CSE 5370: Bioinformatics Homework-1

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Collaboration Statement

I have collaborated with Vijitha Kotapati(1001860730) and Tulasi Sridevi Navuluru(1002010740) to do the programming questions in 1.2, 1.3 and 1.4 by understanding the Fisher's exact test and Bonferroni Correction concepts.

1 Genome Wide Association Studies (GWAS)

You are working as a population geneticist for the government of a large country trying to understand associations between a complex genetic trait (phenotype) and genetic variants in a sequencing study conducted on hundreds of volunteer participants. In this study, there are 50 patients in the case cohort and 100 people in the control cohort. For these participants, 1000 particular SNPs (snp 1, snp 2, ..., snp 1000) are measured and reported (in a real-world study, number of SNPs tested can be several million). These SNPs are either C-alleles or T-alleles. You are required to conclude whether there is significant evidence whether any of the C-allele SNPs contribute to a person's risk of developing the complex trait (Note: this question may be challenging to complete prior to the walk through lecture).

1.1 Generating Your Own Unique Data

We are provided with a python script named datasetGenerator.py. This program will take in our UTA student ID as an argument and generates a unique artificial dataset of the mentioned study. To run the code, simply run:

$\gg$ ***python3 datasetGenerator.py –ID 1002086719***

Running the program will create a file named 1002086719.csv in the same directory this program is located in. This data set has 1000 rows rep- resenting each SNP and 5 columns representing the name of the SNP, number of C-alleles in the case cohort, number of T-alleles in the case cohort, number of C-alleles in the control cohort, and number of T-alleles in the control cohort.

1.2 Fisher's Exact Test

In this scenario, you can represent the data as contingency tables and the effect sizes as odds ratios (please refer to the walk through lecture and slides). For each SNP, if there is significant evidence that the odds ratio for allele C is higher than 1, you can conclude that allele C is among the causes of the complex genetic trait. The Fisher's exact test is a statistical test performed on the contingency tables and tests whether the odds ratio of the underlying populations are close to 1 or not. Using the scipy's fisher exact function, find the p-value associated with each SNP for your data set. Assuming an effective p-value of 5×10^{-8}, which SNPs can be considered statistically significant regarding the complex genetic trait? Based on the documentation of fisher exact function, you need to explain what the null hypothesis of this test is and what it means. Also you need to choose to explain how you choose the alternative argument in this function. You have to provide a file named results.csv containing the p-values for each SNP in the first column and the SNPs that are significant in the second column. You should also report the number of significant SNPs in your written answer.

- The SNPs with odds ratio for allele C that is higher than 1 is considered to be statistically significant regarding the complex genetic trait.
  - Explain what the null hypothesis of this test is and what it means.
  - **Null Hypothesis H_0 = Allele C is among the causes of the complex genetic trait.**
  - **Alternate Hypothesis H_1 = Allele C is not the cause of the complex genetic trait.** The Null Hypothesis H0 adopted for this test means that if allele C causes complex genetic trait when the odds ratio for allele C is higher than 1.
- I have chosen less in the alternative argument in fisher exact function. I have chosen my Alternative hypothesis H_1 as allele c is not the cause of the complex genetic trait which makes odd ratio to be less than 1. We use less as the argument in fisher's exact when the odds ratio of the underlying population is less than one. Hence I have used less as the alternative argument.
- The total number of significant SNPs is **166**

1.3 Corrected P-Values

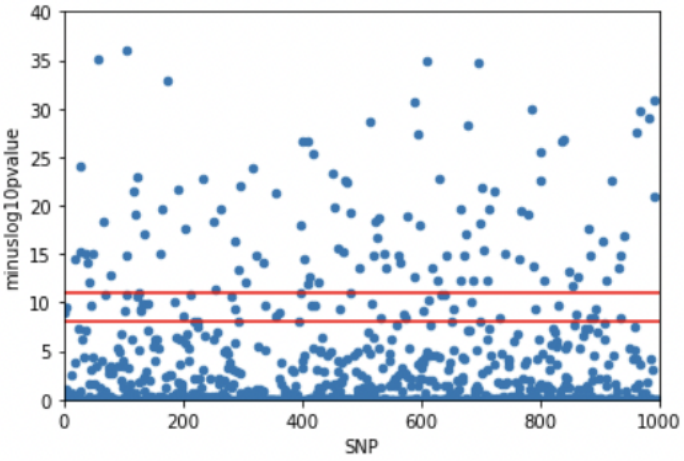
Assuming each association between a SNP and the phenotype is an independent hypothesis, and we want our effective p-value to be 5 × 108 What is our Bonferroni-corrected p-value? How many SNPs are significant under the corrected p-value?

- **The Bonferroni-corrected p-value is** $\frac{\alpha}{n} = \frac{5 \times 10^{-}8}{1000} = 5 \times 10^{-11}$

- **The total number of corrected P values are 119**

1.4 Manhattan Plots

Generate a psuedo Manhattan plot of the log10 (p values) with the original and corrected p-value threshold illustrated. Include a paragraph describing what the Manhattan plot shows.



The X axis in the plot represents SNPs and Y axis represents the associated p values as log10 (p). The blue dots in the plot represents the scattered p values for respective SNPs. The plots between lines represents the threshold.

2 Difficulty Adjustment

Your answers to this section will be used to adjust the difficulty of future assignments in the class.

* How long did this assignment take you to complete?
  - **I completed my assignment in 14 hours.**
* If the assignment took you longer than the 10 hours, which parts were overly difficult?
  - **The Documentation, understanding the question and designing took around 5 hrs . Its challenging yet very interesting to work on this assignment**