

Hybrid Unsupervised Deep Learning Algorithm for Early Detection of Diabetic Retinopathy

A Thesis submitted to the

UPES

For the Award of

Doctor of Philosophy

in

Computer Science and Engineering

By

Huma Naz

February 2025

Supervisor

Dr. Neelu Jyothi Ahuja



School of Computer Science

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Energy Acres, P.O. Bidholi via Prem Nagar,

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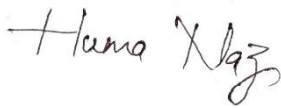
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DECLARATION

I confirm that the thesis titled "Hybrid Unsupervised Deep Learning Algorithm for Early Detection of Diabetic Retinopathy" is my original work, conducted under the supervision of Dr. Neelu Jyothi Ahuja, a Professor of Systemics at the School of Computer Science and Engineering (SOCS), UPES, India. No part of this thesis has been submitted for the conferment of a degree.



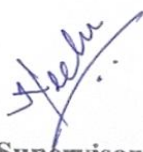
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CERTIFICATE

I hereby confirm that Huma Naz has prepared the thesis titled “Hybrid Unsupervised Deep Learning Algorithm for Early Detection of Diabetic Retinopathy” under my supervision for the purpose of obtaining a PhD degree from UPES. She executed the tasks at the School of Computer Science and Engineering, UPES.



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ABSTRACT

Diabetic retinopathy (DR) represents a significant health issue, responsible for around 10% of global instances of vision impairment in adults. Individuals with diabetes face a risk of blindness that is approximately 20 times higher than that of those without the condition, primarily as a result of complications such as diabetic macular oedema (DME). DR is a condition characterized by damage to the retinal blood vessels, often resulting in eye complications, and classified into two main types: non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR). These types are distinguished by various retinal changes, such as microaneurysms, hemorrhages, and the formation of hard and soft exudates. Symptoms often manifest only in the later stages, leading many individuals with diabetes to remain unaware of their DR until the condition has significantly progressed.

Timely identification and screening are crucial in preventing blindness, with ophthalmologists relying on colour fundus images to assess eye diseases such as DR. However, the significant shortage of ophthalmologists in developing countries requires a novel approach to detecting DR. Conventional approaches, reliant on extensive evaluation by experts, are unfeasible due to the scarcity of these professionals. An unsupervised approach to DR detection has the potential to address this gap by leveraging the automated deep-embedded clustering-based identification, which offers numerous benefits in detecting DR. By diminishing the reliance on human graders and associated costs, it emerges as a valuable diagnostic tool in hospital settings. The proposed work delves into the essential requirements for the optimal execution of unsupervised learning (UL) in deep learning (DL) algorithms for DR classification. Conventional clustering approaches utilize a clustering algorithm on feature vectors extracted using domain-specific knowledge. On the other hand, unsupervised DL techniques combine clustering and feature extraction into a single framework, boosting clustering accuracy on fundus images.

However, due to a lack of supervisory guidance, even the most advanced deep clustering algorithms need help capturing significant discriminative information in the trained representations. By exploring diverse deep clustering algorithms, the investigation focuses on addressing the enhancement of deep neural networks (DNNs) by incorporating clustering algorithms. An investigation of the various clustering algorithms and their insights is studied and discussed.

The Fuzzy C-Means (FCM) method serves as the foundational approach, while the Modified Fuzzy C-Means (MdFCM) algorithm is offered as an upgraded version to address the local optima issue inherent in FCM. Subsequently, the MdFCM algorithm is combined with a Convolutional Neural Network (CNN), resulting in the Fuzzy C-Means Convolutional Neural Network (FCCNN) to enhance clustering accuracy and increase the model's overall performance. The FCCNN provides a systematic method for categorizing DR into specific stages: No DR, Mild DR, Moderate DR, and Severe DR. The study assesses the effectiveness of the MdFCM and FCCNN models by applying metrics, including Unsupervised Clustering Accuracy (ACC), Normalized Mutual Information (NMI). The analysis shows an ACC of 94%, NMI of 95%, and ARI of 92%.

There is a significant lack of affordable remote tools in clinical settings, prompting the proposal of RetinaCare, a web-based application that integrates FCCNN via an Application Programming Interface. This tool aims to overcome the challenges of implementing remote solutions by reducing the need for expert guidance and serving as a preliminary assessment tool for ophthalmologists. The cost of tabletop fundus cameras is often prohibitive for hospitals located in remote and rural regions. Thus, the more cost-effective option, MIIRet Cam, can be utilized for initial ocular assessments, requiring minimal training for hospital staff and eliminating the need for expert assistance. The RetinaCare tool attained an accuracy rate of 80% and a Spearman correlation coefficient of 0.93 by comparing the application grading with the ophthalmologist grading.

The comparative analysis indicates that the suggested outperforms the efficacy of current deep clustering techniques. Additionally, RetinaCare has the potential to serve as a vital resource for ophthalmologists practising in remote areas.

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ACRONYMS

ACC	Unsupervised Accuracy
AC	Accuracy
ARI	Adjusted Rand Index
AUC	Area Under the Curve
CNN	Convolutional Neural Network
CT	Computed Tomography
CHT	Circular Hough Transformation
DCN	Deep Clustering Network
DEC	Deep Embedded Clustering
DL	Deep Learning
DM	Diabetes Mellitus
DR	Diabetic Retinopathy
DSCR	Deep Clustering under Similarity and Reconstruction constraints
EnFCM	Enhanced Fuzzy C Means
FCAE	Fully Convolutional Autoencoder
FCM	Fuzzy C-Means
FCCNN	Fuzzy C Means Convolutional Neural Network
FLICM	Fuzzy Local Information C-Means
HSV	Hue Saturation Value
IHE	Intensity Histogram Equalization
IRMA	Intra-Retinal Microvascular Abnormality
K-DVAE	K-Deep Variational Autoencoder
KL	Kullback-Leibler
MA_s	Microaneurysms
MdFCM	Modified FCM
MIIRET	Made in India (MII) Retina Camera
M-FLMCM	Malleable Fuzzy Local Median C Means
ML	Machine Learning
MSCF	Multi-Scale Correlation Filtering
NMI	Normalized Mutual Information
NPDR	Non-Proliferative Diabetic Retinopathy

OD	Optic Disc
PDR	Proliferative Diabetic Retinopathy
PET	Positron Emission Tomography
RGB	Red Green Blue
ROC	Retinopathy Open Challenge
SAC	Stacked Auto-Encoder
SDEC	Semi-supervised Deep Embedded Clustering
SGD	Stochastic Gradient Decent
SVM	Support Vector Machine
SN	Sensitivity
SP	Specificity
UL	Unsupervised Learning

Chapter I

Introduction

1.1 Medical Image Analysis

The evolution of medical imaging commenced in 1895 with Roentgen's pioneering discovery of X-rays, marking a crucial milestone in diagnostic technology [1]. Several advanced methods are currently utilized in medical diagnostics, including X-rays, computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), mammography, and ultrasound [2]. Each method improves diagnostic accuracy and elevates patient care across different medical fields. To diagnose a disease, a thorough assessment of related organs is required. With the advent of medical image analysis, the study of various organs has evolved from surgical ways to computer-aided diagnosis. Several researchers and data scientists have explored medical imaging modalities to develop automated screening tools.

The core idea is to detect the presence of any visible symptoms of the underlying disease, which includes localizing and segmenting visible symptoms of the underlying disease for prediction. Such tools can help developing countries with high populations and disproportionate medical facilities. They can also be beneficial for community-level testing by medical professionals. Medical images have been analyzed using conventional image processing techniques for many years. Recent developments in high computation facilities, enormous data storage, and image acquisition quality have collectively

contributed to the required automation. Researchers developed pipeline-based algorithms to study the normal and abnormal features in the image [3], [4]. With the rising popularity of machine learning (ML), the extraction of handcrafted features was used for disease prediction. However, the implementation of deep learning (DL) has completely automated the procedure. Techniques such as convolutional neural networks (CNN) are utilized for tasks involving prediction and classification.

1.2 Overview of Diabetic Retinopathy

Diabetes has been widely acknowledged as the primary cause of diabetic retinopathy (DR) [5]. Accurately identifying DR has posed a longstanding challenge for researchers. The blood vessels within the retina exhibit an increased vulnerability to irregular metabolic conditions resulting from fluctuations in glucose levels. These changes result in retinal damage or lesions, collectively known as DR (Williams et al., 2020). Figure 1.1 illustrates the symptoms in a normal eye compared to those in an eye affected by DR. Traditional ocular healthcare practices have faced difficulties in effectively diagnosing DR symptoms. Therefore, an automated system can mitigate the risk of misdiagnosis by decreasing error rates.

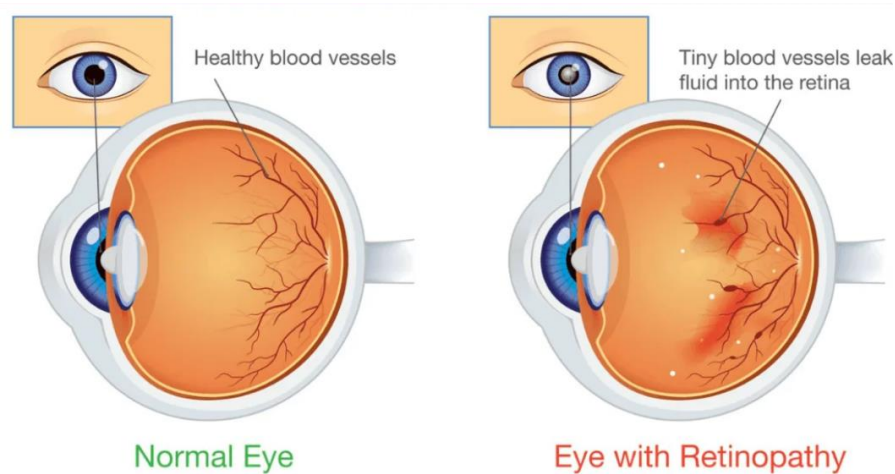


Figure 1.1: Normal Eye and DR Eye (Center, 2012)

Approximately 75% of people impacted by DR reside in underdeveloped nations, highlighting a considerable deficiency in medicinal and diagnostic resources. Moreover, individuals with diabetes possess a 25 times increased probability of obtaining DR and encountering vision impairment compared to non-diabetics (Abbasi et al., 2022). DR occurs when retinal capillaries form lesions that extend to veins and arteries due to changes in vascular architecture, including the loss of pericytes. Microaneurysms (MAs) develop in the capillary walls of compromised capillaries due to the distension of vessel walls. These leakages result in widespread retinal oedema. Exudates develop around the edges of this oedema due to the death of phagocytes. Leaky MAs are generally encircled by 'rings' of exudate (Al-amri et al., 2010). Lesions affecting the retina and causing fluid leakage are identified as background retinopathy, except in the fovea zone.

A considerable shortfall of ophthalmologists and optometrists is projected in nations with limited resources, especially developing countries (Resnikoff et al., 2020). Figure 1.2 presents a statistical correlation between nations with low income and those with high income. However, low-income countries have a density of ophthalmologists per million individuals, one-tenth of the density in high-income countries (Aurangzeb et al., 2021). There are 2.3 optometrists per 10,000 residents in the United Kingdom, indicating a significant shortage in Europe, ranking seventh in optometrist density. Consequently, this global issue has led to restricted access to eye care services, particularly in areas with a high prevalence of diabetes. Alternative methods for detecting and managing diabetes, such as fundus photography, are becoming more critical. Retinal imaging techniques, such as fundus photography, can improve access to ophthalmic treatment in impoverished areas by allowing non-specialists to do these examinations.

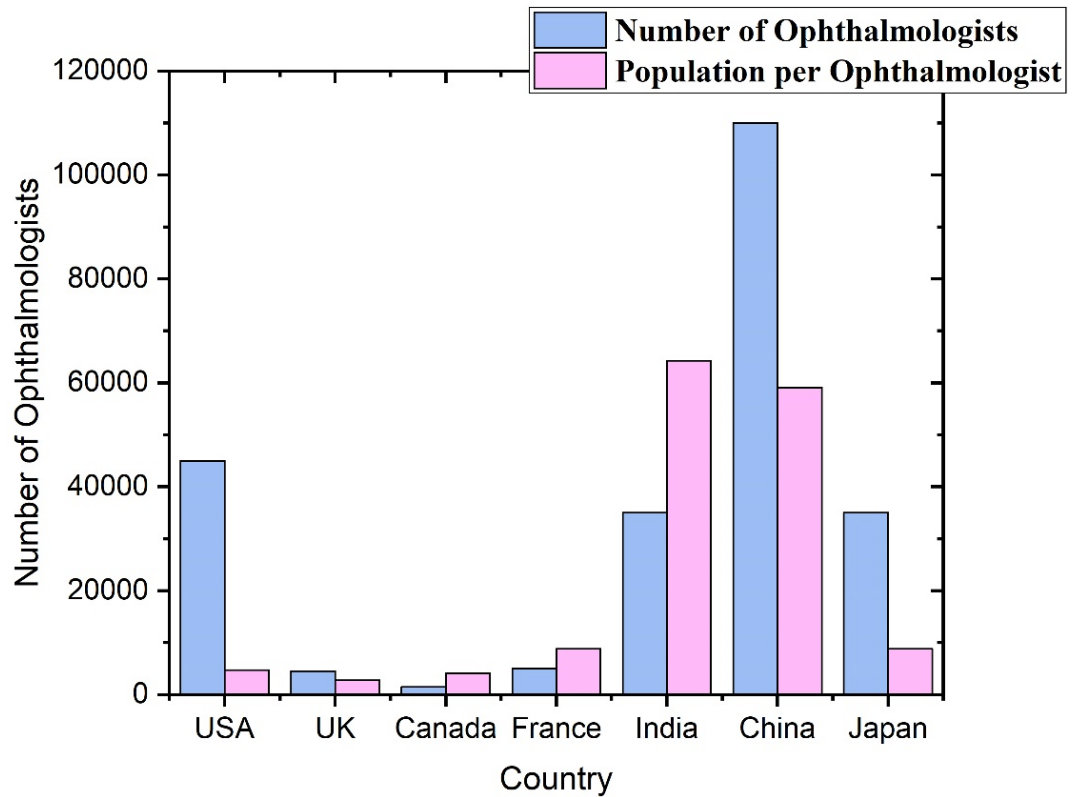


Figure 1.2: Number of Ophthalmologists per Country (Naz, Ahuja, et al., 2024)

1.3 Clinical Features

The retina is the eyeball's innermost lining, made of light-sensitive tissues. A healthy retina has features like an optic disc (OD), blood vessels, macula, and fovea. Figure 1.3 shows the retina and its features. DR occurs with the appearance of various features in the retina and progresses over time. The condition generally includes MAs retinal bleeding, exudates, vitreous bleeding, venous beadings, and neovascularization.

1.3.1 Microaneurysms and hemorrhages: Key Indicators of Red Lesions

Red lesions are recognized as DR's initial symptoms, encompassing Mas and hemorrhages. The initial phases of DR are marked by MAs, which continue to exist as the condition progresses. MAs are classified as sharp red dots covering few pixels, whereas hemorrhages are more significant red patches due to the blood leakage in retinal layers. Consequently, red lesions are crucial for the early detection of DR (Alanazi, 2022).

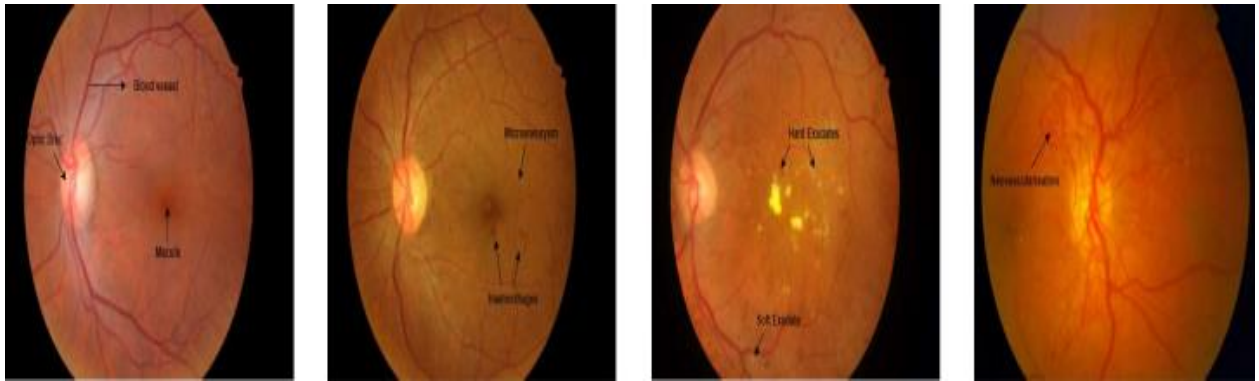


Figure 1.3: Normal and abnormal features in the retina (Naz, Nijhawan, Ahuja, et al., 2024)

1.3.2 Yellow lesions: Exudates

Hard and soft exudates are identified as bright lesions. The leakage of lipids or proteins within the retinal layers in the back section of the eye typically causes these issues (Joshi & Karule, 2018). Hard exudates are dark yellow spots with well-defined boundaries, and soft exudates are defined as white/yellow spots with a cloudy appearance and not very defined boundaries, as shown in Figure 1.4.

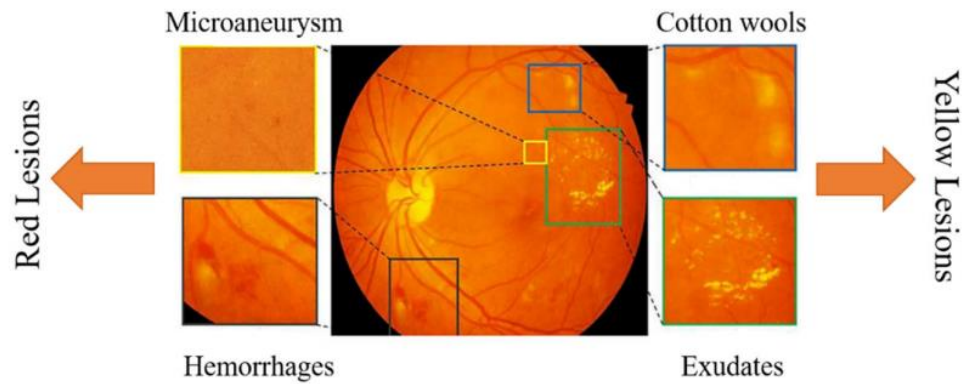


Figure 1.4: Red Lesions and Yellow Lesions (Naz, Nijhawan, Ahuja, et al., 2024)

1.4 Stages of DR

DR is categorized into two main stages: Non-Proliferative Diabetic Retinopathy (NPDR) and Proliferative Diabetic Retinopathy (PDR). The progression of DR is determined by evaluating detailed characteristics and alterations in the retina (Abràmoff et al., 2016). This figure illustrates the difference between the NPDR and PDR, as shown in Figure 1.5. Exudates, MAs, and hemorrhages are typically present in the NPDR stage. In PDR, the blood vessel grows abnormally.

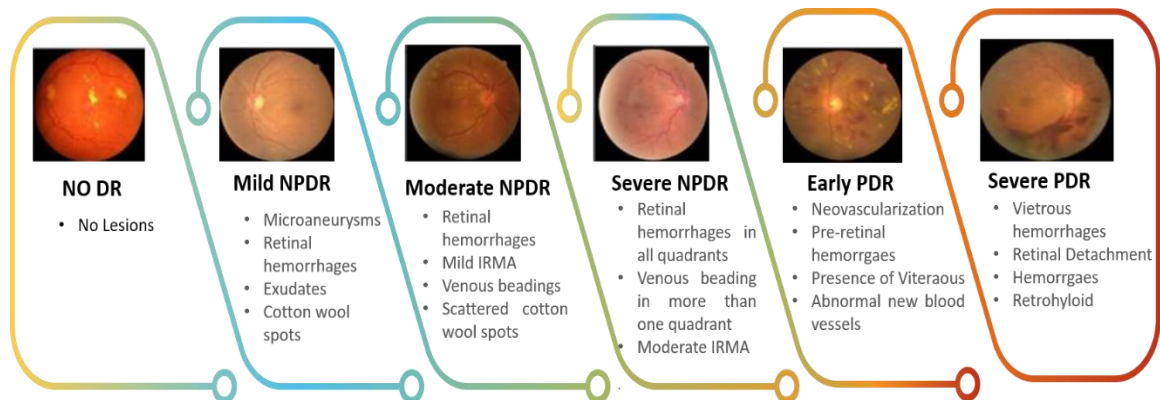


Figure 1.5: Classification of DR Stages (Naz, Ahuja, et al., 2024)

The classification of NPDR stages includes three levels: mild, moderate, and severe, determined by the degree of blood vessel occlusion. As the number of blocked vessels increases, the delivery of oxygen and nutrients to the eye is reduced, which may result in complete vision loss or partial blindness. NPDR signifies the preliminary stage of DR, marked by the lack of new blood vessel formation. At this stage, the walls of the existing blood vessels become compromised, resulting in the formation of small protrusions referred to as MAs. The small vessels sometimes start leaking, which causes damage to the retina. For large retinal vessels, the dilation occurs and later becomes non-uniform.

As the blockage of blood vessels increases, the progression of NPDR changes from mild to severe stages (Bilal, Zhu, et al., 2022). Mild NPDR is considered an early stage of the condition, marked by the presence of at least one microaneurysm or one hemorrhage along with cotton wool spots. Moderate NPDR occurs when numerous MAs or hemorrhages with venous beading are seen. During moderate NPDR, small blood vessels are blocked, affecting the eye's supply of oxygen and nutrients. Severe NPDR occurs when multiple hemorrhages and MAs are seen together with venous beading (Sarwinda et al., 2019). The presence of blood vessels in this region is hindered, resulting in an interruption in the supply of nutrients and oxygen. The fluid leak during NPDR is called oedema and can be seen in the macula of the retina. Once the oedema is visible, treatment is mandatory to avoid permanent blindness.

PDR is recognized as an advanced stage of DR. This condition arises when blood vessels are entirely obstructed, resulting in the development of abnormal new blood vessels within the retina. In PDR, a gelatinous fluid is released from obstructed blood vessels in the center of the eye, and the development of new blood vessels results in damage that may detach the retina, leading to vision loss. Extreme pressure is built on the eyeball; hence, optic nerves are pressed, causing glaucoma. Initially, detecting this disease is essential to saving the patient's vision. For this, continuous checking is required.

1.4.1 Identification of Soft and Hard Retinal Exudates

Soft and Hard retinal exudates are different white-yellow coloured intraretinal features, varying in size from small dots, as illustrated in Figure 1.4. In most cases, exudates comprise extracellular lipids released from abnormal retinal capillaries (Chen et al., 2022). Figure 1.4 illustrates exudates associated with ocular issues, primarily located in the macular region, where lipid accumulation occurs and extends into the central macula. Hard exudates indicate excessive retinal vascular permeability caused by vision threats (Chudzik et al., 2018).

1.4.2 Microaneurysms Detection

Diagnosing MAs is essential in the exposure to DR (Chudzik et al., 2018). MAs are DR's most important warning signs initiated by the primary dilations of slender blood vessels. MAs are round and almost red with small dimensions. The MAs detection is done by Dynamic thresholding and Multi-Scale Correlation Filtering (MSCF) (Dai et al., 2021).

1.4.3 Hemorrhages Detection

The small blood vessels within the conjunctiva are prone to breaking at any time, which causes hemorrhages to occur. This can result in a reddish spot on the sclera, leading to a sub-conjunctival hemorrhage that appears as a bright red or dark red mark on the sclera, the white section of the eye.

1.5 DR Retinal Imaging

Retinal imaging can detect and monitor DR early, preventing severe complications such as vision loss. OCT and OCTA offer detailed insights into the retinal layers and retinal

microvasculature, respectively, through the provision of cross-sectional retina images (as illustrated in Figure 1.6). Ophthalmologists employ fundus photography to examine, diagnose, and track abnormalities in the retina and optic nerve (Ferrara et al., 2023).

Fundus photography, also known as fundoscopy, is a commonly employed technique for examination, diagnosis, and continuous assessment in ophthalmology. A fundus image can capture normal and abnormal features lying on the retina. OCT, colour fundus photography, and OCTA are commonly recommended methods for evaluating and capturing fundus images (Pichi et al., 2017).

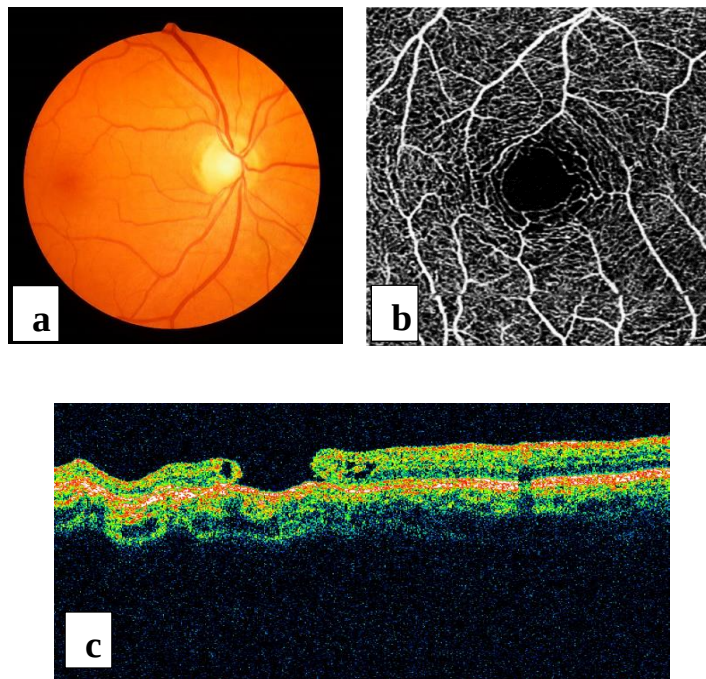


Figure 1.6: Diagnostic Methods for DR: a) Normal Eye Fundus Image Showing OD and Blood Vessels, b) OCT Angiogram Displaying Macular Microvasculature and Foveal Avascular Zone, c) Time-Domain OCT Scan Revealing a Full-Thickness Macular Hole (Naz, Nijhawan, & Ahuja, 2024)

Fundus imaging is a widely used alternative to traditional retinal photography and tabletop fundus cameras. Nowadays, it employs a smartphone camera and software to perform non-invasive fundus imaging (Krishnegowda & Ganesan, 2022). This technique incorporates an additional lens or adapter onto a smartphone camera, enabling the acquisition of a broader field of view and high-resolution images of the fundus (Rajalakshmi et al., 2021). The fundus image is captured by positioning a smartphone close to the eye, utilizing the device's camera. Systems that rely on smartphones require light sources, automated focusing mechanisms, and image enhancement techniques, which are increasingly available and affordable in many contemporary smartphone cameras. This approach holds significant promise for improving access to fundus imaging in areas that are currently underserved.

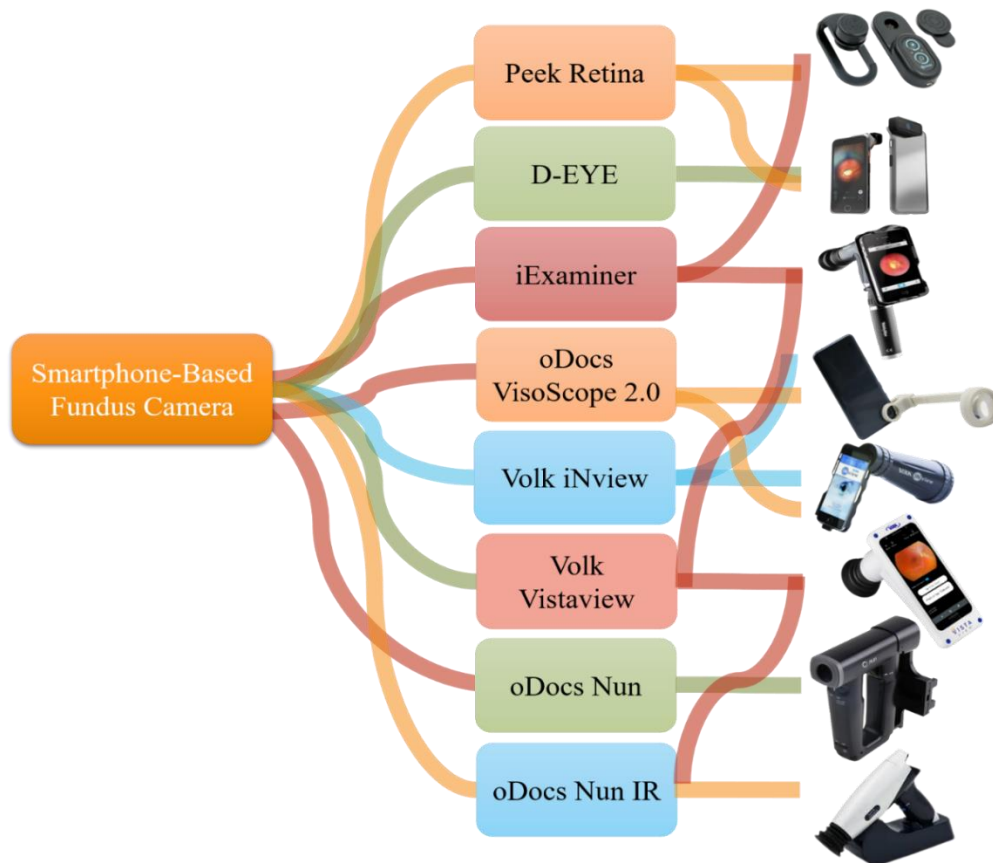


Figure 1.7: Diverse Types of Smartphone Fundus Camera (Naz, Nijhawan, & Ahuja, 2024)

Smartphones' widespread availability and affordability may significantly enhance access to fundus imaging, especially in remote or underdeveloped regions lacking ophthalmologists' services and tabletop fundus cameras. Smartphone-based fundus photography facilitates the seamless exchange of photos with healthcare specialists for remote diagnosis and consultation (Micheletti et al., 2016). There are several market providers for smartphone-based cameras with different features and lighting conditions (Figure 1.7).

1.6 Image Preprocessing

The resolution and quality of fundus images are essential for accurately extracting blood vessels from retinal images. Despite progress in imaging technologies, consistently obtaining high-quality images remains challenging (Sisodia et al., 2017). Therefore, image pre-processing becomes a pivotal step in enhancing image quality before the extraction of vessels. However, a trade-off between quality of enhancement and conserving the structural details of the image is crucial.

To minimize the chances of false positives, background segmentation of the OD and blood vessels is performed before the foreground segmentation of red and yellow lesions. The OD and blood vessels may exhibit intensity and colour attributes that closely resemble those of pathological lesions, such as MAs and hemorrhages. The proposed algorithm can more accurately identify lesions by segmenting and excluding these structures. Consequently, preprocessing techniques, including contrast enhancement and noise reduction, are employed to markedly enhance the clarity and visibility of edges, thereby facilitating more effective background segmentation.

1.6.1 Blood Vessel and OD Extraction

The vessel extraction becomes challenging because the constituent vessels vary in size, shape, and orientation. The vessel's bifurcations, branching, and crossover further complicate the identification process. Therefore, vessel enhancement becomes essential before segmentation. Moreover, The OD segmentation approach is implemented by combining the Circular Hough Transform with morphological closure to reduce false identification of the OD. This method identifies circles with a robust circular reaction, which matches the OD regions. Other circles that do not have a significant circular response are most likely yellow lesions or other deceptive spots.

Segmentation isolates the vessels and OD from all other structures of the fundus image for better lesion detection. The vessel isolation is done using the Fuzzy Inference method. Abrupt changes in intensity are noted at the edges, points, blobs, and lines in the fundus image. In contrast, a consistent intensity distribution is exhibited in the uniform areas, including the background. Other than intensities, additional features such as texture, elongation, and compactness., are also considered for segmenting vessel points. Several image-driven techniques can segment vessels, including thresholding, clustering, and region growing.

1.7 Unsupervised DL

Today, numerous well-established organizations grapple with challenges in effectively managing their data. Additionally, the study of big data presents its own set of demands. Recognizing that ML algorithms offer efficient solutions to intricate tasks, organizations leverage them to address these challenges. Notably, DL algorithms, in particular, significantly enhance model performance and facilitate detailed analysis. Supervised ML algorithms are crucial in predictive analysis, demonstrating the substantial potential to solve diverse problems (Alyoubi et al., 2020).

Conversely, unsupervised ML algorithms exhibit significant capability in uncovering various hidden opportunities. Moreover, clustering algorithms demonstrate proficiency in organizing elements that exhibit comparable characteristics without labelled data (An et al., 2022). This methodology categorizes data according to the insights acquired and the knowledge developed. Techniques like deep embedded clustering (DEC) typically exhibit enhanced performance relative to unsupervised learning (UL), primarily due to their superior clustering abilities.

A broader range of possibilities is unlocked by the proficiency of clustering algorithms in feature learning and cluster assignment (Arcadu et al., 2019). Soft and complex clustering algorithms represent distinct clustering methods utilized in various data applications (Atwany et al., 2022). Due to inherent limitations, clustering algorithms encounter significant challenges when applied to classification problems. Supervised ML algorithms are crucial in predictive analysis, demonstrating the substantial potential to solve diverse issues (Alyoubi et al., 2020). Conversely, unsupervised ML algorithms exhibit significant capability in uncovering various hidden opportunities.

Furthermore, clustering algorithms provide a more accurate grouping of elements with similar features without supervision or labelling (An et al., 2022). This method categorizes data according to derived knowledge and knowledge acquisition. Deep clustering algorithms emerge from the integration of clustering and DL techniques. These algorithms generally surpass UL owing to their superior clustering capabilities. Combining clustering methods with feature learning and cluster assignment enables a broader array of applications (Arcadu et al., 2019). Soft and complex clustering algorithms represent distinct clustering methods utilized in various data applications (Atwany et al., 2022). Due to inherent limitations, clustering algorithms encounter significant challenges when applied to classification problems.

1.8 Proposed Approach

The proposed work aims to improve the properties and efficacy of DL methodologies by incorporating clustering algorithms into their framework. The aim is to facilitate the integration of UL techniques into DL algorithms to improve data categorization efficiency. The proposed approach combines unsupervised and supervised techniques for diagnosing DR using unlabeled fundus pictures.

The present study introduces an optimized Fuzzy C-Means (FCM) algorithm to improve convergence and address the issue of local optima. Additionally, the modified FCM is integrated with CNN to grade DR severity. The suggested approach operates in an unsupervised fashion, employing an unlabeled dataset. However, the efficacy is evaluated against established methodologies, with results indicating that existing techniques are surpassed by the proposed algorithm in the detection of DR. This algorithm has been implemented in a web-based application intended for the identification and categorization of severity levels in patients based on captured or uploaded images in real-time.

Our study aims to examine the severity levels of DR through feature extraction and grading analysis for remote patients. Early detection of DR is crucial for averting potential sight-threatening complications or vision loss. The proposed application serves as a preliminary diagnostic tool, alleviating the workload on a limited number of optometrists/ophthalmologists in developing nations. The proposed study utilizes the Made in India (MII) Ret Cam, a smartphone-based camera, to test the algorithm's performance deployed within the application, employing the Volk 20D lens.

Current advanced techniques in DR detection algorithms primarily concentrate on image classification, depending exclusively on ML. Medical professionals often find these solutions less effective because they lack interpretability. Another existing algorithm, which emphasizes lesion localization or segmentation, is more complex and requires

understanding the differences between abnormalities. Therefore, the proposed work aims to detect DR at any stage, providing the severity percentage and levels. Additionally, it focuses on identifying the initial symptoms of the DR stage, which are commonly found across all stages.

