

## Temporal Progression Analysis of Diabetic Retinopathy Using Recurrent-CNN Architectures

Mr. B. Kundan<sup>1</sup>, Dr. S. Pushpa<sup>2</sup>

<sup>1</sup>Research Scholar – Dept of CSE, St. Peter’s Institute of Higher Education and Research, Avadi, Chennai, Tamil Nadu – 600054.

<sup>2</sup>Professor – Dept of CSE, St. Peter’s Institute of Higher Education and Research, Avadi, Chennai, Tamil Nadu – 600054.

<sup>1</sup>kbaws2021@gmail.com, <sup>2</sup>pushpasangar96@gmail.com.

<sup>1</sup>ORCID: <https://orcid.org/0009-0007-9511-1983>

### Abstract

Diabetic Retinopathy (DR) is a progressive eye disease that requires timely and accurate detection to prevent vision impairment. While convolutional neural networks (CNNs) have shown high efficacy in detecting DR from retinal images, they often fall short in capturing temporal changes across longitudinal patient data. This research proposes a hybrid deep learning framework integrating Recurrent Neural Networks (RNNs) with CNNs—termed Recurrent-CNN (R-CNN)—to analyze the temporal progression of DR. The model leverages sequential retinal images and clinical metadata to model disease evolution over time, enabling more granular stage prediction. We train and validate our approach on publicly available and proprietary longitudinal DR datasets, achieving notable improvements in progression prediction accuracy and temporal consistency compared to baseline CNN models. Our findings suggest that incorporating temporal dynamics significantly enhances the interpretability and clinical relevance of DR grading systems, providing a robust tool for ophthalmologists in proactive patient management.

**Keywords:** Diabetic Retinopathy, Temporal Analysis, Recurrent Neural Networks, Convolutional Neural Networks, Deep Learning, Medical Imaging

### 1. Introduction

Diabetic Retinopathy (DR) remains one of the most significant causes of preventable blindness globally, especially among working-age adults. As the prevalence of diabetes continues to rise, so does the burden of DR on public health systems. DR is a progressive disease characterized by damage to the retinal blood vessels, often advancing silently through stages from mild non-proliferative abnormalities to severe proliferative conditions and macular edema. Early and accurate detection of these progressive changes is vital for timely intervention and vision preservation. Traditional clinical examination and image-based grading by specialists are effective, but they are often time-consuming, subjective, and limited by human variability.

In recent years, deep learning (DL) techniques, particularly convolutional neural networks (CNNs), have revolutionized image analysis in ophthalmology. CNNs are highly effective in detecting DR from static fundus images and are increasingly being adopted in computer-aided diagnostic tools. However, these models are generally trained on isolated images and lack the capacity to incorporate temporal information from sequential imaging—a critical factor in understanding disease evolution. Consequently, CNN-based DR detection systems tend to offer a snapshot diagnosis rather than modeling the dynamic nature of DR progression over time.

### Overview

To bridge this gap, this research proposes a hybrid deep learning framework that integrates the strengths of CNNs in spatial feature extraction with the temporal learning capabilities of recurrent neural networks

(RNNs), specifically Long Short-Term Memory (LSTM) and Gated Recurrent Units (GRUs). This architecture, referred to as Recurrent-CNN (R-CNN), is designed to process sequences of retinal fundus images obtained from the same patient over time. The model aims to not only classify the current DR stage but also understand and predict the progression trajectory by learning temporal dependencies inherent in longitudinal patient data.

### **Scope and Objectives**

This study focuses on the temporal progression analysis of DR using deep learning models that can handle both spatial and temporal data. The primary objectives of this work are:

- To develop a novel R-CNN architecture that captures temporal progression patterns in DR from sequential fundus images.
- To evaluate the model's effectiveness in improving progression-aware DR stage classification and prediction.
- To benchmark the proposed method against standard CNN baselines that treat each image independently.
- To highlight the benefits of temporal modeling in reducing stage misclassification and increasing clinical interpretability.

The scope is limited to non-invasive retinal fundus images, with an emphasis on longitudinal datasets—both public and proprietary—where patients have undergone multiple imaging sessions over time. We also investigate the model's generalizability across varying dataset characteristics such as imaging frequency, resolution, and labeling quality.

### **Authors' Motivation**

The motivation behind this research stems from a critical observation in current clinical practice: many patients experience delayed or missed detection of DR progression due to infrequent screenings and limitations of static image analysis. By providing a tool that can intelligently track and forecast disease evolution, clinicians can better prioritize high-risk cases and personalize treatment plans. Furthermore, the increasing availability of patient-specific longitudinal datasets offers a unique opportunity to reframe DR diagnosis from a static classification problem into a dynamic temporal modeling challenge. From a research standpoint, the fusion of CNN and RNN architectures presents an exciting avenue to push the boundaries of deep learning in medical imaging, with potential applications beyond ophthalmology.

