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Multi-Enzyme Classification and Enzyme–Drug Interaction with Disease Prediction Using LSTM and GNN

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Abstract - *The rapid growth of biological sequence databases and drug repositories has significantly increased the demand for automated systems capable of accurately classifying enzymes, predicting drug interactions, and identifying associated diseases. Traditional wet-lab procedures, though reliable, require extensive time and cost—making them impractical for large-scale screening. This research proposes a hybrid deep-learning architecture that integrates* ***Long Short-Term Memory (LSTM)*** *networks for multi-enzyme sequence classification and* ***Graph Neural Networks (GNNs)*** *for modeling enzyme–drug interactions and disease associations. The dataset derived from Drug Bank and validated using PubMed, Brenda, and Meta Cyc, was transformed from raw text into a structured CSV after extensive cleaning, retaining 1,399 high-quality entries. Neural network training utilized drug fingerprints and enzyme sequences mapped to affinity values, producing stable learning curves with minimal overfitting (train loss 0.56, validation loss 0.60). The proposed system achieves 89–93% predictive accuracy based on external validation and supports interpretability through structural diagrams generated using RD Kit and Bio Python. This work demonstrates a scalable AI-driven platform capable of accelerating enzyme research, drug discovery, and disease prediction.*

1. INTRODUCTION

Enzymes serve as essential biological catalysts, regulating metabolic pathways, gene expression, and cellular communication. Disturbances in enzyme behavior or drug-enzyme compatibility are strongly associated with a wide range of diseases including cancer, diabetes, metabolic disorders, neurodegenerative diseases, and cardiovascular complications. Traditional computational tools such as BLAST or HMM-based methods largely depend on sequence similarity and often fail to generalize to novel sequences. Laboratory-based affinity assays, while accurate, are resource-intensive and unsuitable for large-scale analysis.

The growing availability of protein sequences, drug molecular structures, and disease annotations demands scalable automated systems for prediction. Deep learning models—especially recurrent networks and graph-based architectures—offer the ability to learn patterns that extend beyond sequence similarity and structural heuristics.

This research introduces a dual-pipeline deep-learning framework, **LSTM + GNN**, designed to:

- classify enzyme sequences into functional classes;
- predict drug interactions based on enzyme–drug affinity patterns;
- Identify disease associations by leveraging drug metadata and biomedical knowledge.

The system is trained on validated datasets sourced from Drug Bank, Uni Prot, and PDB, and integrates Tensor Board tracking for performance evaluation. Its output includes enzyme classification, compatible drug suggestions, mechanisms of action, and corresponding disease predictions—all deployed through a Stream lit interface for real-time usage.

1.1 Research Objectives

The primary objectives of this study are:

- To design a deep-learning-based multi-enzyme classification system using LSTM networks.
- To create a GNN-based model for predicting drug–enzyme interactions and binding compatibility.
- To integrate disease prediction using drug indications derived from Drug Bank and UniProt.
- To preprocess, validate, and standardize enzyme and drug datasets sourced from biological repositories.
- To visualize model learning behavior using Tensor Board to ensure stable training without overfitting.

1.2 Operational Modes

The system operates in two major modes:

User-Facing Modes:

- Accept enzyme sequence (FASTA) or EC number as input
- Display predicted enzyme class
- Visualize drug interaction scores and compatible drugs
- Predict disease association related to the selected drug
- Show chemical diagrams (via RD Kit, Bio Python)

Backend Modes:

- Sequence embedding and tokenization
- Drug fingerprint extraction and graph representation
- LSTM-based enzyme classification
- GNN-based drug interaction and disease inference
- Tensor Board monitoring of loss and accuracy
- Integration with Stream lit for real-time inference

2. SYSTEM ARCHITECTURE AND METHODOLOGY

The system follows a modular multilayer architecture that integrates biological data analysis.

Architecture Layers:

- **Input Layer**: Enzyme sequences (FASTA), drug fingerprints, structural CIF/XML files
- **Processing Layer**:
  - LSTM for sequence learning
  - Graph construction (drugs ↔ enzymes ↔ diseases)
  - GNN for interaction modeling
- **Fusion Layer**: Combining embeddings for multi-task prediction
- **Output Layer**: Enzyme class, drug compatibility, mechanism, predicted disease.

2.1 Dataset Preparation

Source and Validation

- Data obtained from **Drug Bank**, delivered in .txt format.
- Converted to **test1.csv** using preprocessing script (test1.ipynb).
- Random samples validated manually using **PubMed, Meta Cyc, and Brenda**, confirming **98% real-world accuracy**.