DR-specific lesion detection using fundus images started with classical image enhancement. Researchers detect abnormalities and pixel-wise classifications and detection. Diverse classical methods include curvelet transform (Johnson et al., 2018), watershed transform (Gupta et al., 2022), and adaptive template matching (Mansour, 2018). State-of-the-art methods include CNN (Chudzik et al., 2018; Ricci & Perfetti, 2007; Salamat et al., 2019) methods for DR detection. In the current study, the suggested method is integrated into a web-based application called “RetinaCare,” which includes various screens, from registration and login to capturing and adjusting the fundus image. These images can be captured using any smartphone-based camera. In the proposed study, the MIIRet Cam was used for testing purposes. The application displays the final grading of DR on the DR classification page, which ranges from mild to severe DR in severity analysis.

Despite notable advancements in early detection methodologies for DR, existing techniques face significant limitations in predictive performance. Current approaches often fail to provide robust and reliable predictive tools, raising concerns about their efficacy in comprehensive DR management (Bilal, Sun, et al., 2022). This challenge is exacerbated by the scarcity of affordable diagnostic tools in clinical settings, particularly in remote and underserved areas. Additionally, many studies focus on datasets from non-Indian populations, which may not generalize well to diverse demographic groups, further limiting the real-world applicability of these methods (Alyoubi et al., 2020).

To address these gaps, there is an urgent need to refine existing strategies and develop innovative methods that enhance diagnostic precision. One promising direction involves the integration of unsupervised and modified DL models with web-based applications. The

proposed tool, RetinaCare, can run as a mobile phone application and detect DR in mild to PDR stages. This application operates smoothly in remote areas and integrates the proposed algorithm. Additionally, the algorithm can be further trained on the fundus images of patients, which will be saved in RetinaCare while detecting DR to enhance its performance. Since the algorithm is unsupervised, labelling is not required.

Moreover, no existing hybrid unsupervised DL algorithm is integrated into a tool that facilitates real-time detection of DR using a smartphone-based fundus camera. The current state-of-the-art unsupervised approaches are primarily based on autoencoders, which consist of encoder-decoder networks. These autoencoder-based deep clustering approaches tend to overfit in data-constrained scenarios due to the requirement of learning the weights of both the encoder and decoder. The proposed tool can be helpful to the medical community as it can serve as a preliminary tool for ophthalmologists and provide a first opinion for doctors. An operator with minimal training and without specialized knowledge can operate the tool. The proposed work offers a transformative solution for medical imaging and scalable healthcare technologies, providing valuable preliminary assessments for ophthalmologists.

1.9 Performance Metrics for the Proposed Approach

Researchers employ a range of evaluation criteria to evaluate the efficacy of the suggested method, which is tailored to the specific characteristics of the algorithm. The proposed methodology is inherently unsupervised; therefore, the chosen performance metrics for this approach include accuracy, normalized mutual information (NMI), and the adjusted Rand Index (ARI). The measurement system is well-suited for evaluating the proposed deep clustering methods on fundus image datasets since they provide a quantitative, interpretable, and comprehensive assessment of clustering quality. These metrics address the unique challenges of working with visual data and are widely adopted within the medical analysis community, promoting interpretability. The following section outlines the description of the metrics.

Unsupervised Accuracy: The unsupervised accuracy (ACC) evaluates the performance of a mapping function (mp) that connects the ground truth (g) to the outcomes of clustering assignments (c), distinguishing it from conventional accuracy metrics. As the UL algorithm produces the final result, aligning the ground truth labels with the output is not feasible. The ACC can be computed with equation 1.1 (Abramoff et al., 2010).

$$ACC = \max_{mp} \frac{\sum_{j=1}^n 1(g_j = mp(c_i))}{n} \quad (1.1)$$

Normalized Mutual Information: This metric compares the similarities between two clusters or the labels of identical data items. A normalized mutual score scales the result from $[0, 1]$ (Naz et al., 2022), Where 0 indicates no correlation and 1 denotes perfect correlation. The formula is given by equation 1.2.

$$NMI = \frac{I(l, c)}{\max(H(l), H(c))} \quad (1.2)$$

The mutual information between label l and its associated cluster c is signified by $I(l, c)$, while entropy is denoted by H .

$$I(X; Y) = \sum_{x \in X} \sum_{y \in Y} \rho(x, y) \cdot \log\left(\frac{\rho(x, y)}{\rho(x) \cdot \rho(y)}\right) \quad (1.3)$$

Entropy measures the uncertainty and can be computed as follows using equation 1.4.

$$H(X) = - \sum_{x \in X} \rho(x) \cdot \log(\rho(x)) \quad (1.4)$$

Adjusted Rand Index: The ARI is utilized as a statistical measure to evaluate the level of similarity between two cluster partitions by analyzing the allocation of data points to their corresponding clusters (Hoffman et al., 2015). ARI is bounded within the interval of $[-1,$

1]. An increased ARI value indicates improved clustering. ARI can be computed using equation 1.5.

$$ARI = \frac{\sum_{ij} \binom{n_{ij}}{2} - [\sum_i \binom{a_i}{2} \sum_j \binom{b_j}{2}] / \binom{n}{2}}{\frac{1}{2} [\sum_i \binom{a_i}{2} \sum_j \binom{b_j}{2}] - [\sum_i \binom{a_i}{2} \sum_j \binom{b_j}{2}] / \binom{n}{2}} \quad (1.5)$$

The total count of samples is represented by n , while the number of samples categorized within the same pair in both the actual and predicted clusters is signified by n_{ij} . Furthermore, a_i represents the count of samples associated with cluster i based on the accurate labels, and the quantity of samples within cluster j is represented by b_j , as determined by the predicted labels.

1.9.1 Average Execution Time: It refers to the average time that is taken for a model or algorithm to process a single instance, such as an image, during its runtime or inference (Geetharamani & Balasubramanian, 2016). It serves as a crucial measure of the efficacy and speed of a model or algorithm in real-world applications. The lower the average execution time, the faster and more responsive the model makes predictions or data processing. The proposed methodology is evaluated through a threefold analysis: visual representation, statistical analysis, and performance analysis.

Three benchmark datasets and a dataset primarily collected for this study are used to assess how well the methodology can generalize across different image resolutions. The proposed algorithm follows a 70%, 30% training, and testing split, which helps evaluate its effectiveness.

1.10 Overview of Existing DR Databases

Clinicians use various imaging techniques, including OCT, fundus photography, and fluorescein angiography, to evaluate and diagnose retinal disorders in clinical optometry.

OCT is used to diagnose retinal vascular abnormalities and assess retinal layer thickness, whereas Fundus images show the retina's inner structures. Numerous datasets with fundus photos are accessible, and researchers have used both proprietary and open-access databases in their study. Several methods can be used to automate DR diagnosis and identify retinal disease. Through performance analysis, the dataset chosen for the developed classifiers should guarantee the accurate diagnosis of the condition.

Dai et al. utilized a substantial dataset of 466,627 fundus pictures from 121,342 individuals diagnosed with diabetes (Dai et al., 2021). Accordingly, Yang et al.(Y. Yang et al., 2017) employed a publicly available DR dataset from Kaggle, consisting of 22,795 images, to train and evaluate the algorithm. Each study utilized 800 fundus images for evaluation and 21,995 images designated for assessing and identifying eye-related issues.

1.10.1 Common DR Databases

Table 1.1 lists datasets used for DR detection in various publications and studies. Some researchers (Bilal et al., 2021; Bilal, Sun, et al., 2022) have used exclusive datasets with limited accessibility, while others have used publicly available data (Grzybowski et al., 2020). Several universities and hospitals have generated comprehensive databases employing diverse camera configurations (Lim et al., 2022). The table further outlines the specifics of the DR Dataset and the camera configurations used in the associated research. The data is organized according to the title of the study and the year it was published.

A detailed summary of the dataset characteristics, including image count, dataset class distribution, and access links to publicly available databases, is provided in Table 4. This signifies that datasets such as IDRiD, APTOS DR challenge dataset, E-optha, Messidor1, Messidor2, STARE, DIARETDB0, and DIARETDB1 have established themselves as recognized benchmarks. Numerous researchers have studied these datasets, concentrating on detecting lesions, screening for DR, and identifying features like hemorrhages, microaneurysms, and exudates (Nagpal et al., 2021). Figure 1.8 offers additional

clarification on the characteristics and particular aspects of the dataset, as detailed in the final column of the table. As shown in Table 1.1, most open-source datasets suffer from class imbalance, as demonstrated by specific analyses of the current dataset. Some of the renowned datasets are the following:

1. Kaggle EyePACS
2. Kaggle APTOS 2019
3. Messidor & Messidor2
4. IDRiD
5. DDR
6. E-optha
7. DiaRetDB1
8. DRiDB

Table 1.1 Overview of Publicly Available DR Datasets

S. No	Dataset Title	Image Count	Class distribution	Access link
1	Kaggle EyePACS Dataset (2016)	A total of 88,702, from which 35,426 were for training and 53,576 for testing	No DR- 73% Mild DR-6% Moderate DR- 15% Severe DR- 2.4% PDR – 2.01%	https://www.kaggle.com/c/diabetic-retinopathy-detection
2	Kaggle APTOS 2019	3662 training images and 1928 test images	No DR- 73% Mild DR-6% Moderate DR- 15% Severe DR- 2.4% PDR - 2.01%	https://www.kaggle.com/c/aptos2019-blindness-detection/data
3	DRIVE (2004)	40 Fundus images (Training Images-20 Testing Images - 20)	exudates hemorrhage - 7 out of 40	https://docs.activelearning.ai/datasets/drive-dataset

4	IDRiD (2021)	Total 516 fundus color images with 4288 x 2848 resolution	DR Retinal Images - 81 Normal Retinal Images - 164	https://idrid.grand-challenge.org/
5	DIARETDB0 (2020)	130 Fundus images	DR Sign – 110 Normal Images -20	https://www.it.lut.fi/project/imageret/diaretdb0/
6	DIARETDB1 (2020)	A collection of 89 images of the fundus.	DR Sign – 84 Normal Images with no Sign of DR -5	https://www.it.lut.fi/project/imageret/diaretdb1/
7	DriDB (2020)	A collection of 50 images of the fundus.	DR Sign – 36 Normal Images with no Sign of DR -14	https://ipg.fer.hr/ipg/resources/image_database#
8	Messidor	A total of 400 images	400 without pupil dilation and 400 with pupil dilation	https://www.adcis.net/en/third-party/messidor/

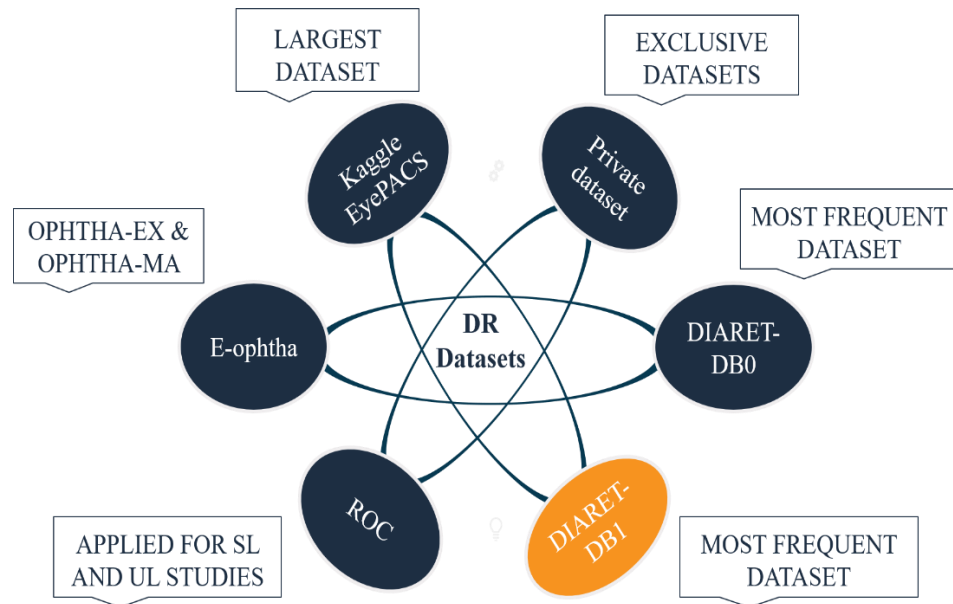


Figure 1.8: Overview of DR Datasets and their Characteristics (Naz, Ahuja, et al., 2024)

1.10.2 Criteria for Database Selection in the Current Study

Most publicly accessible datasets are imbalanced. Moreover, habitat and external conditions impact disease progression. Therefore, the selection of datasets was made after considering several factors. Table 1.2 presents the databases chosen for the research. Furthermore, fundus images were obtained from an eye clinic in western Uttar Pradesh to ensure the findings are applicable and can be evaluated within Indian demographics.

Table 1.2 Dataset Utilized in the Proposed Study

S. No.	Dataset	Number of Images	Dimension
1	IDRiD (Porwal et al., 2020)	103	2848×4288
2	APTOS (Naz et al., 2022)	3662	640 × 480
3	Primary dataset	81	2866 x2866
4	DIARERDB1 (Zago et al., 2020)	89	1500 × 1152

1.11 Motivation

Paradoxically, Individuals in low and middle-income nations are estimated to have a higher likelihood of experiencing diabetes and DR in comparison to those in high-income countries. According to the IDF report, Southeast Asia is considered a hub of diabetes, with 30.6 million suffering from diabetes, as shown in Figure 1.9 (Pratt et al., 2016), and 9.6 million possibly suffering from sight-threatening DR. DM and DR are the most common causes of reduced, premature death and quality-adjusted life-years among old-aged people as well as adults nowadays. The continuous increase in DM and DR cases also leads to a global rise in the unequal planned expenditure on diabetes and the cost of diabetes care in developing countries (Pratt et al., 2016).

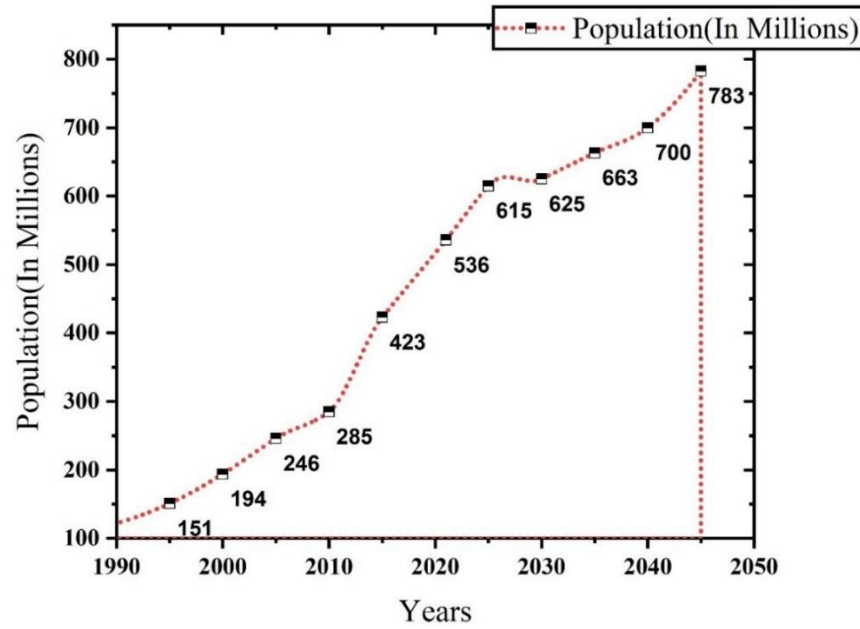


Figure 1.9: Global diabetes prevalence estimates from (2000-2045) (Sun et al., 2022; WHO, n.d.)(Saeedi et al., 2019; Sun et al., 2022; WHO, n.d.)

Several conventional algorithms are available for improving and applying them in DR Detection applications. Nonetheless, most of these methods are linear, making it challenging to approach datasets that require a constant pattern. Additionally, the accuracy of these algorithms may vary based on the dataset size (Chakradar et al., 2021).

The healthcare system in India is very fragile. Implementing the supervised learning process requires significant manual labour and effort for data annotation. Strict regulations govern the dissemination of medical imaging data, and specialists' accessibility for labelling these images is limited, as indicated by the Ophthalmology Database Study of Cataract Surgery 2024 and the 2022 Physician Specialty Data Report, as shown in Figure 1.10. Thus, there is a need for an unsupervised systematic approach to DR Detection and automated labelling.

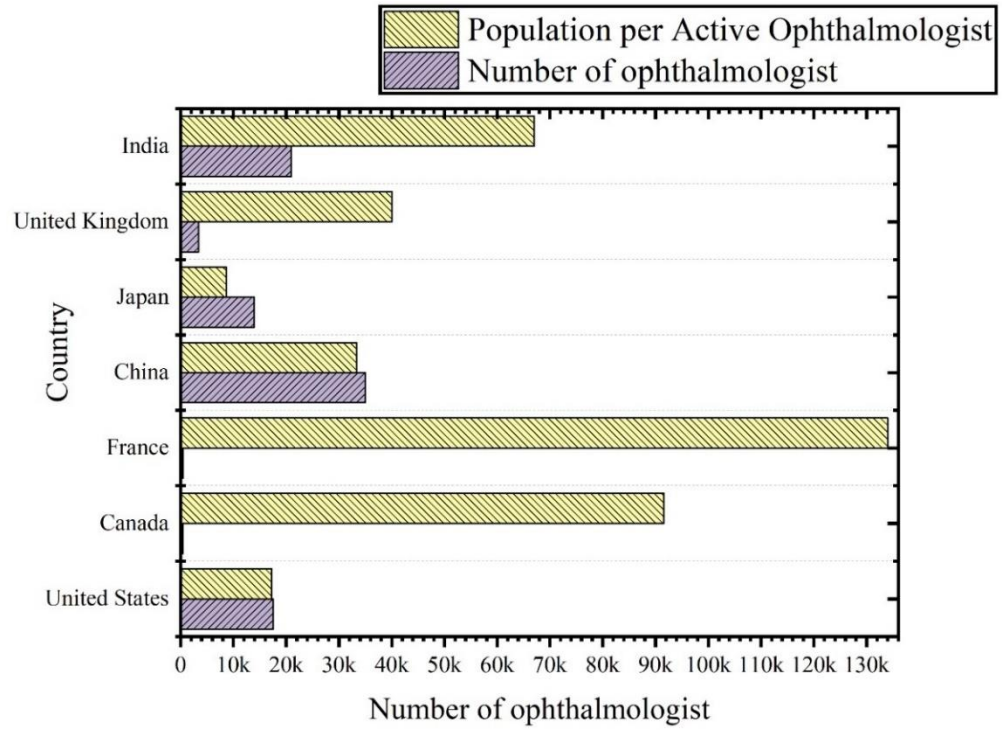


Figure 1.10: Distribution of ophthalmologists by country (Albo et al., 2023; Association of American Medical Colleges, 2023; Buchan et al., 2024)

1.12 Objectives

To enhance the behavior and nature of clustering algorithm with the nature of deep learning methodology. So, the hybrid model of Unsupervised Learning and deep learning algorithm can be implemented for efficient DR classification.

Sub Objectives

1. To develop a pre-processing algorithm for improving the image quality of fundus images.
2. To design a computationally efficient hybrid unsupervised-deep learning algorithm to classify DR stages.
3. To develop a DR detector and recommender system.

1.13 Contributions

The significant contributions of our proposed work include-

1. The proposed work presents an Indian dataset of DR fundus images collected at an Eye Center in northern India. Grayscale and colour preprocessing improve the image quality of raw fundus images.
2. The current study introduces an enhanced iteration of the FCM clustering algorithm, specifically designed to mitigate the challenges associated with local optima inherent to the traditional FCM approach.
3. The proposed work presents a hybrid deep clustering algorithm that combines the proposed modified FCM and CNN for severity grading of the DR fundus images.
4. The proposed work presents RetinaCare, a web-based tool for classifying DR fundus images designed to ease the workload of ophthalmologists and serve as a first opinion in rural locations.
5. The proposed study validates the tool at Shri Mahant Indires (SMI) Hospital, Dehradun, India, with guidance from ophthalmologists.

1.14 Organization of the Thesis

The thesis has been structured into five chapters. A summary of the presented work is briefly described in each chapter.

Chapter 1:

This chapter discusses the importance of medical image analysis in DR diagnostics and severity analysis. It also includes a discussion of the clinical features, retinal imaging, and stages of DR. The literature works on DR detection and classification, red lesion

segmentation, severity grading, and DR diagnosis. Chapter 1 also presents the motivation and contribution of the thesis.

Chapter 2:

This chapter outlines the clustering methods and deep-embedded clustering techniques investigated in the thesis. It discusses the various conventional clustering methods and modified versions for diagnosing DR using fundus images. Moreover, the limitations of autoencoder-based DEC and other clustering methods are also discussed.

Chapter 3:

This chapter offers an in-depth examination of the principal dataset and outlines the preprocessing techniques employed to enhance the quality of fundus images. The original images frequently exhibit artifacts, low contrast, and inconsistent lighting. The Intensity Histogram Equalization (IHE) method was modified to enhance image clarity and address these issues. Furthermore, the OD may occasionally be mistaken for exudates; thus, background segmentation was utilized to eliminate both the OD and blood vessels to enhance the precision of lesion detection.

Chapter 4:

This chapter adopts the unsupervised way of diagnosing DR embedded in DL methods. It discusses the FCM methodology and process to optimize the search space of space for attaining the optimal cluster. The performance of the modified FCM is also concerned with average time and accuracy under noisy and noiseless conditions. Moreover, the process of combining MDFCM with CNN (FCCNN) is also elaborated, and the result is shown using performance metrics such as ACC, NMI, and ARI.

Chapter 5:

This chapter discussed a dedicated DR detection system utilizing a web-based application compatible with any mobile phone. This presents significant benefits for individuals living in remote areas. This application incorporates the proposed algorithm, and image capture is facilitated through the MII ret cam paired with a 20D Volk lens, a cost-effective alternative to expensive table-top fundus cameras. Moreover, the proposed algorithm's real-life testing, the application's flow, and operations are also discussed. Integrating the MIIRet Cam with the application for testing purposes and the complete specifications is covered. The testing scenarios and results are also presented on patients in the hospital setting.

1.15 Summary

The present study advances the field of automated DR detection by integrating an optimized FCM clustering algorithm with CNN for severity grading. In contrast to existing methodologies that predominantly rely on supervised learning or intricate lesion segmentation techniques, the proposed hybrid framework enhances classification accuracy while mitigating the dependency on labeled data. The development of RetinaCare, a web-based diagnostic tool, significantly improves accessibility to DR screening, particularly in remote and underserved regions, thereby addressing critical limitations in contemporary DR detection frameworks. Comparative evaluations demonstrate the superior performance of the proposed approach, characterized by improved convergence rates, reduced susceptibility to local optima, and enhanced feature discrimination. Furthermore, validation conducted at SMI Hospital, Dehradun, corroborates the efficacy and practical applicability of the proposed methodology. These findings underscore the study's contribution to the domain of automated ophthalmic diagnostics, bridging the gap between state-of-the-art deep learning methodologies and real-world clinical implementation.

Chapter II

Investigations on Deep Clustering Methods

2.1 Introduction

As the global population ages, an accompanying rise in cases of eye disease is expected; however, ophthalmic services, particularly in rural and developing areas, have been declining faster than the overall service provision rate. To eliminate preventable blindness worldwide by 2020, the World Health Organization has established "Vision 2020". Many ways to enhance eye health include more education and awareness campaigns, precise diagnoses, and focused preventative measures. As of 2012, the estimated global population of people with visual impairments was 124 million without correction for uncorrected refractive problems, including 37 million who are blind. Avoidable blindness is being reduced due to the global Vision 2020 project, especially ocular infections. Still, more work must be done to combat cataracts, glaucoma, and DR. Much research towards automated detection has focused on DR due to its high occurrence and related impact.

Diabetes is a significant contributor to cardiovascular diseases and physical impairments, with approximately 15% of instances of blindness linked to chronic diabetes. This positions diabetes as the primary cause of vision impairment on a global scale. By 2045, it is projected that 451 million individuals worldwide will be impacted by diabetes, with the number of diagnosed cases rising to 693 million (Cho et al., 2018). Image acquisition systems have improved, but retinal vessel damage is a severe complication. A fundamental retinal abnormality is associated with DR, characterized by a gradual constriction of retinal arteries and a reduction in blood flow within the retina. DR can be detected early in the disease process, significantly reducing a patient's vision loss risk. Several factors can

reduce vision, but macular edema is one of the most common. Retinal abnormalities are critical public health concerns, particularly prevalent in underdeveloped nations. They can be systemic or non-systemic, with systemic abnormalities potentially affecting multiple organs and spreading throughout the body (Franklin & Rajan, 2014).

The significance of retinal fundus images within a computer-aided diagnostic (CAD) system is recognized, enabling precise detection of DR in its early stages. This system performs critical processes such as lesion detection, segmentation, and classification, facilitating timely diagnosis and treatment. Recent researchers have applied CAD and [56] for better disease diagnosis at an early stage. It can also be used as a second opinion for doctors in medical diagnosis.

2.2 Computer-Aided Diagnosis of DR

Over the past few years, image acquisition systems have rapidly improved, as image quality is crucial to identifying diseases and interpreting results. Image acquisition and reconstruction have been enhanced by utilizing diverse imaging techniques, such as MRI, fundus imaging, and X-rays. The ability to extract useful information from many images to analyze features contributing to disease prediction is still challenging. Automated medical image analysis techniques can improve the prediction and interpretation of medical images (Hervella et al., 2020).

Furthermore, automated diagnosis can be beneficial because the number of doctors per population is limited in developing countries, and this method may offer a first opinion/decision for further consultation, reducing the load on ophthalmologists. In recent years, numerous research endeavours have employed ML and DL methodologies to improve the classification accuracy of DR (Iqbal et al., 2022; Yamuna & Maheswari, 2013). Furthermore, DL algorithms have outperformed most ML algorithms recently, facilitating automated feature extraction and medical image interpretation (Franklin & Rajan, 2014). As a result of these enhancements, DL algorithms have been widely

embraced for medical image analysis (Fraz et al., 2017). DL techniques are typically categorized into two main types: supervised learning methods and UL methods.

Most researchers (Kampffmeyer et al., 2019; Kumar et al., 2019; Wang et al., 2015) use supervised methods to analyze medical images, focusing primarily on DR classification. Most of these algorithms are comparable to human performance. In recent years, these systems have exhibited considerable promise in improving medical imaging and advancing healthcare outcomes. Supervised learning techniques require the Availability of labelled or annotated datasets to train predictive models effectively. Models created using labelled data generally demonstrate enhanced performance in real-time situations. The process of labelling data necessitates considerable manual effort (Litjens et al., 2017). Conversely, it has been observed that UL algorithms offer significant benefits for applications in the medical field, as they enable the exploration of new opportunities (Hervella et al., 2020; Y. Zhao et al., 2015). SL methods are limited in uncovering alternative possibilities due to biases inherent in principles.

Regular neural networks project data into representations for supervised tasks, but backpropagation can lead to trivial solutions without output. The challenges encountered in traditional feedforward neural networks are mitigated by integrating clustering loss functions into the auto-encoder architecture. Auto-encoders are used for UL tasks like feature learning and data reconstruction. Auto-encoders capture meaningful data representations and are well-suited for embedding and clustering tasks since they map a lower-dimensional latent space onto input data. However, auto-encoders require training an encoder and a decoder network, which can lead to overfitting and limited data instances. Current deep clustering approaches lack supervision, making them unable to capture discriminative information in learned representations.

2.3 Various Clustering Methods

Traditionally, clustering algorithms use feature vectors derived from domain-specific insights to cluster the resulting features. Meanwhile, DEC methods enable the direct clustering of original images with enhanced performance by integrating feature extraction and clustering into an integrated framework. Supervised learning has considerable potential and can address various challenges. However, the UL approach holds the promise of revealing numerous new opportunities.

The ability to perform cluster assignments and feature learning allows DEC methods to perform at a superior level to UL methods (Sheng et al., 2022). Additionally, the discussion highlights the limitations commonly associated with supervised learning techniques. Conventional neural networks are designed to transform data into a format appropriate for supervised learning applications (Enguehard et al., 2019). The training employs various methods to optimize network weights, including gradient descent and backpropagation. Backpropagation leads to a trivial solution in instances where a neural network lacks an output. In these scenarios, the weights and representations within the network are initialized to zero, regardless of the cost function employed. Consequently, the utilization of feedforward neural networks is not suitable for unsupervised representation learning when they integrate a loss function based on unsupervised clustering.

Previous studies (Fard et al., 2020; Peng et al., 2016; Xie et al., 2016; B. Yang et al., 2017) have demonstrated the integration of cluster losses into the auto-encoding framework to address this issue. An auto-encoder is commonly employed in UL applications, particularly feature extraction and data reconstruction. The architectural framework comprises two primary elements: the encoder and decoder networks. The encoder network transforms the input data into a reduced-dimensional latent space, whereas the decoder network aims to reconstruct this encoded representation to revert it to the original input space. This method allows auto-encoders to effectively capture meaningful data representations, making them suitable for embedding and clustering tasks. Deep clustering that employs autoencoders

involves the integration of a clustering loss function within the latent space that follows the encoding process. This approach enhances clustering efficacy by employing encoded representations. The integration of clustering loss within the encoder network can be achieved by utilizing the constraints inherent to the auto-encoder framework. In contrast, the decoder network does not contribute to the clustering process. The limitations imposed by the auto-encoder enhance the training of both the encoder and decoder networks. In instances where the availability of data examples is constrained, the training of encoder-decoder networks necessitates a parameter count that is approximately double that required for a conventional feedforward neural network. The increased complexity may result in overfitting (Liu et al., 2017). Due to inadequate supervision, deep clustering techniques do not effectively capture discriminatory information in trained representations. Most deep clustering algorithms are encoder-decoder architectures and auto-encoders (Sheng et al., 2022). Auto-encoder-based deep clustering methods may experience overfitting due to the necessity of learning the weights of both encoders and decoders in data-scarce situations.

Deep clustering methodologies utilize DL networks to extract essential representations fed to shallow clustering techniques. Several DL-based architectures are implemented to discover the deep representations for clustering. A new deep clustering model (Xie et al., 2016) has been developed, incorporating a K-means clustering technique, utilizing Student's t-distribution kernel as the distance metric within a stacked auto-encoder (SAC). The incorporation of K-means clustering, using Euclidean distance metrics, within the framework of an autoencoder represents a novel approach to enhancing data (Fard et al., 2020; B. Yang et al., 2017). A series of methods for deep clustering has followed, including convolutional (X. Guo et al., 2017) and contractive auto-encoders (Diallo et al., 2021), (Ren et al., 2019). To improve clustering stability, DCSR optimizes the Adaptive Siamese and Reconstruction losses to deal with similarities (Yu & Wang, 2020), (X. Yang et al., 2019).

The Deep K-means approach proposed [71] is further improved by substituting K-means with hierarchical K-means. The latent embedding and noise counterparts are subjected to reconstruction error using a dual variational auto-encoder framework (L. Yang et al.,

2023). K-Deep Variational Autoencoders (k-DVAEs) are used to get the best results for clustering. These use multiple autoencoders to make better latent models (Caciularu & Goldberger, 2023).

2.4 Auto-Encoders-based Deep Clustering Approach

The deepest layer of the auto-encoder produces representations that are input into independent clustering methods, such as spectral clustering or K-means clustering, according to a significant research paper on DL-based clustering (X. Yang et al., 2019). The optimization process led to a gradual decrease in the reconstruction and clustering loss associated with the auto-encoder. Subsequently, a novel formulation integrating Sparse Autoencoder Clustering (SAC) with sparse subspace clustering techniques was introduced to overcome the challenges of fragmented training methodologies (Elhamifar & Vidal, 2013). The framework (Figure 2.1) shows that the autoencoder demonstrated superior performance to its segmented counterpart, as illustrated.

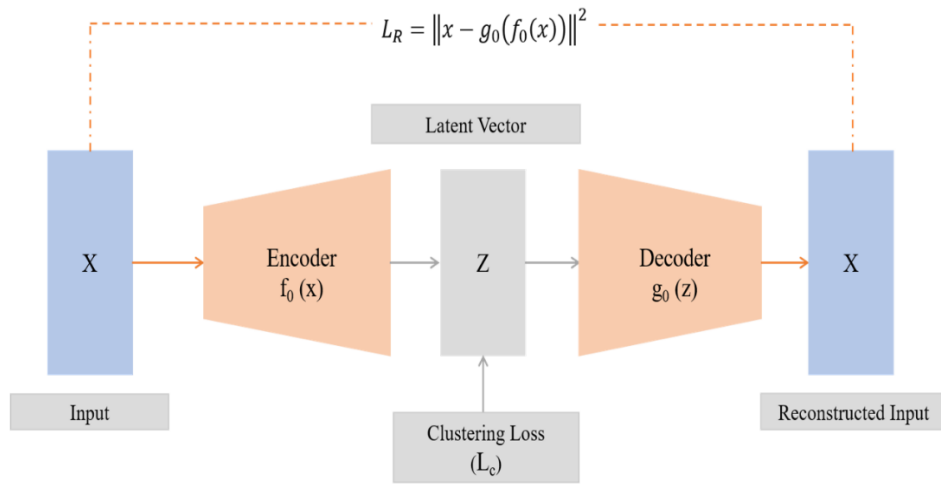


Figure 2.1: Autoencoder Framework with Reconstruction and Clustering Loss (Naz, Ahuja, et al., 2024)

This method incorporates a clustering technique known as k-means clustering assignment with demand response. Three steps must be taken to optimize the process: 1. Reducing dimensions, 2. Reconstructing data, and 3. Promoting regularization based on clusters (Min et al., 2018).

Stochastic Gradient Descent (SGD) is a widely utilized optimization algorithm in ML and DL to minimize the objective function associated with a neural network. This methodology entails the assessment of individual data points z_i alongside the centroid of each cluster μ_j , while the SGD loss function is calculated around the feature space.

$$\frac{\partial L}{\partial z_i} = \frac{\alpha+1}{\alpha} \sum_j \left(1 + \frac{\|z_i - \mu_j\|^2}{\alpha}\right) \times (p_{ij} - q_{ij})(z_i - \mu_j) \quad (2.1)$$

$$\frac{\partial L}{\partial \mu_i} = -\frac{\alpha+1}{\alpha} \sum_j \left(1 + \frac{\|z_i - \mu_j\|^2}{\alpha}\right) \times (p_{ij} - q_{ij})(z_i - \mu_j) \quad (2.2)$$

The gradient loss function $\frac{\partial L}{\partial z_i}$, as specified in equation (2.1), is employed for calculating the general backpropagation $\frac{\partial L}{\partial u_i}$, which facilitates network learning as outlined in equation (2.2). In the context of the Student's t-distribution, the symbol α denotes the degrees of freedom, which is assumed to be equal to 1.

p_{ij} represents the auxiliary target distribution as defined in equation (2.3).

$$p_{ij} = \frac{\frac{q_{ii}^2}{f_j}}{\sum_{j'} \frac{q_{ij}^2}{f_{j'}}} \quad (2.3)$$

The term $f_j = \sum_i q_{ij}$ represents the frequencies associated with soft clustering. The term q_{ij} signifies the probability of sample assignment of i to cluster j using equation (2.4).

$$q_{ij} = \frac{(1+\|z_i-\mu_j\|^2/\alpha)^{-\frac{\alpha+1}{2}}}{\sum_{j'} (1+\|z_i-\mu_{j'}\|^2/\alpha)^{-\frac{\alpha+1}{2}}} \quad (2.4)$$

To identify cluster centers μ_j , the clustering algorithm analyzes the corresponding features z_i after the DNN has completed preliminary learning. As a result of multiple iterations, most clustering algorithms achieve convergence. In this scenario, the state of convergence is defined by minimising the Kullback-Leibler (KL) loss, as described in equation (2.5).

$$L = KL(P\|Q) = \sum_i \sum_j p_{ij} \log \frac{p_{ij}}{q_{ij}} \quad (2.5)$$

Based on the equations in sections 2.3 and 2.4, the clustering algorithm is then calculated using the existing parameters, including z_i, μ_j, p_{ij} and q_{ij} , per equation (2.5). *LC* loss is the loss function associated with clustering. The deep neural network (DNN) computes the reconstruction loss, *LR*, in parallel with updating the learning parameters. This simultaneous operation is essential for preparing the network for further training.