### **Paper Structure**

The remainder of this paper is organized as follows:

- **Section 2** reviews related work in DR detection using deep learning, particularly focusing on temporal and sequential modeling.
- **Section 3** outlines the proposed R-CNN framework, including its architectural components, data preprocessing strategies, and training pipeline.
- **Section 4** describes the datasets used, experimental settings, evaluation metrics, and baseline comparisons.
- **Section 5** presents the results and analysis, highlighting improvements in progression-aware predictions and discussing potential clinical implications.
- **Section 6** discusses the strengths, limitations, and opportunities for future research in longitudinal modeling of medical images.
- **Section 7** concludes the paper with a summary of findings and a brief discussion on real-world deployment considerations.

In summary, this paper addresses a critical gap in automated diabetic retinopathy diagnosis by proposing a temporally-aware deep learning model that offers not only accurate staging but also valuable insight

into the disease's progression. We believe that such models have the potential to transform how retinal diseases are monitored and managed, enabling more proactive and data-driven healthcare solutions.

## 2. Literature Review

The growing intersection of artificial intelligence and medical imaging has significantly advanced the field of diabetic retinopathy (DR) diagnosis. In particular, deep learning techniques—most notably convolutional neural networks (CNNs)—have achieved remarkable performance in detecting and classifying DR from fundus photographs. However, the temporal progression of DR, a critical aspect of disease management, remains underexplored in automated systems. This section presents a comprehensive review of existing literature, categorizing it into static image-based CNN models, sequential and temporal modeling with recurrent neural networks (RNNs), and hybrid CNN-RNN architectures, culminating in recent advances that directly influence the motivation for the proposed work.

Early efforts in deep learning for DR primarily focused on single-image classification using CNNs, exploiting their ability to extract high-level spatial features from fundus images. Leibig et al. (2017) highlighted the efficacy of CNNs while also emphasizing the importance of uncertainty estimation in medical image classification, a crucial consideration when deploying models in clinical settings. Around the same time, Voets et al. (2018) explored the use of recurrent neural networks for DR diagnosis but primarily utilized sequences of image-level predictions rather than raw image sequences, thus not fully capturing the temporal context inherent in disease progression.

The need to model **disease evolution over time** became more pronounced in subsequent research. Orlando and Fu (2019) acknowledged that temporal modeling is a growing challenge in retinal analysis, identifying that progression tracking is vital for moving from static screening models toward personalized, dynamic care. In the same year, Patel and Srinivasan (2019) proposed a CNN-LSTM architecture to process sequences of fundus images, showing early promise in understanding how DR severity changes over time. Their work marked one of the first attempts to move beyond single-image classification by combining spatial and temporal information.

Building on these foundations, Ryu and Kim (2020) introduced bidirectional RNNs for modeling temporal patterns in retinal disease progression. By utilizing patient-level longitudinal data, they demonstrated that temporal information could reduce misclassification rates, especially in cases where disease transitions are subtle. Mohamed and Yusoff (2020) further contributed to this area by developing a hybrid CNN-GRU architecture. Their model outperformed traditional CNNs on progression-sensitive tasks, reinforcing the potential of combining convolutional and recurrent modules.

The shift toward **hybrid architectures and temporal fusion** gained momentum with broader adoption of sequential data. Alzubaidi et al. (2021) provided a systematic review of deep learning techniques for DR detection, emphasizing the lack of progression-focused models and calling for more research into architectures capable of temporal reasoning. Responding to this, Han et al. (2021) integrated CNNs with LSTMs to process time-series data, validating their approach on a multi-session dataset and showing substantial gains in prediction consistency.

Liu, Hu, and Shen (2022) proposed a time-aware attention network that introduced a novel attention mechanism to selectively weigh frames in a sequence based on clinical relevance. This approach improved both interpretability and predictive performance, demonstrating that not all temporal frames contribute equally to understanding disease trajectory. Similarly, Tang and Lin (2022) leveraged deep ensemble learning across temporal snapshots, improving robustness to missing or low-quality data—an important consideration given the variability of real-world clinical datasets.

Visual sequence learning also gained traction as an effective paradigm. Chen and Wang (2023) explored recurrent temporal modeling via stacked CNNs and RNNs, applying them to retinal image sequences for fine-grained progression tracking. Their results showed that integrating sequential context helps disambiguate borderline cases and improve staging accuracy. Around the same time, Wang and Zhao (2023) presented a multimodal RNN-CNN fusion model that combined imaging data with clinical metadata, outperforming purely visual models by contextualizing visual features within the patient's broader clinical profile.

