BiBoNet: An Explainable Deep Learning Framework for Integrating Microbiome and Metabolome Data in Disease Classification

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Keywords: multi-omics, explainable AI, data integration, disease classification

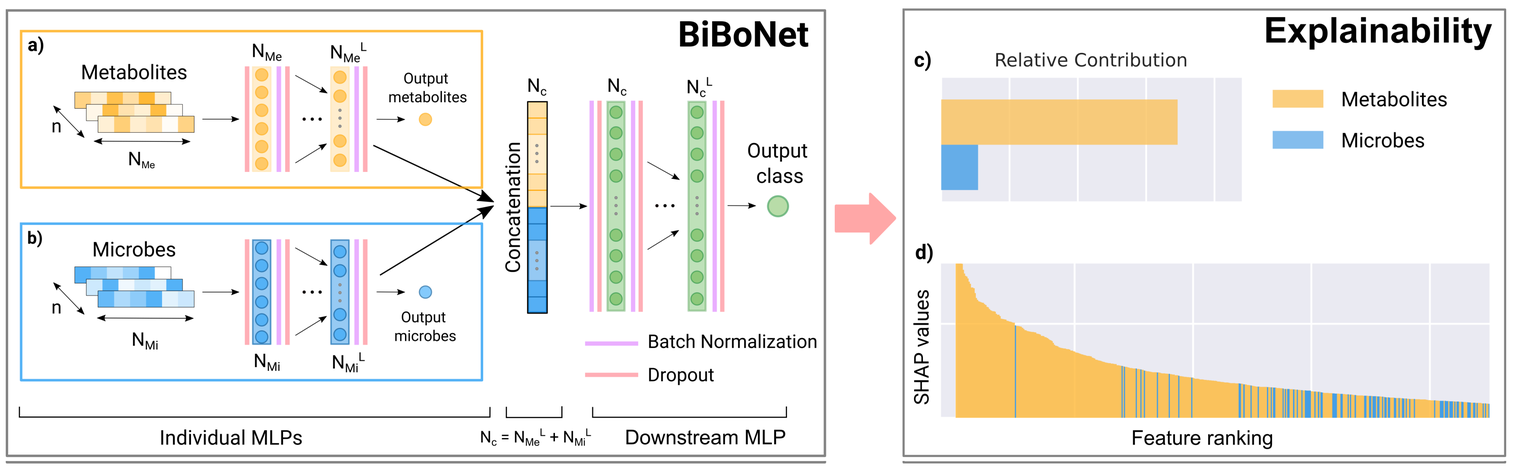
Background

Multi-omics data analysis integrates heterogeneous biological information to reveal novel insights into complex bioinformatics scenarios. In particular, microbiomics and metabolomics are increasingly studied together to understand how microbiome–metabolome interactions relate to host disease. However, the high dimensionality of these data hinders classical statistical approaches, while deep learning (DL) methods, though powerful, often suffer from limited interpretability. This work addresses the trade-off between accuracy and explainability by introducing BiBoNet, a deep learning framework for disease classification that integrates microbiome and metabolome data and incorporates explainability mechanisms.

Methods

Dataset	Disease	Samples (Control)	Metabolites (AP)	Microbes (AP)
iHMP	IBD	105 (26)	5820	8893
PRISM	IBD	155 (26)	8847	163
KIM	CRC	138 (102)	462	170
SINHA	CRC	131 (89)	530	86
YACHIDA	CRC	277 (127)	298	17692