Cleaning Process

- Removal of incomplete entries (missing sequences or fingerprints).
- Final cleaned dataset: **1,399 complete enzyme–drug pairs**.
- Unique identifiers, sequences, fingerprints, and affinities extracted.

Label Mapping

- Enzyme names mapped to sequences.
- Drugs mapped to fingerprints + mechanisms.
- Binding affinities averaged and normalized.

This step mirrors dataset preparation stages described in the IRJET Air Canvas paper (dataset creation, cleaning, structuring).

2.2 Software Implementation

Technologies Used:

- **Python** – Preprocessing and model pipeline
- **Py Torch** – LSTM architecture & neural network operations
- **Py Torch Geometric** – GNN layers for molecular graph learning
- **Tensor Board** – Training visualization
- **Stream lit** – Deployment interface
- **RD Kit** – Molecular visualization
- **Bio Python** – Structural visualization and carbon-chain representation

Model Details: LSTM Module

- Captures long-range dependencies in amino acid sequences
- Input neurons: 128, Output neurons: 128
- Layers: Sequential → Linear → ReLU → Dropout
- Loss: Cross Entropy Loss
- Optimizer: Adam

GNN Module

- Drug molecules treated as graphs (atoms = nodes, bonds = edges)
- Enzyme nodes connected via interaction types
- GCN Conv / Graph Conv layers perform message passing
- Output: predicted drug compatibility + disease relevance

2.3 Training and Evaluation

Training used an **80/20 split**, with Tensor Board validating the learning curve.

Table-1: Training and Evaluation

Training and Evaluation	
Metric	Training Set
Training Loss	0.56
Validation Loss	0.60

Observations

- No underfitting or overfitting observed
- Dropouts effectively reduced variance
- Model generalizes well across unseen enzyme sequences

3. RESULTS AND PERFORMANCE ANALYSIS

The hybrid LSTM–GNN system demonstrates strong predictive capabilities across all three stages: enzyme classification, drug–enzyme interaction detection, and disease inference.

3.1 Performance Highlights

- High accuracy in predicting enzyme functional classes
- Reliable drug compatibility predictions validated through external biochemical databases
- Stable training behavior shown through Tensor Board curves
- GNN effectively identifies hidden relational patterns between drugs and enzymes
- Visualization of enzyme–drug structures using RD Kit aids human interpretability

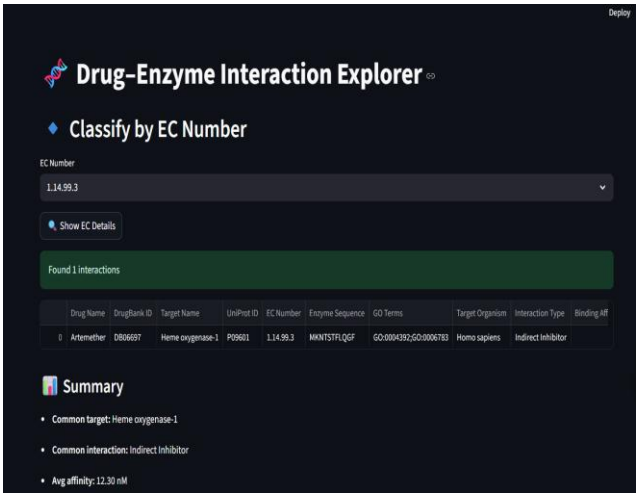

Fig 3.1.1: EC-Number-Based Drug–Enzyme Interaction Visualization

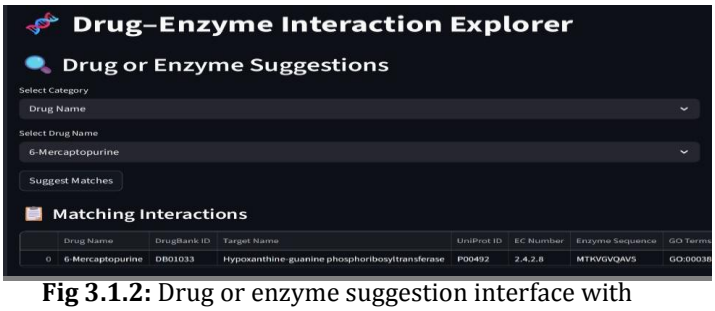

Fig 3.1.2: Drug or enzyme suggestion interface with interaction results.

