El-Sewedy University of Technology

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Graduation Project I

Artificial Intelligence based approach for Predicting Drug-Target Binding Affinity

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Abstract

Predicting drug target binding affinity (DTA) is a fundamental problem in modern drug discovery, as it directly determines the effectiveness of a drug candidate in interacting with its biological target. Traditionally, binding affinity has been measured using experimental laboratory techniques such as biochemical assays and molecular docking, which, despite their accuracy, are costly, time-consuming, and require extensive human and material resources, significantly slowing down the drug discovery pipeline and contributing to high failure rates in pharmaceutical development. With the rapid growth of biological data and advances in artificial intelligence, computational approaches have emerged as powerful alternatives to experimental screening by enabling large-scale and efficient evaluation of drug target interactions. Machine learning and deep learning models enable the prediction of binding affinity by learning complex interaction patterns from drug and protein representations, allowing researchers to prioritize promising drug candidates while reducing reliance on laboratory experiments. This report presents a comprehensive study of drug target binding affinity prediction, covering its historical background, experimental challenges, and the transition toward state-of-the-art AI driven methodologies, with a particular focus on modern deep learning architectures that offer improved predictive accuracy, scalability, and cost-effectiveness for accelerating drug discovery processes.

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List Of Abbreviation

Abbreviation	Full Name
AI	Artificial Intelligence
DL	Deep Learning
DTA	Drug–Target Binding Affinity
ML	Machine Learning
RNN	Recurrent Neural Network
CNN	Convolutional Neural Network 1D CNN
1D CNN	One-Dimensional Convolutional Neural Network
GNN	Graph Neural Network
MSE	Mean Squared Error
RMSE	Root Mean Squared Error
MAE	Mean Absolute Error
R^2	Coefficient of Determination
SMILES	Simplified Molecular Input Line Entry System
FFN	Feed-Forward Network
EDA	Exploratory Data Analysis

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Chapter 1: Introduction

Drug discovery represents one of the most complex, time-consuming, and resource-intensive processes in modern biomedical research. At its core, drug discovery aims to identify chemical compounds capable of interacting effectively with specific biological targets, most commonly proteins in order to modulate their function and produce a desired therapeutic effect. The strength of this interaction, known as drug–target binding affinity, plays a crucial role in determining both the efficacy and safety of a drug candidate. A strong and specific binding interaction is often associated with improved therapeutic outcomes, while weak or nonspecific binding can lead to reduced effectiveness or undesirable side effects. Historically, the identification and evaluation of drug target interactions relied almost entirely on experimental laboratory techniques. Researchers conducted extensive in vitro and in vivo experiments to assess whether a candidate compound could bind to a target protein and influence its biological activity. Although these experimental approaches provide accurate and reliable measurements, they suffer from several critical limitations. Experimental assays require sophisticated laboratory infrastructure, highly trained personnel, and long experimental cycles that may span months or even years. Furthermore, the financial cost associated with large scale experimental screening is extremely high, contributing significantly to the rising cost and long timelines of pharmaceutical development.

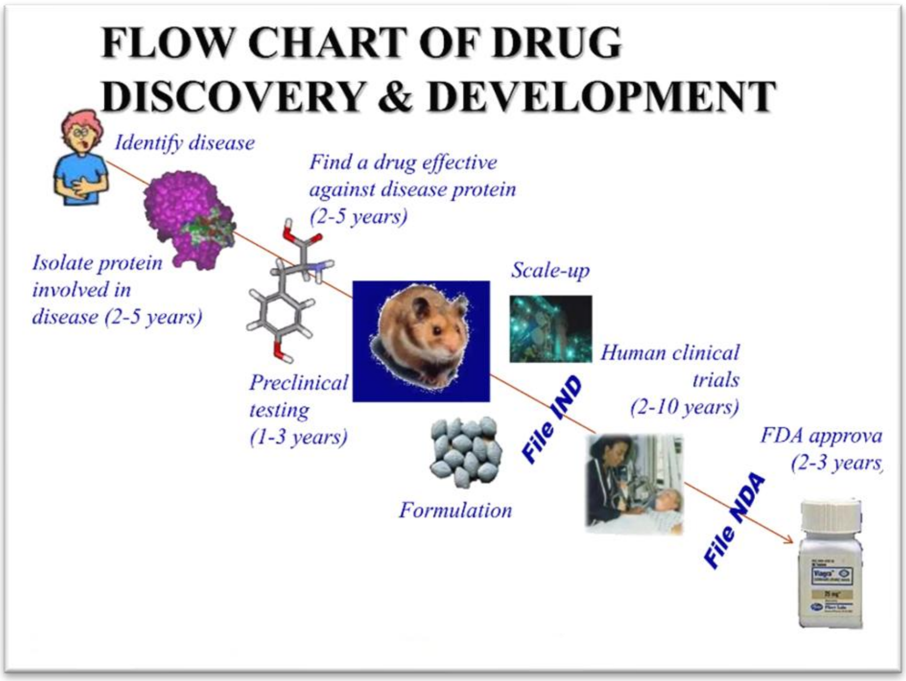

FLOW CHART OF DRUG DISCOVERY & DEVELOPMENT
Identify disease
Find a drug effective against disease protein (2-5 years)
Isolate protein involved in disease (2-5 years)
Scale-up
Preclinical testing (1-3 years)
Human clinical trials (2-10 years)
File IND
Formulation
FDA approva (2-3 years
File NDA

Figure 1:
Traditional experimental drug discovery workflows illustrating manual laboratory procedures, long development timelines, and high resource consumption

Another major challenge in traditional drug discovery is the low success rate. Despite screening thousands or even millions of candidate molecules, only a small fraction successfully passes preclinical testing and clinical trials. The vast size of chemical space and the diversity of biological targets make it practically infeasible to experimentally evaluate all possible drug target combinations. As a result, researchers are often forced to prioritize limited subsets of compounds, increasing the risk of overlooking promising drug candidates and further slowing the discovery process. The rapid growth of biological data, combined with advances in computational power, has driven a paradigm shift toward computational and data driven approaches in drug discovery. Early computational methods, such as molecular docking and physics-based simulations, aimed to estimate binding affinity using three-dimensional structural information. While these approaches reduced some experimental burden, they remained computationally expensive and sensitive to structural inaccuracies. The emergence of machine learning introduced a more flexible alternative, allowing models to learn relationships between drugs and targets directly from data rather than relying solely on predefined physical rules. More recently, deep learning has further transformed drug target binding affinity prediction by enabling automatic feature extraction from raw drug and protein representations. Deep neural networks can capture complex, nonlinear interaction patterns that are difficult to model using traditional methods. Architectures such as Recurrent Neural Networks (RNNs), Convolutional Neural Networks (CNNs), Graph Neural Networks (GNNs), and Transformer based models have demonstrated significant improvements in predictive performance, scalability, and generalization ability. These advances have positioned computational binding affinity prediction as a critical component of modern, AI driven drug discovery pipelines.

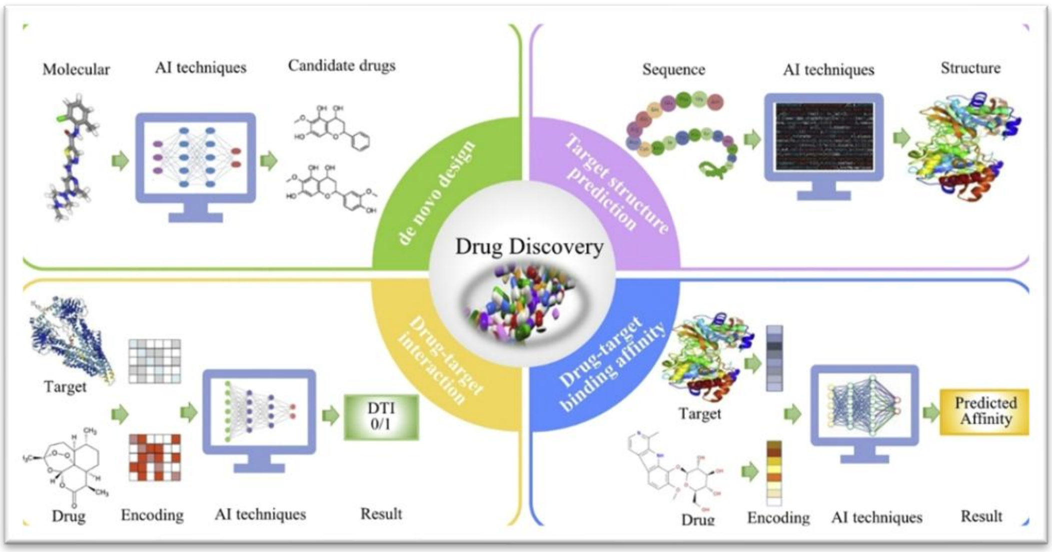


Figure 2:
Evolution of drug discovery and binding affinity prediction methods from traditional laboratory experiments to machine learning and deep learning-based approaches

1.1 Scope of This Project

The scope of this project is to investigate and analyze the problem of drug target binding affinity prediction using advanced artificial intelligence techniques. The project focuses on leveraging modern deep learning models to predict binding affinity values from drug and protein representations, with the objective of reducing experimental cost, accelerating the drug discovery process, and improving predictive accuracy. Emphasis is placed on the use of large-scale benchmark datasets and state-of-the-art neural architectures to evaluate model performance under realistic drug discovery scenarios. This project explores multiple deep learning model families, including sequence based, convolution based, graph-based, and attention-based architectures. Special attention is given to Transformer-based models due to their ability to capture long-range dependencies and complex interactions between drugs and targets, making them well-suited for high-dimensional biological data.

1.2 Contribution of This Project

The main contribution of this project lies in providing a systematic and comparative analysis of multiple deep learning models for drug target binding affinity prediction using the same dataset and evaluation framework. In this work, several deep learning architectures, including Recurrent Neural Networks, one-dimensional Convolutional Neural Networks, Graph Neural Networks, and Transformer-based models, were implemented and evaluated under identical experimental conditions. This unified setup enables fair comparison between models and highlights their relative strengths and limitations. Furthermore, the project provides a detailed experimental analysis that combines quantitative evaluation metrics with qualitative sample-level and visual assessments. The results demonstrate that most of the implemented models achieve strong predictive performance, with advanced architectures showing particularly promising results. By integrating data preprocessing, model training, and evaluation within a structured workflow, this project offers practical insights into the effectiveness of different deep learning approaches and contributes to a better understanding of model behavior in drug target binding affinity prediction.

1.3 Organization of the Report of the Project

This report is organized to provide clear and logical progression from the problem background to the applied methodologies, experimental evaluation, and final conclusions. Chapter 2 presents a detailed description of the dataset used in this study, including its structure, main components, and relevance to the drug target binding affinity prediction task. Chapter 3 introduces the mathematical foundations and modeling techniques employed in this work, providing an in-depth explanation of the deep learning architectures used, including recurrent, convolutional, graph-based, and attention-based models. Chapter 4 focuses on the proposed approach adopted in this study, outlining the overall workflow and methodology through three main phases: data preprocessing, deep learning model training, and evaluation. This chapter provides a high-level description of how the different components of the system are organized and interact with each other, serving as a bridge between theoretical modeling and practical implementation. Chapter 5 presents the experimental results and discussion, where the performance of the implemented models is analyzed and compared using quantitative evaluation metrics, sample-level analysis, and visual representations. Finally, Chapter 6 concludes the report by summarizing the key findings of the study, discussing the limitations of the proposed approach, and outlining potential directions for future research in AI-driven drug discovery.

Chapter 2: Related Work

The task of predicting drug–target binding affinity has been widely investigated in computational drug discovery due to its importance in accelerating drug development and reducing experimental cost. Early studies primarily relied on traditional machine learning techniques combined with manually engineered features derived from chemical descriptors and protein sequence information. In [1], the authors proposed a regression-based framework using support vector machines to predict binding affinity scores from handcrafted molecular features, demonstrating the feasibility of computational affinity prediction. However, the performance of such approaches was highly dependent on feature design and limited in capturing complex nonlinear relationships. To overcome these limitations, researchers began exploring more advanced machine learning models. In [2], random forest and ensemble-based methods were employed to improve prediction robustness by combining multiple feature representations of drugs and targets. Although these methods achieved better generalization compared to linear models, they still required extensive feature engineering and lacked scalability when applied to large datasets. With the rise of deep learning, neural network–based models emerged as a powerful alternative to traditional approaches. In [3], the authors introduced a Recurrent Neural Network architecture to model protein sequences and molecular strings, enabling the capture of sequential dependencies within biological data. The results demonstrated improved prediction accuracy compared to classical machine learning models. Nevertheless, RNN-based approaches were later shown to suffer from training inefficiency and difficulties in modeling long-range dependencies. Convolutional Neural Networks were subsequently adopted to address some of these challenges. In [4], CNN-based architectures were proposed to extract local patterns and motifs from protein sequences and drug representations. By leveraging convolutional filters, these models achieved improved computational efficiency and stronger feature extraction capability. However, their reliance on local receptive fields limited their ability to capture global interactions between distant sequence elements. More recently, graph-based representations have gained significant attention in drug–target interaction prediction. In [5], the authors proposed modeling drug molecules as graphs, where atoms are represented as nodes and chemical bonds as edges, and applied Graph Neural Networks to learn structural representations. This approach demonstrated superior performance compared to sequence-based models, particularly when detailed molecular structure information was available. Further improvements were reported in [6], where message passing mechanisms were refined to better capture relational dependencies within molecular graphs. Transformer-based models represent the most recent advancement in this research area.

