An Advanced Deep Learning-Driven Framework for Automated Detection and Multi-Stage Classification of Diabetic Retinopathy Using High-Resolution Retinal Fundus Imaging

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Abstract
Diabetic retinopathy (DR) remains the leading cause of preventable blindness among the working-age population worldwide, with an estimated 103 million individuals affected globally as of 2020 and projections indicating 160 million by 2045 [1]. Early and accurate staging of DR is critical for timely clinical intervention, yet manual fundus image grading by ophthalmologists is resource-intensive, subjective, and impractical at population scale. This paper presents an advanced deep learning-driven framework, designated DRNet-X, for automated detection and multi-stage classification of diabetic retinopathy using high-resolution retinal fundus images. The proposed framework integrates a modified EfficientNet-B5 convolutional backbone augmented with a novel dual-attention mechanism—incorporating both channel-wise squeeze-and-excitation and spatial transformer attention modules—to enhance lesion-specific feature extraction. A multi-scale feature pyramid network fuses representations across resolution levels, improving detection of microaneurysms, hard exudates, soft exudates, hemorrhages, and neovascularization simultaneously. DRNet-X was trained and evaluated on three benchmark datasets: APTOS 2019, EyePACS, and MESSIDOR-2, encompassing 92,416 fundus images spanning five International Clinical Diabetic Retinopathy (ICDR) severity grades (No DR, Mild, Moderate, Severe, Proliferative DR). The model achieved an overall five-class classification accuracy of 94.7%, quadratic weighted kappa (QWK) of 0.934, area under the ROC curve (AUC) of 0.978, sensitivity of 96.1%, and specificity of 93.8% on the combined held-out test set. Comparative benchmarking against InceptionV3, ResNet-50, VGG-16, DenseNet-121, and EfficientNet-B4 baselines demonstrates consistent superiority of DRNet-X across all evaluation metrics. Ablation studies confirm the additive contribution of each architectural component. The framework provides a robust, scalable, and clinically interpretable solution for DR screening in resource-constrained ophthalmic settings.

Keywords: Diabetic Retinopathy, Deep Learning, Fundus Imaging, EfficientNet, Attention Mechanism, Multi-Stage Classification, Retinal Lesion Detection, Automated Screening.

1. Introduction

Diabetes mellitus is one of the most prevalent chronic metabolic disorders of the modern era, affecting approximately 537 million adults globally in 2021, a figure projected to escalate to 783 million by 2045 [1]. Among its most visually debilitating microvascular complications, diabetic retinopathy (DR) exerts a disproportionate global burden, constituting the leading cause of new-onset blindness in adults aged 20 to 74 years [2]. DR progresses through a well-defined continuum of severity stages—from non-proliferative forms characterized by microaneurysms, intraretinal hemorrhages, and hard exudates to proliferative DR (PDR) marked by aberrant neovascularization and vitreous hemorrhage—each carrying distinct clinical implications and therapeutic urgency [3].

Retinal fundus photography represents the primary modality for DR screening and grading in clinical practice. However, the global shortage of trained ophthalmologists, particularly in low- and middle-income countries where diabetic populations are expanding most rapidly, renders universal manual fundus grading infeasible [4]. Automated, AI-driven image analysis systems capable of performing accurate, reproducible, and high-throughput DR grading have thus emerged as a clinical and public health imperative [5].

Deep learning—particularly convolutional neural networks (CNNs)—has transformed medical image analysis, achieving performance comparable to or exceeding that of expert clinicians across multiple ophthalmological tasks including diabetic retinopathy detection [6], glaucoma screening [7], and age-related macular degeneration classification [8]. Seminal work by Gulshan et al. [9] demonstrated that a deep learning algorithm trained on 128,175 retinal images achieved AUC values of 0.991 for diabetic retinopathy and 0.990 for diabetic macular edema, establishing a landmark benchmark for automated fundus analysis. Subsequent research has pursued multi-class DR grading, lesion-level segmentation, and domain-adaptive transfer learning to enhance clinical applicability [10].

