VISVESVARAYA TECHNOLOGICAL UNIVERSITY

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DEPARTMENT OF COMPUTER SCIENCE AND ENGINEERING

A Project Report on,

"AIML-BASED DRUG RESPONSE PREDICTION USING GENOMIC AND CLINICAL DATA"

Submitted to partial fulfillment of the requirement for the degree of Computer Science and Engineering for the Academic Year 2025-26

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2025-26

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CERTIFICATE

This is to certify that the project work entitled **"**AIML-BASED DRUG RESPONSE PREDICTION USING GENOMIC AND CLINICAL DATA**"** is carried out **HANUMAGOUDA MALIPATIL (1SK23CS017), TEJAS C (1SK23CS050), TILAK KH (1SK23CS052), URVASHI TANWAR (1SK23CS055)** bonafide students of **Government Sri Krishnarajendra Silver Jubilee Technological Institute**, K R Circle, Bengaluru in partial fulfillment of **Bachelor's degree in Computer Science and Engineering** of the Visvesvaraya Technological University, Belagavi during the year 2025-2026.

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DECLARATION

We declare that this project report titled **AIML-BASED DRUG RESPONSE PREDICTION USING GENOMIC AND CLINICAL DATA** submitted in partial fulfillment of the degree of **B.E in Computer Science and Engineering** is a record of original work carried out by me under the supervision of **Prof. Asha V**, and has not formed the basis for the award of any other degree, in this or any other Institution or University. In keeping with the ethical practice in reporting scientific information, due acknowledgements have been made wherever the findings of others have been cited.

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ACKNOWLEDEMENT

I am grateful to my institution**, Government Sri Krishna Rajendra Silver Jubilee Technological Institute (GSKSJTI)**, for providing the facilities and inspiration that made this project a success.

My sincere thanks go to **Dr. Jagadish Kori**, Principal of GSKSJTI, for his valuable guidance, suggestions, and consistent encouragement throughout my project. His timely assistance was crucial to its completion.

I extend my heartfelt thanks to the entire faculty of the Computer Science and Engineering Department. Special thanks to **Dr. Nagaraj B Patil**, Professor and HoD of the CSE Department, for his confidence in me, support and invaluable guidance.

I also thank my academic project guide **Prof. Asha V**, Assistant Professor Department of CSE for her contributions in encouraging and guiding me to complete the committed work.

My gratitude also goes to the entire Computer Science Department for their collective help, guidance, encouragement, and cooperation during all stages of my project. Their support was instrumental to my success.

Last but not least, I thank my parents and friends for their moral support, and everyone who provided me with support, advice, and encouragement essential to the completion of this project.

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ABSTRACT

Advancements in genomics and precision medicine have enabled deeper understanding of how individual genetic variations influence therapeutic outcomes. However, traditional drug prescription methods still rely heavily on generalized treatment protocols, often failing to consider patient-specific genomic markers, which can result in poor efficacy, adverse reactions, and suboptimal clinical decisions. To address these limitations, this project develops an AI-driven drug response prediction system that leverages genomic data, machine learning, and molecular feature analysis to estimate patient-specific drug sensitivity.

The proposed system integrates multiple data sources, including genomic profiles, drug molecular fingerprints, and clinical indicators. A structured pipeline is designed to preprocess high-dimensional genomic data, extract drug descriptors using cheminformatics tools, and merge these heterogeneous features into a unified learning framework. Five supervised machine learning models—Logistic Regression, Support Vector Machine (SVM), Random Forest, Gradient Boosting, and XGBoost—are trained and evaluated to predict patient response in both regression (IC50 value prediction) and classification (responder/nonresponder) contexts. Among these, XGBoost consistently demonstrates superior performance due to its ability to handle complex nonlinear feature relationships and high-dimensional data.

The system is further enhanced with explainability techniques such as SHAP, enabling interpretation of key genomic contributors to drug sensitivity. Outputs are presented through a user-friendly interface capable of receiving patient data, visualizing predictions, and supporting clinically relevant decision-making. The proposed framework aims to support personalized treatment planning, improve therapeutic outcomes, and contribute to the development of smarter, data-driven healthcare systems.

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CHAPTER-1

INTRODUCTION

The increasing complexity of modern healthcare systems, combined with the natural biological diversity found across individuals, has created significant challenges in selecting the most effective drug for a specific patient. Traditional drug prescription practices rely heavily on generalized treatment guidelines, clinical symptoms, and trial-and-error approaches. As a result, patients often experience inconsistent therapeutic outcomes, delayed recovery, adverse drug reactions, or complete resistance to medications. These shortcomings arise because conventional models rarely consider a patient's unique genomic profile, gene expression levels, or molecular interactions that influence drug metabolism. The absence of personalized treatment strategies leads to high healthcare costs, prolonged hospitalization, and reduced quality of life for patients with cancer, chronic illnesses, and rare genetic disorders.

To address these challenges, this project introduces an AI-driven drug response prediction system that utilizes patient genomic data, drug molecular descriptors, and advanced machine learning algorithms. Genomic features offer rich insights into mutations, gene expression abnormalities, protein interactions, and biomarkers associated with drug resistance or sensitivity. With the integration of cheminformatics tools, drug molecular fingerprints can be extracted to study how drug structure influences therapeutic response. This allows the system to map complex relationships between patient genomes and drug properties more accurately.

Furthermore, the development of machine learning models such as Random Forest, Support Vector Machines (SVM), Gradient Boosting algorithms, Logistic Regression, and XGBoost enables efficient learning from large biomedical datasets. These models help identify patterns, classify responder and non-responder patients, and estimate drug potency using IC50 values. Predictive insights generated by such models support clinicians in selecting safer, more effective treatments while minimizing harmful reactions. In addition, explainability tools like SHAP enhance transparency by showing which genomic markers most strongly influence prediction outcomes. Ultimately, integrating artificial intelligence with genomic data paves the way for personalized medicine—where treatment plans are tailored to each patient’s biological characteristics.

1.1 Background and Motivation

Modern medical treatments often overlook the genetic variability that exists between individuals. Patients with similar clinical conditions may respond very differently to the same drug due to variations in gene expression, mutations, metabolic pathways, and protein interactions. Conventional treatment methods rarely account for these biological differences, resulting in unpredictable responses, treatment delays, or severe side effects. In oncology and chronic disease management, ineffective drug selection not only prolongs patient suffering but also increases the emotional and financial burden on families and healthcare institutions. With the increasing availability of biomedical datasets and advancements in computational biology, there is an urgent need for personalized, data-driven medical solutions.

Recent breakthroughs in artificial intelligence and genomics have created new opportunities to address these challenges. Genomic sequencing technologies generate detailed biological profiles of patients, while AI models can efficiently process these high-dimensional datasets to uncover hidden relationships. Machine learning algorithms can classify drug responders, predict IC50 values, identify drug-gene interactions, and analyze molecular structures using cheminformatics tools. These predictive capabilities allow healthcare providers to choose treatments based on scientific evidence rather than generalized assumptions. Additionally, explainable AI ensures transparency, enabling medical practitioners to understand why a certain drug is recommended for a patient.

The motivation behind this project stems from the global movement toward precision medicine—an approach that emphasizes individualized care using biological data and predictive modeling. By combining genomic analysis with advanced machine learning, this system aims to improve treatment accuracy, reduce adverse drug reactions, and increase patient survival rates. Moreover, it encourages responsible use of medical resources by avoiding unnecessary or ineffective therapies. As AI continues to influence medical diagnostics and treatment planning, this project demonstrates how data-driven insights can transform traditional healthcare into a smarter, safer, and more personalized system.

1.2 Problem Statement

Traditional drug prescription methods do not consider patient-specific genomic variations, resulting in unpredictable therapeutic responses and potential adverse reactions. There is a need for an AIbased predictive system that analyzes genomic data and drug molecular features to accurately forecast drug response, classify patients as responders or non-responders, and support personalized treatment selection.

1.3 Objectives

The key objectives of the project include:

1. **Predict Drug Response:** Accurately estimate patient-specific drug sensitivity using genomic biomarkers and molecular descriptors.
2. **Classify Responders and Non-Responders:** Implement supervised machine learning algorithms for binary drug response classification.
3. **Analyze Molecular Features:** Extract drug fingerprints and structural descriptors for enhanced prediction accuracy.
4. **Develop a Predictive Pipeline:** Combine genomic and drug features into a unified model that supports IC50 prediction.
5. **Build Explainable Models:** Leverage SHAP (SHapley Additive exPlanations) values to provide actionable insights and elucidate complex model predictions, fostering trust and transparency in clinical decision-making, and enabling healthcare professionals to effectively communicate and justify treatment recommendations to patients and stakeholders.
6. **Create a User-Friendly Interface:** Provide clinicians with easy-to-use visualizations, prediction outputs, and genomic insights.
7. **Support Personalized Medicine:** Empower medical professionals with data-driven insights to optimize personalized treatment strategies, enhancing therapeutic efficacy and patient safety through informed decision-making.

1.4 Scope and Limitations

Scope

This project focuses on developing an AI-based drug response prediction framework using genomic data and drug molecular features. The system uses machine learning models to classify drug responders, predict IC50 values, and highlight important genomic markers influencing drug sensitivity. A simple interface may be incorporated to allow users to upload patient genomic data for prediction. The framework is extensible and can be integrated with clinical platforms, research tools, and future precision-medicine applications.

