

# Deep Learning Approaches to IBD Patient Classification: A Comparative Study of GNNs and Neural Networks on Olink/UK Biobank Data

Youtube Video: <https://youtu.be/O4Gf38GTlqM>

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## Introduction

Inflammatory bowel disease (IBD), encompassing Crohn's disease (CD) and ulcerative colitis (UC), is a chronic and relapsing disorder with rising global prevalence and substantial clinical heterogeneity. Despite the identification of over 200 genetic risk loci through genome-wide association studies (de Lange et al., 2017; Liu et al., 2015), the biological mechanisms driving patient variability and disease progression remain incompletely understood.

Recent advances in high-throughput proteomics provide new opportunities to uncover molecular signatures associated with disease subtypes, treatment response, and progression (Sun et al., 2018; Zhernakova et al., 2018; Bourgonje et al., 2019; Folkersen et al., 2020). When coupled with scalable machine learning, these data can be leveraged to improve patient stratification and clinical decision-making.

In this study, we analyzed **1983** plasma proteins from **3626** IBD patients and **18,999** controls using Olink® proximity extension assays from the UK Biobank. We conducted a **comparative analysis of deep learning models, including graph neural networks (GNNs) and fully connected neural networks, to evaluate their performance in IBD patient classification** and explore their potential for capturing complex proteomic patterns underlying disease heterogeneity.

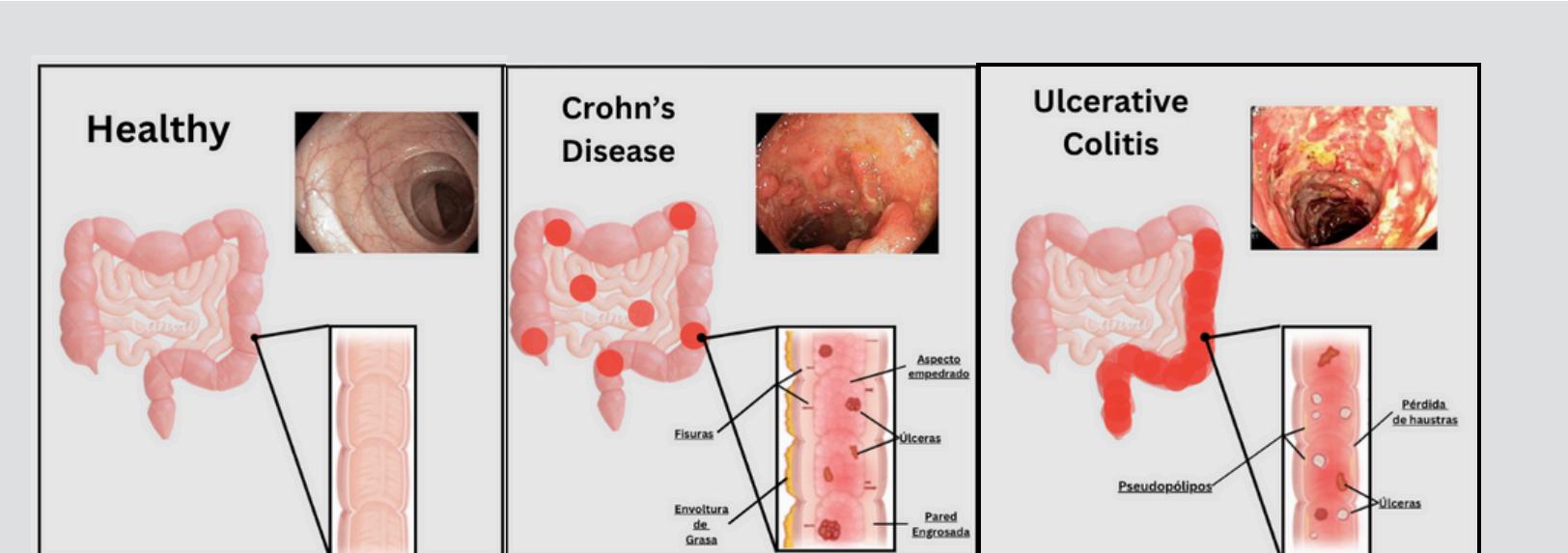
## AIM

We aim to classify IBD patients using neural and graph-based models on plasma proteomics data, uncovering complex protein interactions that may explain disease heterogeneity.

