Machine learning applied to higher order functional representations of omics data reveals biological pathways associated with Parkinson's Disease

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Background

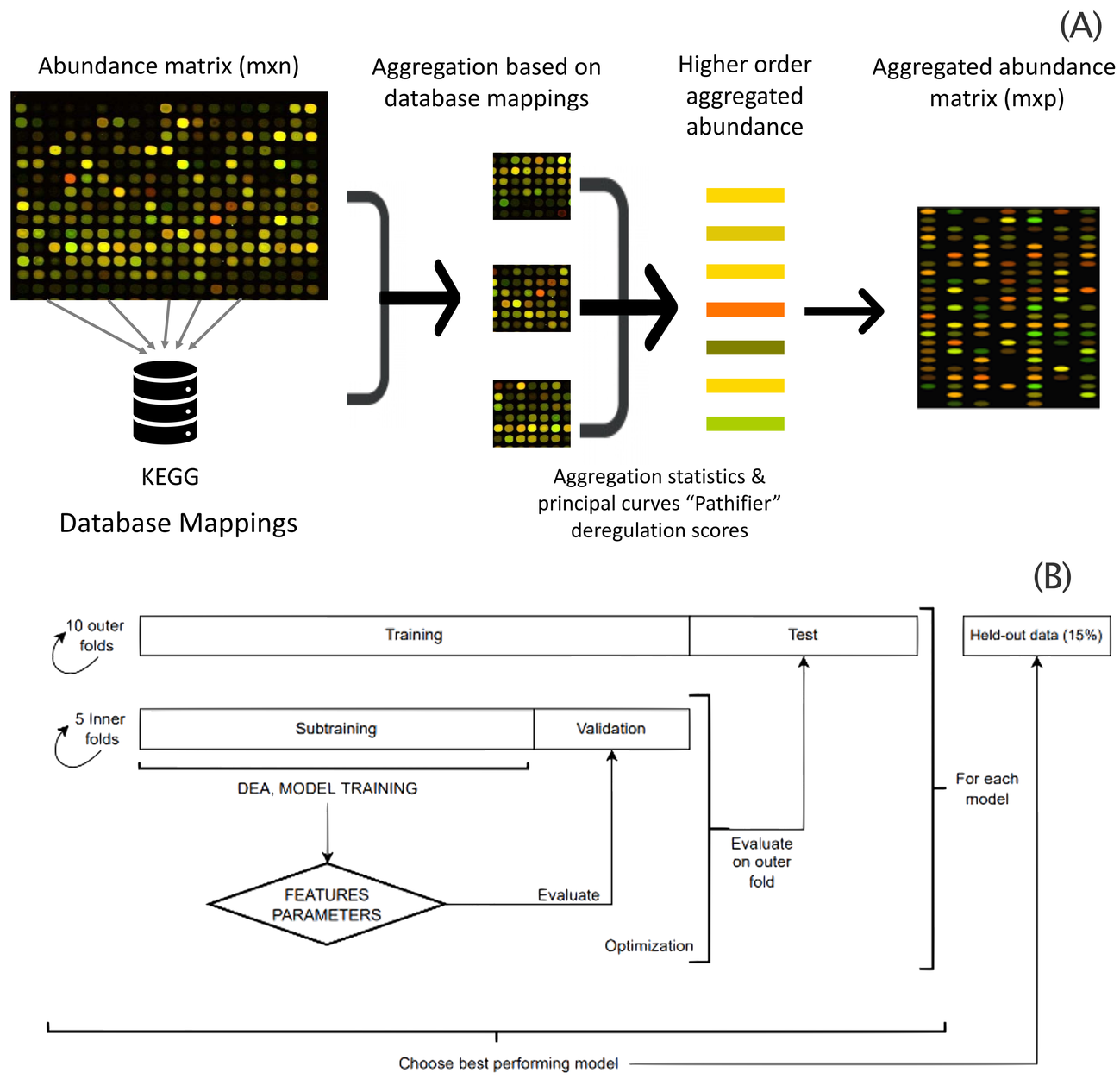
Despite the increasing prevalence of Parkinson's Disease (PD) and research efforts to understand its underlying molecular pathogenesis, early diagnosis of PD remains a challenge.[1]

