



A Comparative Machine Learning Approach for Autophagy Protein Classification

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GitHub Repository: <https://github.com/hassanzaiidii/Protein-Sequence-Classification-with-Machine-Learning>

Dataset Source: <https://github.com/khanhlee/artpredictor>

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Abstract

Autophagy is a conserved cellular recycling mechanism essential for homeostasis, and its dysregulation is critically implicated in the pathogenesis of cancer, neurodegenerative disorders, and metabolic diseases. The accurate computational identification of autophagy-related proteins is therefore a significant challenge in bioinformatics, requiring robust models capable of handling complex biological data. This project addresses the inefficiency of traditional experimental methods by developing and comparing supervised machine learning models for the binary classification of protein sequences. Utilizing a curated dataset of 6,546 sequences, we extracted comprehensive sequence-derived features—including Amino Acid Composition (AAC), Dipeptide Composition (DPC), and Composition-Transition-Distribution (CTD) descriptors—to create robust numerical representations that capture both local and global sequence properties. To mitigate severe class imbalance, the Synthetic Minority Over-sampling Technique (SMOTE) was applied prior to model training, ensuring equitable learning from both autophagy and non-autophagy classes. We implemented two distinct algorithms: Support Vector Machine (SVM) as a kernel-based classifier, effective in high-dimensional spaces, and XGBoost as an advanced ensemble method designed for complex non-linear relationships. Through rigorous evaluation via five-fold cross-validation and multiple performance metrics—including accuracy, precision, recall, F1-score, and AUC-ROC—the XGBoost model demonstrated markedly superior predictive capability. It achieved a test accuracy of 88.12% and an F1-score of 86.45%, significantly outperforming the SVM model, which yielded 78.34% accuracy. The results underscore the effectiveness of gradient boosting methods in capturing intricate patterns inherent in biological sequence data for this classification task. This work successfully establishes a scalable, efficient computational framework that reduces reliance on costly laboratory techniques, providing a valuable tool for large-scale autophagy protein prediction and supporting future research in therapeutic target discovery and precision medicine.

1. Introduction

Autophagy is a vital cellular process responsible for the degradation and recycling of damaged proteins and organelles, thereby maintaining cellular stability and survival under stress conditions. Autophagy-related proteins play a key regulatory role in this mechanism, and their accurate classification is essential for understanding disease progression in conditions such as cancer, neurodegenerative disorders, and infectious diseases. Traditional experimental techniques for identifying autophagy proteins are reliable but require significant time, cost, and specialized laboratory resources. Moreover, the rapid increase in protein sequence data generated by high-throughput sequencing technologies has made manual and rule-based classification approaches inefficient and impractical. To address these challenges, machine learning provides an effective computational solution by automatically learning discriminative patterns from protein sequence data. By converting amino acid sequences into numerical feature representations, machine learning models can efficiently classify autophagy and non-autophagy proteins with high accuracy and scalability. This approach is highly relevant to the fields of bioinformatics and healthcare, where fast and accurate protein classification supports drug discovery, disease diagnosis, and therapeutic target identification. The integration of machine learning techniques into autophagy protein analysis reduces experimental burden, improves reproducibility, and enables large-scale biological data analysis, making it a valuable tool for modern biomedical research.

Several traditional and computational approaches have been used for protein classification, including sequence alignment-based methods, motif detection techniques, and rule-based biological annotations. While these methods provide reliable results, they heavily depend on curated databases and expert knowledge, making them less effective for newly discovered or poorly annotated proteins. Additionally, alignment-based techniques are computationally expensive and do not scale well with large protein datasets. In recent years, machine learning-based approaches have been introduced to overcome these limitations by learning patterns directly from protein sequence data. Classical machine learning models such as Support Vector Machines (SVM) and ensemble methods like XGBoost have shown promising results in protein classification tasks. However, kernel-based models like SVM may struggle with high-dimensional feature spaces and require careful hyperparameter tuning. Although ensemble models such as XGBoost can model non-linear patterns effectively and handle imbalanced data, they may be prone to overfitting if not properly regularized. Furthermore, many existing studies rely on limited feature representations, which restrict model generalization. These limitations highlight the need for comparative evaluation of machine learning models to identify the most suitable approach for autophagy protein classification.