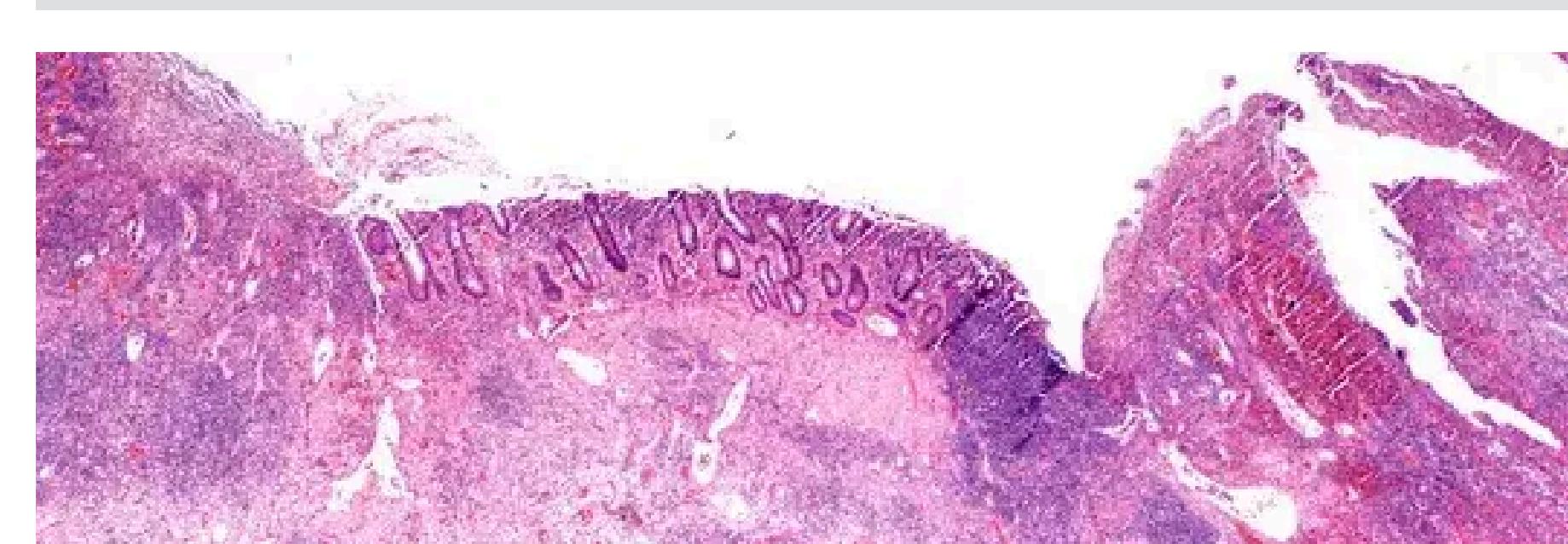
## Context

### The Disease

**Crohn's Disease:** Requires more aggressive treatment over time. [1]



**Ulcerative Colitis:** More predictable course, but can lead to dysplasia or colorectal cancer. [1]



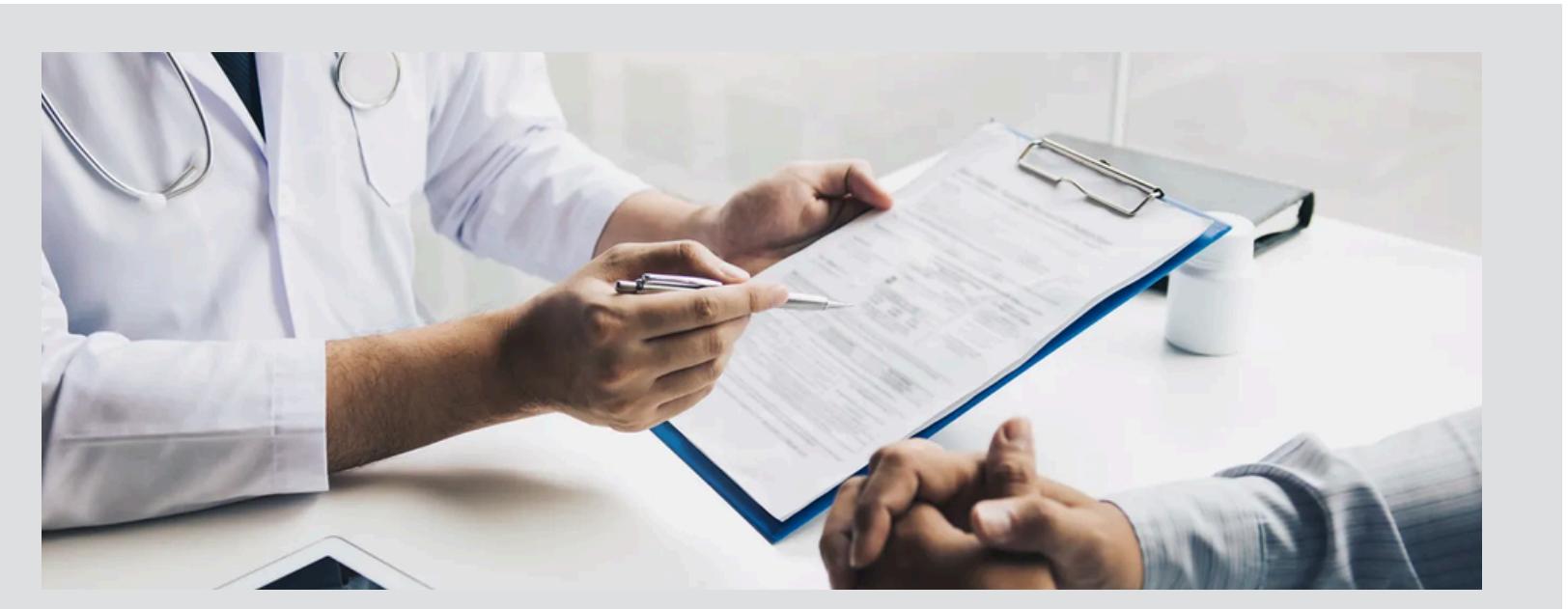
### Evolution of the disease

#### Modern Approach:

- Focus on early intervention and "treat-to-target" strategies. [1]
- Goal: Slow progression, reduce complications, improve outcomes. [1]

### Diagnosis

- Clinical Assessment:** Symptoms like diarrhea, abdominal pain, weight loss. [6]
- Lab Tests** [3]:  
Blood: CRP, ESR, anemia, albumin.  
Stool: Calprotectin, lactoferrin.
- Endoscopy** (colonoscopy with biopsy): Gold standard for diagnosis [3][6].

