Directional association inference challenged by severe dropout in single-cell RNAseq data

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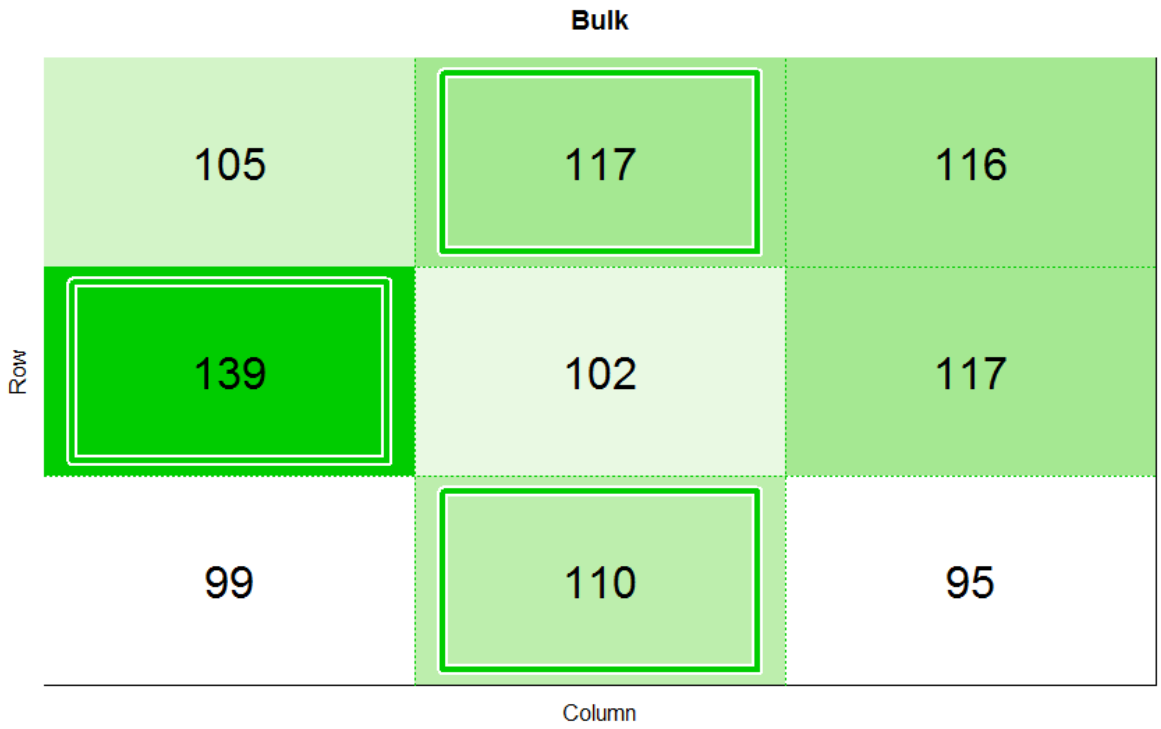
Motivation

- **Single-cell RNA sequencing (scRNA) allows to gain RNA-seq from small amount of initial material. (single cell)**
- **New field of study focus on data from single cell.**
- **scRNA suffers from 0.9 dropout.**
- **Methods for Bulk RNA-seq performs close to random**
- **New methods FunChisq [1].**