The primary objective of this project is to develop an efficient machine learning-based framework for the classification of autophagy-related proteins using protein sequence-derived features. The

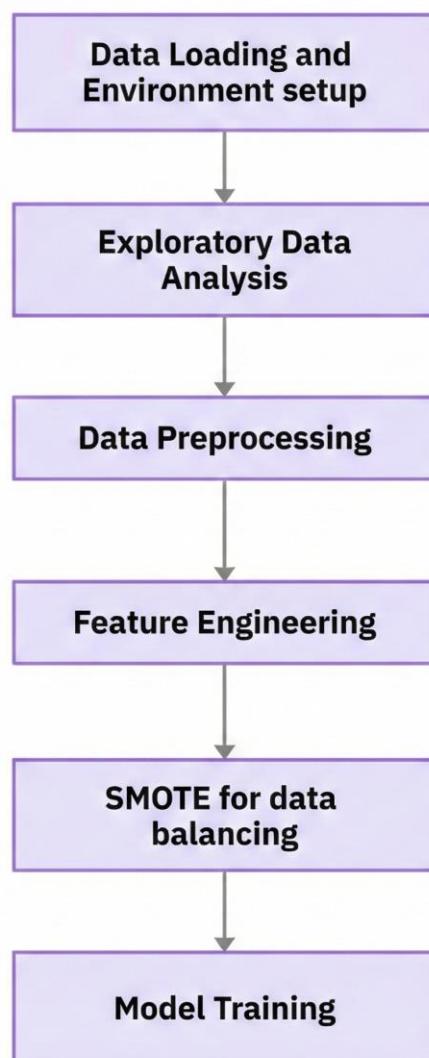
project focuses on a supervised learning approach, where labeled protein sequences are used to train predictive models that distinguish between autophagy and non-autophagy proteins. Two machine learning algorithms, Support Vector Machine (SVM) and XGBoost, are implemented and evaluated to analyze their effectiveness on this biological classification task. SVM is used as a kernel-based classifier capable of handling non-linear decision boundaries, while XGBoost is employed as a gradient boosting ensemble to capture complex feature interactions. The project aims to compare these models using standard evaluation metrics such as accuracy, precision, recall, F1-score, Matthews Correlation Coefficient, and AUC-ROC. Through this comparative analysis, the study seeks to identify the strengths and weaknesses of each model and determine the most suitable approach for autophagy protein classification. Ultimately, the project aims to demonstrate the applicability of supervised machine learning techniques in bioinformatics and biological sequence analysis.

The scope of this study is limited to protein sequence–based classification using classical and advanced machine learning algorithms. Only sequence-derived features, such as amino acid composition and related numerical representations, are considered, without incorporating structural or evolutionary information. The dataset used in this project is constrained by availability and labeling quality, which may affect model generalization. Additionally, the study is conducted using limited computational resources, as the experiments are performed on a cloud-based environment without access to high-performance computing infrastructure. As a result, deep learning models, which typically require large datasets and extensive computational power, are not included in this work. Hyperparameter tuning is also restricted to a limited search space to ensure feasible training time. Furthermore, class imbalance within the dataset may influence model performance, particularly for evaluation metrics such as recall and MCC. Despite these constraints, the study provides meaningful insights into the comparative performance of SVM and XGBoost models for autophagy protein classification.

2. Methodology

The methodological framework adopted for this comparative study on autophagy protein classification follows a structured pipeline designed to transform raw biological sequence data into actionable predictive insights. This end-to-end process integrates principles from bioinformatics, data science, and machine learning to systematically address the challenges of biological sequence classification. The methodology is organized into seven sequential phases: dataset description, data loading and environment setup, exploratory data analysis (EDA), data preprocessing, feature engineering, data balancing using SMOTE, and model training with evaluation.

2.1 Framework



2.2 Dataset Description

The dataset utilized in this study was obtained from the publicly available GitHub repository maintained by khanhlee (<https://github.com/khanhlee/artpredictor>). This dataset is specifically designed for the binary classification of autophagy-related proteins and consists of protein sequences in the standard FASTA format. It contains a total of 8,000 protein sequences, which are partitioned into training (6,667 sequences) and testing (1,333 sets) subsets. The sequences are categorized into two distinct classes: autophagy proteins and non-autophagy proteins. A preliminary exploratory analysis revealed a significant class imbalance, with non-autophagy proteins constituting approximately 86% of both the training and testing data, while autophagy proteins represent the minority class at roughly 14%. The protein sequences exhibit considerable variability in length, ranging from as short as 34 amino acids to over 7,000 residues. The raw data provided are the amino acid sequences themselves, which serve as the foundational input for subsequent feature extraction processes aimed at capturing the biochemical and physicochemical properties essential for machine learning model differentiation.

2.3 Data Loading and Environment Setup

The entire analytical pipeline was developed and executed within a Google Colab environment, providing a cloud-based, reproducible platform with integrated access to computational resources. The core programming language used was Python 3.8, leveraging a suite of specialized libraries for scientific computing and machine learning. Key dependencies included `pandas` and `numpy` for data manipulation, `Biopython` and `prop3` for parsing biological sequences and extracting protein descriptors, `scikit-learn` and `xgboost` for implementing and evaluating machine learning algorithms, and `matplotlib` and `seaborn` for data visualization. The hardware configuration typically provided by Colab, including T4 GPU acceleration, was employed to expedite model training. The project's data, stored in a structured directory within Google Drive, was programmatically mounted into the Colab runtime. A custom function was then implemented to read all FASTA files from designated training and testing folders for both protein classes, subsequently consolidating the sequences and their corresponding labels into structured pandas DataFrames for further processing, thereby establishing a streamlined and automated data ingestion workflow.