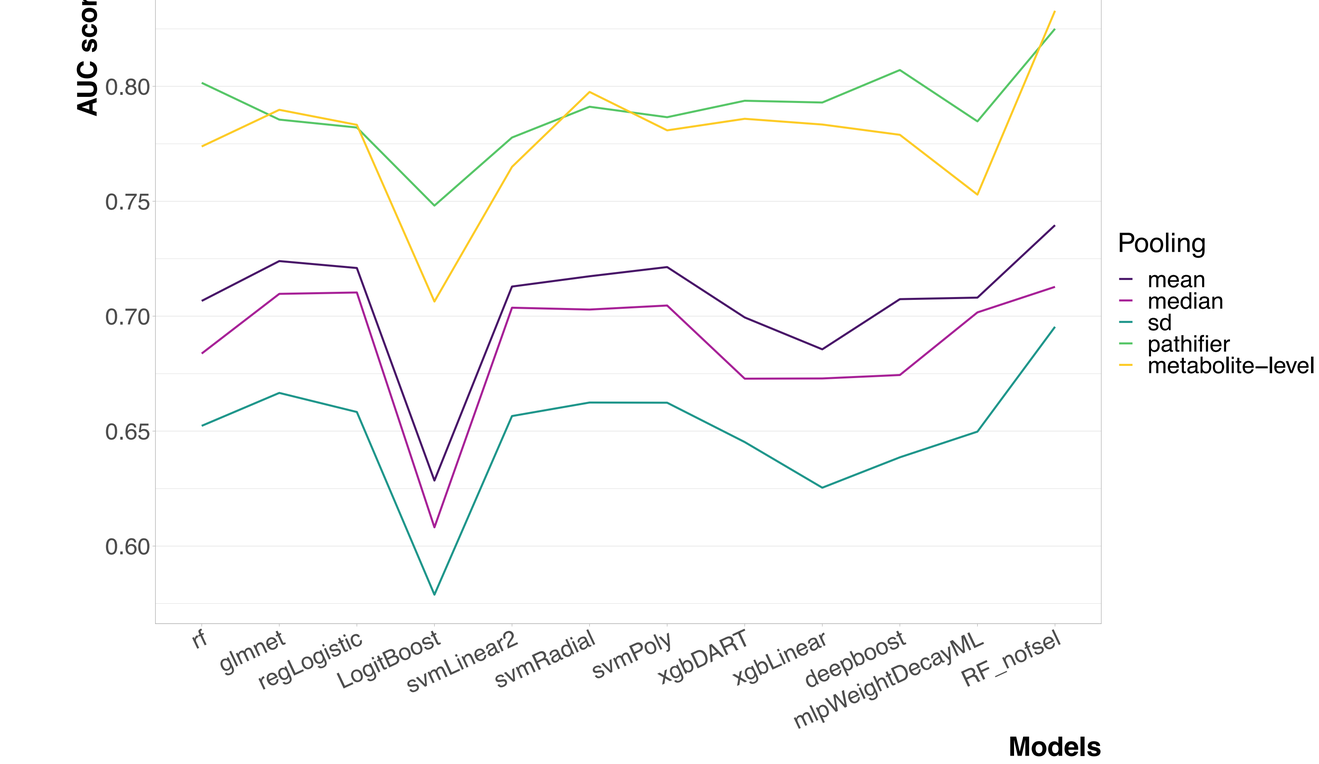
Machine learning analysis of blood-based omics data is a promising non-invasive approach to finding molecular fingerprints associated with PD that may enable an early and accurate diagnosis.[2] However, genes and metabolites don't act isolated. Higher order functional representations of omics data such as pathways allow better and more meaningful interpretation.[3]

Methods

Here, we applied ML classification methods to transcriptomics and metabolomics data from PD case/control studies (PPMI[4] & NCER-PD cohort[5] respectively).

- Higher order functional representations were generated via aggregation statistics (mean, median, sd) and deregulation scores based on principal curves[6] "pathifier scores" (A)
- External two-level cross-validation was used, including nested feature selection (B)
- Models' performance and most relevant predictive features were compared with individual feature level predictors (C)





Conclusions

- Significant AUC scores for cross-validation & external testing.
- Pooled representations of omics data can perform as well as single-level omics predictors to classify PD versus controls samples.
- Plausible biological pathways associated with PD diagnosis.

Limitations:

- Unknown confounders
- Large variability among PD patients makes identifying common trends difficult
- Data represents late stages of the disease

Future work:

- Modelling of other PD prognostic outcomes (e.g. motor dysfunction scores)
- Graph representation of the data via protein-protein interactions, metabolic networks

References

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