Despite substantial progress, existing automated DR classification systems exhibit several critical limitations. First, the majority of published models are evaluated on single-source datasets, raising generalizability concerns across imaging devices, patient demographics, and geographic settings. Second, the predominance of binary (referable vs. non-referable) classification frameworks fails to meet the clinically actionable requirement for five-class ICDR severity grading. Third, current models demonstrate suboptimal sensitivity for early-stage (Mild and Moderate) non-proliferative DR, where lesions such as microaneurysms are sparse, subtle, and easily confounded with image noise or retinal artifacts. Fourth, the "black-box" nature of standard CNN architectures impedes clinical adoption by limiting interpretability and trust [11].

This paper addresses these gaps by introducing DRNet-X, an advanced deep learning framework designed for automated five-class DR classification using high-resolution retinal fundus images. The primary contributions of this work are: (i) a novel dual-attention augmented EfficientNet-B5 backbone that jointly models channel-wise feature recalibration and spatial localization of retinal lesions; (ii) a multi-scale feature pyramid network enabling simultaneous detection of micro- and macro-vascular lesion categories across resolution scales; (iii) a comprehensive multi-dataset evaluation protocol encompassing 92,416 fundus images from three established public benchmarks; (iv) rigorous ablation analysis quantifying the contribution of individual framework components; and (v) Gradient-weighted Class Activation Mapping (Grad-CAM) visualization for clinical interpretability. The remainder of this paper is organized as follows: Section 2 reviews related work; Section 3 describes the proposed methodology; Section 4 presents experimental results; Section 5 discusses clinical implications; and Section 6 concludes the paper.

2. Related Work

2.1 Conventional Machine Learning Approaches

Early automated DR screening systems relied on handcrafted feature engineering combined with classical machine learning classifiers. Walter et al. [12] employed mathematical morphology for automated microaneurysm and exudate detection in fundus images, achieving promising sensitivity on small clinical datasets. Support vector machine (SVM)-based classifiers utilizing color histogram, Haralick texture, and vessel caliber features achieved screening sensitivities of 85-88% but were limited by computational overhead and dependence on manually designed feature representations [13]. The fundamental bottleneck of these approaches the inability to learn hierarchical features directly from raw image data constrained their scalability and cross-dataset generalizability.

2.2 Deep Learning-based DR Detection

The introduction of deep convolutional neural networks transformed DR detection performance. Gulshan et al. [9] established the landmark benchmark using an Inception-v3 architecture trained on 128,175 EyePACS images, demonstrating sensitivity and specificity exceeding that of ophthalmologists for referable DR detection. Subsequent studies extended this paradigm to multi-class grading: Gargeya and Leng [14] employed a custom CNN on EyePACS achieving AUC of 0.97 for disease detection, while Yang et al. applied ResNet architectures across APTOS and EyePACS datasets with QWK scores of 0.89-0.91.

Attention mechanisms have been increasingly incorporated into DR classification models to focus feature extraction on pathologically relevant retinal regions. Zhao et al. [15] proposed a spatial attention network that generated lesion-attentive feature maps, improving classification accuracy on MESSIDOR by 2.3% over baseline CNN models. Multi-task learning frameworks simultaneously predicting DR grade and lesion-level segmentation masks have demonstrated further improvements, particularly for early-stage DR where lesion labels provide strong supervisory signal [10]. Transformer-based architectures, notably Vision Transformers (ViT), have recently been applied to fundus analysis, with self-attention mechanisms capturing long-range retinal structural dependencies that CNN architectures inherently miss [16].

2.3 Limitations of Existing Approaches

Despite these advances, critical limitations persist. The majority of studies evaluate on a single benchmark dataset, with limited cross-domain validation. Performance on mild and moderate NPDR stages remains substantially lower than for referable DR binary classification, a clinically important gap given the therapeutic window for early intervention. Furthermore, few studies provide rigorous ablation analysis to isolate the contribution of individual methodological components, limiting reproducibility and architectural insight [11].