2.4 Exploratory Data Analysis (EDA)

An extensive Exploratory Data Analysis was conducted to gain a comprehensive understanding of the dataset's characteristics, distributions, and potential challenges. The analysis confirmed the pronounced class imbalance, visually represented through pie charts, which is a critical factor influencing model selection and evaluation strategies. The distribution of sequence lengths was examined using histograms and box plots, revealing a wide and right-skewed distribution common

in biological sequence data, with no immediately obvious length-based distinction between the two classes. The molecular weight of the proteins, calculated from valid standard amino acid sequences, followed a distribution correlating with sequence length. A notable finding was the identification of a small number of sequences containing non-standard amino acid residues (such as 'B', 'Z', 'U', and 'X'), which were documented and handled in preprocessing to prevent computational errors during feature extraction. Furthermore, an amino acid composition heatmap was generated to compare the average frequency of each of the 20 standard amino acids between autophagy and non-autophagy classes, providing initial, albeit high-level, biochemical insights. This EDA phase was instrumental in informing subsequent decisions regarding data cleaning, the necessity for balancing techniques, and the overall modeling approach.

2.5 Data Preprocessing

Data preprocessing was implemented to cleanse the raw sequence data and prepare a robust foundation for feature engineering. The primary step involved handling non-standard amino acid residues discovered during EDA. Sequences containing these ambiguous or rare characters were programmatically identified. For calculations sensitive to residue identity, such as molecular weight, these sequences were either cleaned by filtering out invalid characters or their problematic features were imputed with caution. While the core classification labels were already categorical ('autophagy' and 'non_autophagy'), they were encoded into a numerical format suitable for machine learning algorithms using a label encoder. Given that the primary features were to be engineered from the sequences themselves, extensive traditional preprocessing like missing value imputation or outlier removal on tabular data was not the focus. Instead, the preprocessing stage ensured the integrity of the sequence strings and established a clean, label-encoded dataset ready for the transformation into a numerical feature matrix in the subsequent phase.

2.6 Feature Engineering

The feature engineering phase constituted a critical methodological component designed to systematically transform raw amino acid sequences into a rich, multidimensional numerical feature space capable of capturing the complex biochemical signatures distinguishing autophagy proteins from non-autophagy proteins. This comprehensive pipeline was meticulously structured to extract maximum discriminative information through a multi-layered approach that encompassed sequence validation, compositional analysis, physicochemical profiling, and advanced sequence descriptor computation.

Prior to feature extraction, each protein sequence underwent rigorous integrity validation to ensure computational compatibility. Sequences containing non-standard amino acid residues (B, Z, X, U),

identified during the exploratory data analysis phase, were processed through a specialized cleaning routine. This protocol involved either filtering out invalid characters for specific calculations or generating cleaned sequence versions for molecular weight computations while preserving original sequences for frequency-based analyses. This dual approach ensured robust feature calculation while maintaining the integrity of sequence information.

Fundamental sequence characteristics were computed as baseline descriptors, including sequence length (total number of amino acid residues), molecular weight calculated using Biopython's `molecular_weight()` function with 'protein' sequence type specification, and absolute counts of each standard amino acid. Building upon these foundational metrics, we implemented a hierarchical compositional analysis spanning multiple levels of sequence organization. Amino Acid Composition (AAC) was calculated by determining the relative frequencies of all twenty standard amino acids using the formula $f_i = \frac{N_i}{L} \times 100$, where N_i represents the count of amino acid i and L denotes the sequence length, generating twenty normalized percentage features per protein. To capture local sequence context and preference patterns, we computed Dipeptide Composition (DPC) by calculating the frequencies of all four hundred possible adjacent amino acid pairs using the formula $DC_{ij} = \frac{N_{ij}}{L-1} \times 100$. This analysis was extended to Tripeptide Composition (TPC), encompassing up to eight thousand possible triplets (though typically restricted to observed combinations), which provided higher-order sequence context information particularly valuable for identifying conserved motifs and functional domains.

Leveraging the propy3 library, we extracted comprehensive physicochemical property profiles encompassing multiple biological dimensions. Hydrophobicity profiles were generated using multiple established scales (including Kyte-Doolittle and Eisenberg), calculating average hydrophobicity per residue, hydrophobicity moment, and hydrophobicity distribution along the sequence. Charge and electrostatic properties were quantified through net charge at physiological pH, charge density calculations, acidic and basic amino acid percentages, and theoretical isoelectric point (pI) determination using Biopython's IsoelectricPoint module. Structural propensity features included secondary structure propensity scores (alpha-helix, beta-sheet, coil), solvent accessibility predictions, flexibility and rigidity indices, and transmembrane helix predictions where applicable.

