Machine learning to identify pathways in Parkinson Disease?

Poster SOM_3: Machine learning applied to higher order functional representations of omics data reveals biological pathways associated with Parkinson Disease

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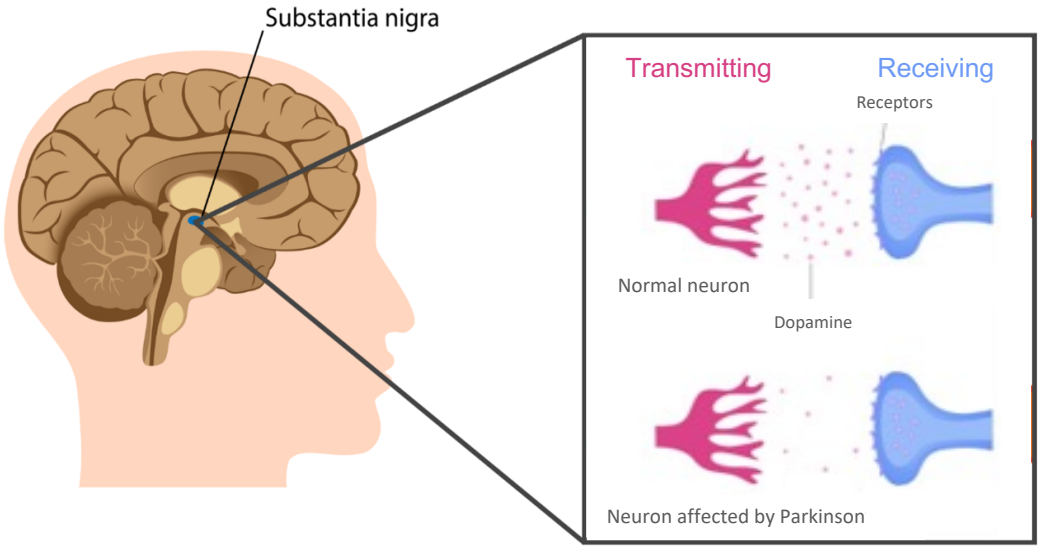
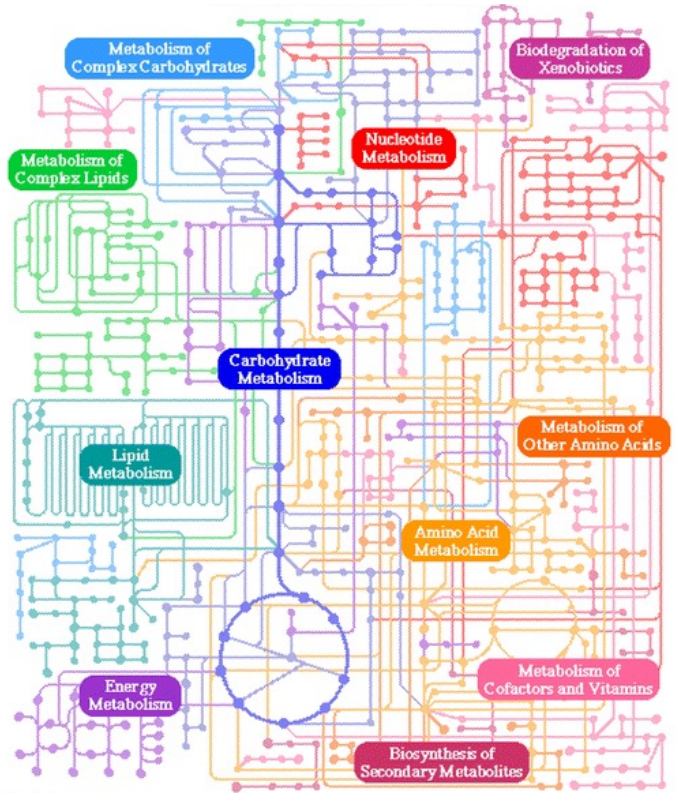
Parkinson's Disease & higher order functional representations



