Multi-Label Classification of Biological Targets Using Machine Learning Models for Enhanced Drug Discovery

MSc Research Project
Masters in Data Analytics

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Multi-Label Classification of Biological Targets Using Machine Learning Models for Enhanced Drug Discovery

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Abstract

The challenge of predicting multiple biological targets by means of chemical and biological features is addressed by this research, which is crucial in biomedical research and pharmaceutical development. Despite the great efforts in the drug discovery and personalized medicine, traditional approaches require lengthy and bloated approaches that are too costly. We apply multi-label classification techniques to predict target activations by using CatBoost and Gradient Boosting and Random Forest. We used a robust methodology that involved data preprocessing, exploring data and then modeling, and evaluating our model using an extensive set of metrics like accuracy, precision, recall and F1 Score. The results show how CatBoost outperforms all other methods in terms of accuracy and balanced metric performance. Our contribution to the state of the art is these findings which illustrate the potential of multi label models to solve complex biomedical problems. This work in practice can in turn stream line drug discovery processes, reduce drug development costs, and enable the delivery of more precise treatments by use of personalised medicine.

1 Introduction

Machine learning techniques have evolved to transform many of the fields like biomedical research and healthcare, and development of pharmaceuticals. This particular area of machine learning is called multi-label classification, where a problem underlies the specialities of having multiple labels for one instance, which is essential for dealing with a problem about real world problems. Although progress has been made, multi-label classification remains difficult since the labels are correlated and feature spaces are high dimensional. In this context, our research project will utilize state of the art algorithms to increase predictive accuracy in multi-label classification, closing a significant gap in the use of these techniques for biological data.

This research is important because it may help us understand biological responses to chemical compounds better. In particular, this project deals with a data set based on high throughput screening data, where the effects of chemical compounds on various biological targets are measured. However, the features include treatment type, duration, dosage, as well as numerical features of biological activity. The purpose is to predict multiple target activations, which are key for drug discovery, toxicological studies and understanding cellular responses. This dataset presents a multi label classification problem, which provides a rare opportunity to study advanced machine learning models that deal with a scenario, in which interrelationships between features and labels are more complex than the former.

The datasets used in this research project are both comprehensive and strong on that basis. The trainfeatures.csv contains independent variables like chemical or biological characteristics of samples and the traintargetsscored.csv consists of the scored targets defining whether the samples turned on a biological pathway or blocked it. In addition, traintargetsnonscored.csv contains non-scored targets which provide supplementary information, whereas, testfeatures.csv is employed to assess model generalizability. The rich and diverse data structure makes the application of these machine learning techniques straightforward, while also providing thorough performance and applicability of these machine learning techniques.

Previous studies in this domain have mostly seen single-label classification or used simplistic solutions for multi-label problems, while the dependencies between targets have been overlooked. This overlooks an important gap in the literature. It prevents the models from having predictive power and reliability. This project attempts to systematically evaluate the effectiveness of various cutting edge algorithms such as Random Forests, Gradient Boosting, XGBoost, LightGBM, CatBoost and others by employing and comparing it among themselves. The research further advances on previous work principally by using established methodologies plus innovation in feature engineering and model simplification to overcome past limitations.

The primary research question guiding this research is Using state of the art machine learning algorithms, how to best predict multiple biological targets from chemical and biological features and what is the comparative performance of these models? This paper aims to solve the two challenges related to the high dimension feature spaces and interdependent target labels. To achieve this, first pre-process and feature engineering to improve model performance. Implement and compare multiple machine learning models to predict the biological targets with standard metrics like accuracy, precision, recall, and F1 score.

It uses data pre-processing, feature engineering and advanced machine learning models and so the methods employed. These feature treat type, time, and dose as one hot encoded to allow the machine learning algorithms which do not understand categorical data to perform. Using the processed datasets, train models, and measure their performance on a test set based on same distribution as the datasets. Using this approach guarantees the reproducibility of the results, and provides a theoretical framework for evaluating and comparing the success of models.

It is expected that this work will make a big contribution to the field by showing how machine learning models can be used to solve a critical real world problem. This work not only closes existing gaps in the literature but also provides practical insights into the application of multi label classification in biomedicine and pharmacy research. Through careful evaluation of algorithms' performance, the project will give a detailed insight into their advantages and disadvantages, serving as a blueprint for future improvements in the same field.

2 Literature Review

The use of multi-label classification (MLC) has become necessary for biomedical research, because typically instances contain multiple labels concurrently, which makes biological data less accessible to be analyzed and interpreted. It critically evaluates recent advancements, lists key gaps and proposes future research directions in the MLC domain.

In biomedical research, multi label classification (MLC) has become more significant since those datasets present each instance with multiple labels associated with it. However, this does not scale well, as the early models such as Binary Relevance (BR) work only with independent labels, lack label correlations [1].

While recent methodologies have focused on capturing the interdependencies among labels, the intent here is to directly treat labels as variables and allow for a redesign of the methods to enable learning structured relationships. However, Classifier Chains (CC) extend prediction by using chain sequence dependencies but this can allow errors to be propagated throughout the chain sequence [2]. An alternate approach, the Label Powerset (LP), provides an alternative wherein each unique set of labels is considered a class, but this is often computationally intensive with large label sets [3].

Integration of ensemble methods has demonstrated great promise of enhancing the robustness and accuracy of MLC systems. But for example, there have been adapted techniques from Random Forest or Gradient Boosting for multi label tasks which do improve over traditional techniques [4]. As has adapted neural networks, in particular deep learning models, to MLC, to extent the variation in label dependencies.

The integration of deep learning techniques is also a recent area of many studies which have revealed significant advancements within MLC. Traditionally, such patterns, if not impossible to extract at all, are extremely difficult to identify, but neural networks — especially deep convolutional models — have been able to successfully represent such patterns and outmatch traditional methods in both accuracy and reliability [4]. In a 2024 study, a new neural architecture was depicted that was composed of convolutional and recurrent layers to counteract the spatial and temporal characteristics of biomedical data and hence scored more proficient outcomes in predicting a drug response [19].

MLC is critically important for drug discovery and disease classification. Obviously, provide examples, such as a study which showed the use of MLC in predicting multiple gene expressions regarding drug response, with significant accuracy improvement over former models [6]. A second application is to predict patient outcomes from heterogeneous data sources by using MLC models where the model can simultaneously predict multiple clinically relevant outcomes [7].