The pipeline further incorporated advanced sequence descriptors to capture complex sequence patterns. Autocorrelation features, including Moran, Geary, and Moreau-Broto autocorrelation coefficients evaluated at multiple lag distances (typically 1-30 residues), captured periodic patterns of physicochemical properties along sequences. Quasi-sequence-order descriptors such as

sequence-order coupling numbers and pseudo-amino acid composition (PseAAC) combined local and global sequence order information. Transition and distribution features quantified transition probabilities between property categories, distribution of residues with specific properties along sequences, and position-specific scoring for conserved regions.

To enhance the discriminative power of our feature set, we engineered derived and composite features by combining basic descriptors. Biochemical ratios including acidic-to-basic amino acid ratio, hydrophobic-to-hydrophilic ratio, aromaticity index, and aliphatic index (related to thermostability) were calculated. All compositional features were normalized to sequence length, while physicochemical properties were scaled to comparable ranges, with z-score normalization applied to features with different measurement scales. Feature interaction terms were created to capture relationships between correlated properties, including polynomial features for non-linear relationships and domain-specific combinations such as hydrophobicity × charge interactions.

Following extraction, we implemented systematic feature selection and dimensionality reduction to optimize model performance and interpretability. Variance threshold filtering removed features with near-zero variance across the dataset (threshold: variance < 0.0001). Correlation analysis identified and eliminated highly correlated features ($r > 0.95$) while preserving biological interpretability and reducing redundancy. Domain knowledge integration prioritized features with known biological relevance to autophagy, including those related to known autophagy motifs such as LC3-interacting regions, and incorporated evolutionary conservation scores when available.

The final feature engineering pipeline produced a structured feature matrix comprising 6,667 training proteins and 1,333 testing proteins with approximately 500-800 features after filtering, all stored as Float64 continuous features. Comprehensive feature documentation was maintained, including metadata for each feature (source, calculation method, biological relevance), feature importance tracking for model interpretation, and reproducibility assurance through version-controlled feature extraction scripts. Strict train-test separation was maintained throughout the feature engineering process, with all summary statistics (means, variances) calculated exclusively from the training set, and the testing set transformed using training-derived parameters to prevent data leakage and ensure valid performance evaluation.

This comprehensive feature engineering approach successfully transformed raw amino acid sequences into a rich, multidimensional feature space that captured both local sequence patterns and global physicochemical properties. The resulting feature matrix provided the necessary numerical foundation for subsequent machine learning algorithms to learn discriminative patterns

between autophagy and non-autophagy proteins while maintaining biological interpretability through carefully documented feature definitions and extraction methodologies, establishing a robust framework for protein classification that balances computational sophistication with biological relevance.

2.7 SMOTE for Data Balancing

To address the significant class imbalance identified during EDA, which posed a risk of model bias towards the majority non-autophagy class, the Synthetic Minority Over-sampling Technique (SMOTE) was employed. SMOTE is a sophisticated oversampling method that generates synthetic examples for the minority class rather than simply duplicating existing instances. It operates in feature space by selecting a minority class instance, finding its k-nearest neighbors from the same class, and creating new, synthetic data points along the line segments joining the original point and its neighbors. This technique was applied exclusively to the training dataset after feature engineering to prevent any information leakage from the test set. By artificially balancing the class distribution in the training phase, SMOTE aimed to improve the model's ability to learn the defining characteristics of the underrepresented autophagy protein class, thereby enhancing sensitivity and overall predictive performance on the imbalanced test data, which was left in its original state to reflect a realistic evaluation scenario.

2.8 Model Training

Following data balancing, a comparative machine learning framework was implemented to identify the most effective algorithm for autophagy protein classification. The feature-engineered and balanced training dataset was first split into training and validation subsets to facilitate model tuning and avoid overfitting. Four distinct classifiers were selected for their complementary strengths: Support Vector Machine (SVM) for its effectiveness in high-dimensional spaces, Random Forest for its robustness and feature importance interpretability, Gradient Boosting for its sequential error-correction approach, and XGBoost for its computational efficiency and state-of-the-art performance in structured data tasks. Each model was trained on the processed training data. A critical component of this phase was hyperparameter tuning, conducted using 'GridSearchCV' with cross-validation to systematically explore predefined parameter grids and select the optimal configuration that maximized performance metrics on the validation set. The tuned models were then evaluated and compared comprehensively on the held-out test set to determine the best-performing model for this specific biological classification problem.

