PiDeeL: Pathway-Informed Deep Learning Model for Survival Analysis and Pathological Classification of Gliomas

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INTRODUCTION

Gliomas are the most common type of brain tumor, accounting for 60% of all primary brain tumors. Glioma patients face a poor prognosis, with a median survival of 18 months. The tumor characteristics include different cell types (e.g., astrocytes, oligodendrocytes), grades (i.e., grade I - IV) and levels of malignancy (i.e., benign, aggressive).

High-Resolution Magic Angle Spinning Nuclear Magnetic Resonance (HRMAS NMR) spectroscopy is a promising technology for tissue analysis with the following advantages:

- Small samples of unprocessed specimen
- Fast sample preparation
- Non-destructive

Relying on tumor malignancy prediction may be insufficient:

- Prolonged survival in malignant glioma
- Rapid progression and low survival in benign glioma

METHODS

1 The surgeon removes primary tumor tissue from the patient's brain and prepares specimens.

2 Prepared samples are sent for HRMAS NMR spectroscopy analysis.

3 HRMAS NMR output spectrum are preprocessed.

4 37 metabolites are quantified via metabolite specific models.

5 PiDeeL transforms metabolite concentrations to survival analysis and pathological classification predictions.

6 Based on this feedback, the surgeon decides to preempt or continue performing the surgery

RESULTS

We compared our model against the following model configurations:

A Baseline models

B
- DeepSurv with 138 neurons in the first hidden layer
- PiDeeL with randomly connected PI-matrix
- PiDeeL with shuffled PI-matrix

C DeepSurv with different dropout rates

D DeepSurv on the varying dataset sizes

Downstream feature importance analysis revealed:

E
- The most important metabolites for survival analysis prediction: Glutamine, Glutamate and Alanine.
- The pathways with the most contribution to the outcome of PiDeeL: Mineral absorption, Alanine-aspartate-glutamate metabolism and mTOR signaling pathway.

PiDeeL was successful for these unanticipated cases:

- PiDeeL predicted long survival for a malignant glioma case where the patient lives 5,656 days after surgery.
- PiDeeL predicted low survival for a benign glioma patient who only lived 42 days.

CONCLUSION

- Accurate feedback on predicted prognosis and survival can help the surgeon.
- Biology-induced sparsity enables training deeper neural networks.
- Integrating prior biological knowledge into neural networks improves performance.
- Increased interpretability on metabolites and pathways supports surgical decision-making.