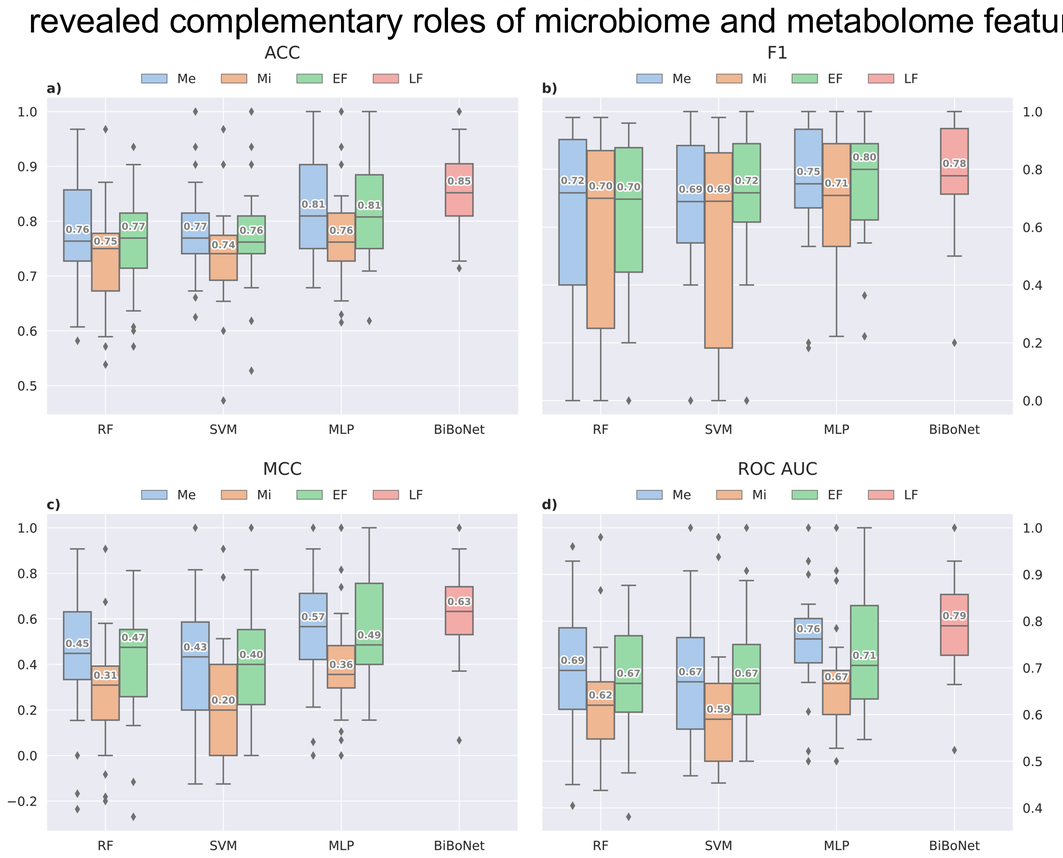
Table 1. Description of the datasets used in this study. Abbreviations – IBD: inflammatory bowel desease, CRC: colorectal cancer, AP: after processing



BiBoNet employs a composite multi-layer perceptron (MLP) architecture based on late integration. Two subnetworks, each trained on a different omics dataset (microbial abundance and metabolic profiles), are fused by concatenating their hidden representations. A downstream MLP processes this combined feature space to perform classification. To enhance interpretability, we apply SHapley Additive exPlanations (SHAP) to compute feature contributions. SHAP values are aggregated to quantify the relative influence of microbiome versus metabolome data, and input features are ranked by importance to provide biological interpretability at the level of individual microbes and metabolites.

Results

We benchmarked BiBoNet against baseline models on five matched microbiome–metabolome datasets related to Inflammatory Bowel Disease (IBD) and Colorectal Cancer (CRC). Performance was evaluated using grid search hyperparameter optimization and five-fold stratified cross-validation. BiBoNet consistently outperformed competing methods in classification accuracy while offering interpretable insights into feature contributions. SHAP analyses revealed complementary roles of microbiome and metabolome features, highlighting key biomarkers associated with disease states.



