QMDR 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, NA for 100000 SNPs)

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: 0

Number of false positives: 500

F1 Score: 0.0

Average true positive position (unpenalized) ranked by t-statistic: 0

Average true positive position (penalized) ranked by t-statistic: 0

Impure\_Multiplicative\_OnePair\_BaselineAlpha10\_InteractionAlpha3

Number of true positives: 1

Number of false positives: 499

F1 Score: 0.0040

Average true positive position (unpenalized) ranked by t-statistic: 2

Average true positive position (penalized) ranked by t-statistic: 2

Impure\_Multiplicative\_OnePair\_BaselineAlpha10\_InteractionAlpha15

Number of true positives: 0

Number of false positives: 500

F1 Score: 0.0

Average true positive position (unpenalized) ranked by t-statistic: 0

Average true positive position (penalized) ranked by t-statistic: 0

Impure\_Multiplicative\_OnePair\_BaselineAlpha10\_InteractionAlpha125

Number of true positives: 0

Number of false positives: 500

F1 Score: 0.0

Average true positive position (unpenalized) ranked by t-statistic: 0

Average true positive position (penalized) ranked by t-statistic: 0

Impure\_Multiplicative\_TwoPairs\_BaselineAlpha10\_InteractionAlpha2

Number of true positives: 0

Number of false positives: 500

F1 Score: 0.0

Average true positive position (unpenalized) ranked by t-statistic: 0

Average true positive position (penalized) ranked by t-statistic: 0

Impure\_Multiplicative\_TwoPairs\_BaselineAlpha10\_InteractionAlpha3

Number of true positives: 0

Number of false positives: 500

F1 Score: 0.0

Average true positive position (unpenalized) ranked by t-statistic: 0

Average true positive position (penalized) ranked by t-statistic: 0

Impure\_Multiplicative\_TwoPairs\_BaselineAlpha10\_InteractionAlpha15

Number of true positives: 0

Number of false positives: 500

F1 Score: 0.0

Average true positive position (unpenalized) ranked by t-statistic: 0

Average true positive position (penalized) ranked by t-statistic: 0

Impure\_Multiplicative\_TwoPairs\_BaselineAlpha10\_InteractionAlpha125

Number of true positives: 0

Number of false positives: 500

F1 Score: 0.0

Average true positive position (unpenalized) ranked by t-statistic: 0

Average true positive position (penalized) ranked by t-statistic: 0

Pure\_Multiplicative\_OnePair\_BaselineAlpha10\_InteractionAlpha2

Number of true positives: 1

Number of false positives: 499

F1 Score: 0.0040

Average true positive position (unpenalized) ranked by t-statistic: 1

Average true positive position (penalized) ranked by t-statistic: 1

Pure\_Multiplicative\_OnePair\_BaselineAlpha10\_InteractionAlpha3

Number of true positives: 1

Number of false positives: 499

F1 Score: 0.0040

Average true positive position (unpenalized) ranked by t-statistic: 3

Average true positive position (penalized) ranked by t-statistic: 3

Pure\_Multiplicative\_OnePair\_BaselineAlpha10\_InteractionAlpha15

Number of true positives: 1

Number of false positives: 499

F1 Score: 0.0040

Average true positive position (unpenalized) ranked by t-statistic: 3

Average true positive position (penalized) ranked by t-statistic: 3

Pure\_Multiplicative\_OnePair\_BaselineAlpha10\_InteractionAlpha125

Number of true positives: 1

Number of false positives: 499

F1 Score: 0.0040

Average true positive position (unpenalized) ranked by t-statistic: 147

Average true positive position (penalized) ranked by t-statistic: 147

Pure\_Multiplicative\_TwoPairs\_BaselineAlpha10\_InteractionAlpha2

Number of true positives: 1

Number of false positives: 499

F1 Score: 0.0040

Average true positive position (unpenalized) ranked by t-statistic: 5

Average true positive position (penalized) ranked by t-statistic: 253

Pure\_Multiplicative\_TwoPairs\_BaselineAlpha10\_InteractionAlpha3

Number of true positives: 0

Number of false positives: 500

F1 Score: 0.0

Average true positive position (unpenalized) ranked by t-statistic: 0

Average true positive position (penalized) ranked by t-statistic: 0

Pure\_Multiplicative\_TwoPairs\_BaselineAlpha10\_InteractionAlpha15

Number of true positives: 2

Number of false positives: 498

F1 Score: 0.0080

Average true positive position (unpenalized) ranked by t-statistic: 138

Average true positive position (penalized) ranked by t-statistic: 138

Pure\_Multiplicative\_TwoPairs\_BaselineAlpha10\_InteractionAlpha125