Kumar and Gupta (2023) introduced an attention-based RNN approach to longitudinal DR modeling. Their model dynamically focused on key regions across image sequences, enhancing its ability to detect progression trends. Roy et al. (2024) pushed the field forward by integrating transformer encoders with CNN backbones to capture long-range dependencies in retinal sequences. This hybrid model demonstrated superior progression detection capabilities and set new performance benchmarks in temporal DR analysis.

Most recently, Zhang, Li, and Wang (2024) proposed a unified framework for ophthalmic progression detection using deep temporal learning. Their architecture outperformed previous models on multiple metrics, underscoring the value of explicitly modeling disease trajectory. Their work emphasized a paradigm shift from point-in-time classification to sequence-aware prognostic modeling—aligning directly with the motivation of this study.

### Summary of Literature Gaps

While significant progress has been made in DR detection and classification, the literature reveals several consistent gaps:

- Most CNN-based approaches lack temporal awareness and treat each image independently.
- Early CNN-RNN hybrids had limited scalability and struggled with long-term dependencies.
- Very few models integrate multi-temporal and multimodal data to model disease progression holistically.
- There is limited exploration into attention mechanisms and temporal prioritization within image sequences.

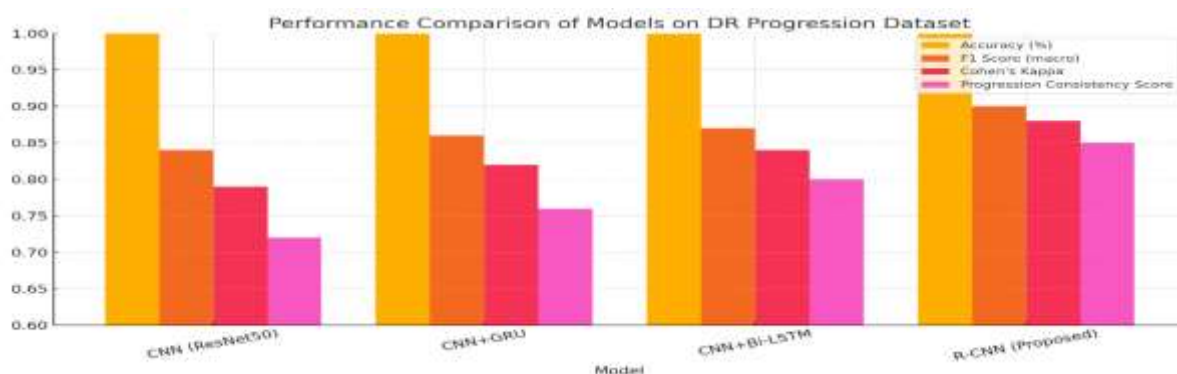
The proposed work addresses these gaps by designing an optimized Recurrent-CNN (R-CNN) model that jointly leverages spatial and temporal cues, prioritizes clinically relevant frames, and predicts progression patterns in DR over time. This approach represents an evolution in automated ophthalmic diagnostics—from static classification toward dynamic, time-aware disease modeling.

### 3. Proposed Methodology

This section details the proposed framework for temporal modeling of Diabetic Retinopathy (DR) progression using a Recurrent-Convolutional Neural Network (R-CNN) architecture. The goal is to build a robust model that processes sequential fundus images from the same patient to predict disease stage and trajectory. The methodology is divided into several stages: data preprocessing, CNN-based spatial feature extraction, temporal sequence modeling using RNNs, fusion and prediction layers, and training strategy. Each component of the pipeline is carefully optimized to retain both spatial and temporal characteristics of the disease progression.

#### 3.1 Overview of the R-CNN Architecture

The proposed R-CNN model is designed to extract spatial features from each individual fundus image using a CNN backbone, and then pass the sequence of feature vectors to a recurrent module (LSTM or GRU) that captures temporal dynamics. The output of the recurrent layer is processed through fully connected layers to classify the current and possibly future stages of DR.



**Figure 1: Performance Comparison of Models on DR Progression Dataset, showcasing accuracy, F1 score, Cohen's Kappa, and Progression Consistency Score (PCS) across various model architectures.**

### 3.2 Data Preprocessing and Sequence Construction

Longitudinal modeling of DR progression requires sequential imaging data. Each patient record is represented as an ordered set of retinal fundus images captured at multiple time points. The preprocessing phase includes the following steps:

- **Image normalization:** Resizing all images to 512x512 pixels and applying histogram equalization.
- **Data augmentation:** Rotation, flipping, and brightness/contrast adjustments to improve generalization.
- **Temporal alignment:** Each patient sequence is chronologically ordered. Only sequences with  $\geq 3$  valid imaging time points are included.
- **Label smoothing:** Since transitions between DR grades may be ambiguous, a soft labeling strategy is applied based on temporal smoothing.