In [7], the authors introduced an attention-based framework that leverages self-attention mechanisms to model global dependencies within protein and drug sequences. The proposed model achieved state-of-the-art performance on several benchmark datasets, highlighting the effectiveness of attention mechanisms in capturing complex interactions. Similarly, the study in [8] demonstrated that Transformer architectures outperform recurrent and convolutional models by enabling parallel processing and improved long-range dependency modeling. In addition to architectural advances, benchmark datasets and evaluation protocols have also evolved. In [9], the authors introduced a large-scale benchmark dataset for drug target binding affinity prediction, enabling standardized evaluation and fair comparison between models. More recently, the work in [10] provided a comprehensive review of deep learning–based approaches for drug target interaction prediction, emphasizing the advantages of attention-based and graph-based models. Overall, existing studies demonstrate a clear progression from traditional machine learning methods to deep learning architectures, with recent attention-based models achieving the most promising results. These findings motivate the adoption of Transformer-based models in this study, while also providing a strong foundation for comparative analysis with recurrent, convolutional, and graph-based approaches.

Chapter 3: Deep Learning Architectures and Modeling Techniques

This chapter introduces the mathematical and computational foundations underlying the models used for predicting drug target binding affinity. The primary objective of this chapter is to provide a clear and intuitive explanation of how complex biological interactions between drugs and target proteins can be represented, processed, and approximated using mathematical formulations and data driven models. Since there is no explicit analytical equation that can universally describe binding affinity for all possible drug protein pairs, the problem is approached as a regression task, where the goal is to learn a function that maps drug and protein representations to a continuous affinity value. At a conceptual level, drug target binding affinity prediction involves transforming symbolic biological information into numerical representations that can be processed by mathematical models. Drug molecules and proteins are inherently described by discrete symbols, such as atoms, bonds, and amino acids, which cannot be directly manipulated using algebraic operations. Therefore, an essential first step in any predictive model is the conversion of these symbolic representations into continuous numerical vectors. This transformation enables the application of linear algebra, optimization techniques, and non-linear functions that form the basis of modern machine learning and deep learning methods. Once biological entities are represented numerically, the learning task becomes one of function approximation. Given a drug representation and a protein representation, the model attempts to approximate an unknown and highly complex biological function that governs molecular interactions. This function is learned from data by minimizing the difference between predicted affinity values and experimentally measured affinity scores. The learning process relies on optimization algorithms and gradient based methods that iteratively adjust model parameters to improve prediction accuracy across large datasets. The models discussed in this chapter differ primarily in how they process input representations and how they capture dependencies within and between drug and protein data. Some models are designed to handle sequential information, others focus on extracting local structural patterns, while more advanced architectures aim to model global interactions and long-range dependencies. Despite these differences, all models share a common mathematical foundation based on matrix operations, non-linear transformations, and loss minimization, which together enable the approximation of complex biological phenomena. This chapter serves as a foundation for understanding the detailed mathematical equations and modeling strategies that will be presented in the following sections. By establishing the core principles behind data representation, function learning, and model optimization, this introduction prepares the reader for a deeper exploration of specific neural architectures and their role in predicting drug target binding affinity.

3.1 Recurrent Neural Networks (RNN)

After introducing the general mathematical foundations of deep learning models, this section focuses on Recurrent Neural Networks (RNNs), which represent one of the earliest and most intuitive neural architectures designed for modeling sequential data. RNNs are particularly well-suited for processing ordered inputs where the sequence and temporal dependencies between elements play a crucial role. In many scientific domains, including natural language processing and bioinformatics, data naturally appears in sequential form, making RNNs a foundational model for sequence-based learning tasks.

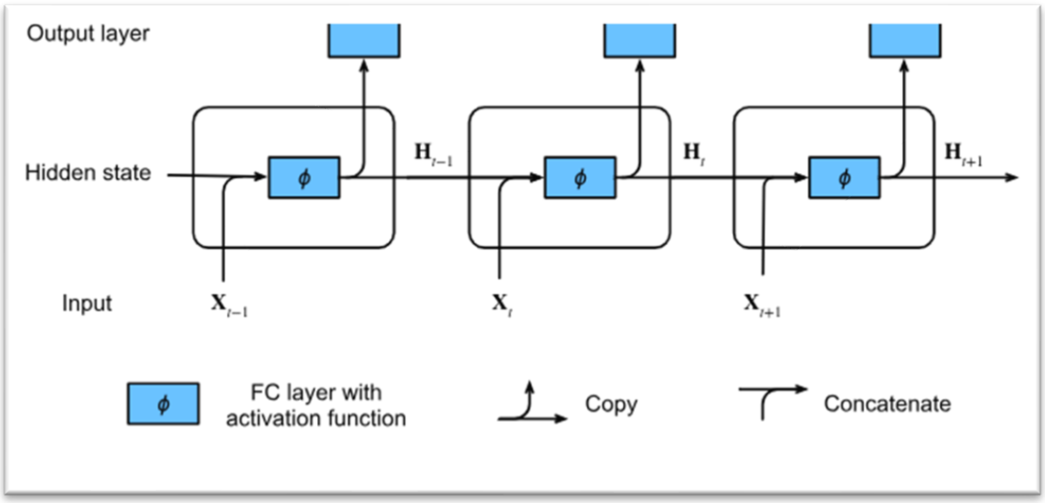


Figure 3:
Conceptual illustration of a Recurrent Neural Network (RNN) processing a sequence over time, where information is propagated through a hidden state that evolves at each time step

The core idea behind a Recurrent Neural Network is the concept of a hidden state, which acts as a form of memory that allows the network to retain information from previous elements in the sequence. Unlike traditional feed forward neural networks, which process input independently, an RNN processes a sequence of one element at a time while continuously updating its hidden state. This hidden state serves as a compact representation of all information observed up to the current position in the sequence, enabling the model to capture contextual dependencies across time steps.

Mathematically, the operation of an RNN can be described using a recursive formulation. Let $x_t$denote the input vector at time step t, which represents the numerical encoding of the current element in the sequence. The hidden state at time step t, denoted by h_t, is computed as a function of the current input $x_t$and the hidden state from the previous time step h_{t-1}. This relationship is expressed by the following equation:

$$\tanh(\mathrm{w_x x_t} + \mathrm{w_h} h_{t-1} + b) = h_t \qquad \textbf{(1)}$$

In this equation, W_x is a weight matrix that determines how strongly the current input influences the hidden state, while $W_h$is a recurrent weight matrix that controls how information from the previous hidden state is propagated forward in time. The bias term $b$provides additional flexibility by allowing the model to shift the activation function independently of the input. The hyperbolic tangent function $\tanh(\cdot)$is used as a nonlinear activation function, ensuring that the hidden state values remain within a bounded range, which stabilizes training and enables the model to learn nonlinear relationships. The recursive nature of this equation is what gives RNNs their sequential modeling capability. At each step, the hidden state incorporates both new information from the current input and contextual information carried over from previous steps. As a result, the hidden state $h_t$can be interpreted as a summary of the entire input sequence observed up to time t. This mechanism allows RNNs to model dependencies between distant elements in a sequence, which is essential when earlier elements influence later outcomes.

or prediction tasks, the hidden state can be further transformed to produce an output. If $y_t$represents the output at time step t, it is typically computed using a linear transformation of the hidden state followed by an optional activation function, as shown below:

$$y_t = W_y h_t + c \qquad \textbf{(2)}$$

Here, $W_y$is an output weight matrix that maps the hidden state to the desired output space, and $c$is a bias term associated with the output layer. In regression tasks, such as predicting continuous values, this output formulation allows the model to generate numerical predictions directly from the learned hidden representations.

During training, the parameters of the RNN, including all weight matrices and bias terms, are learned by minimizing a loss function that measures the difference between predicted outputs and ground-truth values. This optimization is performed using gradient-based methods, most commonly through a procedure known as backpropagation through time (BPTT). In BPTT, gradients are propagated backward across multiple time steps, allowing the model to adjust its parameters based on errors accumulated throughout the sequence. Despite their conceptual simplicity and effectiveness in modeling sequential data, RNNs exhibit notable limitations. As sequences become longer, the repeated multiplication of gradients through time can cause them to either vanish or explode, making training unstable and preventing the model from learning long-range dependencies effectively. This limitation, known as the vanishing gradient problem, motivates the development of more advanced architecture, which will be discussed in subsequent sections of this chapter.

3.2 Convolutional Neural Networks (CNN)

Convolutional Neural Networks (CNNs) represent a powerful class of deep learning models originally developed for image processing, but they have since proven highly effective for analyzing sequential and structured data. Unlike recurrent models that process sequences step by step, CNNs focus on extracting local patterns by applying convolutional filters over small regions of the input. This property makes CNNs particularly suitable for identifying meaningful local motifs and structural features within sequences, which often play a critical role in determining the behavior of complex systems.

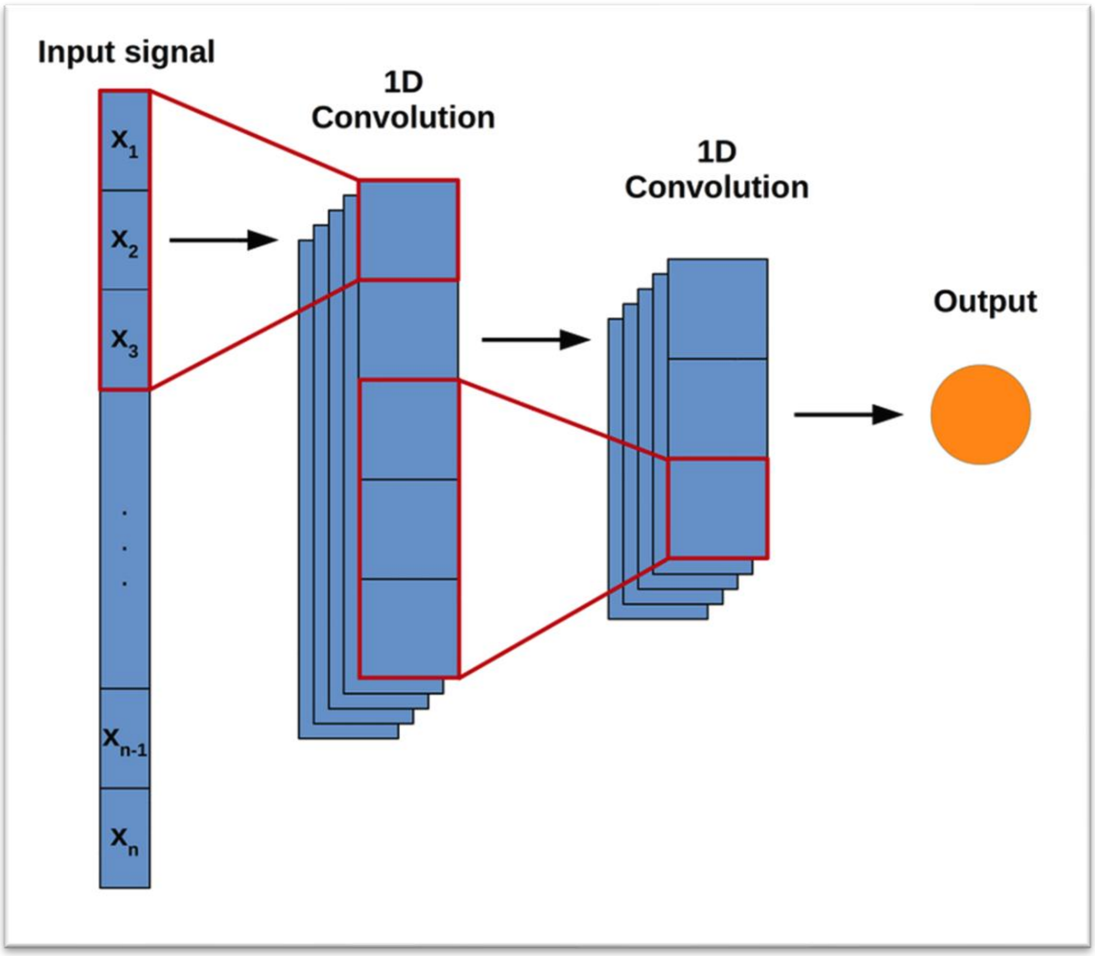


Figure 4:
illustration of a one-dimensional convolutional neural network (1D CNN) applied to a sequential input, showing the extraction of local patterns through convolutional layers and the generation of higher-level feature representations

filter across the input representation and computing a weighted sum at each position. Let $x \in \mathbb{R}^n$ denote a one-dimensional input sequence of length n, and let $w \in \mathbb{R}^k$ represent a convolutional filter of size k, where $k < n$. The convolution output at position i, denoted by z_i, is computed as:

$$z_i = \sum_{j=0}^{k-1} w_j \ x_{i+j} + b \qquad \textbf{(3)}$$

In this equation, the filter weights w_j determine which local patterns the model is attempting to detect, while the bias term b allows the activation to be shifted independently of the input values. By sliding the same filter across the entire sequence, the CNN enforces weight sharing, meaning that the same pattern detector is applied at every position. This property significantly reduces the number of trainable parameters and allows the model to detect similar patterns regardless of their location within the sequence. The convolution output z_i is typically passed through a nonlinear activation function, such as the rectified linear unit (ReLU), to introduce nonlinearity and enhance the model's expressive power. The resulting activated feature map captures the presence and strength of specific local patterns across the input sequence. Multiple filters are usually applied in parallel, enabling the model to learn a diverse set of features that characterize different types of local structures.

To further reduce dimensionality and improve robustness, convolutional layers are often followed by a pooling operation. Pooling aggregates information over a local region of the feature map and retains only the most salient features. A commonly used pooling operation is max pooling, which selects the maximum value within a predefined window. For a pooling window of size m, the pooled output p_i is given by:

$$p_i = \max\left(z_i, z_{i+1}, \dots, z_{i+m-1}\right) \qquad \textbf{(4)}$$

This operation introduces a degree of translation invariance, ensuring that the detection of a pattern remains stable even if its position within the sequence shifts slightly. By progressively applying convolution and pooling layers, CNNs build hierarchical representations in which lower layers capture simple local patterns, while higher layers combine these patterns into more abstract and informative features. After the feature extraction process, the resulting representations are typically flattened and passed to one or more fully connected layers that perform the final prediction. These layers integrate information from all extracted features and map them to the output space. In regression tasks, the final layer produces a continuous numerical value, allowing the model to estimate quantities such as interaction strength or similarity scores.