Algorithm		MLP_{Me}	MLP_{Mi}	MLP_{EF}	BiBoNet
Dataset	**Score**				
iHMP	ACC	0.848 (0.082)	0.781 (0.023)	0.810 (0.030)	**0.886 (0.065)**
	F1	0.902 (0.054)	0.871 (0.016)	0.883 (0.021)	**0.928 (0.041)**
	MCC	0.572 (0.233)	0.229 (0.188)	0.429 (0.079)	**0.672 (0.194)**
	ROC AUC	0.755 (0.105)	0.567 (0.056)	0.654 (0.034)	**0.794 (0.116)**
PRISM	ACC	0.968 (0.035)	0.903 (0.061)	0.968 (0.029)	**0.974 (0.024)**
	F1	0.980 (0.022)	0.939 (0.038)	0.980 (0.018)	**0.984 (0.015)**
	MCC	0.905 (0.105)	0.711 (0.192)	0.907 (0.083)	**0.925 (0.070)**
	ROC AUC	0.939 (0.060)	0.846 (0.112)	0.939 (0.055)	**0.943 (0.053)**
KIM	ACC	0.739 (0.042)	0.761 (0.027)	0.753 (0.017)	**0.797 (0.048)**
	F1	0.422 (0.191)	0.397 (0.146)	0.331 (0.157)	**0.530 (0.176)**
	MCC	0.266 (0.198)	0.294 (0.121)	0.267 (0.123)	**0.421 (0.192)**
	ROC AUC	0.634 (0.104)	0.622 (0.064)	0.602 (0.082)	**0.692 (0.093)**
SINHA	ACC	0.840 (0.016)	0.718 (0.087)	0.855 (0.038)	**0.863 (0.018)**
	F1	0.708 (0.037)	0.496 (0.151)	0.707 (0.132)	**0.754 (0.041)**
	MCC	0.631 (0.033)	0.314 (0.207)	0.674 (0.108)	**0.685 (0.045)**
	ROC AUC	0.780 (0.025)	0.645 (0.095)	0.792 (0.090)	**0.812 (0.037)**
YACHIDA	ACC	0.740 (0.031)	0.679 (0.026)	0.707 (0.049)	**0.758 (0.036)**
	F1	0.747 (0.041)	0.709 (0.015)	0.735 (0.024)	**0.774 (0.035)**
	MCC	0.487 (0.059)	0.360 (0.069)	0.419 (0.105)	**0.518 (0.075)**
	ROC AUC	0.743 (0.029)	0.675 (0.034)	0.704 (0.060)	**0.758 (0.037)**

Table 3. Five-fold stratified cross-validation performance on each dataset. Mean scores calculated over the cross-validation sets are reported with standard deviation in brackets. Subscript Me refers to metabolites, Mi to microbes and EF (early fusion) to input feature concatenation.

Fig. 2. Aggregated results for each fold of a 5-folds cross validation over all datasets for four scoring metrics. Results are grouped by model type. Colours indicate results for metabolites alone (Me, blue), microbes alone (Mi, orange), early fusion (EF, green) and late fusion (LF, red). Numerical values in each box-and-whisker plot correspond to the distribution's median (second quartile).