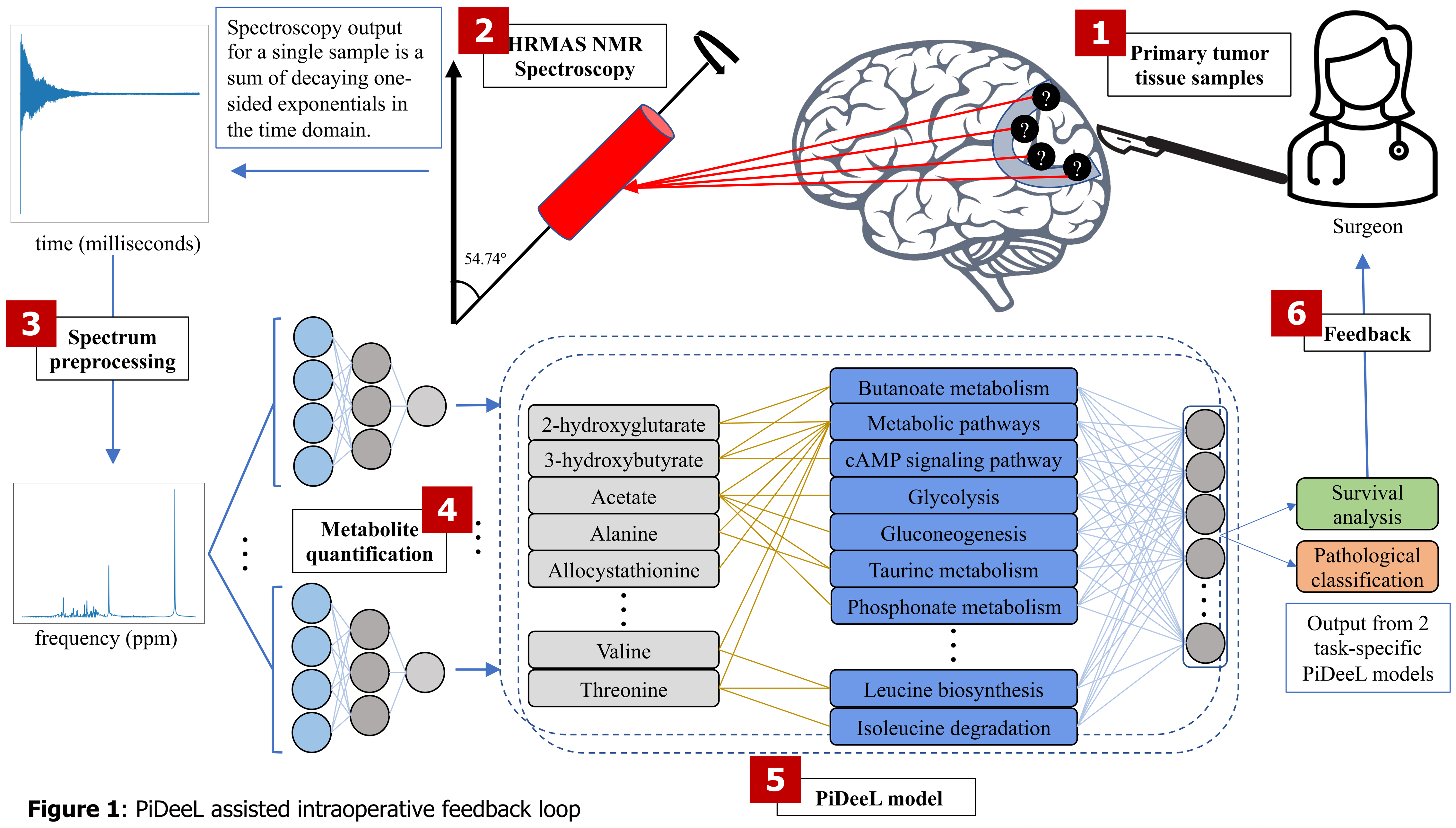

Figure 1: PiDeeL assisted intraoperative feedback loop

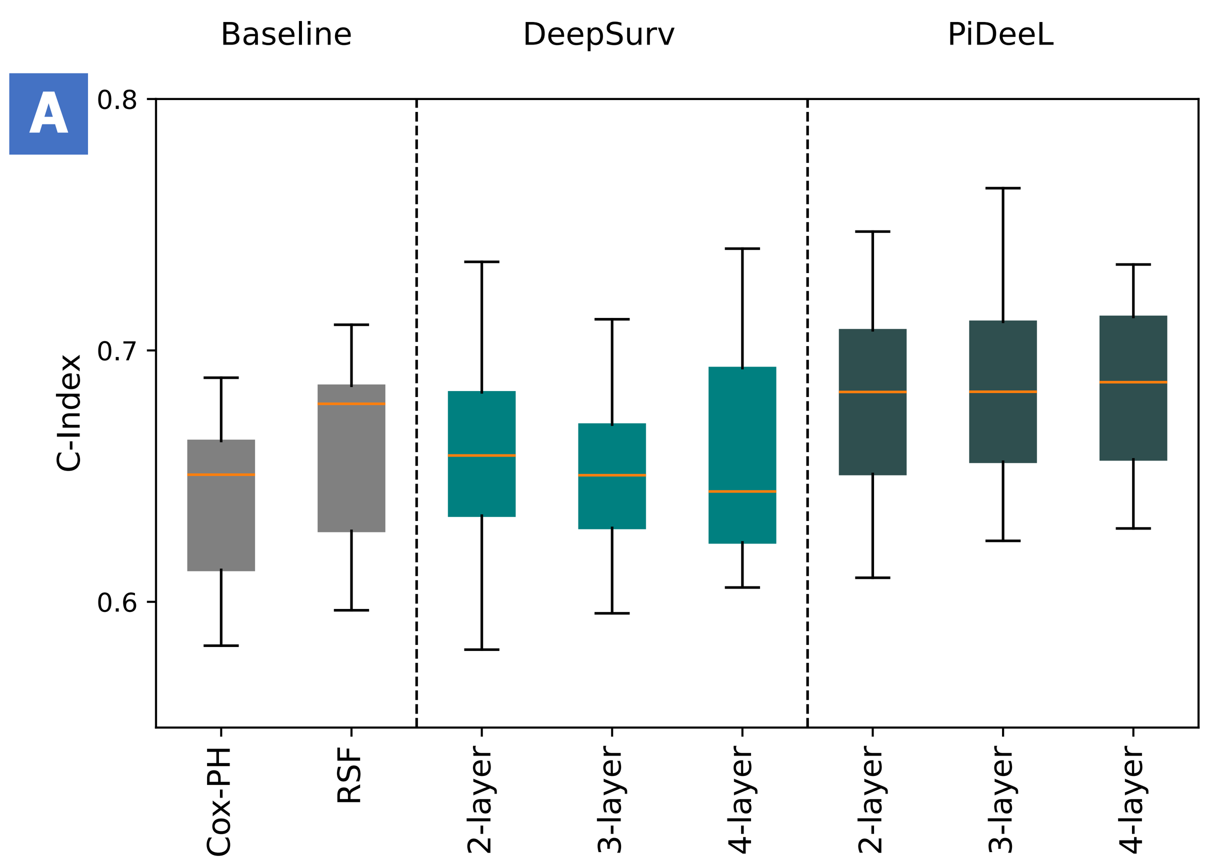