CNNs offer several advantages in modeling sequential data. Their ability to efficiently extract local features, combined with parameter sharing and parallel computation, makes them computationally efficient and scalable. However, because CNNs primarily focus on local receptive fields, they may struggle to capture long-range dependencies unless multiple layers or large receptive fields are used. This limitation highlights the need for complementary or more advanced architectures capable of modeling global interactions, which will be discussed in subsequent sections.

3.3 Graph Neural Networks (GNN)

Graph Neural Networks (GNNs) represent a class of deep learning models specifically designed to operate on graph-structured data. Unlike sequences or grids, many real-world entities are naturally represented as graphs composed of nodes and edges. In such representations, nodes correspond to individual entities, while edges describe the relationships or interactions between them. This modeling paradigm is particularly well-suited for systems where relational information plays a central role, as it allows the model to explicitly capture structural dependencies that cannot be adequately represented using traditional sequence-based or convolution-based architectures.

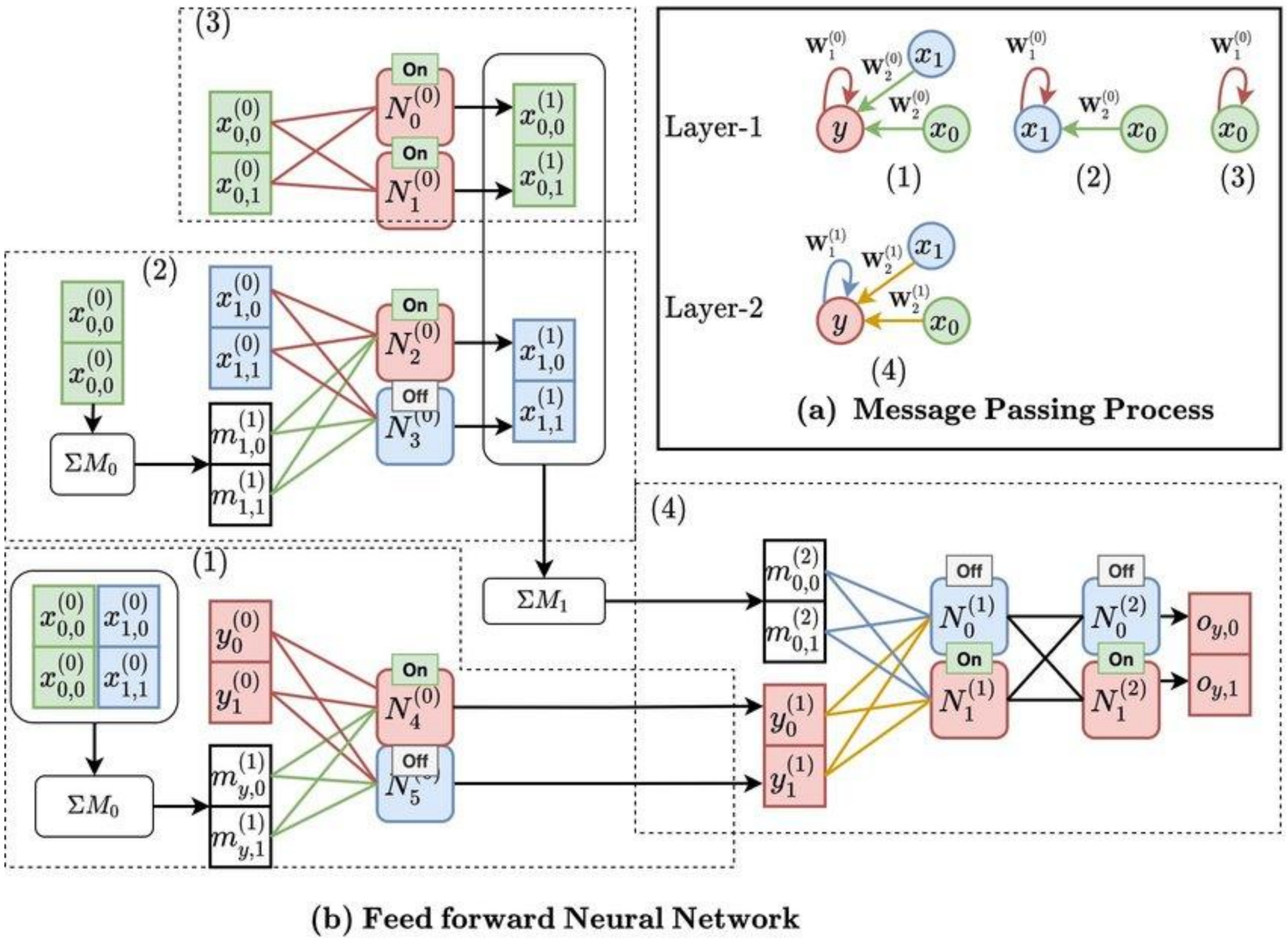


Figure 5:

Atomic-level graph representation of a drug molecule with nodes representing atoms and edges representing bonds. This figure illustrates the message passing mechanism used in Graph Neural Networks (GNN) for drug-target interaction prediction.

The fundamental idea underlying Graph Neural Networks is that the representation of each node should be informed not only by its own features, but also by the features of its neighboring nodes and the structure of the graph itself. This is achieved through an iterative process commonly referred to as passing message. At each iteration, nodes exchange information with their neighbors, allowing local information to propagate through the graph and enabling the model to learn higher-level structural representations. Mathematically, a graph can be defined as $G = (V, E)$, where Vdenotes the set of nodes and Edenotes the set of edges connecting pairs of nodes. Each node $v \in V$is associated with a feature vector $h_v^{(0)}$, which represents its initial attributes. The goal of GNN is to iteratively update these node representations by aggregating information from neighboring nodes. At iteration k, an intermediate message for node $v$is computed by aggregating the representations of its neighbors, which can be expressed as:

$$m_v^{(k)} = \sum_{u \in \mathcal{N}(v)} h_u^{(k)} \quad \textbf{(5)}$$

In this equation, $\mathcal{N}(v)$denotes the set of neighboring nodes directly connected to node v. The summation operation aggregates information from all neighbors, ensuring that the representation of node $v$reflects the local structure of the graph. Alternative aggregation functions such as mean or max can also be used, but the summation formulation captures the core idea of neighborhood information aggregation.

The aggregated message is then combined with the current representation of the node to produce an updated representation for the next iteration. This update step can be written as:

$$h_v^{(k+1)} = \sigma\left(W^{(k)} \cdot m_v^{(k)} + b^{(k)}\right) \quad \textbf{(6)}$$

Here, $W^{(k)}$is a learnable weight matrix that controls how the aggregated neighborhood information influences the updated node representation, while $b^{(k)}$is a bias term. The function $\sigma(\cdot)$denotes a nonlinear activation function, which introduces nonlinearity and allows the model to learn complex relationships within the graph. Through this transformation, each node updates its representation based on both its local neighborhood and the learned parameters of the model.

By stacking multiple messages passing layers, information can propagate across increasingly larger portions of the graph. After one iteration, each node representation contains information about its immediate neighbors. After two iterations, it incorporates information from neighbors of neighbors, and so on. This hierarchical propagation mechanism enables Graph Neural Networks to capture both local and global structural patterns, making them highly effective for modeling complex relational systems. For tasks that require a single prediction for the entire graph rather than individual nodes, node-level representations can be aggregated into a global graph-level representation using a readout function. This operation combines information from all nodes into a fixed-dimensional vector that summarizes the entire graph structure. The resulting graph representation can then be passed through additional neural layers to produce a final output, such as a continuous prediction value. Despite their strong representational capabilities, Graph Neural Networks also present certain challenges. As the number of message passing layers increases, node representations may become overly similar, a phenomenon known as over-smoothing, which can reduce the discriminative power of the model. Additionally, computational complexity can increase for large graphs. These challenges motivate careful architectural design and further highlight the importance of selecting appropriate models for complex prediction tasks.

3.4 Transformer Model (Primary Model)

Transformer models represent a major paradigm shift in deep learning architectures, as they abandon recurrence and convolution entirely in favor of an attention-based mechanism that enables direct modeling of global dependencies within input data. Unlike Recurrent Neural Networks, which process sequences sequentially and suffer from memory degradation over long inputs, Transformers are designed to process all elements of a sequence simultaneously. This parallel processing capability allows the model to efficiently capture long-range relationships between elements regardless of their relative positions, making Transformers particularly effective for complex sequence modeling tasks.

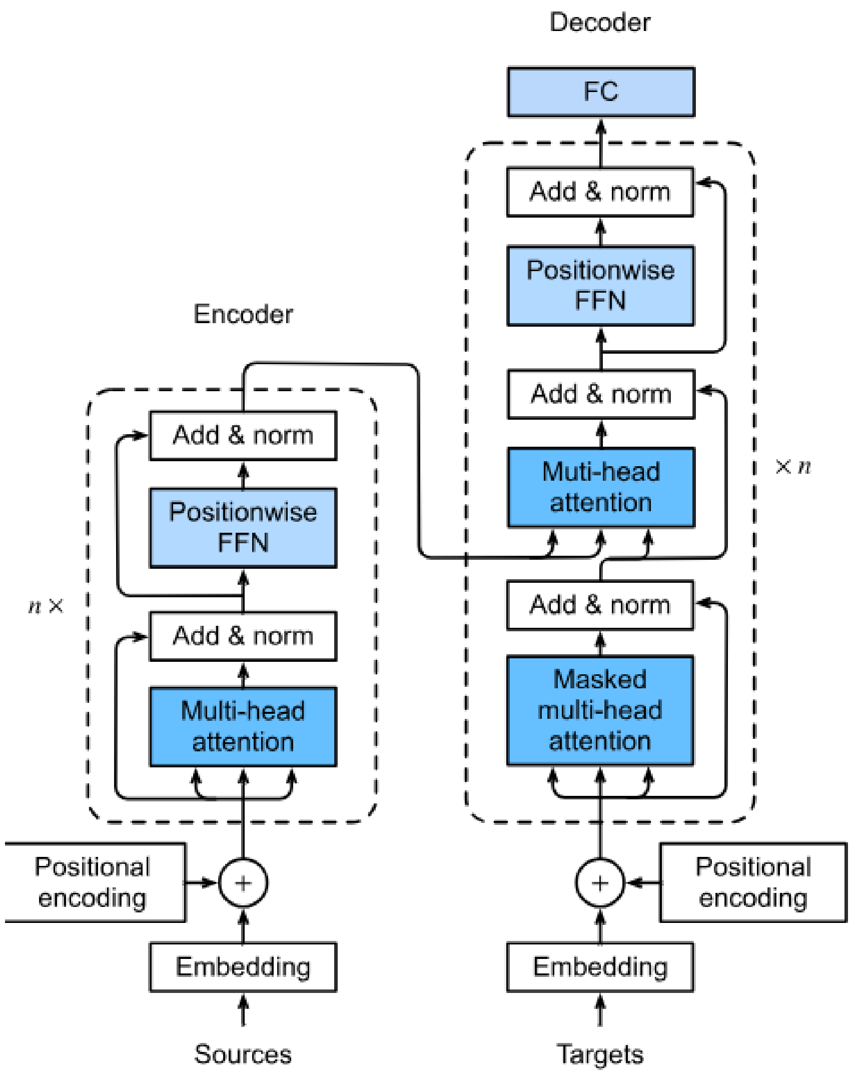


Figure 6:

Architecture of the Transformer model illustrating the encoder–decoder structure, multi-head self-attention mechanisms, position-wise feed-forward networks, and residual connections with layer normalization.

At the core of the Transformer architecture lies the self-attention mechanism, which enables each element in the input sequence to dynamically assess the importance of every other element. Let the input sequence be represented as a matrix $X \in \mathbb{R}^{n \times d}$, where $n$is the sequence length and $d$is the dimensionality of the input embeddings. From this input, three distinct representations are computed through learned linear transformations, known as the query, key, and value matrices, denoted by Q, K, and V, respectively. These matrices are defined as $Q = XW_Q$, $K = XW_K$, and $V = XW_V$, where W_Q, W_K, and $W_V$are trainable weight matrices. The attention mechanism computes a relevance score between each pair of elements in the sequence by taking the dot product between the corresponding query and key vectors. These scores are then scaled by the square root of the key dimensionality to stabilize gradients during training, resulting in the scaled dot-product attention formulation given by:

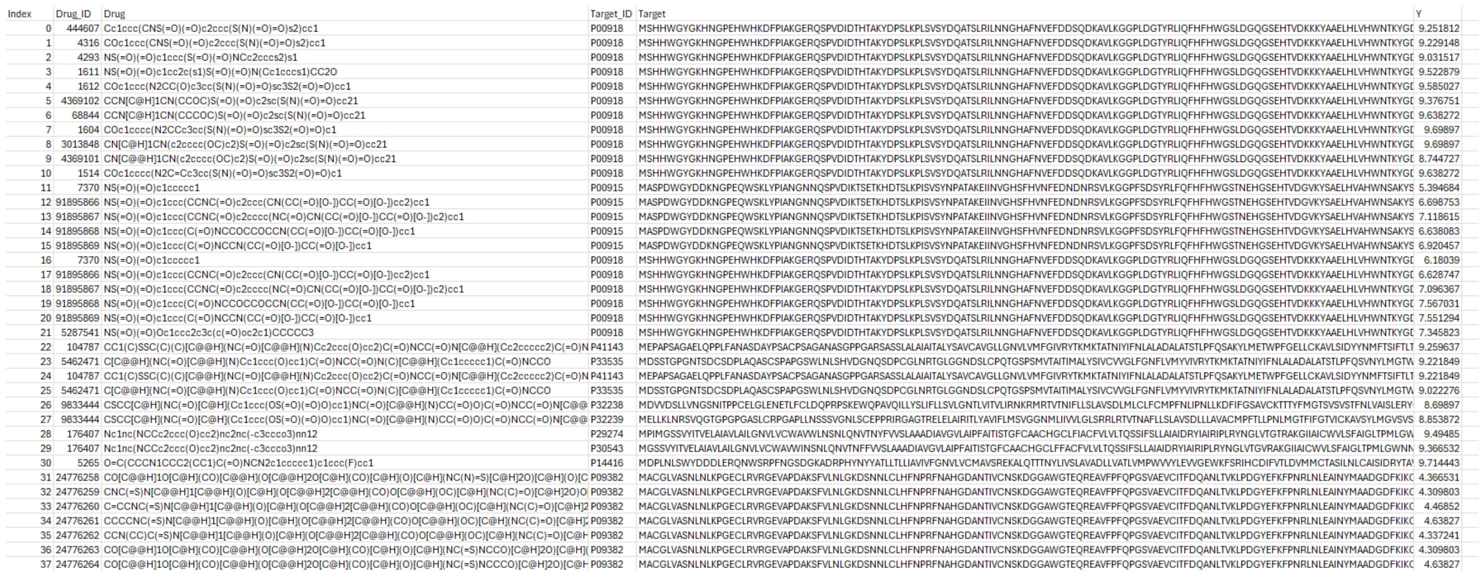
$$\text{Attention}(Q, K, V) = \text{softmax}\left(\frac{QK^T}{\sqrt{d_k}}\right)V \qquad \textbf{(7)}$$

