MIDESP Epistasis Report (with EpiGEN)

Ways of evaluating epistasis detection algorithm performance:

1. Number of interacting pairs (true positives) identified.
2. Number of false positives.
3. Position of true positive(s) (averaged if multiple) when ranked by p-value. If any true positives are missing their position is considered to be the “last” in the list.
   1. The above definition will be referred to as penalized true positive position.
   2. Alternatively, average true positive position can be computed only using the detected true positives. This will be referred to as unpenalized true positive position.
4. Runtime (~1second for 1000 SNPs, >60 minutes for 100000 SNPs)
   1. This is a java application. Was still executing after an hour with 100000 SNPS, however, it may be possible to run in a more optimized fashion.

Compare these performance parameters across:

1. Multiplicative vs Dominant vs Recessive vs XOR Interaction.
2. Interaction Alpha: 1.25, 1.5, 2, 3, 8, 16.
3. Pure vs Impure.

Each EpiGEN dataset is named as follows: PURE/IMPURE (indicates presence of marginal effects) \_ MULTIPLICATIVE/DOMINANT/RECESSIVE/XOR (indicates type of interaction) \_ ONEPAIR / TWOPAIRS / EIGHTPAIRS (indicates number of interacting disease snp pairs) \_ BASELINEALPHA10 (indicates quantitative phenotype value in absence of marginal and interaction effects) \_ InteractionAlpha 1.25/1.5/2/3/8/16 (indicates strength of interaction effect)