Figure 2: Performance comparison of PiDeeL and baseline models

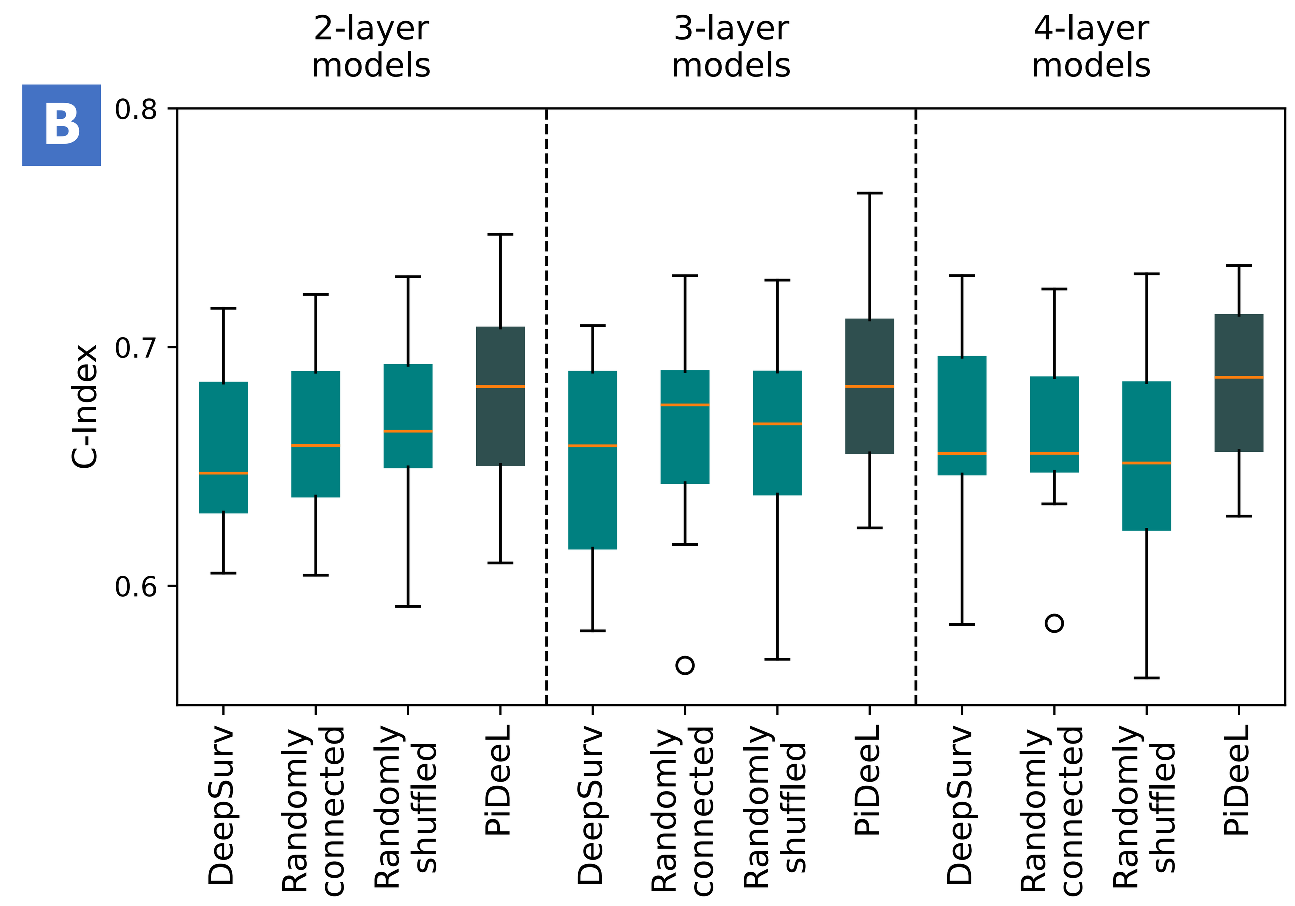

Figure 3: Performance comparison for ablation tests