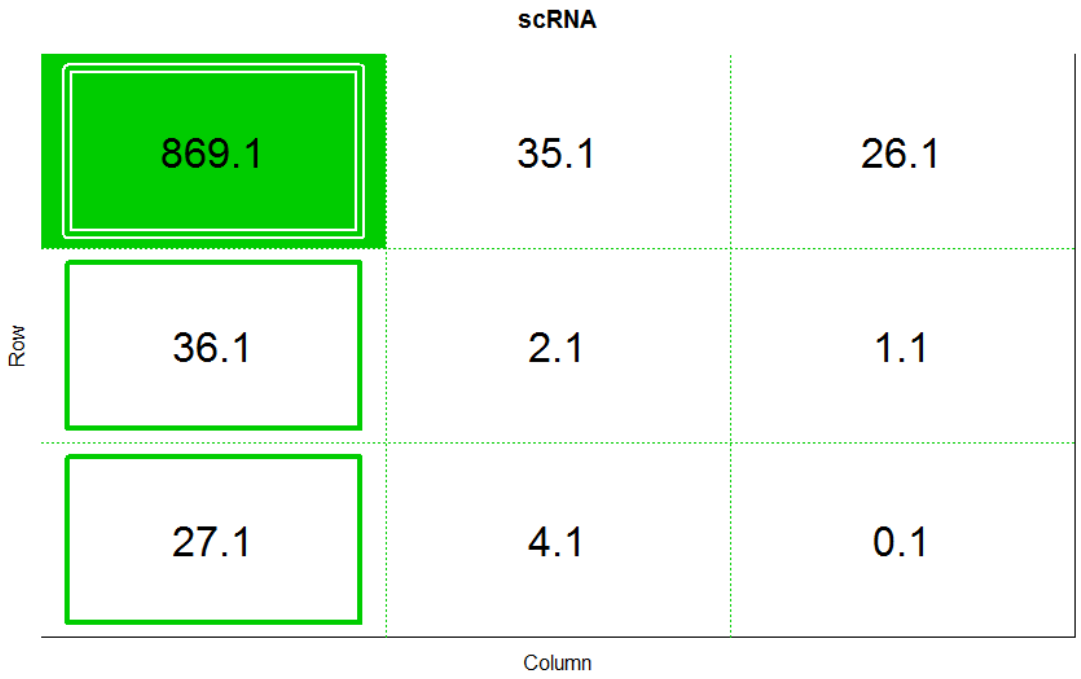
Bulk RNA-seq

- **Input material: multiple cell**
- **No dropout**
- **1000 samples**



Single-cell RNA-seq

- **Input material: single cell**
- **0.9 dropout**
- **1000 samples**



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Methods

1. **Pearson's Correlation test**
2. **Mutual Information**
3. **Conditional Entropy (directional)**
4. **Pearson's χ^2-test**
5. **Functional χ^2-test (directional) [1]**

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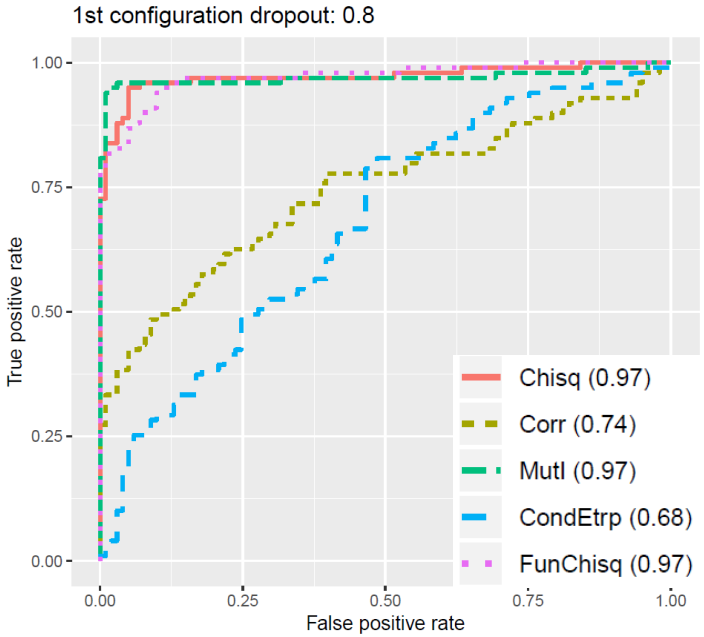
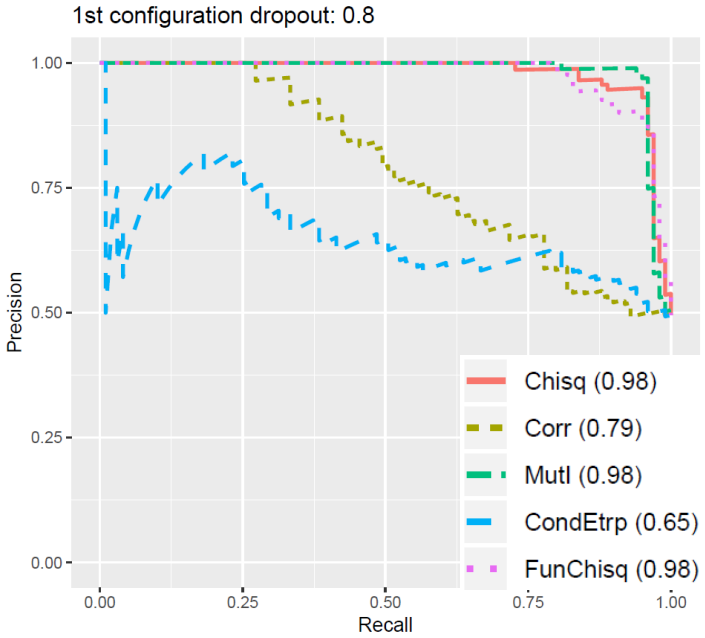
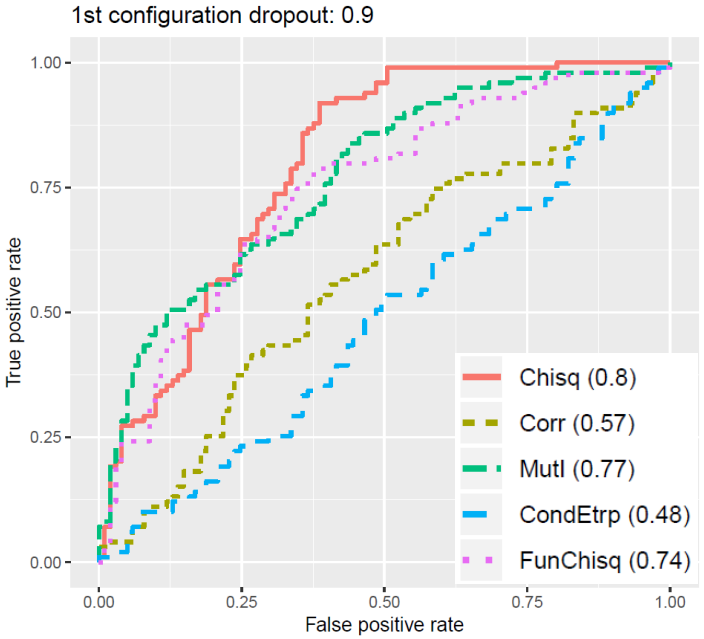
Simulated dataset