**RESULTS (pages 1-11)**

**MULTIPLICATIVE DATASETS**

Impure\_Multiplicative\_OnePair\_BaselineAlpha10\_InteractionAlpha2

Number of true positives: 1

Number of false positives: 48

Average true positive position (unpenalized) ranked by MI: 3

Average true positive position (penalized) ranked by MI: 3

Impure\_Multiplicative\_OnePair\_BaselineAlpha10\_InteractionAlpha3

Number of true positives: 1

Number of false positives: 167

Average true positive position (unpenalized) ranked by MI: 1

Average true positive position (penalized) ranked by MI: 1

Impure\_Multiplicative\_OnePair\_BaselineAlpha10\_InteractionAlpha1.5

Number of true positives: 1

Number of false positives: 28

Average true positive position (unpenalized) ranked by MI: 2

Average true positive position (penalized) ranked by MI: 2

Impure\_Multiplicative\_OnePair\_BaselineAlpha10\_InteractionAlpha1.25

Number of true positives: 0

Number of false positives: 29

Average true positive position (unpenalized) ranked by MI: 0

Average true positive position (penalized) ranked by MI: 0

Impure\_Multiplicative\_TwoPairs\_BaselineAlpha10\_InteractionAlpha2

Number of true positives: 1

Number of false positives: 58

Average true positive position (unpenalized) ranked by MI: 7

Average true positive position (penalized) ranked by MI: 33.5

Impure\_Multiplicative\_TwoPairs\_BaselineAlpha10\_InteractionAlpha3

Number of true positives: 1

Number of false positives: 58

Average true positive position (unpenalized) ranked by MI: 2

Average true positive position (penalized) ranked by MI: 31

Impure\_Multiplicative\_TwoPairs\_BaselineAlpha10\_InteractionAlpha1.5

Number of true positives: 0

Number of false positives: 39

Average true positive position (unpenalized) ranked by MI: 0

Average true positive position (penalized) ranked by MI: 0

Impure\_Multiplicative\_TwoPairs\_BaselineAlpha10\_InteractionAlpha1.25

Number of true positives: 0

Number of false positives: 324

Average true positive position (unpenalized) ranked by MI: 0

Average true positive position (penalized) ranked by MI: 0

Pure\_Multiplicative\_OnePair\_BaselineAlpha10\_InteractionAlpha2

Number of true positives: 1

Number of false positives: 419

Average true positive position (unpenalized) ranked by MI: 1

Average true positive position (penalized) ranked by MI: 1

Pure\_Multiplicative\_OnePair\_BaselineAlpha10\_InteractionAlpha3

Number of true positives: 1

Number of false positives: 1101

Average true positive position (unpenalized) ranked by MI: 1

Average true positive position (penalized) ranked by MI: 1

Pure\_Multiplicative\_OnePair\_BaselineAlpha10\_InteractionAlpha1.5

Number of true positives: 1

Number of false positives: 157

Average true positive position (unpenalized) ranked by MI: 1

Average true positive position (penalized) ranked by MI: 1

Pure\_Multiplicative\_OnePair\_BaselineAlpha10\_InteractionAlpha1.25

Number of true positives: 1

Number of false positives: 18

Average true positive position (unpenalized) ranked by MI: 1

Average true positive position (penalized) ranked by MI: 1

Pure\_Multiplicative\_TwoPairs\_BaselineAlpha10\_InteractionAlpha2

Number of true positives: 1

Number of false positives: 18

Average true positive position (unpenalized) ranked by MI: 3

Average true positive position (penalized) ranked by MI: 11.5

Pure\_Multiplicative\_TwoPairs\_BaselineAlpha10\_InteractionAlpha3

Number of true positives: 2

Number of false positives: 27

Average true positive position (unpenalized) ranked by MI: 3

Average true positive position (penalized) ranked by MI: 3

Pure\_Multiplicative\_TwoPairs\_BaselineAlpha10\_InteractionAlpha1.5

Number of true positives: 2

Number of false positives: 137

Average true positive position (unpenalized) ranked by MI: 3

Average true positive position (penalized) ranked by MI: 3

Pure\_Multiplicative\_TwoPairs\_BaselineAlpha10\_InteractionAlpha1.25

Number of true positives: 1

Number of false positives: 138

Average true positive position (unpenalized) ranked by MI: 1

Average true positive position (penalized) ranked by MI: 70.5

**DOMINANT DATASETS**

Impure\_Dominant\_OnePair\_BaselineAlpha10\_InteractionAlpha8

Number of true positives: 0

Number of false positives: 10

Average true positive position (unpenalized) ranked by MI: 0

Average true positive position (penalized) ranked by MI: 0

Impure\_Dominant\_OnePair\_BaselineAlpha10\_InteractionAlpha16

Number of true positives: 0

Number of false positives: 344