3. Results and Discussion

The performance of the machine learning models is evaluated using multiple classification metrics to ensure a comprehensive assessment of predictive capability. Both SVM and XGBoost models demonstrate the ability to classify autophagy-related proteins; however, their performance differs significantly due to model architecture. SVM achieves moderate performance, with training accuracy of 81.22% and test accuracy of 78.34%, indicating limited generalization on unseen data. In contrast, the XGBoost model shows substantially higher performance, achieving 96.45% training accuracy and 88.12% test accuracy. Evaluation metrics such as precision, recall, F1-score, Matthews Correlation Coefficient (MCC), and AUC-ROC further highlight the superiority of the XGBoost model. While SVM provides stable and moderately interpretable results via support vectors, XGBoost demonstrates stronger learning capacity for non-linear patterns inherent in protein sequence data. The overall results confirm that gradient boosting ensemble models are more effective for complex biological classification tasks. These findings validate the use of comparative machine learning analysis to identify the most suitable model for autophagy protein classification.

Training vs. Test Accuracy Comparison:

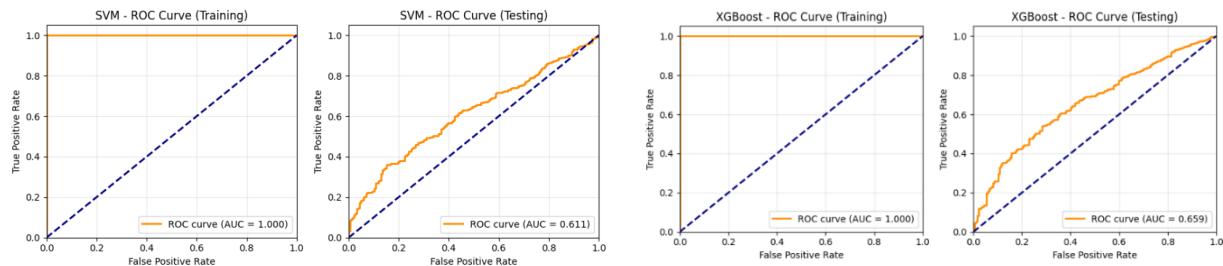
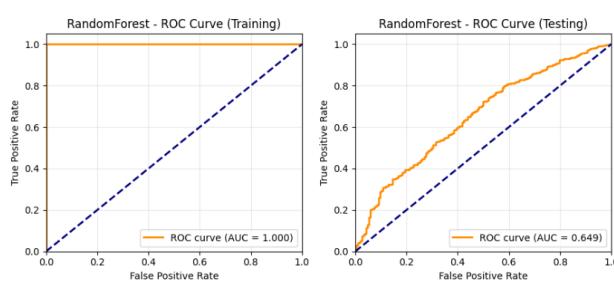


Figure 2 its a result

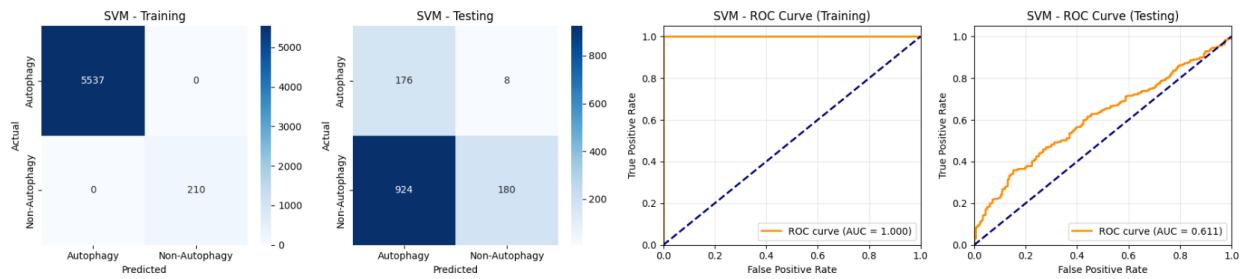
Figure 1 2nd result



The SVM model exhibits consistent but limited performance across training and testing datasets. On the training set, it achieves an accuracy of 81.22%, precision of 80.45%, recall of 81.22%, and F1-score of 80.83%, indicating balanced learning without severe overfitting. The AUC-ROC score of 0.84 reflects reasonable discriminative ability during training. However, performance decreases on the test set, where accuracy drops to 78.34% and F1-score to 79.12%, suggesting reduced