DEC is a stacked autoencoder (SAE) that undergoes end-to-end training like SAE (Diallo et al., 2021). Feature learning within DEC was improved through pairing constraints incorporated by SDEC (Ren et al., 2019).

The DCSR enhanced cluster stability by incorporating adaptive Siamese and reconstruction losses (Y. Li et al., 2022). Spectral clustering losses were also integrated into autoencoders, further improving their performance (X. Yang et al., 2019). A dual variational autoencoder architecture was developed to impose reconstruction errors for both latent embeddings and their noise counterparts, enhancing the overall efficacy of the model [79]. Deep K-means were introduced and later improved by substituting traditional K-means with hierarchical K-means (Huang et al., 2022). Additionally, multiple auto-

encoders in K-DVAE have been proposed to enhance clustering performance by generating superior latent representations (Caciularu & Goldberger, 2023).

An encoder and decoder network must be trained concurrently in the auto-encoder framework. Clustering losses are built into the encoder network; the decoder network is not involved in clustering. A training set of encoders and decoders produces twice as many parameters as a feedforward neural network. This scenario may result in overfitting, mainly if data examples are scarce (Liu et al., 2017).

2.5 Convolutional Neural Network-based Deep Clustering Approaches

The agglomerative clustering is recurrently combined with CNN (J. Yang et al., 2018). This approach divided the time steps into multiple periods, and in each period, clusters and representation learning are merged in forward pass and backward pass, respectively. A CNN is trained simultaneously with the clustering of the resultant features by DeepClust (Caron et al., 2018). As part of a discriminative loss framework, DeepClust performs iterative k-means clustering on the CNN's features, updating weights according to the expected cluster assignment, which is regarded as pseudo-labels. The authors present an advanced clustering framework based on a gated CNN (L. Li & Kameoka, 2018).

Data noise and variation are highly sensitive to CNN-based deep clustering techniques. Additionally, CNNs are primarily used as supervised learning models. The filters in CNNs are learned in a data-driven manner and are not predefined or handcrafted. However, there is no guarantee that each learned filter will be unique. Several reasons include redundancy in training data, learning of local features, random weights initialization, and regularization techniques. Thus, learned representations might be redundant in CNN-based deep clustering approaches (Min et al., 2018).

2.6 Advanced Clustering: Discriminately Boosted Methodology

The DBC Method adheres to the same procedures as DEC, which encompass training, clustering, KL divergence, and the assignment of clusters. CNN-based autoencoders differ significantly in functionality from feedforward-based generic autoencoders. The difference is in the functionality, which improves accuracy over the DEC, mainly when encoding image-centric datasets. The framework consists of two components that correspond with the SAE: (1) the Fully Convolutional Autoencoder (FCAE) and (2) the Detected Body Computer (DBC), as depicted in Figure 2.4. The first section includes the FCAE, whereas the second section features a derivation of a DBC structure based on the FCAE.

The DBC serves as an initial processing step before the soft k-means model classifies clusters during the training phase. An alternative approach to the DEC method will be employed to train the data points. The capability of CNNs to learn image features through the simultaneous analysis of fine and coarse details is acknowledged; however, their utilization in image datasets is not commonly practiced. The assignment of clusters results in differing scores for the features produced by the clustering model. The parameters r_{ij} and s_{ij} are assessed throughout the clustering process. The arrangement of clusters leads to variations in the scores associated with the characteristics generated by the clustering model. The parameters are denoted as r_{ij} and s_{ij} are assessed throughout the clustering procedure.

The soft k- k-means score is articulated as follows:

$$s_{ij} = \frac{(1+\|z_i-\mu_j\|^2)^{-1}}{\sum_j^k (1+\|z_i-\mu_j\|^2)^{-1}} \quad (2.6)$$

According to equation (2.6), the t-distribution kernel can be used to evaluate how similar cluster centers μ_j where ($j \in 1$ to k) are hidden characteristics z_i where ($I \in 1$ to m). The

calculation of the discriminative target distribution is derived from s_{ij} , as illustrated in equation (2.7).

$$r_{ij} = \frac{\frac{s_{ij}^\alpha}{n_j}}{\sum_j^k \frac{s_{ij}^\alpha}{n_j}} \quad (2.7)$$

Where, $n_j = \sum_{l=1}^m s_{lj}^\alpha$ signifies the t-distribution and the degrees of freedom is represented by α . The formulation of the objective function associated with the soft k-means clustering methodology is outlined in equation (2.8).

$$L = KL(R||S) = \sum_{i=1}^m \sum_{j=1}^k r_{ij} \log \frac{r_{ij}}{s_{ij}} \quad (2.8)$$

The selection of the learning rate for the neural network is affected by the clustering algorithm through the computation of gradient descent in each iteration, as outlined in equations (2.9) and (2.10).

$$\frac{\delta L}{\delta z_i} = \frac{1+\alpha}{\alpha} \sum_{j=1}^k (r_{ij} - s_{ij}) \times \frac{z_i - \mu_j}{1 + \|z_i - \mu_j\|^{\frac{2}{\alpha}}} \quad (2.9)$$

$$\frac{\delta L}{\delta \mu_j} = \frac{1+\alpha}{\alpha} \sum_{j=1}^k (r_{ij} - s_{ij}) \times \frac{\mu_j - z_i}{1 + \|\mu_j - z_i\|^{\frac{2}{\alpha}}} \quad (2.10)$$

To enhance network training in each session, L_c is combined with reconstruction loss (L_R). Therefore, DBC is UL, like DEC.

2.7 Deep Clustering Network (DCN) Method

The DCN technique establishes a collaborative operation to efficiently tackle the difficulty of executing UL methodologies in DL. In this method, weights acquired after each training session may be used to cluster in the subsequent category rather than analyzing the abstract feature representation.

Fault tolerance is integrated with clustering techniques, particularly k-means clustering, to improve system resilience and ensure continuity in achieving objectives. Three fundamental actions are included in the optimization criteria of the process: (1) reducing the dimensionality of data, (2) reconstructing data, and (3) enhancing regularization techniques through the utilization of cluster structures. As discussed below, the latent feature space is substituted with the clustering-friendly abstract representation w . $h_i = f(x_i; w), f(.; w): R^M \rightarrow R^R$. The function $f(.; w)$ is defined as the mapping between the weights w linked to a specific input x within the designated hidden layer h_i . The combined dimensionality reduction (DR) and clustering process is articulated in equation (2.11).

$$\min_{w, m, s_i} \hat{L} = \sum_{i=1}^N \|f(x_i; w) - M_{s_i}\|_2^2 \quad (2.11)$$

$$s.t. S_{j,i} \in [0,1], 1^T s_i = 1 \forall i, j$$

Here, Clustering loss or euclidean space distance is represented by $\hat{L}$. A cluster function, referred to as M , is defined that includes the clusters m_k . The assignment vector of the data point i is represented by s_i . Combined with dimensionality reduction and clustering, the k-means method is more effective for low-dimensional data and straightforward for high-dimensional data (Sleman et al., 2021).

2.8 Significance and Challenges

Clustering techniques present constraints and advantages, which vary as per the dimensional characteristics of the dataset. With the increasing complexity of data dimensions, many clustering algorithms struggle to detect commonalities, primarily due to their dependence on distance evaluations among individual data points. DL algorithms mitigate this issue, but spectral clustering techniques require dimensionality reduction. The deep clustering method may be more effective with high-dimensional data if a definitive objective function is established for training the DL algorithm. This approach establishes a comprehensive end-to-end foundation for learning, data dimensionality reduction, and clustering, enabling a manifold of benefits. DNNs can handle extensive data (high dimensionality), covering text, photos, and videos, improving clustering algorithms for low-dimensional learning (Min et al., 2018).

The effectiveness of Autoencoder latent space features for clustering is significantly reduced. Corruption in latent space is a significant risk to all data, and it can sometimes lead to data loss in its entirety. Clustering loss does not reliably maintain local structures, which could lead to difficulties in preserving local structures and misclassifications.

The integration of the clustering algorithm into the DNN model, which is inherently complex, has led to heightened complexity during both the implementation and training phases. DNN and DCN incorporate multiple hyper-parameters that play a critical role in learning, loss estimation, clustering, and performance validation with actual data. The complexity of establishing these hyper-parameters arises from the lack of ground truth in the dataset, leading to diminished interpretability. The optimization of these factors presents significant complexity in execution.

The clustering stage in DCN is regarded as crucial, as it improves the UL performance within the DNN. The natural representation is sometimes aligned with the cluster resulting from the learning process. The primary objectives of this research are greatly influenced

by the importance of this issue, requiring addressing challenges associated with supervision. The proposed algorithm for DR classification addresses challenges, including local minima, overfitting, and dimension-dependent performance.

Chapter III

Retinal Image Enhancement and Background Segmentation

The retinal fundus image acquired from the retina is affected by noise and displays low contrast, which complicates accurate interpretation. Improving the retinal image is an essential initial step before additional processing. Raw medical imaging data often display noise, artefacts, and extraneous features that may mislead even the most advanced analytical DL models. Even with advanced DL techniques, the preprocessing phase remains crucial, as it ensures the delivery of high-quality input data directly linked to the model's performance. Preprocessing enhances image quality, reduces noise, and emphasizes relevant areas, improving the accuracy of segmentation tasks. The segmentation of the OD and blood vessels is essential for differentiating these anatomical features from potential DR lesions, thereby minimizing the risk of false positive diagnoses.

During enhancement, preserving the subtle structural detail of the image and maintaining the contrast is crucial. A novel approach is introduced to tackle the retinal image pre-processing problem. The fundus images are processed using the new IHE techniques. The approach transforms RGB images into the HSI colour space, addresses noise and intensity issues through median filtering, and enhances contrast using the advanced IHE algorithm.

The suggested methodology effectively enhances image contrast, thereby improving the visibility of vascular structures. This chapter progresses as follows: Section 3.1 discusses an overview of retinal image pre-processing and conventional preprocessing approaches.

Section 3.2 presents the background segmentation using circular Hough transform and fuzzy inference-based vessel segmentation. Section 3.3 details the advancement of the proposed methodology, while Section 3.4 presents the experimental results and compares them with existing methods.

3.1 Introduction

Imaging technology has advanced significantly in recent years; however, captured images must undergo essential preprocessing techniques before being used for accurate diagnosis and interpretation. Pre-processing entails the initial refinement of unprocessed data to render it suitable for application. The specific steps involved in pre-processing are generally determined by the particular application. The fundus images present challenges for segmenting vessels and OD and concerns regarding camera artifacts. Non-uniformity, illumination issues, poor contrast, dull or very bright colours, or noise can be found in fundus images.

There are several image processing methods available for handling these problems. These techniques enhance the quality of fundus images, thereby augmenting the algorithm's efficacy. Recently, various image enhancement techniques have been implemented for fundus image pre-processing. Methods designed to improve contrast frequently utilize histogram-based approaches, among which Contrast-Limited Adaptive Histogram Equalization (CLAHE) is a notable instance. To the best of our knowledge, there seems to be a lack of research addressing the challenges associated with insufficient contrast and improper lighting conditions in retinal image capture.

Even while the technologies achieve a uniform illumination image, they do so at the expense of a considerable loss of entropy. However, it is never acceptable, particularly in healthcare imaging, where even a slight loss of relevant information can result in a completely separate diagnosis. Furthermore, most previous approaches suffer from over-enhancement, which has a detrimental effect on the information content. A Modified IHE

algorithm is employed in the proposed study to address these issues by introducing a new pre-processing technique. The method involves transforming RGB images into the HSI colour space, addressing noise and intensity issues through median filtering, and enhancing contrast using the proposed algorithm. It helps in eliminating the over-enhancement issue of traditional methods. This also efficiently maintains the image's actual brightness. The suggested approach does not necessitate any domain transformation. Therefore, it reduces computational complexity.

3.2 Materials & Method

This section briefly overviews several advanced techniques, illustrated in Figure 3.1. It discusses specifically the methods used for comparison with the suggested approach. It also discusses the existing intensity equalization method and joint equalization methods.

The pre-processing step mainly aims at contrast improvement, noise elimination, and inhomogeneity correction. The low contrast in fundus images hinders ophthalmologists from accurately analyzing important eye characteristics, making it difficult to see the delicate vessels. Consequently, improving contrast is an essential goal in analyzing fundus images. Various methods for contrast enhancement have been documented (Sindhusaranya & Geetha, 2023).

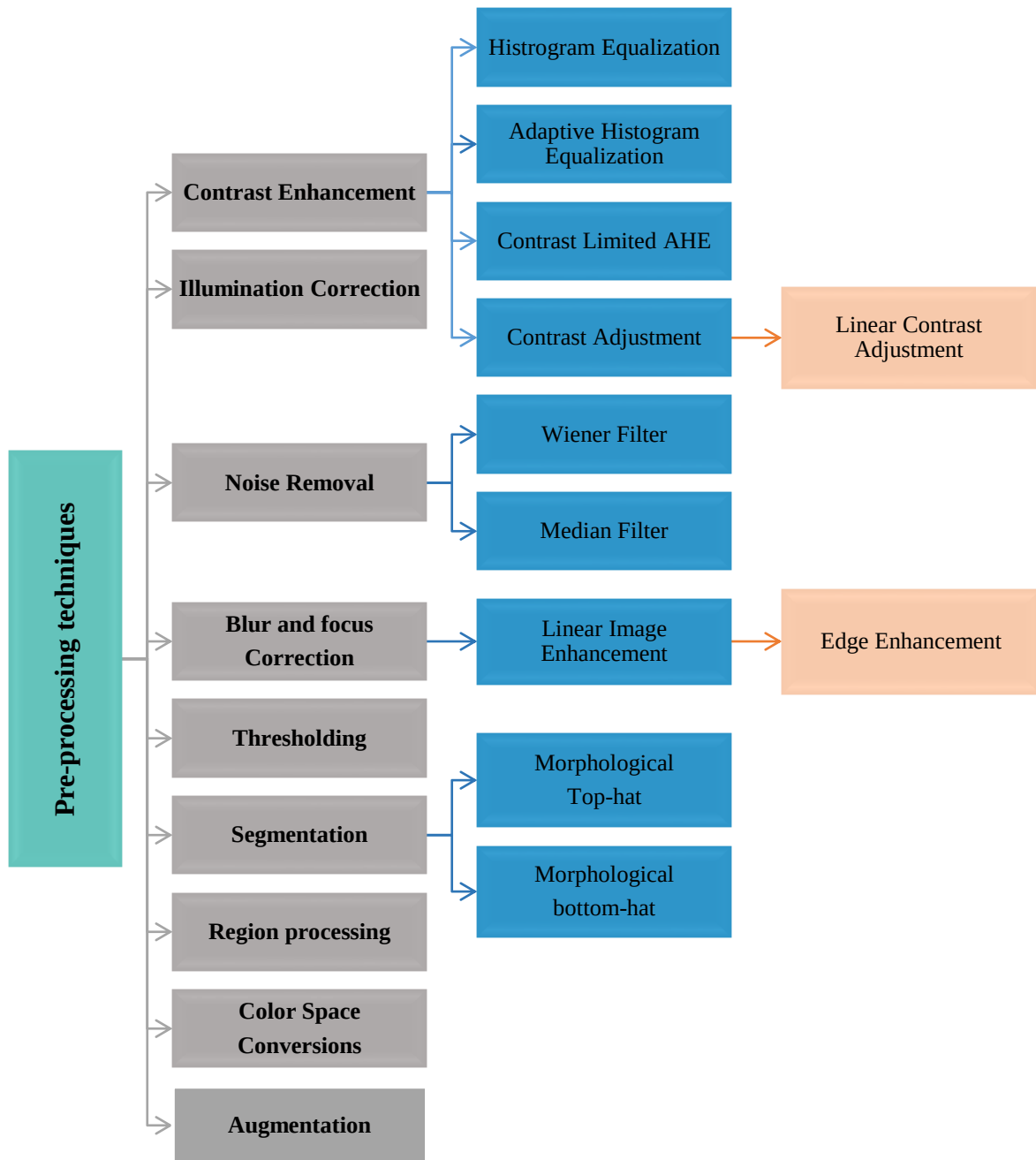


Figure 3.1: Overview of Pre-processing Techniques for DR Image Enhancement
(Naz, Ahuja, et al., 2024)

Recursive sub-image histogram equalization (RSIHE) is an innovative HE approach that preserves an image's average brightness. This methodology involves the iterative segmentation of the histogram into progressively smaller sub-histograms, ultimately improving the image's visual quality (Sim et al., 2007). This technique employs a recursive separation and weighting mechanism that modifies the sub-histograms through a power-law function before applying the histogram equalization process (Kim & Chung, 2008). Similarly, several variants of HE [89] have been developed in contrast enhancement techniques to address the problem of over-enhancement while achieving satisfactory results. The methods mentioned include HE with a plateau constraint [91] and texture HE based on dominant orientation (Dissopa et al., 2021).

Adaptive histogram equalization (AHE) (Dissopa et al., 2021) also enhances regional contrast by calculating multiple histograms for different sections of an image. However, one of its significant drawbacks is the tendency to amplify noise in uniform areas of the image. CLAHE [94] was developed to tackle this problem by limiting the cumulative distribution function (CDF) gradient used during the transformation. By limiting amplification, CLAHE effectively reduces noise enhancement, making it a widely adopted method in the preprocessing of retinal images. Various HE modifications have been explicitly explored to improve fundus image contrast. Singh et al. (Singh & Sabrol, 2021) introduced an innovative methodology aimed at enhancing the contrast and illumination of fundus photographs. This technique utilizes a histogram clipping algorithm incorporating radiance indicator-based histogram equalization (RIHE).

Alhussein et al. (Alhussein et al., 2020) utilized a particle swarm optimization methodology in their research to enhance the contextual adaptation of CLAHE; the proposed strategy aims to improve the context-specificity of the contextual region setting in CLAHE. Budai et al. (Budai et al., 2013) combined histogram stretching with bilateral filtering for preprocessing the retinal image. Bilateral filters help lower the noise and retain the vessel boundaries. Liao et al. (Liao et al., 2014) introduced a novel approach for contrast enhancement that integrates linear stretching techniques with fitting

methodologies. The literature also discusses another technique called power-law transformation (PT), commonly called gamma transformation. This method enhances image contrast by adjusting the intensity of each pixel through exponentiation with a constant value. Power-law transformation is particularly effective for images of highly dark or bright contrast.

Consequently, Dash and Bhoi (Dash & Bhoi, 2018) explored the integration of CLAHE with gamma correction. Despite introducing this novel method, gamma correction showed certain shortcomings in its effectiveness, primarily because of varying lighting conditions and the complex structure of fundus images. The retinex method (Edwin & John, 1971) improves image quality by aligning it with how humans perceive and interpret visuals. It eliminates the impact of uneven lighting in both colour and grayscale images. Hani et al. (Hani et al., 2013) normalized the contrast variation using the based method and performed contrast enhancement using independent component analysis. Zhao et al. (Y. Zhao et al., 2015) employed a retinex-inspired method combined with a bilateral filter to address inconsistencies in the image.

The variability in lighting conditions during acquiring fundus images is often cited as a primary contributor to the observed intensity inhomogeneity within these images. In their research, Leahy et al. (Rani et al., 2017) proposed the application of Laplace interpolation within the image formation model as a method for correcting illumination discrepancies. Although there have been improvements, numerous experimental findings indicate that image enhancement methods rooted in retinex theory continue to face challenges, including halo artifacts, excessive enhancement, and insufficient computational efficiency. Some of the methods in detail are discussed in this section.

3.2.1 Histogram Equalization

HE is recognized as a fundamental method in the field of image processing, mainly to improve the visibility of low-contrast images. It maps the image intensities to the whole

available range of intensity. This approach dramatically increases the overall contrast of an image, but it also results in over-enhancement, which causes a loss of vital content information. Over-enhancement takes place when the process tries to modify the average brightness of an image, aiming to align it with the center of the intensity spectrum (Garg & Jain, 2017).

Various researchers have proposed several modifications to deal with the issues of HE. A relevant strategy for tackling this issue is the implementation of brightness-preserving bi-histogram equalization (BBHE). This technique involves the division of the original histogram into two distinct sub-histograms, which are determined by the mean value of the fundus images. A significant advantage of this methodology is its ability to maintain the mean value of the augmented image in proximity to that of the original image. This characteristic significantly minimizes artifacts, producing more realistic images (Dhal et al., 2021).

The cumulative distribution function serves as the mapping technique employed by HE to determine the output pixel intensity. Let $I(x, y)$ represents a low-contrast retinal image of dimension $R_1 \times R_2 \cdot L$ denotes the quantity of distinct intensity levels. The probability density function, denoted as $p(k)$, is established for a given intensity level represented by the variable k , as articulated in equation (3.1).

$$p(k) = \frac{1}{R_1 \times R_2} n^k \quad (3.1)$$

Here $k = 0, 1, \dots, (L - 1)$ and n^k is the count of pixels with intensity k . Then, the CDF is calculated in equation (3.2) as

$$CDF(k) = \sum_{j=0}^k p(j) \text{ for } k = 0, 1, \dots, (L - 1) \quad (3.2)$$

Then, the output pixel intensities (h_{eq}) are calculated in equation (3.3) using the CDF as follows:

$$h_{eq} = \lceil (L - 1)\{CDF(k) - (CDF(k))_{min}\} \rceil \quad (3.3)$$

$\lceil . \rceil$ denotes the ceiling operation and $(CDF)_{min}$ represents the lowest among the CDF values. The method utilized consists of an explicit procedure for converting grey levels from the original image to its improved version. Nonetheless, peaks in the histogram may result in an over-amplification of specific regions. In order to tackle this issue, numerous modifications to the conventional HE approaches have been documented in academic literature. However, the computational procedure neglects the spatial information of a pixel, which contains attributes common in the surrounding area (Dhal et al., 2021).

3.2.2 Joint Histogram Equalization

The joint histogram equalization (JHE) method incorporates neighbourhood information by first constructing a joint histogram from the source image $I(x, y)$ as well as the mean filtered image $\bar{I}(x, y)$ to incorporate neighbourhood information. Joint histograms $h(l, k)$ represent a matrix $L \times L$ whose entries correspond to the number of instances of grey levels k and l occurring at the exact spatial location I and $\bar{I}$. In equation (3.4), the values $h(l, k)$ indicate the occurrence rate of a pair of pixels (l, k) occurs in both images, and then the 2D CDF function is calculated using equation (3.4) (Agrawal et al., 2022).

$$CDF(l, k) = \sum_{m=0}^k \sum_{n=0}^l h(m, n) \quad (3.4)$$

Finally, the enhanced image pixel intensity h_{eq} is computed using the 2D CDF as in equation (3.5).

$$h_{eq} = round\left[\frac{L-1}{R_1 \times R_2} \{CDF(k) - (CDF(k))_{min}\}\right] \quad (3.5)$$

3.2.3 Contrast-limited Adaptive Histogram Equalization

CLAHE exhibits considerable efficacy in the improvement of retinal images. The process begins with the segmentation of the image into separate, non-overlapping regions of equal dimensions (n_k) ensuring that $\sum_{k=0}^{L-1} n_k = R_1 \times R_2$. Then, the histogram of each region is computed. Each histogram is adjusted to ensure it remains within a specified clipping threshold β . It is calculated beforehand using equation (3.7).

$$\beta = \begin{cases} 1, & \text{if } \frac{\delta R_1 R_2}{L} < 1 \\ \frac{\delta R_1 R_2}{L}, & \text{otherwise} \end{cases} \quad (3.7)$$

Here, δ denotes clip factor $0 < 1 \leq \delta$. The clip limit β restricts the number of grey scales that can be used. Additionally, the total clipped pixel count (n_c) is determined using the clipped histogram's height (h_k) in equation (3.8) (Krishnegowda & Ganesan, 2022).

$$n_c = R_1 \times R_2 - \sum_{k=0}^{L-1} h_k \quad (3.8)$$

Finally, interpolation is used to combine the small sections. CLAHE is utilized in medical imaging because it does not amplify noise excessively. The procedure could, however, have the downside of over-enhancing, leading to fictitious blurs in the output.

3.2.4 Homomorphic Filter

Homomorphic filtering (HF) is based on the illumination-reflectance image formation model and is particularly useful for eliminating multiplicative noise (Abdulla et al., 2012). The process begins with a logarithmic transformation that changes multiplicative components into additive ones, followed by linear filtering to address the noise. However, in many real-world scenarios, the illumination across the image is not uniform, introducing

variations that primarily impact the low-frequency areas and can be viewed as noise. Lastly, an exponential function is applied to counteract the effects of the logarithm.

Various pre-processing methodologies have been utilized in the research outlined in the chosen articles to improve outcomes. Table 3.1 presents a comprehensive overview of the research objectives, the relevant pre-processing methodologies employed, and the respective performance indicators. The approaches are systematically classified and designated with labels ranging from T1 to T8.

Table 3.1 Summary of Preprocessing Techniques and Their Performance Metrics for DR Detection

Objective	T1	T2	T3	T4	T5	T6	T7	T8	Result	Ref No
Identification of retinal Hemorrhages	✓	✗	✗	✓	✓	✓	✗	✗	Sensitivity (SN)-89 Specificity (SP)-87 Accuracy (AC)-89	(Mumtaz et al., 2018)
Automated detection of MA utilizing UL	✓	✗	✗	✓	✗	✗	✓	✗	SN- 48 FROC (Focused Receiver Operating Characteristics)-0.5 FPPI (False Positive Per Image)-43.13	(W. Zhou, Wu, Chen, Wang , et al., 2017)
Retinal vessel extraction	✓	✗	✗	✗	✗	✗	✓	✗	SN-94 SP-96 AC-94	(Vega et al., 2015)
Grading of DR lesion detection	✗	✗	✗	✗	✗	✗	✓	✗	Area Under the Curve-95.9	(Y. Yang et al., 2017)

DR fundus image classification	✓	✗	✗	✗	✗	✗	✗	✗	SN-86.03 SP-97.11 AUC-98.34 AC-92.01	(X. Li et al., 2018)
DR detection using fundus image	✗	✓	✗	✗	✗	✗	✗	✗	SN-95 SP-30 AC-75	(Pratt et al., 2016)
Automated detection of DR	✗	✗	✗	✗	✗	✗	✗	✗	AC-94.5	(Xu et al., 2017)
Retinal vessel segmentation	✓	✓	✗	✗	✓	✗	✗	✗	Precision-84.9 SP-98.01 AC-95.3 AUC-97.44	(Franklin & Rajan, 2014)
Automated screening of NPDR	✓	✗	✗	✓	✗	✓	✗	✗	SN-100 SP-89 AC-94	(Xiao et al., 2017)

*T1-CE, T2-Normalization, T3-Illumination Correction, T4- Thresholding, T5- Green Band Extraction, T6-OD and Blood Vessel Segmentation extraction, T7-Gaussian/median Filter, T8-HE

3.3 Proposed Methodology

The principal aim of retinal image processing is to identify key factors contributing to blindness. Recent research highlights the significance of studying retinal images for predictive insights into major medical disorders affecting the brain, heart, and other vital organs (Mookiah et al., 2021). Pre-processing is crucial in automated DR detection, addressing noise, device variations, poor contrast, blurring, and uneven illumination in retinal fundus images (Storath & Weinmann, 2018). The proposed pre-processing

approach was adapted and refined from various published studies (Bi et al., 2020; Hanúšková et al., 2013) to yield optimal outcomes in fundus image processing. Pre-processing enhances model performance by eliminating noise, enhancing image contrast, and equalizing illumination.

Specific images from the IDRiD (Harangi et al., 2019), Raw Images collected from an Eye center, APTOS, and DIARETDB1 (Naz, Nijhawan, Ahuja, et al., 2024) datasets exhibit significant darkness, as demonstrated in Figure 3.2 (b). Additionally, variations in colour illumination further complicate the analysis. Secondly, it is imperative to eliminate uninformative dark regions within specific images, which becomes particularly important when reducing the image size, as informative areas may become excessively small. Thus, cropping out the uninformative regions intuitively becomes necessary in such cases.

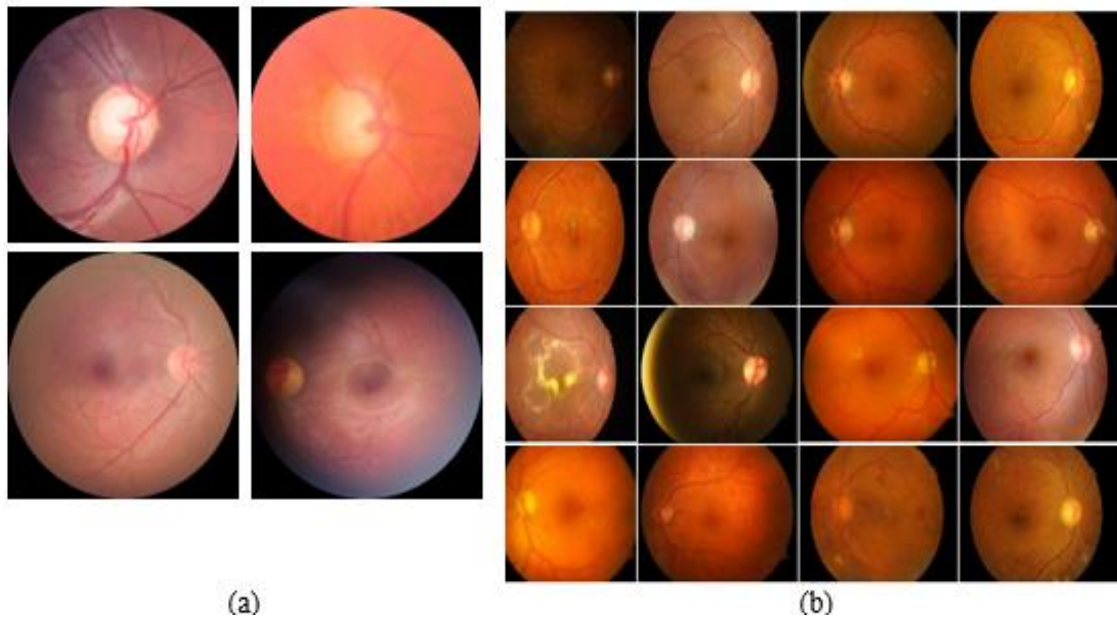


Figure 3.2: Sample Fundus Images from Utilized Dataset (a) Example retinal fundus images from the primary dataset collected at the Shiva Netralaya Centre. (b) Example images from the IDRiD and DIARETDB1 datasets illustrating dark and variably illuminated conditions

This study introduces a new pre-processing technique for DR classification aimed at improving image clarity and feature extraction quality. The method involves transforming RGB images into the HSI colour space, addressing noise and intensity issues through median filtering, and enhancing contrast using the IHE algorithm. In this context, fundus photographs from a publicly accessible and primary database are examined, with the HSI colour space utilized for colour images.

The median filter is a method utilized to minimize noise within the intensity range of an image. The reduction of noise resulting from inconsistent lighting and vignetting effects can be accomplished by using a median filter. This technique entails calculating the median value from a 3×3 -pixel neighbourhood and replacing the affected pixel with this median value. The image undergoes further noise reduction by applying a Gaussian filter, which effectively preserves the integrity of the edges throughout the filtering process.

The HSI colour space separates colour information (Hue and Saturation) from luminance information (intensity) in retinal images, which is crucial for identifying abnormalities like MAs. This separation helps in more accurate feature discrimination. The HSI colour space also helps minimize errors in microaneurysm identification, especially in regions where intensity features alone may not be sufficient. Due to their complexity and computational overhead, the CIE-Lab and XYZ colour spaces were not used. The procedures associated with image pre-processing in this study are illustrated in Figure 3.3. The conversion from the RGB colour space to the HSI colour space, in conjunction with the application of a median filter, facilitates noise reduction and enhances the extraction of intensity features pertinent to OD detection. A proposed IHE technique is used for contrast enhancement, further elaborated in the section.

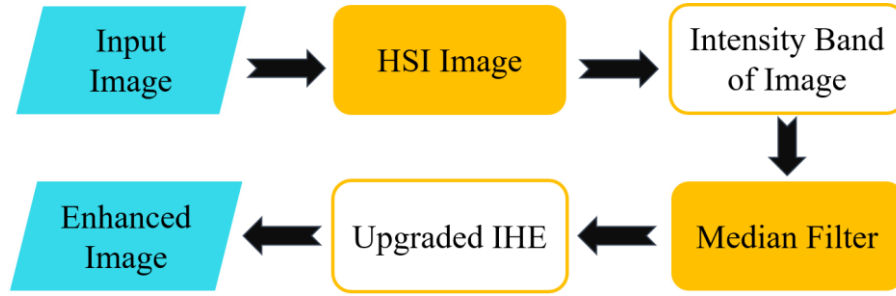


Figure 3.3: Workflow for Image Enhancement in DR Detection (Naz & Jyothi, 2025)

To transform the RGB image into HSI, the pixel values of each component are initially read within the range of [0-255] for conversion. The resulting values, falling within the range of 0-255, are divided by 255 to achieve an output range of [0, 1]. The subsequent phase involves ascertaining the value of θ . This requires evaluating the significance of the component B is $\leq G$, then $H = \theta$, and if $B \geq G$, then $H = 360 - \theta$. The inverse cosine is employed to obtain results in degrees. The hue component is then divided by 360 to get values in the range of [0, 1]. The same method is repeated to determine the saturation and intensity values, resulting in the acquisition of the HSI image.

3.3.1 Contrast Enhancement

Noise-removed image contrast is improved through the proposed IHE algorithm. Unlike CLAHE and other Gaussian enhancement techniques, IHE performs histogram equalization through the image's under-radiance calculation. The image processing tasks were implemented using the latest versions of MATLAB R2024a and Python 3.11.4, with each program handling specific tasks. A proposed IHE algorithm was implemented in Python for CE using MATLAB for noise removal, intensity band extraction, and RGB to HSI colour space conversion.

By exploiting ξ , a tuneable parameter, the histograms can be divided into sub-histograms by computing split values. An accumulated histogram and normalized count are calculated from equations (3.6) and (3.7).

$$\alpha_c(i) = \frac{\phi(i)}{\epsilon} \text{ for } 0 \leq i \leq I - 1 \quad (3.6)$$

$$\Gamma(k) = \sum_{i=0}^k \alpha_c(i) \text{ for } 0 \leq i \leq I - 1 \quad (3.7)$$

In the field of image processing, the histogram of an image is denoted by ϕ . The variable I denotes the total intensity levels present within the image, whereas ϵ indicates the total pixel count within the image and represents the corresponding intensity values. Normalized histogram count and accumulated histogram count are the parameters Γ and α_c respectively for a given image Γ_p , which is a controlling parameter and can be calculated using equation (3.8).

$$\sum_{j=0}^{\Gamma_p} \Gamma(j) \approx \xi \text{ for any } 0.1 \leq \xi \leq 0.9 \quad (3.8)$$

S_v represents the split value that can be calculated using equation (3.9).

$$S_v = (I - 1) - \Gamma_p - 1 \quad (3.9)$$

The tuneable parameter, ξ , and the enhancement level is inversely proportional. Furthermore, an increase in the parameter ξ corresponds to a rise in the value of Γ_p . The initial sub-histogram is derived from a lower value of ξ , while the subsequent sub-histogram is generated from a comparatively higher value of ξ .

The initial and secondary sub-histograms undergo separate equalization procedures. Low-intensity pixels can be mapped to high-intensity pixels due to the extendedness of the first sub-histogram. However, the second sub-histogram has a lower range to extend as the pixel values are already high. This saves the higher-intensity pixels from over-enhancement.