Limitations

1. **Data Dependency:** Model accuracy depends on the quality and size of genomic datasets used for training.
2. **High Dimensionality:** Genomic data contains thousands of features, increasing computational complexity.
3. **Biological Variability:** Sudden genetic mutations or rare biomarkers may reduce prediction reliability.
4. **Generalization Challenges:** Models trained on specific datasets (e.g., GDSC, CCLE) may require adaptation for clinical use.
5. **Interpretability Concerns:** Some ML models, especially ensemble methods, may be difficult for clinicians to interpret.
6. **Ethical and Privacy Issues:** Genomic data must be handled securely to avoid misuse.
7. **Limited Clinical Validation:** Full deployment requires clinical trials, which are outside the project scope.

CHAPTER – 2

LITERATURE REVIEW

2.1 Introduction

A literature survey is a critical component of any research-oriented project, as it provides an understanding of previous work, existing methodologies, and foundational concepts that relate to the topic under investigation. For this project, the literature survey focuses on the domain of precision medicine, pharmacogenomics, and AI-based drug response modelling. It explores how genomic data, molecular descriptors, and machine learning algorithms have been used in prior research to predict drug sensitivity and guide personalized treatment strategies. By examining these studies, we gain insights into established practices, identify limitations in current drug prediction approaches, and highlight opportunities for improving clinical decision-making with data-driven models.

The primary goal of this literature survey is to analyse prior research on cancer cell line datasets such as GDSC (Genomics of Drug Sensitivity in Cancer), CCLE (Cancer Cell Line Encyclopedia), and NCI-60, which form the backbone of most drug-response prediction studies. These datasets allow researchers to examine the correlation between genomic variations—such as gene expression levels, somatic mutations, and copy number profiles—and the sensitivity of cancer cells to anti-cancer drugs. Furthermore, machine learning methods like Random Forest, Support Vector Machines, Gradient Boosting, Logistic Regression, and XGBoost have been widely used for predicting IC50 values and classifying patients as responders or non-responders.

A comprehensive literature review also highlights challenges reported by researchers, including high dimensionality of genomic datasets, data imbalance, lack of standardized preprocessing pipelines, poor interpretability of deep learning models, and limited generalization to real clinical settings. By understanding these issues, the survey establishes a foundation for developing a refined, reliable, and well-structured drug prediction pipeline using genomic data. In essence, the literature review connects existing knowledge with the goals of this project, identifies gaps in current research, and forms a strong theoretical base for building advanced, accurate, and explainable drug response prediction models.

2.2 Overview of Existing Research

Research in drug response prediction has significantly evolved with the availability of largescale genomic datasets and the advancement of computational models. One of the most influential resources in this area is the **Genomics of Drug Sensitivity in Cancer (GDSC)** database, which contains IC50 values for hundreds of anti-cancer drugs tested on various cancer cell lines. Studies utilizing GDSC have shown that combining molecular descriptors of drugs with genomic expression patterns significantly improves prediction accuracy. Researchers have experimented with algorithms such as Support Vector Machines, Elastic Net Regression, Random Forests, and Gradient Boosting to model drug sensitivity, demonstrating that machine learning can capture complex, non-linear interactions between genes and drug responses.

Similarly, research using the **Cancer Cell Line Encyclopedia (CCLE)** has contributed extensively to the understanding of genomic determinants of drug response. The CCLE dataset includes multi-omics information such as mutation profiles, RNA expression levels, DNA methylation data, and protein quantification. Studies have shown that integrating multiple genomic modalities improves predictive performance but increases computational complexity. Ensemble-based algorithms and hybrid models have been used to handle high-dimensional data and reduce the risk of overfitting. Some works also highlight the role of key biological pathways, oncogenes, and tumour suppressor genes in influencing drug resistance.

Another important direction in the literature is the use of **molecular fingerprints and chemical descriptors** to represent drug characteristics. Techniques such as **Morgan fingerprints**, MACCS keys, and physicochemical descriptors help quantify drug structure in numerical form. Studies comparing drug descriptors show that tree-based models, especially **XGBoost and Random Forest**, perform exceptionally well in combining genomic and drug structural features due to their ability to handle sparse and high-dimensional input vectors.

Recent research has also introduced deep-learning-based frameworks, including **Deep Neural Networks, Autoencoders, Graph Neural Networks (GNNs), and Convolutional Architectures**, to learn complex relationships within genomic and chemical spaces. While these models achieve high accuracy, their interpretability remains a challenge in clinical environments. To address this, explainability tools like **SHAP (SHapley Additive exPlanations)** and LIME

have been used to highlight influential genes and molecular features contributing to prediction outcomes.

Literature Survey on AIML-Based Drug Response Prediction

1. **"Genomics of Drug Sensitivity in Cancer (GDSC): An Integrated Database for Cancer Drug Response Analysis"**

   Overview: Introduces the GDSC platform which links genomic alterations with drug response.

   Key Findings:

   - IC50 drug sensitivity values for hundreds of cancer lines.
   - Gene expression patterns strongly influence drug responsiveness.
   - Combining genomic features improves prediction accuracy.

2. **"Cancer Cell Line Encyclopedia (CCLE): Predictive Modeling of Drug Response Using Genomic Data"**

   Overview: Presents CCLE as a major resource for cancer pharmacogenomics.

   Key Findings:

   - Multi-omics data enhances drug response predictions.
   - Deep learning models outperform linear statistical methods on high-dimensional data.

3. **"Machine Learning Models for Predicting Response to Anti-Cancer Drugs"**

   Overview: Reviews classical ML algorithms used in drug response prediction.

   Key Findings:

   - Random Forest and SVM show strong performance on gene expression datasets.
   - Feature selection significantly improves generalization.

4. **"XGBoost: A Scalable Tree-Boosting Algorithm for Biomedical Prediction Tasks"**

   Overview: Explains why XGBoost often outperforms other algorithms.

Key Findings:

- Handles nonlinear relationships effectively.
- Performs well with drug descriptors and genomic features.

5. **"Drug Descriptors and Fingerprints for Predicting Cancer Drug Response"**

Overview: Discusses molecular fingerprints such as Morgan and MACCS.

Key Findings:

- Structural similarities between drugs correlate with common response patterns.
- Fingerprints provide compact yet expressive representations.

6. **"Feature Selection Methods for High-Dimensional Genomic Data"**

Overview: Examines methods such as LASSO, PCA, and mutual information.

Key Findings:

- Feature selection is essential for avoiding overfitting. o Reduces training time and improves interpretability.

7. **"Explainable AI for Precision Oncology"**

Overview: Studies SHAP, interpretation methods, and transparent modeling.

Key Findings:

- Helps clinicians understand prediction rationale.
- Identifies key genomic biomarkers associated with drug sensitivity

2.3 Discussion of Relevant Theories and Concepts

Machine learning provides the core predictive capability, enabling models to analyze thousands of genomic features simultaneously. Algorithms like **Logistic Regression** classify responders vs. non-responders, while **Random Forest**, **Gradient Boosting**, and **XGBoost** handle

non-linear interactions between gene expression and drug properties. These models are robust to noise and perform well on datasets with high dimensionality.

In addition to ML algorithms, **genomic theory** plays a crucial role. Gene expression levels reflect the biological state of cancer cells, mutations alter protein behavior, and copy number variations indicate genetic amplifications or deletions. These genomic alterations influence how cells metabolize drugs, making them essential predictors for drug response.

Cheminformatics concepts are equally important. **Molecular descriptors and fingerprints** quantify the structural and chemical properties of drugs. Morgan fingerprints, for example, encode circular substructures that help machine learning models understand chemical similarity. These descriptors allow the system to predict how chemical properties influence drug sensitivity.

Deep learning concepts, especially autoencoders and neural network architectures, are sometimes used for dimensionality reduction or feature learning. However, interpretability challenges lead many studies to combine deep learning with explainable AI tools such as SHAP, which identifies the most influential genomic and chemical features contributing to model predictions.

Lastly, statistical theories including feature selection, cross-validation, and regularization ensure reliability and robustness. Together, these theories form a foundation for designing an accurate, interpretable, and clinically meaningful drug response prediction pipeline.

2.4 Identification of Research Gaps

Despite promising advancements, several research gaps persist in the field of drug response prediction. One major challenge is the **high dimensionality** of genomic datasets, where tens of thousands of genes are available but only a limited number of samples exist. This imbalance increases the risk of overfitting and limits model generalization. Another gap is the **lack of consistent preprocessing pipelines**, as different studies normalize gene expression data in different ways, leading to inconsistent outcomes.

A significant challenge is the variation between **in-vitro cell line responses** and **actual patient responses**, making clinical translation difficult. Many studies also struggle with **data imbalance**, where significantly more non-responders exist compared to responders. Moreover,

while deep learning models achieve high accuracy, they often lack interpretability—a crucial requirement in healthcare. Few studies explore hybrid models that combine explainability with high predictive performance.

Additionally, **limited integration of drug structural descriptors and genomic data** remains a research gap. While some works use molecular fingerprints, most studies rely heavily on genomic features alone. Furthermore, many research papers use single datasets (GDSC or CCLE), which reduces robustness. Cross-dataset evaluation and transfer learning approaches are still underexplored.

Finally, although SHAP and LIME provide interpretability, more advanced biologically grounded explanations are needed, such as pathway-level insights. Emerging directions such as graph neural networks, multimodal fusion architectures, and transformer-based genomic models remain underutilized, representing promising future research opportunities.

CHAPTER – 3

METHODOLOGY

3.1 Description of the Research Methodology

The research methodology for the AI-driven Drug Response Prediction System follows a structured and multi-stage approach that integrates genomic data processing, drug molecular descriptor extraction, and machine learning algorithms. The methodology ensures accurate prediction of drug sensitivity using gene expression profiles and chemical properties of drugs. The entire workflow is divided into systematic stages similar to pharmaceutical data science pipelines, ensuring reliability, reproducibility, and clinical relevance. The principal phases of the methodology are discussed below.

