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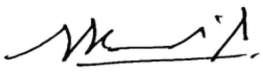

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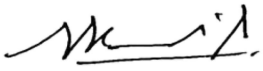

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This thesis is dedicated to GOD and my beloved family.

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Ritesh Sharma

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Abbreviations

Abbreviation	Description
AI	Artificial Intelligence
AMR	Antimicrobial Resistance
AMPs	Antimicrobial Peptides
AVPs	Antiviral Peptides
AFPs	Antifungal Peptides
ABPs	Antibacterial Peptides
MIC	Minimum Inhibitory Concentration
WHO	World Health Organization
RBCs	Red Blood Cells
AUC	Area Under Curve
ELMo	Embeddings from Language Models
HCF	Handcrafted Features
PESTV	Pretrained Embeddings from Seq2vec
OHE	One-Hot Encoding
XGBoost	Extreme Gradient Boosting
SVM	Support Vector Machine
RF	Random Forest
LR	Logistics Regression
NB	Naive Bayes

Abbreviation	**Description**
KNN	K-Nearest Neighbour
ANN	Artificial Neural Network
CM	Classification Module
ERT	Extremely Randomized Trees
AB	AdaBoost
GB	Gradient Boosting
ReLU	Rectified Linear Unit
ICL	Independent Component Layer
Adam	Adaptive Moment Estimation
FDA	Food and Drug Administration
Bi-GRU	Bidirectional Gated Recurrent Unit
Bi-LSTM	Bidirectional Long Short-Term Memory
BiTCN	Bidirectional Temporal Convolutional Network
CNN	Convolutional Neural Network
LIME	Local Interpretable Model-agnostic Explanations
IC	Independent Component
GF	Genomic Features

List of Symbols

Symbol	Description
z_t	update gate
r_t	reset gate
h_t	candidate state
i_t	input gate
o_t	output gate
f_t	forget gate
L	loss function
η	learning rate
σ	activation function
x_t	embedding vector of the amino acid

Preface

The discovery of antibiotics revolutionized modern healthcare and increased the lifespan of humans by more than twenty years, but their unregulated use has resulted in antimicrobial resistance (AMR). AMR kills at least 7 lakh people in poor and middle-income countries each year, and the WHO ranks it as one of the top ten public health hazards. To counteract this condition, novel antimicrobial compounds are required, and antimicrobial peptides (AMPs) show promise in this regard. AMPs are proteins produced by diverse organisms naturally and can be classified into multiple groups, such as antiviral (AVPs), antifungal (AFPs), and antibacterial peptides (ABPs).

To avoid the high costs and time associated with identifying novel AMPs in the lab, researchers use *in-silico* tools for preliminary screening of natural sources. However, the existing tools available for this purpose have poor performance, which limits their applicability for wet-lab researchers. Thus, we have proposed AI-based frameworks for identifying AFPs, AVPs, and ABPs from natural sources in different studies.

All amino acids are not equally important in classifying a peptide. Existing AI-based tools do not provide information about the essential amino acids responsible for classifying a peptide. Therefore, we developed an explainable framework that not only classifies the peptides but also provides information about the essential amino acids responsible for classifying a peptide.

The WHO categorizes bacteria into three categories (critical, high, and medium), and the ESKAPEE pathogens are a major threat as they range from high to critical

WHO-priority pathogens. Earlier studies can identify ABPs from natural resources but do not provide minimum inhibitory concentration (MIC) values against the ESKAPEE pathogens. Thus, for identifying optimal ABPs (which work at low MIC), wet-lab researchers have to test the identified ABPs against ESKAPEE pathogens at different concentrations, leading to a loss of time and money. To address this issue, we proposed a framework that predicts the MIC values for ABPs against ESKAPEE pathogens. The proposed framework can help identify optimal ABPs that can work at low MICs against the entire ESKAPEE group of bacteria.

Peptide toxicity is a major hurdle in the development of therapeutic peptides. Hemolytic activity against red blood cells is one of the key factors to consider when evaluating peptide toxicity. High hemolytic activity can lead to anemia and other blood disorders, making highly hemolytic peptides unsuitable for pharmaceutical use. However, discovering low hemolytic peptides is a labor-intensive and time-consuming process that involves testing on mammalian red blood cells. To address this, we proposed a framework to identify low hemolytic therapeutic peptides.

All the frameworks we developed as part of different studies have also been made available as web applications. The wet-lab researchers can use these tools to narrow the search space while discovering low hemolytic AMPs active against different pathogens.