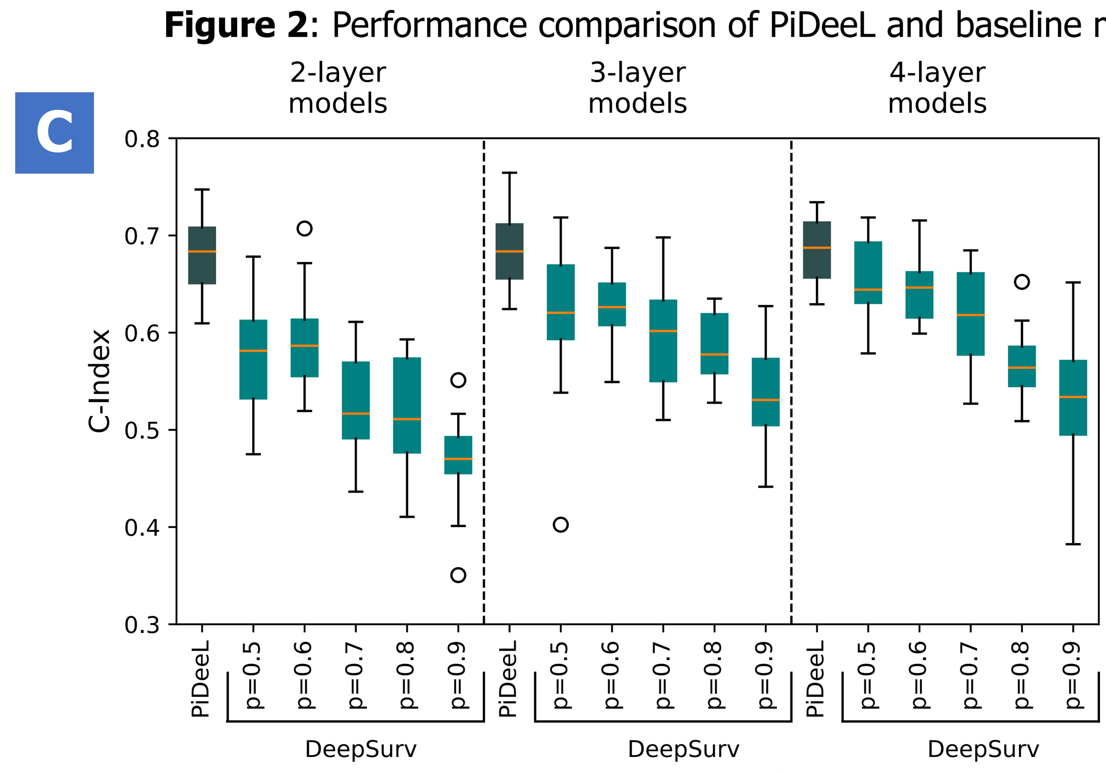

Figure 4: Performance comparison of PiDeeL and DeepSurv with dropout

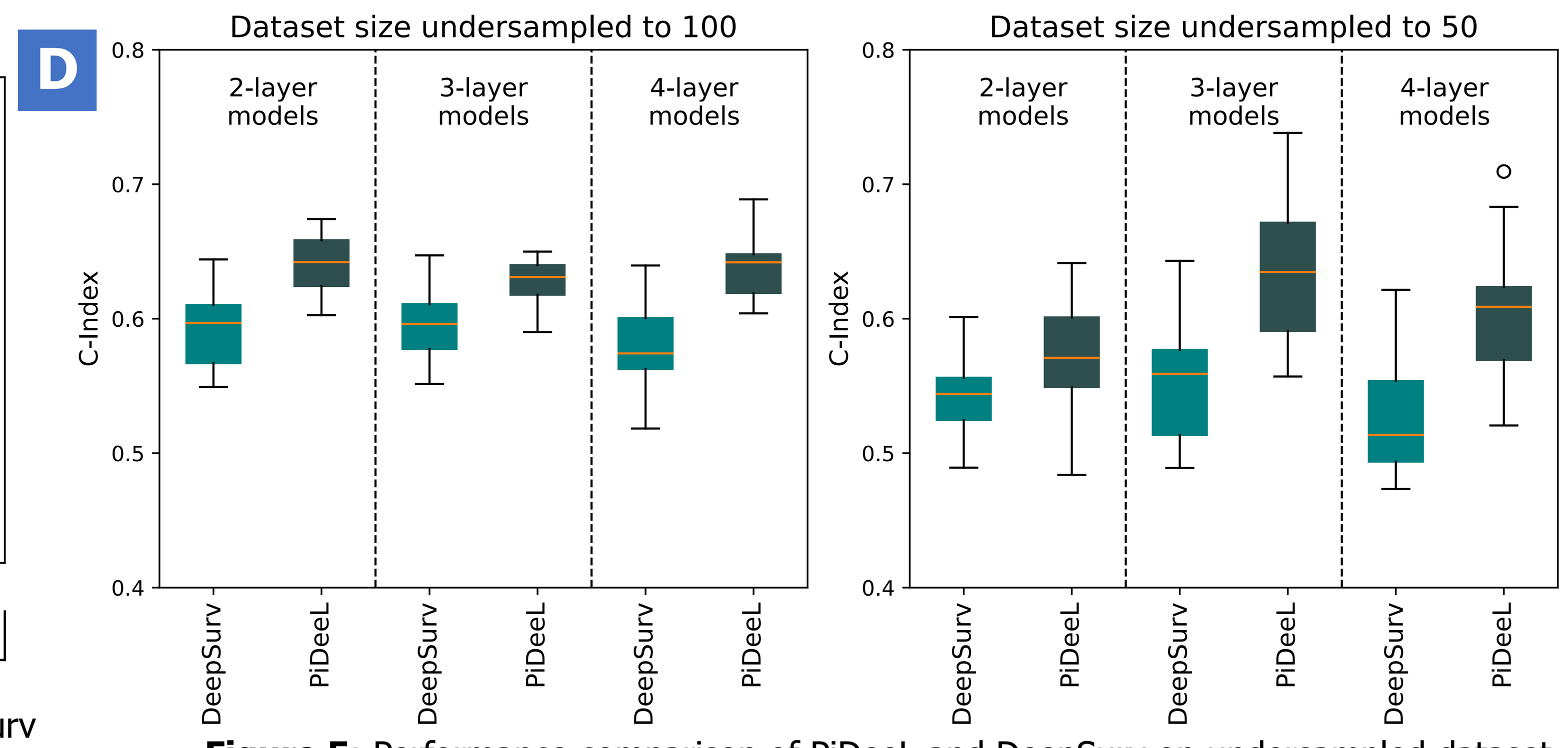