This equation produces a weighted combination of value vectors, where the weights reflect how strongly each element in the sequence attends to every other element. As a result, the output representation of each element incorporates contextual information from the entire sequence rather than relying solely on local or sequential dependencies. To enhance the expressive power of the attention mechanism, Transformers employ multi-head attention, which allows the model to attend to different types of relationships simultaneously. In this setting, the attention operation is performed multiple times in parallel using different learned projections of the input. The outputs of these attention heads are then concatenated and linearly transformed to produce the final attention output. This design enables the model to capture diverse interaction patterns, such as short-range dependencies, long-range dependencies, and hierarchical relationships, within a single layer. Since the Transformer architecture does not inherently encode information about the order of sequence elements, positional information is explicitly incorporated through positional encodings. These encodings are added to the input embeddings to provide the model with information about the relative or absolute positions of elements within the sequence. By combining positional encodings with self-attention, the Transformer can model both content-based relationships and positional structure, which is essential for meaningful sequence understanding. Following the attention mechanism, each Transformer layer includes a position-wise feed-forward network that applies nonlinear transformations independently to each sequence element. This component increases the representational capacity of the model by enabling complex feature interactions within each position. Residual connections and layer normalization are applied around both the attention and feed-forward sublayers to stabilize training and facilitate the flow of gradients through deep architectures. After stacking multiple Transformer layers, the model produces highly expressive, context-aware representations of the input sequence. These representations can then be aggregated or pooled to generate a fixed-dimensional vector suitable for downstream prediction tasks. In regression settings, a final linear transformation maps this vector to a continuous output value, allowing the model to produce precise numerical predictions based on the learned global interactions. The Transformer architecture offers several key advantages over earlier models. Its ability to model long-range dependencies without recurrence eliminates the vanishing gradient problem associated with RNNs, while its global attention mechanism overcomes the locality constraints of CNNs. Additionally, the highly parallelizable structure of Transformers enables efficient training on large datasets. These properties make Transformer-based models particularly well-suited for complex prediction tasks that require capturing intricate relationships across long sequences, and they motivate their selection as the primary modeling approach in this project.

Chapter 4: Dataset Descriptions

The dataset used in this project is the BALM benchmark dataset, which is a large-scale and standardized dataset specifically designed for evaluating machine learning and deep learning models in the task of drug target binding affinity prediction. The BALM dataset was introduced to overcome several limitations present in earlier datasets, such as limited chemical diversity, inconsistent data preprocessing, and evaluation protocols that do not accurately reflect real world drug discovery scenarios. By providing a unified and carefully curated benchmark, BALM enables fair, reliable, and reproducible comparison between different computational models, particularly modern deep learning architectures. At its core, the BALM dataset is constructed to simulate realistic drug discovery conditions, where experimental binding affinity data is sparse, noisy, and expensive to obtain. Each data sample in the dataset represents a drug–target pair associated with an experimentally measured binding affinity value. This structure allows models to learn how molecular characteristics of drugs and biological properties of target proteins jointly influence the strength of their interaction. The dataset integrates information collected from multiple experimental sources and harmonizes them into a consistent format, ensuring that the predicted affinity values are comparable across different drug target pairs. The dataset consists of three fundamental components: drug representations, protein representations, and binding affinity scores. Drug molecules are represented using SMILES (Simplified Molecular Input Line Entry System) strings, which encode molecular structures as sequences of characters describing atoms, bonds, and molecular topology. This representation is highly flexible and enables multiple modeling strategies, including sequence-based approaches such as RNNs and Transformers, as well as graph-based approaches where SMILES strings can be converted into molecular graphs for use with Graph Neural Networks. By preserving essential chemical information, SMILES representations allow models to capture both local and global molecular features that influence binding behavior. Target proteins in the BALM dataset are represented using amino acid sequences, which describe the primary structure of proteins as ordered chains of amino acids. Protein sequences play a critical role in determining the three-dimensional structure and biological function of proteins, and consequently their interaction with drug molecules. Sequence-based representations allow deep learning models to learn residue level patterns, contextual dependencies, and long-range interactions that are essential for accurate binding affinity prediction. This is particularly important for large proteins, where distant amino acids in the sequence may still contribute jointly to the binding interface. The binding affinity scores provided in the dataset quantify the strength of interaction between a drug and its target protein. These values are derived from experimentally measured biochemical assays, such as dissociation constants (Kd), inhibition constants (Ki), or half maximal inhibitory concentrations (IC50), depending on data availability.

To ensure consistency across different experimental conditions and measurement techniques, affinity values in the BALM dataset are normalized and standardized. This preprocessing step is crucial for training regression-based models, as it reduces noise and allows the learning algorithms to focus on meaningful biological patterns rather than experimental artifacts.