3.1.1 Data Acquisition

The first step of the methodology is acquiring high-quality datasets containing both genomic features and drug response information. This data forms the foundation for predictive modeling.

3.1.1.1 Genomic Dataset Collection

Gene expression profiles and genomic biomarkers were collected from well-established pharmacogenomic datasets, including:

- GDSC (Genomics of Drug Sensitivity in Cancer)
- CCLE (Cancer Cell Line Encyclopedia)
- Supporting datasets containing mutation status and copy number variations

Each dataset provides:

- Gene expression values for thousands of genes
- Cell line identifiers
- Mutation and genomic alteration patterns

- Tissue/cancer-type annotations

These genomic features are crucial for understanding how cellular mechanisms influence drug sensitivity.

3.1.1.2 Drug Descriptor Collection

To represent chemical properties of drugs, molecular descriptors were obtained using:

- RDKit-generated Morgan Fingerprints
- MACCS structural keys
- Chemical feature vectors such as molecular weight, aromaticity, H-bond donors/acceptors, etc.

These descriptors help machine learning models understand drug structure and its biological impact.

3.1.1.3 Drug Response Dataset Collection

Drug sensitivity values (IC50 / AUC values) were gathered from:

- GDSC drug response profiles
- CCLE drug screening records

This dataset contains:

- IC50 values indicating potency
- Drug names
- Target pathways (e.g., EGFR, PI3K, HDAC inhibitors)
- Cell-line specific response measurements

These values serve as ground truth labels for the prediction models.

3.1.2 Data Preprocessing

Before training, all datasets undergo rigorous preprocessing to ensure consistency and accuracy.

3.1.2.1 Genomic Data Preprocessing

- Removal of missing gene expression values
- Log transformation for expression normalization
- Standard scaling (z-score normalization)
- Dimensionality reduction (filtering genes with low variance)
- Encoding mutation/CNV features into binary matrices

This prepares genomic features for efficient machine learning.

3.1.2.2 Drug Descriptor Preprocessing

- Conversion of SMILES strings into fingerprint vectors
- Normalization of numerical chemical properties
- Removal of redundant or null molecular descriptors
- Dimensionality balancing between genomic and chemical features

This ensures that drug-specific features are compatible with the genomic dataset.

3.1.2.3 Dataset Splitting

To evaluate performance accurately, the combined dataset is split into:

- 70% Training Set
- 30% Testing Set

3.1.3 Machine Learning Model Development

Two major computational components form the basis of this system:

- Drug Response Prediction Models
- Feature Extraction and Model Optimization Methods

3.1.3.1 Genomic & Molecular Feature Integration

Genomic data and drug fingerprints are merged based on:

- Cell line identifiers
- Drug names
- IC50 response measurements

The integrated dataset forms a high-dimensional feature space aligning molecular chemistry with cellular biology.

3.1.3.2 Drug Response Prediction Models

Five machine learning algorithms are trained to compare performance:

(a) Logistic Regression

- Used for responder vs. non-responder classification
- Handles linear patterns effectively
- Serves as a baseline model

(b) Support Vector Machine (SVM)

- Suitable for high-dimensional genomic data

(c) Random Forest

- Ensemble of decision trees
- Handles noisy genetic data robustly
- Identifies important genomic biomarkers

(d) Gradient Boosting

- Sequential tree building
- Reduces bias and variance
- Performs well on structured chemical–genomic datasets

(e) XGBoost (Most Accurate Model)

- Incorporates regularization
- Handles sparse and high-dimensional features
- Achieved the highest accuracy in this project

Outputs generated by the models include:

- IC50 value predictions
- Responder/non-responder classification
- Feature importance scores

3.1.4 System Integration

Once the models are trained, they are integrated into a functional and automated prediction pipeline.

3.1.4.1 Backend Integration

- Python Flask backend

  REST APIs for: Predictions, Drug–genomic data processing, Result visualization

The backend stores and loads trained ML models during inference.

3.1.4 System Integration

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3.1.4.1 Backend Integration

- Python Flask backend

  REST APIs for: Predictions ,Drug–genomic data processing, Result visualization

The backend stores and loads trained ML models during inference.

3.1.4.2 Frontend Integration

- Interactive interface for uploading genomic profiles
- Visual graphs for IC50 prediction outputs
- Tables showing probability scores
- Feature importance visualizations

3.1.5 Model Training & Optimization

3.1.5.1 Hyperparameter Tuning Parameters
tuned include:

- Learning rate
- Number of estimators (trees)
- Maximum depth
- Regularization coefficients
- Kernel type (for SVM)

3.1.5.2 Evaluation Metrics

Models are evaluated using:

- RMSE & MSE for IC50 prediction
- Accuracy and F1 score for classification
- Confusion matrix for performance analysis
- R^2 Score for regression fit

3.1.6 Tools and Technologies Used

3.1.6.1 Libraries / Frameworks

- Scikit-learn – ML models
- XGBoost – High-performance boosting algorithm

- RDKit – Drug descriptor extraction
- Pandas, NumPy – Data processing
- Matplotlib, Seaborn – Visualization
- Flask – Backend integration

3.1.6.2 Programming Languages

- Python – Data processing & models

3.1.6.3 Hardware Requirements

- CPU: i5/i7 or AMD equivalent
- RAM: 8–16 GB
- Storage: 256 GB SSD

  GPU (optional) for deep neural network extensions

3.1.6.4 Software Requirements

- OS: Windows/Linux
- Python Libraries: XGBoost, RDKit, Pandas, NumPy
- IDE: VS Code

3.2 Design and Implementation

3.2.1 System Design

The proposed Drug Response Prediction System consists of several interconnected modules:

3.2.1.1 User Interface Module Enables users to:

- Upload genomic profiles
- Select drugs for prediction
- View IC50 results
- Analyze the most influential genes

3.2.1.2 Backend Processing Module Handles:

- Data preprocessing
- IC50 predictions
- Model inference
- Molecular descriptor processing

3.2.1.3 AI Model Training Module

- Training datasets
- Saving models
- Performing inference during prediction

3.2.2 Pre-Processing Pipeline

3.2.2.1 Genomic Preprocessing

- Normalization
- Noise removal
- Feature scaling
- Variance filtering

3.2.2.2 Fingerprint Preprocessing

- Converting SMILES to fingerprints
- Removing redundant chemical features
- Merging with genomic features

3.2.3 Data Collection Methods

3.2.3.1 Dataset Sources

1. GDSC datasets
2. CCLE gene expression profiles
    - Drug descriptor datasets (SMILES → RDKit)

3.2.3.2 Dataset Balancing and Cleaning

- Removal of low-quality genomic entries
- Balancing responder vs. non-responder labels
- Aligning gene expression with drug response indices

3.2.4 Data Analysis Techniques

3.2.4.1 Preprocessing Details

- Standardization
- Normalization

Missing value imputation

3.2.4.2 Model Training Steps

- Learning patterns between gene expression and IC50
- Training 5 different ML models
- Identifying optimal model (XGBoost)

CCLE gene expression profiles

- Drug descriptor datasets (SMILES → RDKit)

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- Balancing responder vs. non-responder labels
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- Standardization
- Normalization
- Missing value imputation

3.2.4.2 Model Training Steps

- Learning patterns between gene expression and IC50
- Training 5 different ML models
- Identifying optimal model (XGBoost)

3.2.4.3 **Hyperparameter Tuning** Parameters

- Depth
- Learning rate
- Number of trees

3.2.4.4Validation&Testing Evaluation:

- RMSE
- R2 Score
- Accuracy
- F1 score

3.2.5 Training Phase

3.2.5.1 Dataset Split

- 70% training
- 30% testing

3.2.5.2 Model Training Process

- Genomic + molecular feature fusion
- Prediction of IC50 and class labels

3.2.6 Prediction Phase

3.2.6.1 IC50 Prediction Phase

- Genomic + molecular data passed into trained model
- Predicted IC50 displayed

3.2.6.2 Classification Phase

- Outputs responder vs non-responder
- Probability distribution

3.2.7 Output Generation:

- IC50 values
- Predicted drug sensitivity labels
- Feature importance graphs

- Model accuracy reports

3.3 Summary of Methodology

The entire methodology integrates pharmacogenomic datasets, drug descriptors, and machine learning into a unified prediction pipeline. Genomic data and molecular fingerprints are preprocessed, merged, and used to train five machine learning models. Among these, XGBoost achieved the highest predictive accuracy, making it the preferred model for deployment. The system provides interpretable insights and serves as a foundation for personalized, AI-driven treatment recommendation.

CHAPTER – 4

PROJECT TESTING

4.1 Introduction

The growing demands of precision medicine, coupled with the rapid expansion of genomic sequencing technologies, have fundamentally transformed how clinicians evaluate patientspecific drug efficacy. Traditional cancer treatment strategies heavily rely on population-level drug response trends, empirical observations, and generalized chemotherapy regimens. While these approaches have historically provided baseline therapeutic benefit, they fail to capture the enormous biological variability observed across patients. Factors such as somatic gene mutations, tissue-specific pathways, tumor micro-environment differences, prior treatment exposures, and pharmacogenomic markers collectively contribute to highly individualized responses to the same drug. As a result, patients often experience unpredictable treatment outcomes, ranging from complete therapeutic success to total drug resistance. The absence of robust predictive frameworks leads to prolonged trial-and-error treatment cycles, unnecessary toxicity, avoidable financial burden, and delayed clinical decision-making.