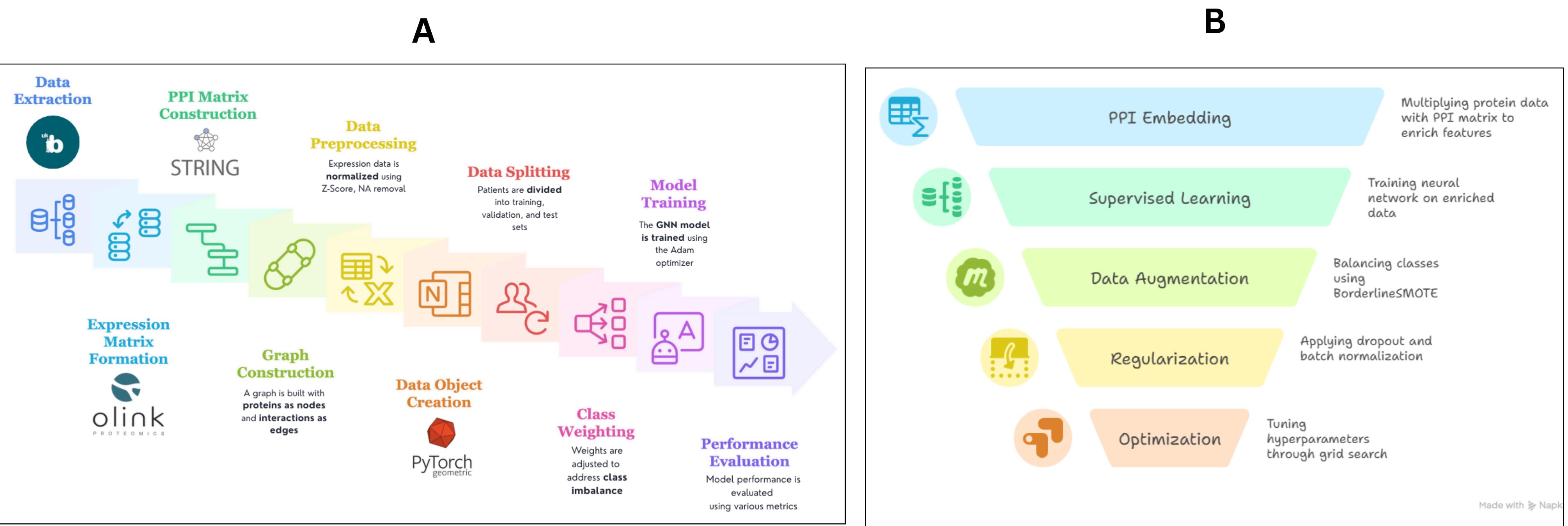


### Challenges

- Non-specific symptoms and overlap with other GI conditions. [3]\*
- Variable disease patterns between individuals. [3][7]
- No definitive non-invasive biomarkers. [3][8]
- Reliance on invasive testing and exclusion of other diseases. [8]



## Methodology



### Protein Embedding Generation

A two-layer Graph Convolutional Network (GCN) or Graph Attention Network (GAT) learns context-aware embeddings for each protein. The GCN/GAT processes initial protein features (expression levels across patients) by aggregating information from neighboring proteins within the PPI (protein-protein interaction) network via learnable weights.

### Patient Embedding Construction

Unique patient-specific embeddings are constructed by taking a weighted sum of the learned protein embeddings, where the weights are the patient's individual protein expression level. This integrates network context with personalized expression profiles.

### Patient Classification

The generated patient embeddings are then fed into a multi-layer perceptron (MLP) for binary classification. The MLP consists of several fully connected layers, interspersed with Batch Normalization and Dropout for robust learning, outputting class logits.

