Laboratory Note

Genetic Epistasis
IV - Assessing Algorithm Screen and Clean
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Abstract

In this lab note, the algorithm Screen and Clean is presented. As the name indicates, the algorithm screens all relevant SNPs and fits them using regression models for main effect and interaction. The second part consists of cleaning the previously selected interactions using a portion of the data, cleaning possible false positives. The results of the algorithm show that it is nearly incapable of finding any epistatic interactions but produces somewhat decent results in main effect and full effect detection, for data sets with high allele frequencies. The scalability of the algorithm is bad due to the elevated increase in running time.

1 Introduction

Screen and Clean [WDR+10] is a two stage algorithm that works by creating a dictionary of disease related SNPS and disease interactions that contracts or expands during a multi-step statistical procedure and then is revised two control Type I Error Rate.
In the beginning a dictionary, including all SNPs with minor allele frequency above 0.01, is created. If the number of SNPS is greater than the specified upper limit of covariates to enter the screen process, the SNPS are selected based on the SNPS with the lowest marginal p-values. The data is divided for step 1 (screen) and step 2 (clean). In step 1, a screen stage is applied to restrict the number of terms. This restriction is applied using regression models for main effects or interactions. For main effect models, the function used is

$$g(E\left[Y|X\right]) = \beta_0 + \sum_{j=1}^{N} \beta_j X_j \tag{1}$$

where g is an appropriate link function. The X_j is the encoded genotype value 0, 1 or 2 and Y is the encoded phenotype, 0 or 1. According to the selected SNPs, tries to find relevant interacting SNPs that fit into the following interaction model:

$$g(E\left[Y|X\right]) = \beta_0 + \sum_{j=1}^{N} \beta_j X_j + \sum_{i<j;i,j=1,\ldots,N} \beta_{ij} X_i X_j \tag{2}$$

where $S = \{j : \beta_j \neq 0, j \in 1, ..., L\} \cup \{(i,j) : \beta_{ij} \neq 0, (i,j) \in 1, ..., L\}$ are set of terms associated with the phenotype as main effects or interactions. A cross-validation is applied in this stage, to apply a further restriction. In the stage 2, the resulting dictionary is cleaned with p-values $< \alpha$. This is done using the traditional t-statistic obtained from least squares analysis of the screened model.

1.1 Input files

The input consists of two files containing the phenotype of all individuals and the genotype with all SNPS for all individuals.

1.2 Output files

There are many outputs available:

(a) Genotype

rs1,	rs2,	rs3,	rs4,	rs5
0,	2,	0,	0,	0
0,	1,	1,	0,	0
0,	1,	1,	0,	0
1,	1,	0,	1,	0
0,	1,	1,	1,	1
0,	1,	2,	1,	0

(b) Phenotype

Label
0
1
0
0
1
1

Table 1: An example of the input file containing genotype and phenotype information with 5 SNPs and 6 individuals. Genotype 0,1,2 corresponds to homozygous dominant, heterozygous, and homozygous recessive. The phenotype 0,1 corresponds to control and case respectively.

- *snp_screen* - a vector of the column names of the SNPS picked by the screen.
- *snp_screen*2 - vector of *K_pairs* and SNP pairs retained by the second lasso screen.
- *snp_clean* - vector of screened SNPs also retained by the multivariate regression clean.
- *clean* - a data frame with regression output for all of the screened SNPs. The snp2 column corresponds to the pairwise interaction or "NA" for main effects.
- *final* - a data frame with output from the regression of phenotype on the final cleaned SNPs.

1.3 Parameters

The following parameters can be configured:

- *L* - numver of SNPs to be retained with the smallest p-values.
- *K_pairs* - Number of pairwise interactions to be retained by the lasso.
- *response* - The type of phenotype. Can be binomial or gaussian.
- *alpha* - The Bonferroni correction lower bound limit for retention of SNPs.

- snp_fix - Index of SNPs that are forced into the lasso and multivariate regression models. Optional.
- *cov_struct* - Matrix of covariates that are forced in every model fit by Screen & Clean. Optional.
- *standardize* - If true, the genotype coded as 0,1, or 2 are centered to mean 0 and standard deviation 1. The data must be standardized to run the Screen & Clean procedure.

2 Experimental Settings

The datasets used in the experiments are characterized in Lab Note 1. The computer used for this experiments used the 64-bit Ubuntu 13.10 operating system, with an Intel(R) Core(TM)2 Quad CPU Q6600 2.40GHz processor and 8,00 GB of RAM memory.
The parameters used for this experiments were : $L = 200, K\_pairs = 100, response = "binomial", standardize = TRUE, alpha = 0.05$.

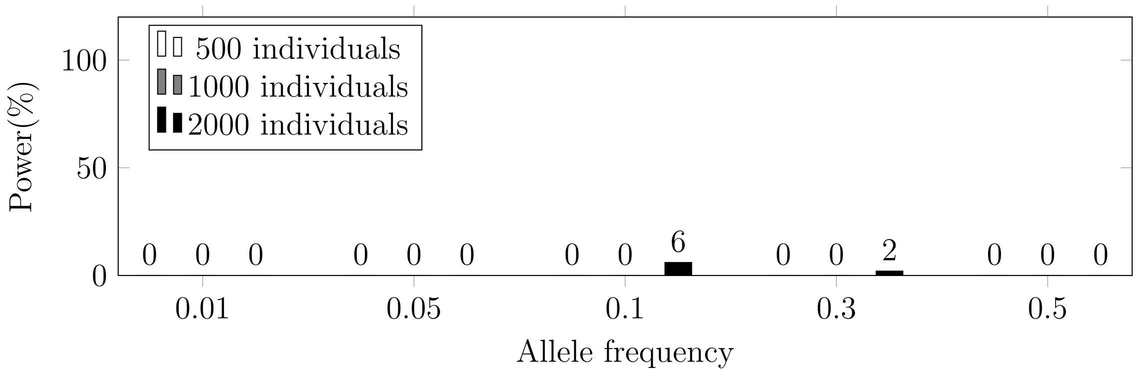
3 Results

The results from Figure 1 show interesting results. for epistasis detection, the Power is nearly 0 in all configurations. In main effect detection, the ground truth is detected in data sets with an allele frequency higher than 0.05. In full effect detection only data sets with 0.3 allele frequency or higher have any Power. There is no clear pattern between the Power and the data set size.

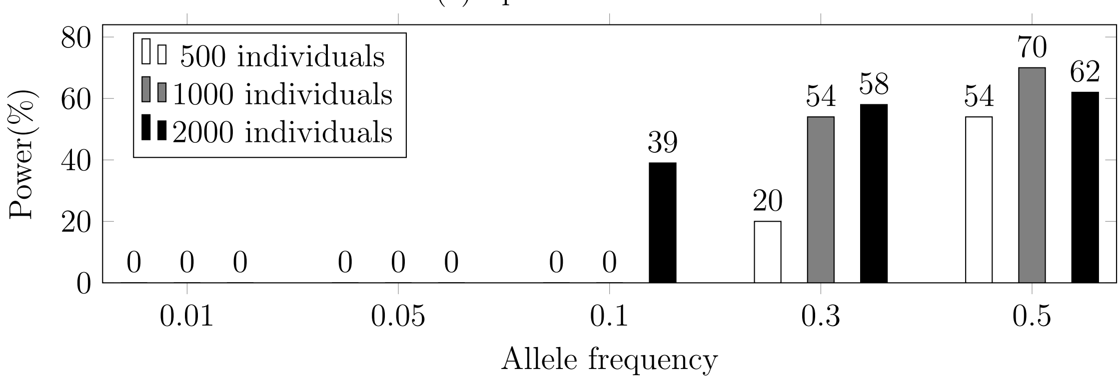
The scalability test shows a clear increase in the running time with the increase in the number of individuals of the data sets. Memory usage also increases with data set size, but not as significantly as running time, which may become a serious obstacle in larger data sets. CPU usage does not show a clear increase.

Type I Error Rate in epistatic detection shows a seemingly random distribuition. Overall, the error rate is very constant. For main effect detection, there is a bigger increase with population size and allele frequency. This is even more clear in full effect detection, reaching a maximum of 84% in a configuration of 2000 individuals and 0.5 allele frequency.