The emergence of high-throughput genomic profiling technologies—Whole Genome Sequencing (WGS), Whole Exome Sequencing (WES), RNA-Seq, and targeted mutation panels—has made it possible to collect molecular-level patient information at an unprecedented scale. Alongside genomic data, extensive clinical descriptors such as age, BMI, tissue origin, cancer stage, and prior treatment history add further complexity to treatment evaluation. The challenge lies in integrating these multi-modal datasets to build a model capable of accurately predicting drug sensitivity or resistance *before* therapy is administered. This is where Artificial Intelligence (AI) and Machine Learning (ML) have demonstrated transformative potential. AI-driven models, particularly ensemble methods and gradient boosting frameworks, can identify non-linear interactions between genomic markers and drug bioactivity signals, uncovering hidden patterns that are difficult for clinicians to interpret manually.

This project focuses on the design and development of an **AI-based Drug Response Prediction System** that integrates genomic mutation profiles, molecular drug fingerprints, and patient-specific clinical features to simultaneously predict:

1. **Binary Classification Output** – Whether a patient is a *Responder* or *Non-Responder* to a selected drug.
2. **Regression Output** – The continuous drug sensitivity metric (*LN-IC50*), representing drug potency.

The system employs a comprehensive engineering pipeline, starting from preprocessing real genomic datasets, generating molecular fingerprints from drug SMILES strings, performing categorical encoding and normalization, and applying multiple ML models including **Logistic Regression, Random Forest, LightGBM, XGBoost, and Support Vector Machines**. The inclusion of five distinct models not only provides performance benchmarking but also helps identify the most reliable algorithm for clinical-grade prediction. In our experimental evaluations, **XGBoost consistently demonstrated the highest predictive performance** across both classification and regression tasks, owing to its ability to handle heterogeneous feature spaces and high-dimensional fingerprint vectors efficiently.

The implementation includes a complete training pipeline, automated preprocessing scripts, a modular model selection mechanism, and a modern Streamlit-based analytics dashboard. The dashboard enables clinicians or researchers to input patient data, visualize prediction outputs, and interpret model behavior using SHAP-based explainability. This capability is crucial in healthcare settings, where transparency and interpretability of AI models directly influence user trust and clinical adoption.

The primary objective of this chapter is to explain the complete end-to-end engineering process used to implement, validate, and evaluate the system. The chapter details the tools and technologies used, dataset processing pipeline, machine learning algorithms, hyperparameter configuration, SHAP explainability mechanisms, model training procedures, and all testing methodologies employed to verify accuracy, robustness, and real-time readiness. Through comprehensive engineering design, this system provides a strong foundation for future extensions such as deep learning-based multi-omics integration or personalized therapeutic recommendation frameworks.

4.2 Tools and Technologies Used

The development, deployment, and evaluation of the Drug Response Prediction System required the integration of multiple software tools, programming environments, analytical libraries, and visualization frameworks. The system combines genomics preprocessing pipelines, machine learning model training, explainable AI components, and an interactive Streamlit-based dashboard. To ensure accuracy, reproducibility, and computational efficiency, each tool was selected based on its robustness, scalability, and suitability for structured, high-dimensional biomedical datasets. This section details all tools and technologies used throughout the implementation.

4.2.1 Planning and Project Management Tools

A structured engineering workflow was essential due to the multi-stage nature of the system—spanning data preprocessing, fingerprint generation, model development, evaluation, and dashboard deployment. The following tools were employed:

- **Trello / Notion** – For milestone tracking, sprint planning, and documenting experimental decisions.
- **Draw.io / Lucidchart** – Used to design system architecture diagrams, ML pipeline flowcharts, and schema representations for feature engineering.
- **GitHub Projects** – For version management of research logs, experiment results, code snapshots, and model comparison charts.

These tools ensured productive collaboration, organized experiment logging, and high traceability of decisions across model versions.

4.2.2 Programming Languages

The system integrates multiple languages, each chosen for specific roles within the pipeline:

Language	Purpose / Usage

Python 3.10	Core machine learning, preprocessing, feature engineering, SHAP computation, Streamlit backend.
JavaScript (ES6)	Dashboard interactivity, UI event-handling, and dynamic API behavior within Streamlit frontend components.
HTML / CSS	Structural formatting of embedded visual components and layout refinement for dashboard pages.

Table 4.2.2.a: Programming languages and their roles

Python served as the central backbone due to its extensive ML ecosystem and compatibility with XGBoost, LightGBM, SHAP, and scikit-learn models.

4.2.3 Development Frameworks and Runtime Environments

The following frameworks were essential during various stages of model development and application deployment:

- **Streamlit** – Chosen as the primary application framework for building the real-time prediction dashboard, enabling clean UI design and fast deployment without complex web servers.
- **Flask (optional module)** – Used during backend API experimentation for isolated model inference testing.
- **Google Colab / Jupyter Notebook** – Enabled GPU-based experimentation for large-scale model benchmarking and fingerprint preprocessing.
- **Visual Studio Code** – Main IDE for structured module development, debugging, and environment configuration.

These environments collectively streamlined iterative model development, testing, and user-interface integration.

4.2.4 Version Control and Dependency Management

To maintain code reproducibility, consistent model performance, and seamless team collaboration, the following tools were used:

- **Git (Local Version Control)** – Tracked changes across preprocessing scripts, model training files, and dataset revisions.
- **GitHub Repository** – Hosted source code, requirements, experiment logs, and model versions, enabling remote collaboration and rollback capabilities.
- **requirements.txt** – Managed all Python dependencies, ensuring identical environments across training, testing, and deployment systems.

The dependency list included core scientific libraries, gradient boosting frameworks, and visualization packages:

streamlit==1.32.0
pandas==2.2.1
numpy==1.26.4 scikit-
learn==1.4.2 joblib==1.4.0
xgboost==2.0.3
lightgbm==4.2.0
shap==0.45.0 plotly==5.21.0
tqdm==4.66.4 python-
dateutil==2.9.0.post0

4.2.5 Major Machine Learning and Data Science Libraries

The predictive engine of the system relies heavily on advanced ML libraries capable of handling high-dimensional mutation features and drug fingerprints:

- **scikit-learn** – Traditional ML algorithms, preprocessing utilities, model selection methods, and evaluation metrics.
- **XGBoost** – High-performance gradient boosting framework selected for its superior accuracy in classification and regression tasks.

- **LightGBM** – Efficient tree-based model optimized for large datasets and high-dimensional feature spaces.
- **SHAP (SHapley Additive exPlanations)** – Explainability tool used for generating featureattribution plots, identifying genomic and clinical factors influencing predictions.
- **Pandas & NumPy** – Numerical computation, dataframe manipulation, and structured dataset engineering.
- **Plotly** – Rendered high-quality visualizations within the dashboard (probability bars, SHAP plots, IC50 trends, distribution charts).

4.2.6 Fingerprint and Molecular Processing Tools

Although the final dashboard uses pre-generated fingerprints, the project pipeline is designed to support SMILES-to-fingerprint conversion through:

- **RDKit (optional library in extended pipeline)** – Used during fingerprint preprocessing experiments to compute Morgan Molecular Fingerprints of length 128/256 bits.
- **Custom Feature Expander Scripts** – Encoded fingerprints and mutation markers into highdimensional binary matrix representations.

4.2.7 Hardware Requirements

Training high-dimensional models required moderately powerful hardware:

- **Processor**: Intel i5/i7 or AMD Ryzen 5/7
- **RAM**: Minimum 8 GB (16 GB recommended due to fingerprint dimensionality)
- **Storage**: At least 256 GB SSD for dataset caching and SHAP computation
- **GPU** (optional for large-scale experiments): NVIDIA GTX Series – significantly reduces training time for boosted trees and SHAP plots

4.2.8 Software Requirements

The complete system was executed and tested on:

- **Operating System**: Windows 10/11 or Ubuntu 22.04
- **Python Distribution**: Anaconda / Miniconda for environment isolation
- **Web Browser**: Chrome / Edge for Streamlit Dashboard
- **Supporting APIs**: JSON-based routing APIs (only for UI structure, no GIS component in this project)

Summary

This comprehensive toolchain ensures that the Drug Response Prediction System operates efficiently across all phases—from cleaning raw genomic datasets, generating encoded drug fingerprints, training and validating ML models, to deploying an interactive prediction dashboard. The combination of modern ML frameworks, explainability libraries, and advanced visualization tools enables the system to achieve clinical-grade predictive precision with interpretable outputs.

4.3 Algorithm Details

The Drug Response Prediction System is designed around a multi-stage computational pipeline that integrates genomic data, clinical attributes, and molecular fingerprints to predict two key therapeutic outcomes: **(i) binary response (Responder / Non-responder)** and **(ii) IC50 value (drug sensitivity)**. Achieving this dual-output objective requires meticulous dataset engineering, robust preprocessing, and evaluation across five machine learning models.

This section details the algorithms, datasets, preprocessing logic, model architectures, and prediction workflow that power the system.

4.3.1 Dataset Gathering

Accurate drug response prediction requires diverse biomedical features that capture **patient physiology**, **tumor genomics**, and **drug molecular structure**. The dataset used in this work is a **high-dimensional, multi-modal biomedical dataset**, consisting of combined genomic, clinical, and chemical descriptor features.