Average true positive position (unpenalized) ranked by MI: 0

Average true positive position (penalized) ranked by MI: 0

Impure\_Dominant\_TwoPairs\_BaselineAlpha10\_InteractionAlpha8

Number of true positives: 2

Number of false positives: 2486

Average true positive position (unpenalized) ranked by MI: 1871.5

Average true positive position (penalized) ranked by MI: 1871.5

Impure\_Dominant\_TwoPairs\_BaselineAlpha10\_InteractionAlpha16

Number of true positives: 0

Number of false positives: 10

Average true positive position (unpenalized) ranked by MI: 0

Average true positive position (penalized) ranked by MI: 0

Pure\_Dominant\_OnePair\_BaselineAlpha10\_InteractionAlpha8

Number of true positives: 1

Number of false positives: 637

Average true positive position (unpenalized) ranked by MI: 1

Average true positive position (penalized) ranked by MI: 1

Pure\_Dominant\_OnePair\_BaselineAlpha10\_InteractionAlpha16

Number of true positives: 1

Number of false positives: 323

Average true positive position (unpenalized) ranked by MI: 1

Average true positive position (penalized) ranked by MI: 1

Pure\_Dominant\_TwoPairs\_BaselineAlpha10\_InteractionAlpha8

Number of true positives: 0

Number of false positives: 99

Average true positive position (unpenalized) ranked by MI: 0

Average true positive position (penalized) ranked by MI: 0

Pure\_Dominant\_TwoPairs\_BaselineAlpha10\_InteractionAlpha16

Number of true positives: 0

Number of false positives: 129

Average true positive position (unpenalized) ranked by MI: 0

Average true positive position (penalized) ranked by MI: 0

**RECESSIVE DATASETS**

Impure\_Recessive\_OnePair\_BaselineAlpha10\_InteractionAlpha8

Number of true positives: 0

Number of false positives: 10

Average true positive position (unpenalized) ranked by MI: 0

Average true positive position (penalized) ranked by MI: 0

Impure\_Recessive\_OnePair\_BaselineAlpha10\_InteractionAlpha16

Number of true positives: 0

Number of false positives: 10

Average true positive position (unpenalized) ranked by MI: 0

Average true positive position (penalized) ranked by MI: 0

Impure\_Recessive\_TwoPairs\_BaselineAlpha10\_InteractionAlpha8

Number of true positives: 0

Number of false positives: 905

Average true positive position (unpenalized) ranked by MI: 0

Average true positive position (penalized) ranked by MI: 0

Impure\_Recessive\_TwoPairs\_BaselineAlpha10\_InteractionAlpha16

Number of true positives: 0

Number of false positives: 10

Average true positive position (unpenalized) ranked by MI: 0

Average true positive position (penalized) ranked by MI: 0

Pure\_Recessive\_OnePair\_BaselineAlpha10\_InteractionAlpha8

Number of true positives: 0

Number of false positives: 544

Average true positive position (unpenalized) ranked by MI: 0

Average true positive position (penalized) ranked by MI: 0

Pure\_Recessive\_OnePair\_BaselineAlpha10\_InteractionAlpha16

Number of true positives: 0

Number of false positives: 478

Average true positive position (unpenalized) ranked by MI: 0

Average true positive position (penalized) ranked by MI: 0

Pure\_Recessive\_TwoPairs\_BaselineAlpha10\_InteractionAlpha8

Number of true positives: 0

Number of false positives: 49

Average true positive position (unpenalized) ranked by MI: 0

Average true positive position (penalized) ranked by MI: 0

Pure\_Recessive\_TwoPairs\_BaselineAlpha10\_InteractionAlpha16

Number of true positives: 0

Number of false positives: 139

Average true positive position (unpenalized) ranked by MI: 0

Average true positive position (penalized) ranked by MI: 0

**CONTROL DATASETS**

Pure\_Control\_TwoPairs\_BaselineAlpha10

Number of true positives: 0

Number of false positives: 535

Average true positive position (unpenalized) ranked by MI: 0

Average true positive position (penalized) ranked by MI: 0

Pure\_Control\_OnePair\_BaselineAlpha10

Number of true positives: 0

Number of false positives: 506

Average true positive position (unpenalized) ranked by MI: 0

Average true positive position (penalized) ranked by MI: 0

Pure\_Control\_EightPairs\_BaselineAlpha10

Number of true positives: 0

Number of false positives: 535

Average true positive position (unpenalized) ranked by MI: 0

Average true positive position (penalized) ranked by MI: 0

Impure\_Control\_TwoPairs\_BaselineAlpha10

Number of true positives: 0

Number of false positives: 506

Average true positive position (unpenalized) ranked by MI: 0