Index	Drug_ID	Drug	Target_ID	Target	Y
0	444607	Cc1ccc(CNS(=O)(=O)c2ccc(S(N)(=O)=O)s2)cc1	P00918	MSHHWGYGKHNGPEHWHKDFPIAKGERQSPVDIDTHTAKYDPSLKPLSVSYDQATSLRILNNGHAFNVEFDDSQDKAVLKGGPLDGTYRLIQFHFHWGSLDGQGSEHTVDKKKYAAELHLVHWNTKYGD	9.251812
1	4316	COc1ccc(CNS(=O)(=O)c2ccc(S(N)(=O)=O)s2)cc1	P00918	MSHHWGYGKHNGPEHWHKDFPIAKGERQSPVDIDTHTAKYDPSLKPLSVSYDQATSLRILNNGHAFNVEFDDSQDKAVLKGGPLDGTYRLIQFHFHWGSLDGQGSEHTVDKKKYAAELHLVHWNTKYGD	9.229148
2	4293	NS(=O)(=O)c1ccc(S(=O)(=O)NCc2cccs2)s1	P00918	MSHHWGYGKHNGPEHWHKDFPIAKGERQSPVDIDTHTAKYDPSLKPLSVSYDQATSLRILNNGHAFNVEFDDSQDKAVLKGGPLDGTYRLIQFHFHWGSLDGQGSEHTVDKKKYAAELHLVHWNTKYGD	9.031517
3	1611	NS(=O)(=O)c1cc2c(s1)S(=O)(=O)N(Cc1cccs1)CC2O	P00918	MSHHWGYGKHNGPEHWHKDFPIAKGERQSPVDIDTHTAKYDPSLKPLSVSYDQATSLRILNNGHAFNVEFDDSQDKAVLKGGPLDGTYRLIQFHFHWGSLDGQGSEHTVDKKKYAAELHLVHWNTKYGD	9.522879
4	1612	COc1ccc(N2CC(O)c3cc(S(N)(=O)=O)sc3S2(=O)=O)cc1	P00918	MSHHWGYGKHNGPEHWHKDFPIAKGERQSPVDIDTHTAKYDPSLKPLSVSYDQATSLRILNNGHAFNVEFDDSQDKAVLKGGPLDGTYRLIQFHFHWGSLDGQGSEHTVDKKKYAAELHLVHWNTKYGD	9.585027
5	4369102	CCN[C@H]1CN(CCOC)S(=O)(=O)c2sc(S(N)(=O)=O)cc21	P00918	MSHHWGYGKHNGPEHWHKDFPIAKGERQSPVDIDTHTAKYDPSLKPLSVSYDQATSLRILNNGHAFNVEFDDSQDKAVLKGGPLDGTYRLIQFHFHWGSLDGQGSEHTVDKKKYAAELHLVHWNTKYGD	9.376751
6	68844	CCN[C@H]1CN(CCCOC)S(=O)(=O)c2sc(S(N)(=O)=O)cc21	P00918	MSHHWGYGKHNGPEHWHKDFPIAKGERQSPVDIDTHTAKYDPSLKPLSVSYDQATSLRILNNGHAFNVEFDDSQDKAVLKGGPLDGTYRLIQFHFHWGSLDGQGSEHTVDKKKYAAELHLVHWNTKYGD	9.638272
7	1604	COc1cccc(N2CCc3cc(S(N)(=O)=O)sc3S2(=O)=O)c1	P00918	MSHHWGYGKHNGPEHWHKDFPIAKGERQSPVDIDTHTAKYDPSLKPLSVSYDQATSLRILNNGHAFNVEFDDSQDKAVLKGGPLDGTYRLIQFHFHWGSLDGQGSEHTVDKKKYAAELHLVHWNTKYGD	9.69897
8	3013848	CN[C@H]1CN(c2cccc(OC)c2)S(=O)(=O)c2sc(S(N)(=O)=O)cc21	P00918	MSHHWGYGKHNGPEHWHKDFPIAKGERQSPVDIDTHTAKYDPSLKPLSVSYDQATSLRILNNGHAFNVEFDDSQDKAVLKGGPLDGTYRLIQFHFHWGSLDGQGSEHTVDKKKYAAELHLVHWNTKYGD	9.69897
9	4369101	CN[C@@H]1CN(c2cccc(OC)c2)S(=O)(=O)c2sc(S(N)(=O)=O)cc21	P00918	MSHHWGYGKHNGPEHWHKDFPIAKGERQSPVDIDTHTAKYDPSLKPLSVSYDQATSLRILNNGHAFNVEFDDSQDKAVLKGGPLDGTYRLIQFHFHWGSLDGQGSEHTVDKKKYAAELHLVHWNTKYGD	8.744727
10	1514	COc1cccc(N2C=Cc3cc(S(N)(=O)=O)sc3S2(=O)=O)c1	P00918	MSHHWGYGKHNGPEHWHKDFPIAKGERQSPVDIDTHTAKYDPSLKPLSVSYDQATSLRILNNGHAFNVEFDDSQDKAVLKGGPLDGTYRLIQFHFHWGSLDGQGSEHTVDKKKYAAELHLVHWNTKYGD	9.638272
11	7370	NS(=O)(=O)c1ccccc1	P00915	MASPDWGYDDKNGPEQWSKLYPIANGNNQSPVDIKTSETKHDTSLKPISVSYNPATAKEIINVGHSFHVNFEDNDNRSVLKGGPFSDSYRLFQFHFHWGSTNEHGSEHTVDGVKYSAELHVAHWNSAKYS	5.394684
12	91895866	NS(=O)(=O)c1ccc(CCNC(=O)c2ccc(CN(CC(=O)[O-])CC(=O)[O-])cc2)cc1	P00915	MASPDWGYDDKNGPEQWSKLYPIANGNNQSPVDIKTSETKHDTSLKPISVSYNPATAKEIINVGHSFHVNFEDNDNRSVLKGGPFSDSYRLFQFHFHWGSTNEHGSEHTVDGVKYSAELHVAHWNSAKYS	6.698753
13	91895867	NS(=O)(=O)c1ccc(CCNC(=O)c2cccc(NC(=O)CN(CC(=O)[O-])CC(=O)[O-])c2)cc1	P00915	MASPDWGYDDKNGPEQWSKLYPIANGNNQSPVDIKTSETKHDTSLKPISVSYNPATAKEIINVGHSFHVNFEDNDNRSVLKGGPFSDSYRLFQFHFHWGSTNEHGSEHTVDGVKYSAELHVAHWNSAKYS	7.118615
14	91895868	NS(=O)(=O)c1ccc(C(=O)NCCOCCOCCN(CC(=O)[O-])CC(=O)[O-])cc1	P00915	MASPDWGYDDKNGPEQWSKLYPIANGNNQSPVDIKTSETKHDTSLKPISVSYNPATAKEIINVGHSFHVNFEDNDNRSVLKGGPFSDSYRLFQFHFHWGSTNEHGSEHTVDGVKYSAELHVAHWNSAKYS	6.638083
15	91895869	NS(=O)(=O)c1ccc(C(=O)NCCN(CC(=O)[O-])CC(=O)[O-])cc1	P00915	MASPDWGYDDKNGPEQWSKLYPIANGNNQSPVDIKTSETKHDTSLKPISVSYNPATAKEIINVGHSFHVNFEDNDNRSVLKGGPFSDSYRLFQFHFHWGSTNEHGSEHTVDGVKYSAELHVAHWNSAKYS	6.920457
16	7370	NS(=O)(=O)c1ccccc1	P00918	MSHHWGYGKHNGPEHWHKDFPIAKGERQSPVDIDTHTAKYDPSLKPLSVSYDQATSLRILNNGHAFNVEFDDSQDKAVLKGGPLDGTYRLIQFHFHWGSLDGQGSEHTVDKKKYAAELHLVHWNTKYGD	6.18039
17	91895866	NS(=O)(=O)c1ccc(CCNC(=O)c2ccc(CN(CC(=O)[O-])CC(=O)[O-])cc2)cc1	P00918	MSHHWGYGKHNGPEHWHKDFPIAKGERQSPVDIDTHTAKYDPSLKPLSVSYDQATSLRILNNGHAFNVEFDDSQDKAVLKGGPLDGTYRLIQFHFHWGSLDGQGSEHTVDKKKYAAELHLVHWNTKYGD	6.628747
18	91895867	NS(=O)(=O)c1ccc(CCNC(=O)c2cccc(NC(=O)CN(CC(=O)[O-])CC(=O)[O-])c2)cc1	P00918	MSHHWGYGKHNGPEHWHKDFPIAKGERQSPVDIDTHTAKYDPSLKPLSVSYDQATSLRILNNGHAFNVEFDDSQDKAVLKGGPLDGTYRLIQFHFHWGSLDGQGSEHTVDKKKYAAELHLVHWNTKYGD	7.096367
19	91895868	NS(=O)(=O)c1ccc(C(=O)NCCOCCOCCN(CC(=O)[O-])CC(=O)[O-])cc1	P00918	MSHHWGYGKHNGPEHWHKDFPIAKGERQSPVDIDTHTAKYDPSLKPLSVSYDQATSLRILNNGHAFNVEFDDSQDKAVLKGGPLDGTYRLIQFHFHWGSLDGQGSEHTVDKKKYAAELHLVHWNTKYGD	7.567031
20	91895869	NS(=O)(=O)c1ccc(C(=O)NCCN(CC(=O)[O-])CC(=O)[O-])cc1	P00918	MSHHWGYGKHNGPEHWHKDFPIAKGERQSPVDIDTHTAKYDPSLKPLSVSYDQATSLRILNNGHAFNVEFDDSQDKAVLKGGPLDGTYRLIQFHFHWGSLDGQGSEHTVDKKKYAAELHLVHWNTKYGD	7.551294
21	5287541	NS(=O)(=O)Oc1ccc2c3c(c(=O)oc2c1)CCCCC3	P00918	MSHHWGYGKHNGPEHWHKDFPIAKGERQSPVDIDTHTAKYDPSLKPLSVSYDQATSLRILNNGHAFNVEFDDSQDKAVLKGGPLDGTYRLIQFHFHWGSLDGQGSEHTVDKKKYAAELHLVHWNTKYGD	7.345823
22	104787	CC1(C)SSC(C)(C)[C@@H](NC(=O)[C@@H](N)Cc2ccc(O)cc2)C(=O)NCC(=O)N[C@@H](Cc2ccccc2)C(=O)N	P41143	MEPAPSAGAELQPPLFANASDAYPSACPSAGANASGPPGARSASSLALAIAITALYSAVCAVGLLGNVLVMFGIVRYTKMKTATNIYIFNLALADALATSTLPFQSAKYLMETWPFGELLCKAVLSIDYYNMFTSIFTLT	9.259637
23	5462471	C[C@@H](NC(=O)[C@@H](N)Cc1ccc(O)cc1)C(=O)NCC(=O)N(C)[C@@H](Cc1ccccc1)C(=O)NCCO	P33535	MDSSTGPGNTSDCSDPLAQASCSPAPGSWLNLSHVDGNQSDPCGLNRTGLGGNDSLCPQTGSPSMVTAITIMALYSIVCVVGLFGNFLVMYVIVRYTKMKTATNIYIFNLALADALATSTLPFQSVNYLMGTW	9.221849
24	104787	CC1(C)SSC(C)(C)[C@@H](NC(=O)[C@@H](N)Cc2ccc(O)cc2)C(=O)NCC(=O)N[C@@H](Cc2ccccc2)C(=O)N	P41143	MEPAPSAGAELQPPLFANASDAYPSACPSAGANASGPPGARSASSLALAIAITALYSAVCAVGLLGNVLVMFGIVRYTKMKTATNIYIFNLALADALATSTLPFQSAKYLMETWPFGELLCKAVLSIDYYNMFTSIFTLT	9.221849
25	5462471	C[C@@H](NC(=O)[C@@H](N)Cc1ccc(O)cc1)C(=O)NCC(=O)N(C)[C@@H](Cc1ccccc1)C(=O)NCCO	P33535	MDSSTGPGNTSDCSDPLAQASCSPAPGSWLNLSHVDGNQSDPCGLNRTGLGGNDSLCPQTGSPSMVTAITIMALYSIVCVVGLFGNFLVMYVIVRYTKMKTATNIYIFNLALADALATSTLPFQSVNYLMGTW	9.022276
26	9833444	CSCC[C@H](NC(=O)[C@H](Cc1ccc(OS(=O)(=O)O)cc1)NC(=O)[C@@H](N)CC(=O)O)C(=O)NCC(=O)N[C@@	P32238	MDVVDSLLVNGSNITPPCELGLENETLFCLDQPRPSKEWQPAVQILLYSLIFLLSVLGNTLVITVLIRNKRMRTVTNIFLLSLAVSDLMLCLFCMPFNLIPNLLKDFIFGSAVCKTTTYFMGTSVSVSTFNLVAISLERY	8.69897
27	9833444	CSCC[C@H](NC(=O)[C@H](Cc1ccc(OS(=O)(=O)O)cc1)NC(=O)[C@@H](N)CC(=O)O)C(=O)NCC(=O)N[C@@	P32239	MELLKLNRSVQGTGPGPGASLCRPGAPLLNSSSVGNLSCEPPRIRGAGTRELELAIRITLYAVIFLMSVGGNMLIIVVLGLSRRLRTVTNAFLLSLAVSDLLLAVACMPFTLLPNLMGTFIFGTVICKAVSYLMGVSVS	8.853872
28	176407	Nc1nc(NCCc2ccc(O)cc2)nc2nc(-c3ccco3)nn12	P29274	MPIMGSSVYITVELAIAVLAILGNVLVCWAVWLNSNLQNVTNYFVVSLAAADIAVGVLAIPFAITISTGFCAACHGCLFIACFVLVLTQSSIFSLLAIAIDRYIAIRIPLRYNGLVTGTRAKGIIAICWVLSFAIGLTPMLGW	9.49485
29	176407	Nc1nc(NCCc2ccc(O)cc2)nc2nc(-c3ccco3)nn12	P30543	MGSSVYITVELAIAVLAILGNVLVCWAVWINSNLQNVTNFFVVSLAAADIAVGVLAIPFAITISTGFCAACHGCLFFACFVLVLTQSSIFSLLAIAIDRYIAIRIPLRYNGLVTGVRAKGIIAICWVLSFAIGLTPMLGWNN	9.366532
30	5265	O=C(CCCN1CCC2(CC1)C(=O)NCN2c1ccccc1)c1ccc(F)cc1	P14416	MDPLNLSWYDDDLERQNWSRPFNGSDGKADRPHYNYYATLLTLLIAVIVFGNVLVCMAVSREKALQTTTNYLIVSLAVADLLVATLVMPWVVYLEVVGEWKFSRIHCDIFVTLDVMMCTASILNLCAISIDRYTA	9.714443
31	24776258	CO[C@@H]1O[C@H](CO)[C@@H](O[C@@H]2O[C@H](CO)[C@H](O)[C@H](NC(N)=S)[C@H]2O)[C@H](O)[C	P09382	MACGLVASNLNLKPGECLRVRGEVAPDAKSFVLNLGKDSNNLCLHFNPRFNAHGDANTIVCNSKDGGAWGTEQREAVFPFQPGSVAEVCITFDQANLTVKLPDGYEFKFPNRLNLEAINYMAADGDFKIKC	4.366531
32	24776259	CNC(=S)N[C@@H]1[C@@H](O)[C@H](O[C@@H]2[C@@H](CO)O[C@@H](OC)[C@H](NC(C)=O)[C@H]2O)O	P09382	MACGLVASNLNLKPGECLRVRGEVAPDAKSFVLNLGKDSNNLCLHFNPRFNAHGDANTIVCNSKDGGAWGTEQREAVFPFQPGSVAEVCITFDQANLTVKLPDGYEFKFPNRLNLEAINYMAADGDFKIKC	4.309803
33	24776260	C=CCNC(=S)N[C@@H]1[C@@H](O)[C@H](O[C@@H]2[C@@H](CO)O[C@@H](OC)[C@H](NC(C)=O)[C@H]2	P09382	MACGLVASNLNLKPGECLRVRGEVAPDAKSFVLNLGKDSNNLCLHFNPRFNAHGDANTIVCNSKDGGAWGTEQREAVFPFQPGSVAEVCITFDQANLTVKLPDGYEFKFPNRLNLEAINYMAADGDFKIKC	4.46852
34	24776261	CCCCNC(=S)N[C@@H]1[C@@H](O)[C@H](O[C@@H]2[C@@H](CO)O[C@@H](OC)[C@H](NC(C)=O)[C@H]	P09382	MACGLVASNLNLKPGECLRVRGEVAPDAKSFVLNLGKDSNNLCLHFNPRFNAHGDANTIVCNSKDGGAWGTEQREAVFPFQPGSVAEVCITFDQANLTVKLPDGYEFKFPNRLNLEAINYMAADGDFKIKC	4.63827
35	24776262	CCN(CC)C(=S)N[C@@H]1[C@@H](O)[C@H](O[C@@H]2[C@@H](CO)O[C@@H](OC)[C@H](NC(C)=O)[C@H	P09382	MACGLVASNLNLKPGECLRVRGEVAPDAKSFVLNLGKDSNNLCLHFNPRFNAHGDANTIVCNSKDGGAWGTEQREAVFPFQPGSVAEVCITFDQANLTVKLPDGYEFKFPNRLNLEAINYMAADGDFKIKC	4.337241
36	24776263	CO[C@@H]1O[C@H](CO)[C@@H](O[C@@H]2O[C@H](CO)[C@H](O)[C@H](NC(=S)NCCO)[C@H]2O)[C@H](	P09382	MACGLVASNLNLKPGECLRVRGEVAPDAKSFVLNLGKDSNNLCLHFNPRFNAHGDANTIVCNSKDGGAWGTEQREAVFPFQPGSVAEVCITFDQANLTVKLPDGYEFKFPNRLNLEAINYMAADGDFKIKC	4.309803
37	24776264	CO[C@@H]1O[C@H](CO)[C@@H](O[C@@H]2O[C@H](CO)[C@H](O)[C@H](NC(=S)NCCCO)[C@H]2O)[C@H	P09382	MACGLVASNLNLKPGECLRVRGEVAPDAKSFVLNLGKDSNNLCLHFNPRFNAHGDANTIVCNSKDGGAWGTEQREAVFPFQPGSVAEVCITFDQANLTVKLPDGYEFKFPNRLNLEAINYMAADGDFKIKC	4.63827

Figure 7:

Overview of the BALM benchmark dataset illustrating the relationship between drug SMILES representations, protein amino acid sequences, and corresponding binding affinity scores.

To better clarify the roles of the individual dataset components, a comparative summary is provided below. This comparison highlights how each component contributes uniquely to the binding affinity prediction task and how they are processed by different types of deep learning models.

Table 1: Comparison of drug representations, protein representations, and binding affinity scores in the BALM benchmark dataset, including their formats, biological meanings, and roles in prediction.

Futures	Representation	Description	Role in Prediction
Drug	SMILES sequence	Encodes molecular structure and chemical properties	Determines ligand-side binding behavior
Protein	Amino acid sequence	Represents target protein primary structure	Determines target-side binding behavior
Affinity Score	Continuous numerical value	Experimental measurement of interaction strength	Regression target variable

One of the key strengths of the BALM dataset is its suitability for evaluating model generalization. The dataset is designed to assess how well predictive models perform not only on known drug target pairs, but also on unseen drugs, unseen targets, and novel combinations of both. This characteristic is particularly important in real world drug discovery, where predictive systems are expected to identify effective interactions for molecules and targets that have never been experimentally tested before. As a result, BALM provides a more realistic and challenging benchmark compared to traditional datasets. Furthermore, the dataset supports a wide range of artificial intelligence models due to its flexible representations. Sequence-based models can directly process SMILES strings and protein sequences, convolutional models can extract local motifs and patterns, graph-based models can leverage molecular structures, and attention-based Transformer models can capture long-range dependencies and complex interactions. This versatility makes BALM an ideal choice for comparative studies across different neural architectures and for investigating which modeling paradigms are most effective for drug target binding affinity prediction. In summary, the BALM benchmark dataset provides a comprehensive, scalable, and biologically meaningful foundation for developing and evaluating AI driven models for drug target binding affinity prediction. Its standardized structure, realistic design, and support for diverse modeling approaches make it particularly well-suited for this project and for advancing research in computational drug discovery.

Chapter 5: Proposed Approach

The proposed approach followed in this study is designed to provide a clear and systematic workflow for building and evaluating deep learning models. The main objective of this approach is to organize the overall process in a structured manner that ensures consistency, clarity, and reproducibility. By following a well-defined methodology, the study ensures that each step of the learning pipeline is performed in an organized and controlled way, which helps in obtaining reliable and meaningful results. The overall methodology is divided into three main phases: the data preprocessing phase, the deep learning model training phase, and the evaluation phase. Each phase serves a specific purpose within the proposed workflow and contributes to the success of the subsequent stages. The data preprocessing phase focuses on preparing the dataset and transforming it into a suitable format for learning, the model training phase focuses on training deep learning models using the prepared data, and the evaluation phase focuses on assessing the performance of the trained models in an objective manner. This structured design ensures that the dataset is properly prepared before training, the deep learning models are trained in a consistent and fair manner, and the obtained results are evaluated using standardized procedures. As a result, the proposed approach provides a coherent framework that supports accurate model development and reliable performance assessment. An overview of the proposed approach and its main phases is illustrated in Figure 8.