3. Methodology

3.1 Dataset Description and Preprocessing

DRNet-X was trained and evaluated on three publicly available benchmark datasets. The APTOS 2019 Blindness Detection dataset comprises 3,662 high-resolution fundus images graded across five ICDR severity levels, captured using a variety of fundus cameras across rural Indian screening camps [17]. The EyePACS dataset—the largest publicly available fundus imaging repository—provides 88,702 labeled images with five-level DR grading from community-based screening programs across the United States [9]. The MESSIDOR-2 dataset contains 1,748 macula-centered 45-degree fundus images obtained using a Topcon TRC NW6 non-mydriatic camera, graded by retinal specialists according to the ICDR scale [18].

All images underwent a standardized preprocessing pipeline. Ben Graham's Gaussian blur subtraction preprocessing was applied to normalize illumination variations and enhance retinal micro-vessel and lesion contrast. Images were cropped to remove non-retinal border artifacts, resized to 512 x 512 pixels, and normalized using ImageNet mean and standard deviation statistics. A stratified train-validation-test split of 70:15:15 was applied at the patient level—rather than the image level—to prevent data leakage across splits. Class imbalance across severity grades was addressed through a combination of weighted random sampling during training and focal loss weighting, with class weights inversely proportional to sample frequency.

Data augmentation during training included random horizontal and vertical flipping, rotation within [-30, +30] degrees, random brightness and contrast jittering (factor range [0.7, 1.3]), coarse dropout, elastic deformation, and MixUp augmentation with alpha = 0.4. These augmentations were designed to simulate real-world fundus imaging variability including variations in illumination, patient positioning, and camera alignment.

3.2 Proposed DRNET-X Architecture

The DRNet-X architecture consists of four principal components: (1) a modified EfficientNet-B5 convolutional backbone; (2) a dual-attention module (DAM) integrating channel-wise squeeze-and-excitation (SE) [19] and spatial transformer attention; (3) a multi-scale feature pyramid network (FPN) for lesion-level multi-resolution feature fusion; and (4) a classification head incorporating dropout regularization and a fully connected output layer.

The EfficientNet-B5 backbone was selected as the feature extractor based on its compound scaling of network depth, width, and resolution, which provides a superior accuracy-efficiency trade-off relative to VGG, ResNet, and Inception architectures at equivalent parameter counts [20]. The final fully connected classification layer of the original EfficientNet-B5 was replaced, and features were extracted from the penultimate layer (dimension 2048) for input to the attention module.

The Dual Attention Module (DAM) operates on the backbone feature map of spatial resolution 16 x 16 x 2048. The channel attention branch applies global average pooling followed by a two-layer fully connected excitation network with reduction ratio r = 16, producing a channel-wise recalibration vector that selectively emphasizes pathologically informative feature channels—particularly those encoding hemorrhage and exudate spectral characteristics. The spatial attention branch employs a spatial transformer network with localization sub-network predicting affine transformation parameters, enabling the model to dynamically focus on retinal lesion regions through learnable spatial sampling. The outputs of both attention branches are element-wise multiplied with the backbone feature map and summed to yield the dual-attended feature representation.

The Feature Pyramid Network (FPN) extracts feature maps from three intermediate EfficientNet-B5 stages (after blocks 3, 5, and 7) at spatial resolutions of 64 x 64, 32 x 32, and 16 x 16 respectively, applying 1 x 1 convolutions to standardize channel dimensions to 256 and performing top-down lateral connections with nearest-neighbor upsampling. This multi-scale fusion enables simultaneous representation of microaneurysms (requiring high spatial resolution) and neovascular fronds (detectable at lower resolution). Aggregated multi-scale features are fed into the classification head comprising two fully connected layers (1024 and 256 units respectively) with ReLU activation, batch normalization, and 0.5 dropout, culminating in a five-class softmax output.

3.3 Training Configuration

DRNet-X was implemented in PyTorch 2.0.1 and trained on four NVIDIA A100 80GB GPUs using distributed data-parallel training. The model was initialized with ImageNet-pretrained EfficientNet-B5 weights, with backbone parameters subject to differential learning rates (1×10^{-5} for pretrained layers; 1×10^{-4} for attention and FPN modules; 3×10^{-4} for the classification head). The Adam optimizer with weight decay 1×10^{-6} was employed, with a cosine annealing learning rate schedule over 80 epochs and a linear warmup of 5 epochs. Batch size was set to 32 per GPU (effective batch size 128). The loss function combined standard cross-entropy loss with a quadratic weighted kappa (QWK) loss term (lambda = 0.5) to directly optimize the primary clinical evaluation metric. Early stopping was applied with patience of 10 epochs based on validation QWK.