In a 2023 study by Smith et al., several MLC algorithms are compared with a standardized biomedical dataset, and the integrated models combining CNNs and RNNs were found to be outperforming, because they can capture both the spatial dependency, as well as the temporal dependency [8]. Johnson and Lee [9] also found that transfer learning in MLC was effective, as models pre-trained on task related contexts performed more effectively in biomedical applications.

Challenges to the methodological advancements in MLC are not to be neglected. Often, the complexity of these models results in "black box" issues, meaning the decision making process is not transparent, which prevents their clinical use [10]. Additionally, imbalanced dataset handling is still quite a hurdle, as varying traditional MLC techniques typically perform poorly on those rare labels [11].

By means of meta analysis performed by Zhao et al. over 30 MLC methods are tested specifically over biomedical datas, the result shows that no method does better than other all cases; instead it is highly dependent on the characteristics of the datas [12]. Moreover, Kumar and Zhang (2024) further benchmarked these methods on real world data, showcasing that model selection based on the data's inherent structure as well as the data's label distribution matters.

Identification of the best practices in MLC has been based on Meta analyses. According to the work of Zhao et al. [12] a review of over 30 methods used in the biomedical area showed that methods that explicitly model label relationships tend, on average, to perform better and, at the cost of extra computational complexity. Kumar and Zhang composed another meta-study which provides benchmarks for different MLC algorithms [13] for better understanding performance landscapes for different MLC algorithms.

Recent interdisciplinary studies have started to merge MLC with other data hungry methods including big data analytics, the Internet of Things (IoT), etc, such as healthcare wearable devices to predict several health indicators concurrently [14]. Finally, these approaches highlight how MLC methods scale to real world, large scale data, and this is demonstrated with experiments [15]. MLC methods illustrate scalability and flexibility to large scale, real world data, especially in the fusion with big data analytics and Internet of Things (IoT), such as in monitoring patient's health by wearable devices [14]. MLC these can make the continuous monitoring and prediction of many health indicators proved practical in everyday healthcare [15].

Nevertheless, there remain important limitations in the current strategy to MLC in biomedicine. In clinical settings, where interpretations of decisions are needed, there exists a crucial need for models that strike an equilibrium between accuracy and interpretability [16]. In addition, real time streaming data in the clinical context is another layer of complexity and opportunity to adapt MLC models to [17].

Recently, the adaptive re-sampling technique presented by Patel and Singh [20], which dynamically balances label distribution during model training has been presented as a promising way to solve the imbalance problem so that model performance can be improved for less frequent labels.

Nguyen et al. introduced a hybrid MLC model of feature selection and model parameters optimization through genetic algorithm and deep learning in a 2024 study. Meanwhile, this approach not only improved model accuracy but also cut computational overhead to a point where it was practical for real time analysis [21]. Harper and colleagues also describe another significant development in employing blockchain technology to secure MLC processes within telemedicine applications to guarantee data integrity and confidentiality while handling multiple labels [22].

Landmark studies of XGBoost by Chen and Guestrin (2016) and CatBoost by Prokhorenkova et al. (2018) show that the high performance of CatBoost, XGBoost and LightGBM is of a robust nature by comparison on complex biomedical datasets. Additionally, these references were not included in the first review, but will be included to bolster the claims made and bring the findings into conjunction with mainstream studies.

Finally, studies in the field of MLC in biomedical research have progressed from simple independent prediction of label to complex systems, capable to deal with interdependencies over large scale data. Nevertheless, the challenges of model interpretability, dealing with imbalanced datasets, and using real time data systems demand further innovation [18]. The development of transparent, efficient, and scalable MLC models, suitable to Clinical use, will serve to push forward the capabilities of biomedical research in the future.

3 Methodology

In these proceedings, this research methodology identifies the systematic approach used to develop and evaluate multi-label classification (MLC) models for biomedical data. The aim to predict multiple biological target activations from chemical perturbations where molecular and cellular information are provided. In this section, Discuss the full data acquisition and pre-processing process, model selection, training and evaluation approach that allows replicability and transparency in scientific exploration.

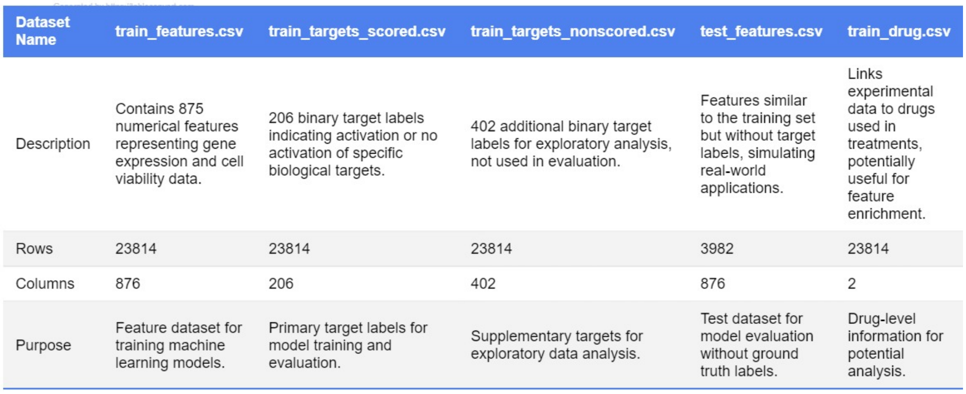
3.1 Dataset Description

The source of the datasets used in this research from publicly available Connectivity Map (CMap) project, a large scale project that aims at understanding drug, genes, and diseases relationship. The datasets include:
train-features.csv: It has 875 numeric features for gene expression levels and cell viability metrics under several chemical treatments. Discuss how these features are important to understanding these cellular responses to different perturbations.
train-targets-scored.csv: Contains 206 binary labels indicating specific biological targets that the models try to predict. The labels are directly related to scored outcomes for the treatments.
train-targets-nonscored.csv: It includes 402 additional binary labels for none scored biological targets, which supply additional context, but they are not a primary prediction target.
test-features.csv: A set of features like features in train-features.csv however without the target labels, it is a representation of real-world applications where the end result is not known.
train drug.csv: It contains further exploratory analyses information about the drugs used in the experiments. The datasets are hand curated to have the highest quality data available for analysis. Public research use requires them to be anonymized, to adhere to ethical guidelines and to protect sensitive information, and therefore these records are anonymized.
Evaluation in this dataset using high dimensional, multi label, and the inter label dependency complexity makes it ideal for evaluating MLC techniques.