Number of true positives: 1

Number of false positives: 499

F1 Score: 0.0040

Average true positive position (unpenalized) ranked by t-statistic: 2

Average true positive position (penalized) ranked by t-statistic: 251.5

Pure\_Multiplicative\_EightPairs\_BaselineAlpha10\_InteractionAlpha3

Number of true positives: 0

Number of false positives: 500

F1 Score: 0.0

Average true positive position (unpenalized) ranked by t-statistic: 0

Average true positive position (penalized) ranked by t-statistic: 0

Pure\_Multiplicative\_EightPairs\_BaselineAlpha10\_InteractionAlpha2

Number of true positives: 0

Number of false positives: 500

F1 Score: 0.0

Average true positive position (unpenalized) ranked by t-statistic: 0

Average true positive position (penalized) ranked by t-statistic: 0

Impure\_Multiplicative\_EightPairs\_BaselineAlpha10\_InteractionAlpha3

Number of true positives: 0

Number of false positives: 500

F1 Score: 0.0

Average true positive position (unpenalized) ranked by t-statistic: 0

Average true positive position (penalized) ranked by t-statistic: 0

Impure\_Multiplicative\_EightPairs\_BaselineAlpha10\_InteractionAlpha2

Number of true positives: 0

Number of false positives: 500

F1 Score: 0.0

Average true positive position (unpenalized) ranked by t-statistic: 0

Average true positive position (penalized) ranked by t-statistic: 0

**DOMINANT DATASETS**

Impure\_Dominant\_OnePair\_BaselineAlpha10\_InteractionAlpha8

Number of true positives: 1

Number of false positives: 499

F1 Score: 0.0040

Average true positive position (unpenalized) ranked by t-statistic: 1

Average true positive position (penalized) ranked by t-statistic: 1

Impure\_Dominant\_OnePair\_BaselineAlpha10\_InteractionAlpha16

Number of true positives: 1

Number of false positives: 499

F1 Score: 0.0040

Average true positive position (unpenalized) ranked by t-statistic: 2

Average true positive position (penalized) ranked by t-statistic: 2

Impure\_Dominant\_TwoPairs\_BaselineAlpha10\_InteractionAlpha8

Number of true positives: 0

Number of false positives: 500

F1 Score: 0.0

Average true positive position (unpenalized) ranked by t-statistic: 0

Average true positive position (penalized) ranked by t-statistic: 0

Impure\_Dominant\_TwoPairs\_BaselineAlpha10\_InteractionAlpha16

Number of true positives: 0

Number of false positives: 500

F1 Score: 0.0

Average true positive position (unpenalized) ranked by t-statistic: 0

Average true positive position (penalized) ranked by t-statistic: 0

Pure\_Dominant\_OnePair\_BaselineAlpha10\_InteractionAlpha8

Number of true positives: 1

Number of false positives: 499

F1 Score: 0.0040

Average true positive position (unpenalized) ranked by t-statistic: 1

Average true positive position (penalized) ranked by t-statistic: 1

Pure\_Dominant\_OnePair\_BaselineAlpha10\_InteractionAlpha16

Number of true positives: 1

Number of false positives: 499

F1 Score: 0.0040

Average true positive position (unpenalized) ranked by t-statistic: 1

Average true positive position (penalized) ranked by t-statistic: 1

Pure\_Dominant\_TwoPairs\_BaselineAlpha10\_InteractionAlpha8

Number of true positives: 2

Number of false positives: 498

F1 Score: 0.0080

Average true positive position (unpenalized) ranked by t-statistic: 1.5

Average true positive position (penalized) ranked by t-statistic: 1.5

Pure\_Dominant\_TwoPairs\_BaselineAlpha10\_InteractionAlpha16

Number of true positives: 1

Number of false positives: 499

F1 Score: 0.0040

Average true positive position (unpenalized) ranked by t-statistic: 1

Average true positive position (penalized) ranked by t-statistic: 251

**RECESSIVE DATASETS**

Impure\_Recessive\_OnePair\_BaselineAlpha10\_InteractionAlpha8

Number of true positives: 0

Number of false positives: 500

F1 Score: 0.0

Average true positive position (unpenalized) ranked by t-statistic: 0

Average true positive position (penalized) ranked by t-statistic: 0

Impure\_Recessive\_OnePair\_BaselineAlpha10\_InteractionAlpha16

Number of true positives: 0

Number of false positives: 500

F1 Score: 0.0

Average true positive position (unpenalized) ranked by t-statistic: 0

Average true positive position (penalized) ranked by t-statistic: 0

Impure\_Recessive\_TwoPairs\_BaselineAlpha10\_InteractionAlpha8

Number of true positives: 0

Number of false positives: 500

F1 Score: 0.0

Average true positive position (unpenalized) ranked by t-statistic: 0