Source: Adapted from shutterstock

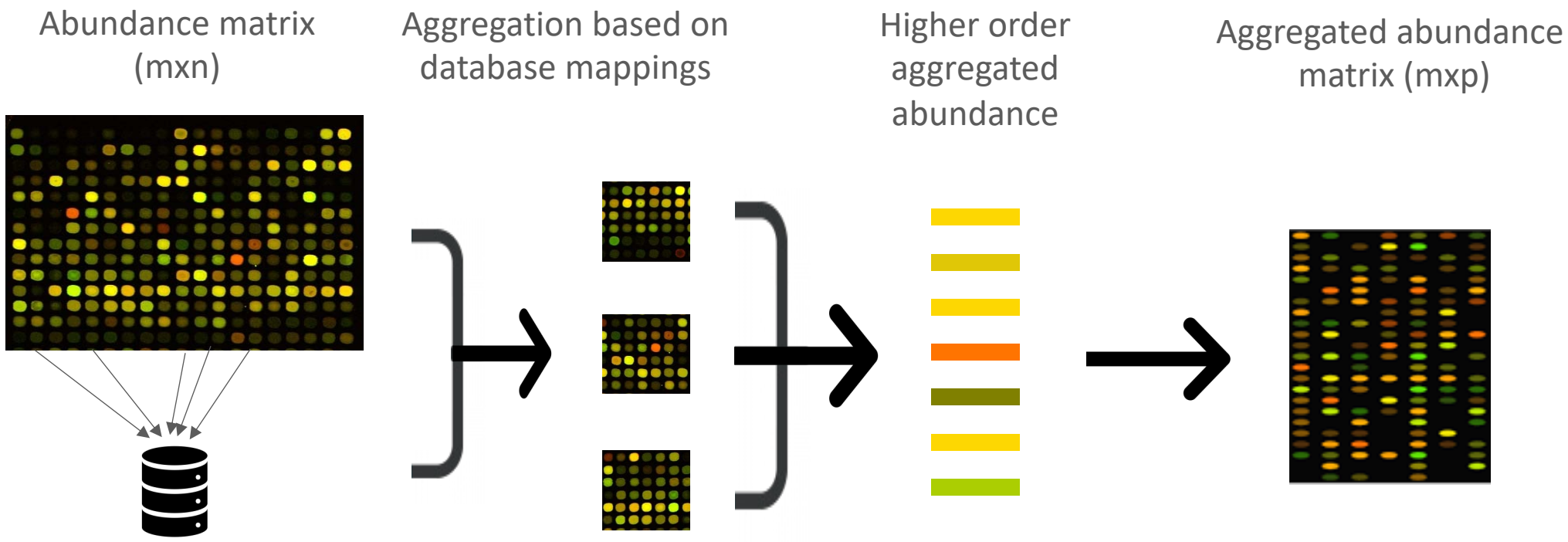
- Single gene mutations?
- Mitochondrial genetics?
- Environmental factors (toxins)?

Diagnosis is clinical & difficult



Schematic representation of metabolic networks
Source: The Origin and Evolution of Metabolic Pathways: Why and How did Primordial Cells Construct Metabolic Routes?