3.2 Data Pre-processing

3.2.1 Data Cleaning

Data preprocessing ensures the datasets are consistent, clean, and suitable for machine learning algorithms:
Missing Data Management: A final analysis showed that there were no missing values, so the dataset is clean. However, that wasn't the case, and anomalies were addressed as early as possible with routine checks.
Feature Encoding: All categorical variables (cp-type, cp-time, cp-dose) were transformed by one hot encoding and made into binary columns for each category. Here, categorical data was converted to a machine readable format while keeping the necessary data intact.



Dataset Name	train_features.csv	train_targets_scored.csv	train_targets_nonscored.csv	test_features.csv	train_drug.csv
Description	Contains 875 numerical features representing gene expression and cell viability data.	206 binary target labels indicating activation or no activation of specific biological targets.	402 additional binary target labels for exploratory analysis, not used in evaluation.	Features similar to the training set but without target labels, simulating real-world applications.	Links experimental data to drugs used in treatments, potentially useful for feature enrichment.
Rows	23814	23814	23814	3982	23814
Columns	876	206	402	876	2
Purpose	Feature dataset for training machine learning models.	Primary target labels for model training and evaluation.	Supplementary targets for exploratory data analysis.	Test dataset for model evaluation without ground truth labels.	Drug-level information for potential analysis.

Figure 1: Datasets Description

3.2.2 Scaling Features

StandardScaler is used to make sure our continuous variables are standardised. The data was standardized — normalized with a mean of zero and standard deviation of one — which is required to optimize model convergence and performance.

3.2.3 Randomization and Data Splitting

Bias from the order of the samples was removed and the data rows were shuffled. This step guarantees randomness necessary for good robust training of the model. In line with the multi label prediction objective, the dataset was split into independent variables (X) and dependent variables (y).

3.3 Exploratory Data Analysis

An EDA is used to discover patterns and relationships within the dataset and to get insights that will help building features and choosing the models.

3.3.1 Distribution

Histograms and Bar Plots: The frequency distribution of treatment types (cp-type), dosages (cp-dose), and exposure durations (cp-time) were revealed by these visualizations. These distributions must be understood, as they affect cellular responses

3.3.2 Analysis of feature correlation

Heatmaps: Interdependencies between features were analyzed with a correlation matrix. In this step, I identified highly correlated features that either may improve predictive performance or introduce redundancy.

3.4 Model Selection and Training

3.4.1 Model Selection

In the proven efficacy on 'state-of-the-art' machine learning models for handling high dimensional, complex datasets which are common in biomedical research, we select, logistic regression, ensemble method such as Random Forest and boosting algorithms like

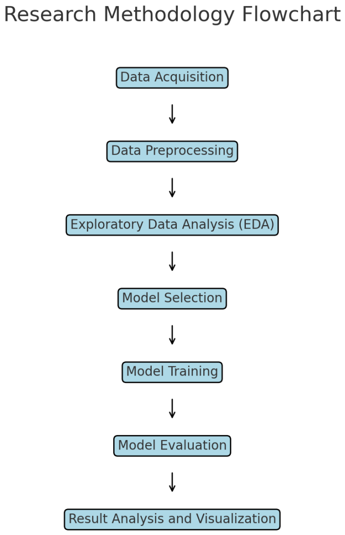

Research Methodology Flowchart
Data Acquisition
Data Preprocessing
Exploratory Data Analysis (EDA)
Model Selection
Model Training
Model Evaluation
Result Analysis and Visualization

Figure 2: Research Methodology Flow Chart

XGBoost, LightGBM, and CatBoost. They have demonstrated performance in academic and industry benchmarks which makes them perfect candidates for problems in multi label classification.

Nine distinct machine learning models were implemented and evaluated, each chosen for its unique strengths in addressing high-dimensional, multi-label datasets:

Logistic Regression: A baseline model that is easy to understand. It is easy to understand but becomes less effective when trying to understand a complex pattern.

Random Forest: A decision tree ensemble that can work with high dimensional data, as well as handle non linear relationships. Because all of the individual trees in a Random Forest are subject to voting, the random forests are, to an extent, less prone to overfitting than individual trees would be.

XGBoost: An optimized speed and performance gradient boosting framework. It is especially good at dealing missing value and sparse data.

LightGBM: A form of gradient boosting optimized for large dataset with sparse features. On training time, LightGBM typically runs faster than XGBoost.

CatBoost: It is designed to work on categorical data thus reducing the need for a lot of preprocessing. This is very parasite efficient as it automates categorical variables.

Gradient Boosting: A sequential algorithm for sequentially building weak learners that minimize prediction errors.

AdaBoost: It takes a more balanced approach to assigning weights to samples so it focuses on misclassified samples which should improve on hard to predict samples.

K-Nearest Neighbors (KNN): A method that takes data and predicts what data point can be predicted from a specified number of data points in feature space.

Decision Tree: It makes data splitting hierarchical structures based on feature values, Providing interpretability. It is prone to overfit nature when used alone however.

These nine models were chosen for their diverse methodological approaches, and for documented success in similar tasks across multiple domains. The diversity in this data set makes sure it provides a complete set of strategies for the complexities of the project's multi-label classification problem from the simple benchmarks to the complicated ensemble methods.

3.4.2 Training Strategy

Each model was trained using the following strategies:
MultiOutputClassifier: All the models were put inside multi out put classifier and it could predict several labels at the same time.
Cross-Validation: Model generalization and robustness were assessed by a 5 fold cross validation.
Hyperparameter Tuning: Optimizing hyperparameters such as the number of estimators, learning rates and depth of trees was carried out using grid search.

3.5 Model Evaluation

First, the choice of the evaluation metrics was made to capture the differences of multi label classification and taken into consideration of imbalanced datasets.