3.3.2 Intensity Histogram Equalization Technique

The IHE algorithm, as illustrated in Figure 3.4, operates by calculating the absolute difference between the intensity values, denoted as ω_1 and ω_2 , which are derived through equation 3.10. The improved image is created using the two sub-histograms obtained in the previous step. The intensity values, denoted as ω_1 and 2, are computed through a recursive process until the absolute difference between them falls below a predetermined error threshold, denoted as e . In this context, the threshold value is set at 0.002. The subsequent section delineates the comprehensive algorithmic procedures.

IHE Algorithm

- 1 Calculate a histogram $\emptyset$ for an input image.
 - 2 Acquire intensity values for the input image using equation (3.10) with I set to 256.

$$\omega_1 = \frac{\sum_{i=0}^{I-1} \emptyset(i)}{I \cdot \sum_{i=0}^{I-1} \emptyset(i)} \quad (3.10)$$
 - 3 Determine the split value S_v as outlined in equation 3.9.
 - 4 Divide the histogram into sub-histograms $\emptyset_l$ for the intensity value from 0 to S_v and $\emptyset_u$ for the range $S_v + 1$ to $I - 1$.
 - 5 Equalize histograms $\emptyset_l$ and $\emptyset_u$ within their respective intensity range.
 - 6 The process outlined in Step 2 is reiterated to determine the intensity values ω_2 of the equalized image.
 - 7 Continue executing steps 1-6 until the condition $|\omega_1 - \omega_2| \leq e$ is satisfied.
 - 8 Integrate $\emptyset_l$ and $\emptyset_u$ to re-establish histogram $\emptyset$.
-

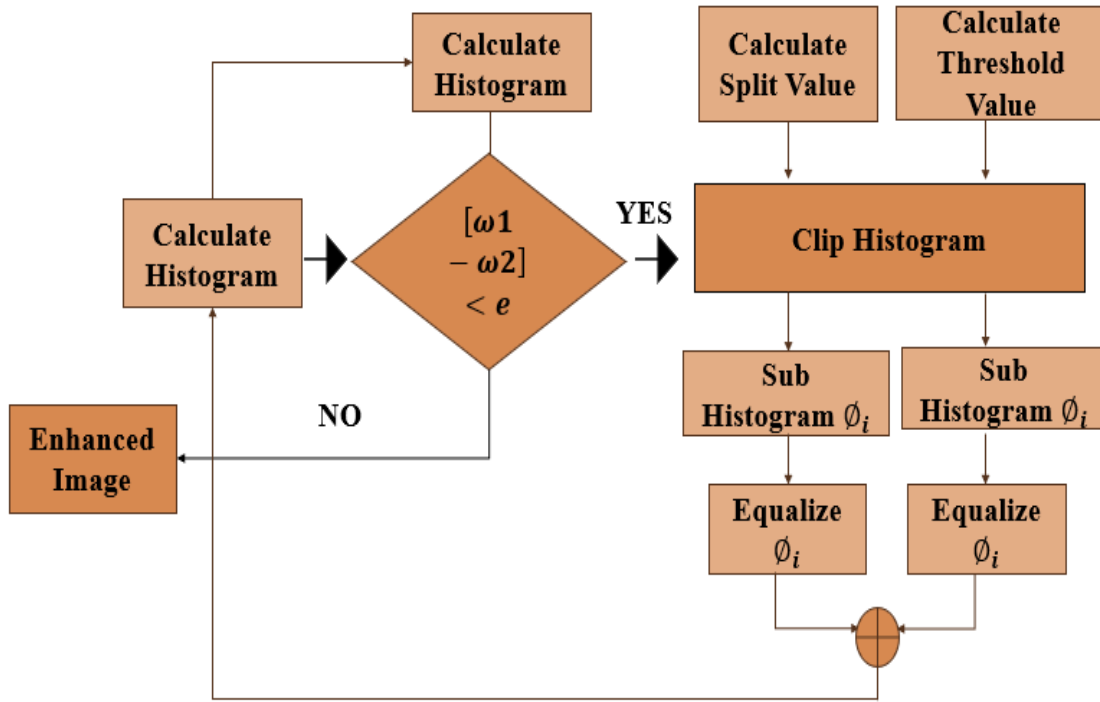


Figure 3.4: IHE Flow chart

The median filter serves as a proficient technique for mitigating noise within the intensity spectrum of an image. This method effectively mitigates disturbances arising from inconsistent lighting conditions and vignetting effects by computing the median value within a 3×3 -pixel neighbourhood. Following this, the pixel recognized as noisy is replaced with the median value, thus improving the overall contrast. The image is subjected to additional noise reduction by applying a Gaussian filter, effectively maintaining edge integrity during filtering. Figure 3.5 depicts the various phases of image pre-processing utilized in a clinical database.

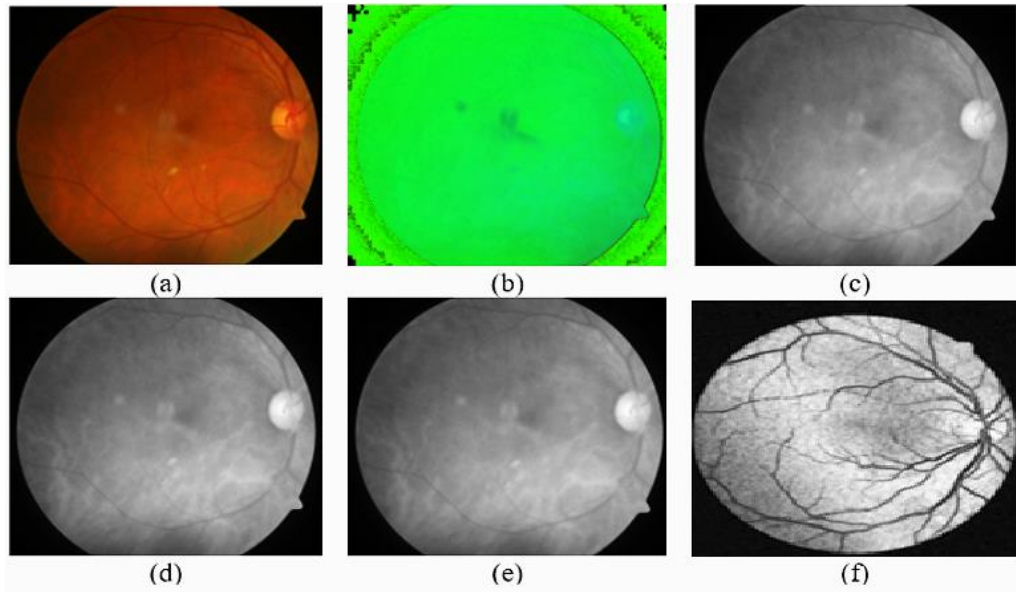


Figure 3.5: Pre-processing steps (a) RGB Image (b) HSV Image (c) Intensity band of image (d) Median Filtered Image using I band (e) Gaussian filtered image (f) IHE Image with circle cropping.

3.3.3 Colour Fundus Image Preprocessing

However, some vital information can be lost due to the nature of grayscale image preprocessing. MAs, tiny red dots that appear in the retina, contain critical colour information that is crucial in accurate diagnosis. The loss of colour details during preprocessing may obscure these vital features. The color fundus images are also processed to preserve and enhance structural and colour-related information. This approach helps to retain the critical features that aid in identifying retinal abnormalities more effectively.

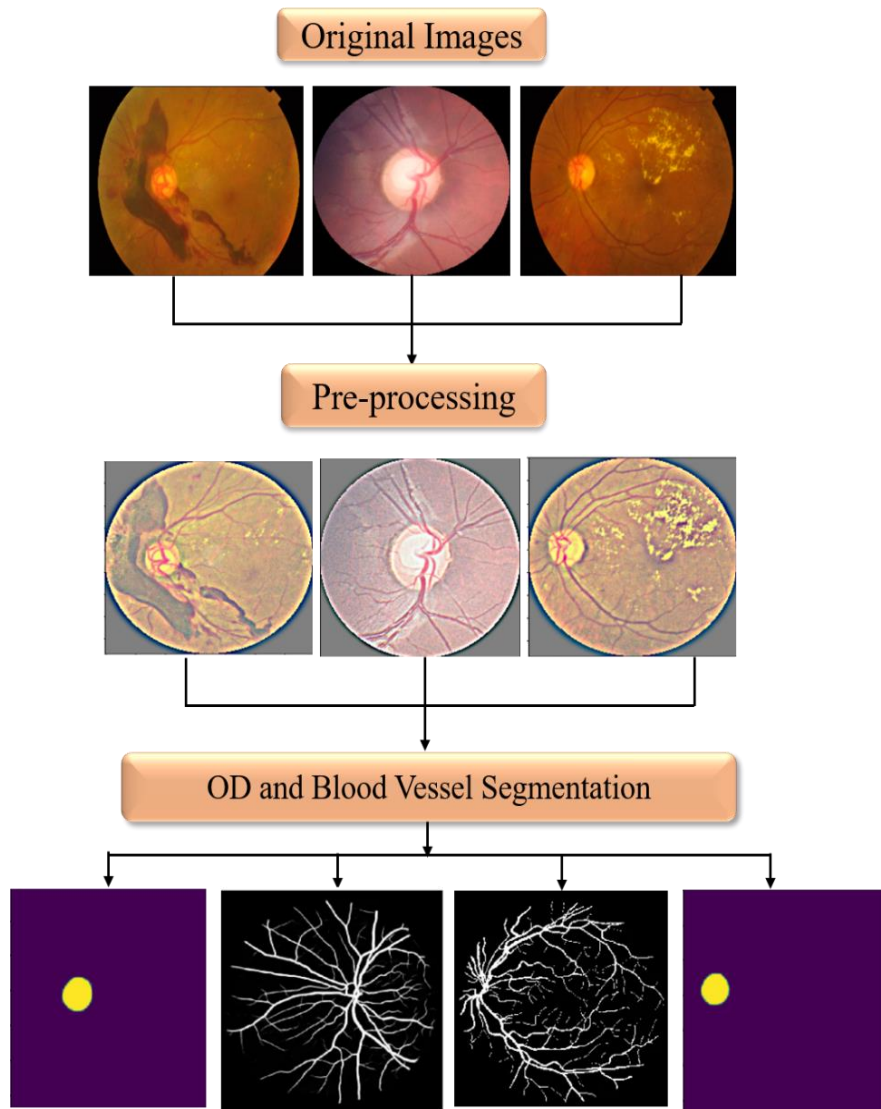


Figure 3.6: Color Image Preprocessing and Background Segmentation

An alternative methodological approach for the extraction of colour features during the pre-processing phase of fundus image analysis is depicted in Figure 3.6. The images are converted from RGB to BGR format to facilitate further processing. A pre-processing method addresses lighting conditions and dark areas (Salamat et al., 2019). This method includes rescaling the images to a consistent radius (300 to 500 pixels) for uniformity. The local average colours are then subtracted, with 50% of the average colour mapped to grey.

Furthermore, the images are reduced to 90% of their original dimensions to alleviate boundary effects. A circle cropping technique removes uninformative black areas that may be present in some images.

This technique enables the cropping of uninformative areas. While this process may result in the loss of some scabs or cotton wools, it effectively eliminates black regions that do not contain relevant information. The primary objective of the proposed research is to identify yellow and red lesions in specific regions of the retina.

3.4 Background Segmentation

Background segmentation in fundus images refers to separating the foreground (the essential structures of the retina) from the background (typically the irrelevant or non-informative parts of the image). Fundus photographs offer an extensive depiction of the posterior segment of the eye, which includes anatomical components such as the retina, optic disc, macula, and the associated vascular system. The utilization of these images is crucial for the identification and diagnosis of various ocular disorders, such as DR, glaucoma, and age-related macular degeneration.

The principal objective of background segmentation is to detect and separate regions of interest, including blood vessels, the OD, and the macula while eliminating non-essential areas. This technique enhances the examination and processing of critical elements within the image. Effective segmentation enables accurate disease detection and diagnosis by enhancing retinal structure visibility and reducing noise.

3.4.1 Optic Disc Segmentation

The OD is a highly concentrated region inside a fundus picture. Researchers commonly determine the OD by analyzing its morphological characteristics, luminance, and

dimensions. Numerous algorithms have been introduced as significant methodologies for the segmentation of the OD. There are two main types of algorithms. The initial element involves the identification of the OD within a retinal image. This localization process entails ascertaining the OD's precise position in the visual representation of the retina. The subsequent element focuses on the segmentation of the OD area. The delineation of the OD within a retinal image facilitates the isolation of this particular anatomical region.

Gagnon et al. [114] designed a method for detecting ocular degeneration, macular conditions, and retinal networks by applying pyramidal decomposition, template matching, and confidence assignment. Claudius et al. (Geetharamani & Balasubramanian, 2016) developed a method for detecting OD in colour fundus images using a cascade classifier. The accuracy was 100% for standard retinal images and 75% for images depicting pathological conditions.

Ravishankar et al. (Ravishankar et al., 2009) identified prominent blood vessels and employed their intersections to ascertain the OD's location. Youssif et al. used directional and 2-D Gaussian-matched filters for OD detection (Youssif et al., 2008). Fleming et al. (Fleming et al., 2006) used Hough transform and template matching for OD and fovea detection. Rangayyan et al. (Rangayyan et al., 2010) used a Gabor filter-based approach to locate the OD center, but it has high computational complexity. In the proposed approach, object detection is segmented using Morphological opening, morphological closing, and erosion for shape segmentation.

After obtaining the enhanced image, the next step is eliminating the OD from the picture, as shown in Figure 3.7, to avoid interference during MA detection, as both share similar characteristics. Morphological opening, morphological closing, and erosion are the binary operations that detect OD from the fundus image (Saranya et al., 2022). Cavities in various areas become more prominent during erosion, and other minor details are eliminated.

During dilation, the cavities among the area become smaller by adding an extra pixel layer at the boundaries, and minor details are retained. These are the general edge-preserving methods (Salongcay et al., 2022). A morphological closing operation is performed as a preliminary step to attain the desired shape of the OD within the enhanced image. This closing operation is characterized by a sequence that begins with dilation, which is subsequently followed by erosion. In contrast, the process of morphological opening encompasses an initial phase of erosion followed by a subsequent phase of dilation. An image threshold is then performed to acquire a binary representation.

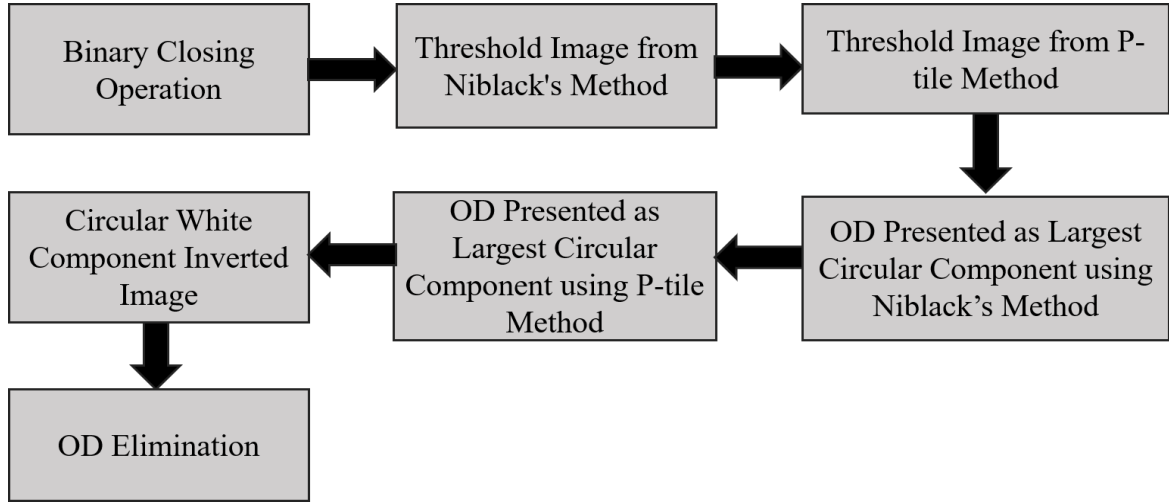


Figure 3.7: Steps for OD Elimination

An image Ω is obtained as the output of the threshold operation that contains the connected region C_i . Moreover, it can be equated as in equation (3.11).

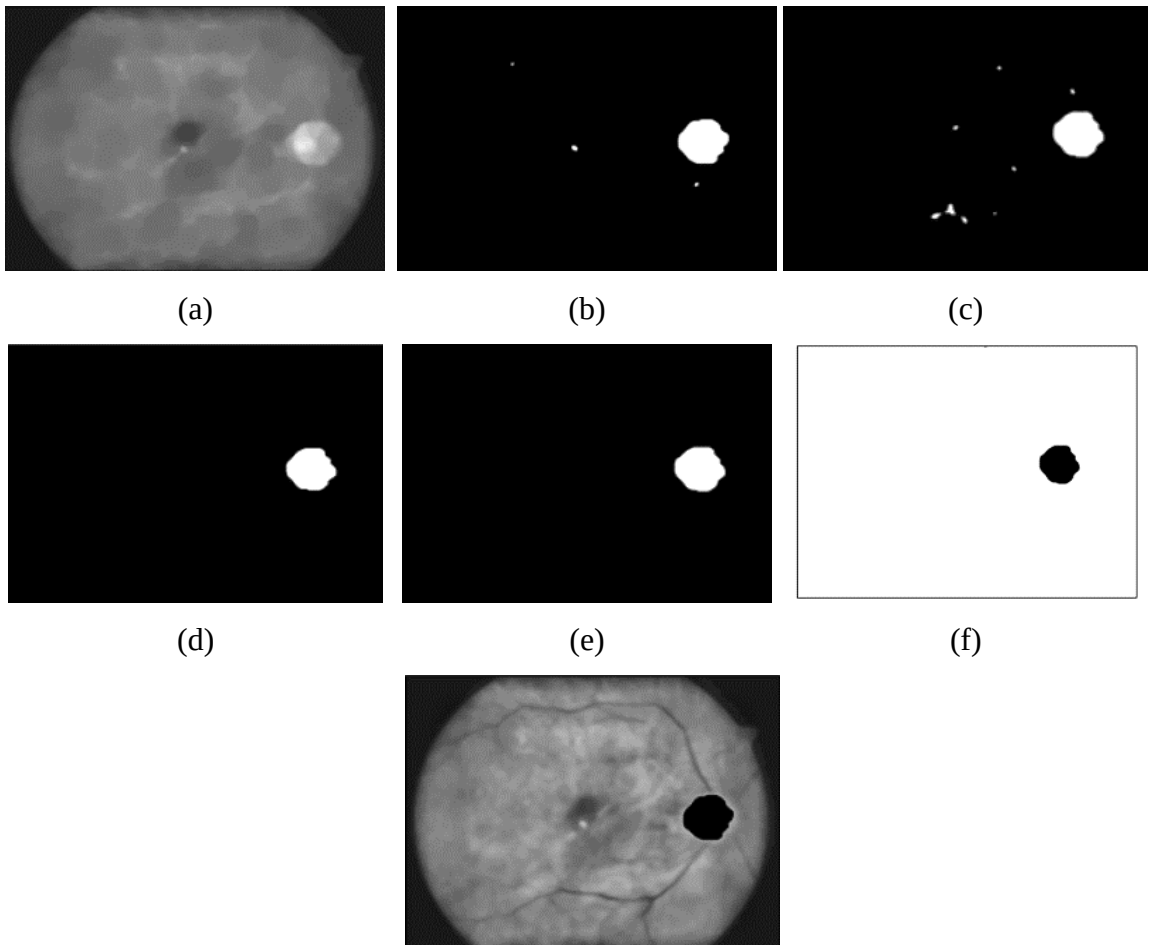
$$\Omega = \cup_{k \in m} C_k, C_i \cap C_j = 0, \forall i, j \in m, i \neq j \quad (3.11)$$

k denotes the connected components in the enhanced image, where m varies from 1 to k . Compared to the background, additional pixels are detected in the details, which contain a disc-shaped structure that is associated with C_i , which is essentially the OD. The process allows for effective segmentation of OD from the remainder of C_i . Here, C_i contains R_i which forms the most significant component. The conciseness of R_i can be measured

using equation (3.12). Additionally, the variable m ranges from 1 to k , where k represents the total count of connected components identified within the enhanced image. When analyzing the background, extra pixels are detected in the details, uncovering a disc-shaped structure linked to C_i , which aligns with the OD. Consequently, a successful segmentation of OD from the other structures of C_i has been accomplished. C_i includes R_i which represents the most crucial element. The assessment of R_i conciseness can be achieved using equation (3.12).

$$C(R_i) = 4\pi \frac{A(R_i)}{P^2(R_i)} \quad (3.12)$$

Where, $A(R_i)$ denotes the pixel count within the i^{th} region, while $A(R_i)$ also refers to the pixel count in the vicinity of the region (R_i). The findings are illustrated in Figure 3.7.



(g)

Figure 3.8: OD elimination process (a) morph closing operation on IHE processed image (b) threshold image using Niblick's method (c) threshold image using p-tile method (d) most significant circular section using Niblick's method (e) most significant circular section using p-tile method (f) IHE image (g) OD eliminated image.

Percentile (p-tile) and Nilblack's methods (Taghizadeh & Mahzoun, 2011) are used to determine the threshold technique to obtain the binary image (Bin Rais et al., 2004). There are more significant contrasts in the OD region of the image than in other areas. The percentage is calculated as the measure of brightness, and it is assumed that in the fundus image, approximately 2% of brightness is for the OD. This percentage assumption calculates the binary image using the p-tile algorithm. The highest compactness value is obtained by one of the connected components that form the OD. This method is superior to the existing Circular Hough Transformation (CHT), as mentioned by (Long et al., 2019). The OD elimination is depicted in Figure 3.8.

This method identifies circles with a robust circular reaction, which matches the OD regions. Other circles that do not have a significant circular response are most likely yellow lesions or other deceptive spots. Figure 3.9 illustrates the images that have undergone preprocessing utilizing colour fundus techniques.

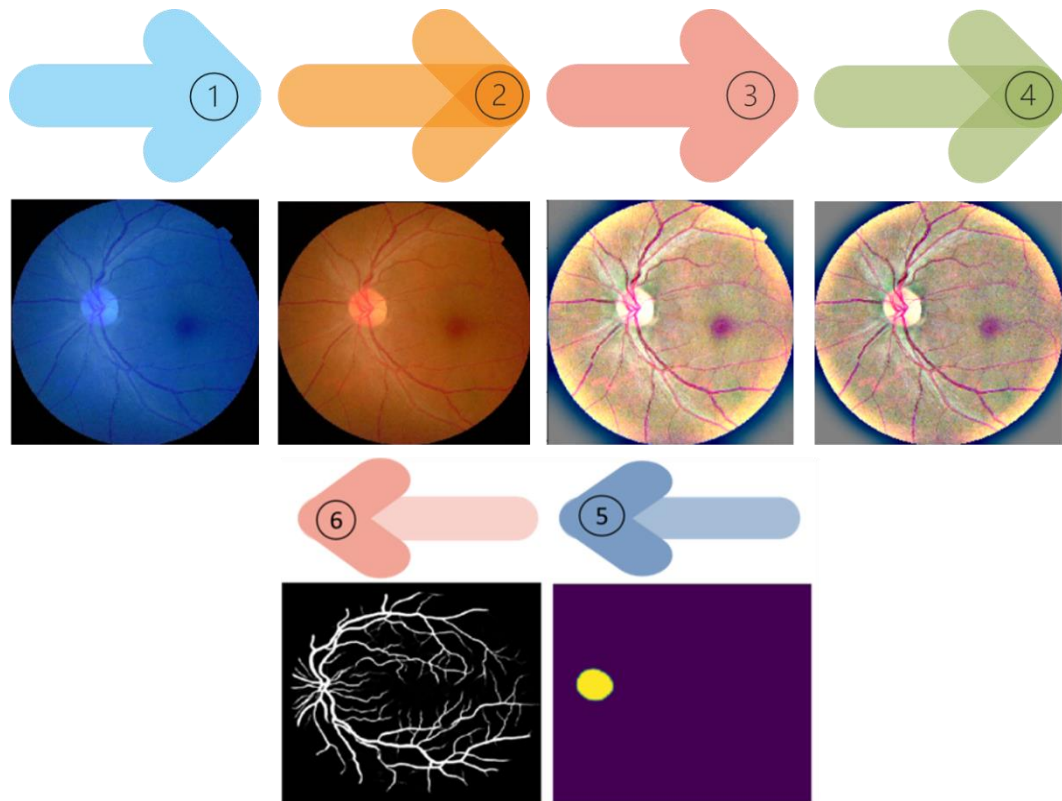


Figure 3.9: Steps for Color Fundus Image Preprocessing and Background Segmentation

3.4.2 Blood Vessel Segmentation

Blood vessels are essential pathways that facilitate circulating blood throughout the entire body, including the retina. As if they were tree branches, retinal vessels have a complex structure with varying widths, with their most comprehensive portions at their origins and narrowest portions at their ends. In fundus images, thin vessels exhibit low contrast, resulting in seamless integration with the background. An unhealthy retina can have abnormalities like dark lesions, bright lesions, abnormal vessel growth, and venous beading.

Different researchers have suggested various segmentation techniques for extracting blood vessels. Moccia presented several noteworthy findings regarding blood vessel segmentation in this review (Moccia et al., 2018). Data categorization methods can be broadly classified into two primary categories: supervised learning and UL. In unsupervised methodologies, various techniques such as matched filtering, morphological operations, profile modelling, active contour models, and multi-scale approaches are employed for retinal vessel segmentation. In their article, Hoover et al. [125] presented the concept of recurrent threshold probing on MF response images.

According to Zhang et al. (Zhang et al., 2010), the Gaussian-based MF approach undergoes thresholding according to the first-order derivative of the initial filter. Researchers have explored various techniques in supervised vessel structure segmentation (Paris et al., 2011; Ricci & Perfetti, 2007; Soares et al., 2006; Staal et al., 2004). Soares et al. (Soares et al., 2006) explored Gaussian mixture model-based classification followed by the 2-D Gabor wavelet transform coefficient at diverse scales. This miss-match leads to the loss of true positives. Also, OD regions with vessel-like profiles can lead to false positives.

3.4.2.1 Fuzzy Inference based blood vessel Segmentation

Blood vessels are characterized as representations of curved singularities. These tubular structures exhibit a continuously varying width. The segmentation of an extensive vessel map utilizing two-dimensional pictures is a difficult task. This research presents a methodology for segmenting blood vessels in fundus images utilizing fuzzy inference systems.

The utilization of Fuzzy Inference systems for the segmentation of blood vessels presents significant advantages in the realm of edge detection, thereby differentiating it from traditional edge detection methodologies (Ricci & Perfetti, 2007). The fuzzy approach is particularly advantageous as it effectively handles uncertainty in the available information, providing more robust and accurate results (Mishra et al., 2020).

The present research emphasizes enhancing edge information extracted from input fundus images and refining the output through a fuzzy logic-based approach. The following subsection details the algorithm developed for the fuzzy inference-based blood vessel segmentation technique to achieve this. As illustrated in Figure 3.10, sample fundus images from the utilized dataset, along with their extracted blood vessels, visually demonstrate the effectiveness of this method.

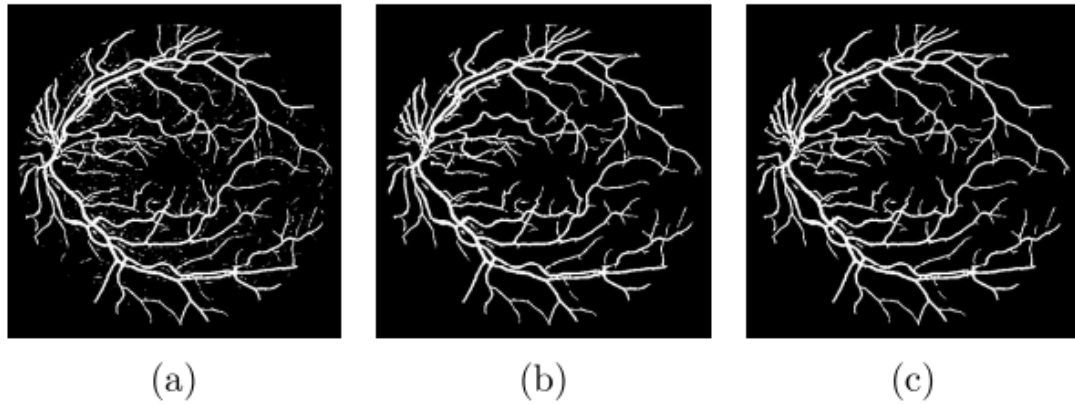


Figure 3.10: Blood Vessel Segmentation from APTOS and DIARETDB1 Dataset

Algorithm: Fuzzy Inference-based Blood Vessel Segmentation

Input: OD segmented image

Output: Blood vessel segmented image

Start

Step 1: Scale the input image to regulate it.

Step 2: Apply convolution in the x and y directions to obtain image gradients.

Step 3: Establish a fuzzy inference system to facilitate the segmentation of blood vessels, wherein the Gaussian membership function is utilized for defining membership degrees

Step 4: Analyze the blood vessel segmentation output for each row of pixels in the image I (x, y) utilizing the corresponding rows as I_x and I_y as the image gradient of the towards x & y direction is specified as follows;

$$I(x, y) = \text{white for } I_x = 0 \text{ and } I_y = 0; \text{ for background}$$

$$I(x, y) = \text{black for } I_x \neq 0 \text{ and } I_y \neq 0; \text{ for edge}$$

Stop

3.5 Result and Discussion

A total of four distinct fundus image datasets were employed to assess the efficacy of the proposed preprocessing technique. Chapter 1 discusses the specifics of each of the datasets. This study used APTOS (Sikder, 2019), Fundus images, and DIARETDB1 and IDRiD datasets. Each set of images has a different FoV, illumination, dimensions, and contrast.

This section assesses the suggested approach for preprocessing retinal images for the 20 sample images (S1-S20). The proposed methodology is evaluated using publicly available datasets, namely APTOS and IDRiD, and proprietary datasets assembled explicitly for the proposed study. The validation of the algorithm is conducted through the application of multiple performance metrics, including the Contrast Improvement Index (CII), the Absolute Mean Brightness Error (AMBE), and the Peak Signal-to-Noise Ratio (PSNR).

3.5.1 Contrast Improvement Index (CII)

The Contrast Improvement Index (CII) assesses the enhancement of contrast in fundus photographs by analyzing the disparity in contrast between the processed image and its original image. The mathematical representation is achieved by comparing the contrasts between the enhanced and original images. Equation (3.13) illustrates how contrast is typically quantified by subtracting the maximum intensity from the minimum or using the standard deviation.

$$CII = \frac{C_{enhanced}}{C_{original}} \quad (3.13)$$

Where C represents the contrast of the image.

3.5.2 Absolute Mean Brightness Error (AMBE)

The AMBE method quantifies the luminance disparity between original and enhanced images. As outlined in equation (3.14), a reduced AMBE value signifies more remarkable brightness preservation. The process involves calculating the absolute disparity between the intensity values of the original image ($M_{original}$) and those of the enhanced image ($M_{enhanced}$).

$$AMBE = | M_{original} - M_{enhanced} | \quad (3.14)$$

3.5.3 Peak Signal-to-Noise Ratio (PSNR)

A PSNR is a metric utilized to evaluate the quality of an enhanced image to its original counterpart. The PSNR is expressed in decibels (dB) and is calculated using the MSE between the two images. A higher PSNR value implies less distortion, indicating superior quality. According to equation (3.15), the PSNR measures distortion.

$$PSNR = 10 \cdot \log_{10} \left(\frac{MAX_I^2}{MSE} \right) \quad (3.15)$$

In the context of an 8-bit fundus image, the symbol MAX_I represents the highest possible pixel intensity value, which is quantified as 255. The experimental outcomes of the proposed methodology are presented in Figures 3.11 and 3.12, encompassing the APTOS, IDRiD, and primary datasets.

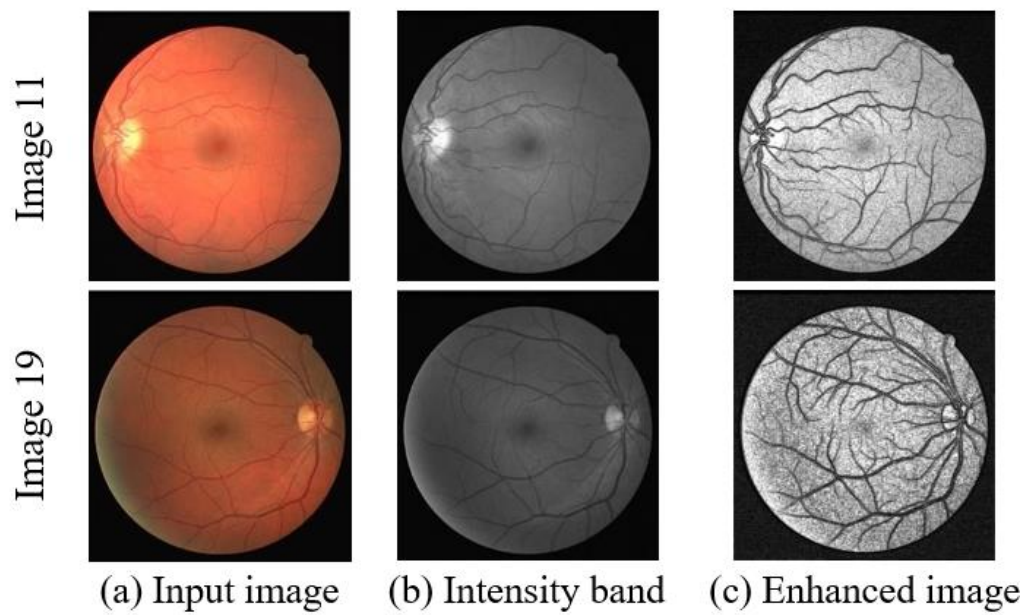


Figure 3.11: Proposed Preprocessing Results for APTOS Sample Images

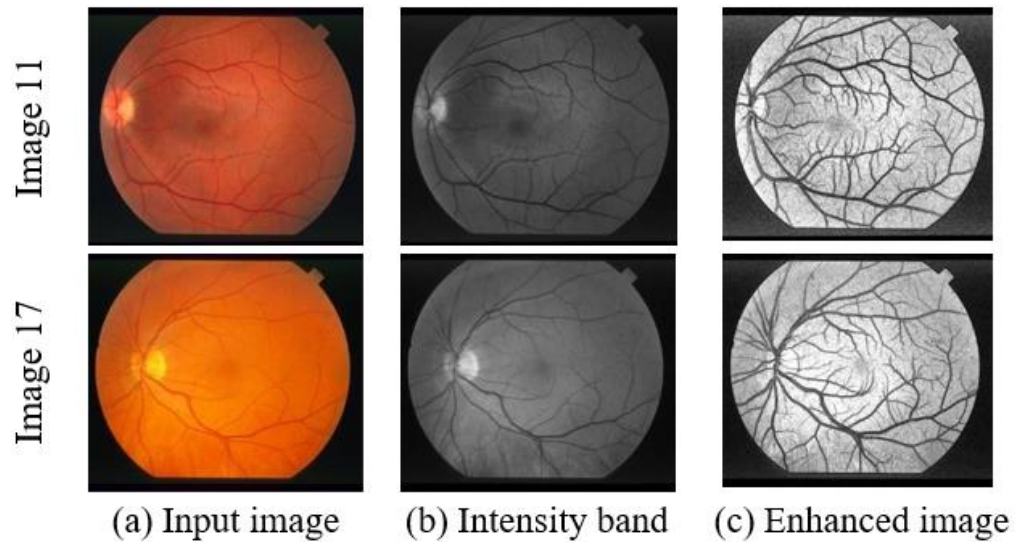


Figure 3.12: Proposed Preprocessing Results for IDRiD and Primary Dataset Sample Images

Figure 3.11 illustrates the pre-processed images corresponding to Image 11 and Image 19 from the APTOS database to the original input images. Specifically, Figures 3.11 (a) and 3.11 (b) present the original colour fundus images alongside the extracted intensity bands for each respective image. Figure 3.11 (c) illustrates the improved image generated using the suggested preprocessing technique.