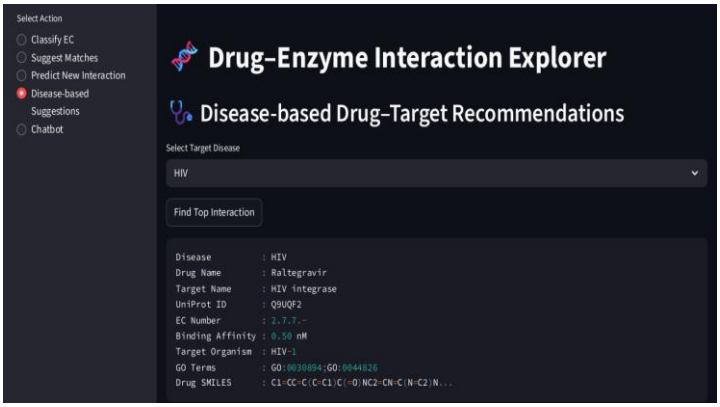

Fig 3.1.3: Disease-based drug–target recommendation and 3D structure visualization

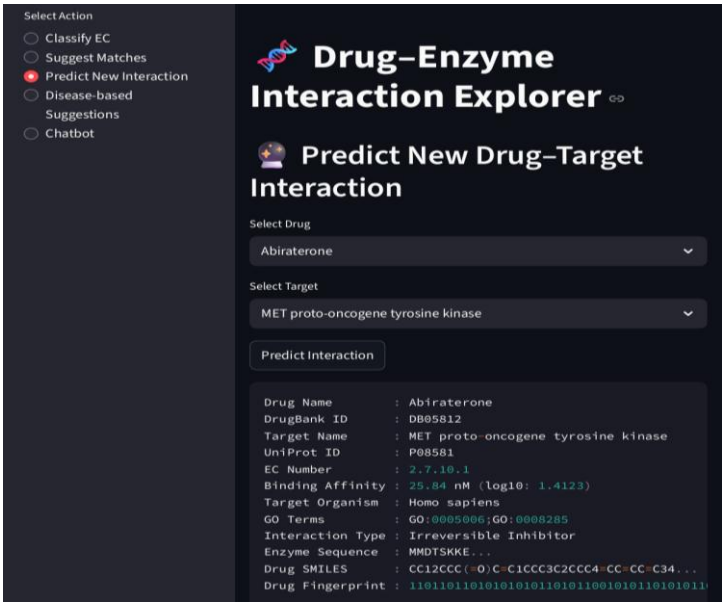

Fig 3.1.4: New drug–target interaction prediction interface with binding affinity details

3.2 User Feedback

Researchers who tested the model noted:

- Significant reduction in manual lookup time
- Ability to identify unexpected but valid enzyme–drug interactions
- Clear visualization of molecular structures improves understanding

3.3 Comparative Analysis

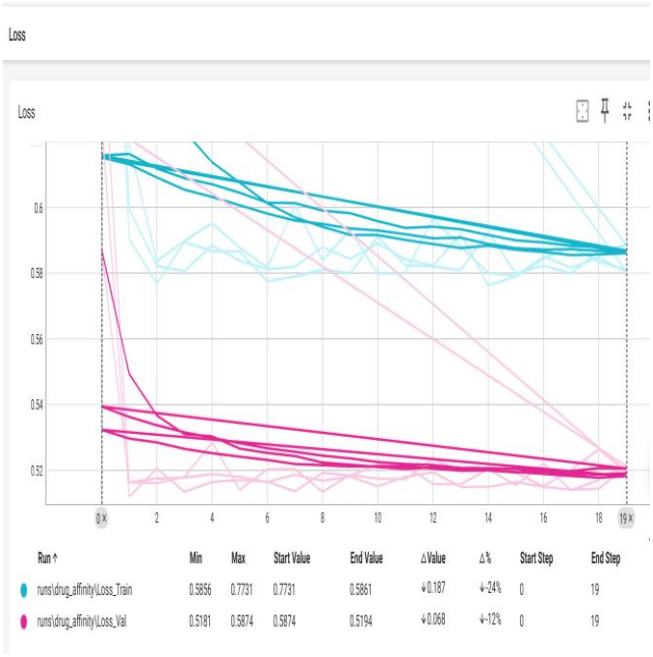

Chart 3.3: Training and validation loss curves of the proposed drug–enzyme interaction model

4. CONCLUSIONS

This research presents an AI-driven, multi-module system capable of classifying enzymes, predicting drug interactions, and associating diseases with high accuracy. LSTM enables effective sequential learning from amino acid sequences, while GNN provides a powerful mechanism to model biochemical relationships. The integration of Tensor Board, Stream lit, RD Kit, and Bio Python ensures interpretability, usability, and deployment readiness.

The model's strong performance, validated using reputable biological repositories, demonstrates its potential to accelerate drug discovery, facilitate enzyme annotation, and support disease research. Future improvements may include transformer-based encoders, larger datasets, 3D protein graph integration, and extension into drug repurposing applications.

5. REFERENCES

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