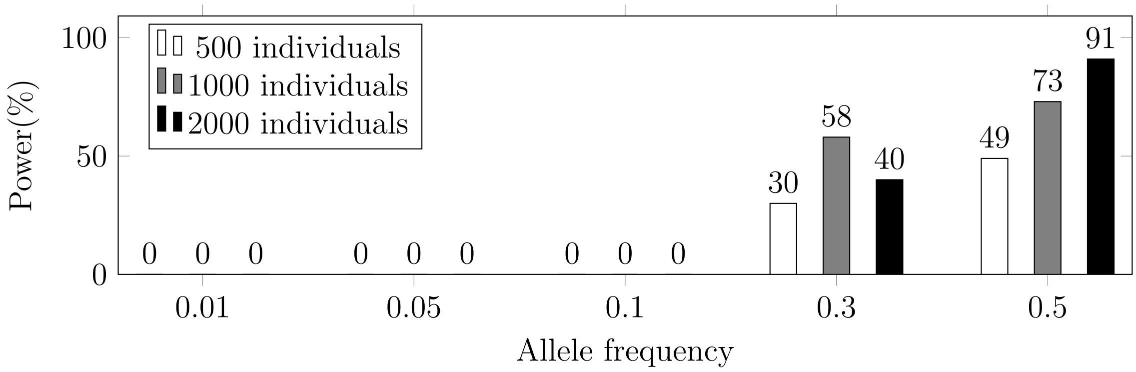
From Figure 4 and Figure 5 there is only an indication of Power for data sets with 2000 individuals, except for full effect data sets, exacly the same as with the odds ratio variance. The prevalence variation shows a small Power



(a) Epistasis

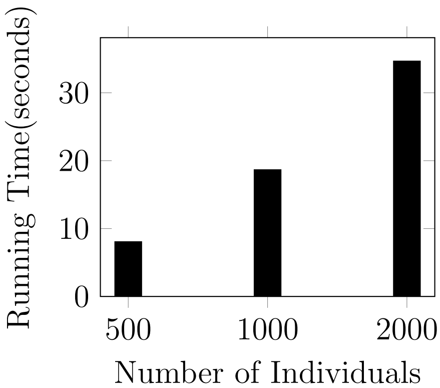


(b) Main Effect

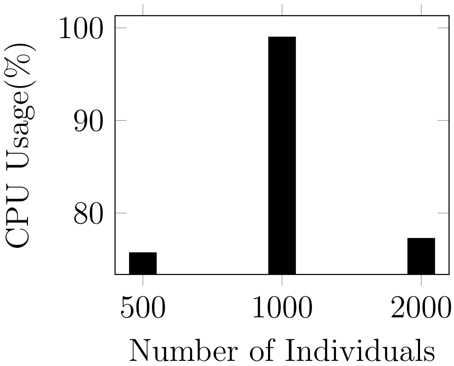


(c) Full Effect

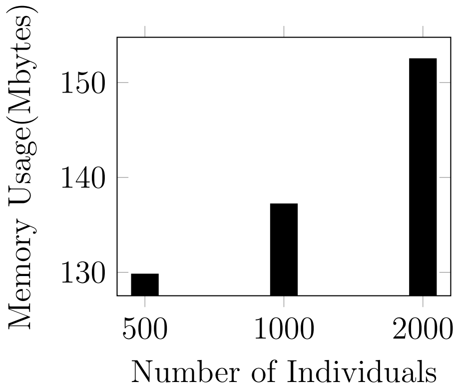
Figure 1: Average Power by allele frequency. For each frequency, three sizes of data sets were used to measure the Power, with odds ratio of 2.0 and prevalence of 0.02. The Power is measured by the amount of data sets where the ground truth was amongst the most relevant results, out of all 100 data sets. (b), (a), and (c) represent main effect, epistatic and main effect + epistatic interactions.



(a) Average running time.

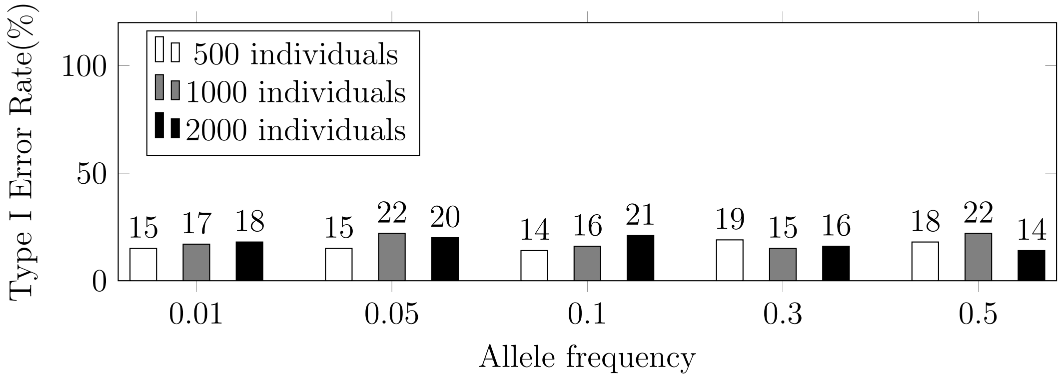


(b) Average CPU usage.

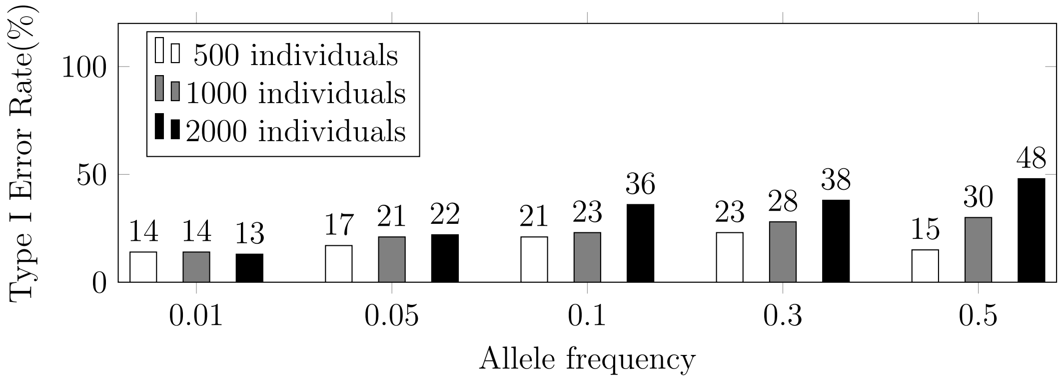


(c) Average memory usage.

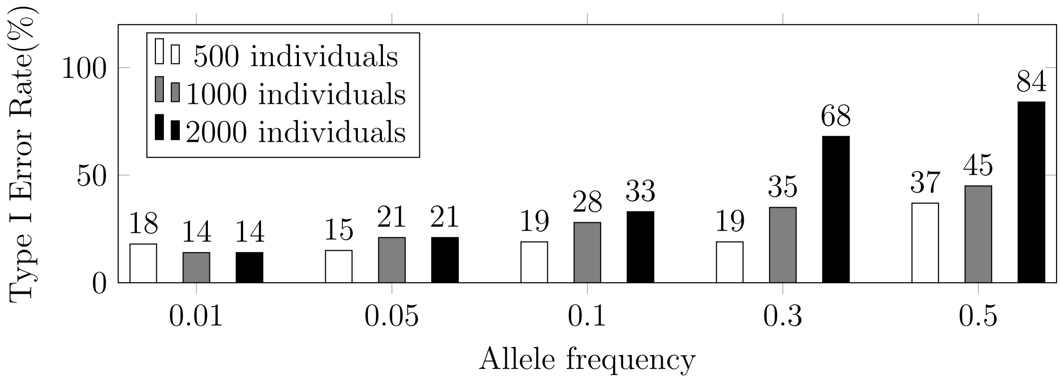
Figure 2: Comparison of scalability measures between different sized data sets. The data sets have a minor allele frequency is 0.5, 2.0 odds ratio, 0.02 prevalence and use the full effect disease model.