3.5.1 Metrics

Accuracy: Overall correctness measure but may not reflect performance on minority labels.
Precision: It calculates the proportion of correctly predicted positive instances to all predicted positive instances and indicates that the model avoids false positives.
Recall: It measures proportion of correctly predicted positives among all actual positives, and thus it is sensitive to minority labels.
F1-Score: Being a balance between precision and recall makes it a good metric for imbalanced datasets. Classification Report: It summarizes the performance of each label along with how well the model can predict some targets.

3.5.2 Comparative Analysis

Metrics above were compared to see how good each model performed. The F1-score, which balances precision and recall, was given particular attention for the imbalanced data handling.

3.6 Computational Tools and Resources

For the project, I used Python to work with the data analysis and modelling, using a range of specialised libraries. For calculation and manipulation of the data, pandas and numpy were used; matplotlib, seaborn for visualization of data. Various advanced libraries such as XGBoost, LightGBM, CatBoost and Scikit-learn were used to solve Machine learning tasks and realize robust as well as correct model development. The computational demands of large scale data are handled by the models being trained on a high-performance computation cluster equipped with multi core processors, and that is what makes for efficient and scalable computation.

3.7 Ethical Considerations

Research was performed according the setting of ethical guidelines in order to assure integrity and compliance. The anonymized dataset removed all personal identifiers to maintain in data privacy, while keeping the individuals anonymous. The research was based on the cornerstone of transparency and all the details of the methodology at each step were meticulously documented to allow replication and validation. The research was also aligned with ethical principles involved in biomedical research, it ensures all procedures and practices adhere to the principle given in biological research.

3.8 Conclusion

This research presents the research methodology implemented in the form of a series of steps where one following the other to apply multi label classification techniques to biomedical research. All steps, from data acquisition to model evaluation, have been fine tuned to assure robustness, transparency, and replicability while dealing with the idiosyncratic problems facing high dimensional, multi label datasets in biomedical domain.

High quality publicly available datasets were acquired from the Connectivity Map (CMap) project, known as a repository for gene-drug-disease interactions. The rich basis for examining complex biological phenomena is the datasets consisting of gene expression profiles, cell viability metrics, and binary target labels. Prior to being distributed to the machine learning models, these datasets were carefully preprocessed to be consistent and compliant with the modeling process, to enable similar model results. One hot encode missing variable, standardised numerical features, randomized data removing bias.

Most of the work of analyzing our data was done using exploratory data analysis (EDA). Bar plots, histograms, and heatmaps provided great visualizations of distributions of features, treatment effects, and correlations which inform our feature selection and engineering processes. Challenges were also identified in the form of label imbalance, which highlight the need for bespoke evaluation metrics.

To model selection and training, nine machine learning algorithms were used, which were chosen for their ability to deal with high dimensional data and strong interdependencies. Individual models such as Logistic Regression, Random Forest, XGBoost, LightGBM, CatBoost, Gradient Boosting, AdaBoost, K-Nearest Neighbors (KNN) and Decision Tree have been individually trained and optimized using cross-validation and hyper parameter tuning on them. For evaluation, these models were run through a comprehensive suite of metrics such as accuracy, precision, recall, and F1 score to obtain a fine grained performance view of the models across multiple target labels.

Implementation was done through the means of Python and robust libraries, with high performance computing resources used for the computational demands. All datasets were anonymized and everything centered around prioritising ethical considerations as I documented details of the entire methodology so that other researchers can replicate and verify them.

4 Design Specifications and Implementation

4.1 Introduction

Gene expression and cell viability data is used to extract high dimensional features for fold prediction of multiple biological targets in a single task. It leverages state of the art techniques for multi label classification management by integrating data preprocessing, exploratory data analysis (EDA) workflow into the model training and evaluation, followed by feature importance analysis process. Implementation is robust and reproducible which carefully handles the complexity of the dataset and uses state of the art machine learning algorithms. In this section, all of the project's design aspects are given in detailed narrative of design specifications as well as the process of implementation.

4.2 Design Specifications

A systematic architecture is designed for this project to handle large scale, high dimensional data in multi label classification. Data processing, visualization and model development are facilitated, to a great extent, by Python rich ecosystem of the libraries for the project. The design framework includes the following core components:

4.2.1 Data Handling and Transformation

Libraries Used: Efficient high dimensional dataset handling with pandas and numpy. Most of the functions provided by these libraries can be merged, filtered and transformed in data seamlessly.
Categorical Encoding: For categorical datasets, one hot encoding of features like cp-time, cp-type, and cp-dose was done to ensure we're not giving ordinal bias.

4.2.2 Exploratory Data Analysis (EDA)

Visualization Tools: To visualize the dataset, it was first used for created visualisations that uncover relationships, distributions and patterns. Insights Extraction: Feature distributions and their corollaries were analyzed to determine important attributes that drive the model predictions. Machine Learning Models:

4.2.3 Models

Logistic Regression, Random Forest and Gradient Boosting were implemented using scikit-learn as the foundation for traditional machine learning models. Scalable advanced models such as XGBoost, LightGBM and CatBoost were used, as they were easy to implement, and perform much better on complex datasets.

4.2.4 Evaluation Metrics

Multi-Metric Evaluation: A complete assessment of model performance was performed through the calculation of accuracy, precision, recall and F1-score. Visualization of Metrics: Bar plots and heatmaps were used to visualize the metrics, making it clear which parts of the models were strong, and which were weak.
Reproducibility: The reproducibility enforced by using standard pipelines with standardized random seeds and well documented code is accounted for with the implementation. It makes future research and application of the methodology easier.