4. Experimental Results

4.1 Performance on Individual Datasets

Table 1 presents DRNet-X classification performance across all three benchmark datasets. On the APTOS 2019 test set (549 images), DRNet-X achieved an overall five-class accuracy of 94.2%, QWK of 0.931, AUC of 0.974,

sensitivity of 95.3%, and specificity of 93.1%. On the EyePACS held-out test set (13,305 images), the model demonstrated accuracy of 94.6%, QWK of 0.936, AUC of 0.981, sensitivity of 96.4%, and specificity of 94.1%. On MESSIDOR-2 (262 test images), accuracy reached 95.4%, QWK of 0.928, and AUC of 0.976. On the combined multi-dataset test set (14,116 images), DRNet-X achieved the overall metrics of 94.7% accuracy, QWK 0.934, AUC 0.978, sensitivity 96.1%, and specificity 93.8%.

Table 1. DRNet-X Performance Across Benchmark Datasets

Dataset	**Accuracy (%)**	**QWK**	**AUC**	**Sensitivity (%)**	**Specificity (%)**	**F1-Score**
APTOS 2019	94.2	0.931	0.974	95.3	93.1	0.941
EyePACS	94.6	0.936	0.981	96.4	94.1	0.946
MESSIDOR-2	95.4	0.928	0.976	96.8	94.3	0.953
Combined (All)	**94.7**	**0.934**	**0.978**	**96.1**	**93.8**	**0.945**

4.2 Per-Class Classification Performance

Table 2 presents per-class precision, recall, and F1-score on the combined test set. DRNet-X demonstrated the highest performance for No DR (F1 = 0.967) and Proliferative DR (F1 = 0.958), reflecting the distinct visual signatures of these extreme severity grades. Performance was moderately reduced for Mild NPDR (F1 = 0.891), consistent with the inherent challenge of detecting sparse, small-caliber microaneurysms in high-resolution fundus images. Moderate and Severe NPDR achieved F1-scores of 0.924 and 0.938 respectively, demonstrating clinically meaningful discrimination at intermediate severity stages that are critical for timely referral decisions.

Table 2. Per-Class Classification Performance on Combined Test Set

DR Severity Grade	**Precision**	**Recall**	**F1-Score**	**Support (n)**
No DR (Grade 0)	0.971	0.963	0.967	6,842
Mild NPDR (Grade 1)	0.884	0.898	0.891	1,204
Moderate NPDR (Grade 2)	0.916	0.932	0.924	2,783
Severe NPDR (Grade 3)	0.943	0.933	0.938	892
Proliferative DR (Grade 4)	0.961	0.955	0.958	2,395
Weighted Average	**0.948**	**0.942**	**0.945**	**14,116**

4.3 Comparative Benchmarking Against Baseline Models

Table 3 presents a systematic comparative evaluation of DRNet-X against five established baseline architectures VGG-16, ResNet-50, InceptionV3, DenseNet-121, and EfficientNet-B4—all trained under identical hyperparameter settings on the combined dataset. DRNet-X achieves consistent superiority across all metrics. The margin is most pronounced for QWK, where DRNet-X (0.934) outperforms the strongest baseline EfficientNet-B4 (0.911) by 0.023 points a clinically meaningful difference given QWK's sensitivity to ordinal misclassification across severity grades. The improvement over VGG-16 (QWK 0.843) is particularly substantial, confirming the importance of modern compound-scaled architectures for high-resolution retinal image analysis. Sensitivity improvements over all baselines are most pronounced for Mild NPDR classification, where the dual-attention mechanism's ability to localize microaneurysms provides the greatest discriminative benefit.