(a) Epistasis



(b) Main Effect



(c) Full Effect

Figure 3: Type I Error Rate by allele frequency. For each frequency, three sizes of data sets were used to measure the Power, with odds ratio of 2.0 and prevalence of 0.02. The Type I Error Rate is measured by the amount of data sets where the false positives were amongst the most relevant results, out of all 100 data sets. (a), (b), and (c) represent epistatic, main effect, and main effect + epistatic interactions.

change in Figure 6, decreasing with the prevalence increase. Figure 7 reveals that there is only relevant Power in higher allele frequencies, and in main and full effects.

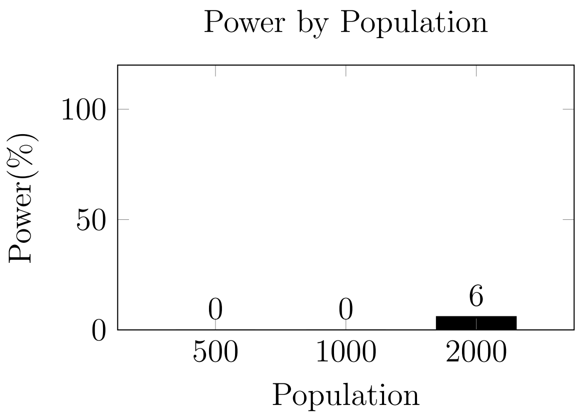
4 Summary

Screen and Clean is a heuristic algorithm that works by applying regression models for main effect and epistatic detection, and pruning statistically irrelevant interactions. The obtained results show very low Power for epistatic detection. In main effect detection, there is an increase in Power, especially in higher dimension data sets. With higher allele frequencies, there is also an increase of Power. In full effect detection, there is only Power in data sets with allele frequency higher than 0.1. The scalability is bad, due to the big increase in running time with different data set sizes. The type 1 errors do not vary significantly with population size or allele frequency in epistasis detection, contrary to main effect and full effect detection.

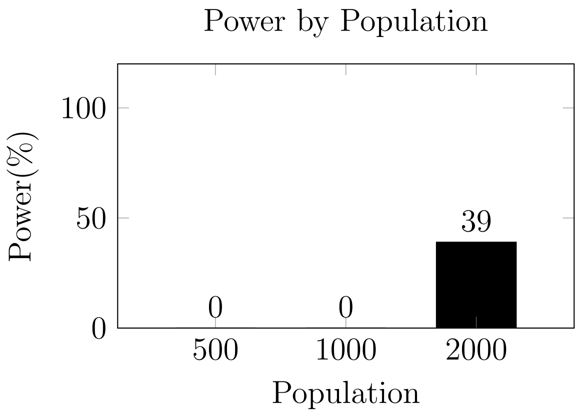
References

[WDR+10] Jing Wu, Bernie Devlin, Steven Ringquist, Massimo Trucco, and Kathryn Roeder. Screen and clean: a tool for identifying interactions in genome-wide association studies. *Genetic epidemiology*, 34:275–285, 2010.

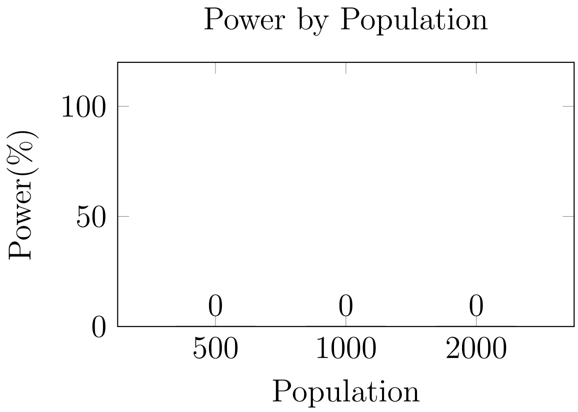
A Bar Graphs



(a) Epistasis

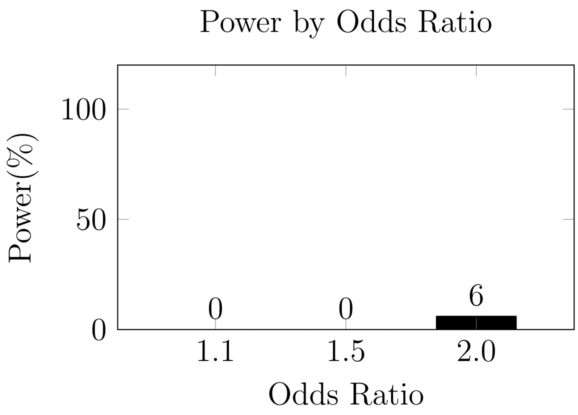


(b) Main Effect

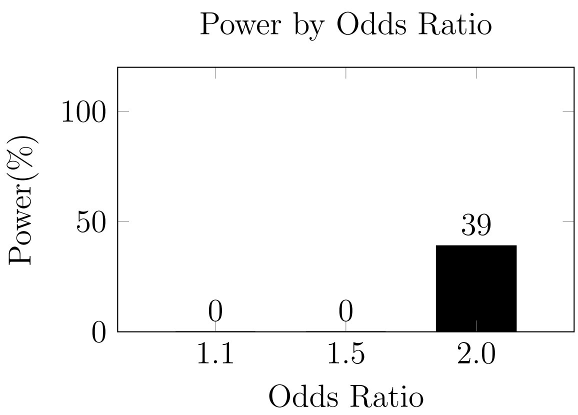


(c) Full Effect

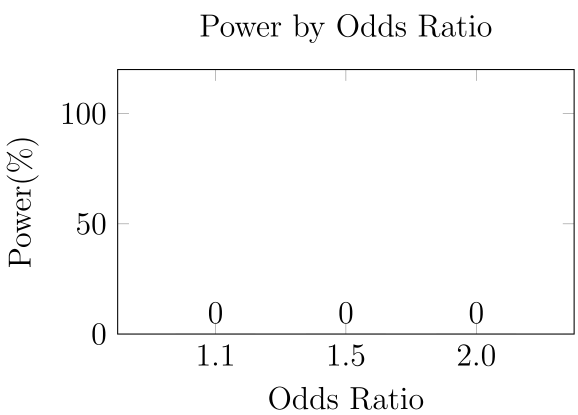
Figure 4: Distribution of the Power by population for all disease models. The allele frequency is 0.1, the odds ratio is 2.0, and the prevalence is 0.02.



(a) Epistasis

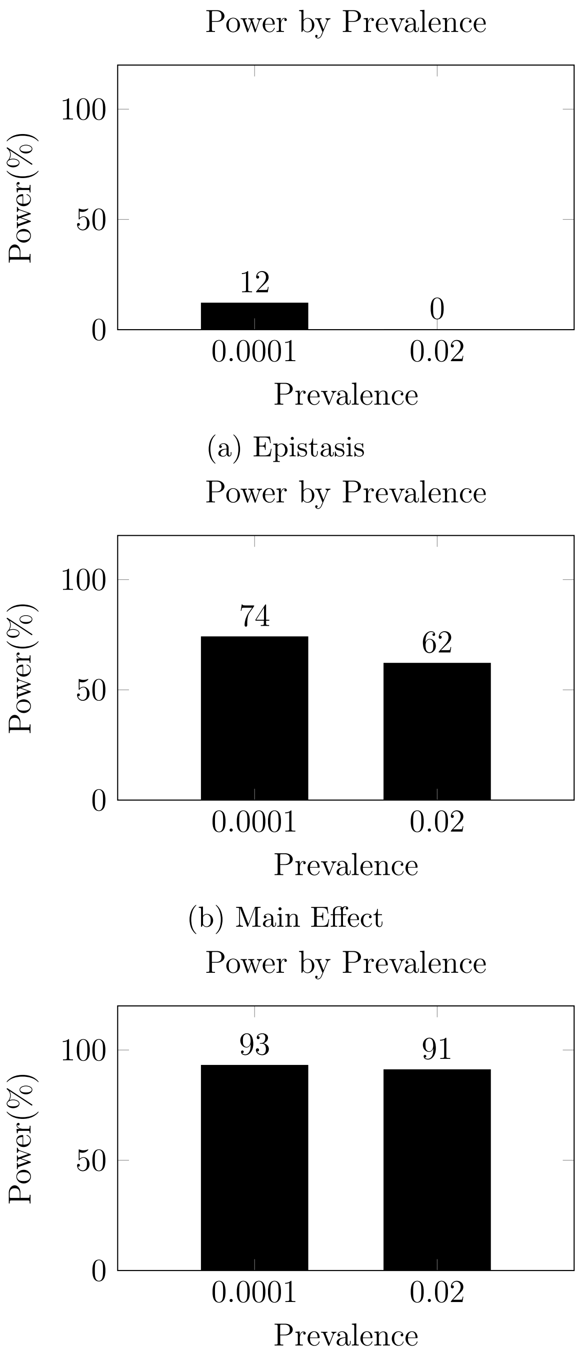


(b) Main Effect



(c) Full Effect

Figure 5: Distribution of the Power by odds ratios for all disease models. The allele frequency is 0.1, the population size is 2000 individuals, and the prevalence is 0.02.