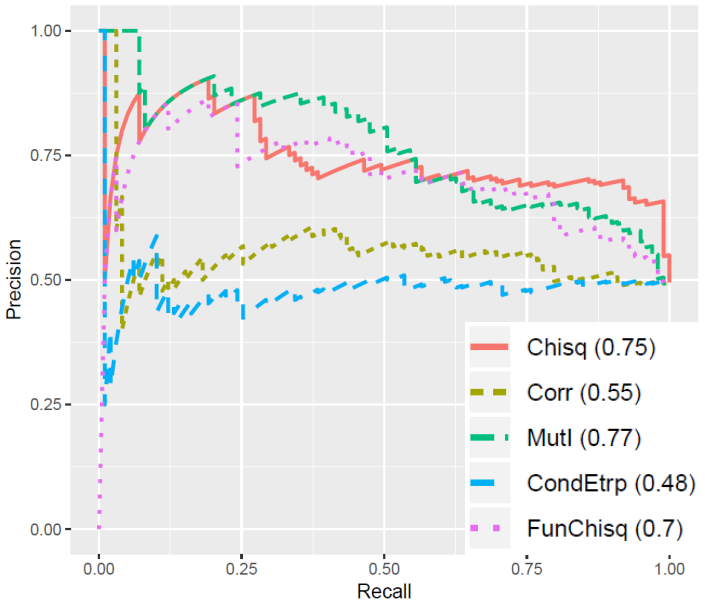
- **Size: 200 tables**
- **Dimension : 3x3**
- **Samples: 1000**
- **Noise: 0.0, 0.2**
- **Dropout: 0.2, 0.8, 0.9, 0.99**
- **Configurations:**
    1. **Detection of relationship**
    2. **Detection of relationship direction**