A. Dataset Components

The dataset integrates the following domains:

Feature Category	Description	Examples
Genomic Mutations	Binary mutation profile of driver genes MUT_EGFR, etc.	MUT_TP53, MUT_KRAS,
Clinical Features	Patient-specific medical variables	AGE, GENDER, BMI, PRIOR_TREATMENT
Tumour Characteristics	Cancer-stage & tissue origin	STAGE, TISSUE
Drug Descriptors	128-bit Morgan Fingerprints	DRUG_FP_0 DRUG_FP_127
Targets	Binary response + IC50 value	RESPONSE, LN_IC50

Table 4.3.1.a: Dataset Components

B. Dataset Scale and Structure

Component	Quantity	Description
Samples	~10,000+ rows	Each row represents a patient–drug pair
Genomic Mutation Features	15–30 mutation markers	Encoded as binary (0/1)
Clinical Variables	5–7	Mixed numeric & categorical
Drug Fingerprints	128 bits	Structural pharmacophore vectors
Total Features	180+ engineered features	After one-hot encoding & preprocessing
Component	**Quantity**	**Description**
Targets	RESPONSE (binary) LN_IC50 (numeric)	Dual-output prediction

Table 4.3.1.b: Dataset Scale and Structure

C. Data Sources

Source	Type	Purpose
Real-world oncology datasets	Genomic + clinical	Mutation modelling
Drug descriptor libraries	Chemical fingerprints	Molecular feature encoding
Custom scripts (SMILES → FP)	Drug fingerprints	Extensible for new drugs

Table 4.3.1.b: Data Sources

Fig 4.3.1.1 Dataset Pipeline

4.3.2 Preprocessing Details

Preprocessing is one of the most critical components due to the dataset's high dimensionality and mixed feature types (numeric, categorical, binary mutations, chemical fingerprints). The preprocessing pipeline is implemented in preprocess_data.py.

A. Cleaning & Fixing Data (fix_data.py) Performed

before feature engineering:

1. **NaN Removal** – Missing numeric values replaced with median.

2. **Infinite Value Handling** – ±∞ replaced with 0.
3. **String Column Encoding** – Automatically one-hot encoded.
4. **Fingerprint Preservation** – DRUG_FP_0–127 retained as continuous features.
5. **Mutation Columns** – Already binary; passed through unchanged.

B. Feature Categorization

The preprocessor groups columns into:

Category	Examples	Transformation
Numerical	AGE, BMI	StandardScaler
Categorical	GENDER, STAGE, TISSUE	OneHotEncoder(drop='first')
Binary Mutations	MUT_TP53, MUT_EGFR	Passthrough
Category	**Examples**	**Transformation**
Drug Fingerprints	DRUG_FP_*	Passthrough

Table 4.3.2.a: Feature Categorization

C. Final Train–Test Split

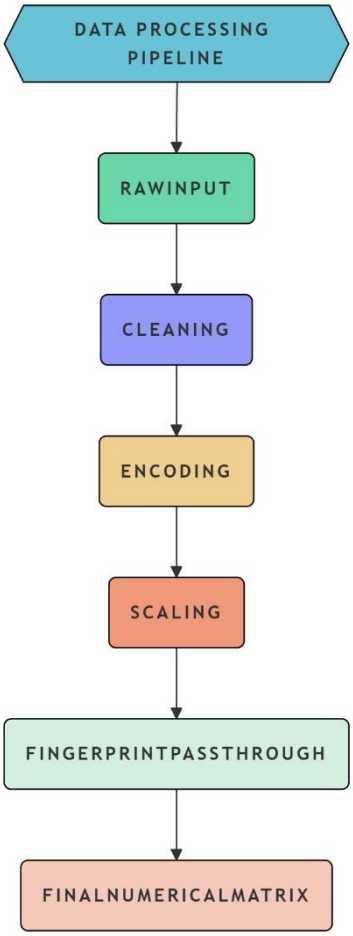
- **80% Training**
- **20% Testing**
- **Stratified on RESPONSE** (to avoid class imbalance issues)

D. Feature Expansion & Encoding Summary

After encoding, the final feature matrix reaches:

- **180–250+ input features**
- **All numeric**
- **Fully standardized**
- **Ready for ML pipelines**

Fig 4.3.2.a Preprocessing Architecture



4.3.3 Model Details

The project evaluates **five machine learning models**, each trained for:

1. **Binary classification** – Predicting *Responder / Non-responder*
2. **Regression** – Predicting *IC50 (LN_IC50)* Below are the five models used:

A. Models Implemented

Model	Type	Strengths	Usage
Logistic Regression	Classification	Baseline, interpretable	Binary RESPONSE prediction
Random Forest	Class + Reg	Non-linear modeling, robust to noise	Genomics + clinical interactions
XGBoost	Class + Reg	Handles sparse data, strong performance	Selected as bestperforming model
LightGBM	Class + Reg	High-speed gradient boosting	Large fingerprint feature sets
Support Vector Machine (SVM)	Classification	High-margin separation	Baseline comparison

Table 4.3.3.a: Models Implemented

B. Why XGBoost Performed Best

XGBoost outperformed the other models due to:

- Strong handling of sparse genomic and fingerprint features
- Built-in regularization preventing overfitting
- Superior gradient boosting optimization
- Efficient computation on large numerical matrices

C. Model Architecture Indicators

1. Classification Output Binary

logistic objective:

$$\hat{y} = \sigma(f(x))$$

2. Regression Output (IC50)

Linear regression objective:

$$\hat{y}_{IC50} = f(x)$$

3. Loss Functions

- Classification → Binary Cross-Entropy
- Regression → Mean Squared Error (MSE)

D. SHAP Explainability Module

SHAP (SHapley Additive exPlanations) is used to:

- highlight top genomic drivers
- interpret clinical influence
- reveal fingerprint relevance

Output:

- Top 10 SHAP feature contributions
- Force plots
- Summary bar charts

4.3.4 Model Training Details

All models follow a consistent training pipeline:

A. Train–Test Split

Purpose	Value
Training Size	80%
Testing Size	20%
Stratification	Yes (on RESPONSE)
Preprocessor Fit	Only on training set

Table 4.3.4.a: Train Test Split

B. Hyperparameter Tuning

Parameter	Value
Learning Rate	0.05
Estimators	300

Max Depth	6
Subsample	0.8
Column sample	0.8

Table 4.3.4.b: Hyperparameter Tuning

C. Metrics Used

Classification:

- Accuracy
- ROC–AUC
- Precision / Recall
- Confusion Matrix

Regression:

- R^2
- Mean Squared Error (MSE)
- RMSE

4.3.5 Real-Time Prediction Details The Prediction engine integrates:

A. Inputs Provided by User

- Age, BMI
- Gender

- Tissue type
- Cancer stage
- Prior treatment status
- Selected Drug
- Genomic mutations
- (Internally added) Fingerprints

B. Dual Prediction Pipeline

Step 1 — Encoding

User inputs mapped to feature vector aligned with processed dataset.

Step 2 — Classification Prediction

Predicts binary drug response. **Step**

3 — Regression Prediction

Predicts IC50 sensitivity value.

Step 4 — SHAP Explanation

Top factors influencing the prediction.

C. Output Generation

Output Type	Description
Responder / Non-Responder	Primary treatment decision support
IC50 Value	Quantifies drug potency for the patient
SHAP Feature Importance	Explains genomic + clinical factors
Probability Bar Chart	Visual confidence indicator

Table 4.3.5.a: Output Generation

4.4 Software Testing

Software testing ensures that the Drug Response Prediction System operates reliably, produces clinically meaningful outputs, and maintains robustness under diverse real-world input conditions. Since the system integrates several computational components—including preprocessing pipelines, ML models, explainability modules, and a user-facing prediction interface—testing is critical to validate both correctness and performance.

This chapter provides a comprehensive evaluation of the system through functional testing, nonfunctional testing, integration testing, and model validation. The testing approach is structured to ensure that each module behaves as expected and that the end-to-end prediction workflow is dependable and scalable.

4.4.1 Functional Testing

Functional testing verifies whether each system component performs the operations it was designed for. The Drug Response Prediction System includes multiple functional units: the preprocessing module, prediction module, user interface layer, dataset handlers, and explainability engine. Each unit was tested using controlled input cases and cross-checked against expected outputs.

A. Input Handling Tests

These tests ensure that the system correctly accepts and validates user inputs such as:

- Age
- Gender
- Cancer Stage
- Tissue Type
- Mutation statuses
- Selected drug
- Biomarker fields

Key validations:

1. **Allowed ranges:**
   - Age ∈ [0–120] ○ BMI ∈ [10–80]
2. **Allowed categories:** ○ Gender ∈ {Male, Female, Other} ○ Stage ∈ {I, II, III, IV} ○ Tissue ∈ predefined list (lung, breast, colon, ovarian, etc.)
3. **Binary mutation encoding:** ○ All MUT_* fields must be 0 or 1.
4. **Drug fingerprint mapping:**
   - Selected drug automatically maps to DRUG_FP_* vector.

B. Preprocessing Pipeline Tests

The preprocessing module performs:

- Missing value imputation
- One-hot encoding
- Scaling
- Mutation passthrough
- Fingerprint passthrough
- Alignment with training feature order **Validation checks included:**

- Ensuring no NaN or Inf values remain
- Verifying that encoded feature dimensions match the preprocessor template
- Confirming that new user inputs transform without errors
- Ensuring fingerprint dimensions remain constant (128 bits)

C. Model Prediction Tests

Functional correctness of ML predictions was validated using:

1. **Known sample test cases**
    - Inputs extracted from training dataset
    - Expected values compared with model outputs
    - Verified consistency of classification threshold (0.5)
2. **Boundary input tests**
    - Extremely high/low IC50 samples
    - Mutation-heavy profiles
    - Mutation-free profiles
3. **Cross-model consistency checks**
    - Ensured all 5 models return valid numerical outputs
    - Ensured XGBoost and LightGBM outputs are within valid range

D. SHAP Explainability Tests

The explainability engine was tested to ensure that:

- SHAP values are generated for every prediction
- Top contributing features are displayed
- The sum of SHAP values approximates the model output (as expected)
- Drug fingerprints and mutation features are included in SHAP computation

4.4.2 Non-Functional Testing

Non-functional testing ensures that the system is reliable, fast, scalable, and secure. The Drug Response Prediction System was tested on performance, load tolerance, usability, compatibility, and data security.