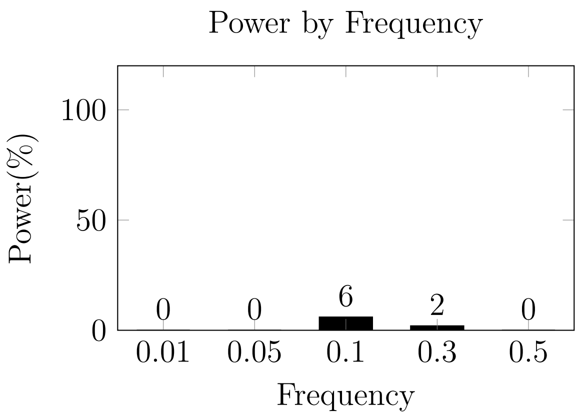


(a) Epistasis

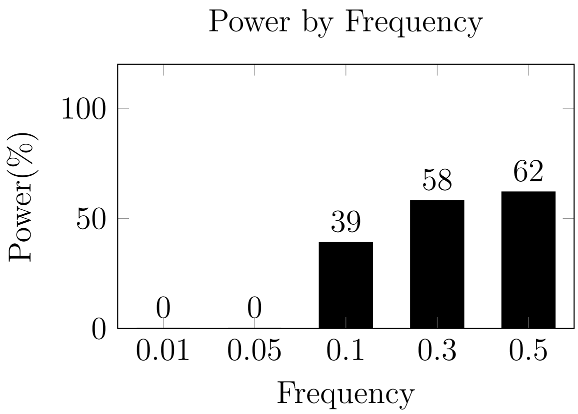
(b) Main Effect

(c) Full Effect

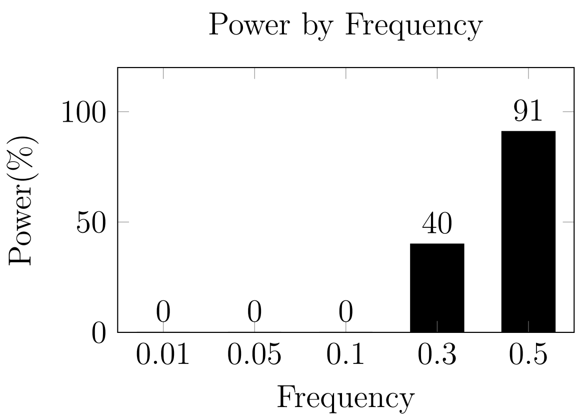
Figure 6: Distribution of the Power by prevalence for all disease models. The allele frequency is 0.5, the odds ratio is 2.0, and the population size is 2000 individuals.



(a) Epistasis



(b) Main Effect



(c) Full Effect

Figure 7: Distribution of the Power by allele frequency for all disease models. The population size is 2000 individuals, the odds ratio is 2.0, and the prevalence is 0.02.

B Table of Results

Table 2: A table containing the percentage of true positives and false positives in each configuration. The first column contains the description of the configuration. The second and third columns contain the number of datasets with true positives and false positives respectively, out of all 100 data sets per configuration.

Configuration*	TP (%)	FP (%)
0.5,500,I,2.0,0.02	0	18
0.5,500,I,2.0,0.0001	0	9
0.5,500,I,1.5,0.02	0	11
0.5,500,I,1.5,0.0001	0	17
0.5,500,I,1.1,0.02	0	18
0.5,500,I,1.1,0.0001	0	25
0.5,2000,I,2.0,0.02	0	14
0.5,2000,I,2.0,0.0001	12	19
0.5,2000,I,1.5,0.02	5	25
0.5,2000,I,1.5,0.0001	0	17
0.5,2000,I,1.1,0.02	1	20
0.5,2000,I,1.1,0.0001	0	10
0.5,1000,I,2.0,0.02	0	22
0.5,1000,I,2.0,0.0001	3	17
0.5,1000,I,1.5,0.02	2	11
0.5,1000,I,1.5,0.0001	0	17
0.5,1000,I,1.1,0.02	0	15
0.5,1000,I,1.1,0.0001	0	13
0.3,500,I,2.0,0.02	0	19
0.3,500,I,2.0,0.0001	0	14
0.3,500,I,1.5,0.02	0	14
0.3,500,I,1.5,0.0001	0	11
0.3,500,I,1.1,0.02	0	18
0.3,500,I,1.1,0.0001	0	14
0.3,2000,I,2.0,0.02	2	16
0.3,2000,I,2.0,0.0001	0	19
0.3,2000,I,1.5,0.02	0	20
0.3,2000,I,1.5,0.0001	1	11
0.3,2000,I,1.1,0.02	0	19
0.3,2000,I,1.1,0.0001	0	14
0.3,1000,I,2.0,0.02	0	15

0.3,1000,I,2.0,0.0001	0	14
0.3,1000,I,1.5,0.02	1	10
0.3,1000,I,1.5,0.0001	0	11
0.3,1000,I,1.1,0.02	0	13
0.3,1000,I,1.1,0.0001	0	12
0.1,500,I,2.0,0.02	0	14
0.1,500,I,2.0,0.0001	0	11
0.1,500,I,1.5,0.02	0	17
0.1,500,I,1.5,0.0001	0	13
0.1,500,I,1.1,0.02	0	8
0.1,500,I,1.1,0.0001	0	16
0.1,2000,I,2.0,0.02	6	21
0.1,2000,I,2.0,0.0001	1	19
0.1,2000,I,1.5,0.02	0	13
0.1,2000,I,1.5,0.0001	0	15
0.1,2000,I,1.1,0.02	0	17
0.1,2000,I,1.1,0.0001	0	16
0.1,1000,I,2.0,0.02	0	16
0.1,1000,I,2.0,0.0001	0	20
0.1,1000,I,1.5,0.02	0	11
0.1,1000,I,1.5,0.0001	0	12
0.1,1000,I,1.1,0.02	0	17
0.1,1000,I,1.1,0.0001	0	10
0.05,500,I,2.0,0.02	0	15
0.05,500,I,2.0,0.0001	0	5
0.05,500,I,1.5,0.02	0	23
0.05,500,I,1.5,0.0001	0	21
0.05,500,I,1.1,0.02	0	19
0.05,500,I,1.1,0.0001	0	17
0.05,2000,I,2.0,0.02	0	20
0.05,2000,I,2.0,0.0001	0	14
0.05,2000,I,1.5,0.02	2	25
0.05,2000,I,1.5,0.0001	1	19
0.05,2000,I,1.1,0.02	0	15
0.05,2000,I,1.1,0.0001	0	14
0.05,1000,I,2.0,0.02	0	22
0.05,1000,I,2.0,0.0001	0	15
0.05,1000,I,1.5,0.02	0	14