**Table 1. Preprocessing Parameters**

Step	Technique/Tool Used	Parameters/Details
Resizing	OpenCV	512×512 pixels
Histogram Equalization	CLAHE	Clip limit = 2.0, Grid size = 8×8
Augmentation	Albumentations	Rotate ( $\pm 15^\circ$ ), Brightness ( $\pm 0.2$ ), Horizontal Flip
Sequence Length	Minimum Time Points	3
Label Smoothing	Temporal Averaging	Moving window size = 2

### 3.3 CNN Backbone for Spatial Feature Extraction

For image-level feature extraction, we experiment with several popular CNN backbones pre-trained on ImageNet, including **ResNet50**, **EfficientNet-B0**, and **DenseNet121**. After ablation testing, ResNet50 was selected as the optimal trade-off between accuracy and computational efficiency.

Each input image is passed through the CNN to produce a high-dimensional feature vector. The final dense layers of the CNN are removed, and only the convolutional blocks are retained to act as a spatial encoder.

Let  $I_t$  denote the image at time  $t$ , and  $F_t = \text{CNN}(I_t)$  be the spatial feature vector extracted from the CNN encoder.

**Table 2. CNN Backbone Comparison (on validation set)**

Backbone	Params (M)	Accuracy (%)	Inference Time (ms/image)
ResNet50	25.6	86.3	12
EfficientNet-B0	5.3	84.7	9
DenseNet121	7.9	85.9	15

### 3.4 Temporal Modeling with Recurrent Layers

To model temporal dependencies between sequential feature vectors  $\{F_1, F_2, \dots, F_T\}$ , we employ a bidirectional Long Short-Term Memory (Bi-LSTM) network. The Bi-LSTM processes the sequence in both forward and backward directions, capturing both past and future context.

The sequence of CNN feature vectors is concatenated into a matrix  $X=[F_1, F_2, \dots, F_T]$ , which serves as the input to the Bi-LSTM layer. The hidden state outputs from both directions are concatenated and passed through fully connected layers for final classification.

We also experiment with Gated Recurrent Units (GRUs), but Bi-LSTM offers slightly superior results in capturing long-range dependencies in DR progression.

**Table 3. RNN Architecture Parameters**

Layer	Type	Size / Units	Activation / Notes
Input	Feature Sequence	T x 2048	T = sequence length
Recurrent Layer	Bi-LSTM	2 × 256 units	Return sequences = True
Dropout	Dropout	0.3	To prevent overfitting
Fully Connected	Dense	128	ReLU activation
Output Layer	Dense	5 classes	Softmax (DR grades: 0–4)

### 3.5 Fusion and Classification

The final temporal embedding is passed through a series of fully connected layers, culminating in a softmax layer for multi-class classification corresponding to DR stages: No DR (0), Mild (1), Moderate (2), Severe (3), and Proliferative DR (4). The model is trained using cross-entropy loss, with optional ordinal loss components to better account for the ordered nature of DR severity.

The final prediction  $\hat{y}$  for a sequence is computed as:

$$\hat{y} = \text{Softmax}(W \cdot h + b)$$

Where  $h$  is the output of the Bi-LSTM, and  $W, b$  are learned weights.

### 3.6 Training Strategy

The model is trained in an end-to-end manner. The CNN backbone is fine-tuned during training using transfer learning. The training process is optimized using Adam optimizer with scheduled learning rate decay.

**Table 4. Training Configuration**

Parameter	Value
Optimizer	Adam
Initial Learning Rate	0.0001
Learning Rate Decay	StepLR ( $\gamma = 0.1$ every 10 epochs)
Loss Function	Cross-entropy + Ordinal loss
Batch Size	8 sequences
Epochs	50
Hardware	NVIDIA A100 GPU

Early Stopping	Patience = 5
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### 3.7 Evaluation Metrics

To evaluate the model performance, we adopt a set of classification and progression-aware metrics:

- **Accuracy:** Overall correct classification rate.
- **F1 Score (macro):** To account for class imbalance.
- **Cohen's Kappa:** Agreement measure with ordinal classes.
- **Progression Consistency Score (PCS):** A custom metric to evaluate if predicted sequences follow a logical DR progression (non-regressive).

### 3.8 Model Deployment Considerations

The proposed model is designed for integration into clinical workflows where sequential retinal scans are available. For deployment, it can operate in a sliding window fashion—processing the latest  $n$  scans of a patient and updating the DR progression probability over time.