### Training and Evaluation

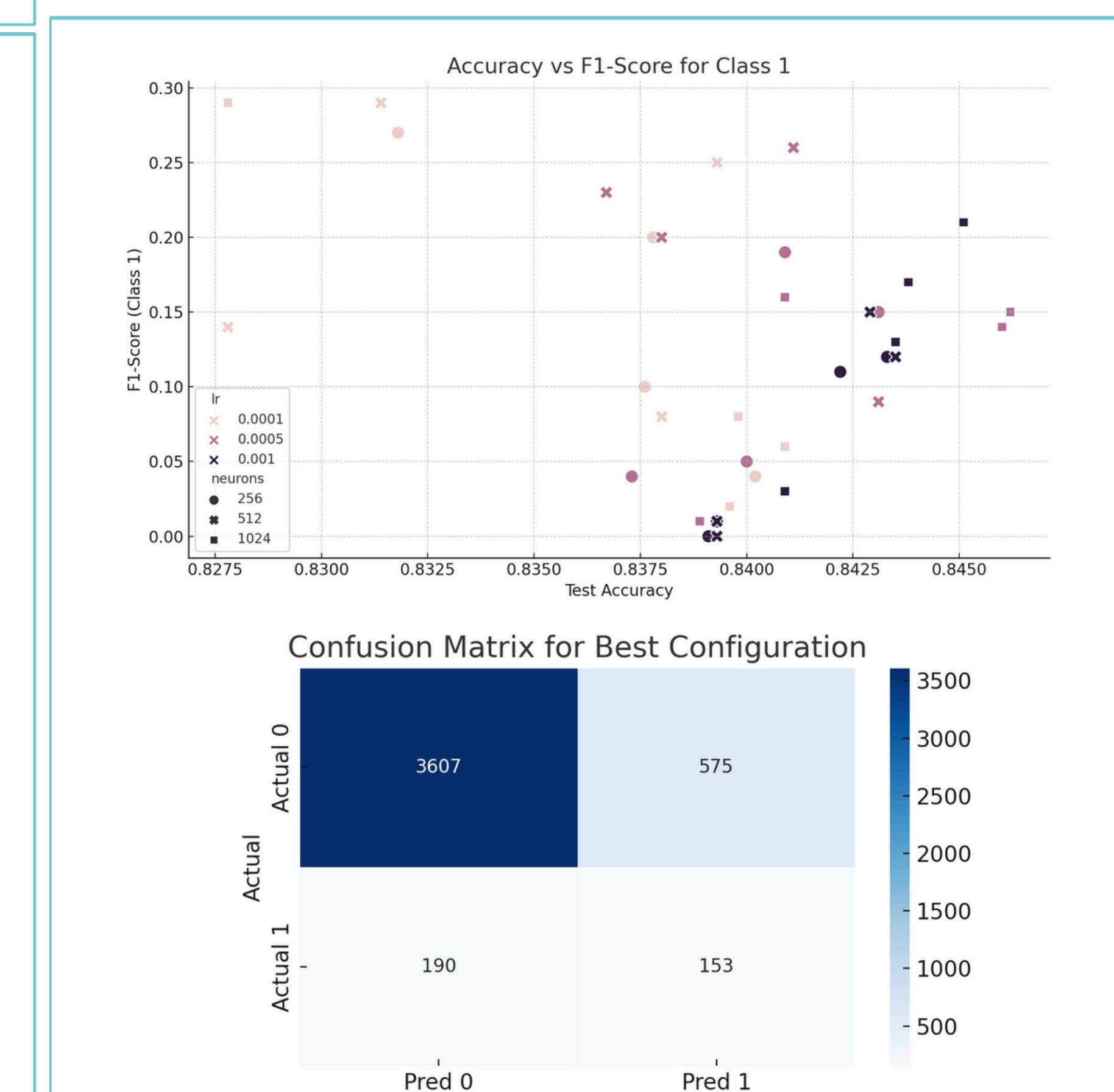
**Loss Function:** Weighted Cross-Entropy Loss is utilized to address potential class imbalance, applying pre-calculated weights (wc) to each class's contribution to the total loss.

**Optimizer:** The Adam optimizer is used for model parameter updates.

**Hyperparameter Optimization:** GAT learning vs GCN learning

**Evaluation Metrics:** Model performance is assessed using accuracy, and critically, F1-score, Recall, Precision for the positive (minority) class, and AUC-ROC, providing a comprehensive view of classification effectiveness on the test set.

## Results



- For the classical NN result:**
  - Selected Configuration: 0.0001
  - Number of neurons (first dense layer): 512
  - Batch size: 32
  - Epochs: 40
- Performance Metrics:**
  - Test Accuracy: 83.14%
  - F1-Score (Class 1 – Diseased): 0.29
  - Precision (Class 1): 0.45
  - Recall (Class 1): 0.21
  - F1-Score (Class 0 – Healthy): 0.90

## Discussion

- The results indicate that traditional deep neural networks can perform well in distinguishing between healthy individuals and IBD patients when enhanced with protein-protein interaction context. Incorporating focal loss helped mitigate the effects of class imbalance by reducing the impact of easy negative samples during training. The use of SMOTETomek further improved the representativeness of the minority class in the training dataset.
- However, the relatively low recall and F1-score for the disease class suggest that the model still struggles to capture complex patterns associated with IBD. This could be due to the biological complexity of the disease, the presence of noise in high-dimensional proteomics data, or limitations in the interaction matrix used.
- Neither model performs outstandingly in classifying the minority class ("Diseased"), with both showing a low and identical F1-score of 0.29. The classical neural network demonstrates higher precision (0.45), indicating fewer false positives, but its low recall (0.21) suggests it misses many actual sick cases.

- The Graph Neural Network (GCN) achieves a higher recall (0.51), enhancing its ability to detect sick patients, though at the cost of more false positives (precision of 0.20). Its higher AUC also indicates better overall class discrimination. *The choice between models depends on the clinical context and whether it is more important to reduce false negatives or false positives.*

**Future work could explore hybrid models, feature selection methods, or integrate clinical metadata to further enhance prediction performance.**

## References

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