Results 1st Configuration

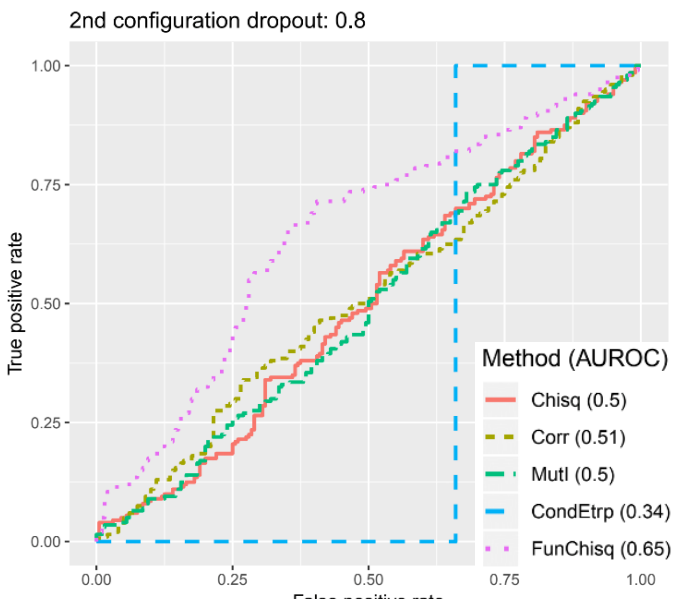


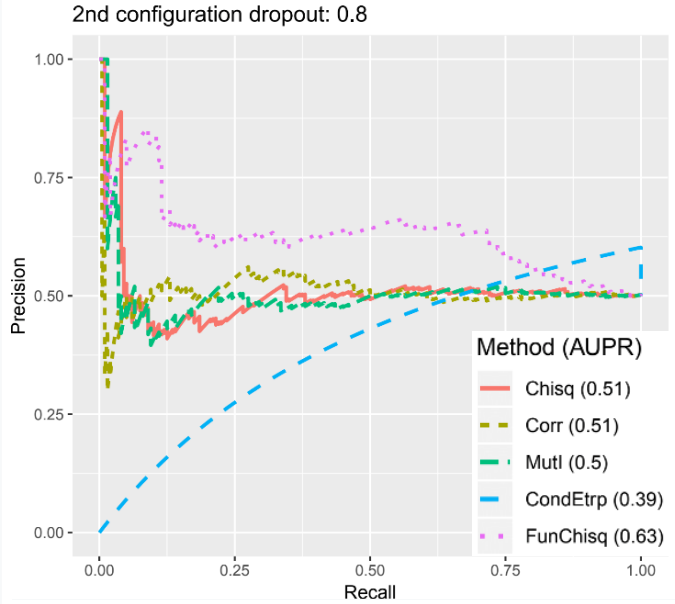


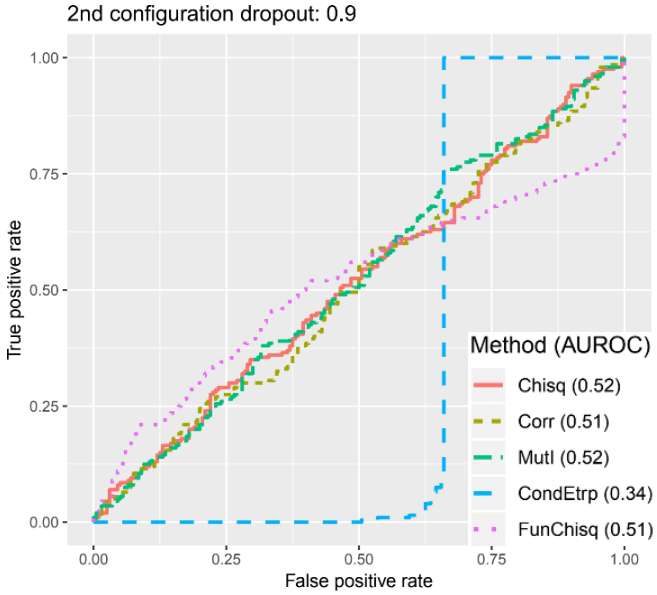


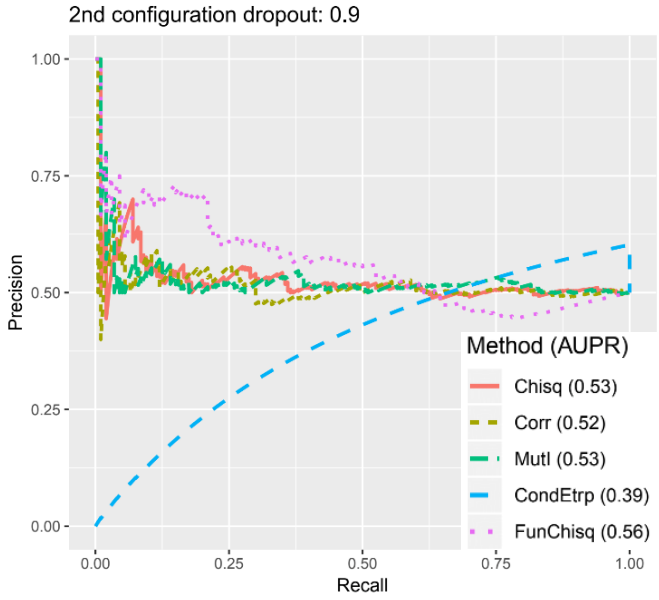


Results 2nd Configuration









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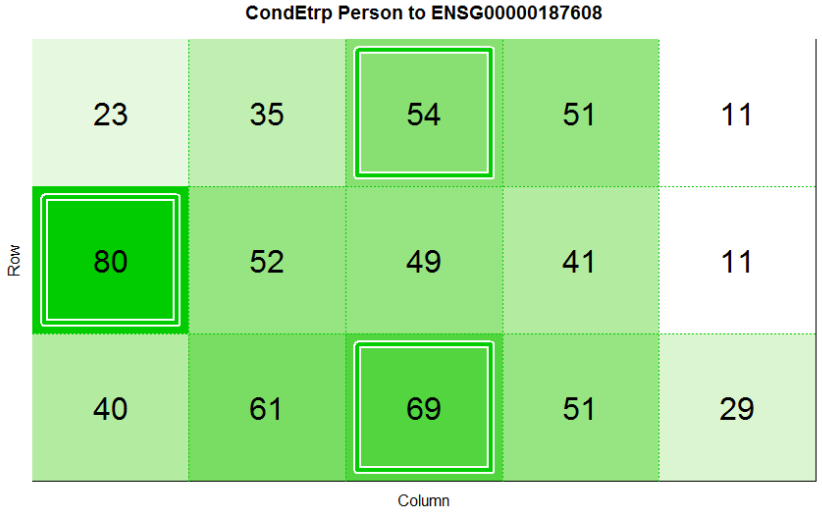
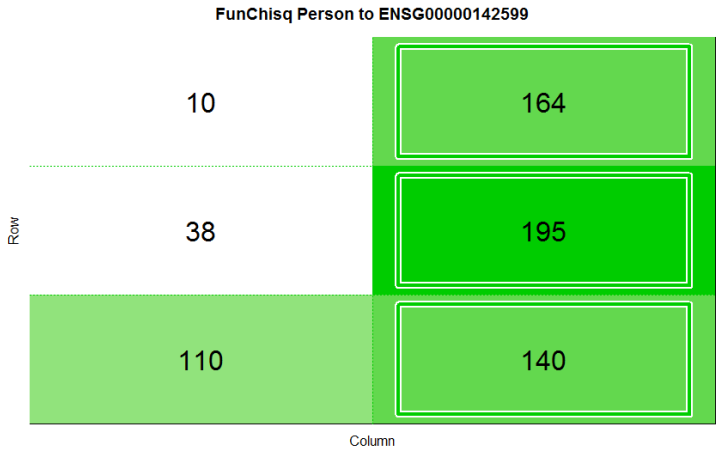
Real dataset biological background