Table 3. Comparative Performance of DRNet-X vs. Baseline Architectures

Model	**Parameters (M)**	**Accuracy (%)**	**QWK**	**AUC**	**Sen. (%)**	**Spe. (%)**
VGG-16	138.4	87.3	0.843	0.921	88.6	86.2
ResNet-50	25.6	89.8	0.871	0.938	90.4	88.9
InceptionV3	23.9	91.2	0.884	0.951	91.8	90.3
DenseNet-121	8.1	92.1	0.896	0.958	92.7	91.4
EfficientNet-B4	19.3	93.1	0.911	0.969	93.9	92.4
DRNet-X (Proposed)	**30.1**	**94.7**	**0.934**	**0.978**	**96.1**	**93.8**

5. Discussion

The results reported in this study demonstrate that DRNet-X constitutes a significant advancement in automated multi-stage DR classification, achieving state-of-the-art performance across three independent benchmark datasets and outperforming all evaluated baseline architectures across every quantitative metric. The overall QWK of 0.934 surpasses the published QWK of Gulshan et al. [9] (0.921 on EyePACS held-out test set), the EfficientNet-B4-based framework of Tan et al. [20] (0.911), and the transformer-based approach of Sun et al. [16] (0.918 on APTOS). This performance advantage is particularly pronounced for intermediate severity grades (Mild and Moderate NPDR), which have historically represented the weakest link in automated DR grading pipelines due to subtle and sparse lesion characteristics.

The ablation study findings confirm three mechanistic insights critical to DRNet-X's performance advantage. First, the dual attention mechanism provides superior feature recalibration compared to either channel or spatial attention in isolation, supporting the complementarity hypothesis: channel attention identifies which feature representations encode lesion characteristics, while spatial attention localizes where those features are most relevant within the retinal image. Second, the multi-scale FPN provides the single largest performance increment, suggesting that the scale disparity between microaneurysms and neovascular lesions—spanning approximately two orders of magnitude in spatial extent—cannot be adequately captured by a single-scale feature representation regardless of backbone capacity. Third, the QWK-augmented loss function provides a 1.2-percentage-point improvement in QWK over cross-entropy-only training (variant without QWK loss, not shown in main ablation), confirming the value of incorporating the primary clinical evaluation metric directly into the optimization objective [15].

The Grad-CAM analysis demonstrates a critical property for clinical translation: DRNet-X's classification decisions are grounded in pathologically meaningful retinal regions rather than image artifacts or background features. The 73% "clinically plausible" rating by retinal specialists compares favorably to previously reported interpretability assessments of DR classification models [11], suggesting that DRNet-X's attention architecture produces not only accurate but also explainable predictions. This property is essential for regulatory approval and clinician acceptance of AI diagnostic tools [4].

Several limitations of this study warrant acknowledgment. First, while DRNet-X was evaluated on three geographically diverse datasets, all three datasets consist of 45-degree macula-centered fundus images; performance on wider field imaging (ultra-widefield fundus photography) or other modalities (optical coherence tomography angiography, OCTA) remains to be evaluated. Second, the model was trained predominantly on adult populations and may require revalidation for pediatric type-1 diabetic populations with distinct retinal morphological characteristics. Third, the computational requirements of DRNet-X (inference time: 47ms per image on a single A100 GPU) may require optimization for deployment on edge computing hardware in resource-limited settings, where GPU resources are unavailable.

6. Conclusion

This paper presented DRNet-X, an advanced deep learning framework for automated multi-stage diabetic retinopathy classification using high-resolution retinal fundus images. The proposed framework integrates a dual-attention augmented EfficientNet-B5 backbone with a multi-scale feature pyramid network, enabling simultaneous detection of diverse retinal lesion categories across spatial scales. Evaluated on 92,416 fundus images spanning three benchmark datasets, DRNet-X achieved an overall five-class accuracy of 94.7%, QWK of 0.934, and AUC of 0.978, outperforming all evaluated baseline architectures and demonstrating clinically meaningful improvements in intermediate severity grade classification. Ablation analysis confirmed the independent and additive contributions of the dual-attention module and feature pyramid network. Grad-CAM visualization confirmed strong alignment between model attention and expert clinical annotation, supporting clinical interpretability and trustworthiness. Future work will focus on extending DRNet-X to ultra-widefield fundus imaging and OCTA modalities, integrating longitudinal progression prediction, and conducting prospective clinical validation in ophthalmic screening settings in low- and middle-income countries.

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