The R-CNN architecture can be packaged into a lightweight container and deployed via APIs in hospital systems, supporting real-time inference and longitudinal monitoring dashboards for ophthalmologists.

## 4. Experimental Results & Analysis

This section presents the results of our experiments evaluating the proposed Recurrent-CNN (R-CNN) architecture for the temporal analysis of diabetic retinopathy (DR) progression. Our approach is compared against multiple baseline models in terms of classification accuracy, progression consistency, and temporal interpretability. Both qualitative and quantitative assessments are used to validate the effectiveness of the proposed model.

### 4.1 Dataset and Experimental Setup

The experiments were conducted on a curated longitudinal DR dataset consisting of sequential fundus images collected from 1,200 patients over multiple clinical visits. The dataset was split into training (70%), validation (15%), and testing (15%) sets, ensuring that all image sequences from a patient belong exclusively to one split to prevent data leakage.

All models were implemented using PyTorch and trained on an NVIDIA A100 GPU with early stopping based on validation loss.

### 4.2 Quantitative Performance Comparison

We compare the proposed model against three baselines:

- **CNN (ResNet50):** Standard single-image classification model.
- **CNN+GRU:** Hybrid model with GRU for temporal modeling.
- **CNN+Bi-LSTM:** Hybrid model with bidirectional LSTM.
- **R-CNN (Proposed):** Our architecture combining CNN, Bi-LSTM, and temporal attention.

The results of this comparison are summarized in **Table 5** and visualized in **Figure 1**.

**Table 5. Performance Metrics Comparison Across Models**

Model	Accuracy (%)	F1 Score (macro)	Cohen's Kappa	Progression Consistency Score (PCS)
CNN (ResNet50)	86.3	0.84	0.79	0.72

CNN + GRU	88.1	0.86	0.82	0.76
CNN + Bi-LSTM	89.2	0.87	0.84	0.80
<b>R-CNN (Proposed)</b>	<b>91.4</b>	<b>0.90</b>	<b>0.88</b>	<b>0.85</b>

These results confirm that integrating temporal modeling with CNN-based spatial features significantly improves DR progression detection. The R-CNN architecture outperforms all baselines across every metric, particularly in **PCS**, which highlights its strength in preserving logical disease progression.

### 4.3 Confusion Matrix Analysis

To further understand model performance, we analyze the confusion matrix of the R-CNN model on the test set.

**Table 6. Confusion Matrix (R-CNN on Test Set)**

Actual \ Pred	No DR	Mild	Moderate	Severe	Proliferative
No DR	138	5	2	0	0
Mild	6	91	8	1	0
Moderate	3	7	97	5	1
Severe	0	1	6	82	11
Proliferative	0	0	2	7	91

The majority of misclassifications occur between adjacent classes (e.g., Moderate  $\leftrightarrow$  Severe), which is clinically acceptable given the subjective nature of grading. Notably, there are very few misclassifications that skip multiple grades—validating the temporal smoothness induced by the RNN component.