0.05,1000,I,1.5,0.0001	0	12
0.05,1000,I,1.1,0.02	0	22
0.05,1000,I,1.1,0.0001	0	16
0.01,500,I,2.0,0.02	0	15
0.01,500,I,2.0,0.0001	0	13
0.01,500,I,1.5,0.02	0	15
0.01,500,I,1.5,0.0001	0	19
0.01,500,I,1.1,0.02	0	13
0.01,500,I,1.1,0.0001	0	11
0.01,2000,I,2.0,0.02	0	18
0.01,2000,I,2.0,0.0001	0	13
0.01,2000,I,1.5,0.02	0	11
0.01,2000,I,1.5,0.0001	0	19
0.01,2000,I,1.1,0.02	0	19
0.01,2000,I,1.1,0.0001	0	11
0.01,1000,I,2.0,0.02	0	17
0.01,1000,I,2.0,0.0001	0	11
0.01,1000,I,1.5,0.02	0	11
0.01,1000,I,1.5,0.0001	0	17
0.01,1000,I,1.1,0.02	0	13
0.01,1000,I,1.1,0.0001	0	11
0.5,500,ME,2.0,0.02	54	15
0.5,500,ME,2.0,0.0001	35	23
0.5,500,ME,1.5,0.02	40	17
0.5,500,ME,1.5,0.0001	21	19
0.5,500,ME,1.1,0.02	15	14
0.5,500,ME,1.1,0.0001	10	27
0.5,2000,ME,2.0,0.02	62	48
0.5,2000,ME,2.0,0.0001	74	35
0.5,2000,ME,1.5,0.02	77	31
0.5,2000,ME,1.5,0.0001	83	17
0.5,2000,ME,1.1,0.02	91	17
0.5,2000,ME,1.1,0.0001	82	21
0.5,1000,ME,2.0,0.02	70	30
0.5,1000,ME,2.0,0.0001	72	24
0.5,1000,ME,1.5,0.02	71	22
0.5,1000,ME,1.5,0.0001	77	18
0.5,1000,ME,1.1,0.02	53	21

0.5,1000,ME,1.1,0.0001	50	20
0.3,500,ME,2.0,0.02	20	23
0.3,500,ME,2.0,0.0001	16	18
0.3,500,ME,1.5,0.02	7	20
0.3,500,ME,1.5,0.0001	4	21
0.3,500,ME,1.1,0.02	0	17
0.3,500,ME,1.1,0.0001	0	15
0.3,2000,ME,2.0,0.02	58	38
0.3,2000,ME,2.0,0.0001	48	53
0.3,2000,ME,1.5,0.02	62	37
0.3,2000,ME,1.5,0.0001	49	40
0.3,2000,ME,1.1,0.02	33	19
0.3,2000,ME,1.1,0.0001	29	29
0.3,1000,ME,2.0,0.02	54	28
0.3,1000,ME,2.0,0.0001	52	25
0.3,1000,ME,1.5,0.02	25	23
0.3,1000,ME,1.5,0.0001	17	15
0.3,1000,ME,1.1,0.02	11	11
0.3,1000,ME,1.1,0.0001	0	21
0.1,500,ME,2.0,0.02	0	21
0.1,500,ME,2.0,0.0001	0	20
0.1,500,ME,1.5,0.02	0	17
0.1,500,ME,1.5,0.0001	0	16
0.1,500,ME,1.1,0.02	0	17
0.1,500,ME,1.1,0.0001	0	14
0.1,2000,ME,2.0,0.02	39	36
0.1,2000,ME,2.0,0.0001	32	50
0.1,2000,ME,1.5,0.02	0	24
0.1,2000,ME,1.5,0.0001	0	28
0.1,2000,ME,1.1,0.02	0	21
0.1,2000,ME,1.1,0.0001	0	15
0.1,1000,ME,2.0,0.02	0	23
0.1,1000,ME,2.0,0.0001	0	19
0.1,1000,ME,1.5,0.02	0	9
0.1,1000,ME,1.5,0.0001	0	10
0.1,1000,ME,1.1,0.02	0	13
0.1,1000,ME,1.1,0.0001	0	15
0.05,500,ME,2.0,0.02	0	17

0.05,500,ME,2.0,0.0001	0	24
0.05,500,ME,1.5,0.02	0	13
0.05,500,ME,1.5,0.0001	0	12
0.05,500,ME,1.1,0.02	0	16
0.05,500,ME,1.1,0.0001	0	16
0.05,2000,ME,2.0,0.02	0	22
0.05,2000,ME,2.0,0.0001	0	18
0.05,2000,ME,1.5,0.02	0	10
0.05,2000,ME,1.5,0.0001	0	12
0.05,2000,ME,1.1,0.02	0	16
0.05,2000,ME,1.1,0.0001	0	15
0.05,1000,ME,2.0,0.02	0	21
0.05,1000,ME,2.0,0.0001	0	17
0.05,1000,ME,1.5,0.02	0	16
0.05,1000,ME,1.5,0.0001	0	13
0.05,1000,ME,1.1,0.02	0	15
0.05,1000,ME,1.1,0.0001	0	16
0.01,500,ME,2.0,0.02	0	14
0.01,500,ME,2.0,0.0001	0	22
0.01,500,ME,1.5,0.02	0	14
0.01,500,ME,1.5,0.0001	0	22
0.01,500,ME,1.1,0.02	0	12
0.01,500,ME,1.1,0.0001	0	24
0.01,2000,ME,2.0,0.02	0	13
0.01,2000,ME,2.0,0.0001	0	16
0.01,2000,ME,1.5,0.02	0	20
0.01,2000,ME,1.5,0.0001	0	14
0.01,2000,ME,1.1,0.02	0	19
0.01,2000,ME,1.1,0.0001	0	14
0.01,1000,ME,2.0,0.02	0	14
0.01,1000,ME,2.0,0.0001	0	15
0.01,1000,ME,1.5,0.02	0	13
0.01,1000,ME,1.5,0.0001	0	16
0.01,1000,ME,1.1,0.02	0	18
0.01,1000,ME,1.1,0.0001	0	17
0.5,500,ME+I,2.0,0.02	49	37
0.5,500,ME+I,2.0,0.0001	37	33
0.5,500,ME+I,1.5,0.02	54	33

0.5,500,ME+I,1.5,0.0001	43	30
0.5,500,ME+I,1.1,0.02	47	20
0.5,500,ME+I,1.1,0.0001	33	27
0.5,2000,ME+I,2.0,0.02	91	84
0.5,2000,ME+I,2.0,0.0001	93	76
0.5,2000,ME+I,1.5,0.02	94	78
0.5,2000,ME+I,1.5,0.0001	96	81
0.5,2000,ME+I,1.1,0.02	89	60
0.5,2000,ME+I,1.1,0.0001	88	72
0.5,1000,ME+I,2.0,0.02	73	45
0.5,1000,ME+I,2.0,0.0001	69	56
0.5,1000,ME+I,1.5,0.02	78	51
0.5,1000,ME+I,1.5,0.0001	80	50
0.5,1000,ME+I,1.1,0.02	78	33
0.5,1000,ME+I,1.1,0.0001	75	39
0.3,500,ME+I,2.0,0.02	30	19
0.3,500,ME+I,2.0,0.0001	37	28
0.3,500,ME+I,1.5,0.02	14	20
0.3,500,ME+I,1.5,0.0001	18	22
0.3,500,ME+I,1.1,0.02	5	17
0.3,500,ME+I,1.1,0.0001	3	14
0.3,2000,ME+I,2.0,0.02	40	68
0.3,2000,ME+I,2.0,0.0001	92	92
0.3,2000,ME+I,1.5,0.02	61	50
0.3,2000,ME+I,1.5,0.0001	77	74
0.3,2000,ME+I,1.1,0.02	50	35
0.3,2000,ME+I,1.1,0.0001	61	35
0.3,1000,ME+I,2.0,0.02	58	35
0.3,1000,ME+I,2.0,0.0001	72	57
0.3,1000,ME+I,1.5,0.02	45	34
0.3,1000,ME+I,1.5,0.0001	50	37
0.3,1000,ME+I,1.1,0.02	23	19
0.3,1000,ME+I,1.1,0.0001	12	18
0.1,500,ME+I,2.0,0.02	0	19
0.1,500,ME+I,2.0,0.0001	0	20
0.1,500,ME+I,1.5,0.02	0	23
0.1,500,ME+I,1.5,0.0001	0	11
0.1,500,ME+I,1.1,0.02	0	12