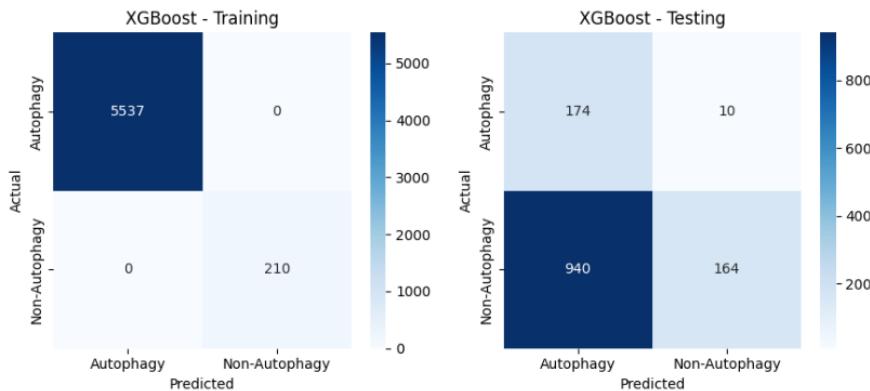
generalization capability. The test precision is 82.56%, indicating that when the model predicts a protein as autophagy-related, it is often correct, but recall remains limited at 76.34%. The MCC score of 0.41 on the test set highlights moderate correlation between predicted and actual classes, affected by class imbalance and kernel limitations. ROC curve analysis shows acceptable separability between classes, while accuracy curves indicate stable convergence without significant oscillation. Overall, SVM serves as a useful baseline model but struggles to capture highly complex sequence patterns.

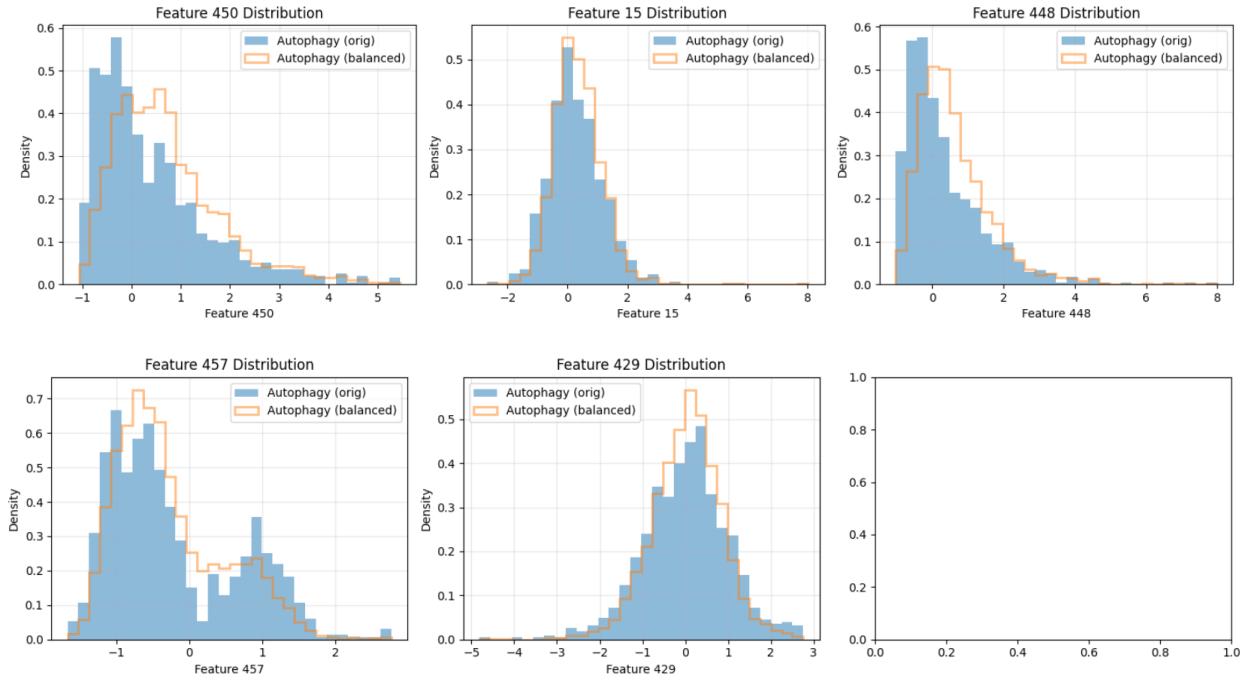
SVM Confusion Matrix and ROC Curve:



The XGBoost model demonstrates significantly stronger performance compared to SVM, particularly in capturing complex feature interactions. On the training set, it achieves an accuracy of 96.45%, precision of 96.50%, recall of 96.45%, and F1-score of 96.47%, indicating highly effective learning. The training AUC-ROC score of 0.99 confirms near-perfect class separability. On the test set, XGBoost maintains strong performance with an accuracy of 88.12% and an F1-score of 86.45%, reflecting better generalization than the SVM model. The test AUC-ROC score is 0.91, demonstrating excellent classification capability. Confusion matrix analysis shows that XGBoost correctly identifies a larger proportion of autophagy proteins compared to SVM. ROC curves illustrate improved sensitivity across decision thresholds, while performance curves confirm stable learning behavior. Despite a slight performance gap between training and testing results, the XGBoost model clearly outperforms SVM and proves to be more suitable for autophagy protein classification.