- Dataset gained from Tung et al. [2]
- single-cell Fluidigm C1 platform
- three C1 replicates from three human induced pluripotent stem cell (iPSC) lines
- unique molecular identifiers (UMI) to all samples
- The paper is focused on finding source of variation in gene expression data.
    - Genotype
    - UMI counts are biased

Real dataset

- **Subset of 40 genes**
- **Configurations:**
  1. **Person vs Gene (true) and Gene vs Person (false) only for differentially expressed genes.**
  2. **Person vs Gene (true for differentially expressed genes)**





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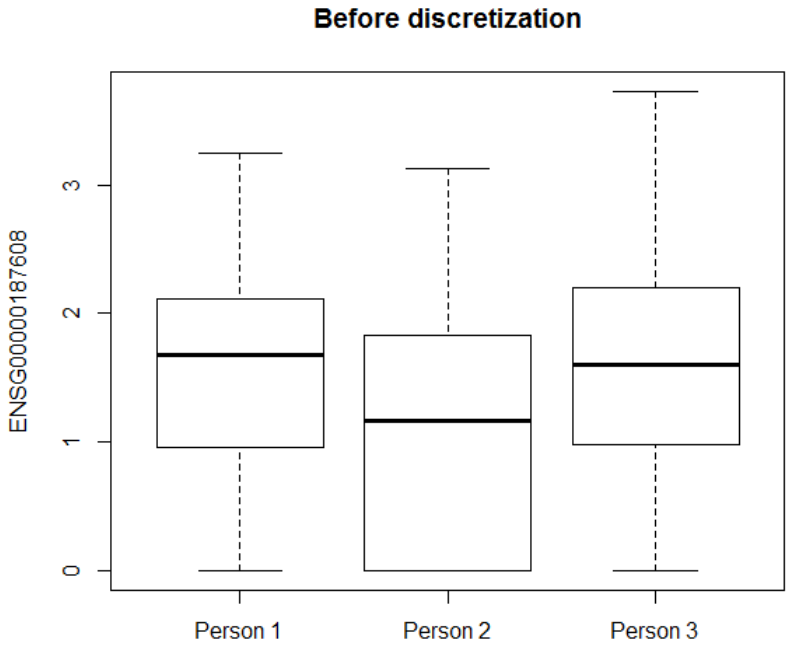
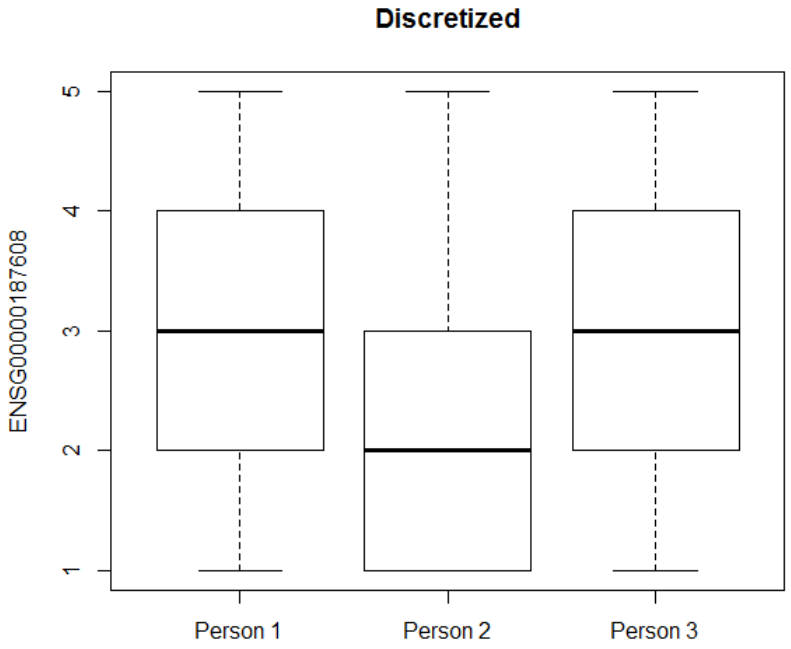
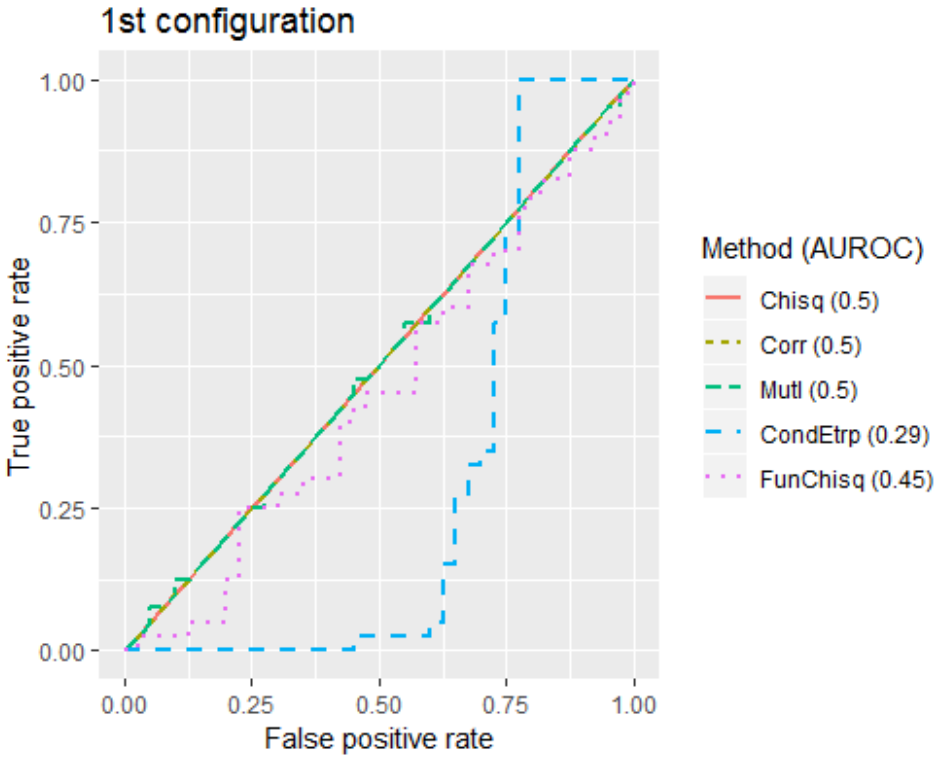
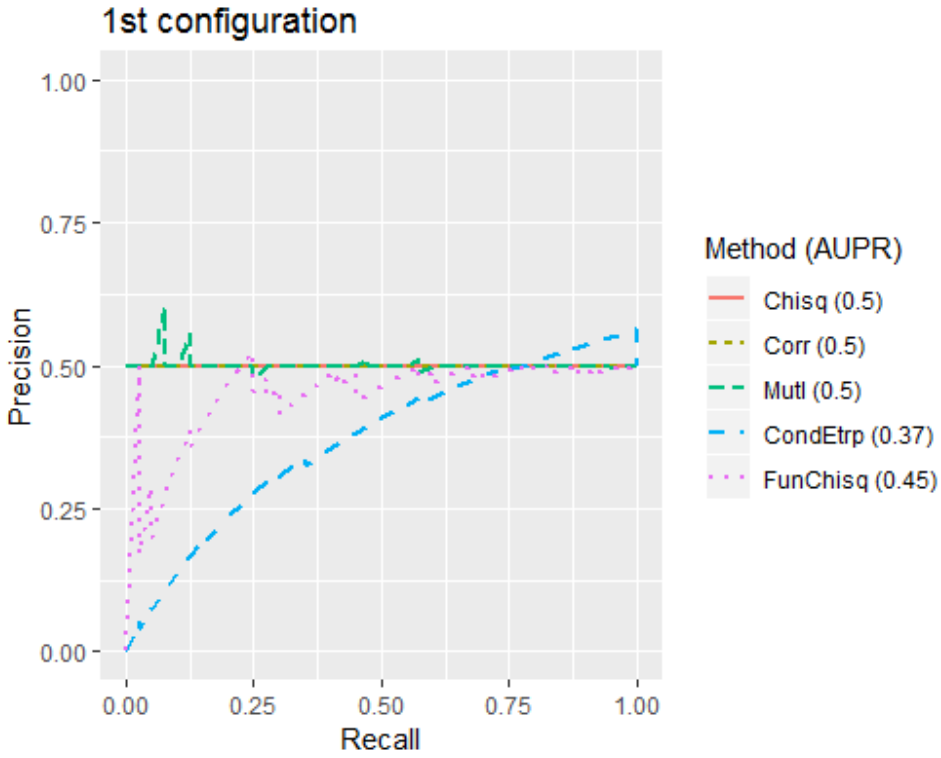
Data discretization