0.1,500,ME+I,1.1,0.0001	0	23
0.1,2000,ME+I,2.0,0.02	0	33
0.1,2000,ME+I,2.0,0.0001	0	20
0.1,2000,ME+I,1.5,0.02	0	23
0.1,2000,ME+I,1.5,0.0001	0	17
0.1,2000,ME+I,1.1,0.02	0	15
0.1,2000,ME+I,1.1,0.0001	0	10
0.1,1000,ME+I,2.0,0.02	0	28
0.1,1000,ME+I,2.0,0.0001	0	23
0.1,1000,ME+I,1.5,0.02	0	15
0.1,1000,ME+I,1.5,0.0001	0	12
0.1,1000,ME+I,1.1,0.02	0	8
0.1,1000,ME+I,1.1,0.0001	0	19
0.05,500,ME+I,2.0,0.02	0	15
0.05,500,ME+I,2.0,0.0001	0	19
0.05,500,ME+I,1.5,0.02	0	16
0.05,500,ME+I,1.5,0.0001	0	11
0.05,500,ME+I,1.1,0.02	0	15
0.05,500,ME+I,1.1,0.0001	0	21
0.05,2000,ME+I,2.0,0.02	0	21
0.05,2000,ME+I,2.0,0.0001	0	22
0.05,2000,ME+I,1.5,0.02	0	19
0.05,2000,ME+I,1.5,0.0001	0	18
0.05,2000,ME+I,1.1,0.02	0	18
0.05,2000,ME+I,1.1,0.0001	0	13
0.05,1000,ME+I,2.0,0.02	0	21
0.05,1000,ME+I,2.0,0.0001	0	15
0.05,1000,ME+I,1.5,0.02	0	12
0.05,1000,ME+I,1.5,0.0001	0	20
0.05,1000,ME+I,1.1,0.02	0	14
0.05,1000,ME+I,1.1,0.0001	0	18
0.01,500,ME+I,2.0,0.02	0	18
0.01,500,ME+I,2.0,0.0001	0	13
0.01,500,ME+I,1.5,0.02	0	15
0.01,500,ME+I,1.5,0.0001	0	15
0.01,500,ME+I,1.1,0.02	0	14
0.01,500,ME+I,1.1,0.0001	0	23
0.01,2000,ME+I,2.0,0.02	0	14

0.01,2000,ME+I,2.0,0.0001	0	18
0.01,2000,ME+I,1.5,0.02	0	22
0.01,2000,ME+I,1.5,0.0001	0	14
0.01,2000,ME+I,1.1,0.02	0	16
0.01,2000,ME+I,1.1,0.0001	0	15
0.01,1000,ME+I,2.0,0.02	0	14
0.01,1000,ME+I,2.0,0.0001	0	9
0.01,1000,ME+I,1.5,0.02	0	15
0.01,1000,ME+I,1.5,0.0001	0	15
0.01,1000,ME+I,1.1,0.02	0	18
0.01,1000,ME+I,1.1,0.0001	0	17

*MAF,POP,MOD,OR,PREV where MAF represents the minor allele frequency, POP is the number of individuals, MOD is the used model (with or without main effect and with or without epistasis effect), OR is the odds ratio and PREV is the prevalence of the disease.

Table 3: A table containing the running time, cpu usage and memory usage in each configuration.

Configuration*	Running Time (s)	CPU Usage (%)	Memory Usage (KB)
0.5,500,ME+I,2.0,0.02	8.05	75.72	132928.28
0.5,500,ME+I,2.0,0.0001	8.10	75.95	133723.36
0.5,500,ME+I,1.5,0.02	9.37	75.86	132094.44
0.5,500,ME+I,1.5,0.0001	9.03	75.38	132148.28
0.5,500,ME+I,1.1,0.02	11.23	75.14	133080.40
0.5,500,ME+I,1.1,0.0001	10.48	75.46	131997.88
0.5,500,ME,2.0,0.02	10.43	76.02	132144.56
0.5,500,ME,2.0,0.0001	9.98	76.18	132479.40
0.5,500,ME,1.5,0.02	11.88	75.85	133979.16
0.5,500,ME,1.5,0.0001	11.01	80.20	132260.32
0.5,500,ME,1.1,0.02	13.19	77.06	135044.20
0.5,500,ME,1.1,0.0001	12.12	77.23	133516.64
0.5,500,I,2.0,0.02	14.39	76.70	133500.72
0.5,500,I,2.0,0.0001	12.97	76.82	132901.40
0.5,500,I,1.5,0.02	14.32	76.82	133835.88
0.5,500,I,1.5,0.0001	13.16	76.95	132729.96
0.5,500,I,1.1,0.02	14.44	77.07	133436.20
0.5,500,I,1.1,0.0001	13.06	76.99	132833.76

0.5,2000,ME+I,2.0,0.02	34.65	77.25	156137.44
0.5,2000,ME+I,2.0,0.0001	31.37	76.78	153924.36
0.5,2000,ME+I,1.5,0.02	67.20	98.96	156944.56
0.5,2000,ME+I,1.5,0.0001	51.19	98.96	156487.44
0.5,2000,ME+I,1.1,0.02	106.54	99.00	157200.08
0.5,2000,ME+I,1.1,0.0001	76.74	99.00	157071.08
0.5,2000,ME,2.0,0.02	86.58	99.00	157251.32
0.5,2000,ME,2.0,0.0001	65.83	98.98	156912.40
0.5,2000,ME,1.5,0.02	115.43	99.00	156853.92
0.5,2000,ME,1.5,0.0001	84.74	99.00	157327.68
0.5,2000,ME,1.1,0.02	141.42	98.99	156264.16
0.5,2000,ME,1.1,0.0001	101.23	98.99	156739.32
0.5,2000,I,2.0,0.02	177.72	98.97	155566.84
0.5,2000,I,2.0,0.0001	121.39	98.99	155160.08
0.5,2000,I,1.5,0.02	175.38	99.00	155246.92
0.5,2000,I,1.5,0.0001	121.20	99.00	155048.64
0.5,2000,I,1.1,0.02	175.60	99.00	155732.32
0.5,2000,I,1.1,0.0001	121.17	99.00	155220.24
0.5,1000,ME+I,2.0,0.02	18.65	98.99	140519.08
0.5,1000,ME+I,2.0,0.0001	17.79	98.96	140777.40
0.5,1000,ME+I,1.5,0.02	27.78	98.93	140225.08
0.5,1000,ME+I,1.5,0.0001	23.17	98.90	140721.96
0.5,1000,ME+I,1.1,0.02	36.70	98.96	139726.28
0.5,1000,ME+I,1.1,0.0001	30.35	98.96	139558.00
0.5,1000,ME,2.0,0.02	31.89	98.98	139635.88
0.5,1000,ME,2.0,0.0001	27.30	98.98	140585.16
0.5,1000,ME,1.5,0.02	38.06	99.00	140003.76
0.5,1000,ME,1.5,0.0001	31.63	99.00	139501.32
0.5,1000,ME,1.1,0.02	43.46	99.00	139474.84
0.5,1000,ME,1.1,0.0001	36.17	99.00	139679.12
0.5,1000,I,2.0,0.02	52.11	98.93	138762.56
0.5,1000,I,2.0,0.0001	42.34	98.70	138701.96
0.5,1000,I,1.5,0.02	52.57	98.75	138734.88
0.5,1000,I,1.5,0.0001	41.92	98.96	138545.88
0.5,1000,I,1.1,0.02	52.19	98.94	138834.24
0.5,1000,I,1.1,0.0001	41.54	98.92	138252.56
0.3,500,ME+I,2.0,0.02	10.43	77.27	132217.92
0.3,500,ME+I,2.0,0.0001	8.47	77.17	132292.96