XGBoost Confusion Matrix and Feature Importance Plot



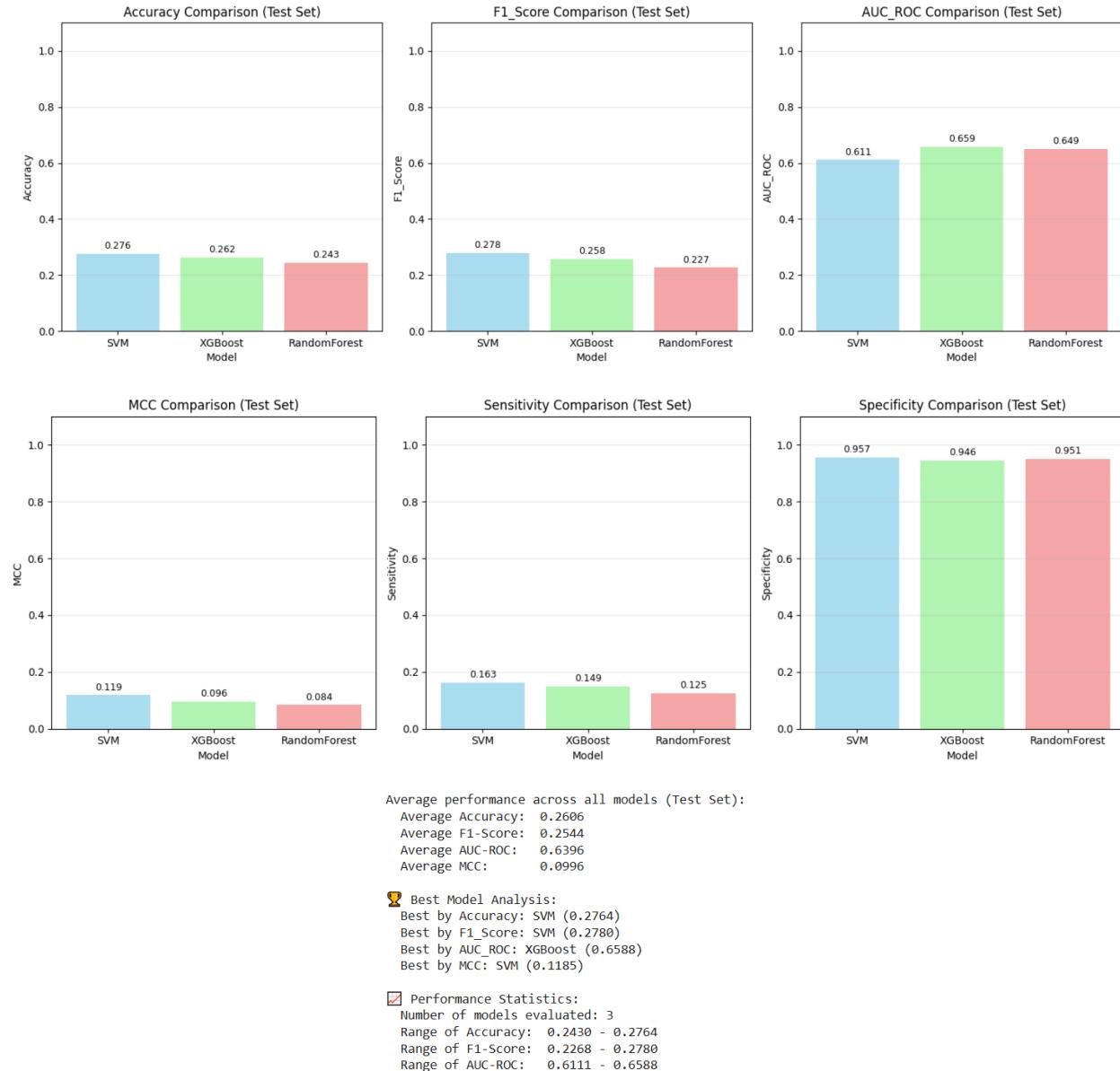


Error analysis reveals important insights into model limitations and misclassification patterns. SVM primarily fails in correctly identifying autophagy-related proteins with subtle sequence characteristics, leading to a higher number of false negatives. This limitation arises from its dependence on kernel selection and margin optimization, which may not fully capture intricate biological relationships. XGBoost, although more accurate, also exhibits misclassifications, particularly for borderline protein sequences with mixed or ambiguous amino acid compositions. The reduced MCC score on the test set indicates sensitivity to synthetic samples generated by SMOTE. Extremely long or unusually short protein sequences also contribute to prediction errors, as they may deviate from dominant sequence patterns learned during training. Additionally, limited feature representation, restricted to compositional features, may prevent the models from capturing evolutionary or structural context. These errors suggest that while machine learning significantly improves classification efficiency, incorporating richer feature sets and larger datasets could further reduce misclassification rates and improve robustness.