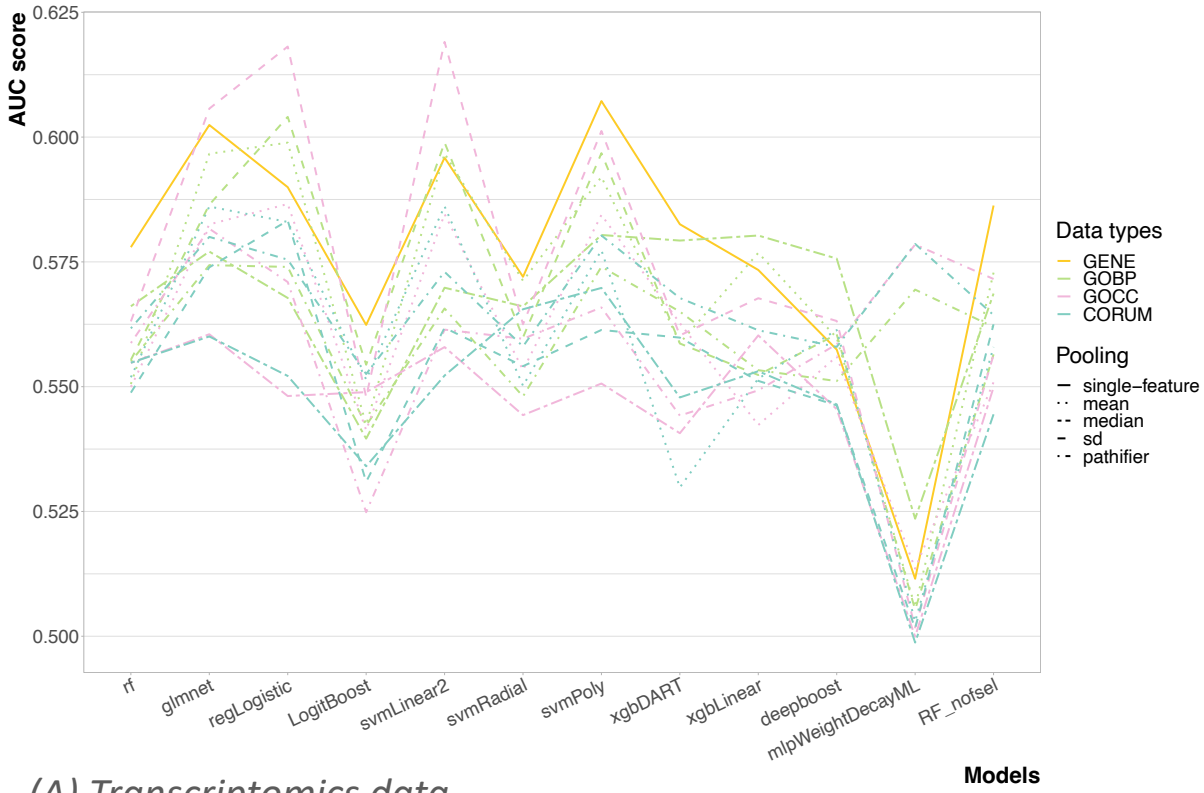
Aggregating omics data into higher order functional features



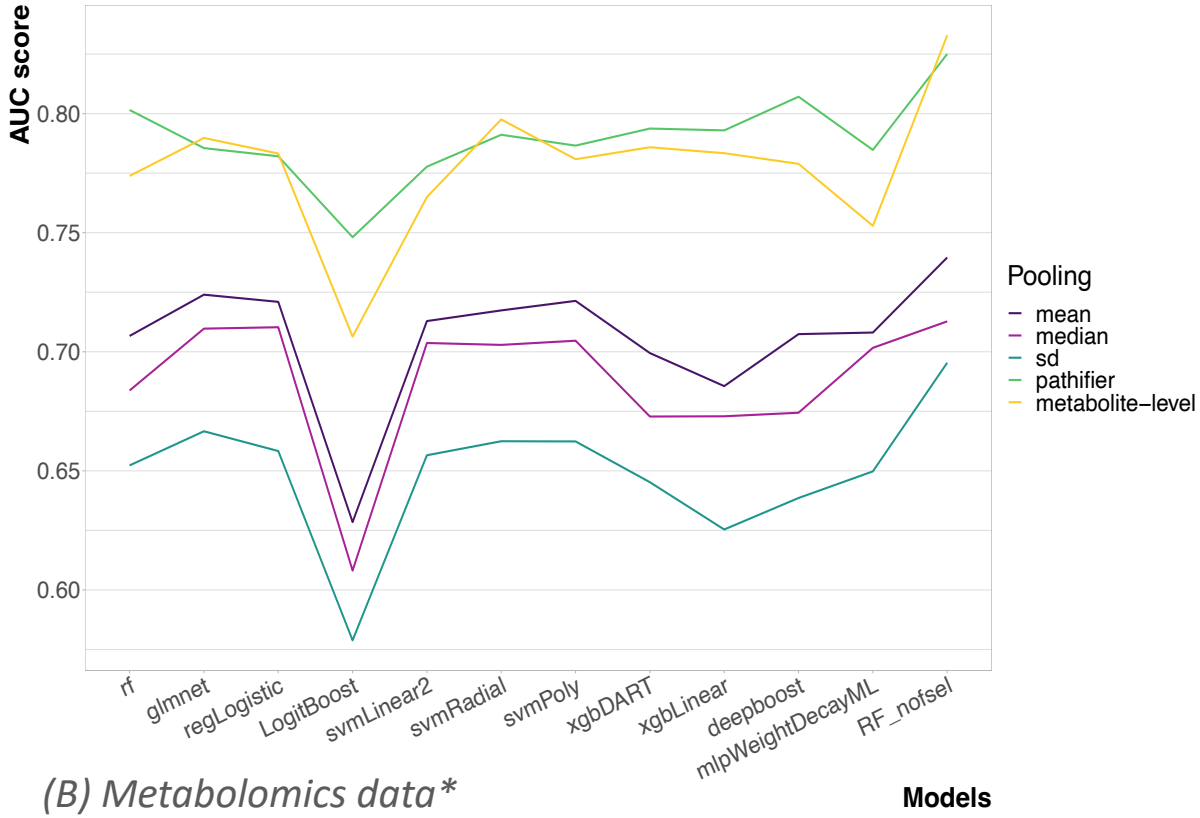
KEGG = Kyoto Encyclopedia of Genes and Genomes
m = number of samples
n = number of single-level features (i.e. genes, metabolites, etc)
p = number of higher order functional aggregates (e.g. number of pathways)