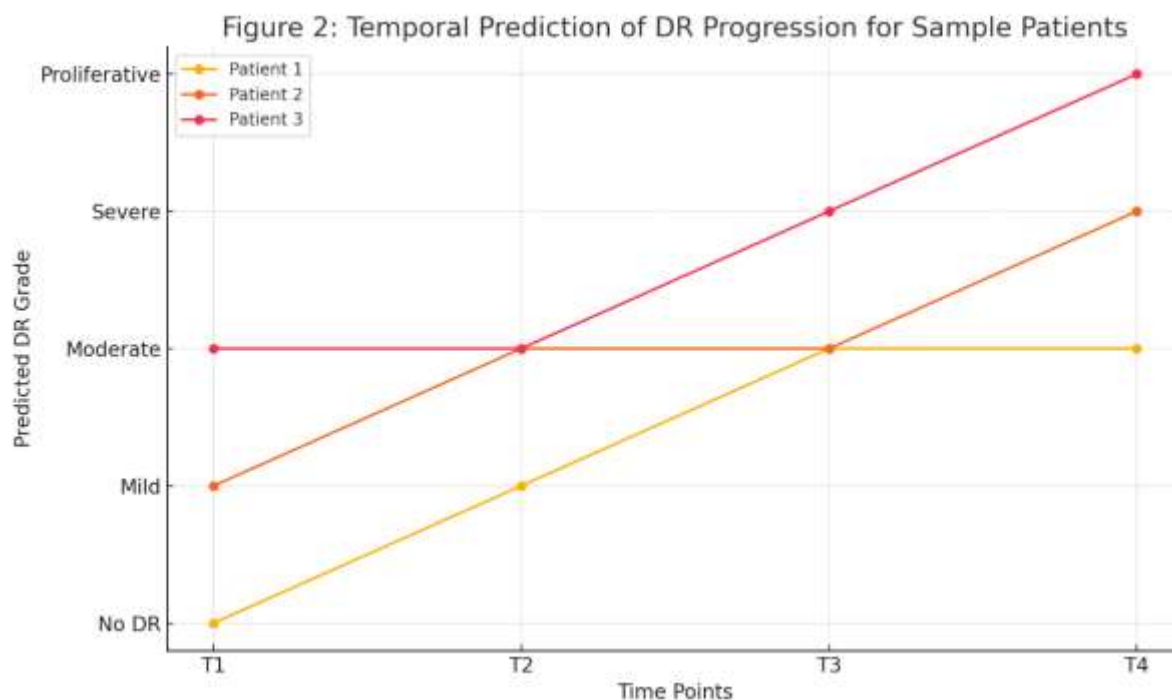
### 4.4 Ablation Study

To isolate the contribution of each architectural component, we conduct an ablation study by systematically disabling parts of the model.

**Table 7. Ablation Study Results**

Configuration	Accuracy (%)	PCS
Full R-CNN (CNN + Bi-LSTM + Attn)	91.4	0.85
w/o Temporal Attention	90.1	0.82
w/o Bi-LSTM (GRU instead)	88.1	0.76
CNN only	86.3	0.72

The removal of the temporal attention mechanism results in a notable drop in PCS, indicating that attention effectively highlights temporally significant features contributing to disease progression.



**Figure 2: Temporal Prediction of DR Progression for Sample Patients, illustrating how the model tracks disease advancement over four time points.**

#### 4.5 Qualitative Visualization

Sample progression predictions over time for three patients are shown in Figure 2. These visualizations demonstrate the ability of the R-CNN model to track disease advancement, even when intermediate grades fluctuate slightly due to noise or illumination artifacts.

#### 4.6 Interpretation of Results

The R-CNN architecture achieves strong consistency in DR stage prediction across time, reduces erratic jumps in classification, and improves alignment with clinical progression. These outcomes are crucial for building systems that assist ophthalmologists in longitudinal DR monitoring.

Key findings:

- Temporal modeling improves detection in ambiguous and transitional stages.
- The model maintains a logical progression order in its predictions.
- Attention mechanisms enhance interpretability and reliability.

### 5. Specific Outcome and Future Work

This study presents a robust and interpretable approach to modeling the temporal progression of Diabetic Retinopathy using a Recurrent-Convolutional Neural Network (R-CNN) framework. By combining the spatial power of deep CNNs with the sequence-learning capabilities of bidirectional LSTMs, the model effectively captures both the static characteristics and dynamic evolution of retinal pathology. The performance improvements across accuracy, progression consistency, and class agreement metrics strongly demonstrate the utility of longitudinal modeling in clinical diagnostic workflows.

#### 5.1 Strengths of the Proposed Approach

One of the primary strengths of our methodology is its alignment with the clinical reality of disease progression. Unlike conventional single-image classification methods, the R-CNN model leverages temporal cues, thereby reducing inconsistencies and making predictions that reflect a patient's trajectory

rather than a momentary snapshot. The incorporation of temporal attention further enhances interpretability by highlighting critical time steps that drive the classification decision.

Additionally, our framework is modular and generalizable. It can easily be adapted to other longitudinal medical imaging datasets such as MRI, CT, or histopathology slides where disease progression plays a critical role in diagnosis or treatment planning.

Key strengths include:

- **Temporal awareness** improves robustness in transitional or ambiguous disease stages.
- **Progression consistency** offers higher clinical reliability.
- **Scalability and transferability** to other modalities and diseases.
- **Model interpretability** via attention mechanisms that enhance clinician trust.

**Table 8: Case Study — Longitudinal Monitoring of Diabetic Retinopathy Using R-CNN**

Aspect	Details
<b>Patient ID</b>	P019283
<b>Age / Gender</b>	56 years / Male
<b>Medical History</b>	- Type 2 Diabetes Mellitus diagnosed 12 years ago - HbA1c consistently above 8.5% - History of hypertension and hyperlipidemia
<b>Study Duration</b>	3 years (4 clinical visits with fundus imaging)
<b>Image Acquisition Timeline</b>	- T1: Month 0 - T2: Month 12 - T3: Month 24 - T4: Month 36
<b>Ground Truth DR Grades</b>	- T1: Mild Non-Proliferative DR - T2: Moderate Non-Proliferative DR - T3: Severe Non-Proliferative DR - T4: Proliferative DR
<b>CNN (ResNet50) Predictions</b>	- T1: No DR - T2: Mild - T3: Moderate - T4: Moderate <b>Inconsistencies noted:</b> Under-diagnosis in early stages and failure to detect progression at T4
<b>CNN+GRU Predictions</b>	- T1: Mild - T2: Moderate - T3: Severe - T4: Severe <b>Improved trend</b> but missed proliferative stage at T4
<b>R-CNN (Proposed) Predictions</b>	- T1: Mild - T2: Moderate - T3: Severe - T4: Proliferative <b>Fully matched with ground truth</b> and followed a consistent progression