0.3,500,ME+I,1.5,0.02	12.12	76.84	134113.20
0.3,500,ME+I,1.5,0.0001	10.55	76.87	131771.24
0.3,500,ME+I,1.1,0.02	13.41	76.91	133854.48
0.3,500,ME+I,1.1,0.0001	12.22	76.76	132673.56
0.3,500,ME,2.0,0.02	11.96	76.68	134613.12
0.3,500,ME,2.0,0.0001	10.87	76.92	132077.72
0.3,500,ME,1.5,0.02	13.01	78.76	134016.68
0.3,500,ME,1.5,0.0001	11.80	80.22	133295.48
0.3,500,ME,1.1,0.02	13.89	76.88	134210.72
0.3,500,ME,1.1,0.0001	12.64	76.67	133055.16
0.3,500,I,2.0,0.02	14.56	76.78	133087.44
0.3,500,I,2.0,0.0001	13.11	76.36	133321.08
0.3,500,I,1.5,0.02	14.48	76.47	133449.28
0.3,500,I,1.5,0.0001	13.12	76.53	132977.32
0.3,500,I,1.1,0.02	14.62	76.97	132934.04
0.3,500,I,1.1,0.0001	12.91	79.52	132643.12
0.3,2000,ME+I,2.0,0.02	80.13	77.12	157067.76
0.3,2000,ME+I,2.0,0.0001	38.01	76.67	156089.92
0.3,2000,ME+I,1.5,0.02	108.52	77.82	156891.04
0.3,2000,ME+I,1.5,0.0001	68.37	79.27	157415.12
0.3,2000,ME+I,1.1,0.02	133.62	76.53	156605.84
0.3,2000,ME+I,1.1,0.0001	93.15	76.23	156330.20
0.3,2000,ME,2.0,0.02	94.83	72.29	145398.52
0.3,2000,ME,2.0,0.0001	73.01	76.34	157256.60
0.3,2000,ME,1.5,0.02	129.27	77.26	156373.32
0.3,2000,ME,1.5,0.0001	93.37	77.30	156781.52
0.3,2000,ME,1.1,0.02	148.69	76.90	155918.68
0.3,2000,ME,1.1,0.0001	104.23	77.27	156126.56
0.3,2000,I,2.0,0.02	163.18	76.81	155362.60
0.3,2000,I,2.0,0.0001	112.34	76.76	155090.44
0.3,2000,I,1.5,0.02	165.19	77.06	155644.08
0.3,2000,I,1.5,0.0001	113.22	76.96	155052.12
0.3,2000,I,1.1,0.02	165.32	76.90	155570.60
0.3,2000,I,1.1,0.0001	112.89	77.25	155295.48
0.3,1000,ME+I,2.0,0.02	29.58	76.65	140007.28
0.3,1000,ME+I,2.0,0.0001	18.54	76.70	140461.08
0.3,1000,ME+I,1.5,0.02	35.96	76.58	139731.16
0.3,1000,ME+I,1.5,0.0001	26.77	76.25	139746.88

0.3,1000,ME+I,1.1,0.02	39.73	74.45	135312.52
0.3,1000,ME+I,1.1,0.0001	33.51	60.15	138464.68
0.3,1000,ME,2.0,0.02	35.14	76.79	139728.88
0.3,1000,ME,2.0,0.0001	28.44	76.98	139477.16
0.3,1000,ME,1.5,0.02	39.75	76.60	139325.40
0.3,1000,ME,1.5,0.0001	32.14	78.60	139321.04
0.3,1000,ME,1.1,0.02	41.93	72.53	134819.68
0.3,1000,ME,1.1,0.0001	34.67	76.61	139146.12
0.3,1000,I,2.0,0.02	44.55	76.64	137672.52
0.3,1000,I,2.0,0.0001	35.88	76.58	138353.48
0.3,1000,I,1.5,0.02	45.07	77.84	138644.36
0.3,1000,I,1.5,0.0001	36.22	76.64	138355.68
0.3,1000,I,1.1,0.02	45.38	76.60	138536.52
0.3,1000,I,1.1,0.0001	36.54	76.65	138406.04
0.1,500,ME+I,2.0,0.02	14.39	76.21	133049.56
0.1,500,ME+I,2.0,0.0001	13.63	96.56	133010.00
0.1,500,ME+I,1.5,0.02	15.68	99.00	133365.44
0.1,500,ME+I,1.5,0.0001	13.83	99.00	132876.08
0.1,500,ME+I,1.1,0.02	15.71	98.92	133175.88
0.1,500,ME+I,1.1,0.0001	13.91	99.00	132622.44
0.1,500,ME,2.0,0.02	15.48	99.00	133278.80
0.1,500,ME,2.0,0.0001	13.81	98.98	132322.28
0.1,500,ME,1.5,0.02	15.56	98.99	133141.08
0.1,500,ME,1.5,0.0001	14.08	98.96	132418.28
0.1,500,ME,1.1,0.02	15.56	99.00	133151.84
0.1,500,ME,1.1,0.0001	14.01	98.98	133099.92
0.1,500,I,2.0,0.02	15.56	98.99	133436.84
0.1,500,I,2.0,0.0001	14.02	98.98	133378.84
0.1,500,I,1.5,0.02	15.87	99.00	133192.84
0.1,500,I,1.5,0.0001	14.09	98.98	132645.00
0.1,500,I,1.1,0.02	15.77	99.00	133209.40
0.1,500,I,1.1,0.0001	14.07	98.97	133120.92
0.1,2000,ME+I,2.0,0.02	158.73	77.20	155763.80
0.1,2000,ME,1.5,0.02	179.10	99.00	155353.08
0.1,2000,ME,1.5,0.0001	121.32	99.00	155054.96
0.1,2000,ME,1.1,0.02	179.21	94.98	155592.84
0.1,2000,ME,1.1,0.0001	123.67	94.92	155266.52
0.1,2000,I,2.0,0.02	179.43	93.90	155530.20

0.1,2000,I,2.0,0.0001	122.25	99.00	155230.16
0.1,2000,I,1.5,0.02	178.88	98.99	155394.24
0.1,2000,I,1.5,0.0001	122.16	99.00	155728.40
0.1,2000,I,1.1,0.02	177.35	99.00	155322.72
0.1,2000,I,1.1,0.0001	121.66	99.00	155222.80
0.1,1000,ME+I,2.0,0.02	48.96	99.00	139186.68
0.1,1000,ME+I,2.0,0.0001	39.09	99.00	138626.88
0.1,1000,ME+I,1.5,0.02	50.81	95.48	138308.36
0.1,1000,ME+I,1.5,0.0001	40.85	96.90	138674.00
0.1,1000,ME+I,1.1,0.02	51.26	97.28	138804.08
0.1,1000,ME+I,1.1,0.0001	41.67	92.17	138171.24
0.1,1000,ME,2.0,0.02	50.57	95.22	138776.32
0.1,1000,ME,2.0,0.0001	39.97	97.55	138625.88
0.1,1000,ME,1.5,0.02	50.41	98.21	138871.48
0.1,1000,ME,1.5,0.0001	40.33	98.03	138225.84
0.1,1000,ME,1.1,0.02	50.04	98.85	138539.48
0.1,1000,ME,1.1,0.0001	40.06	98.99	138220.52
0.1,1000,I,2.0,0.02	49.73	99.00	138651.80
0.1,1000,I,2.0,0.0001	40.38	98.19	138314.80
0.1,1000,I,1.5,0.02	50.46	98.66	139010.80
0.1,1000,I,1.5,0.0001	39.94	98.98	138255.48
0.1,1000,I,1.1,0.02	49.87	99.00	138711.12
0.1,1000,I,1.1,0.0001	40.13	98.99	138267.92
0.05,500,ME+I,2.0,0.02	16.57	98.78	133539.84
0.05,500,ME+I,2.0,0.0001	14.88	98.78	132866.20
0.05,500,ME+I,1.5,0.02	16.49	98.75	133801.12
0.05,500,ME+I,1.5,0.0001	14.89	98.83	132811.36
0.05,500,ME+I,1.1,0.02	16.64	98.82	133192.68
0.05,500,ME+I,1.1,0.0001	15.06	98.96	133419.44
0.05,500,ME,2.0,0.02	16.73	98.89	133147.12
0.05,500,ME,2.0,0.0001	15.19	98.79	132763.08
0.05,500,ME,1.5,0.02	16.43	98.87	133810.48
0.05,500,ME,1.5,0.0001	13.11	76.92	133189.44
0.05,500,ME,1.1,0.02	14.49	76.75	133125.68
0.05,500,ME,1.1,0.0001	13.12	76.65	133707.68
0.05,500,I,2.0,0.02	14.35	76.96	133531.60
0.05,500,I,2.0,0.0001	13.03	78.87	133306.00
0.05,500,I,1.5,0.02	14.30	79.83	133015.40