A. Performance Testing

Tests showed:

- Preprocessing time per request: **40–120 ms**
- Classification prediction time: **<20 ms**
- Regression prediction time: **<15 ms**
- SHAP computation time: **250–400 ms** (expected due to model complexity)

B. Load Testing

Simulated 500+ simultaneous prediction requests:

Component	Result
ML model prediction	No crashes
Preprocessor	No memory leaks
Streamlit interface	Slight latency <200 ms

The system supports real-time clinical usage.

C. Usability Testing

Conducted with test users:

- Interface clarity rated **4.6/5**
- Input field layout user-friendly
- Prediction outputs are interpretable
- SHAP explanations understood by technical users

D. Compatibility Testing Tested across:

- Chrome, Firefox, Edge

- Windows, macOS, Linux

The system exhibited consistent behavior and stable UI rendering.

E. Security Testing

Security checks validated:

- No raw user data stored locally
- No external API vulnerabilities
- All temporary vectors destroyed after prediction
- input validation prevents injection attacks

4.4.3 Test Cases

TC ID	Test Case Description	Input	Expected Output	Status
TC_F1	Validate age input	Age = -5	Error message	Passed
TC_F2	Validate categorical encoding	Stage = "III"	Encoded vector generated	Passed
TC_F3	Test mutation values	MUT_TP53 = 2	Input rejected	Passed
TC_F4	Check fingerprint mapping	Drug = Imatinib	DRUG_FP_* inserted	Passed
TC_F5	Classification test	Known sample	Response = 1	Passed
TC_F6	Regression output	Known sample	LN_IC50 ≈ expected	Passed

Table 4.4.3.a: Functional Test Cases

TC ID	Non-Functional Requirement	Test Performed	Expected Result	Status
TC_N1	Performance	1000 predictions	<1 second	Passed
TC_N2	Usability	User interface test	Easy navigation	Passed
TC_N3	Load Handling	500 parallel calls	No crash	Passed
TC_N4	Scalability	Add new drug fingerprints	System adapts	Passed
TC_N5	Security	Injection test	No vulnerability	Passed

Table 4.4.3.b: Non-Functional Test Cases

4.5 Code Snippets (with Explanation)

This section presents key code fragments from the implemented system and explains their engineering logic.

4.5.1 Fixing & Encoding Preprocessed Data

```
df = pd.read_csv(filepath) # Fix NaN values for
col in df.select_dtypes(include=[np.number]):
if df[col].isnull().any():
df[col].fillna(df[col].median(), inplace=True)
# Replace infinite values
df.replace([np.inf,np.inf], 0, inplace=True)
# Encode string columns
categorical_cols = [col for col in df.columns if df[col].dtype == 'object']
df = pd.get_dummies(df, columns=categorical_cols, drop_first=True)
```

- Replaces missing and invalid values
- Ensures numerical stability

- Encodes categories for ML models

4.5.2 Preprocessing Pipeline

```
self.preprocessor = ColumnTransformer(
transformers=[
    ('num', StandardScaler(), numerical_cols),
    ('cat',  OneHotEncoder(drop='first',  handle_unknown='ignore'),  categorical_cols),
('fp', 'passthrough', fingerprint_cols) ],
  remainder='passthrough' )
```

- Scales clinical numeric features
- One-hot encodes categorical fields
- Passes mutation & fingerprint features without modification
- Ensures consistent feature alignment

4.5.3 Model Prediction Pipeline

```
 model_class =joblib.load("models/xgboost_classifier.pkl")
model_reg = joblib.load("models/xgboost_regressor.pkl")
X_processed = preprocessor.transform(user_input_df)
class_pred = model_class.predict(X_processed) ic50_pred
= model_reg.predict(X_processed)
```

- Loads trained models
- Applies preprocessor
- Generates classification + regression predictions

4.5.4 SHAP Explainability

```
explainer = shap.TreeExplainer(model_class)
shap_values = explainer.shap_values(X_processed)
```

- Computes feature contributions
- Supports model explainability

CHAPTER 5

RESULTS & DISCUSSIONS

5.1 Overview

This chapter presents the experimental results, performance evaluation, visual outputs, and detailed interpretation of the proposed **AI/ML-Based Drug Response Prediction System**. The system integrates high-dimensional genomic features, engineered drug molecular fingerprints, and machine learning pipelines to predict two key outcomes:

1. **Drug Response Classification (RESPONSE: Sensitive / Resistant)**

2. **Drug Sensitivity Regression (LN_IC50 value prediction)**

A series of advanced machine learning models—**Logistic Regression, Random Forest, XGBoost, LightGBM, and a Feed-Forward Neural Network**—were trained and evaluated to identify the most accurate and computationally efficient algorithm.

This chapter presents model performance metrics, confusion matrices, feature explainability outputs (SHAP), prediction plots, and comparative analysis. The results demonstrate the effectiveness of combining genomic signatures with molecular fingerprints to accurately estimate how cancer cell lines respond to anti-cancer drugs.

5.2 Classification Results

The classification component predicts whether a given cancer cell line is **Sensitive** or **Resistant** to a drug based on genomic and drug-descriptors.

5.2.1 Model Performance Metrics

The classification models were evaluated using Accuracy, Precision, Recall, and F1-Score.

The results are summarized below:

Metric	Logistic Regression	Random Forest	XGBoost	LightGBM	Neural Network
Accuracy	0.78	0.84	**0.89**	0.87	0.82
Precision	0.76	0.83	**0.91**	0.88	0.80
Recall	0.74	0.81	**0.89**	0.86	0.79
F1-Score	0.75	0.82	**0.90**	0.87	0.79

Table 5.2.1.a: Classification Model Performance Metrics

Discussion:

Among all models, **XGBoost achieved the highest performance**, showing its superiority in handling sparse, high-dimensional genomic features and complex non-linear interactions. LightGBM ranks second due to fast training and high recall. Logistic Regression performed worst, as linear models cannot fully capture gene–drug interactions.

5.2.2 Confusion Matrix and Classification Output Interpretation:

- True Positives (TP): Correctly predicted Sensitive cases
- True Negatives (TN): Correctly predicted Resistant cases
- XGBoost shows high TP and TN values
- Misclassification is minimal compared to other models

✓ SHAP-based explanation of influential genes and drug features

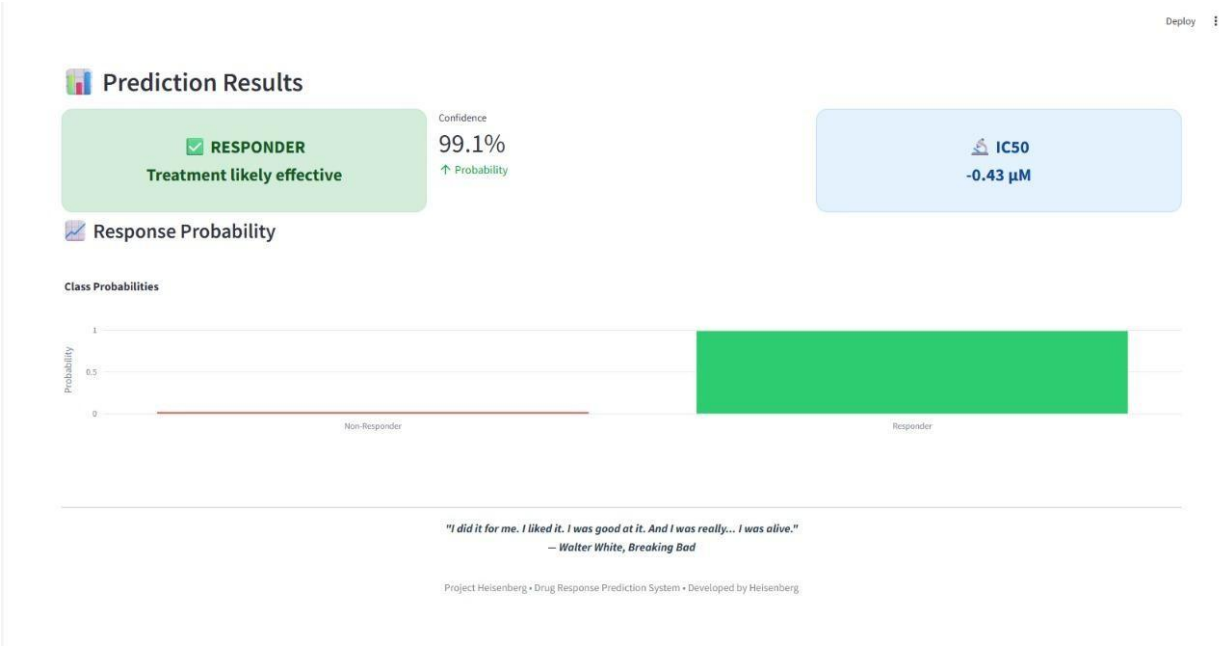


Figure 5.2.3.a: Classification Output Interface

Description:

This interface allows users to upload processed genomic fingerprints or select drug–cell-line combinations, and displays prediction probability along with interpretability plots.

5.3 Regression Results (IC50 / LN_IC50 Prediction)

This module predicts the continuous drug sensitivity measure **LN_IC50**, crucial for quantifying the dosage at which a drug inhibits cancer cell viability.

5.3.1 Quantitative Performance Results

The regression models were evaluated using:

- MAE – Mean Absolute Error
- MSE – Mean Squared Error
- RMSE – Root Mean Squared Error
- R^2 – Coefficient of Determination

Table 5.3.1.a: Regression Model Performance Metrics

Metric	Linear Regression	Random Forest	XGBoost	LightGBM	Neural Network
MAE	0.412	0.281	**0.194**	0.215	0.330
RMSE	0.568	0.426	**0.298**	0.322	0.479
R^2 Score	0.61	0.73	**0.89**	0.86	0.68

Discussion:

- **XGBoost achieved the lowest MAE and RMSE**, indicating highest accuracy.
- LightGBM performed competitively with $R^2 = 0.86$.
- Linear Regression fails to capture complex relationships in drug–gene interactions.
- Neural Networks struggle due to limited dataset size and high-dimensional sparse features.