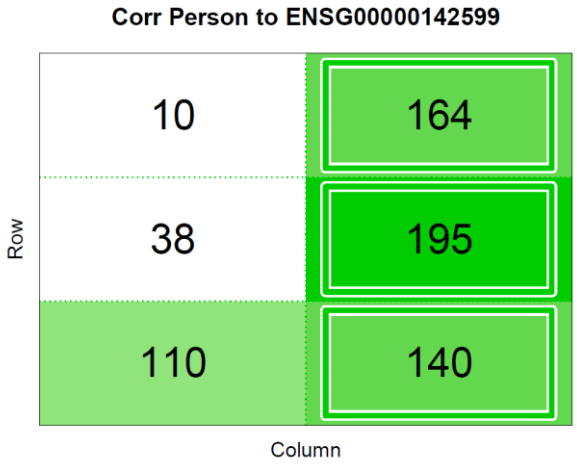


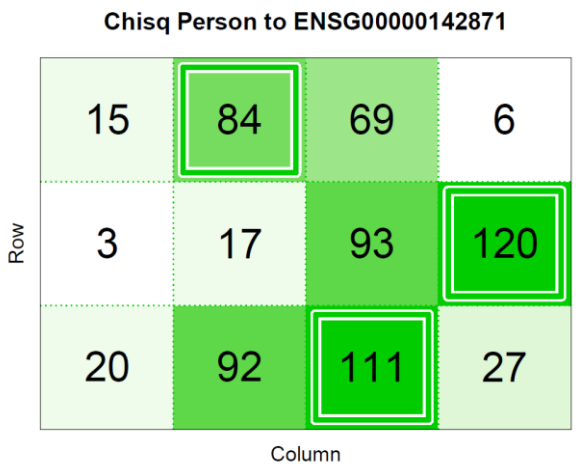
Results 1st configuration

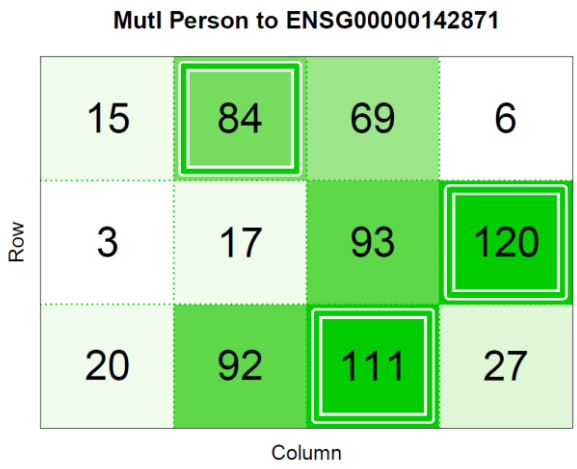




Tables with strongest inference for each method

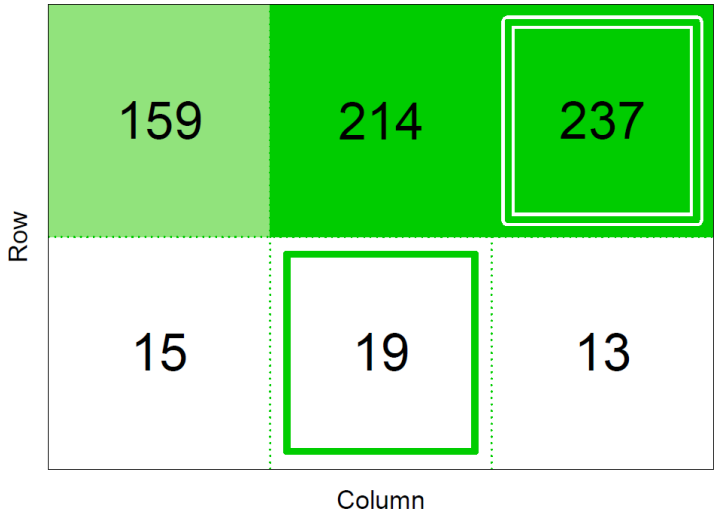




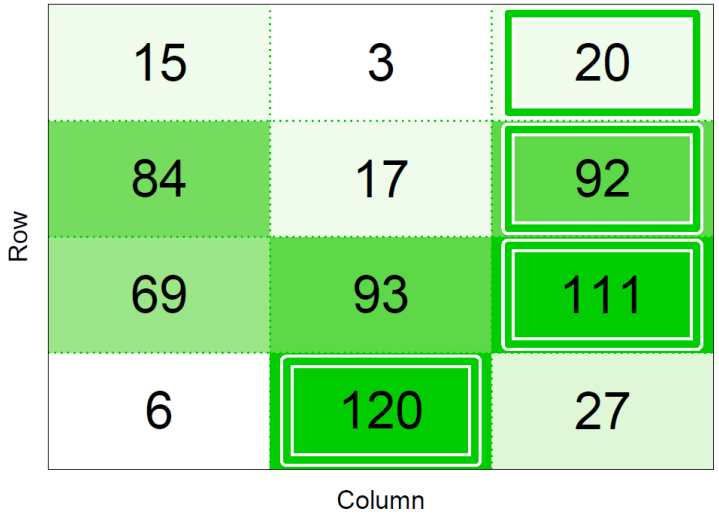


Tables with strongest inference for each method

CondEtrp ENSG00000215910 to Person



FunChisq ENSG00000142871 to Person



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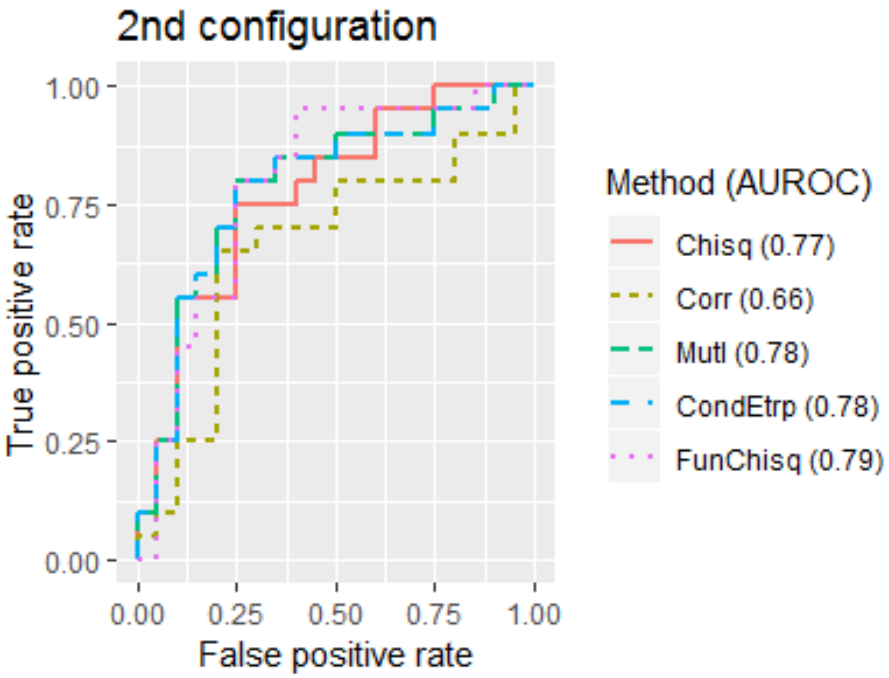
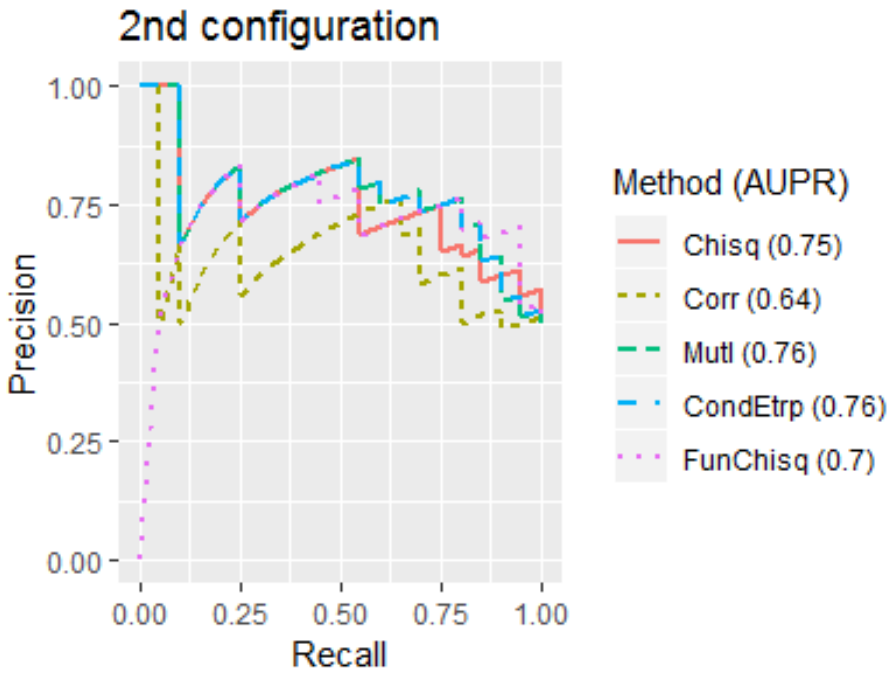
Results 2nd configuration





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Conclusion

- **Simulated dataset**
- **Real dataset**
- **Future work**
  - **Answer How many samples are needed to gain at least 70% accuracy?**
  - **Add test for multiple noise**
  - **Process whole real dataset**

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References

[1] Zhang, Y., & Song, M. (2013). Deciphering interactions in causal networks without parametric assumptions. *arXiv preprint arXiv:1311.2707*.

[2] Tung, P.Y., Blischak, J. D., Hsiao, C. J., Knowles, D. A., Burnett, J. E., Pritchard, J. K., &Gilad, Y. (2017). Batch effects and the effective design of single cell gene expression studies. Sci Rep, 7, 39921.