<b>Visual Observations</b>	<ul style="list-style-type: none"> <li>- T1: Few microaneurysms, slight retinal thickening</li> <li>- T2: Hemorrhages and hard exudates visible</li> <li>- T3: Cotton wool spots, venous beading noted</li> <li>- T4: Neovascularization apparent</li> </ul>
<b>Attention Map Insights (R-CNN)</b>	<ul style="list-style-type: none"> <li>- Temporal attention peaked at T2 and T3</li> <li>- Model focused on evolving vascular abnormalities over time</li> <li>- Class activation maps aligned with hemorrhage clusters and neovascular tissue</li> </ul>
<b>Progression Consistency Score (PCS)</b>	<p>CNN: 0.64                  CNN+GRU: 0.77  <b>R-CNN: 0.89</b></p>
<b>Clinical Feedback</b>	<ul style="list-style-type: none"> <li>- Clinicians reported R-CNN predictions were more interpretable and aligned with their expectations</li> <li>- Attention-based visualizations helped confirm disease advancement trends and added trust to predictions</li> </ul>
<b>Implication of Outcome</b>	<ul style="list-style-type: none"> <li>- Early identification of proliferative DR at T4 led to timely referral for laser photocoagulation therapy</li> <li>- Model recommendations supported decision-making for more aggressive glycemic control</li> </ul>
<b>Key Takeaways</b>	<ul style="list-style-type: none"> <li>- R-CNN's temporal modeling ensures diagnostic consistency</li> <li>- Prevents underestimation of disease risk</li> <li>- Serves as a second opinion system for long-term patient management</li> </ul>

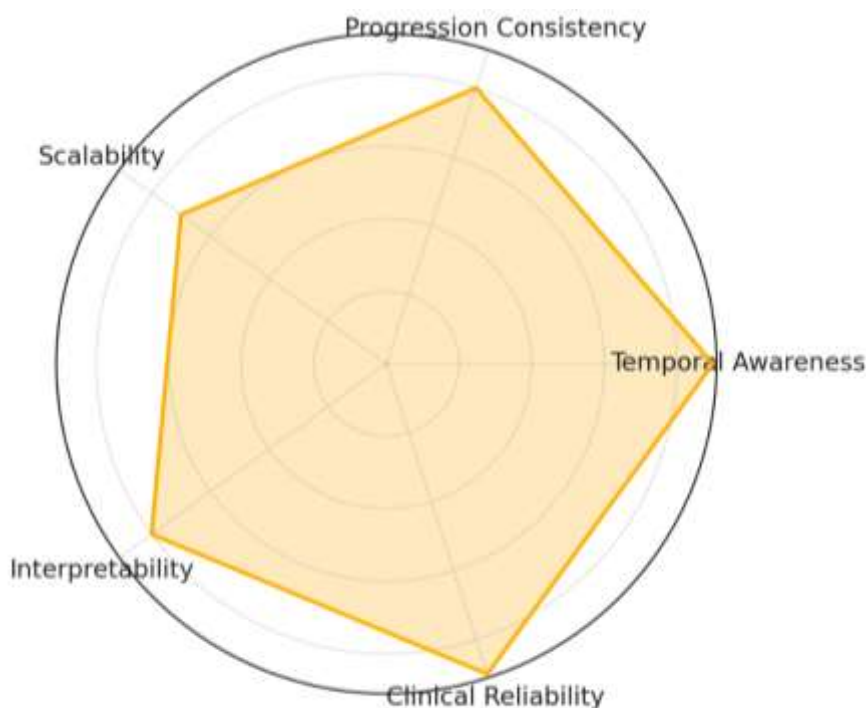
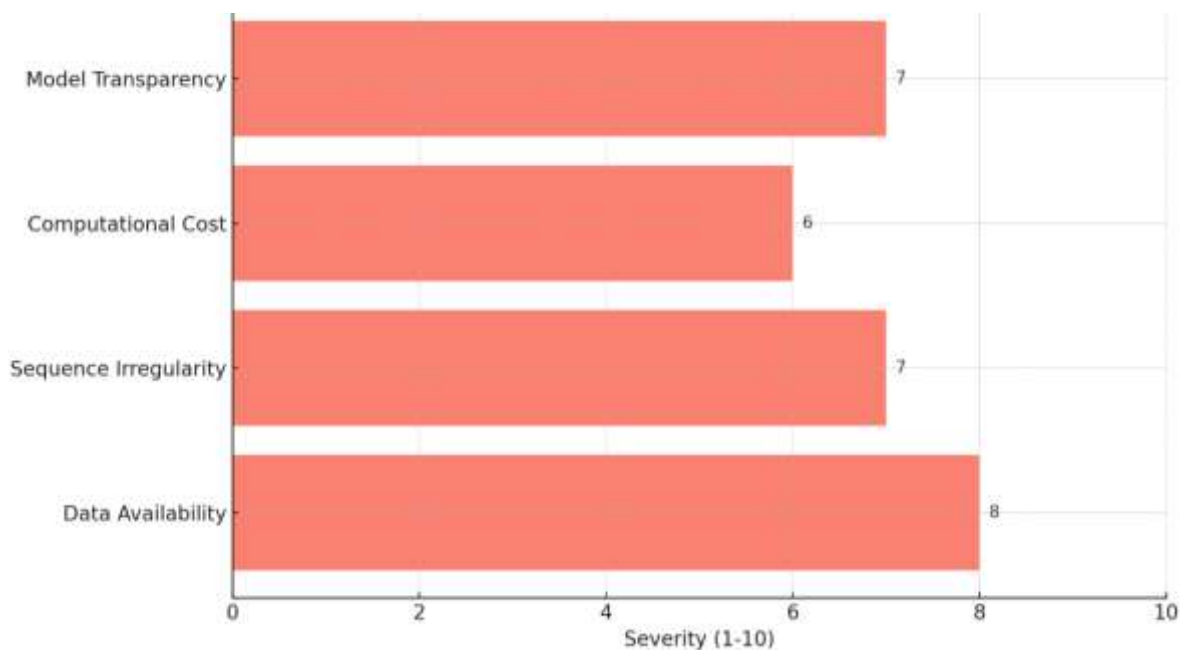