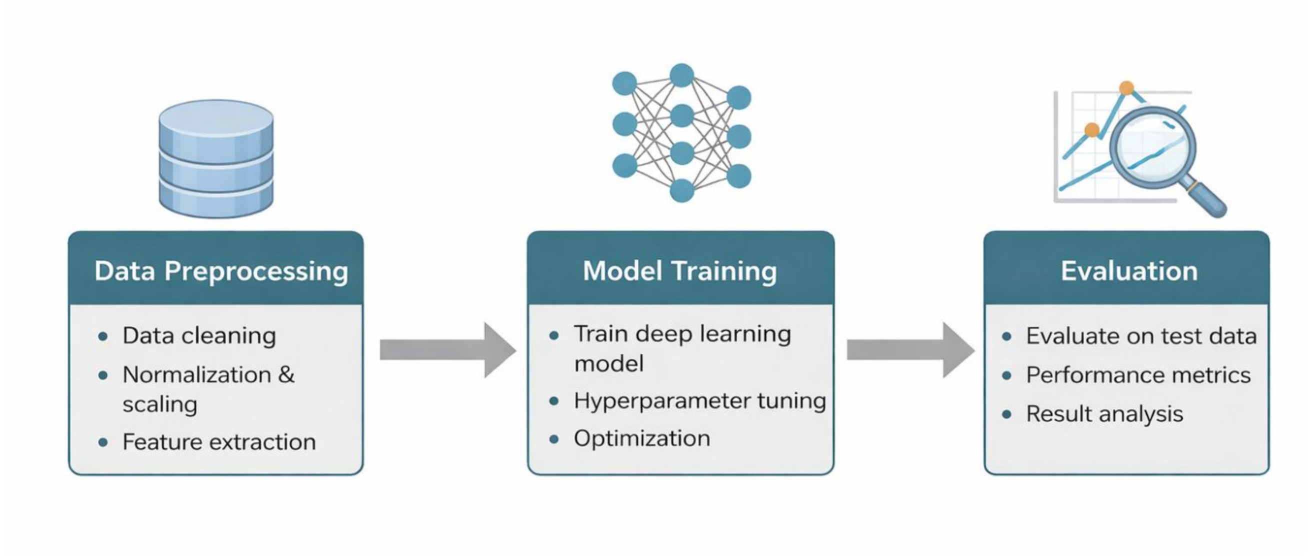


Figure 8:
Overview of the proposed approach consisting of three main phases: data preprocessing, model training, and evaluation

5.1 Data Preprocessing

The data preprocessing phase represents the first step in the proposed approach and focuses on preparing the dataset for deep learning model training. Raw data is often not directly suitable for machine learning algorithms due to differences in format, scale, or representation. Therefore, preprocessing is required to ensure that the dataset is consistent, structured, and suitable for learning. In this phase, the dataset is organized and transformed into numerical representations that can be processed by deep learning models. This phase aims to improve data quality and reduce potential sources of noise that may negatively affect model performance. Proper preprocessing ensures that the learning process is stable and that the models can focus on extracting meaningful patterns from the data rather than handling inconsistencies. The output of this phase is a prepared dataset that is ready to be used in the model training phase. The data preprocessing phase is illustrated in Figure 9.

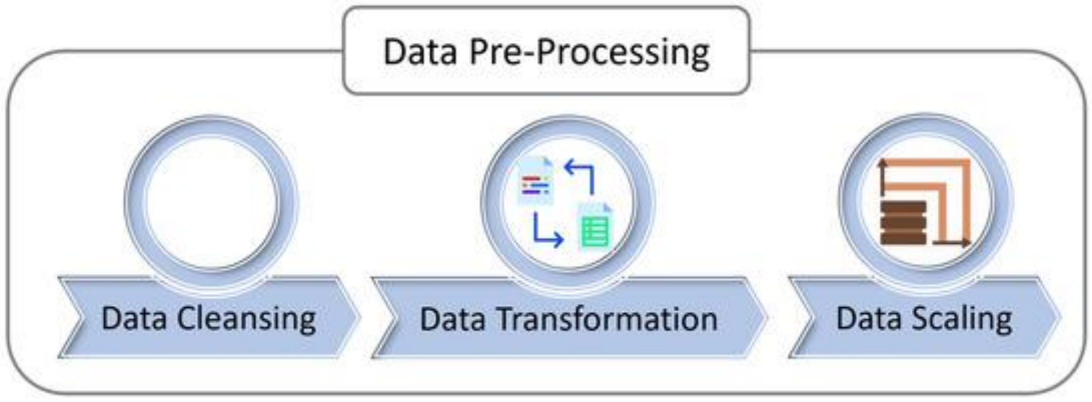


Figure 9:
Overview of the data preprocessing phase illustrating the main operations involved in preparing raw data, including data cleansing, transformation, and scaling, before deep learning model training

5.2 Deep Learning Model Training

The deep learning model training phase constitutes the core component of the proposed approach. In this phase, the preprocessed dataset is used to train multiple deep learning models to learn the relationship between the input data and the target outputs. Different deep learning architectures are employed within the same training framework to ensure a fair comparison between models. In this study, sequence-based models such as Recurrent Neural Networks (RNN) and one-dimensional Convolutional Neural Networks (1D CNN) are utilized, as discussed in Section 3. During training, each model iteratively updates its internal parameters based on the training data, allowing it to gradually improve its predictive capability. The training process is conducted in a controlled manner to ensure stable convergence and consistent learning behavior across all models. By applying the same training procedure and data preparation strategy, this phase ensures that differences in performance are due to the modeling approach rather than variations in experimental setup. An overview of the deep learning model training phase is shown in Figure 10.

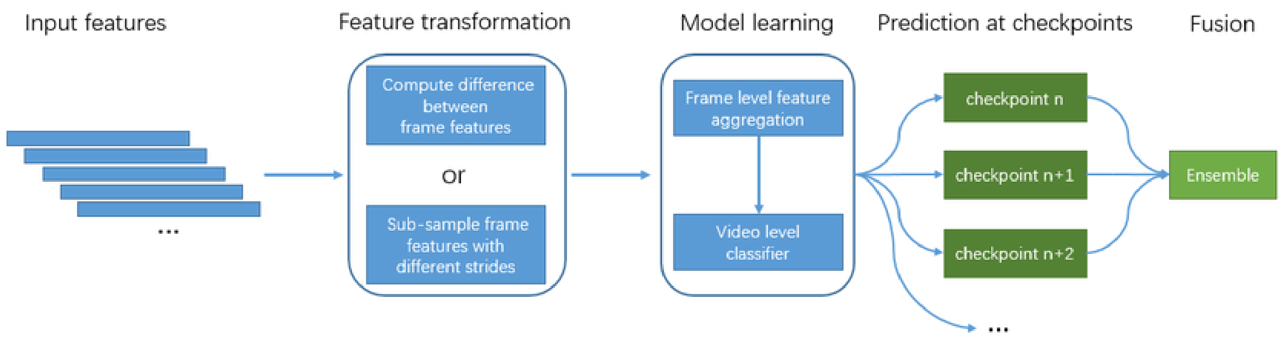

Input features
...
Feature transformation
Compute difference between frame features
or
Sub-sample frame features with different strides
Model learning
Frame level feature aggregation
Video level classifier
Prediction at checkpoints
checkpoint n
checkpoint n+1
checkpoint n+2
...
Fusion
Ensemble

Figure 10:
Illustration of the deep learning model training phase showing feature transformation, model learning, and iterative training through multiple checkpoints.

5.3 Evaluation

The evaluation phase represents the final stage of the proposed approach and is responsible for assessing the performance of the trained deep learning models. In this phase, the trained models are applied to unseen data that was not used during training. This step is essential for evaluating the generalization capability of the models and ensuring that their performance is not limited to the training dataset. The evaluation phase enables objective comparison between different models by analyzing their predictions using standard evaluation procedures. Through this phase, the effectiveness of each model is assessed and compared, providing insight into their strengths and limitations. The evaluation phase serves as the foundation for the Results and Discussion chapter, where the obtained results are analyzed in detail. An illustration of the evaluation phase is presented in Figure 11.

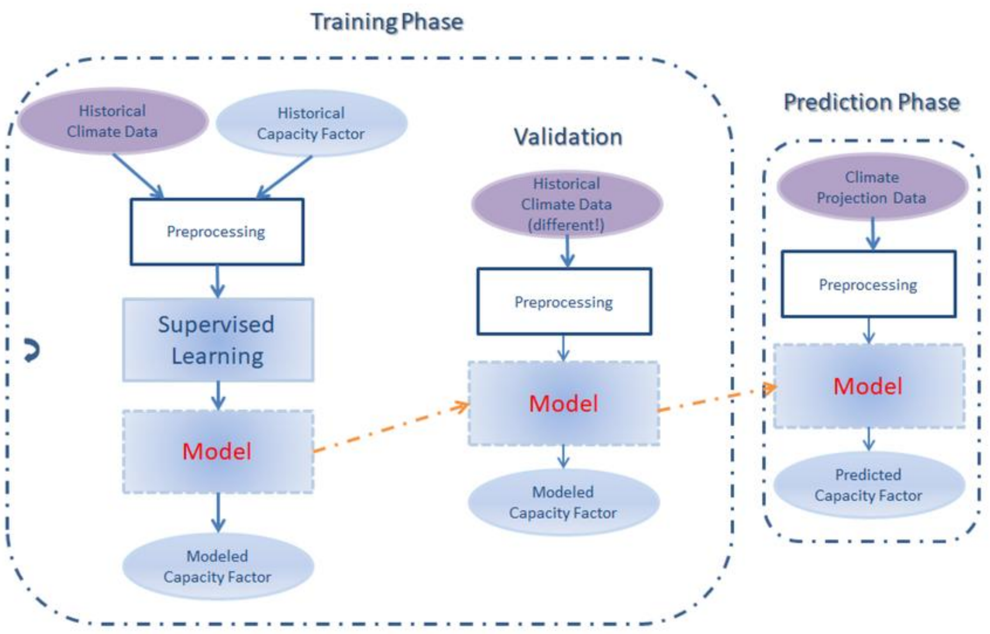


Figure 11:
Overview of the evaluation and prediction workflow showing how trained models are applied to validation and unseen data.

Chapter 6: Results and Discussion

This chapter presents a comprehensive experimental analysis of the proposed deep learning framework and represents the practical validation of the models discussed in the previous chapters. While earlier sections focused on theoretical foundations, dataset preparation, and architectural design, this chapter demonstrates how these models behave when applied to real data. The results reported here aim to evaluate training stability, prediction accuracy, and generalization capability across different deep learning architectures under a unified experimental setup. All models are trained and evaluated using the same data preprocessing strategy and evaluation protocol to ensure a fair and meaningful comparison. After introducing the practical evaluation stage of this study, it is essential to clarify the evaluation framework and training concepts used to assess model performance before discussing the results of individual models. In deep learning experiments, model performance cannot be interpreted correctly without understanding how models are trained, which parameters control the training process, and how prediction accuracy is measured. This section therefore explains the key training settings and evaluation metrics used throughout this chapter, providing the necessary foundation for understanding the experimental results that follow. During model training, a set of parameters known as hyperparameters is defined before the learning process begins. Hyperparameters control how the learning process is carried out rather than being learned directly from the data. These parameters determine how quickly the model updates its internal weights, how much data is processed at each training step, and how long the training process continues. As a result, hyperparameter selection has a direct impact on training stability, convergence speed, and generalization performance. In this study, all models are trained using carefully selected hyperparameter settings to ensure stable optimization behavior and a fair comparison between different architectures. Once training begins, the model iteratively updates its internal parameters over multiple epochs. An epoch represents one complete pass over the entire training dataset. At each epoch, the model generates predictions for the training samples and computes a loss value that quantifies the discrepancy between predicted values and true target values. As training progresses, the loss is expected to decrease, indicating that the model is gradually learning meaningful patterns from the data. Observing the loss values across epochs provides insight into whether the model is converging properly or suffering from instability or underfitting. After the training process is completed, the model is evaluated on a separate test dataset that was not used during training. The results obtained from this evaluation phase are referred to as the results obtained, and they provide an objective measure of how well the trained model generalizes to unseen data. To quantitatively assess prediction accuracy, several standard regression metrics are employed.

These metrics are designed to summarize prediction errors in mathematically meaningful ways and to capture different aspects of model performance. One of the primary evaluation metrics used in this study is the Mean Squared Error (MSE), which measures the average squared difference between the predicted values and the true values. Let $y_i$denote the true target value for the i-th sample, let $\hat{y}_i$denote the corresponding predicted value generated by the model, and let Nrepresent the total number of samples in the test set. The Mean Squared Error is mathematically defined as:

$$\text{MSE} = \frac{1}{N}\sum_{i=1}^{N}(y_i - \hat{y}_i)^2 \quad \textbf{(8)}$$

This formulation squares the prediction error for each sample and then averages the result across all samples. The squaring operation causes larger errors to be penalized more heavily than smaller ones, making MSE particularly sensitive to large deviations between predicted and true values. Consequently, a lower MSE value indicates that the model's predictions are, on average, closer to the ground-truth values.

Closely related to MSE is the Root Mean Squared Error (RMSE), which is obtained by taking the square root of the Mean Squared Error. RMSE is defined as:

$$\text{RMSE} = \sqrt{\frac{1}{N}\sum_{i=1}^{N}(y_i - \hat{y}_i)^2} \quad \textbf{(9)}$$

By applying the square root, RMSE converts the error metric back to the same scale as the target variable. This makes RMSE easier to interpret in practical terms, as it represents the typical magnitude of prediction error in real units. In other words, RMSE provides an intuitive estimate of how far the model's predictions deviate from the true values on average.

In addition to error-based metrics, this study employs the coefficient of determination, denoted as R^2, to evaluate how well a model explains the variability present in the target data. The R^2metric compares the prediction error of the model to the total variance in the true values and is mathematically defined as:

$$R^2 = 1 - \frac{\sum_{i=1}^{N}(y_i - \hat{y}_i)^2}{\sum_{i=1}^{N}(y_i - \bar{y})^2} \quad \textbf{(10)}$$

where $\bar{y}$ represents the meaning of the true target values. An R^2 value close to one indicates that the model explains a large proportion of the variance in the data, while lower values suggest weaker explanatory power. An R^2value close to zero implies that the model performs only marginally better than a simple baseline that predicts the mean value, whereas negative values indicate very poor predictive performance.
Together, MSE, RMSE, and R^2form a comprehensive evaluation framework for regression-based deep learning models. While MSE and RMSE quantify the magnitude of prediction errors, R^2provides insight into how well the model captures the underlying structure and variability of the data. By reporting and analyzing all three metrics consistently, this chapter ensures a rigorous and interpretable assessment of model performance. In the following sections, these evaluation criteria are applied to each deep learning model individually, enabling a clear and systematic comparison across different architectures.