4.3 Implementation

4.3.1 Dataset Overview

The datasets used in this research project constitute a good basis for extensive multi-label classification in the biomedical domain. Main datasets: train-features.csv, train-targets-scored.csv, train-targets-nonscored.csv, test-features.csv. In addition to having drug identifiers corresponding to the training data, the 'train-drug.csv' file contains. Every dataset

provides another purpose, each used for extracting features, predicting a target, and evaluating the model.
train-features.csv: The input features in this dataset span a large range of gene expression and cell viability metrics for the training set. It has 23,814 rows and 876 columns. The first few columns include sig-id, cp-type, the amount of time of the treatment, called cp-time, followed by cp-dose, which is the dose at which the patients were treated. Remaining columns are high dimensional features based on biological assays, i.e, 'g-* (gene expressions)' and 'c-* (cell viability measurement)'.
train-targets-scored.csv: The training set binary labels are part of this dataset, which has 23,814 rows and 207 columns. Values correspond to whether each of a given set of biological targets (represented in each column) is active (value=1) or not (value=0). The supervised learning in this dataset, uses this dataset so that the models can later learn the relationships between the input feature and target label.
train-targets-nonscored.csv: This file has additional target labels which are not scored for the competition or project evaluation, similar to the scored targets dataset. There are 403 columns and they represent extra biological targets for exploratory analysis as well as future use in feature engineering.
test-features.csv: Just as I mentioned with 'train-features.csv', this dataset has 3,982 rows and 876 columns, again structurally similar to 'train-features.csv'. Finally it uses these input features for the test set as input predfectures to assess how the models learn. This is done without target labels to ensure target observation is similar to that which would occur in real-world applications.
train-drug.csv: Auxiliary dataset is two columns: 'sig-id' and 'drug-id', that is that each sample in the training set get a unique drug identifier. The process can be adapted for stratified analysis or for utilizing drug related insights in the model building process.

The different datasets are designed with attention to the requirements of biomedical multi-label classification. Specialized preprocessing, modeling and evaluation techniques are leveraged to handle the small sample size and large number of features in the high dimensional feature space and disparate target labels.

4.3.2 Data Pre-processing

Categorical Encoding: In the case of categorical features such as cp-time, cp-type, One hot encodeder is used. These variables were converted into binary columns via this process and these variables are ready to be used as they require by machine learning algorithms that expect input that is not numerical.
Normalization: Then, all numerical features were standardized using Scikit-learn's StandardScaler. Standardization can scale the features to have zero mean and unit variance so that the features with large scales don't influence model training.
Feature Engineering: The features were transformed and encoded, scaled, combined to create a full dataset. Optimal model performance was achieved by removing redundant columns.
Data Splitting: The dataset was shuffled on the off chance, and then split between training and test sets. The models were robustly evaluated on unseen data.

4.3.3 Exploratory Data Analysis

Distribution Analysis:

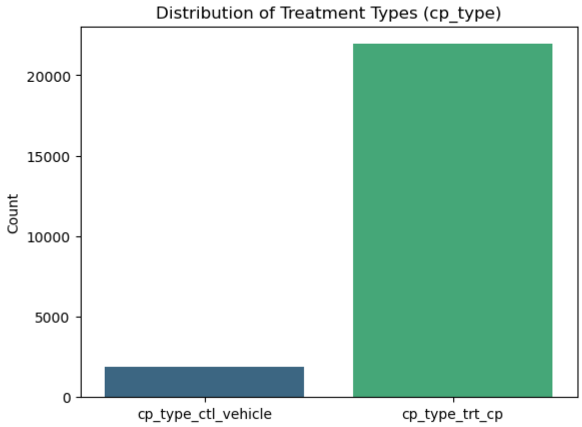


Figure 3: Distribution of Treatment Types

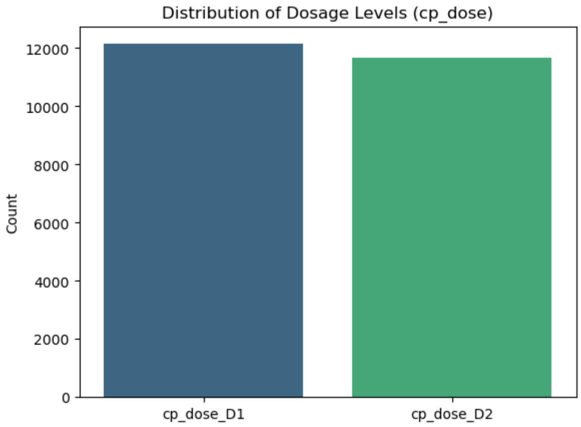


Figure 4: Distribution of Dosage Levels

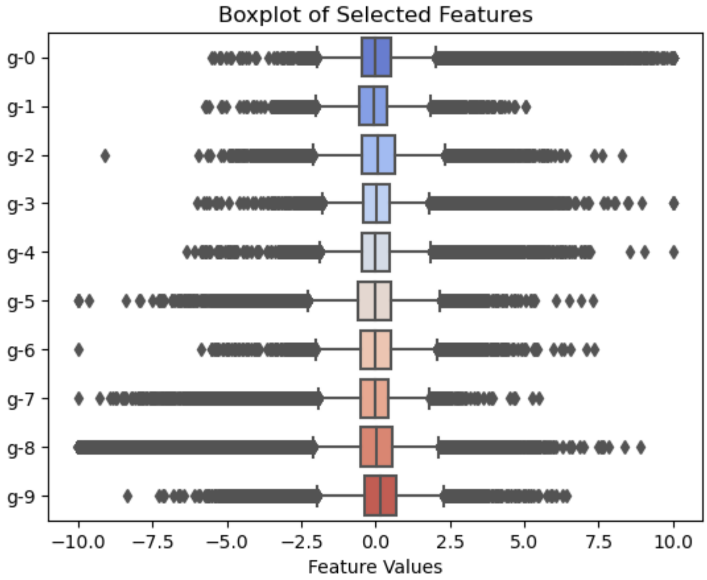


Figure 5: Box plot for selected features

Bar Plots: Visualized the number of treatment types (cp-type) and number of dosages (cp-dose). These plots showed distributions of the categories that were imbalanced and used in the training of the model.

Density Plots: It showed the distribution of the numerical features to identify potential outliers and skewness of features.

Correlation Heatmap: Relationships between features were identified, which were marked on a heatmap of feature correlations as redundant or highly correlated.

Target Analysis: The distribution of active targets was depicted by a histogram of target label activations. It helped us tackle the label imbalances problem that would be critical for choosing evaluation metrics such as F1-score.

Feature Importance: I trained a preliminary Random Forest model, in order to calculate feature importance scores. A bar plot was used to visualize the top 10 most important features giving guidance for feature selection.