Average true positive position (penalized) ranked by MI: 0

Impure\_Control\_OnePair\_BaselineAlpha10

Number of true positives: 0

Number of false positives: 722

Average true positive position (unpenalized) ranked by MI: 0

Average true positive position (penalized) ranked by MI: 0

Impure\_Control\_EightPairs\_BaselineAlpha10

Number of true positives: 2

Number of false positives: 186

Average true positive position (unpenalized) ranked by MI: 3.5

Average true positive position (penalized) ranked by MI: 142.625

**ADDITIONAL DATASETS:**

Pure\_XOR\_EightPairs\_BaselineAlpha10\_InteractionAlpha16

Number of true positives: 7

Number of false positives: 269

Average true positive position (unpenalized) ranked by MI: 42.714285714285715

Average true positive position (penalized) ranked by MI: 72

Pure\_XOR\_EightPairs\_BaselineAlpha10\_InteractionAlpha8

Number of true positives: 6

Number of false positives: 260

Average true positive position (unpenalized) ranked by MI: 24.833333333333332

Average true positive position (penalized) ranked by MI: 85.375

Pure\_Multiplicative\_EightPairs\_BaselineAlpha10\_InteractionAlpha3

Number of true positives: 5

Number of false positives: 444

Average true positive position (unpenalized) ranked by MI: 136.8

Average true positive position (penalized) ranked by MI: 254.25

Pure\_Multiplicative\_EightPairs\_BaselineAlpha10\_InteractionAlpha2

Number of true positives: 2

Number of false positives: 67

Average true positive position (unpenalized) ranked by MI: 37

Average true positive position (penalized) ranked by MI: 61.75

Impure\_XOR\_EightPairs\_BaselineAlpha10\_InteractionAlpha16

Number of true positives: 2

Number of false positives: 77

Average true positive position (unpenalized) ranked by MI: 3.5

Average true positive position (penalized) ranked by MI: 60.875

Impure\_XOR\_EightPairs\_BaselineAlpha10\_InteractionAlpha8

Number of true positives: 1

Number of false positives: 78

Average true positive position (unpenalized) ranked by MI: 4

Average true positive position (penalized) ranked by MI: 70.5

Impure\_Multiplicative\_EightPairs\_BaselineAlpha10\_InteractionAlpha3

Number of true positives: 1

Number of false positives: 78

Average true positive position (unpenalized) ranked by MI: 3

Average true positive position (penalized) ranked by MI: 70.375

Impure\_Multiplicative\_EightPairs\_BaselineAlpha10\_InteractionAlpha2

Number of true positives: 0

Number of false positives: 79

Average true positive position (unpenalized) ranked by MI: 0

Average true positive position (penalized) ranked by MI: 0

**DISCUSSION (Page 12-13)**

Unpenalized true positive positions by interaction type.

Multiplicative:3,1,2,0,7,2,0,1,1,1,1,3,3,3,1,136.8,37,3,0

Dominant: 0, 0, 1871.5, 0, 1, 1, 0, 0

Recessive: 0, 0, 0, 0, 0, 0, 0, 0

Control: 0, 0, 0, 0, 0, 3.5

XOR: 42.71,24.8,3.5,4

From this point onward assume all true positive positions are penalized.

Multiplicative Interaction Average True Positive Positions (note that 0 means no true positives were detected): 3,1,2,0,33.5,31,0,0,1,1,1,1,11.5,3,3,70.5,254.25,61.75,70.375,0

Dominant Interaction Average True Positive Positions: 0, 0, 1871.5, 0, 1, 1, 0, 0

Recessive Interaction Average True Positive Positions: 0, 0, 0, 0, 0, 0, 0, 0

Control: 0, 0, 0, 0, 0, 142.625

XOR: 72,85.375,60.875,70.5

Notably MIDESP did not detect any recessive interactions unlike Matrix and Plink epistasis.

Pairs Detected (# of SNP pairs correctly detected / total # of interacting disease SNP pairs) – only count if at least one pair was detected: 1/1, 1/1, 1/1, 1/2, 1/2, 1/1, 1/1, 1/1, 1/1, 1/2, 2/2, 2/2, 1/2, 7/8, 6/8, 5/8, 2/8, 2/8, 1/8, 1/8, 2/2, 1/1, 1/1

Now let us examine when MIDESP could detect multiplicative interaction.

Multiplicative Interaction Average True Positive Position Clustered by Interaction Alpha:

Interaction Alpha 1.25: 0,0,1,70.5

Interaction Alpha 1.5: 2,0,1,3

Interaction Alpha 2.0: 3,33.5,1,11.5,61.75,0

Interaction Alpha 3.0: 1,31,1,3,254.25,70.375

Clear trend here that interactions with larger effect were more easily detectable. These results are similar to that of Plink’s Epistasis and Matrix Epistasis.

Multiplicative Interaction Average True Positive Position Clustered by Pure Status:

Pure: 1,1,1,1,11.5,3,3,70.5,254.25,61.75

Impure: 3,1,2,0,33.5,31,0,0,70.375,0

Pure epistasis is easier to detect as expected.

Notably, all multiplicative pure interactions with alpha >= 2 were detected.