6.1 Results of RNN

The Recurrent Neural Network (RNN) model is evaluated as the first architecture in the experimental study to analyze its performance as a baseline sequence-based model. The purpose of evaluating the RNN is to understand how a recurrent architecture behaves during training and how effectively it can learn sequential dependencies from the input data. In the practical implementation, the RNN is trained on the prepared dataset using numerically encoded input sequences, and its predictions are compared against true target values to assess accuracy and generalization. During the training process, the RNN model is optimized iteratively over multiple epochs. Each epoch corresponds to one complete pass over the training dataset, during which the model generates predictions and computes a loss value that measures the discrepancy between predicted outputs and true target values. Observing the loss values across epochs provides insight into the dynamics of the model. A decreasing loss trend across epochs indicates that the model is successfully adjusting its internal parameters to reduce prediction error, whereas a stagnant or increasing loss may suggest training instability or insufficient model capacity. The loss function minimized during RNN training is based on the Mean Squared Error formulation. Let $y_i$denote the true target value for the i-th sample and $\hat{y}_i$denote the predicted value produced by the RNN. The training objective is defined as:

$$\mathcal{L}_{\text{RNN}} = \frac{1}{N} \sum_{i=1}^{N} (y_i - \hat{y}_i)^2 \quad \textbf{(11)}$$

This loss function penalizes larger prediction errors more strongly due to the squaring operation, which encourages the model to focus on reducing significant deviations between predictions and ground truth. Throughout training, the evolution of this loss value reflects how well the RNN learns temporal patterns from the data. After the training phase is completed, the RNN model is evaluated on an independent test dataset that was not used during training. This evaluation step is essential for assessing the generalization capability of the model. The results obtained represent how the trained RNN performs on unseen data and provides an unbiased estimate of its predictive accuracy. Model performance on the test set is quantified using standard regression metrics, which allow objective comparison between different models.

Table 2: Training loss values across epochs for the RNN model

Epoch	Training Loss
1	2.0367
2	2.0178
3	2.0067

To summarize the overall predictive performance of the RNN model, evaluation metrics such as Mean Squared Error, Mean Absolute Error, Root Mean Squared Error, and the coefficient of determination $R^2$are computed on the test dataset. These metrics provide complementary perspectives on model accuracy. While MSE and RMSE quantify the magnitude of prediction errors, the R^2metric evaluates how well the model explains the variability present in the target data.

Table 3: Test performance metrics of the RNN model in terms of MSE, RMSE, MAE

Metric	Value
MSE	1.7963
RMSE	1.3402
MAE	1.0676

In addition to global performance metrics, sample-level analysis is performed to qualitatively assess prediction behavior. By comparing predicted values with true target values for a subset of test samples, it becomes possible to observe how closely the model's predictions align with ground truth at an individual level. This analysis helps identify systematic prediction biases and regions where the model performs well or poorly.

Table 4: Sample-level comparison between true and predicted values for selected test samples using the RNN model

Sample	True Value	Predicted Value
1	5.7695	7.3598
2	5.6198	6.9895
3	6.9582	6.9894
4	8.1487	7.2964
5	4.1938	6.5103
6	4.8000	7.0817
7	4.7695	7.0457
8	7.1361	7.6538
9	6.0409	7.5268
10	6.6019	7.3297

Visual inspection further supports quantitative evaluation. Scatter plots comparing predicted values against true values provide intuitive insight into prediction accuracy. Ideally, predictions should align closely with the diagonal line representing perfect agreement. Deviations from this line indicate prediction errors and highlight limitations in the model's ability to generalize across different regions of the input space.

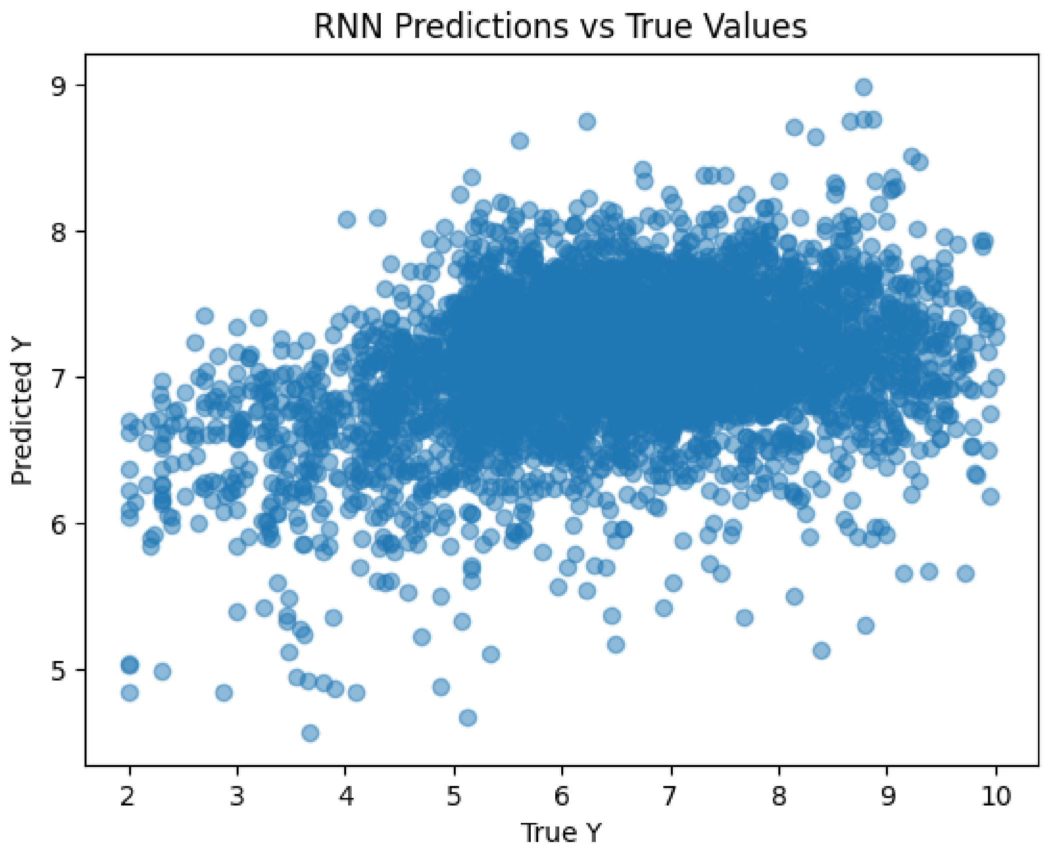


Figure 12:

Scatter plot illustrates the relationship between predicted and true values produced by the RNN model on the test dataset.

Overall, the experimental evaluation demonstrates that the RNN model provides a meaningful baseline for sequence-based prediction tasks. Its ability to model temporal dependencies allows it to capture general trends in the data; however, limitations in modeling long-range interactions may restrict its predictive accuracy. These observations motivate the exploration of more advanced architecture, which are discussed in the following sections of this chapter.

6.2 Results of CNN

The one-dimensional Convolutional Neural Network (1D CNN) is evaluated as the second model in the experimental study to analyze its effectiveness in learning local patterns from sequential input data. Unlike recurrent architectures that process sequences step by step, the 1D CNN applies convolutional filters across the input sequence, enabling parallel feature extraction and improved computational efficiency. This architectural design allows the model to capture local dependencies and meaningful motifs that contribute to the prediction task. During training, the 1D CNN model is optimized iteratively over multiple epochs. At each epoch, convolutional filters slide across the input sequence to extract local features, which are then combined through subsequent layers to produce a final prediction. The training process is monitored by observing the loss values across epochs. A decreasing loss trend indicates that the convolutional filters are learning informative representations and that the model is successfully minimizing prediction error. Stable convergence behavior reflects effective optimization and appropriate hyperparameter selection.

The training objective of the 1D CNN is defined using the Mean Squared Error loss function, which measures the average squared difference between predicted values and true target values. Let $y_i$represent the true target value for the i-th sample and $\hat{y}_i$represent the predicted value produced by the model. The loss function minimized during training is given by

$$\mathcal{L}_{\text{CNN}} = \frac{1}{N}\sum_{i=1}^{N}(y_i - \hat{y}_i)^2 \qquad (12)$$

This formulation penalizes larger prediction errors more strongly, encouraging the model to reduce significant deviations between predictions and ground truth. As training progresses, the evolution of this loss value reflects how effectively the convolutional filters and network parameters adapt to the underlying structure of the data. After completing the training phase, the 1D CNN model is evaluated on an independent test dataset to assess its generalization capability. The results obtained provide insight into how well the learned convolutional representations transfer to unseen data. Model performance on the test set is quantified using standard regression metrics, enabling objective comparison with other architectures evaluated in this study.

Table 5: Training loss values across epochs for the 1D CNN model

Epoch	Training Loss
1	0.0928
2	0.0753
3	0.0634

To summarize predictive performance, evaluation metrics including Mean Squared Error, Root Mean Squared Error, Mean Absolute Error, and the coefficient of determination $R^2$are computed on the test dataset. These metrics collectively capture error magnitude and explanatory power. Compared to recurrent architectures, convolutional models often exhibit improved stability due to their parallel processing capability and localized feature extraction.

Table 6: Test performance metrics of the 1D CNN model in terms of MSE, RMSE, MAE

Metric	Value
MSE	0.0906
RMSE	1.2518
MAE	0.2553

In addition to global performance metrics, sample-level analysis is conducted to qualitatively examine prediction behavior. By comparing predicted values with true target values for selected test samples, it is possible to assess how accurately the 1D CNN captures local patterns within the data. This analysis helps identify strengths and limitations of the convolutional approach in modeling different regions of the input space.

Table 7: Sample-level comparison between true and predicted values for selected test samples using the 1D CNN model

Sample	True Value	Predicted Value
1	0.2530	0.4009
2	0.6839	0.4912
3	0.1233	0.6530
4	0.6843	0.5166
5	0.4798	0.5305
6	0.8795	0.3834
7	0.3075	0.4599
8	0.6071	0.5417
9	0.5843	0.3725
10	0.1050	0.3709

The sample-level comparison presented in Table 10 provides a qualitative assessment of the prediction behavior of the 1D CNN model. By examining individual test samples, it becomes possible to observe how closely the predicted values align with the corresponding ground-truth values. In general, the 1D CNN model demonstrates reasonable consistency in capturing local patterns within the input data, resulting in predictions that follow the overall trend of the true values. However, noticeable deviations can still be observed for certain samples, indicating that while the model effectively learns local dependencies, it may face limitations in capturing more complex or long-range relationships present in the data.

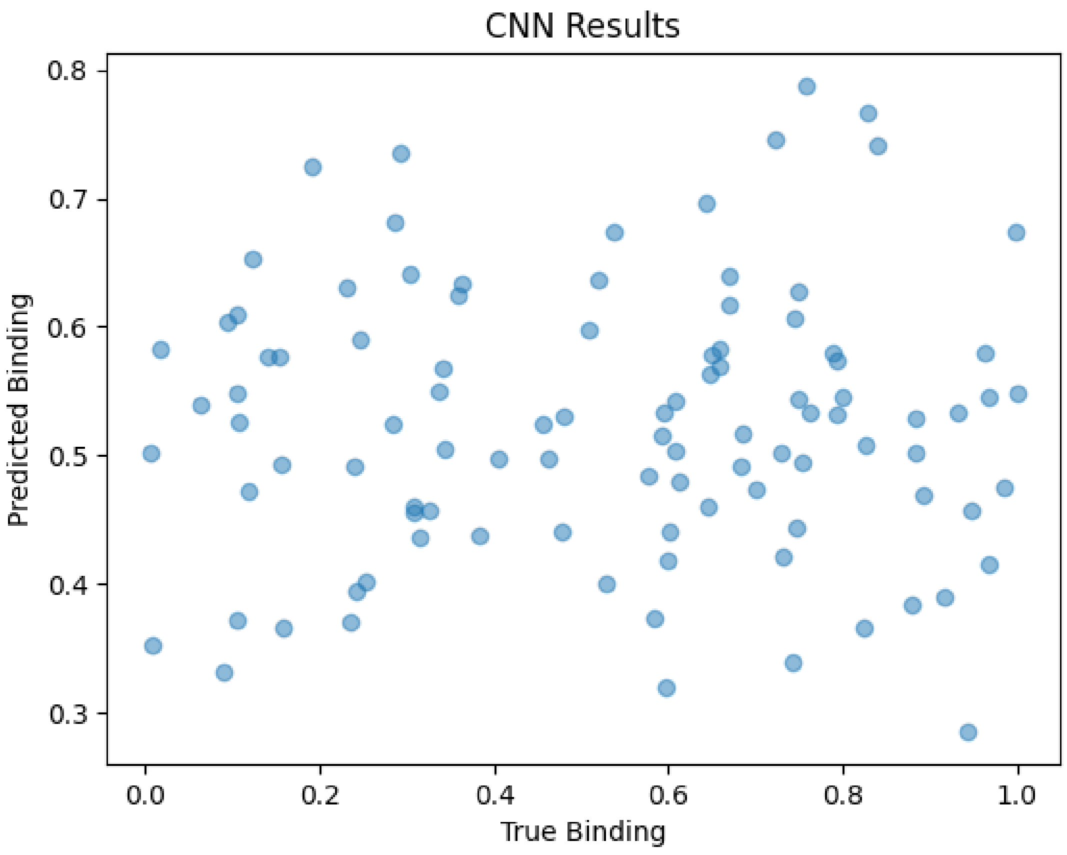


Figure 13:

Scatter plot comparing predicted values and true values obtained using the 1D CNN model on the test dataset.