Explainability

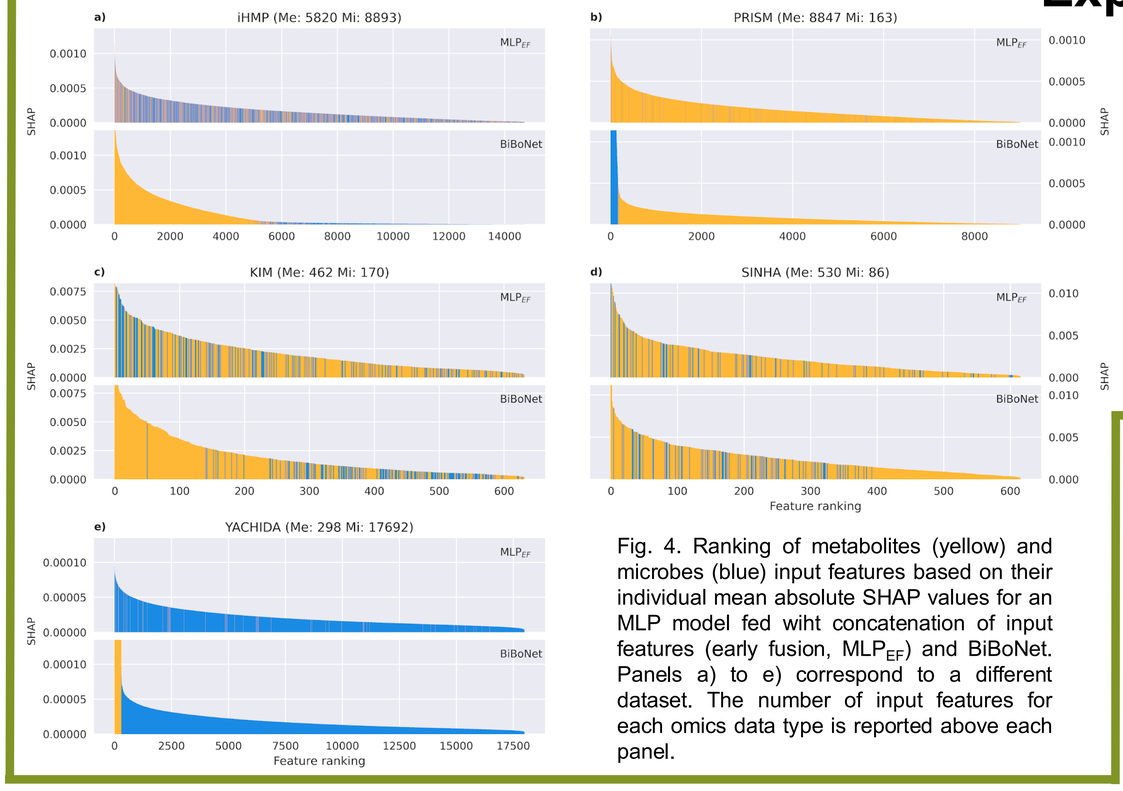
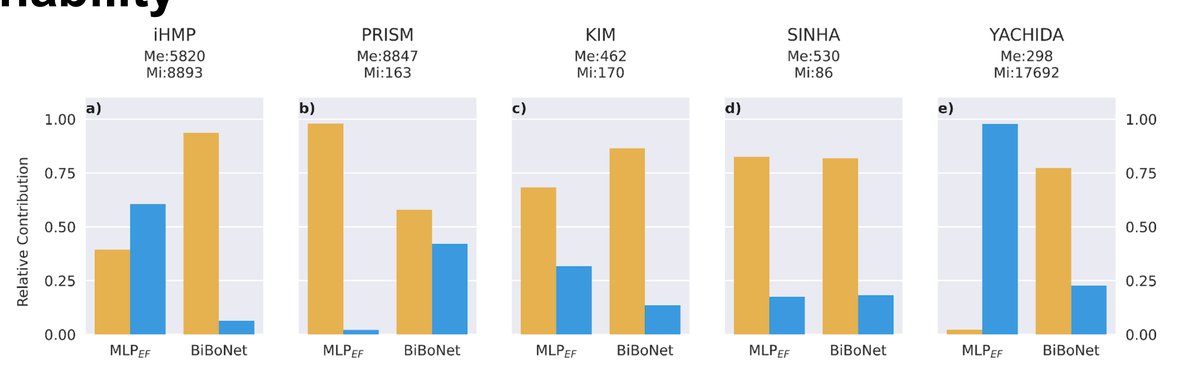


Fig. 4. Ranking of metabolites (yellow) and microbes (blue) input features based on their individual mean absolute SHAP values for an MLP model fed wiht concatenation of input features (early fusion, MLP_{EF}) and BiBoNet. Panels a) to e) correspond to a different dataset. The number of input features for each omics data type is reported above each panel.



Conclusion

This study demonstrates that BiBoNet effectively integrates microbiome and metabolome data for disease prediction while addressing the critical need for model transparency in healthcare applications. By combining accuracy with interpretability, BiBoNet supports biologically meaningful discoveries and enhances trust in deep learning approaches for multi-omics analysis.