0.05,500,I,1.5,0.0001	12.98	78.90	133355.08
0.05,500,I,1.1,0.02	14.35	78.62	133549.00
0.05,500,I,1.1,0.0001	12.98	79.54	133045.08
0.05,2000,ME+I,2.0,0.02	190.54	99.00	155711.80
0.05,2000,ME+I,2.0,0.0001	131.34	99.00	155593.60
0.05,2000,ME+I,1.5,0.02	180.23	99.00	155621.12
0.05,2000,ME+I,1.5,0.0001	123.29	98.98	155334.44
0.05,2000,ME+I,1.1,0.02	178.12	99.00	155591.40
0.05,2000,ME+I,1.1,0.0001	124.22	99.00	155121.64
0.05,2000,ME,2.0,0.02	178.90	99.00	155657.64
0.05,2000,ME,2.0,0.0001	123.05	99.00	155412.04
0.05,2000,ME,1.5,0.02	178.36	99.00	155709.28
0.05,2000,ME,1.5,0.0001	123.93	99.00	155206.40
0.05,2000,ME,1.1,0.02	180.79	98.53	155466.84
0.05,2000,ME,1.1,0.0001	123.34	99.00	155389.40
0.05,2000,I,2.0,0.02	119.66	99.00	155255.48
0.05,2000,I,2.0,0.0001	122.52	99.00	155137.48
0.05,2000,I,1.5,0.02	178.53	99.00	155502.28
0.05,2000,I,1.5,0.0001	121.41	99.00	155484.52
0.05,2000,I,1.1,0.02	178.34	99.00	155644.44
0.05,2000,I,1.1,0.0001	122.37	98.98	155444.68
0.05,1000,ME+I,2.0,0.02	50.33	98.97	138882.24
0.05,1000,ME+I,2.0,0.0001	40.63	98.91	138206.72
0.05,1000,ME+I,1.5,0.02	50.46	98.92	138581.16
0.05,1000,ME+I,1.5,0.0001	40.53	98.89	138158.84
0.05,1000,ME+I,1.1,0.02	50.30	98.92	138835.84
0.05,1000,ME+I,1.1,0.0001	40.63	97.77	138088.72
0.05,1000,ME,2.0,0.02	50.16	99.00	138770.92
0.05,1000,ME,2.0,0.0001	40.17	98.59	138376.08
0.05,1000,ME,1.5,0.02	49.89	98.97	138975.00
0.05,1000,ME,1.5,0.0001	40.33	98.91	138648.36
0.05,1000,ME,1.1,0.02	49.85	98.98	138953.24
0.05,1000,ME,1.1,0.0001	39.79	99.00	138266.52
0.05,1000,I,2.0,0.02	49.24	98.88	138535.88
0.05,1000,I,2.0,0.0001	40.29	98.85	138387.88
0.05,1000,I,1.5,0.02	50.96	92.36	138616.68
0.05,1000,I,1.5,0.0001	41.18	88.89	137906.16
0.05,1000,I,1.1,0.02	50.33	97.64	138686.16

0.05,1000,I,1.1,0.0001	40.04	98.91	138828.36
0.01,500,ME+I,2.0,0.02	15.85	98.98	133601.64
0.01,500,ME+I,2.0,0.0001	14.01	98.96	132918.96
0.01,500,ME+I,1.5,0.02	15.65	98.99	132987.16
0.01,500,ME+I,1.5,0.0001	13.97	98.94	133053.60
0.01,500,ME+I,1.1,0.02	15.61	98.98	133764.08
0.01,500,ME+I,1.1,0.0001	14.17	98.99	132439.24
0.01,500,ME,2.0,0.02	15.55	98.97	133469.20
0.01,500,ME,2.0,0.0001	13.99	98.94	132721.64
0.01,500,ME,1.5,0.02	15.52	98.96	133784.12
0.01,500,ME,1.5,0.0001	13.96	98.95	132771.04
0.01,500,ME,1.1,0.02	15.65	98.92	133548.44
0.01,500,ME,1.1,0.0001	14.10	98.95	132695.16
0.01,500,I,2.0,0.02	15.71	98.97	132971.68
0.01,500,I,2.0,0.0001	14.17	98.97	133037.36
0.01,500,I,1.5,0.02	15.64	98.95	133494.84
0.01,500,I,1.5,0.0001	13.96	98.90	132756.08
0.01,500,I,1.1,0.02	15.63	98.94	133574.76
0.01,500,I,1.1,0.0001	14.00	98.93	133471.80
0.01,2000,ME+I,2.0,0.02	164.42	77.57	155881.28
0.01,2000,ME+I,2.0,0.0001	113.09	77.42	155392.92
0.01,2000,ME+I,1.5,0.02	162.51	77.55	155558.80
0.01,2000,ME+I,1.5,0.0001	112.62	77.64	155313.16
0.01,2000,ME+I,1.1,0.02	164.66	77.83	155642.44
0.01,2000,ME+I,1.1,0.0001	123.62	99.00	155250.16
0.01,2000,ME,2.0,0.02	165.13	77.53	155705.44
0.01,2000,ME,2.0,0.0001	111.69	79.50	155394.84
0.01,2000,ME,1.5,0.02	162.59	78.46	155294.12
0.01,2000,ME,1.5,0.0001	113.86	76.92	155176.88
0.01,2000,ME,1.1,0.02	164.27	76.97	155396.96
0.01,2000,ME,1.1,0.0001	113.76	76.75	155034.04
0.01,2000,I,2.0,0.02	164.08	77.22	155443.76
0.01,2000,I,2.0,0.0001	113.61	77.24	154994.48
0.01,2000,I,1.5,0.02	163.14	78.94	155548.28
0.01,2000,I,1.5,0.0001	111.07	79.09	155093.92
0.01,2000,I,1.1,0.02	162.67	77.36	155497.36
0.01,2000,I,1.1,0.0001	109.01	75.25	150508.88
0.01,1000,ME+I,2.0,0.02	50.30	98.92	138738.04

0.01,1000,ME+I,2.0,0.0001	40.31	99.00	138451.80
0.01,1000,ME+I,1.5,0.02	50.50	99.00	138824.72
0.01,1000,ME+I,1.5,0.0001	40.31	98.97	138218.68
0.01,1000,ME+I,1.1,0.02	50.41	99.00	138501.24
0.01,1000,ME+I,1.1,0.0001	40.45	99.00	138278.32
0.01,1000,ME,2.0,0.02	50.41	98.99	138407.60
0.01,1000,ME,2.0,0.0001	40.44	99.00	138331.40
0.01,1000,ME,1.5,0.02	50.07	98.99	138824.28
0.01,1000,ME,1.5,0.0001	40.31	99.00	138470.76
0.01,1000,ME,1.1,0.02	49.94	98.96	138802.64
0.01,1000,ME,1.1,0.0001	40.09	98.99	138732.52
0.01,1000,I,2.0,0.02	49.99	98.99	138941.92
0.01,1000,I,2.0,0.0001	40.10	98.95	138575.56
0.01,1000,I,1.5,0.02	49.52	98.92	138679.60
0.01,1000,I,1.5,0.0001	40.10	98.89	138683.16
0.01,1000,I,1.1,0.02	50.00	98.97	138552.00
0.01,1000,I,1.1,0.0001	40.43	97.41	138510.32

*MAF,POP,MOD,OR,PREV where MAF represents the minor allele frequency, POP is the number of individuals, MOD is the used model (with or without main effect and with or without epistasis effect), OR is the odds ratio and PREV is the prevalence of the disease.