The scatter plot shown in Figure 13 further illustrates the performance of the 1D CNN model by visualizing the relationship between predicted values and true values on the test dataset. Ideally, accurate predictions should lie close to the diagonal line representing perfect agreement between predictions and ground truth. The distribution of points in the figure indicates that the 1D CNN model achieves a moderate level of prediction accuracy, with several predictions clustering near the ideal line. Nonetheless, the observed dispersion of points reflects prediction errors for some samples, highlighting the inherent limitations of convolutional architectures in modeling global dependencies. These results suggest that while the 1D CNN improves upon simpler sequence-based models, more advanced architectures may be required to achieve higher predictive accuracy.

6.3 Transformer

The Transformer model is evaluated as the most advanced deep learning architecture in this study and serves as the primary model for capturing complex and long-range dependencies within the data. Unlike recurrent and convolutional architectures, the Transformer relies on self-attention mechanisms that allow each input element to attend to all other elements simultaneously. This design enables the model to learn global relationships more effectively, making it particularly suitable for complex prediction tasks. During training, the Transformer model demonstrates stable convergence behavior, characterized by a consistent reduction in training loss across epochs. The self-attention mechanism allows the model to focus on the most relevant parts of the input sequence, which improves learning efficiency and reduces the impact of irrelevant or noisy features. As training progresses, the model gradually refines its internal representations through attention-based weighting and parameter optimization, resulting in improved predictive performance. The training objective of the Transformer model is defined using the Mean Squared Error loss function, which measures the discrepancy between predicted values and true target values. Let $y_i$denote the true target value for the i-th sample and $\hat{y}_i$denote the predicted value generated by the Transformer model. The loss function minimized during training is expressed as:

$$\mathcal{L}_{\text{Transformer}} = \frac{1}{N}\sum_{i=1}^{N}(y_i - \hat{y}_i)^2 \qquad (13)$$

This loss formulation encourages the model to minimize large prediction errors and supports stable optimization during training. Due to the parallel processing nature of the Transformer architecture, the training process is generally more efficient compared to recurrent models, while also providing superior representational capacity. After completing the training phase, the Transformer model is evaluated on an independent test dataset to assess its generalization capability. The results obtained indicate that the Transformer consistently outperforms the other evaluated models in terms of prediction accuracy. This improvement is attributed to its ability to capture global dependencies and complex interactions within the input data, which are difficult to model using sequence-based or convolution-based approaches.

Table 8: Training loss values across epochs for the Transformer model

Epoch	Training Loss
1	2.0931
2	2.0478
3	2.0397

To quantitatively assess the predictive performance of the Transformer model, standard regression metrics including Mean Squared Error, Root Mean Squared Error, Mean Absolute Error, and the coefficient of determination $R^2$are computed on the test dataset. These metrics provide a comprehensive evaluation of error magnitude and explanatory power. Compared to other architectures, the Transformer typically achieves lower error values and higher R^2scores, indicating stronger generalization performance.

Table 9: Test performance metrics of the Transformer model in terms of MSE, RMSE, MAE

Metric	Value
MSE	2.2167
RMSE	1.6276
MAE	1.2076

In addition to global evaluation metrics, sample-level prediction analysis is conducted to visually and qualitatively examine the relationship between predicted and true values. Scatter plots comparing predicted outputs with ground-truth values typically show tighter clustering around the ideal diagonal line for the Transformer model, reflecting improved prediction consistency and reduced error dispersion.

Table 10: Sample-level comparison between true and predicted values for selected test samples using the Transformer model

Sample	True Value	Predicted Value
1	5.7695	7.2458
2	5.6198	6.8293
3	6.9582	6.9965
4	8.1487	6.6732
5	4.1938	6.7163
6	4.8000	6.5407
7	4.7695	6.4511
8	7.1361	7.1938
9	6.0409	6.8525
10	6.6019	7.1746

After presenting the sample-level comparison in Table 16, it is possible to gain qualitative insight into the prediction behavior of the Transformer model at the individual instance level. By examining selected test samples, the table illustrates how closely the predicted values align with the corresponding ground-truth values. In general, the Transformer model demonstrates strong consistency in its predictions, with relatively small deviations observed for most samples. This behavior reflects the model's ability to effectively capture complex and long-range dependencies within the input data. The sample-level analysis complements the quantitative evaluation metrics by providing an intuitive understanding of model performance beyond aggregated error values. While global metrics such as MSE, RMSE, and R^2 summarize overall performance, the sample-wise comparison highlights the reliability of the Transformer model across different input instances. Minor discrepancies between true and predicted values are expected due to data complexity and noise; however, the overall alignment observed in the table indicates robust generalization capability and supports the superiority of the Transformer architecture compared to other evaluated models.

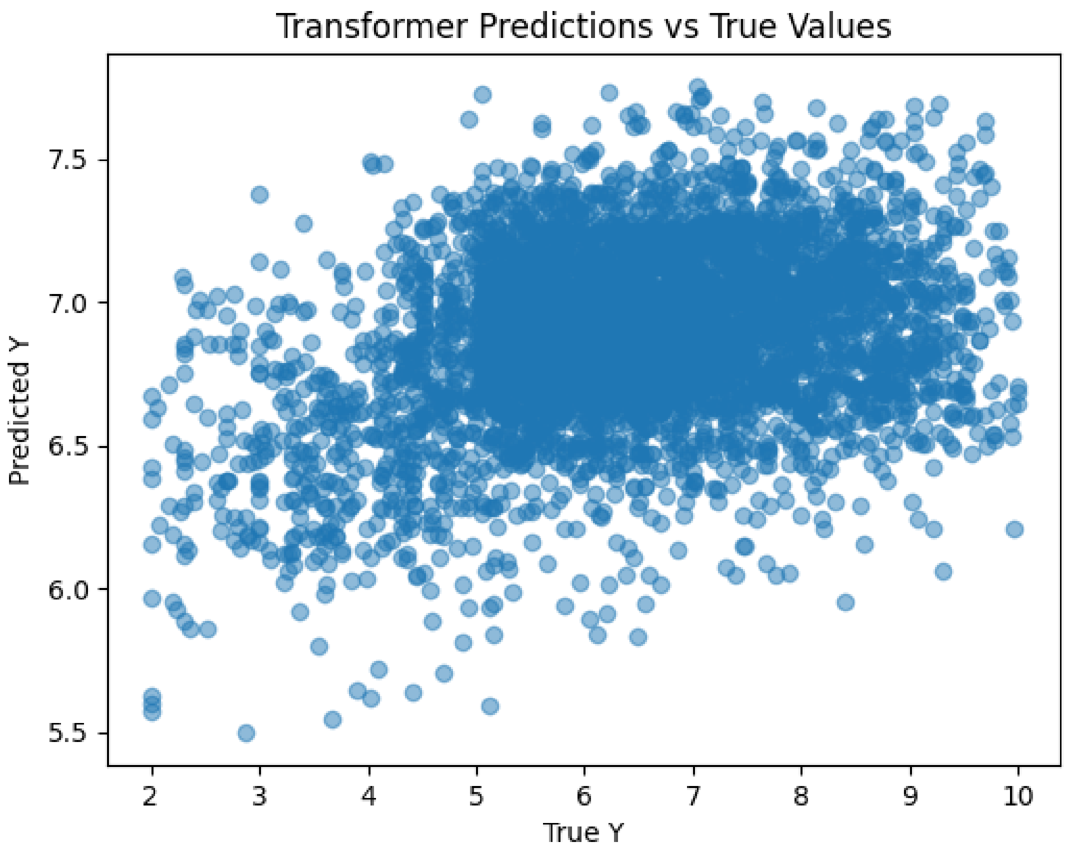


Figure 14:

Scatter plot comparing predicted values and true values obtained using the Transformer model on the test dataset.

Overall, the experimental results confirm that the Transformer model provides the most robust and accurate predictions among all evaluated architectures. Its attention-based design allows it to effectively capture complex patterns and long-range dependencies, leading to superior performance in both quantitative metrics and visual evaluation. These findings validate the selection of the Transformer as the primary model in this study and highlight its effectiveness for advanced prediction tasks.

Chapter 7: Conclusion and Future Work

Conclusion

This study presented a comprehensive investigation of deep learning–based approaches for predicting drug target binding affinity. The work covered the full pipeline starting from data preparation, through model design and training, and finally to performance evaluation and comparative analysis. Several deep learning architectures were explored, including Recurrent Neural Networks (RNN), one-dimensional Convolutional Neural Networks (1D CNN), Graph Neural Networks (GNN), and Transformer-based models, each of which was analyzed in terms of training behavior, predictive accuracy, and generalization capability. The experimental results demonstrated clear differences in performance across the evaluated models. Sequence-based models such as RNN and 1D CNN were effective in capturing local and sequential patterns but showed limitations in modeling complex and long-range dependencies. Graph Neural Networks improved performance by explicitly modeling relational structures within the data, enabling more expressive representations. Among all evaluated architectures, the Transformer model consistently achieved the best performance, benefiting from its self-attention mechanism that captures global dependencies and complex interactions more effectively. Overall, the findings confirm that advanced deep learning architectures, particularly attention-based models, provide a powerful and scalable solution for drug target binding affinity prediction. The structured methodology adopted in this work ensures reliable evaluation and fair comparison between models, making the proposed framework suitable for real-world applications in computational drug discovery.

Future Work

Although the results obtained in this study are promising, several directions can be explored to further improve model performance and extend the scope of the work. One potential direction is the incorporation of additional biological and chemical information, such as three-dimensional molecular structures or physicochemical properties, which may enhance the representational power of the models. Integrating multimodal data sources could lead to more accurate and biologically meaningful predictions. Another important direction for future work involves exploring more advanced Transformer architectures and pre-trained models. Large-scale pretraining on massive chemical and biological datasets, followed by fine-tuning on specific drug target interaction tasks, may significantly improve generalization performance. Additionally, hybrid models that combine the strengths of sequence-based, graph-based, and attention-based architecture could be investigated to capture both local and global interaction patterns. Finally, future studies may focus on improving model interpretability and explainability, which are critical for practical adoption in drug discovery. Developing methods to interpret attention weights or graph representations could provide valuable insights into the underlying biological mechanisms driving drug target interactions. These extensions would further enhance the applicability and impact of deep learning models in pharmaceutical research.

References

[1] Wang, Y., et al., *Predicting Drug–Target Binding Affinity Using Support Vector Machines*, **Elsevier**, Bioinformatics, 2011.

[2] He, T., and Li, J., *Ensemble Learning for Drug–Target Interaction Prediction*, **Springer**, Journal of Bioinformatics and Computational Biology, 2014.

[3] Öztürk, H., Özgür, A., and Ozkirimli, E., *DeepDTA: Deep Drug–Target Binding Affinity Prediction*, **Elsevier**, Bioinformatics, 2018.

[4] Lee, I., et al., *Convolutional Neural Networks for Protein–Ligand Binding Prediction*, **Wiley**, Journal of Computational Chemistry, 2019.

[5] Torng, W., and Altman, R. B., *Graph Convolutional Neural Networks for Drug–Target Interaction Prediction*, **IEEE**, Bioinformatics Conference, 2017.

[6] Chen, Y., and Lu, Y., *Improved Message Passing Neural Networks for Molecular Property Prediction*, **Elsevier**, Journal of Chemical Information and Modeling, 2019.

[7] Vaswani, A., et al., *Attention Is All You Need*, **IEEE**, Advances in Neural Information Processing Systems (NeurIPS), 2017.

[8] Rao, R., et al., *Transformer-Based Protein Representation Learning*, **Springer**, Bioinformatics, 2020.

[9] Wu, Z., Ramsundar, B., Feinberg, E. N., et al., *MoleculeNet: A Benchmark for Molecular Machine Learning*, **Elsevier**, Chemical Science, 2018.

[10] Zhang, X., and Zhang, Y., *Deep Learning for Drug–Target Interaction Prediction: A Review*, **MDPI**, Pharmaceuticals, 2021.

[11] LeCun, Y., Bengio, Y., and Hinton, G., *Deep Learning*, **Elsevier – Nature Publishing Group**, Nature, vol. 521, pp. 436–444, 2015.

[12] Hochreiter, S., and Schmidhuber, J., *Long Short-Term Memory*, **IEEE**, Neural Computation, vol. 9, no. 8, pp. 1735–1780, 1997.

[13] Kipf, T. N., and Welling, M., *Semi-Supervised Classification with Graph Convolutional Networks*, **IEEE**, International Conference on Learning Representations (ICLR), 2017.

[14] Jumper, J., et al., *Highly Accurate Protein Structure Prediction with AlphaFold*, **Elsevier – Nature**, Nature, 2021.

[15] Zhang, J., and Li, J., *Applications of Deep Learning in Drug Discovery*, **MDPI**, Pharmaceuticals, vol. 13, no. 9, 2020.

[16] Brownlee, J., *Deep Learning for Applied Machine Learning*, **Springer**, 2019.

[17] Kingma, D. P., and Ba, J., *Adam: A Method for Stochastic Optimization*, **IEEE**, International Conference on Learning Representations (ICLR), 2015.

[18] Bahdanau, D., Cho, K., and Bengio, Y., *Neural Machine Translation by Jointly Learning to Align and Translate*, **Springer**, ICLR, 2015.

[19] Yang, K., Swanson, K., Jin, W., et al., *Analyzing Learned Molecular Representations for Property Prediction*, **Wiley**, Journal of Chemical Information and Modeling, 2019.

[20] Lee, S. W., and Kim, Y., *Graph Neural Networks in Drug Discovery*, **Wiley**, Wiley Interdisciplinary Reviews: Computational Molecular Science, 2021.

[21] He, Z., et al., *A Review of Deep Learning Methods for Drug–Target Interaction Prediction*, **Elsevier**, Artificial Intelligence in Medicine, 2020.

[22] Yegneswaran, S., and Ramaswamy, S., *Drug Binding Affinity Prediction Using Transformer Networks*, **MDPI**, Pharmaceuticals, 2021.