Similarly, Figure 3.12 illustrates the resultant images for two distinct samples (Image 11 and Image 17) sourced from the IDRiD database. The results demonstrate a significant enhancement in the differentiation between vascular structures and their adjacent background, leading to improved visibility of the vessels in the resultant images compared to the initial green channel for both sets of images. An assessment of the suggested methodology was conducted utilizing a diverse range of established contrast enhancement techniques, such as HE, CLAHE, Power-law Transformation (PT), Discrete Wavelet Transform (DWT), and Homomorphic Filtering (HF), which were applied to both datasets. Table 3.2 compares the CII across different techniques utilized on images from the APTOS, IDRiD, and Primary datasets.

Table 3.2 Comparison of CII for various techniques on the applied database for this study

Images	HE	CLAHE	PT	DWT	HF	IHE (Proposed Method)
S1	2.82	3.31	1.13	0.10	1.07	4.63
S2	2.37	3.05	1.13	0.40	1.00	5.59
S3	2.29	2.31	1.13	0.33	1.12	3.44
S4	1.67	3.84	1.13	0.10	1.03	8.18
S5	3.21	3.20	1.14	0.09	1.12	4.94
S6	2.66	2.39	1.14	0.52	1.00	3.14
S7	1.60	3.32	1.14	0.29	1.06	4.92
S8	2.76	2.89	1.12	0.28	0.99	6.32
S9	4.74	4.27	1.15	0.29	1.02	7.87
S10	2.35	3.22	1.13	0.12	1.14	6.36
S11	2.03	3.00	1.14	0.01	1.09	5.53
S12	2.93	3.09	1.14	0.10	1.03	4.58

S13	2.62	3.57	1.14	0.19	1.10	5.46
S14	2.48	3.08	1.13	0.34	1.03	5.88
S15	1.43	3.97	1.12	0.51	1.02	7.59
S16	3.08	2.87	1.14	0.28	1.02	4.17
S17	3.26	2.86	1.14	0.36	0.80	4.65
S18	3.33	3.45	1.15	0.23	0.95	3.90
S19	2.10	2.40	1.13	0.35	1.11	4.00
S20	3.26	3.04	1.14	0.23	1.10	5.61
Average	2.65	3.16	1.14	0.26	1.04	5.34

Table 3.2 demonstrates that the method under consideration achieves an average CII value of 5.34, the highest recorded among the evaluated techniques. Which further specifies a more significant intensity disparity between the vessels and the background. Moreover, Table 3.3 compares the proposed approach for brightness preservation quantification AMBE among various methodologies on the diverse image samples from APTOS, IDRiD, and the Primary dataset.

Table 3.3 Comparison of AMBE for various techniques on the used database

Images	HE	CLAHE	PT	DWT	HF	IHE (Proposed Method)
S1	54.76	16.66	59.18	69.68	60.69	35.48
S2	50.36	14.81	64.33	74.24	64.35	39.82
S3	76.60	23.01	36.84	48.97	39.55	58.95
S4	61.60	17.06	52.39	63.21	52.11	29.62
S5	71.26	19.66	42.25	53.97	44.78	29.62
S6	57.81	15.40	56.11	66.87	56.47	13.70
S7	60.97	17.57	53.03	63.88	54.60	49.89
S8	65.16	15.98	48.55	59.76	48.66	32.57
S9	45.78	10.52	69.08	78.48	68.13	34.66
S10	73.17	20.49	40.55	52.29	43.32	39.15
S11	53.79	14.38	60.66	70.83	60.87	59.79
S12	59.47	16.27	54.78	65.76	56.01	38.70
S13	49.63	13.85	64.75	74.59	65.96	28.83

S14	60.05	17.41	53.19	64.39	54.63	33.76
S15	83.02	23.80	31.37	42.71	33.54	35.53
S16	48.42	13.41	65.80	75.61	66.21	08.35
S17	38.38	07.50	77.43	85.71	72.59	21.25
S18	46.46	11.88	67.96	77.48	67.57	37.86
S19	74.66	22.82	39.14	50.96	41.55	38.70
S20	63.62	17.23	49.57	60.91	51.67	28.83
Average	59.75	16.49	54.35	65.02	55.16	33.76

Table 3.4 Comparison of PSNR for various techniques on the applied database

Images	HE	CLAHE	PT	DWT	HF	IHE (Proposed Method)
S1	35.87	28.17	32.37	38.93	37.33	39.62
S2	37.11	28.49	31.78	37.67	36.03	35.20
S3	39.60	28.03	32.56	39.60	38.37	39.01
S4	35.72	27.84	32.31	38.91	37.76	35.07
S5	33.57	29.13	32.40	30.36	38.72	35.07
S6	24.73	29.79	31.56	32.69	36.95	35.30
S7	34.60	29.37	32.23	39.60	38.29	35.94
S8	37.05	30.68	32.01	37.74	36.47	37.79
S9	33.76	28.71	32.31	40.09	38.69	37.90
S10	37.90	31.23	31.90	37.11	35.48	41.47
S11	35.98	29.37	32.19	38.82	37.55	37.66
S12	33.59	29.01	32.17	30.26	38.23	38.21
S13	34.42	29.22	31.87	39.69	37.61	44.69
S14	34.81	29.39	31.96	39.44	37.78	34.54
S15	31.20	26.70	32.25	41.79	39.24	36.13
S16	37.07	29.12	32.10	37.77	36.46	38.61
S17	38.48	30.86	31.46	36.40	34.86	40.15
S18	34.39	26.50	32.47	39.84	38.45	31.85
S19	31.92	25.72	32.34	40.40	35.31	39.80
S20	31.36	25.94	32.27	31.58	39.17	37.59
Average	34.59	28.69	32.12	37.36	37.44	37.47

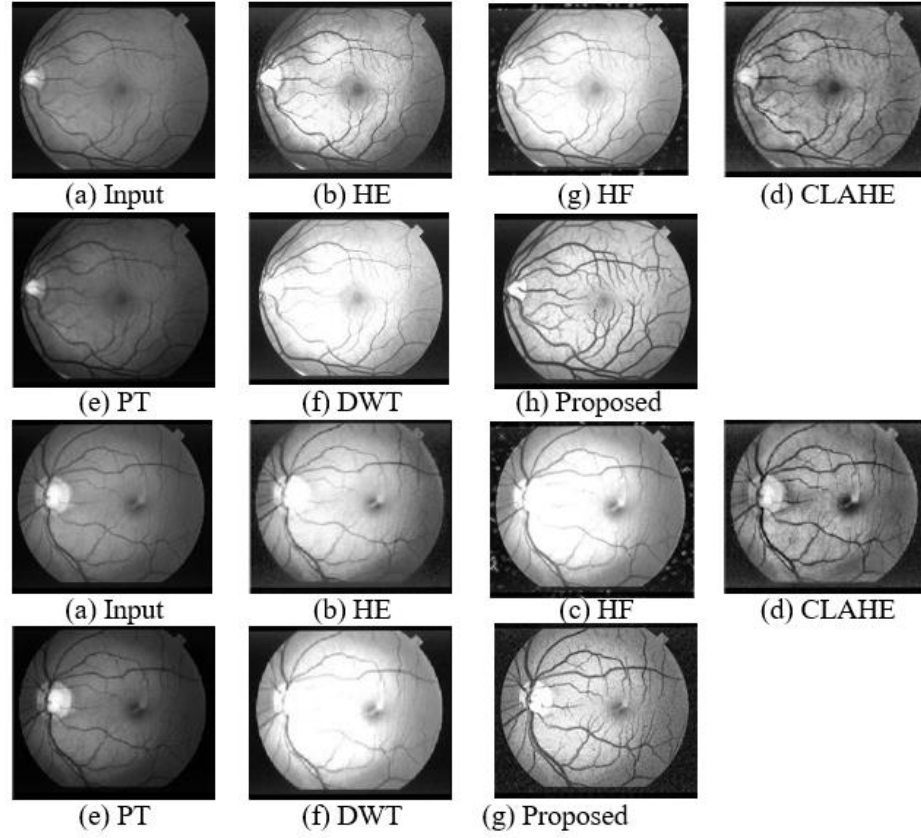


Figure 3.13: Comparison of Proposed Approach with HE, HF, CLAHE, PT, and DWT Techniques on the Applied Database

Table 3.3 presents the average AMBE value achieved using the proposed method for the applied dataset 50.77. The CLAHE technique yields the lowest value of 16.49, while the proposed method yields the second lowest AMBE value. HE, CLAHE, PT, DWT, and HF enhanced images are presented individually in Table 3.4 for the APTOS, IDRiD, and Primary databases. High PSNR values indicate excellent image detail preservation.

The proposed methodology demonstrates the highest PSNR for the utilized dataset, as indicated in Table 3.4. The suggested method demonstrates robust performance according to the specified evaluation metrics. The proposed framework improves image contrast using HE and JHE techniques but blurs regions near the OD due to grey-level mapping.

CLAHE preserves image brightness, whereas HE, JHE, and CLAHE methods exhibit darkening effects, potentially misinterpreting finer vascular structures.

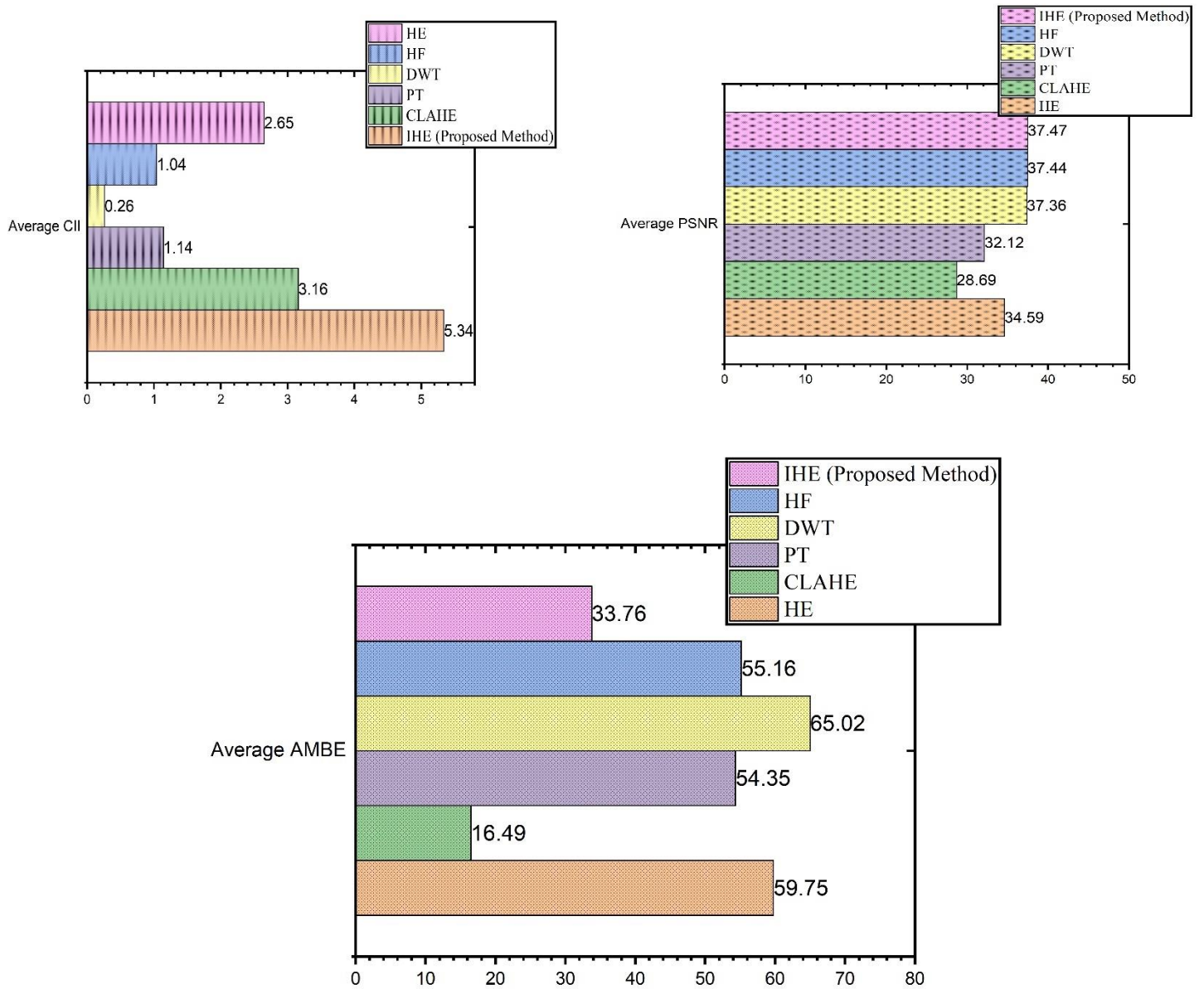


Figure 3.14: Graphical representation of the mean values of the evaluation parameters across diverse methods

The proposed method improves contrast at vessel boundaries while avoiding fuzzy edges, leading to pronounced vessel highlights. Figure 3.13 displays contrast-enhanced images devoid of lesions, utilizing various techniques in conjunction with the applied database from this study. Figure 3.14 illustrates the graphical representation of the average values derived from multiple performance analyses conducted to evaluate the applied algorithm.

3.6 Summary

This chapter presents a new pre-processing technique for DR classification aimed at enhancing image clarity and feature extraction. The approach converts RGB images into the HSI colour space, addressing noise and intensity issues through median filtering and improving contrast using the IHE algorithm. Fundus photographs from exclusive and publicly available databases are processed. Background segmentation separates blood vessels and the OD, thus reducing false positive signals in DR classification. The algorithm under investigation is compared to prominent contemporary techniques, utilizing metrics such as CII, PSNR, and AMBE, which indicate superior performance. The enhanced preprocessing framework significantly improves feature discrimination and strengthens classification robustness under varying lighting conditions and image quality constraints, establishing its efficacy over contemporary techniques and contributing to the advancement of automated DR diagnosis.

Chapter IV

Fuzzy C Means Convolutional Neural Network

The traditional clustering method extracts features from feature vectors derived from domain-specific knowledge. DL approaches combine feature learning and clustering to cluster original images with higher direct performance. Regular neural networks project data into representations for supervised tasks, learning network weights through gradient descent and backpropagation techniques. The backpropagation process can lead to a simplistic outcome characterized by null weights and representations within the neural network. This phenomenon suggests that traditional feedforward neural networks may not be appropriate for tasks involving unsupervised representation learning. The integration of an unsupervised clustering loss does not alter the fundamental nature of this simplistic methodology.

Investigations into deep clustering (Miotto et al., 2017) methodologies have addressed the challenges associated with clustering loss functions by incorporating them within auto-encoder architecture. The system comprises two primary components: an encoder network and a decoder network, utilized for UL tasks such as feature extraction and data reconstruction. They capture meaningful data representations, making them suitable for embedding and clustering tasks. Deep clustering methodologies that utilize auto-encoders integrate the clustering loss within the latent space subsequent to the encoding process.

4.1 FCM Clustering: Methodology and Extensions

The study explores the challenges in clustering algorithms and discusses the evolution of k-means, a popular and influential method. This approach employs Euclidean distance metrics to establish clusters and categorizes data into k distinct clusters according to user-defined parameters.

The procedure operates within a spatial context, utilizing the mean to determine the centroid for each cluster. Iterative methodologies continue to operate until a state of convergence is reached, thereby minimizing the spatial disparity between data points and their corresponding cluster centroids (Zheng et al., 2015). The flow structure of the FCM is shown in Figure 4.1. The proposed algorithm operates under a UL paradigm characterized by numerous sub-optimal states contingent upon the initial value selected. The k-means clustering algorithm is widely regarded as an effective and simple method for the classification of data (Wikaisuksakul, 2014). The k-means algorithm is characterized by its objective function, denoted as J , articulated in equation (4.1).

$$J = \sum_{i=1}^m \sum_{k=1}^K w_{ij} \|x^i - \mu_k\|^2 \quad (4.1)$$

Let m signify the quantity of data points, while k indicates the predetermined total number of clusters as defined by the user. x^i represent the data point in the i^{th} vector, while μ_k denotes the K_{th} cluster center, and $w_{ij} = 1$ for data point x^i if it is a member of the cluster k ; otherwise, $w_{ij} = 0$.

The k-means clustering algorithm provides a fundamental basis for the formulation of the FCM algorithm (Verma et al., 2016). The FCM method represents a soft clustering technique that outperforms the k-means algorithm in detecting overlapping clusters. This iterative technique minimises the objective function while assessing convergence through squared error metrics. FCM operates under the UL framework and forms clusters based on

random initialization. The methodology consists of three key stages: determining the Cluster Center, calculating the Membership Function, and objective function. The assessment of the convergence process is conducted utilizing square error analysis. The objective function pertinent to FCM is articulated in equation (4.2).

$$J_{iter} = \sum_{i=1}^N \sum_{j=1}^{nc} [M^f \left\| D_{x_i - C_j} \right\|^2] \quad (4.2)$$

N signifies the total number of data points within the data vector, while nc refers to the user-defined number of clusters that can be specified based on individual requirements. M^f is a membership function given by equation (4.3).

$$M^f \left(\frac{d_{ji}}{d_{ki}} \right) = M_{iter} = \frac{1}{\left[\sum_{k=1}^{nc} \left(\frac{d_{ji}}{d_{ki}} \right)^{\frac{2}{f-1}} \right]} \quad (4.3)$$

Distance measurements between data points D_{x_i} and cluster centers C_j are represented by d_{ji} and d_{ki} , which are calculated using the Euclidean distance method. According to equation (4.4), C_j represents a cluster center, which can be defined as $\left\| D_{x_i - C_j} \right\|$ and $\left\| D_{x_i - C_j} \right\|$. M^f represents a fuzzification factor.

$$C_j = \frac{\sum_{i=1}^N M^f D_{xi}}{\sum_{i=1}^N M^f} \quad (4.4)$$

The FCM process is as mentioned below.

1. The FCM process is defined through the initialization of nc, f , and the convergence state S_c .
2. A random cluster C_j center and randomly assigned membership function M_{rand}^f are initiated by the FCM based on the UL process.

3. The cluster center C_j is calculated iteratively using equation (4.4).
4. The objective function J_{iter} is computed according to equation (4.2), and the convergence state is assessed as outlined below.
5. The Objective function J_{iter} is calculated using equation (4.2), and the state of the convergence is checked as mentioned below.

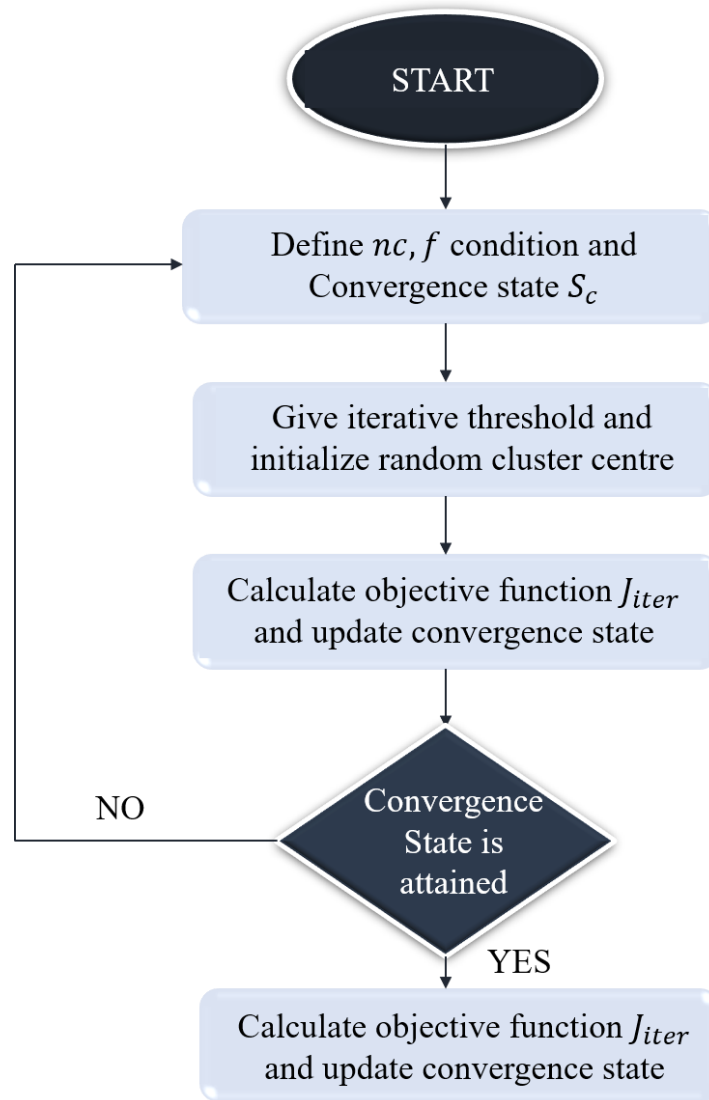


Figure 4.1: Schematic Representation of the FCM Algorithm

6. $J_{iter} - J_{iter-1} < S_c$, the disparity between the present objective function and the previously determined objective function is assessed and verified concerning the established stopping criteria, denoted as S_c .

While FCM demonstrates enhanced performance outcomes, the issue of local optima significantly increases the computational complexity necessary to achieve convergence, which may remain unattainable in specific scenarios. Consequently, the fuzzification factor f has been introduced. Numerous algorithms have been developed to address the limitations identified in FCM.

$$J_{iter} = \sum_{i=1}^N \sum_{j=1}^{nc} \left[M^f \|D_{x_i} - C_j\|^2 \right] + \frac{a}{N_R} \sum_{i=1}^N \sum_{j=1}^c \left[M^f \|D_{x_i} - C_j\|^2 \right], r \in N_i \quad (4.5)$$

Where N_R denotes the cardinality, while a represents a constant employed for adjustment or enhancement.

$$M^f = \frac{(\|D_{x_i} - C_j\|^2)^{\frac{a}{N_R} \sum_{r \in N_i} \|D_{x_i} - C_j\|^2}^{\frac{1}{f-1}}}{\sum_{n=1}^c (\|D_{x_i} - C_j\|^2)^{\frac{a}{N_R} \sum_{r \in N_i} \|D_{x_i} - C_j\|^2}^{\frac{1}{f-1}}} \quad (4.6)$$

$$C_j = \frac{\sum_{i=1}^N M^f (D_{x_i} + \frac{a}{N_R} \sum_{r \in N_i} D_{x_r})}{(1+a) \sum_{i=1}^N M^f} \quad (4.7)$$

According to equations (4.5), (4.6), and (4.7), the FCM variant algorithms have objective functions, membership functions, and cluster centers. Likewise, equations (4.8) and (4.9) explain how the algorithms are adjusted for FCM version 1 and version 2.

$$\epsilon_i = \frac{1}{1+a} \left(D_{x_i} + \frac{a}{N_R} \sum_{j \in N_i} x_j \right) \quad (4.8)$$

Additionally, D_{x_i} is substituted with ϵ_i to formulate an Enhanced Fuzzy C-Means (EnFCM), resulting in a reduction of the time complexity associated with the clustering process.

$$S_{ij} = \begin{cases} e^{-\max(|p_i-p_j|, |q_i-q_j|) / \lambda_s - \frac{\|D_{x_i}-D_{x_j}\|^2}{\lambda_g \sigma_i^2}} \\ 0 \end{cases} \quad (4.9)$$

In the data matrix, the i_{th} element serves as the focal point of the local window described by (p_i, q_i) , but the j_{th} element is regarded as a surrounding value concerning this center. Scaling factors (λ_s and λ_g) are introduced to optimize performance.

$$\sigma_i = \sqrt{\frac{\sum_{j \in N_i} \|x_i - x_j\|^2}{N_R}} \quad (4.10)$$

$$\epsilon_i = \sqrt{\frac{\sum_{j \in N_i} \|x_i - x_j\|^2}{N_R}} \quad (4.11)$$

Where, S_{ij} represents the similarity between a particular data point and its neighbouring point, employed for gradient differentiation. The amalgamation of Equations (4.9), (4.10), and (4.11) with the Fuzzy C-Means (FCM) methodology is referred to as the Fast Generalized FCM (FGFCM) approach. The FCM algorithm has seen numerous improvements over time. An essential modification of this approach is the Fuzzy Local Information C Means (FLICM), which integrates an innovative fuzzy factor referred to as f_{ki} , as outlined in equation (4.12).

$$f f_{ki} = \sum_{j \in i, i \neq j} \frac{1}{d_{ij+1}} (1 - M)^f \|D_{x_i} - C_j\|^2 \quad (4.12)$$

Equation (3.12) measures the proximity of individual data points to their neighbouring points, thus maintaining local information during the clustering process. The term $f f_{ki}$ affects both the membership and objective functions in the FCM framework, as shown in equations (4.13) and (4.14).

$$J_{iter} = \sum_{i=1}^N \sum_{j=1}^{nc} [M^f \|D_{x_i - C_j}\|^2 + f f_{ki}] \quad (4.13)$$

$$M_{iter} = \frac{1}{\left[\sum_{k=1}^{nc} \left(\frac{d_{ji} + f f_{ki}}{d_{ji} + f f_{ki}} \right)^{\frac{1}{f-1}} \right]} \quad (4.14)$$

The characteristics of Fuzzy Local Information C-Means (FLICM) assess the similarity of fuzzy local data, efficiently protecting it from noise and irrelevant information. The parameter referred to as $f f_{ki}$ in the procedure is recognized as the empirical adjustment parameter. This segment comprehensively examines the proposed methodology developed following the FLICM framework.

4.2 Modified Fuzzy C Means Clustering (MdFCM)

The FCM method employs a soft clustering approach, distinguishing itself from k-means by its capability to identify mutual clusters where data points may belong to more than one cluster. The FCM algorithm is a recursive method to optimize a specific objective function. Convergence assessment is performed by examining reductions in mean square error. As FCM operates under the UL paradigm, it initiates the clustering process with random selections (Birtolo & Ronca, 2013; W. Zhou, Wu, Chen, Yi, et al., 2017). The FCM process

involves three stages: (i) Cluster Centre, (ii) Membership Function, and (iii) Objective Function shown below. The objective function of the FCM is given by (4.15).

$$J_{iter} = \sum_{i=1}^N \sum_{j=1}^{nc} \left[M^f \left\| D_{x_i - c_j} \right\| \right] \quad (4.15)$$

N represents the quantity of data points in the data vector, whereas nc denotes the number of clusters, which can be determined by the user. M^f represents a membership function defined by (4.16).

$$M^f \left(\frac{d_{ji}}{d_{ki}} \right) = M_{iter} = \frac{1}{\left[\sum_{k=1}^{nc} \left(\frac{d_{ji}}{d_{ki}} \right)^{\frac{2}{f-1}} \right]} \quad (4.16)$$

Where d_{ji} and d_{ki} represent the distance measurements between the data point D_{xi} and the cluster center C_j which can be represented $\|D_{xi} - C_j\|$ and $\|D_{xi} - C_k\|$ explicitly using the Euclidean distance method, The fuzzification factor, denoted as f is a parameter used in the fuzzification process. The cluster center, denoted as C_j (equation 4.17) is often obtained from the M^f , which represents the specified cluster.

$$C_j = \frac{\sum_{i=1}^N M^f D_{xi}}{\sum_{i=1}^N M^f} \quad (4.17)$$

Despite FCM yielding better results, the limitation arising from local optima amplifies the time complexity required to achieve convergence. In certain instances, convergence may not be attained. Given the nature of the problem, numerous algorithms have been proposed based on FCM to achieve global optima with improved time complexity. Existing versions of FCM have been revised to improve the robustness of the clustering method. These improvements include facilitation techniques such as fuzzification, local optima minimization, contour region similarity assessment, noise tolerance, reduction in execution

time, and enhanced parameter selection. The proposed MdFCM algorithm incorporates the median adjustment parameter F_{mmfi} .

$$J_{iter} = \sum_{i=1}^N \sum_{j=1}^{nc} \left[M^f \|D_{x_i} - C_j\|^2 + F_{mmfi} \right] \quad (4.18)$$

$$F_{mmfi} = \sum_{i \in N_i} \frac{Med(W_{ij})}{Med(W_{ij})+1} \|D_{x_i} - C_j\|^2 \quad (4.19)$$

$$C_{pre_j} = \frac{\sum_{i=1}^N M^f D_{x_i}}{\sum_{i=1}^N M^f} \quad (4.20)$$

$$C_{adjM} = Med(\|C_{old_j} - C_{pre_j}\|) \quad (4.21)$$

$$C_{adj} = \frac{C_{adjM}}{Max(P_v)} \quad (4.22)$$

$$C_j = (C_{pre_j})^{\frac{1}{C_{adj}}} \quad (4.23)$$

$$M_{iter} = \frac{1}{\sum_{k=1}^{nc} \left(\frac{d_{ji} + F_{mmfi}}{d_{ki} + F_{mmfi}} \right)^{\frac{1}{f-1}}} \quad (4.24)$$

As demonstrated in equations (4.18-4.24), the derivative form of an objective function, cluster center, and membership function is modified by the Median adjustment parameter F_{mmfi} . The F_{mmfi} is the only factor accountable for making the algorithm optimal and effective. The following are the steps for running this algorithm.

[1]. The FCM algorithm begins by initializing parameters, such as the desired number of clusters, the fuzzy factor, convergence criteria (indicating the convergence status), and the maximum allowable iterations.

[2]. To streamline the clustering process, the data utilized is referred to as the Data vectors D_{x_i} . This vector is subjected to fuzzification and afterwards reorganized according to a random membership function.

- [3]. The dimension $N \times nc$ is utilized to generate random memberships, and its variants exhibit a soft clustering nature, implying the mutual association of data points in two or more clusters. Here, N represents the total number of data points available in D_{x_i} , and nc , signifying the user-determined number of clusters is utilized.
- [4]. As the procedure is iterative, the membership function M^f is calculated at each iteration using the latest cluster center C_j . If the convergence state is not achieved based on this calculation, a new M^f is computed.
- [5]. The proposed version of the FCM algorithm distinguishes itself from other iterations by employing a distinct method for calculating its cluster center C_j in contrast to C_{prej} wherein the membership function M^f is a crucial factor. One of the primary objectives of this approach is to minimize iterations, thereby achieving the shortest possible convergence time.
- [6]. The distance between the prior cluster center and the present cluster is computed as C_{adjM} as per equation (18) to promote better parameter selection and faster convergence.
- [7]. The C_{prej} is then rectified to generate the final cluster center C_j . The F_{mmfi} is updated with a new M^f , which stimulates the nature of the ideal result. The procedure is repeated until the convergence state is attained.

4.3 Modified Fuzzy C Means Convolutional Neural Network (FCCNN)

CNN inherits characteristics from Artificial Neural Networks, encompassing aspects such as neuron in-plantation, learnable weights, biases, and more. As a DL algorithm, CNN effectively extracts extensive information from images, streamlining the classification process. CNN enhances in-depth feature extraction by combining sub-sampling layers,

convolution filters, and pooling stages. Fully connected layers are responsible for learning and categorizing data based on the provided training.

Notably, CNN employs a multilayer perception technique with minimal pre-processing, earning its designation as a Shift Invariant / Space Invariant Artificial Neural Network due to its feature collection with in-variance in the data. CNN comprises two layers: convolution and classification, as shown in Figure 4.2. This sequential process enhances the network's intricacy while minimizing the number of parameters. The convolution layer employs convolution filters, which can vary in dimensions like 3x3 and 5x5, to emphasize gradients in the spatial domain. The pooling layer includes local and global layers responsible for reducing data dimensions.

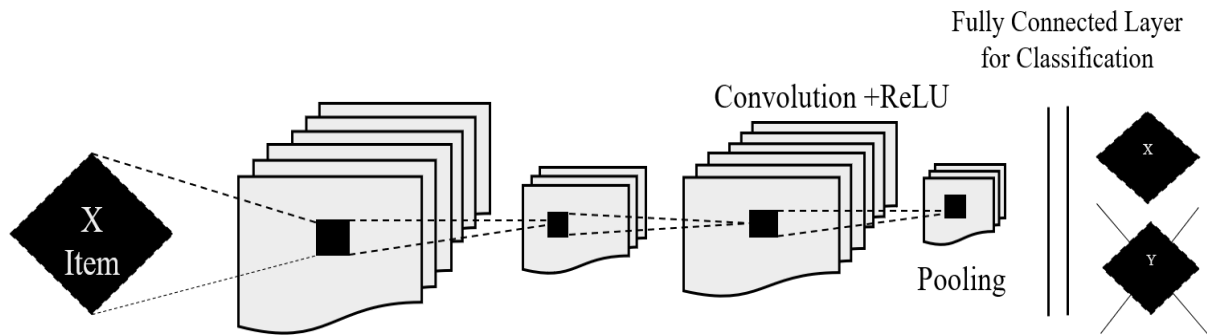


Figure 4.2: Fundamental CNN architecture: spatial reduction and feature depth

The primary method for aggregating data is via averaging. The last layer is a Multi-Layer Perceptron (MLP), operating as a fully connected layer that enables learning and classification tasks. Performance improvements are attained through the incorporation of weights into the learning framework. Shift-invariant neural network learning techniques extract features during the convolution phase. The FCCNN is structured in alignment with the CNN architecture, as detailed below.

The primary objective of the FCCNN proposal is to integrate DL methodologies with an updated version of the FCM algorithm (K. Le Zhou et al., 2014). The MdFCM addresses traditional FCM's limitations. It focuses on mitigating the impact of distances between neighbouring pixels, preserving details during preprocessing, enhancing the fuzzification process concerning local and spatial data values, improving resistance to noise, and refining parameter selection strategies. The parameter augmentation from CNN is subject to reformulation, and the FCCNN is delineated as follows.

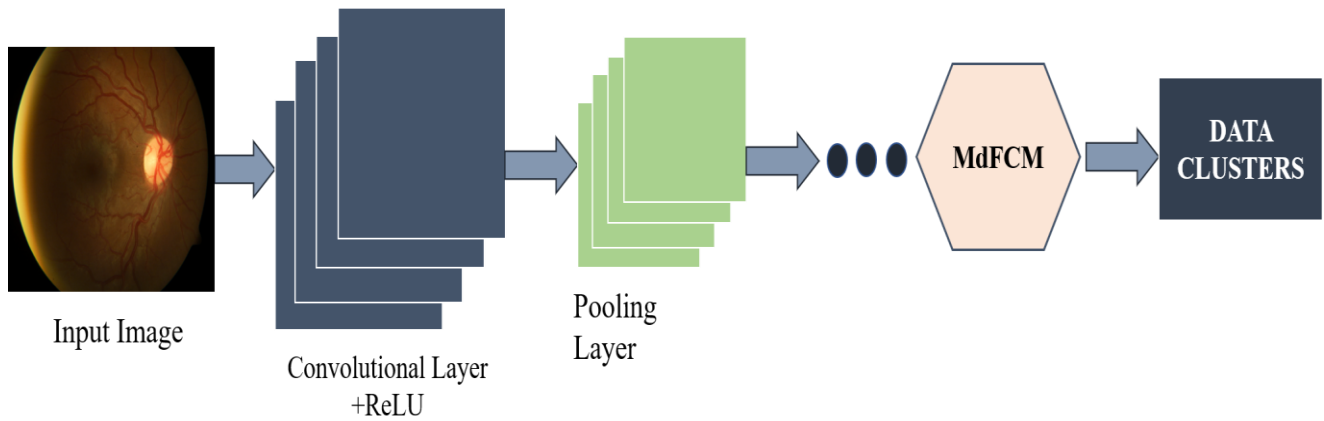


Figure 4.3: Systematic Operations of FCCNN

- [1]. Section III outlines that a CNN comprises two main components: the Convolution Layer and the Fully Connected Layer, which are utilized for data learning and classification.
- [2]. Here, FCCNN is formed by enhancing the Convolution layer of CNN. (Classification section of the CNN is omitted).
- [3]. The FCCNN, an inherited and modified version of FCM, implements the clustering option, MdFCM, with significant modifications.