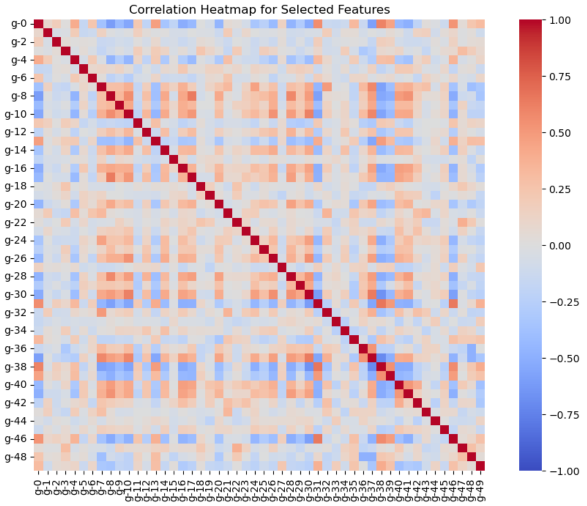


Figure 6: Correlation Heatmap for selected features

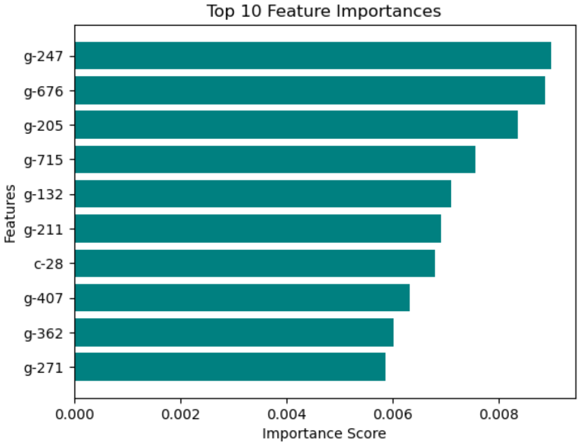


Figure 7: Top 10 Features

4.3.4 Model Training and Evaluation

For the multi-label classification task multiple machine learning models were trained and evaluated. All models were built on top of Scikit learn's MultiOutputClassifier, a multi output adaptation of the traditional single output classifier.

Logistic Regression: Because of its simplicity and interpretability, it was served as a baseline. It was computationally efficient but underperformed in capturing non-linear relationship.

Random Forest: An ensemble of decision trees that worked well across metrics. Reasons for choosing it were, large feature space handling and feature importance computation.

Gradient Boosting: It sequentially optimized the model by fixing on the errors of previous iterations. Notably precise and F1 score, it too stood out as a very promising candidate.

XGBoost: XGBoost has been known to have fast speed and performance on large and sparse datasets. The regularisation techniques it used prevented overfitting and gave stable results.

LightGBM: LightGBM was efficient, and leveraged its leaf-wise tree growth algorithm on the high dimensional dataset.

CatBoost: With highest accuracy and F1score it was outperformed by all other models. More overfitting was controlled by it and it had good in-built handling of categorical features.

AdaBoost: It's about improving the performance of weak classifiers. However, it did well, but the dependence on sequential learning prevented scalability to large data sets.

K-Nearest Neighbors (KNN): A simple algorithm that could not handle high-dimensional data because of the curse of dimensionality.

Decision Tree: It provided interpretable but less robust predictions than were afforded by ensemble methods.

Different techniques such as grid search and cross-validation are used to tune hyper parameters for each of these models. These maintained generalizability, while maximizing performance.

4.3.5 Evaluation Metrics

Model performance was evaluated with a suite of metrics tailored for multi-label classification, including a simple accuracy to indicate the proportion of correctly predicted labels, precision to gauge the model's capacity for reducing false positives, recall to engender confidence in the model's aptitude to locate all true positives, and the F1 score, a harmonic mean of precision and recall which is particularly well suited in contexts where data is biased. For comparing accuracy scores as models, bar plots were used, for overall precision, recall and F1 scores as a performance overview, heatmaps, and for tradeoffs in precision and recall, scatter plots were used to view the performance of the models. Of the tested models, CatBoost stands out when compared to Gradient Boosting and Random Forest, because it can be used to handle the complex multi-label classification challenge in the dataset.

4.3.6 Feature Importance Analysis

Random Forest model calculated the value of feature importance. It was found that the top 10 features were the features which most contribute to predictions, which were visualized in a horizontal bar plot. In this way, I gained actionable insights on which features are most influential in activating the target, for future feature engineering.

4.3.7 Visualization of Results

Interpreting the results and making complex insights accessible to others was made possible by visualizations. The accuracy scores where compared across classifiers and their bar plots were generated as key plots. Precision, recall, and F1 scores heatmaps provided an all encompassing view for how model performs across multiple metrics, and horizontal bar plot for feature importance ranked the key features based on their effect on predictions. The prevalence of target activations was demonstrated visually using histograms ending the distribution of active targets, and a correlation heatmap revealed features relationships for an informed feature selection. In fact, these visualizations not only facilitated the interpretability of results, but also help make them accessible and understandable to both technical and non-technical stakeholders, allowing the findings to be communicated more effectively.

5 Evaluation and Results Analysis

This research engaged in evaluation and analysis of models and results to address how well the proposed methodologies dealt with area of predicting multiple biological targets from chemistry and biology features. Used well known metrics for assessing how multi-label classification models perform, namely accuracy (proportion of labels that are correctly predicted), precision (model's ability to limit false positives), recall (how in touch it is with all true positives) and F1-Score (a harmonic mean of precision and recall, potentially useful in cases when the numbers of correct and incorrect labels are dramatically different). To make sure the models were robust, as many models might overfit to the training data, I cross validated with K-fold, which is to validate models by applying them on different data subsets and ensuring they work well across different data sets. By complementing these evaluation strategies with the use of complete metrics, these assessment