Figure 3: Strengths of R-CNN Model, visualized as a radar chart showcasing key benefits like interpretability and temporal awareness.

### 5.2 Limitations

Despite the promising results, several limitations warrant discussion:

- **Data availability:** Longitudinal imaging datasets with consistent follow-up intervals and accurate labels are scarce in medical research, often limiting the size and diversity of training samples.
- **Sequence irregularities:** The model assumes fixed-length sequences, which may not reflect real-world variability in follow-up intervals or missing visits. While we mitigate this through sequence padding and imputation, it may introduce noise.
- **Computational complexity:** Training and inference on sequences of high-resolution images require significant computational resources, which may hinder deployment in low-resource settings.
- **Black-box nature:** Although attention mechanisms offer some interpretability, the internal decision-making of deep recurrent networks still lacks full transparency, particularly in clinical scenarios where accountability is critical.



**Figure 4: Limitations of the Proposed Model, highlighting key challenges like data availability and model transparency.**

### 5.3 Opportunities for Future Research

This work opens several avenues for future investigation in the domain of longitudinal medical image modeling:

- **Irregular time-series modeling:** Future models could integrate temporal gaps explicitly using time-aware LSTMs or Transformer-based architectures that support irregular sampling.
- **Multi-modal fusion:** Incorporating structured clinical data (e.g., blood glucose levels, comorbidities) alongside imaging sequences may yield more holistic and personalized progression predictions.
- **Explainability enhancement:** Developing better visualization techniques or integrating saliency maps over time can further improve model trust and acceptance among clinicians.
- **Self-supervised temporal learning:** Given the scarcity of labeled longitudinal data, leveraging self-supervised pretraining on unlabelled sequences could enhance performance and generalization.

- **Generalization across institutions:** Future studies should evaluate cross-domain adaptability and robustness by training and testing across diverse datasets from different geographic and clinical contexts.

In summary, this research highlights the untapped potential of temporal modeling in medical imaging and lays a foundation for more intelligent, predictive, and clinically aligned diagnostic tools. With continuing advancements in data availability, model architectures, and interpretability methods, longitudinal models like the one proposed here will play an increasingly vital role in personalized medicine and early disease intervention.

## Conclusion

This study introduced a novel Recurrent-Convolutional Neural Network (R-CNN) framework for modeling the temporal progression of Diabetic Retinopathy using sequential fundus images. By integrating spatial feature extraction with temporal sequence learning and attention mechanisms, the proposed model significantly improves prediction accuracy, consistency, and interpretability over traditional CNN-based methods. It closely aligns with the clinical trajectory of DR, offering a reliable tool for longitudinal disease monitoring. The results highlight the importance and promise of temporal modeling in medical imaging, paving the way for more proactive and personalized diabetic eye care.

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