Results: Predictive PD diagnosis with ML models

Line charts of crossvalidated AUC scores from models & pooling types on transcriptomics (A) and metabolomics (B) data



(A) Transcriptomics data



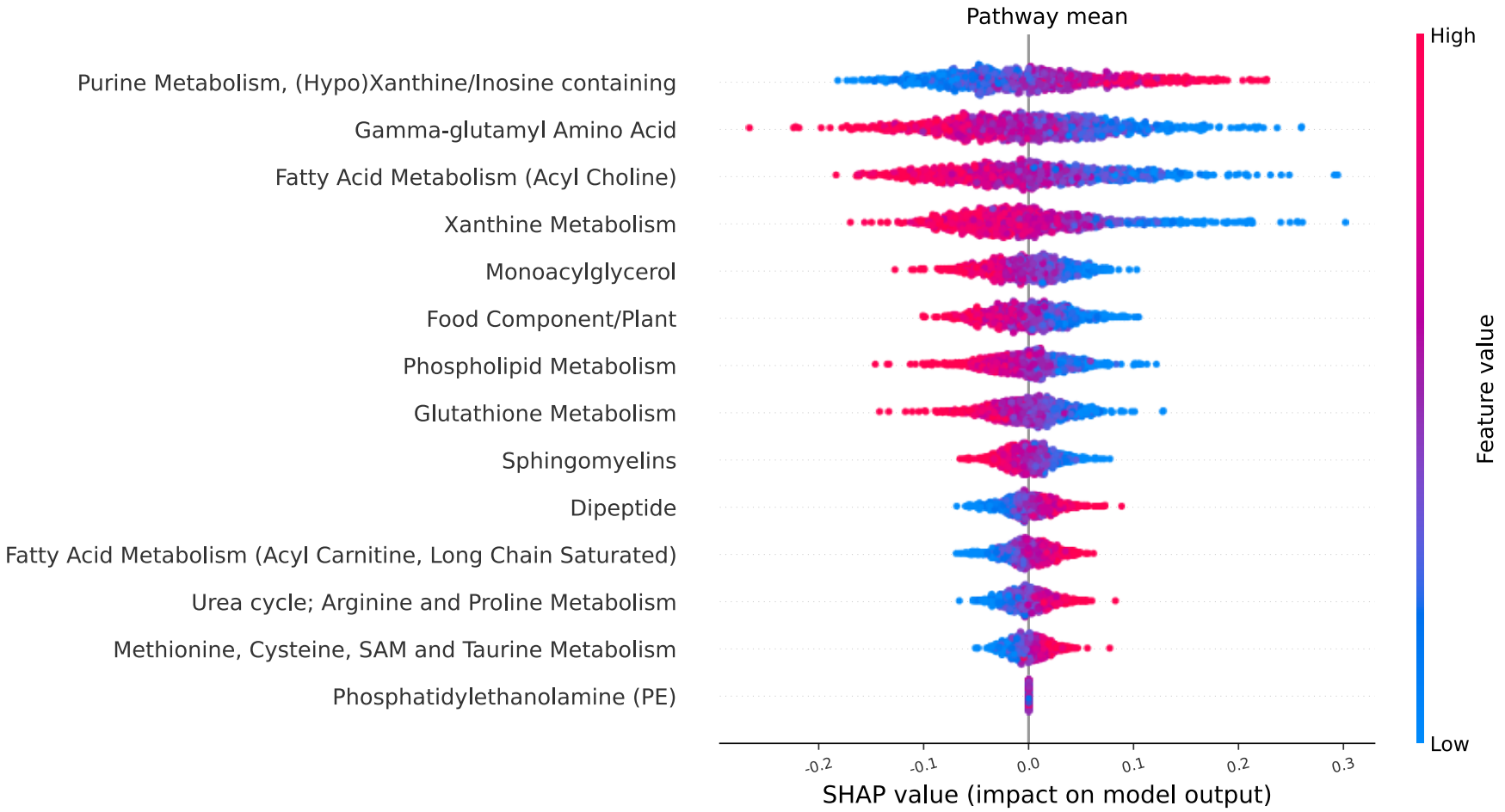
*(B) Metabolomics data**

**Pooling aggregations based on KEGG*

External two-level cross-validation was used including nested feature selection

Results: Relevant features from predictive diagnosis PD/HC

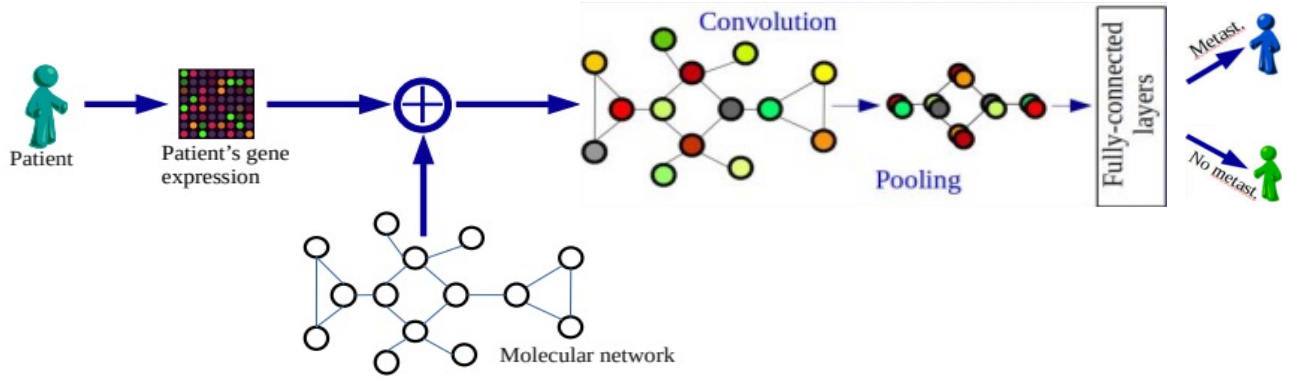
Shap values of (pooled mean -aggregated) KEGG metabolic pathways predictors on regularized logistic regression model



Limitations & outlook for future analyses

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

- ➡ Modelling other PD prognostic outcomes (e.g. motor dysfunction scores)
- ➡ Use a graph representation of the data via protein-protein interactions and metabolic networks



Gene expression profile as a graph signal of the molecular network

Source: Chereda, H., 2022. Explaining decisions of graph convolutional neural networks for analyses of molecular subnetworks in cancer [Doctoral thesis, Georg-August-Universität Göttingen]

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Find my poster here!

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