Figure 5: Performance comparison of PiDeeL and DeepSurv on undersampled dataset

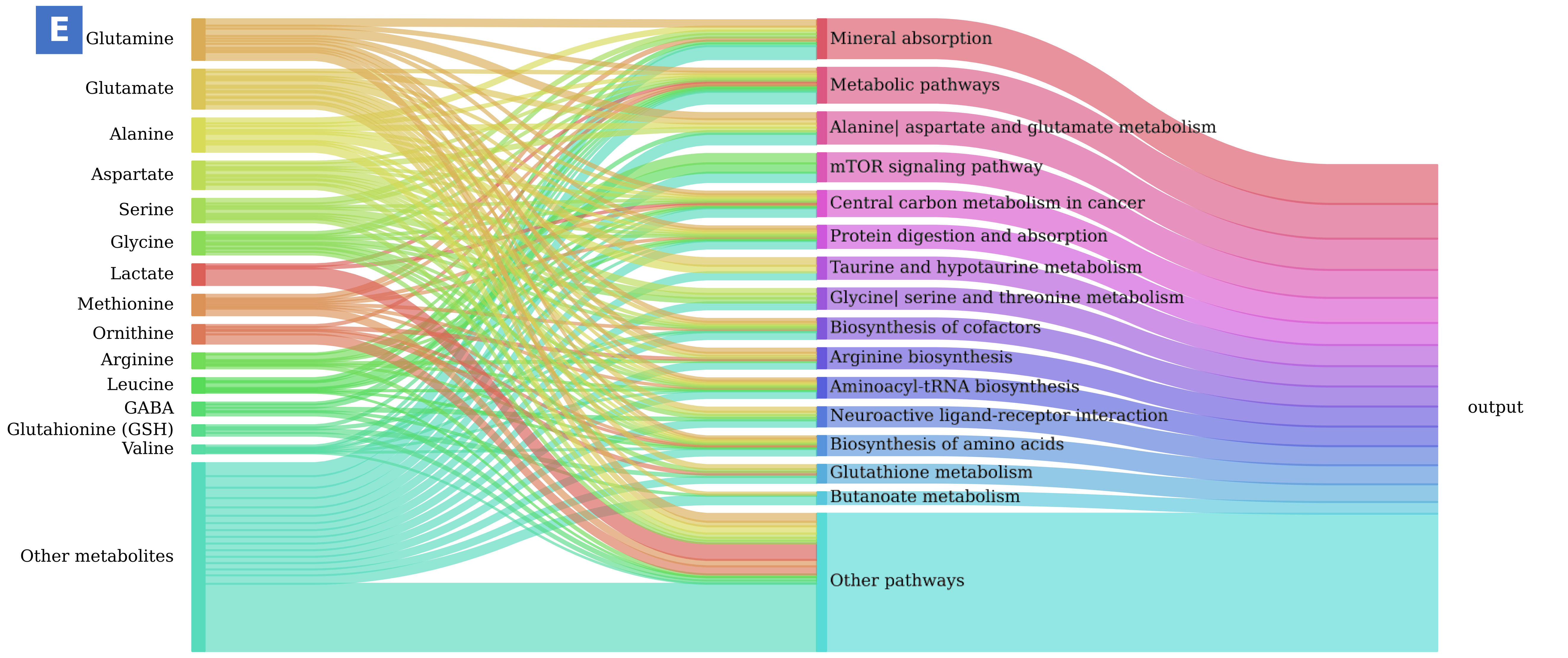

Figure 6: Sankey diagram visualizing the relative importance of metabolites and pathways for PiDeeL.

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