- [4]. The FCCNN, an inherited and modified version of FCM, implements the clustering option, MdFCM, with significant modifications.
- [5]. The procedure of the proposed FCCNN, as depicted in Figure 4.3, offers a comprehensive overview of its associated actions. The data in 1D, 2D, 3D, or other formats is entered into the convolutional layer of the CNN, where it undergoes convolutional filtering. The filter size will be established according to the data, for instance, 3×3 , 5×5 .

The filtering technique aims to separate the gradient properties of the dataset, which are deemed essential parts. Low-frequency data is generally lacking due to the considerable computational time required to assess all aspects. After the filtering phase, attention will transition to data pooling, wherein the data will be down-sampled to a lower resolution to enable convolutional filtering. The analysis will emphasize gradient specifics during the convolutional filtering and pooling phases to enhance the extraction of significant features. This approach is designated as the Convolution Network (ConNet).

The ConNet generates gradient outcomes by employing diverse convolutional filter banks during each pooling step. After each pooling phase, the ConNet produces gradient results using various convolutional filter banks (X. Yang et al., 2019). The identified features are subsequently used in the execution of the FCM algorithm. The ConNet architecture is designed with each stage producing six feature slices. Given four stages, the total number of slices accumulates to 12. The quantity of stages in the ConNet is directly related to the number of convolutional filters utilized. The execution of FCM clustering is performed following the collection of the featured slices, following equation (4.25).

$$F_{VF} = \sum_{j \in N_{i,i \neq j}} \frac{\text{Mean}(w_{ij})}{\text{Mean}(w_{ij})+1} \|D_{x_i} - C_j\|^2 \quad (4.25)$$

Where, D_{x_i} represents data in vector format while C_j denotes a Cluster Center generated in the current iteration. Equation (4.25) shows that the F_{VF} (Fuzzy Value Factor), which is crucial for enhancing the FCM algorithm, particularly in overcoming its inherent limitations (Gong et al., 2013). The proposed method enhances traditional FCM by integrating the median from the designated window. The average value of the window, as indicated in equation (4.26), signifies the mean of the data derived from the input slices of the convolutional filter.

$$J_{cs,cf,Iter} = \sum_{i=1}^N \sum_{j=1}^{nc} \left[MF^{cs,cf,Iter} \|D_{x_i} - C_j\|^2 + F_{VF} \right] \quad (4.26)$$

The notation $MF^{cs,cf,Iter}$ represents the membership function associated with the featured slices relevant to the selected Convolution Stage, Convolution Filter, and Iteration. N represents the number of elements in the dataset, whereas nc indicates the total number of clusters.

The FCM and its modified variant utilize the mathematical model during the iterations. The proposed method uses a stack of featured slices generated by multiple convolutional filters, and the iterative process is carried out through recursive terms. Equation (4.26) outlines the mathematical model of the objective function $J_{cs,cf,Iter}$ which is specifically designed to evaluate convergence. $J_{cs,cf,Iter}$ is calculated for each iteration according to the convergence criteria $(J_{cs,cf,Iter} - J_{cs,cf,Iter}) < C_s$.

$$C_{adj} = \frac{Mean\left(\left\|C_{old-j} - \frac{\sum_{i=1}^N MF^{cs,cf,Iter} D_{x_i}}{\sum_{i=1}^N MF^{cs,cf,Iter}}\right\|\right)}{Max(D_{x_i})} \quad (4.27)$$

$$C_j = \left(\frac{\sum_{i=1}^N MF^{cs,cf,Iter} D_{x_i}}{\sum_{i=1}^N MF^{cs,cf,Iter}} \right)^{\frac{1}{C_{adj}}} \quad (4.28)$$

C_{old-j} denotes the cluster center derived from the prior iteration, whereas C_{adj} pertains to the modifications applied to the cluster mean values. Cluster centers are generally established by computing the mean or median of the membership function to address the challenges linked with traditional clustering methods. The method for determining the cluster center has been modified using a particular equation. The computation of the cluster center begins with the application of the equation C_{adj} (4.27), which is formulated by averaging the previous cluster C_{old-j} with the newly calculated cluster.

The percentage difference is calculated by dividing the computed value by the maximum value in the input data. The computation of C_j is executed following equation (4.28). This cluster center is employed to develop the subsequent membership function. The percentage difference is calculated by dividing the computed value by the maximum input data value. The calculation of C_j is based on equation (4.29), and this cluster center produces the subsequent membership function.

$$MF^{cs,cf,Iter} = \frac{1}{\sum_{k=1}^{nc} \left(\frac{D_{j_i} + F_{VF}}{D_{k_i} + F_{VF}} \right)^{\left(\frac{1}{f-1} \right)}} \quad (4.29)$$

The total number of cluster centers the user requires determines the membership stacks. The factor f facilitates the decomposition of the membership function components, enabling the transformation of data back to an approximate original state through the defuzzification utilizing this factor. The current membership function will be incorporated into the objective function to evaluate its adherence to the convergence criteria.

4.4 Result and Discussion

The proposed methodology is evaluated through a dual analysis framework incorporating visual representation and performance assessment. The system functions with the proposed algorithm, and the model is assessed based on various criteria, including (a) ARI, (b) ACC, and (c) NMI. Chapter 1 offers an in-depth analysis of these performance metrics.

4.4.1 Visual Representation

The proposed algorithm is evaluated utilizing APTOS, IDRiD, DIARETDB1 samples, and a primary dataset. The evaluation is carried out in two modes: (1) Testing with a noiseless image and (2) Testing with a noisy image. The upgraded algorithm incorporates noise tolerance by considering the noise variance σ that affects the data. The algorithm simulates real-world conditions with noisy images by introducing high-frequency noise to a certain percentage of image pixels (Pratt et al., 2016). This allows for assessing the algorithm's performance under challenging conditions and evaluating its robustness. The experimental results indicate that the proposed algorithm outperforms traditional FCM variants and current clustering algorithms in managing noisy images, leading to more precise segmentation results.

Moreover, the upgraded algorithm significantly improves the detection of red and yellow lesions, as shown in Figure 4.4. The proposed algorithm effectively distinguishes lesion regions from the surrounding background. Figure 4.5 presents the results of lesion detection compared with the ground truth for the corresponding fundus images.

This enables precise identification and delineation of red and yellow lesions, providing vital information for diagnosis and treatment planning. To evaluate the proposed algorithm's effectiveness, its performance is compared with several recognized versions of FCM algorithms, including FCM, EnFCM, FLICM, and Malleable Fuzzy Local Median C

Means (M-FLMCM). Nonetheless, the k-means algorithm, which utilizes hard clustering, is omitted from the comparison.

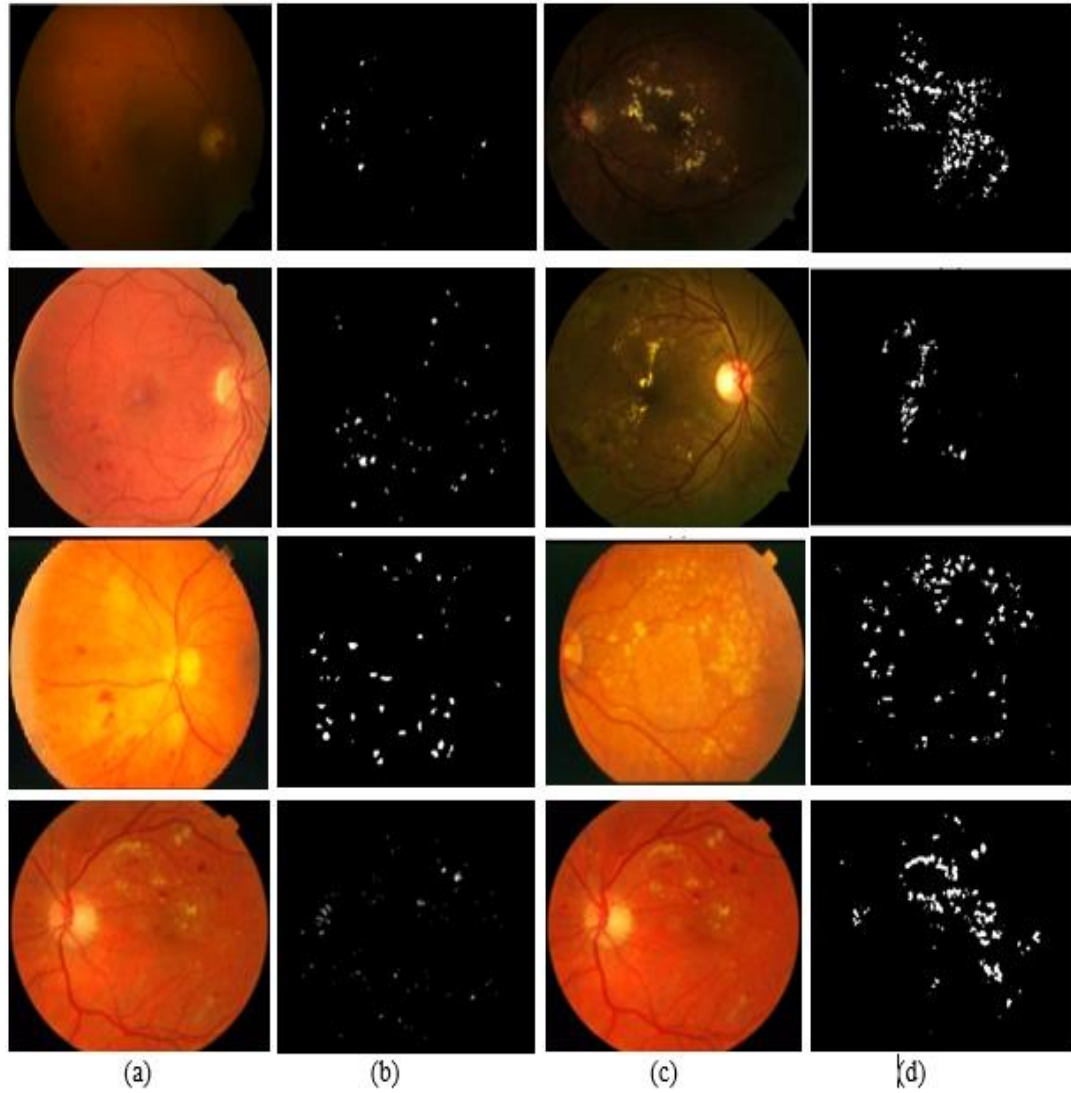


Figure 4.4: Visual representation of experimental results of red and yellow lesion detection: columns a & c denote the original fundus images obtained from DIARETDB1, IDRiD, and the primary dataset. Column B presents the red lesions detected from the original fundus images, and column d shows the yellow lesions detected from the original fundus images.

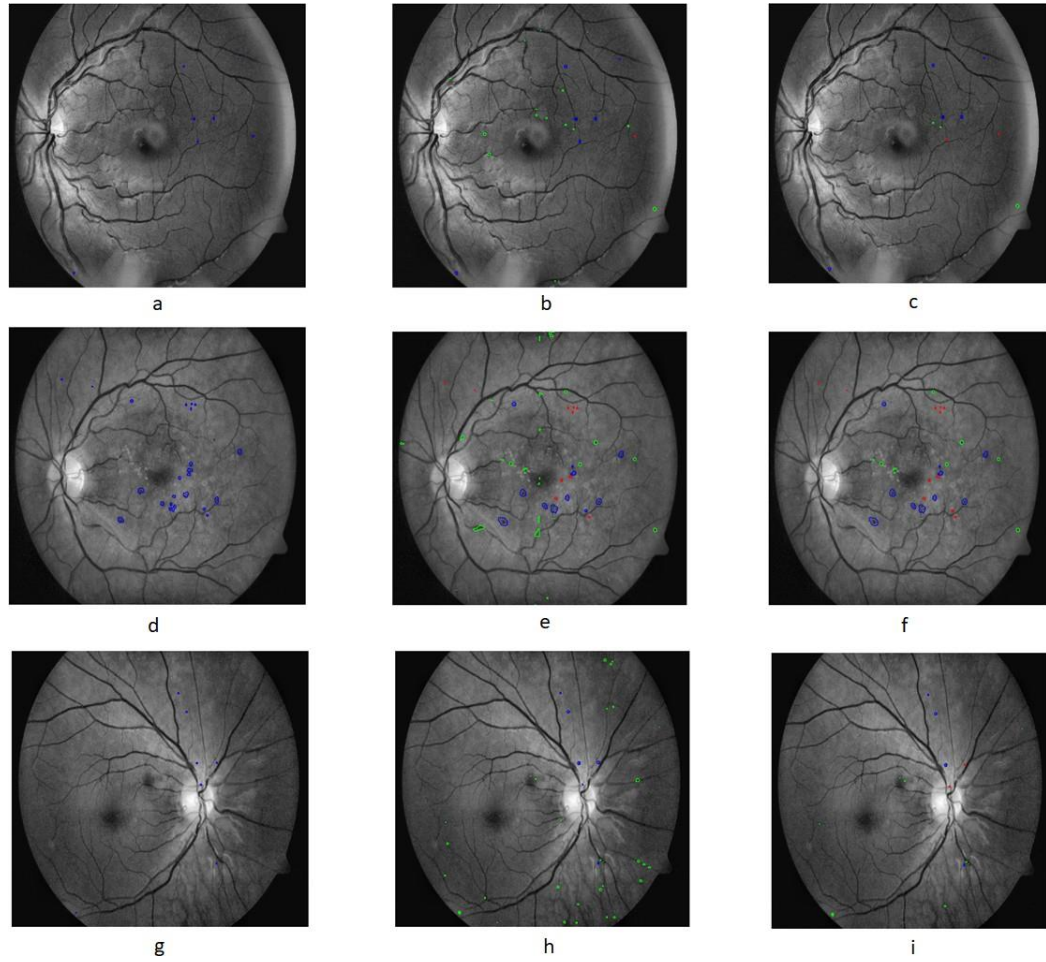


Figure 4.5: Ground truths: (a), (d), and (g), segmentation results using MdFCM (b), (e), and (h), result after false-positives removal: (c), (f) and (i). Red corresponds to false negative candidates, and green represents the false positive, and true positive candidates are true positive in blue.

4.4.2 Performance Analysis

The assessment is conducted in noisy and original conditions to ascertain the algorithm's efficacy. The frequency of the noise can fluctuate, affecting real-time data. This study employs high-frequency noise for the analysis. The noise levels are calibrated to four

distinct intensities, ranging from 0 to 1: 0.2 (20% of the information is compromised), 0.4 (40% compromised), 0.6 (60% compromised), and 0.8 (80% compromised). This validation indicates that MdFCM attains a superior accuracy rate compared to alternative algorithms. MdFCM is an iterative clustering method that categorizes data into clusters, assigning each data point to a specific cluster with a defined degree of membership.

In the proposed algorithm, convergence occurs when the membership coefficients and cluster centroids stabilize, indicating that the algorithm has reached a stable solution (Rezaee et al., 2017). Monitoring runtime in FCM can help assess its performance and efficiency, especially in comparison to other clustering algorithms or variations of FCM. Thus, Table 4.3 shows the average duration that various algorithms require to process cluster data. Each algorithm initiates its iteration from random starting points, and subsequent iterations require additional time for the clustering process.

Table 4.3 displays five distinct segmentation runs along with their corresponding recorded times. Table 4.1 compares the accuracy of FCM with alternative methods in a noiseless environment, demonstrating that MdFCM outperforms the other algorithms evaluated. Furthermore, Table 4.2 presents the results under a noisy condition for seven samples.

Table 4.1: Analysis of modified FCM to different methods for accuracy in a noiseless condition

Samples	K-Means	FCM	DEC	MdFCM
S1	82.107	82.993	83.825	96.57
S2	79.042	79.76	85.047	97.97
S3	70.961	71.822	78.883	95.02
S4	73.863	74.861	82.789	97.41
S5	72.611	73.638	80.68	96.03
S6	73.13	73.46	74.55	99.03
S7	73.863	74.861	82.789	95.99

Table 4.2: Analysis of modified FCM to different methods for precision in noisy environments

σ	K-Means	FCM	DEC	MdFCM
0.2	90.56	91.12	93.13	95.23
0.4	84.26	84.85	88.11	91.45
0.6	76.61	80.17	84.93	86.60
0.8	61.78	66.74	73.17	80.69

Table 4.3: Analysis of clustering algorithms concerning time complexity (in seconds)

Run No	K-Means	FCM	DEC	MdFCM
1	14.6	20.45	19.96	16.22
2	14.24	20.11	20.31	17.54
3	15.61	19.91	19.45	17.21
4	14.78	20.22	19.29	16.34
5	14.76	19.86	19.82	17.02

The MdFCM employs a fuzzy median technique that enables the determination of a median value by considering adjacent pixels, distinguishing it from others, and enhancing the overall accuracy (Rajendran et al., 2016). The medical images exhibited more defined regions due to minimal grayscale variation. The proposed algorithm is structured to effectively extract minor differences within the data neighbourhood for cluster formation.

A performance evaluation was carried out to analyze the FCM algorithm and compare it to leading algorithms in the industry. Tables 4.4 and 4.5 demonstrate the accuracy of different modified FCM variants in noisy and noiseless environments. Understanding the behaviour of the image requires careful consideration of various noise levels (variance). As a result, various noise variances (σ) were analyzed, emphasizing the influence of noise intensity on the data. Figures 4.7 and 4.8 provide a comparative analysis of clustering algorithms in terms of average accuracy under both noiseless and noisy conditions, respectively. Furthermore, runtime is an essential consideration in evaluating the clustering

algorithm, as the primary objective of this study is to enhance this algorithm within the DNN framework. The results demonstrate that the proposed MdFCM algorithm exhibits outstanding performance, with its average accuracy from the standard dataset surpassing that of the existing FCM version, as illustrated in Table 4.6.

Table 4.4: Performance analysis of FCM variants compared to MdFCM under noiseless conditions

Samples	FCMs	EnFCM	FLICM	M-FLMCM	MdFCM
S1	92.38	92.69	93.69	94.63	96.57
S2	89.09	89.23	90.04	96.01	97.97
S3	80.01	80.11	81.08	89.05	95.02
S4	83.12	83.38	84.51	93.46	97.41
S5	81.75	81.97	83.13	91.08	96.03
S6	93.13	93.46	94.55	98.53	99.03
S7	93.14	93.52	94.73	95.69	95.99

Table 4.5: Performance analysis of FCM variants compared to MdFCM under noisy conditions (σ : 0.2 to 0.8)

σ	FCMs	EnFCM	FLICM	MdFCM	M-FLMCM
0.2	91.12	91.09	92.21	93.13	95.23
0.4	84.26	85.28	86.65	88.11	91.45
0.6	76.31	80.31	81.52	84.93	86.60
0.8	61.78	64.91	66.17	71.37	80.69

Table 4.6: Performance analysis of FCM variants compared to MdFCM for average time complexity (in seconds)

Run No	FCMs	EnFCM	FLICM	MdFCM	M-FLMCM
1	20.45	19.96	16.76	16.25	16.22
2	20.11	20.31	17.33	16.18	17.54
3	19.91	19.45	17.02	16.32	17.21
4	20.22	19.29	17.67	17.06	16.34
5	19.86	19.82	17.29	16.92	17.02

4.4.3 Parametric Analysis of Proposed Approach (FCCNN)

The segmentation results of the hybrid unsupervised (FCCNN) algorithm were evaluated against other algorithms to assess statistical significance. Furthermore, it can address various challenges, including the complexity of the model, difficulties in implementation and training, problems in hyperparameter tuning, and issues related to clustering (Shan, 2018). To assess the algorithm's performance, it is essential to compare and analyze its resulting metrics and standardize the metric. (a) ACC (b) NMI (c) ARI. The evaluation of our proposed approach discussed in Chapter 1 is done on three DR image datasets: APTOS, IDRiD, and Primary Dataset. Given that the number of clusters in the datasets is fixed, conventional clustering assessment metrics such as ACC, NMI, and ARI are typically used in experiments. The proposed model's performance is assessed against four state-of-the-art techniques for comparison.

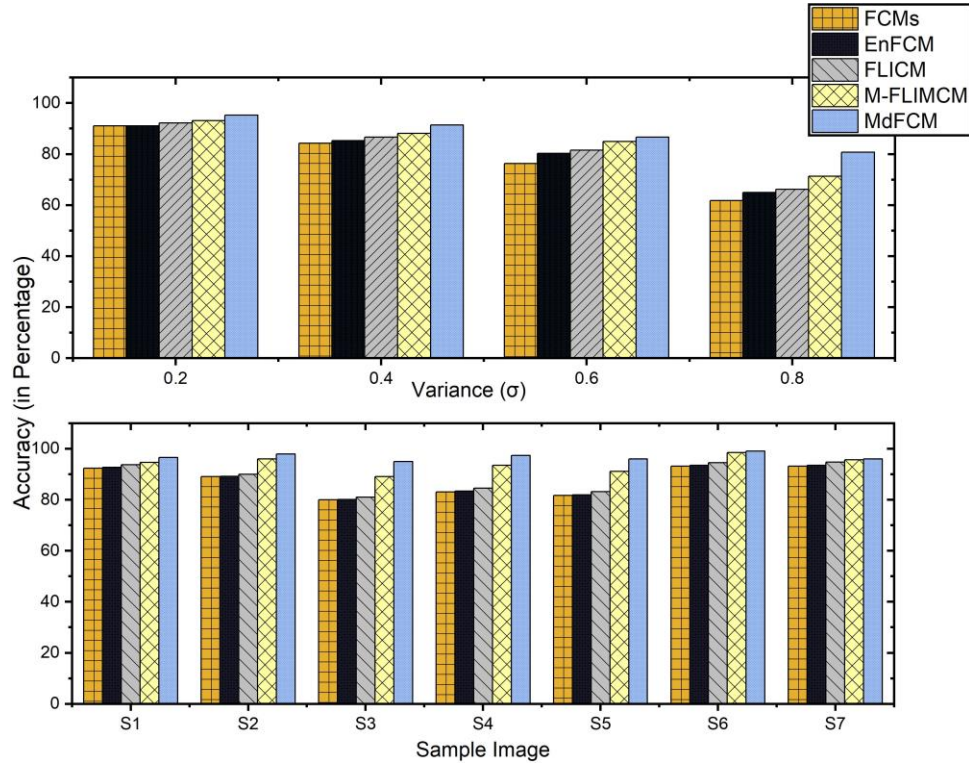


Figure 4.6: Performance analysis of MdFCM for average accuracy under noisy and noiseless conditions (S1 - S7)

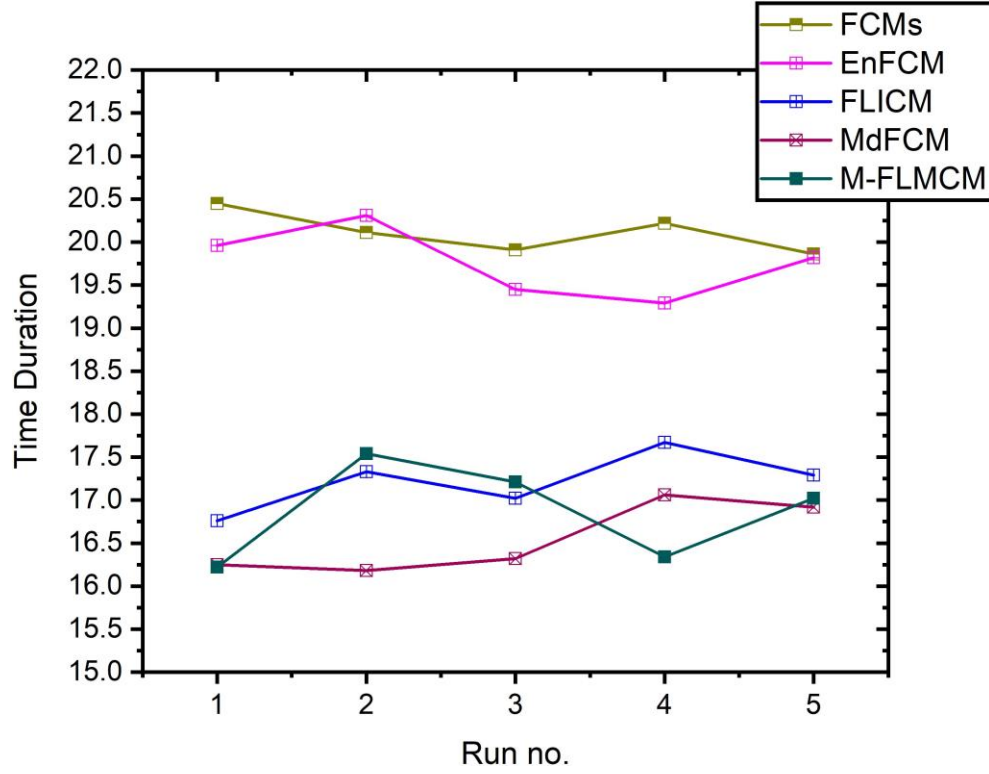


Figure 4.7: Performance analysis of MdFCM for average time complexity (in seconds)

4.4.4 Comparative Analysis

The comparative analysis evaluates the proposed technique against state-of-the-art unsupervised methods using parameters such as ACC, NMI, and ARI. Additionally, it is assessed against the latest CNN architectures and recent proposed work in DR detection. The computational efficiency of MdFCM is comparable to the base FCM algorithm, but it demonstrates improved performance in detecting DR, achieving better accuracy in noisy and noiseless conditions.

Table 4.7 demonstrates the efficacy of the proposed algorithm. Training and testing are performed on applied datasets to evaluate the model's reliability and limitations. An

analysis of the model's performance against leading algorithms demonstrates that the proposed approach achieves better outcomes. The results are depicted in Figures 4.9, 4.10, and 4.11, showcasing the outcomes for each parameter (ACC, NMI, and ARI).

The main objective of this study is to enhance the capability of UL in the DL method, as demonstrated by the results (Geetharamani & Balasubramanian, 2016). Moreover, the proposed research utilizes the MIIRet Cam as a smartphone-based camera to test the algorithm's performance deployed within the application (RetinaCare), employing the Volk 20D lens in the SMI Hospital, Dehradun.

Table 4.7: Comparison of FCCNN with state-of-the-art algorithms on applied datasets using ACC, NMI, and ARI

Method	Evaluation metrics	IDRiD	APTOS	DIARETDB	Primary dataset
K-Means	ACC	0.658	0.91	0.712	0.618
	NMI	0.531	0.72	0.779	0.698
	ARI	0.414	0.79	0.464	0.448
Deep Clustering Network (DCN)	ACC	0.59	0.81	0.742	0.674
	NMI	0.626	0.78	0.614	0.75
	ARI	0.344	0.81	0.543	0.611
Deep K-Means (DKM)	ACC	0.712	0.78	0.64	0.54
	NMI	0.523	0.71	0.63	0.413
	ARI	0.431	0.72	0.51	0.332
Efficient Deep Embedded Subspace Clustering (EDESC)	ACC	0.632	0.82	0.70	0.621
	NMI	0.731	0.87	0.6331	0.677
	ARI	0.221	0.74	0.386	0.502
FCCNN	ACC	0.742	0.94	0.785	0.885
	NMI	0.811	0.95	0.71	0.841
	ARI	0.802	0.92	0.811	0.79

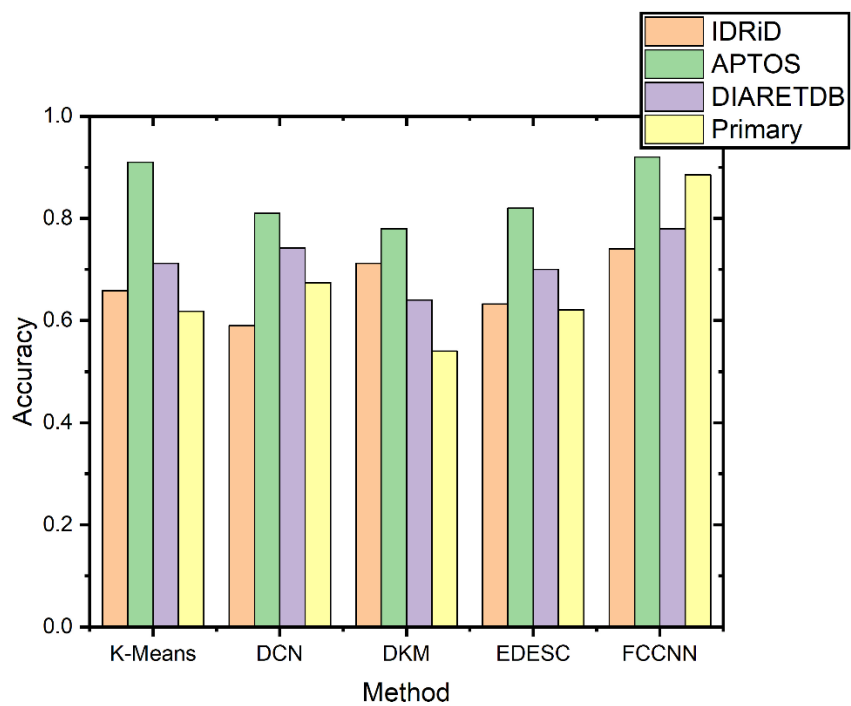


Figure 4.8: Comparison of ACC of state-of-the-art algorithms on applied datasets

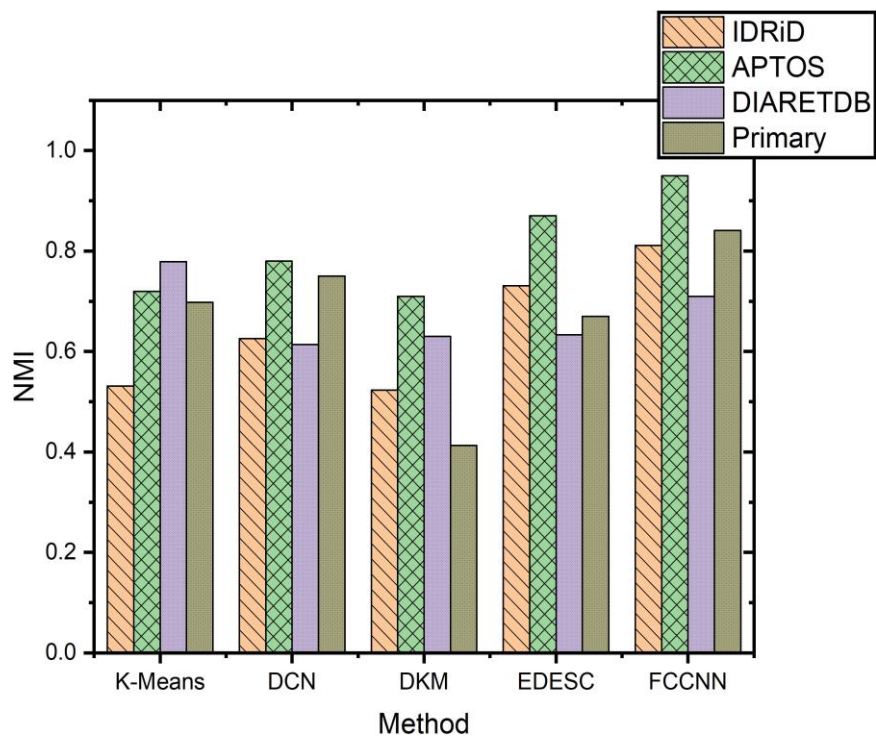


Figure 4.9: Comparison of NMI of state-of-the-art algorithms on applied datasets

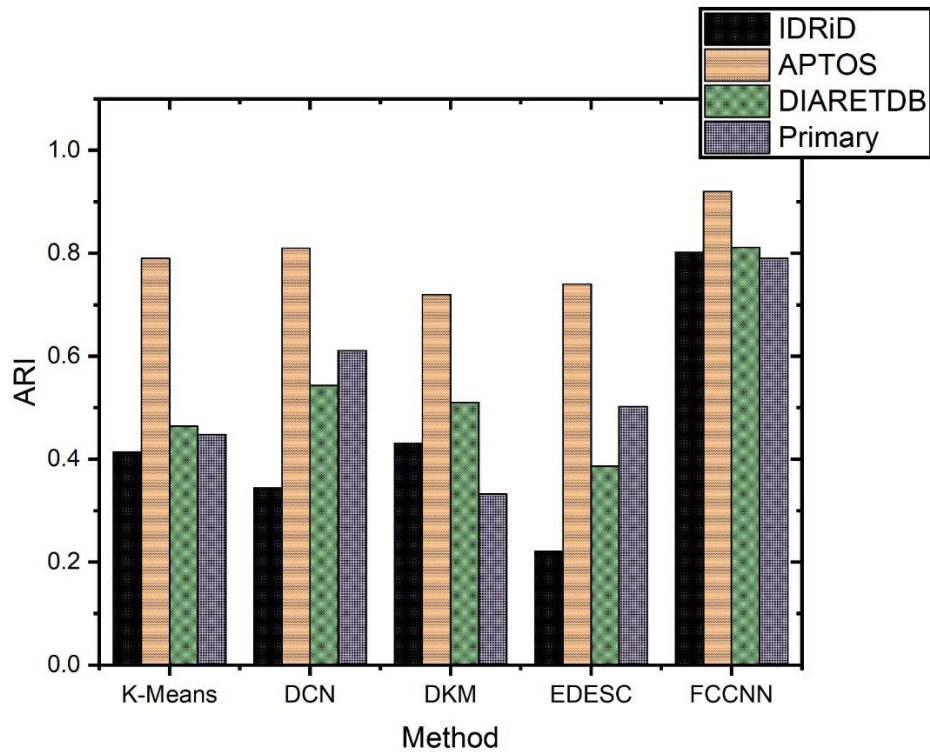


Figure 4.10: Comparison of ARI of state-of-the-art algorithms on applied datasets

Table 4.8: Comparative analysis with existing models

Technique	Overall Accuracy	Precision/NMI	Recall/ARI
VGG16	81.03%	80%	80%
ResNet50 with Attention Model	89%	84%	83%
DesNet121	85.16%	85%	85%
VGG19	87.76%	87%	86%
Proposed Model	94%	95%	92%

The proposed research is assessed in relation to existing CNN models using the performance metrics outlined in Table 4.8, along with advanced methods for DR classification described in Table 4.9. The results demonstrate enhanced performance relative to the current CNN models and the more sophisticated techniques. Furthermore,

the characteristics of the presented work render it more appropriate for execution in distant environments, and performance can be enhanced with further gathered photos and unlabeled data.

Table 4.9: Comparison with Recent Work for DR detection

S. No	Method	Dataset	Performance Analysis	Ref
1	EfficientNet DenseNet	APTOS+ Kaggle	EfficientNet: Accuracy 88% Precision = 90% Recall = 98% DenseNet Accuracy = 76% Precision = 67% Recall = 91%	(Mohanraj , 2023)
2	ResNet101 ResNet50 VGG16	STARE, DIARETDB0, HRF, XHO	Average Training Accuracy = 97% Average Testing Accuracy = 91.5%	(Asia et al., 2022)
3	Parallel CNN	APTOS, Kaggle	Accuracy = 91% (Kaggle) Accuracy = 97% (APTOS)	(Nahiduzz aman et al., 2023)
4	CNN with Residual Blocks	DR 2015 Data Colored resized	Accuracy = 95% Precision = 94% Recall = 94%	(Kommara ju & Anbarasi, 2024)
5	Proposed Method	Kaggle, DIARETDB1, IDRiD and Primary Dataset	Accuracy = 94% ARI = 95% NMI = 91%	

4.4.4.1 Computational Efficiency

The time complexity of the FCM algorithm is primarily determined by the following factors:

1. Number of data points (N): The total number of points in the dataset.
2. Number of clusters (C): The number of clusters into which the data points are divided.
3. Number of iterations (t): The number of iterations the algorithm runs until convergence.