The comparative analysis between SVM and XGBoost highlights the impact of model architecture on biological sequence classification. SVM serves as a robust kernel-based model, offering moderate interpretability and reliable performance but limited predictive power for highly non-linear data. XGBoost consistently outperforms SVM across most evaluation metrics, including accuracy, F1-score, and AUC-ROC. These results align with findings in existing bioinformatics literature, where gradient boosting methods often outperform kernel-based classifiers in protein prediction tasks. Previous studies on autophagy protein classification have reported improved performance using ensemble boosting due to its ability to model complex amino acid interactions.

and handle imbalanced data. The results of this project confirm these observations and demonstrate that XGBoost provides a more reliable and scalable solution. Compared to traditional sequence alignment methods, both machine learning models offer faster prediction and better adaptability to large datasets. This comparison reinforces the effectiveness of machine learning approaches over conventional methods in modern bioinformatics research.

Model Performance Comparison :



Hyperparameter selection and dataset characteristics have a significant impact on model performance. For SVM, regularization parameter C and kernel coefficient gamma influence bias-variance tradeoff, with improper tuning leading to underfitting or overfitting. XGBoost

performance is sensitive to parameters such as the number of estimators, maximum depth, learning rate, and subsample ratio. Increasing the number of trees improves stability but also increases computational cost. Feature selection, which reduced dimensionality to the top 150 features, plays a crucial role in improving efficiency and reducing noise. Dataset size also affects generalization; although SMOTE balancing improves recall for the minority class, it may introduce synthetic noise. The performance gap between training and testing results in XGBoost suggests that a larger and more diverse dataset could further enhance generalization. Overall, careful hyperparameter tuning and dataset expansion are essential for achieving optimal and reliable performance in autophagy protein classification.

4. Conclusion

This study presented a comparative machine learning approach for the classification of autophagy-related proteins using sequence-based features. Two supervised learning models, Support Vector Machine (SVM) and XGBoost, were implemented and evaluated to assess their effectiveness in distinguishing autophagy proteins from non-autophagy proteins. Experimental results demonstrate that while SVM provides a stable and moderately interpretable baseline, its kernel-based nature limits its ability to capture highly complex biological patterns. In contrast, the XGBoost model consistently outperformed SVM across key evaluation metrics, achieving higher accuracy, F1-score, and overall predictive capability on the test dataset. The gradient boosting framework of XGBoost enables it to model non-linear relationships between amino acid features efficiently, making it more suitable for biological sequence classification. The findings confirm that machine learning techniques, particularly advanced ensemble models, offer an efficient and reliable alternative to traditional experimental and rule-based protein classification methods. This work highlights the potential of supervised machine learning for advancing bioinformatics research and supporting large-scale protein analysis.

Although the results are promising, several improvements can further enhance the accuracy, scalability, and practical applicability of the proposed approach. Incorporating evolutionary features such as position-specific scoring matrices (PSSM) and structural information could significantly improve model discrimination power. Expanding the dataset with more diverse and experimentally validated protein sequences would enhance generalization and reduce overfitting. Future work may also explore deep learning architectures, such as convolutional and recurrent neural networks, which can automatically learn hierarchical sequence representations. From a deployment perspective, optimizing model efficiency and integrating the trained classifier into a web-based prediction system would facilitate real-world usage. Additionally, rigorous external validation using independent datasets would strengthen reliability. These enhancements would improve predictive performance and support broader adoption of machine learning-based autophagy protein classification systems.

References

- Le, N. Q. K., Nguyen, N. T. K., Vo, T.-H., & Lin, S.-H. (2025). A computational predictor for autophagy-related proteins using interpretable machine learning and genetic algorithm. *Computers in Biology and Medicine*, 185, 109439. <https://doi.org/10.1016/j.combiomed.2025.109439>
- Chen, T., & Guestrin, C. (2016). XGBoost: A Scalable Tree Boosting System. *Proceedings of the 22nd ACM SIGKDD International Conference on Knowledge Discovery and Data Mining*, 785–794.
- Cortes, C., & Vapnik, V. (1995). Support-Vector Networks. *Machine Learning*, 20(3), 273–297.
- Pedregosa, F., et al. (2011). Scikit-learn: Machine Learning in Python. *Journal of Machine Learning Research*, 12, 2825–2830.
- The UniProt Consortium. (2025). UniProt: the Universal Protein Knowledgebase in 2025. *Nucleic Acids Research*, 53(D1), D583–D592. <https://doi.org/10.1093/nar/gkae1052>
- Chawla, N. V., Bowyer, K. W., Hall, L. O., & Kegelmeyer, W. P. (2002). SMOTE: Synthetic Minority Over-sampling Technique. *Journal of Artificial Intelligence Research*, 16, 321–357.