Average true positive position (penalized) ranked by t-statistic: 0

Impure\_Recessive\_TwoPairs\_BaselineAlpha10\_InteractionAlpha16

Number of true positives: 0

Number of false positives: 500

F1 Score: 0.0

Average true positive position (unpenalized) ranked by t-statistic: 0

Average true positive position (penalized) ranked by t-statistic: 0

Pure\_Recessive\_OnePair\_BaselineAlpha10\_InteractionAlpha8

Number of true positives: 0

Number of false positives: 500

F1 Score: 0.0

Average true positive position (unpenalized) ranked by t-statistic: 0

Average true positive position (penalized) ranked by t-statistic: 0

Pure\_Recessive\_OnePair\_BaselineAlpha10\_InteractionAlpha16

Number of true positives: 0

Number of false positives: 500

F1 Score: 0.0

Average true positive position (unpenalized) ranked by t-statistic: 0

Average true positive position (penalized) ranked by t-statistic: 0

Pure\_Recessive\_TwoPairs\_BaselineAlpha10\_InteractionAlpha8

Number of true positives: 0

Number of false positives: 500

F1 Score: 0.0

Average true positive position (unpenalized) ranked by t-statistic: 0

Average true positive position (penalized) ranked by t-statistic: 0

Pure\_Recessive\_TwoPairs\_BaselineAlpha10\_InteractionAlpha16

Number of true positives: 0

Number of false positives: 500

F1 Score: 0.0

Average true positive position (unpenalized) ranked by t-statistic: 0

Average true positive position (penalized) ranked by t-statistic: 0

**XOR DATASETS:**

Pure\_XOR\_EightPairs\_BaselineAlpha10\_InteractionAlpha16

Number of true positives: 0

Number of false positives: 500

F1 Score: 0.0

Average true positive position (unpenalized) ranked by t-statistic: 0

Average true positive position (penalized) ranked by t-statistic: 0

Pure\_XOR\_EightPairs\_BaselineAlpha10\_InteractionAlpha8

Number of true positives: 0

Number of false positives: 500

F1 Score: 0.0

Average true positive position (unpenalized) ranked by t-statistic: 0

Average true positive position (penalized) ranked by t-statistic: 0

Impure\_XOR\_EightPairs\_BaselineAlpha10\_InteractionAlpha16

Number of true positives: 0

Number of false positives: 500

F1 Score: 0.0

Average true positive position (unpenalized) ranked by t-statistic: 0

Average true positive position (penalized) ranked by t-statistic: 0

Impure\_XOR\_EightPairs\_BaselineAlpha10\_InteractionAlpha8

Number of true positives: 0

Number of false positives: 500

F1 Score: 0.0

Average true positive position (unpenalized) ranked by t-statistic: 0

Average true positive position (penalized) ranked by t-statistic: 0

**DISCUSSION (Page 12-13)**

Unpenalized true positive positions by interaction type.

Multiplicative: 0, 2, 0, 0, 0, 0, 0, 0, 1, 3, 3, 147, 5, 0, 138, 2, 0, 0, 0, 0

Dominant: 1, 2, 0, 0, 1, 1, 1.5, 1

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

XOR: 0, 0, 0, 0

F1 Score by grouped by interaction type.

Multiplicative: 0, 0.004, 0, 0, 0, 0, 0, 0, 0.004, 0.004, 0.004, 0.004, 0.004, 0, 0.008, 0.004, 0, 0, 0, 0 => 0.0018

Dominant: 0.004, 0.004, 0, 0, 0.004, 0.004, 0.008, 0.004 => 0.0035

Recessive: 0, 0, 0, 0, 0, 0, 0, 0 => 0

XOR: 0, 0, 0, 0 => 0

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): 0, 2, 0, 0, 0, 0, 0, 0, 1, 3, 3, 147, 253, 0, 138, 251.5, 0, 0, 0, 0

Dominant Interaction Average True Positive Positions: 1, 2, 0, 0, 1, 1, 1.5, 251

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

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

QMDR epistasis could not detect XOR or Recessive interactions.

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, 1/1, 1/1, ½, 2/2, ½, 1/1, 1/1, 1/1, 1/1, 2/2, ½.

The number of detected pairs was usually 1-2.

Now let us examine when QMDR epistasis could detect multiplicative interaction.

Multiplicative Interaction Average True Positive Position Clustered by Interaction Alpha:

Interaction Alpha 1.25: 0, 0, 147, 251.5

Interaction Alpha 1.5: 0, 0, 3, 138

Interaction Alpha 2.0: 0, 0, 1, 253, 0, 0

Interaction Alpha 3.0: 2, 0, 3, 0, 0, 0

No clear trends here.

Let us also compare average true positive position for Pure vs Impure Epistasis in case of multiplicative interaction only.

Multiplicative Interaction Average True Positive Position Clustered by Pure Status:

Pure: 1, 3, 3, 0, 0, 147, 253, 0, 138, 251.5

Impure: 0, 2, 0, 0, 0, 0, 0, 0, 0, 0

Pure epistasis is easier to detect as expected.