The FCM algorithm entails calculating membership values for each data point across all clusters, which operates at a complexity of $O(NC)$, followed by updating the cluster centers based on these membership values, also at $O(NC)$. This process is repeated until convergence is achieved. Therefore, the overall time complexity for each iteration is $O(NC)$; consequently, for t iterations, the total time complexity amounts to $O(t * NC)$.

MdFCM (Modified Fuzzy C Means)

The Breakdown of the time complexity for each step for Modified FCM is shown based on the provided equations:

- Objective Function (J_{iter})

Complexity: $O(N * NC)$

Reason: The calculation involves a constant number of operations for each N data point and NC cluster.

- Median Adjustment Parameter (F_{mmfi})

Complexity: $O(N * |Ni|)$

Reason: For each data point i , the sum over its neighbourhood is $O(N * |Ni|)$. If the neighbourhood size is assumed to be constant (or small compared to N), the complexity is effectively $O(N)$.

- Preliminary cluster center for cluster j (C_{pre_j})

Complexity: $O(N)$

Reason: The sum over N data points involves a constant number of operations per point.

- The adjusted median of the previous cluster center and Preliminary cluster center (C_{adjM})

Complexity: $O(N \log N)$

Reason: Calculating the median requires sorting, which is $O(N \log N)$.

- Final cluster center (C_j)

Complexity: $O(1)$

Reason: This involves a constant number of operations.

- Membership value (Miter)

Complexity: $O(NC * N)$

Reason: Summing over NC clusters for each N data point.

Total Complexity per Iteration: The total complexity per iteration of the algorithm can be obtained by summing up the complexities of each step:

$O(N * NC)$ from J_{iter} calculation.

$O(N * |Ni|)$ from F_{mmfi} calculation.

$O(N)$ from C_{prej} calculation.

$O(N \log N)$ from C_{adjM} calculation.

$O(1)$ from C_j calculation.

$O(NC * N)$ from M_{iter} calculation.

The dominant terms are $O(N * NC)$, $O(N * |Ni|)$, and $O(N \log N)$, where $|Ni|$ is typically small or constant. Hence, the complexity per iteration is $O(N * NC) + O(N * |Ni|) + O(N \log N)$. Assuming $|Ni|$ is a small constant, the complexity simplifies to $O(N * NC + N \log N)$

Suppose $NC \gg \log N$ (which is the case in clustering with many clusters); the complexity per iteration can be approximated as $O(N * NC)$. Thus, Total Complexity for t Iterations:

The time complexity $O(t * N * NC)$ is analogous to that of FCM; however, convergence can be expedited through the adaptive modification of cluster centers utilizing median computations and adaptive factors to guarantee more precise and stable updates. This diminishes oscillations and expedites convergence. The proposed method is evaluated against leading techniques. The results indicate that it outperforms these methods when applied to the Indian dataset from Kaggle and other sources, utilizing an unsupervised approach. This approach does not require any labelling for new training of the model and outperforms the latest available CNN architectures.

4.5 Summary

This chapter presents two novel algorithms based on a deep clustering approach named MdFCM and FCCNN proposed for DR classification. The MdFCM represents a novel version of the foundational FCM algorithm, designed to optimize fuzzification, minimize local optima, assess contour region similarity, tolerate noise, reduce execution time, and improve parameter selection.

FCCNN is proposed with hybridization of MdFCM and base CNN model to leverage clustering's capability to group similar data patterns before feature extraction by CNN, enhancing DR classification accuracy and improving the robustness of feature learning. Thus, a complete research analysis was performed using MdFCM and FCCNN algorithms on the exclusive and publicly accessible DR Dataset. The proposed methods in both experimental groups exceed the available top techniques. A significant challenge faced during the research is the matter of time complexity. The proposed algorithm exhibits enhanced performance compared to current models; however, its execution time poses a considerable limitation, highlighting a significant avenue for future research.

Chapter V

RETINACARE: A WEB APPLICATION

DR poses a significant risk of vision loss. There are approximately 2.6% of cases of blindness globally, which can be attributed to DR (F. Li et al., 2022). Individuals with diabetes must undergo regular screening to identify DR in its initial phases. Conventionally, the detection of DR involves clinicians examining retinal images to assess the morphology and characteristics of different types of lesions. The identified lesions include MAs, hemorrhages, and soft and hard exudates of lipids and proteins in blood vessels(Y. Zhou et al., 2023). Despite the global prevalence of any form of DR being 27.0% between 2015 and 2019(Thomas et al., 2019), early stages of DR, including referable DR, exhibit no distinct symptoms. The absence of apparent symptoms contributes to the challenge of detecting DR in its initial phases, as the condition can progress significantly before affecting vision. Nonetheless, detecting and treating DR can lower the risk of vision impairment by as much as 57%(Treatment & Retinopathy, 1991).

Regular screening and ongoing monitoring are vital for people with diabetes during the early NPDR to identify individuals at risk of developing PDR(Maclennan et al., 2014; Oh et al., 2021; Owsley et al., 2006). Research shows that many diabetes patients forego the necessary annual eye examinations due to prolonged examination times, lack of symptoms, and limited access to retinal specialists(Chou et al., 2014). Laser therapy and intravitreal anti-vascular endothelial growth factor injections have shown efficacy in detecting and intervening in cases of proliferative DR(Flaxel et al., 2020), thereby mitigating potential complications(P. Y. Zhao et al., 2023). It is imperative to ascertain individuals with PDR to facilitate prompt intervention accurately. The predominant approach for identifying the

presence of neovascularization involves the utilization of eye examinations and colour fundus images(Naz et al., 2022).

Overcoming these challenges involves applying AI methodologies to identify and diagnose DR. In 2016, Gulshan et al.(Gulshan et al., 2016) proposed DL method to assess DR, utilizing a dataset of approximately 0.13 million training photos. The algorithm demonstrated exceptional performance, with AUC values ranging from 0.97 to 0.99 for identifying referable DR. Abramoff et al.(Abramoff et al., 2016) also presented an automated approach employing DR detection on open-access datasets using CNN. Subsequently, several researchers(Gargeya & Leng, 2017; Sahlsten et al., 2019; Sayres et al., 2019) have also emphasized DL technology to classify DR. CNN has been employed in the automated classification of eye diseases such as age-related macular degeneration, retinopathy of prematurity, and glaucoma.

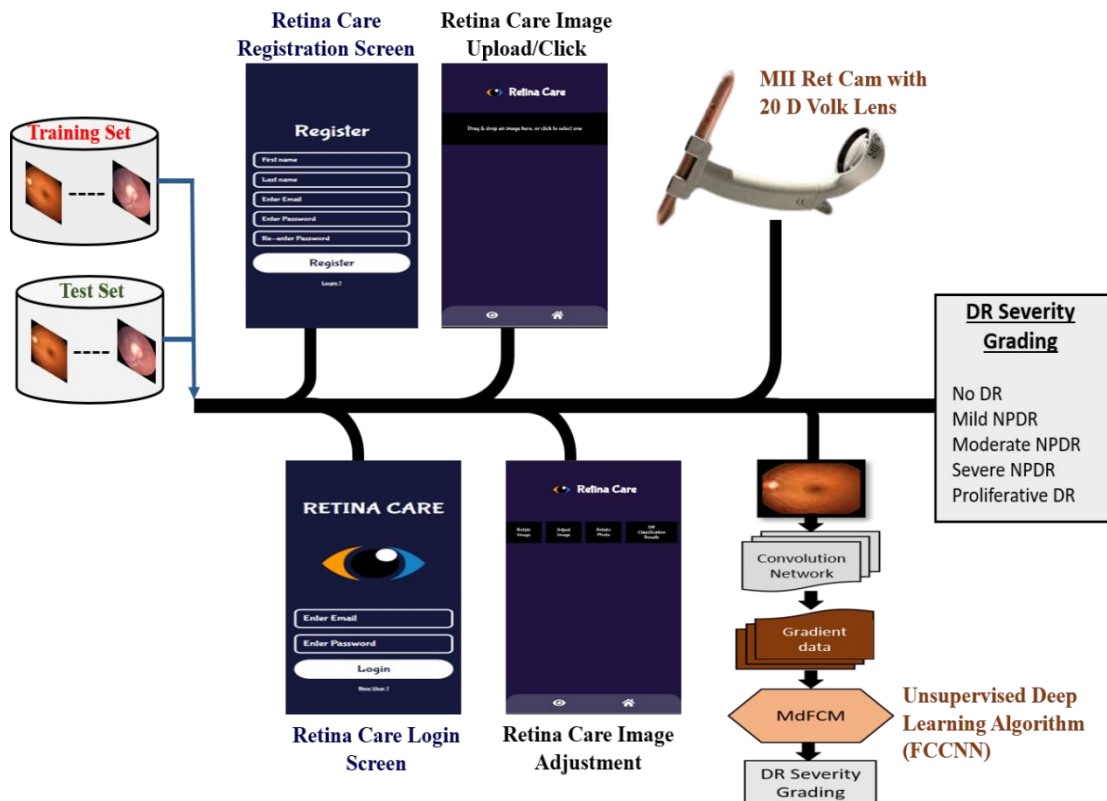


Figure 5.1: Overview of the Retina Care system for DR detection and severity grading

Despite notable technological advancements, there remains a lack of models effectively utilized for real-time applications in remote or limited-resource settings. This deficiency highlights the need for a tool to optimize the grading and detection of DR, thus reducing the burden on healthcare systems and professionals. The proposed development of a standalone application seeks to enhance the speed and accuracy of DR grading, tackling critical issues related to early detection and management, particularly in regions with limited access to specialized medical services. This initiative underscores the essential function of advanced.

The present study introduces an unsupervised DL algorithm that integrates the optimized FCM algorithm with the CNN method (Figure 5.1). This algorithm is implemented in a web-based application (RetinaCare) designed for the detection and assessment of severity levels in patients based on captured or uploaded images. Our study aims to examine the severity levels of DR through feature extraction and grading analysis for remote patients. Early detection of DR is crucial for averting potential sight-threatening complications or vision loss. The proposed application serves as a preliminary diagnostic tool, alleviating the workload on a limited number of optometrists/ophthalmologists in developing nations. The proposed study utilizes the MIIRet Cam, a smartphone-based camera, to test the algorithm's performance deployed within the application, employing the Volk 20D lens.

In the realm of DR, extensive research has unveiled a distinctive set of lesions in the retinas of individuals living with DM over an extended period (X. Li et al., 2018; Nazir et al., 2019). This complex condition prompted the researcher(Pires et al., 2019) to focus on two levels of control. The first involves meticulous diabetes management, regulating glycemia and serum lipid levels to reduce the risk of DR development. The second tier involves the clinical application of laser therapy, proving beneficial in preventing further progression and visual impairment by addressing permeable blood vessels and eliminating proliferative vessels (Orlando et al., 2017; Qummar et al., 2019; Wan et al., 2018).

Automated screening techniques have played a pivotal role in DR detection. Sinthanayothin et al.(Biruntha & Narmadha, 2022) developed a method to analyze fundus images for crucial Non-Proliferative DR (NPDR) indicators. Characteristics of NPDR were autonomously determined using advanced methodologies, such as recursive region-expanding segmentation algorithms and the "Moat Operator." Concurrently, Jena et al. (Jena et al., 2023) enhanced image quality by focusing on the green channel using CLAHE and introduced a novel DR screening method based on asymmetric DL features extracted by U-Net.

Venturing into predictive algorithms, Reddy et al. (Venkaiahppalaswamy et al., 2023) explored optimal methods for DR severity classification. Their study scrutinized algorithms such as Random Forest, Decision Tree, Adaptive Boosting, and Bagging alongside a novel approach employing a Support Vector Machine with a Gaussian kernel. The findings revealed that the Support Vector Machine with Gaussian kernel outperformed its counterparts, achieving an impressive accuracy rate of 81.3%.

Aziz et al. (Aziz et al., 2023) emphasized the potential benefits for ophthalmologists by incorporating a secondary interpreter to expedite traditional screening procedures. Meanwhile, Nage et al.(Nage et al., 2023) focused on early-stage Diabetic Macular Edema (DME) detection through a three-step preprocessing method. The IDRiD and MESSIDOR datasets were employed to evaluate proposed models, showcasing an accuracy of 80.7%. The classification of DR images(Venkaiahppalaswamy et al., 2023) utilized a hybrid binocular Siamese approach with DL. Further evaluations using DIARETDB0 (DB0) and DIARETDB1 (DB1) datasets demonstrated a high accuracy of 94% on DB0 and 94.83% on DB1. Nahiduzzaman et al.(Nahiduzzaman et al., 2023) introduced an automated approach for DR detection, demonstrating efficiency in preprocessing and feature extraction.

Lastly, Guo & Peng(Y. Guo & Peng, 2022) proposed the use of (CARNet) for automatic multi-lesion segmentation in DR. This model optimally utilized fine local features and

coarse global features. Hemamalini et al.(Hemamalini & Kumar, 2022) introduced OSR-FCA, an Outlier-based Skimpy Regularization Fuzzy Clustering Approach, and showcased improved performance by including regularization in the fuzzy membership objective function with sparseness clustering algorithms.

5.1 Material and Methods

The proposed DR detection system is designed to identify DR features for severity analysis and grading, utilizing a dedicated application compatible with any mobile phone. Particularly beneficial for patients in remote areas, this application incorporates the FCCNN algorithm for efficient DR detection. Image capture is facilitated through the MIIRet cam paired with a 20D Volk lens, a cost-effective alternative to expensive table-top fundus cameras. The application serves as an initial diagnostic tool, offering patients a preliminary opinion and guiding them toward further consultation with an ophthalmologist or optometrist for comprehensive evaluation.

Ethical clearance has been obtained from the ethics committee at SMI Hospital in Dehradun. A panel of six members evaluated the research proposal and granted permission to proceed with the study. The IEC approval certificate can be found in Annexure I.

5.1.1 RetinaCare System: Interface Design and Functionality

The proposed DR detection system works with the RetinaCare application, enabling the uploading or capturing of fundus images that can be classified based on specific characteristics, including MAs, hemorrhages, soft exudates, and hard exudates. Users can register and log in to record DR patients for further training (Figure 5.2). The display interface illustrates the severity classification of DR as determined from the supplied image. Furthermore, users can modify several parameters, such as brightness, contrast, and rotation. After adjusting the image, users can confirm it, triggering the DR classification process. This workflow is crucial for effective DR assessment.

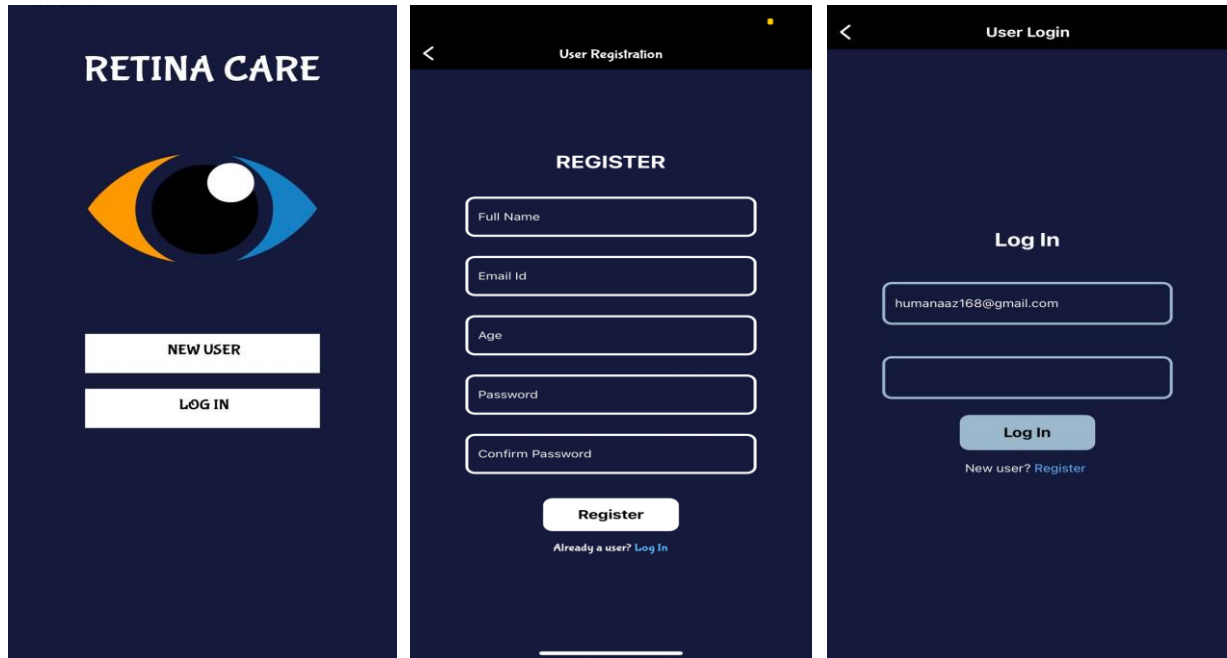


Figure 5.2: Retina Care Register and Login Screen

The ConfirmImageScreen makes adjustments before DR classification, and the RetakePhotoScreen allows users to capture a new image. After capturing, users can confirm the image or retake it (Figure 5.3). The confirmed image is then processed on the DRClassification screen for further processing. Given the suboptimal nature of mobile cameras for capturing fundus images, the proposed study employs the MIIRet camera equipped with a 20D Volk lens. This smartphone-based camera is particularly well-suited for deployment in remote areas. Notably, the camera seamlessly attaches to Android and iPhone devices, facilitating the efficient capture of fundus images. Further details on the camera specifications are illustrated in subsequent sections.

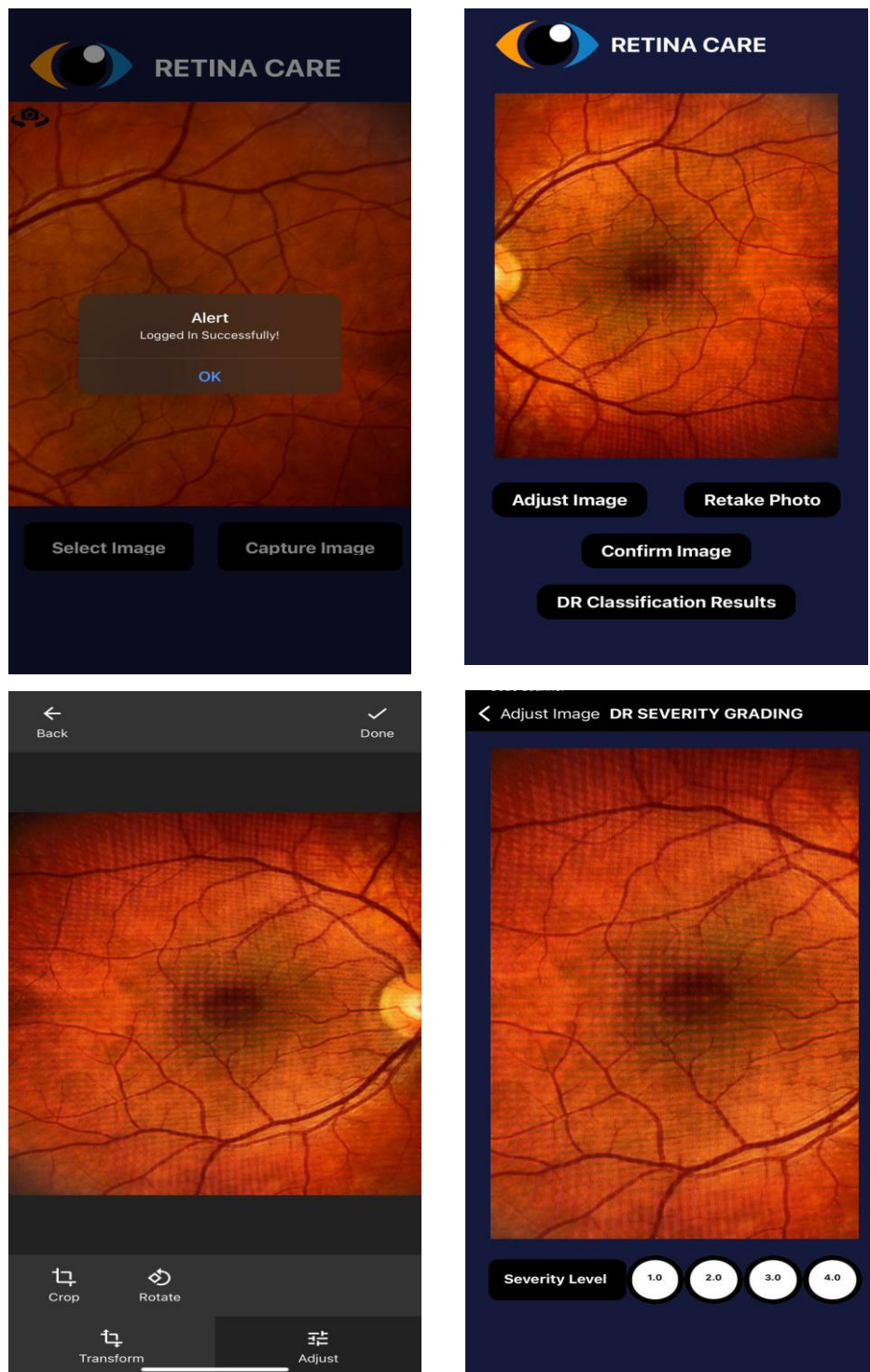


Figure 5.3: Retina Care ImageCapture and Control Screen

5.1.2 MongoDB Integration for Backend Data Management

For database and backend operations, the proposed application uses the MongoDB database. MongoDB is a NoSQL database with a versatile format similar to JSON, or BSON (Binary JSON), for storing data. MongoDB operates without the conventional structures of tables, rows, or predefined schemas that are characteristic of traditional relational database management systems. The system employs collections and documents as its primary organizational framework instead of traditional data structures. A collection is akin to a table in relational databases, while a document is comparable to a row. However, documents in MongoDB are stored in a more flexible format, allowing for different structures within the same collection, without needing a predefined schema.

A MongoDB document comprises key-value pairs, where the key is a string, and the value can take various forms, including strings, numbers, arrays, or even nested documents. The flexible schema of MongoDB is well-suited for applications dealing with unstructured or semi-structured data, as well as for those where the data model frequently changes. Figure 5.4 illustrates an example of stored patient information within the MongoDB dataset cluster.

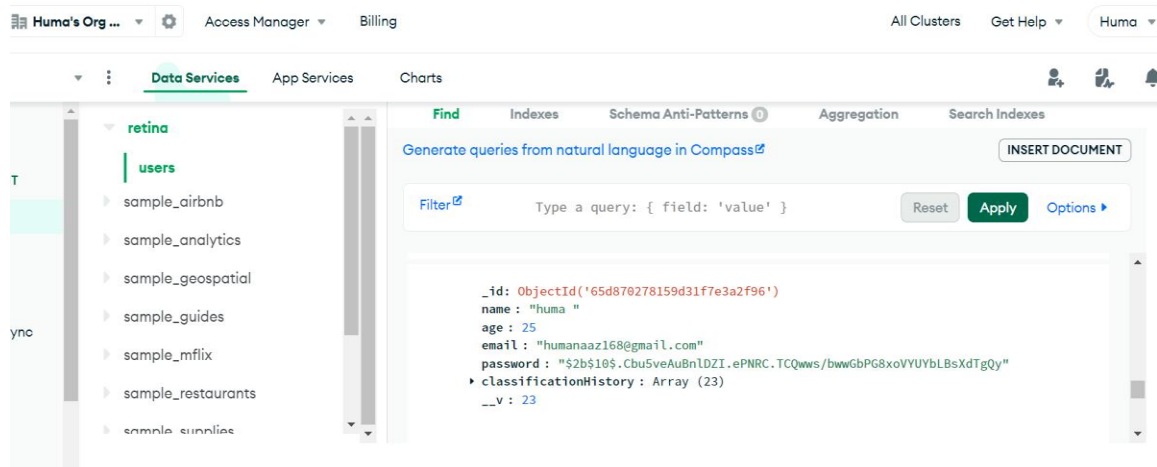


Figure 5.4: DR Patient's data Collected in the Cloud (Mondo DB database)

5.1.3 Make in India (MII)Ret Camera

Digital fundus imaging is widely used for diagnosing and managing DR, but its accessibility is limited in underdeveloped countries due to patient morbidity, high equipment costs, and optometrist shortages(Prayogo et al., 2023). Smartphones have revolutionized fundus imaging by integrating with slit-lamp devices, leading to the need for cost-effective, portable tools like the Make in India (MII)Ret Cam, which is essential in the healthcare landscape. Researchers(Chitkara et al., 2023; Sharma, 2017) have pursued contributing to the healthcare landscape of developing countries by investigating the potential of a MIIRet Cam for large-scale screenings, exemplified by the 20-D lens(Sharma et al., 2015). The MIIRet Cam is a budget-friendly, pioneering smartphone-based fundus camera designed to acquire central and peripheral retinal images, as shown in Figure 5.5. The device incorporates dedicated slots to accommodate a smartphone, featuring a built-in camera and a 20-D lens. Notably, the camera is adaptable to any 20D lens; however, the Volk or Ocular 20D lens is recommended for optimal fundus image capture. The specifications for the MIIRet Cam(Prayogo et al., 2023) are detailed in Table 5.1.

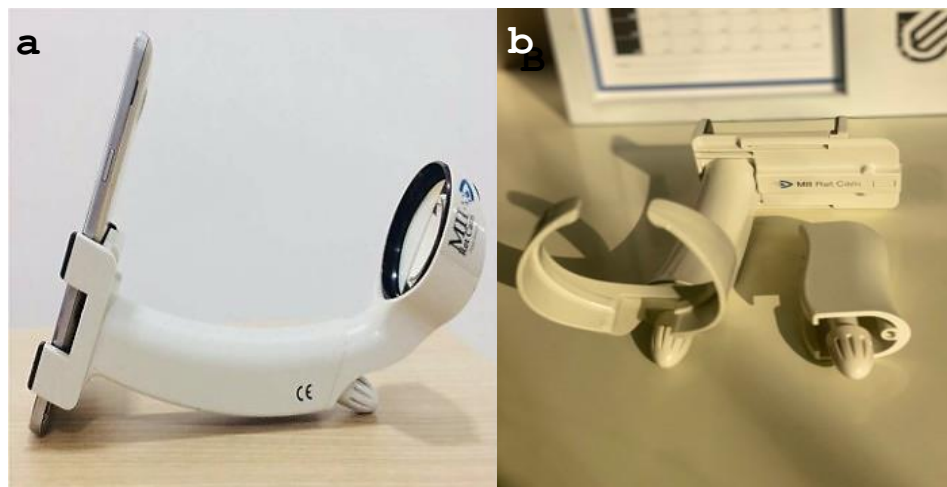


Figure 5.5: MIIRet Cam equipped with iPhone and 20 D lens B) MII Ret Cam

Table 5.1: MIIRet Cam Details

MIIRet Cam (Device Characteristics)	
Compatible with	iPhone/ Smartphone
Principal of Work	Indirect ophthalmoscopy method
Illumination Source	Built-in smartphone flash
Lens Type	20 D lens
Reference Standard	Indirect ophthalmoscopy
Retail Price	\$245–380
MIIRet Cam (Image Protocol)	
Mydriatic	Yes
Field of View	20–40

Several researchers(Behera & Pradhan, 2017; Chitkara et al., 2023; Kaur et al., 2020) have conducted pilot studies utilizing the MIIRet Cam to assess the camera's performance in fundus photo documentation, Purtscher's retinopathy, and DR detection. A research study carried out by Taranpreet et al. (Chitkara et al., 2023), examined a 3-year-old girl following a severe accident was examined, revealing signs suggestive of Purtscher's retinopathy in the right eye through MIIRet Cam-assisted smartphone-based fundus imaging. Meanwhile, the left eye exhibited a regular fundus examination. Lekha et al.(Lekha, n.d.) found that using Multiple Sequential Fluorescein Angiography, 78.57% of preterm infants with retinopathy of prematurity (ROP) could be accurately tracked and treated using serial imaging.

Ethical clearance has been obtained from the ethics committee at SMI Hospital in Dehradun. A panel of six members evaluated the research proposal and granted permission to proceed with the study. The IEC approval certificate can be found in Annexure I.

5.2 Result and Discussion

5.2.1 Demographic and Clinical Characteristics

The research encompassed 120 fundus images gathered from 60 participants. Table 5.2 illustrates the demographic and clinical characteristics of the 60 subjects. A higher proportion of the patients were male (55%; n=34), all identified as Asian. The average age of the participants was calculated to be 53 years, accompanied by a standard deviation of 14.17 years. The average BMI stood at 32.6 kilograms per square meter.

The standard deviation for diastolic blood pressure was 8.7, while for systolic blood pressure, it was 22.4. The average systolic blood pressure recorded was 136.8 mmHg, showing a significant number of patients with type 2 diabetes. The prevalence of DM was 80% out of 60 individuals. The mean haemoglobin A1c level was 8.0%, with a standard deviation of 2.0. Table 5.2 also shows comprehensive information regarding the visual features observed at eye level in the 120 fundus images.

Table 5.2: Demographic and Clinical Characteristics of the Participant

N=60	Total fundus Images=120
Male = 34	N = 68
Female = 26	N = 52
Mean Age	53
Std dev of Age	14.17
Std dev of Glucose (Fasting)	98.38
Std dev of diastolic blood pressure	8.7
Std dev of systolic blood pressure	22.4
Type 1/2 diabetic patients	48
Asian (Indian)	100%

5.2.2 Data Collection and Imaging Process

Two ophthalmologists from SMI Hospital performed a grading assessment to provide specialized recommendations. Figure 5.6 outlines the geographical parameters relevant to the research. The performance metrics of the algorithm and RetinaCare are assessed separately to evaluate the effectiveness of the proposed diagnostic instrument. Fundus images were acquired under the supervision of Dr. Priyanka Gupta, an MBBS in General Medicine and MS in Ophthalmology, at SMI Hospital in Dehradun, as depicted in Figure 5.9. Figures 5.7 and 5.8 present the patient information and fundus images acquired using the MIIRet camera.

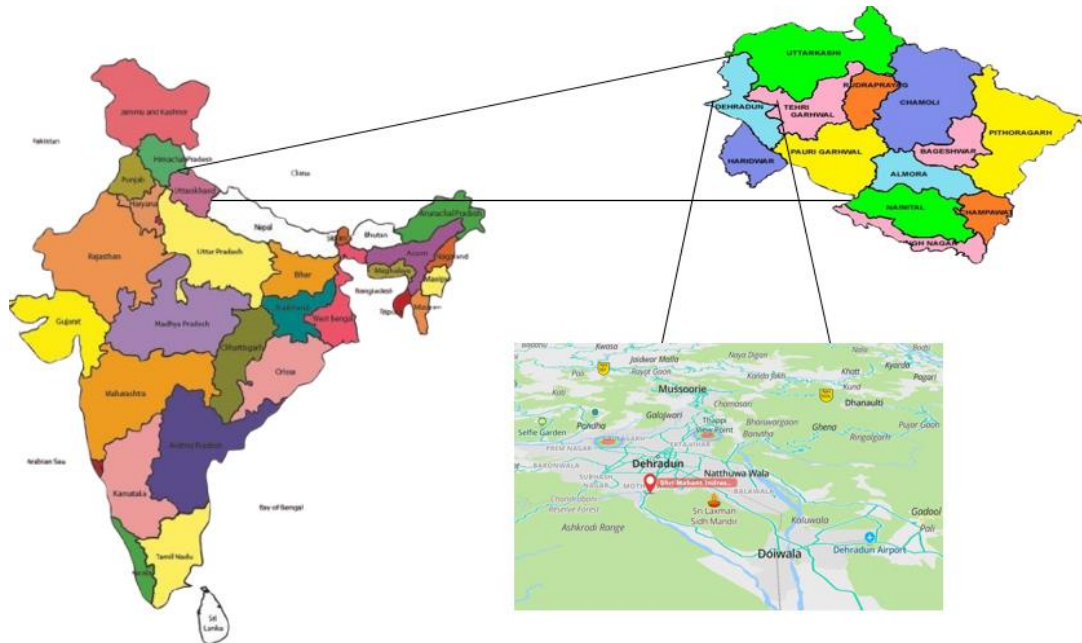


Figure 5.6: Geographical Study Map for DR Detection

Subjects	Eye	Gender	Age	Diabetic	Systolic BP	Diastolic BP	Sugar (fasting)	Ophthalmologist Grading	Application Grading
P1L	Left	Male	20.0	No	118.0	76.0	NaN	Mild NPDR	Mild NPDR
P1R	Right	Male	20.0	No	118.0	76.0	NaN	NO DR	Mild NPDR
P2L	Left	Male	64.0	yes	115.0	78.0	220.0	Moderate NPDR	Mild NPDR
P2R	Right	Male	64.0	yes	115.0	78.0	220.0	Severe NPDR	Severe NPDR
P3L	Left	Male	69.0	yes	120.0	90.0	119.0	PDR	PDR

Figure 5.7: DR Patient's data was collected at SMI hospital and an ophthalmologist-graded

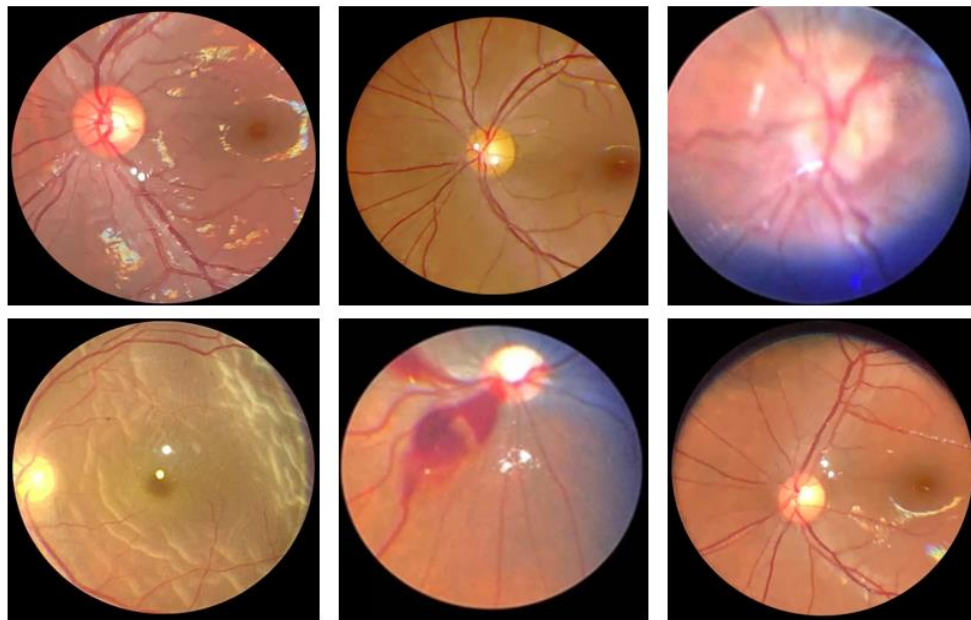


Figure 5.8: Fundus Images Captured with MIIRet Cam

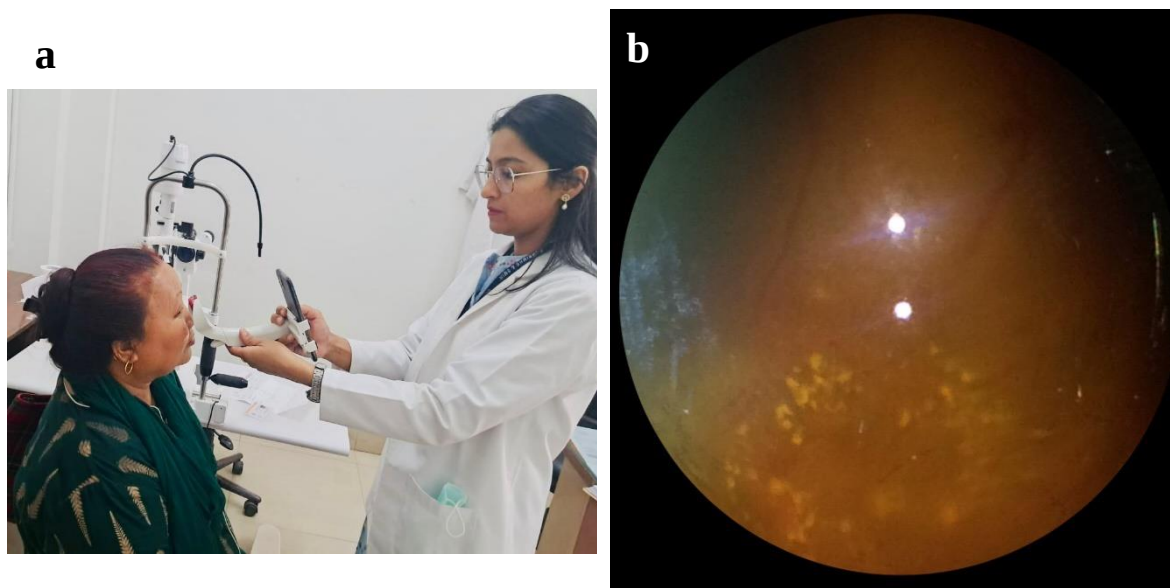


Figure 5.9: Dr Priyanka Gupta capturing DR fundus images using MIIRet cam smartphone-based fundus camera at SMI, Indires Hospital Dehradun (b) Fundus Image Captured with MIIRet Cam with moderate grading

Later, the images are carefully analyzed with RetinaCare to evaluate true and false positives and negatives, following the ophthalmologist's grading guidelines closely, as shown in Figure 5.10. The flow chart to assess the patients' grading is shown in Figure 5.11. After successful authentication through the application, the evaluator details are saved into the MongoDB database. Upon successful login, multiple fundus images can be taken, retaken, and uploaded using the application. Each grade for fundus analysis is also saved to the dataset.