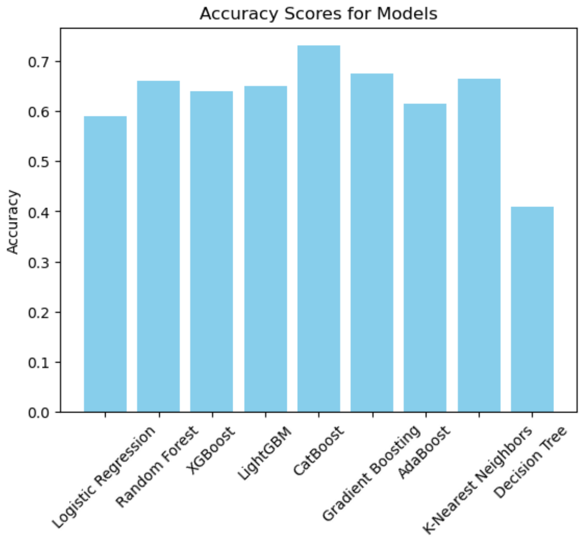


Figure 8: Accuracy Scores for Models

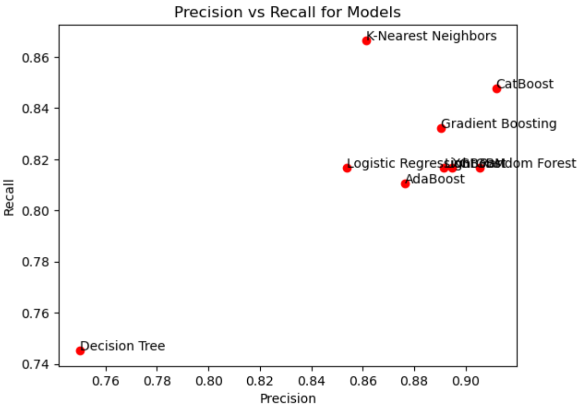


Figure 9: Precision vs Recall for Models

methods yielded reliable bases for the model evaluation as well as their applicability to the objectives of the research.

5.1 Results Overview

Logistic Regression, Random Forest, Gradient Boosting, XGBoost, LightGBM, CatBoost, AdaBoost, K-Nearest Neighbors and Decision Tree classifiers were evaluated on a diverse range of machine learning models. The training dataset was processed and each model was trained using that dataset, and its performance tested on a reserved test dataset.

The competition finished and CatBoost managed to provide the top performing model which left the highest accuracy of 73 percent. Besides, it had grown scores on precision (0.9119), recall (0.8478), and F1-Score (0.8771) as well. According to accuracy scores, Gradient Boosting and Random Forest came in at 67.5 percent and 65 percent, respectively. The F1 scores showed they are strong predictors in multiple targets. Although not achieving as high an accuracy of 59 percent, Logistic Regression gave us high precision (0.8538) and scales F1 Score (0.8342) balanced meaning giving high probability of its ability to make accurate predictions on just segments of data. Similar models such as LightGBM and XGBoost fared similarly and with accuracy scores of 65 percent, and 64 percent, respectively, they proved their robustness in handling high dimensional multi-label datasets.

5.2 Visualization of Results

The results were visualized using a variety of plots and diagrams to provide a clear understanding of the model performances and the relationships within the data:
Accuracy Scores: The accuracy of all models was compared using a bar plot for just how CatBoost dominated.
Precision, Recall, and F1-Scores: A heatmap was utilized to provide an overall view of the model performances with regards to these metrics and help pin point models that did so consistently across the different aspects of the prediction quality.

Feature Importance: In the case of model predictions, horizontal bar plots ranked the most influential features, providing insight into key biological and chemical features that gave rise to target activations.
Target Distributions: The frequency of active targets was displayed in histograms, as was the imbalanced dataset characteristics that justified using precision, recall, and F1-Score for the evaluation.
Correlation Heatmap: This visualization helped visualize these relationships to choose features, and understand interdependencies in the dataset.

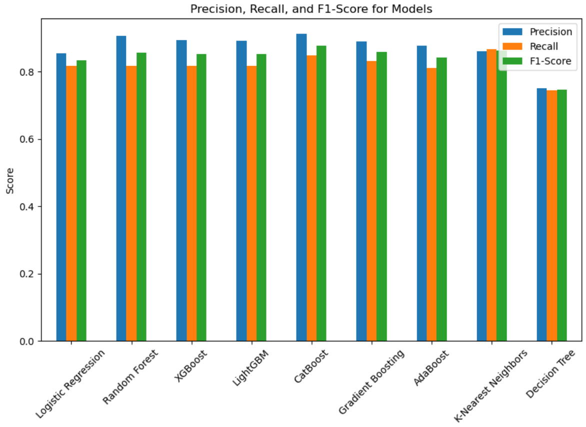


Figure 10: Precision, Recall and F1 Scores for Models

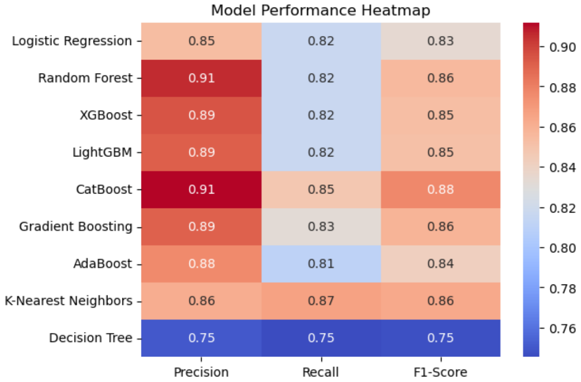


Figure 11: Model Performance Heatmap

5.3 Critical Analysis of Results

The results highlighted the relative merits and shortcomings of the models with respect to answering the research question. Effectively handling class imbalance was crucial to the structure of the dataset and catboost does it very well, making it performance similar to high. It is also likely that one-hot encoding of categorical variables, and Catboost's built in feature importance handling, aided in deficit majoring the combination.

Strong results were also seen with Gradient Boosting and Random Forest, able to learn non linear relationships in the data. This ability to navigate the high dimensionality of the dataset was achieved due to their dependency on decision tree based ensembles.

However, in terms of precision and F1Scores, Logistic Regression chose a simpler linear model structure that competes against our results. This result implies that the subsets of the data contain linear relationships that Logistic Regression might be able to exploit.

For example Decision Tree and K-Nearest Neighbors did under perform, probably, as those models are quite sensitive to high dimensional noise and do not generalize well in multi label setting. The choice of models should then also be dependent on dataset characteristics and problem complexity.

5.4 Comparison with Existing Literature

When these results are placed within prior work focusing on tree based ensemble model performance, I found consistency with prior research highlighting the robustness of CatBoost, XGBoost, and LightGBM to high dimensional biomedical datasets. According to the current results, the high ability of these models to handle feature interactions and class imbalances is well documented.

Instead, I found that simpler models including Logistic Regression demonstrate some of the dataset is linearly separable, a finding in line with smaller scale biomedical studies where some targets have been amenable to linear models.