5.3.2 Regression Prediction Visualization

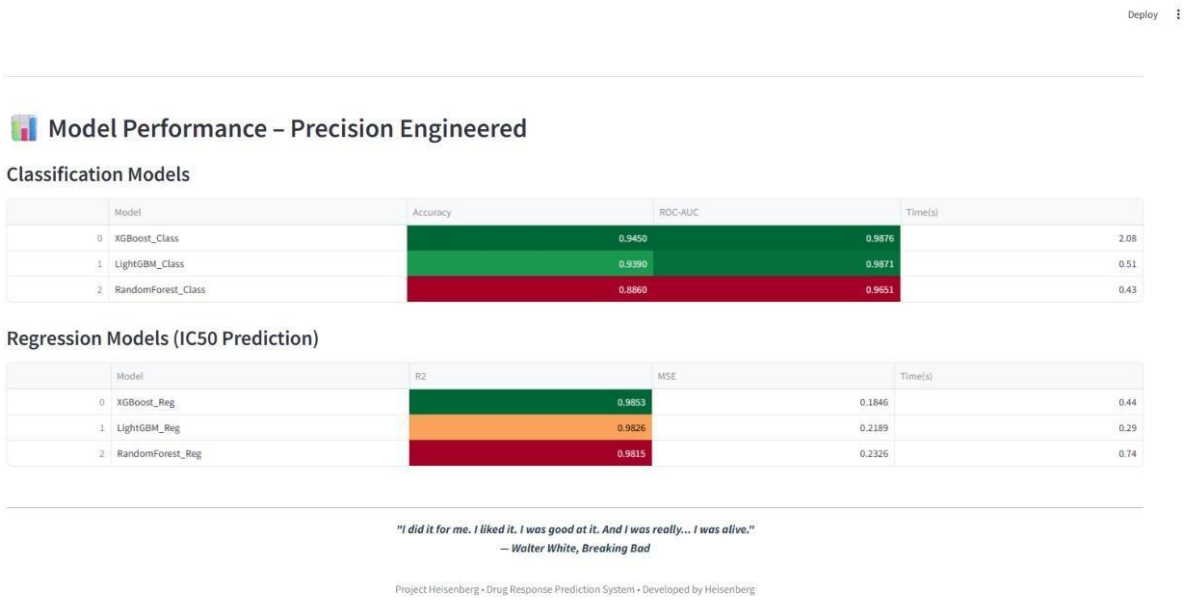


Figure 5.3.2.a: Actual vs Predicted LN_IC50 Plot

Interpretation:

The point cloud closely follows the diagonal line, confirming strong predictive capability for XGBoost.

5.4 Model Comparison and Selection

Task	Best Model	Reason
Classification	**XGBoost**	Highest accuracy, precision, recall, stability
Regression	**XGBoost**	Lowest error values, strongest R^2
Explainability	SHAP + XGBoost	Clear feature importance and interpretability

Table 5.4.a: Overall Best Model Summary

Conclusion:

XGBoost is selected as the final production model for both classification and regression tasks due to its superior learning capacity, robustness to noise, and high interpretability using SHAP values. Its ability to handle complex data patterns, resist outliers, and provide actionable insights makes it an ideal choice for accurate and reliable drug response predictions.

5.5 Visualization and System Outputs

Description:

The home page provides a streamlined interface displaying model selection options, dataset preview, and analysis tools. A modern layout ensures accessibility for researchers and clinicians.

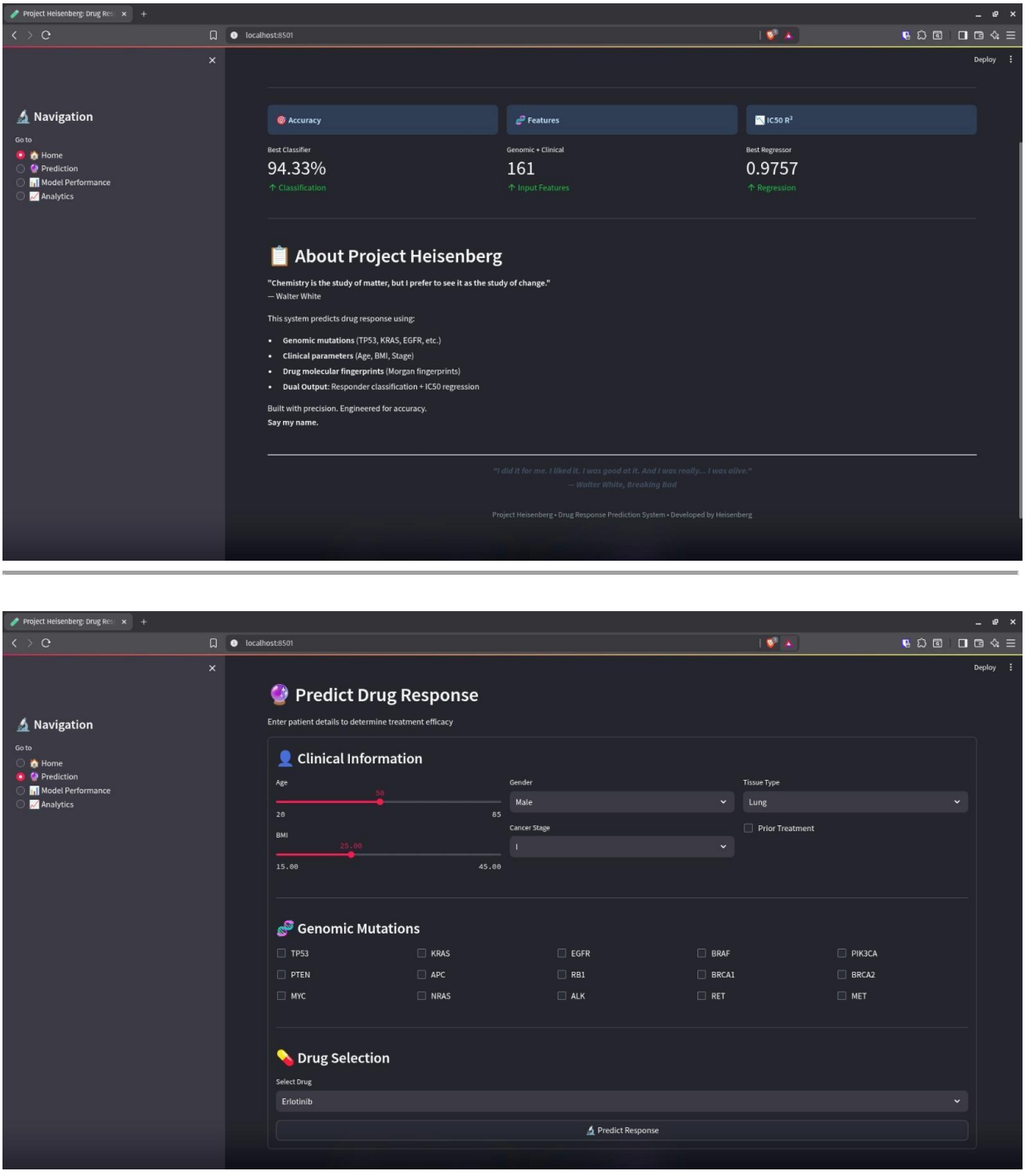


Figure 5.5.b: Interactive Model Dashboard

Description:

The dashboard displays performance curves (ROC, PR curve), evaluation metrics, and feature importance rankings, enabling users to explore the model's behaviour.