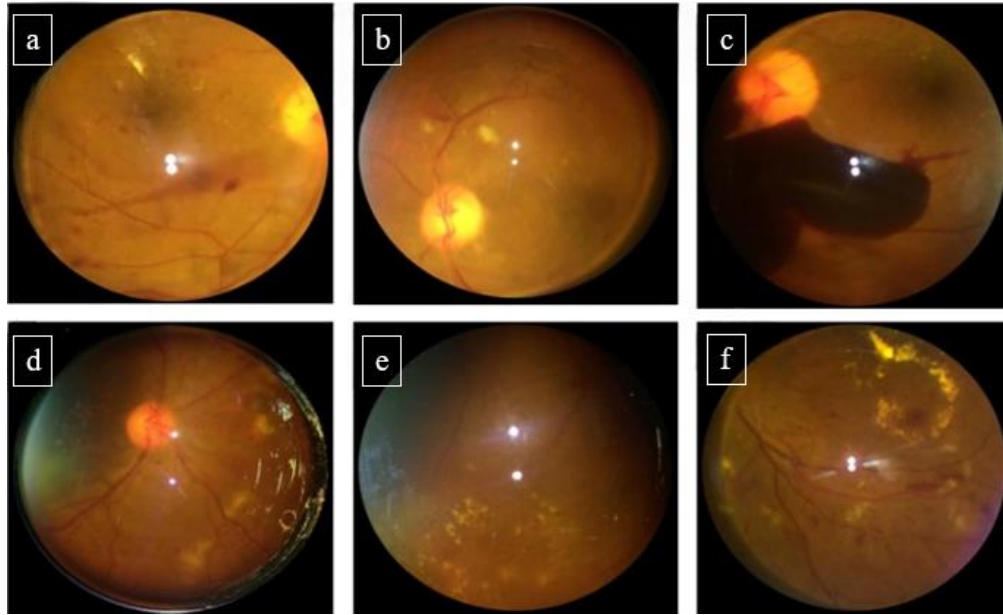


Figure 5.10: DR fundus images captured using MIIRet cam smartphone-based fundus camera at SMI, IndiresH Hospital Dehradun, India with severity grading from ophthalmologist a) Severe NPDR b) Moderate NPDR c) Severe NPDR d) Moderate NPDR e) Moderate NPDR f) Severe NPDR

The evaluation of DR, from Mild NPDR to PDR, is based on the criteria established by the Early Treatment DR Study and the American Academy of Ophthalmology guidelines. The evaluation of RetinaCare using a scoring system from 0 to 4 has been conducted following the defined categories.

5.2.3 Image Analysis and Grading

This proposed approach leverages the Fast Application Programming Interface (API) to create a RESTful web service that facilitates image classification. Fast API is a modern web framework in Python designed to build APIs quickly and efficiently. It supports asynchronous programming, making it well-suited for handling requests and performing tasks concurrently, such as image uploads and processing.

In RESTful web services, this API adheres to REST principles by defining endpoints that interact with resources via HTTP. The /ping endpoint corresponds to a GET request, serving as a health check to confirm the server is running. The /predict endpoint uses a POST request to accept an uploaded image file, making it part of a resource-based interaction. Clients can send image data to this endpoint, and the server responds with the predicted image class and confidence score, adhering to the stateless nature of RESTful services, where each request contains all the information needed for processing.

Thus, Fast API efficiently handles Hypertext Transfer Protocol (HTTP) requests and responses, ensuring quick development and performance. At the same time, the design follows RESTful principles to provide an organized and scalable API. MongoDB serves as the database where user information and prediction results are stored. Here is how MongoDB interacts with the system based on the flowchart:

1. **User Login/Signup:** When a user logs in or signs up, their details (such as username, email, and password) are verified or added to the MongoDB database. If the user is new, their details are inserted as a new document in the MongoDB collection. If they are returning users, their login details are validated against existing records.
2. **Image Upload:** A user can upload an image for analysis after successfully logging in. Upon transmitting the image to the Node.js server, the system verifies the user's information, including their classification as a new or returning user. The information is recorded in a MongoDB database.
3. **Prediction and Storage:** Once the image is sent from the Node.js server to the FCCNN API Server for prediction, the prediction results are generated. These results, image metadata, and user details are returned to the Node.js server.
4. **Storing Results in MongoDB:** The predicted data (like the classification result and confidence score) is then stored in the MongoDB database, which ensures that for each user, the image, prediction results, and other relevant details (such as timestamps) are saved in a structured format for future reference. Each user might

have a document in MongoDB that is updated with new prediction results whenever they upload a new image.

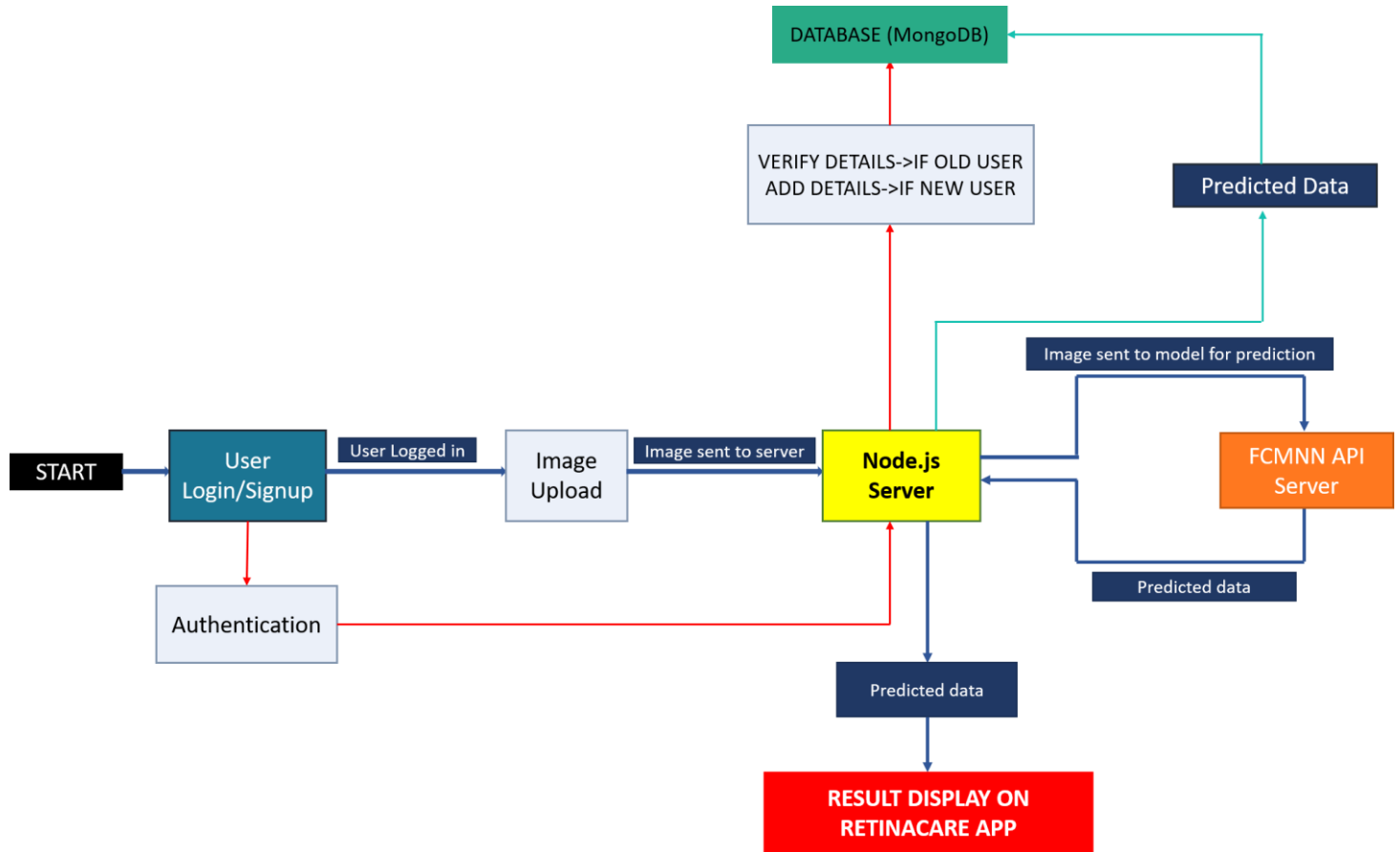


Figure 5.11: Flow Chart for Image flow through API for DR Severity Grading

The MIIRet captured images from DR patients are evaluated against the labelled pictures using the step-by-step process as shown below:

1. Each classification is assigned a specific numerical label: a value of 1 indicates mild severity, 2 corresponds to moderate severity, 3 signifies severe severity, and 4 represents

2. Collect the annotated dataset of MIIRet cam-captured fundus pictures graded by ophthalmologists (Figure 7) and utilize the RetinaCare application to grade the same set of fundus pictures and record the grades (1-4) assigned by the application.
3. Draw a Confusion Matrix and Calculate TP (True Positive), TN (True Negative), FP (False Positive), and FN (False Negative).
4. Calculate the performance metrics (Accuracy, precision, recall, and f-measure) using the confusion metrics.
5. Assess the performance of RetinaCare by examining the calculated metrics.

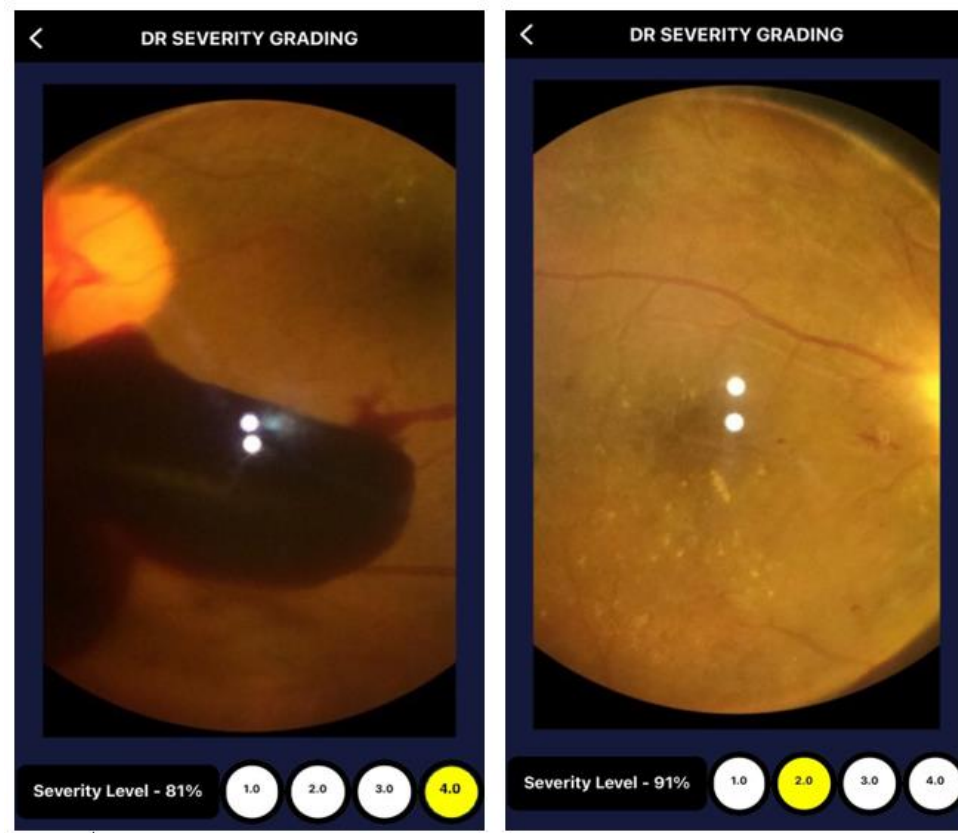


Figure 5.12: RetinaCare- DR Fundus Images Testing with Moderate and Severe Grading Matching with Ophthalmologist Grading

5.2.4 Performance Evaluation of RetinaCare

The fundus images are tested against all the labelled MIIRet cam images provided by the ophthalmologist, as shown in Figure 5.10. Using a confidence percentage, the DRClassification screen in the RetinaCare app shows how severe the condition is (Figure 5.12). It also assigns a grade from 1 to 4. Grade 1 indicates Mild NPDR, Grade 2 indicates Moderate NPDR, Grade 3 signifies Severe NPDR, and Grade 4 refers to PDR. RetinaCare has shown impressive results with a 96 TP. Figure 5.12 shows the confusion matrix utilized to evaluate instances from RetinaCare.

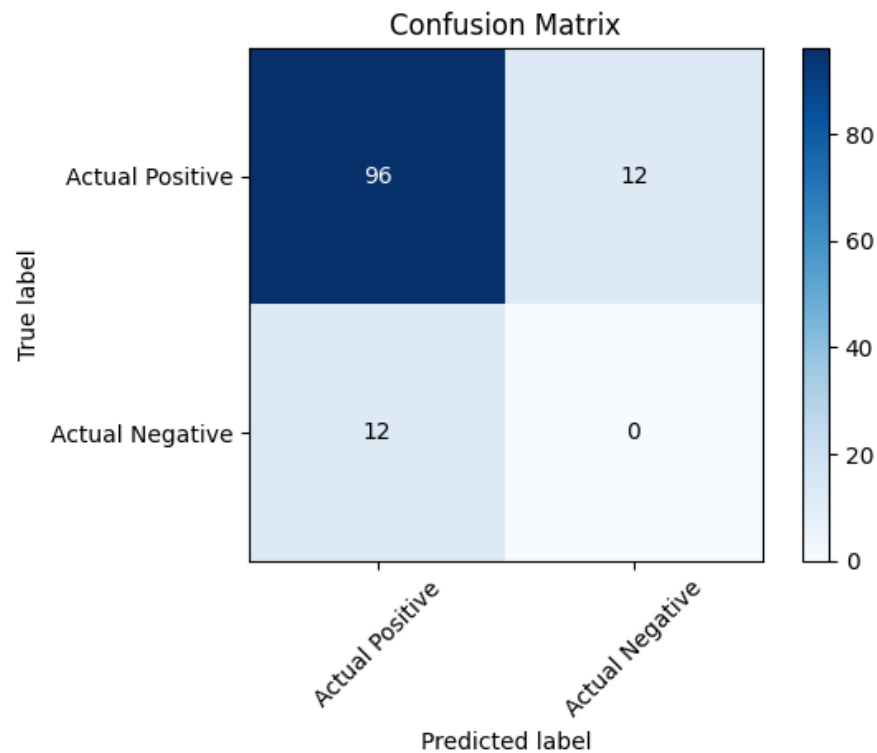


Figure 5.13: Visual Representation of Confusion Matrix

The algorithm's performance is assessed using a confusion matrix, which evaluates metrics including accuracy, precision, recall, and F-measure, as shown in Figure 5.13. The accuracy metric indicates that the algorithm correctly classifies 80% of all patients. The algorithm's precision and recall are 88%, indicating high overall accuracy. Still, low false positives and false negatives show a low rate of positive cases among correctly predicted positives and all actual positive cases.

5.2.5 Correlation with Ophthalmologist Grading

The correlation between the grading given by ophthalmologists and application is evaluated using Spearman's correlation coefficient. Figure 5.14 presents a comparative analysis of the grading conducted by the ophthalmologist and that from RetinaCare.

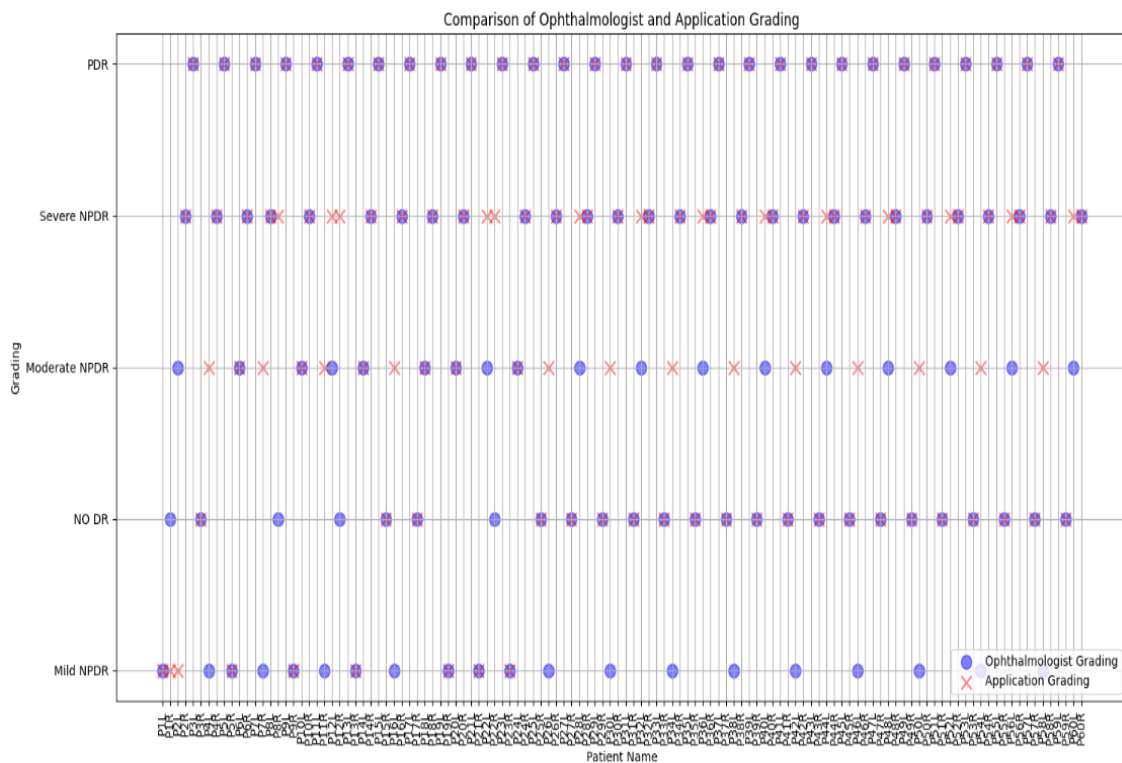


Figure 5.14: Comparison of ophthalmologist and application grading for DR across different patients

The correlation matrix is shown in Figure 5.15. The coefficient value is 0.9363780027609252, indicating a high correlation between the ophthalmologist and application grading. Spearman's correlation coefficient ρ can be calculated using the equation (8).

$$\rho = 1 - \frac{6 \sum d_i^2}{n(n^2-1)} \quad (8)$$

Where d_i indicates the difference in ranks for each paired observation, whereas n signifies the total number of observations. The graphical depiction of this performance is presented in Figure 5.16.

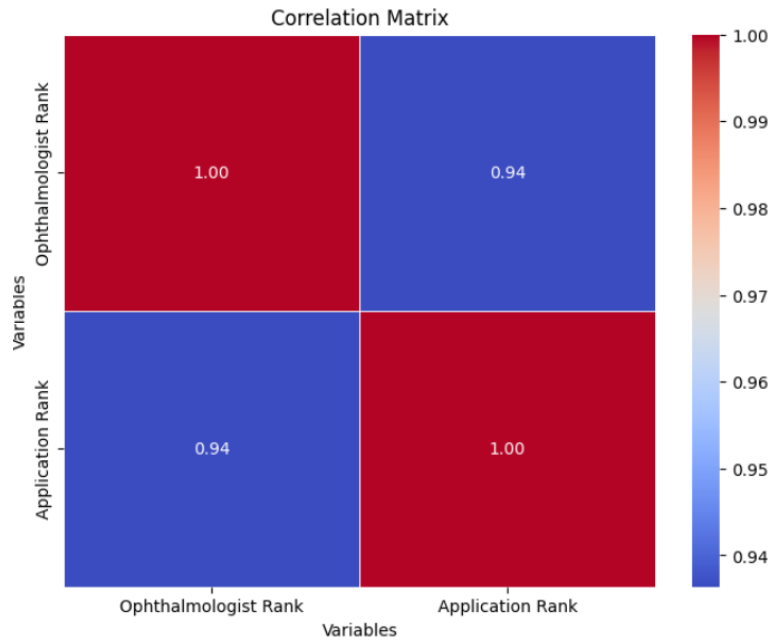


Figure 5.15: Correlation Matrix of RetinaCare and Ophthalmologist Rank

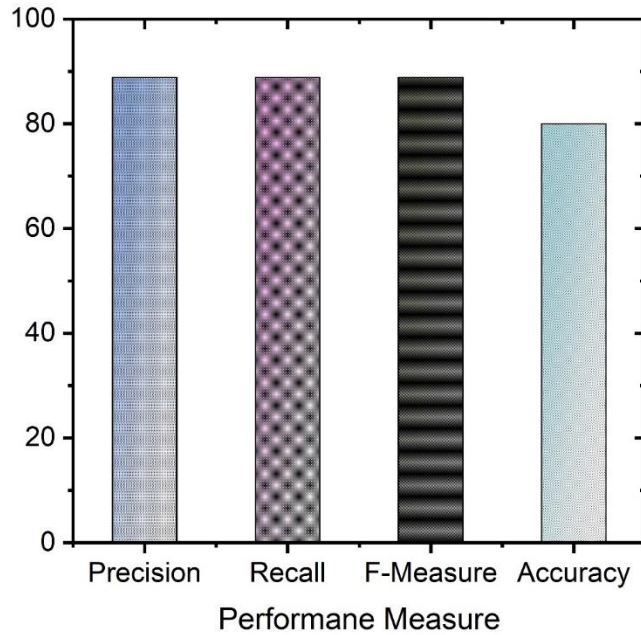


Figure 5.16: Performance Evaluation for RetinaCare

5.3 Summary

This chapter introduces a web application tool that integrates the proposed FCCNN model as an API, creating an efficient DR detection and severity grading platform from mild NPDR to PDR. Real-time testing with DR patients was conducted at SMI Hospital, yielding a high accuracy rate. The MIIRet cam was employed as a portable fundus camera, making the setup especially beneficial for remote areas lacking ophthalmologists or advanced equipment like tabletop fundus cameras. This tool serves as a preliminary diagnostic aid for patients, providing alerts in severe cases to prompt timely medical consultation. Enhancements in the tool's interpretability and performance are needed to improve diagnostic clarity for both doctors and patients.

Chapter VI

CONCLUSION

Conventional clustering techniques generate feature vectors based on domain-specific knowledge and subsequently implement a clustering algorithm on these features. In contrast, DL methodologies combine feature extraction and clustering within a unified framework, allowing for the direct clustering of original images with enhanced performance. The proposed research investigates various deep clustering algorithms to gain insights into the challenges of improving DNN through unsupervised clustering techniques. This study examines the necessary approaches for effectively applying the UL framework to the DNN to mitigate the reliance on labelled data for training the algorithm. A comprehensive review of clustering algorithms is performed, accompanied by an evaluation of the results.

Furthermore, the topic of local optima in FCM is examined, resulting in the development of the MdFCM algorithms. The results of the modified version of FCM in clustering are computed and based on these analyses, and the MdFCM is enhanced with the CNN for the DR classification. The following statements present the findings obtained from the current research.

1. This study introduces a new pre-processing technique for contrast enhancement. Greyscale and colour fundus preprocessing are performed for background segmentation of the OD and blood vessel segmentation.
2. The proposed work presents a modified version of the Fuzzy C-means clustering algorithm to overcome FCM's local optima problem.

3. The suggested work presents a hybrid deep clustering algorithm that combines the proposed modified FCM and CNN for severity grading of the DR fundus images.
4. The proposed algorithms achieved an accuracy rate of 94%, outperforming existing models.
5. Experiments were conducted using standard and primary datasets collected from an eye center in India.
6. The algorithms demonstrated an NMI score of 95% and an ARI score of 92%, indicating robust clustering performance.
7. A web-based tool, RetinaCare, was developed to validate the algorithm's performance, incorporating MIIRet Cam, a smartphone-based camera.
8. The RetinaCare tool is validated at SMI Hospital, India, where it is tested on 60 patients.
9. During clinical validation, the RetinaCare tool achieved an accuracy level of 80%, showcasing its practical applicability.

6.1 Future Directions

The proposed approach can be extended for glaucoma detection using a DIGS Pro handheld Camera. As glaucoma increasingly emerges as a primary cause of blindness, with projections estimating its impact on approximately 80 million individuals worldwide by 2020 and an anticipated rise to 111.8 million by 2040, this extension provides substantial opportunities for the timely recognition and management of this challenging eye condition. There is still a need to enhance the existing methods to improve performance in DR detection. This section analyzes potential directions for future research and the challenges researchers must address to improve the effectiveness of DR classification, as depicted in Figure 6.1.

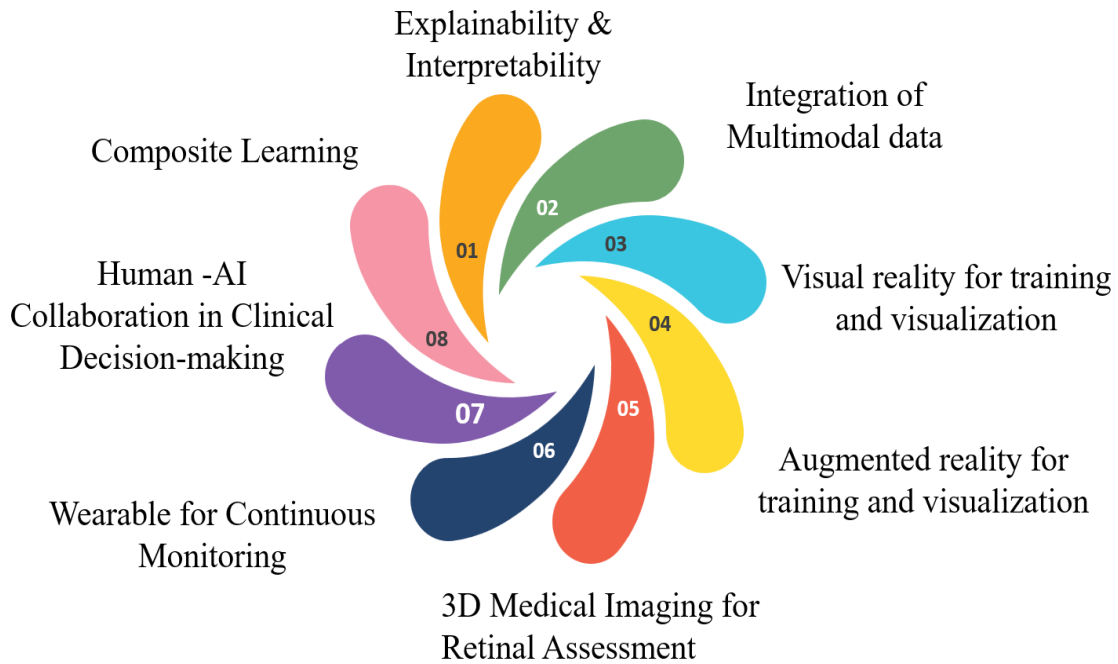


Figure 6.1: Future directions for DR detection (Gauslund, 2022)

6.1.1 Explainability and Interpretability: Achieving clarity in DL models utilized to detect DR presents a significant challenge. Improving model explainability is essential to earn healthcare professionals' trust. Future research should aim to create models communicating the rationale behind their predictions, making their decision-making processes transparent and easy to understand.

6.1.2 Combining Multimodal Data: The integration of data from various imaging modalities, such as OCT and fundus photography, poses a significant challenge in the field. Future research should focus on methods for integrating diverse data modalities to facilitate a comprehensive assessment of the progression and severity of DR.

6.1.3 Leveraging Augmented and Virtual Reality for Visualization: The utilization of virtual and augmented reality (VR/AR) technologies in research concerning DR is anticipated to enhance medical education and visualization methodologies substantially. Future projects aim to advance immersive VR and AR technologies to support healthcare practitioners in training for diabetic retinopathy diagnosis.

6.1.4 Advanced 3D Medical Imaging Methods for Retinal Evaluation: Advances in 3D medical imaging will offer more precise assessments for DR detection. This includes innovations in 3D OCT and other imaging methods that capture volumetric data, helping to reveal subtle structural changes linked to DR with greater clarity.

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List of Publications

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Journal Publications

- (1) Naz, H., Nijhawan, R., & Ahuja, N. J. (2022). An automated unsupervised deep learning-based approach for diabetic retinopathy detection. *Medical & Biological Engineering & Computing*, 60(12), 3635-3654.
- (2) Naz, H., Nijhawan, R., & Ahuja, N. J. (2024). Clinical utility of handheld fundus and smartphone-based camera for monitoring diabetic retinal diseases: a review study. *International Ophthalmology*, 44(1), 1-28.
- (3) Naz, H., Ahuja, N. J., & Nijhawan, R. (2024). Diabetic retinopathy detection using supervised and unsupervised deep learning: a review study. *Artificial Intelligence Review*, 57(5), 1-66.
- (4) Naz, Huma, and Neelu Jyothi Ahuja. "A novel contrast enhancement technique for diabetic retinal image pre-processing and classification." *International Ophthalmology* 45.1 (2024): 11.
- (5) Case Study on Detection of Retinal Abnormalities with Unsupervised Deep Learning Using Retina Care: A Standalone Application. Under Review in *Neural Computing and Applications*.

Conference Proceedings

- (1) Naz, H., Nijhawan, R., & Ahuja, N. J. (2022, October). DT-DL Based Hybrid Approach for Early Detection of Diabetes Using PIMA Dataset. In 2022 10th International Conference on Reliability, Infocom Technologies and Optimization (Trends and Future Directions) (ICRITO) (pp. 1-6). IEEE.
- (2) Naz, H., & Ahuja, N. J. (2024, March). RetinaCare: Diabetic Retinopathy Detection with VGG16-based Web Application. In 2024 11th International Conference on Reliability, Infocom Technologies and Optimization (Trends and Future Directions) (ICRITO) (pp. 1-6). IEEE.

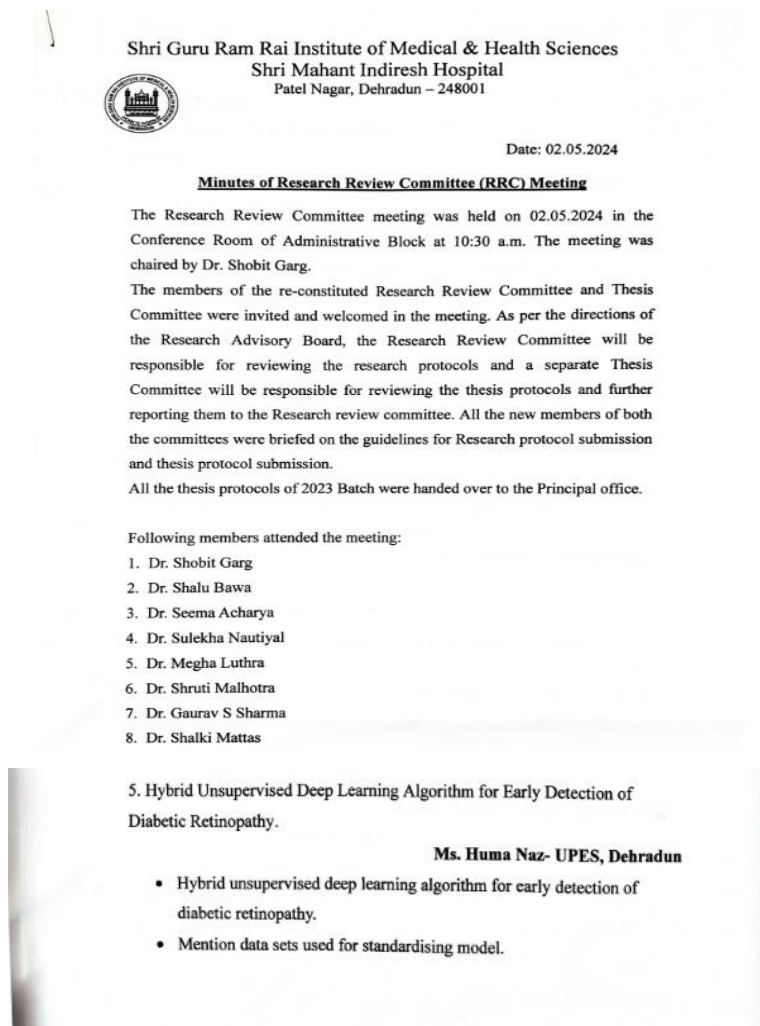
Other Journal Publications

- (1) Naz, H., Nijhawan, R., Ahuja, N. J., Al-Otaibi, S., Saba, T., Bahaj, S. A., & Rehman, A. (2023). Ensembled Deep Convolutional Generative Adversarial Network for Grading Imbalanced Diabetic Retinopathy Recognition. *IEEE Access*, 11, 120554-120568.
- (2) Naz, H., Nijhawan, R., Ahuja, N. J., Saba, T., Alamri, F. S., & Rehman, A. (2024). Micro-segmentation of retinal image lesions in diabetic retinopathy using energy-based fuzzy C-Means clustering (EFM-FCM). *Microscopy Research and Technique*, 87(1), 78-94.
- (3) Naz, H., Saba, T., Alamri, F. S., Almasoud, A. S., & Rehman, A. (2024). An Improved Robust Fuzzy Local Information K-Means Clustering Algorithm for Diabetic Retinopathy Detection. *IEEE Access*.

Annexure I

The ethics committee at SMI Hospital, Dehradun, reviewed the research proposal, and approval was given to proceed with the study. A minute-of-meeting screenshot and an ethical certificate confirming this approval are shown below. The complete minutes of the meetings can be accessed through:

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Institutional Ethics Committee (IEC)
Reference No. SGRR/IEC/05/24
Patel Nagar, Dehradun-248001
(Registration No. ECR/710/Inst/UK/2015/RR-21)



Certificate

Institutional Ethics Committee has reviewed the research protocol entitled "Hybrid Unsupervised Deep Learning Algorithm for Early Detection of Diabetic Retinopathy".

by **Huma Naz**, Junior Research Fellow from Dept. of School of Computer Science & Engineering, UPES, Dehradun.

The research proposal is found to conform to Institutional Ethics Committee regulations and has been **Approved**.

Yours sincerely



Address for correspondence: Institutional Ethics Committee, Administrative Block, SGRRIM&HS, Patel Nagar, Dehradun-248001.

Huma Naz

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