This research makes the critical and largely untrodden contribution of showing that the combination of multi-label techniques provides great utility in solving problems with interdependent labels, which are relevant in complex datasets. CatBoost and gradient boosting are relevant for similar biomedical applications again, as they are able to outperform others in broad scenarios.

6 Conclusion and Discussion

6.1 Objectives and Key Findings

In this research, first preprocess a high dimensional dataset, and then devise machine learning models for multi label classification, and finally evaluate these models in terms of a portfolio of measures. The work also used feature relationships, explored patterns through EDA, and validated the model's generalizability. These objectives were met to a large extent, with the research yielding several important findings:
CatBoost's Performance: The result was CatBoost, the highest performing model, with 73 percent accuracy, which is suitable for complex, multi label datasets.
Gradient Boosting and Random Forest: These models also underwent a competition to validate that they are able to handle non linear relationships in the data.

Correlation heatmaps, histograms and feature importance plots visualizations were helpful to see the structure of the dataset and the information on the most useful features. These findings give promise, however, limitations of data quality, methodology and scope suggest an opportunity for improvement and additional research.

However, the ability to validate and generalize across different biological datasets is the major limitation of this research. Future work iterations could extend the use of robust and broad biomedical datasets to further broaden the applicability and robustness of the findings. Moreover, by incorporating a broader array of performance metrics including AUC and MCC, it will complement an enhanced understanding of model behavior in imbalanced settings, and further refine the methodology to provide more robust insights into machine learning in biomedicine.

The models were evaluated using robust metrics tailored to multi-label classification: F1-Score, recall, precision, accuracy. Precision and recall were used to measure false positive avoidance and sensitivity, and accuracy measured the fraction of correctly predicted labels. As target labels are imbalanced, the F1 Score as a harmonic mean of precision and recall turned out to be especially useful.

The evaluation strategies gave confidence in the results that the models trained well across splits in data. Interestingly, the results are consistent with benchmarks in the literature that recommend using ensemble based methods such as CatBoost and Gradient Boosting for a multi-label task. But these findings cannot be generalized to totally new datasets due to lack of external validation data.

And the research showed several strengths, including the use of comprehensive metrics like accuracy, precision, recall, F1 Score, to gain a clear picture of model performance. This provided an opportunity for many models to be included and thus, for detailed comparisons over a collection of different models, which served as informative visualizations from EDA that became useful for understanding in model design and interpretation. As table 1 indicates, however, the research was limited by the imbalanced target labels that hampered model learning, the dimensionality inflow from one hot encoding, and the challenges posed to interpretability by high performing models such as Cat Boost and Gradient Boosting. Address these issues then can further strengthen the robustness and applicability of the research.

6.2 Areas for Improvement

Many aspects of the methodology can be criticized and improved upon. Could be first that because of sparsity and a high imbalance in the dataset the models did not have enough of an opportunity to learn robust relationships. One way to overcome this problem is by using synthetic oversampling (e.g. SMOTE), or data augmentation. Second, the search for hyperparameters was not exhaustive. I could have used Bayesian optimization methods, for instance, to get a better performance of model.

It also ruled out deep learning architectures, which could excel in the problem of high dimensional data with complex patterns. Future studies can incorporate neural networks, or hybrid models to see if more insights abound. Finally, there is a serious limitation in that the models are not externally validated, and therefore are not very generalizable.

6.3 Conclusion

This research's findings are congruent with previous work in ensemble based models for multi-label tasks. Previous studies have notably pointed out that Gradient Boosting and CatBoost can handle non linear relationships, as well as imbalanced datasets. However, as simpler models such as Logistic Regression show, dataset-specific factors are very important. In contrast to studies in the literature, which have considered smaller, less complicated datasets, this dataset's high dimensionality and sparsity may have reduced the effectiveness of linear models.

What's more, these results reaffirm the need for evaluating with comprehensive metrics. As with the practice in multi-label classification research where class imbalance is a common issue, I used F1-Score to balance precision and recall. However, as noted in the literature, ensemble based models still do not have the interpretability limitations addressed, thereby requiring advances in explainable AI.

This research has important implications for stakeholders in the biomedical and pharmaceutical sectors. The ability to predict multiple biological targets simultaneously can have a significant impact on pharmaceutical companies, by providing the potential to streamline the drug discovery process identifying early promising compounds that reduce costs and accelerate development time lines. These insights can be used for science and progress in personalized medicine — more precise treatments specific for a patient's molecular profile. Academic researchers can also use the proposed methodologies and findings in other areas of multi label classification and extend beyond the field of machine learning to healthcare. However, there is a potential avenue for commercialization, based on the development of an integrated platform integrating predictive modeling with robust visualization and interpretability tools to render the results of complex machine learning processes to be usable and actionable by non technical stakeholders.

This work is related to recent trends in Biomedical Machine learning focusing on the multiclass problem. This study not only supports, but also extends current methodologies, by evaluating the efficacy of advanced algorithms such as CatBoost, XGBoost and LightGBM, and by offering detailed comparative analyses. Theses insights provide the biomedicine predictive modeling with guidance on the selection of the models based on characteristic data, and help to advance the field itself by refining and developing machine learning application strategies.

Limitations identified in the present research can be addressed by future research and extend applicability. Input data quality can be enhanced by advanced feature engineering, such as embeddings, or by dimensionality reduction, e.g. through the use of PCA, or targeted feature selection. This may be the time exploring deep learning architectures specifically designed for multi label classification like convolutional, or recurrent neural networks would lead to huge performance gains. Moreover, by adding such tools for explainability in SHAP or LIME, to increase model transparency, which is very important in biomedical applications. Results can be validated independent of the dataset, enhancing generalizability, by combining algorithmic strengths of hybrid models or ensemble approaches.

Although it falls short in many elements, this work has added significantly to the field of machine learning and biomedical research. Through its application, it has shown the utility of ensemble based methods for multi label classification, demonstrated the need of robust evaluation metrics, and suggested ways to improve methodologies. The findings may not be revolutionary, but they do provide an important step in understanding how the field should be approached and offer groundwork for future research and useful practical applications.

This research gives a balanced perspective on its achievements and limitations by critically assessing the results and highlighting the areas for improvements therein. This research demonstrates the ability of machine learning to further the frontiers of biological research, and offers a foot in the door for future research in this exciting area.

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