each database and tool.
- A final script that produces an output CSV file, accompanied by brief documentation.
- Include any material you think is necessary for understanding your work.

Important Notes

- You are encouraged to document your workflow and decisions made during the task.
- Please ensure that your submission is well-organized and easily understandable.
- Using LLM assistance is permissible, provided that it is reviewed and acknowledged.

Best of luck!