**S9 Table. Comparison of power of gene-based association tests for models with interactions. Power for machine learning based on empirical distribution of test statistic from 5000 simulations.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Value | Phenotype distribution | #SNP(#TAS) | GATES | LinearRegression | SKAT | Ensemble learning |
| Power | *P~N(0,1)+0.20\*snp1\*snp2\*snp9\*snp10* | 10(4) | 6.0[4.0-8.4] | 6.0[4.0-8.4] | 6.6[4.5-9.1] | 5.8[3.9-8.2] |
| Power | *P~N(0,1)+0.002\*snp1 +0.002\*snp2 +0.12\*snp1\*snp2 + 0.18\*snp3\*snp4* | 5(4) | 99.6[98.5-99.9] | 99.6[98.5-99.9] | 100[99.2-100.0] | 97.4[95.5-98.6] |
| Power | *P~N(0,1)+0.25\*snp1\*snp2\*snp3* | 5(3) | 7.4[5.2-10.0] | 8.8[6.4-11.6] | 15.0[11.9-18.4] | 25.4[21.6-29.4] |
| Power | *P ~N(0,1)+0.3\*snp1\*snp2\*snp3* | 5(3) | 10.8[8.2-13.8] | 12.0[9.2-15.1] | 18.6[15.2-22.2] | 39.0[34.7-43.4] |
| Power | *P~N(0,1)+0.35\*snp2\*snp3\*snp4* | 5(3) | 8.8[6.4-11.6] | 9.8[7.3-12.7] | 26.4[22.5-30.4] | 54.0[49.5-58.4] |
| Power | *P~N(0,1)+0.45\*snp2\*snp3\*snp4* | 5(3) | 18.0[14.7-21.6] | 21.2[17.6-25.0] | 43.8[39.3-48.2] | 80.2[76.4-83.6] |
| Power | *P~N(0,1)+0.65\*snp1\*snp2\*snp3\*snp8\*snp9\*snp10* | 10(6) | 5.8[3.9-8.2] | 4.0[2.4-6.1] | 7.8[5.6-10.5] | 6.8[4.7-9.3] |
| Power | *P~N(0,1)+0.002\*snp1 +0.002\*snp2 + [0.2\*(1+snp1)/(1+snp2)] + 0.3\*snp4\*snp5* | 5(4) | 98.2[96.6-99.1] | 99.6[98.5-99.9] | 99.6[98.5-99.9] | 92.8[90.1-94.9] |
| Power | *P~N(0,1)+0.002\*snp1 +0.002\*snp2 +0.3\*snp1\*snp2 + 0.2\*snp3\*snp4* | 5(4) | 99.8[98.8-99.9] | 100.0[99.2-100.0] | 100.0[99.2-100.0] | 100.0[99.2-100.0] |

TAS denotes the number of trait associated SNPs. Machine learning test is based on ensemble learning variation 1 with the following components: multiple linear regression, support vector machine with linear kernel and random forests with mtry = 1 and ntree = 1000.