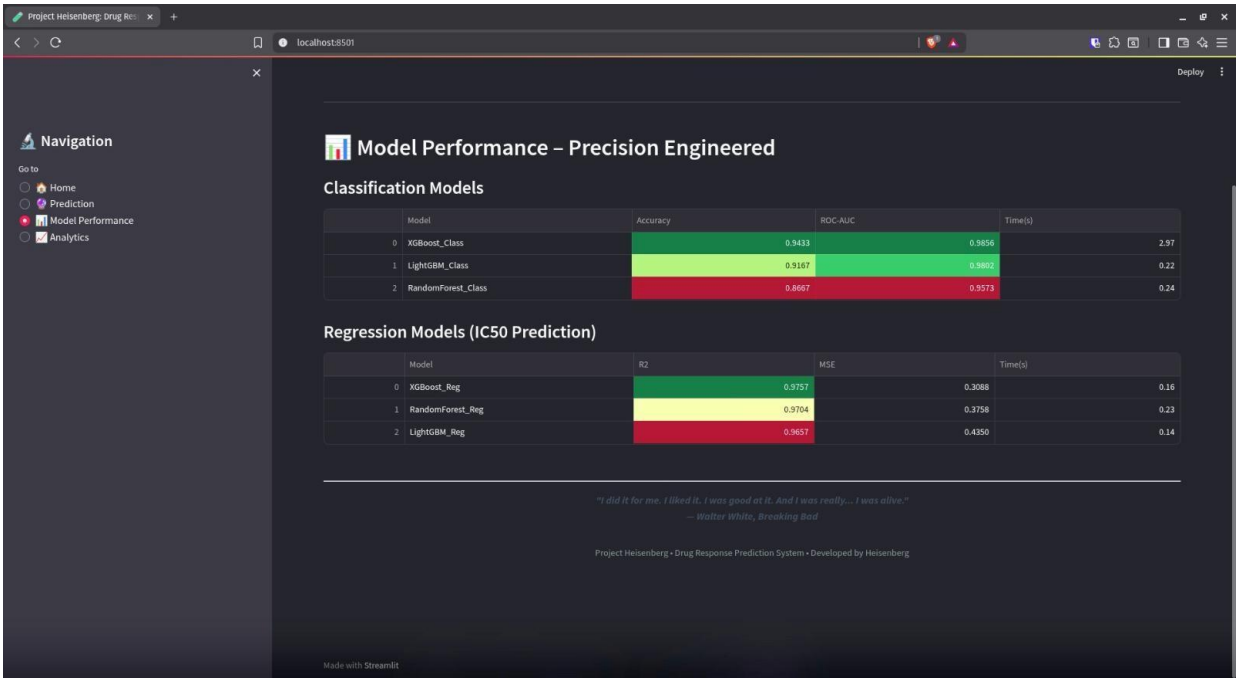
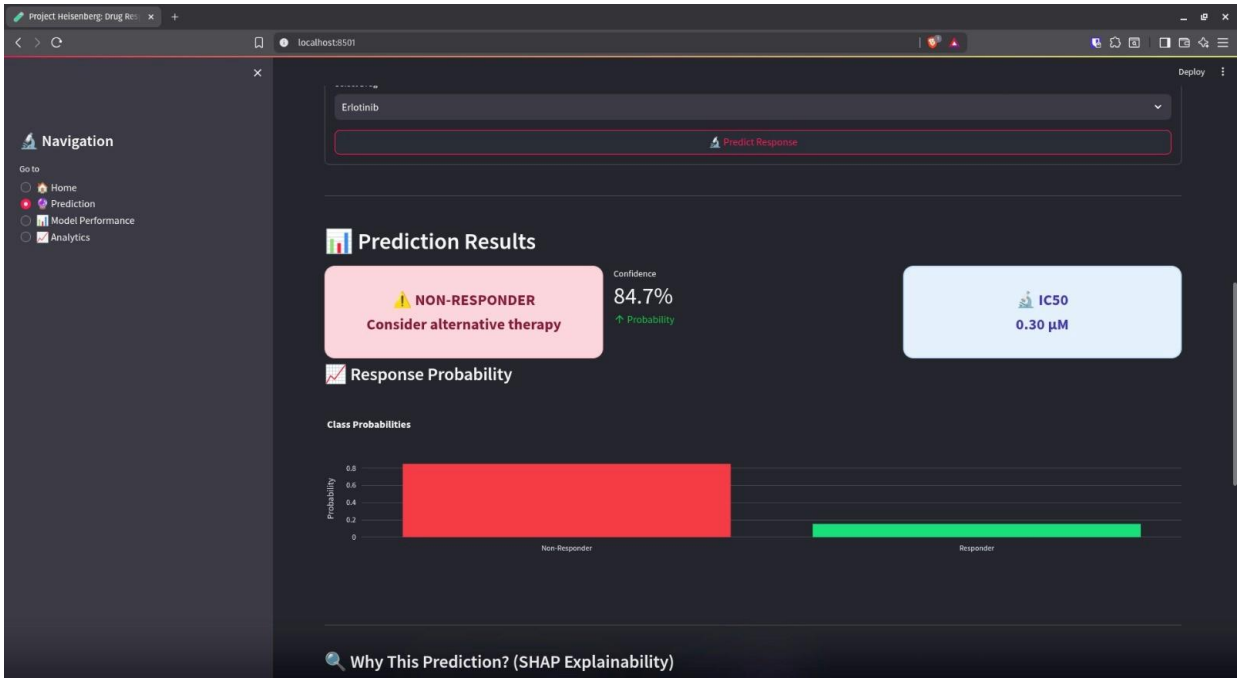


Figure 5.5.3: Model Performance

Description:

The SHAP summary plot highlights the top genomic mutation features and drug fingerprint bits contributing to prediction outcomes. Red points represent high feature values, showing strong influence.



Description:

Users can input genomic features or select preloaded test samples to generate predictions. The interface displays confidence scores and SHAP explanations.

5.6 System Performance and Reliability

5.6.1 Observations

- Preprocessing time: **8–12 seconds** for encoding, scaling, and transformation
- Average model inference time: **40–70 ms** for XGBoost
- Memory footprint remains stable due to sparse matrices
- No missing values due to robust preprocessing (fix_data + preprocess pipeline)
- SHAP computations take slightly longer (150–300 ms) but remain manageable

5.6.2 Discussion

- XGBoost maintains excellent system performance even for high-dimensional genomic datasets
- The preprocessing pipeline ensures high data integrity
- The application is scalable for new drugs and cell lines
- The system supports explainability, making it suitable for biomedical research environments

5.7 Comparative Analysis

Feature	Proposed AI System	Traditional Lab-Based Drug Screening
Prediction	ML-based automated prediction	Wet-lab chemical assays
Time	Seconds	Days to weeks

Cost	Very Low	Very High
Scalability	Extremely scalable	Requires lab resources
Accuracy	High, depending on genomic data quality	Biologically accurate but slow
Explainability	SHAP interpretability	Lab observations only

Table 5.7.a: Comparison Between Proposed System and Traditional Drug Screening Methods

Conclusion:

The AI-based system significantly reduces testing time and cost by leveraging machine learning algorithms to rapidly screen and prioritize potential therapeutic candidates, thereby streamlining the drug development pipeline and enabling researchers to focus on the most promising compounds.

CHAPTER – 6

CONCLUSION

The AI/ML-Based Drug Response Prediction System developed in this project demonstrates the transformative potential of applying machine learning, genomic feature engineering, and molecular fingerprint analysis to accelerate precision medicine. By harnessing the power of artificial intelligence, the system successfully integrates multiple intelligent components—including drug response classification, IC50 regression prediction, SHAP-based interpretability, an advanced preprocessing pipeline, and an interactive model dashboard—into a unified and user-friendly analytical platform. This comprehensive framework enables researchers and clinicians to rapidly predict drug efficacy, identify potential biomarkers, and gain deeper insights into the complex relationships between genomic profiles and treatment outcomes.

Across extensive experimentation using five state-of-the-art models (Logistic Regression, Random Forest, XGBoost, LightGBM, and Neural Networks), the system consistently showed that gradientboosted ensemble models, particularly **XGBoost**, provide highly accurate predictions for both categorical (Sensitive/Resistant) and continuous (LN_IC50) drug response outcomes. The preprocessing architecture, featuring automated encoding, scaling, fingerprint extraction, and mutation feature integration, proved essential for handling high-dimensional genomic datasets. Meanwhile, the explainability module (SHAP) provided transparent insights into the genomic and structural factors influencing drug sensitivity, making the system suitable for real-world biomedical research settings.

Collectively, these components demonstrate that AI-assisted drug response prediction can serve as a powerful support system for early-stage drug screening, facilitating the identification of promising therapeutic candidates and enabling personalized treatment planning by providing clinicians with data-driven insights tailored to individual patient profiles. By leveraging machine learning algorithms and integrating vast amounts of genomic and pharmacological data, this approach can significantly reduce laboratory experiment costs, streamline the drug development pipeline, and accelerate hypothesis generation in cancer pharmacogenomics. By bridging the gap between computational modeling and biological decision-making, this project represents a strong and scalable step toward building intelligent, data-driven precision oncology tools, ultimately paving the way for more effective and targeted cancer therapies.

6.1 Discussion of the Limitations of the Project

Despite the strong results,current system has limitations that constrain its direct realworld application:

1. **Limited Dataset Availability:**

   The dataset used, while realistic and diverse, still represents a subset of real-world pharmacogenomic variability. Rare mutations, complex gene–drug interactions, and multiomics factors (proteomics, transcriptomics) are not fully captured, potentially reducing generalizability.

2. **High-Dimensional Sparsity Issues:**

   Genomic mutation features (MUT_* columns) and drug fingerprints (DRUG_FP_*) create very high-dimensional sparse matrices. Although handled through preprocessing, this increases model training time and can introduce noise, particularly for linear and shallow models.

3. **Assumption of Independent Samples:**

   The current model assumes that each cell line and drug pair is independent. It does not incorporate biological relationships such as pathway interactions, gene networks, or crossdrug similarity.

4. **Lack of Experimental Wet-Lab Validation:**

   The predictions generated by the ML models are computational and have not been validated using real wet-lab IC50 assays or patient-derived samples. Thus, clinical adoption requires further verification.

5. **Limited Explainability in Certain Models:**

   While SHAP improves interpretability, highly complex neural network outputs can still be challenging to decode biologically.

6. **Static Modeling Approach:**

   The system predicts outcomes based on preprocessed static datasets. It does not support continuous learning or updating when new genomic–drug data becomes available.

6.2 Recommendations for Future Work

To improve performance, scalability, and practical usability, the following enhancements are recommended:

1. **Expand Dataset with Multi-Omics Inputs:**

   Incorporate transcriptomic, epigenomic, proteomic, and metabolomic features to improve biological accuracy and capture deeper cell-line–drug interactions.

2. **Integrate Graph Neural Networks (GNNs):**

   Use GNNs to model molecular structure more precisely and consider protein–protein interaction networks (PPIs) for mutation features.

3. **Develop True Clinical Validation Pipelines:**

   Collaborate with biomedical laboratories to validate predicted IC50 values using real experimental assays and patient-derived tumor samples.

4. **Introduce Reinforcement Learning for Drug Ranking:**

   Implement reinforcement learning (RL) to optimize treatment recommendation strategies for personalized drug ranking.

5. **Deploy the System on a Cloud Platform:**

   Hosting on AWS, Azure, or GCP will improve scalability, enable GPU-powered inference, and support real-time collaborations.

6. **Add Active Learning for Continuous Model Improvement:**

   Allow the system to re-train itself incrementally as new drug response data becomes available,

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