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DEVELOPMENT AND EVALUATION OF A TRANSFER LEARNING-BASED FRAMEWORK FOR EARLY DETECTION AND CLASSIFICATION OF DIABETES MELLITUS THROUGH MEDICAL IMAGING AND BIOCHEMICAL DATA

Hussein Fadhil Abdulabbas ABEDI

Master's Thesis

Supervisor

Asst. Prof. Dr. Ayça KURNAZ TÜRKBEN

İstanbul, 2023

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The thesis titled DEVELOPMENT AND EVALUATION OF A TRANSFER LEARNING-BASED FRAMEWORK FOR EARLY DETECTION AND CLASSIFICATION OF DIABETES MELLITUS THROUGH MEDICAL IMAGING AND BIOCHEMICAL DATA prepared HUSSEIN FADHIL ABDULABBAS ABEDI and submitted on 21/12/2023 has been **accepted unanimously** for the degree of Master of Science in Information Technologies.

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I hereby declare that this thesis meets all format and submission requirements of a Master's thesis.

I hereby declare that all information and data presented in this graduation project has been obtained in full accordance with academic rules and ethical conduct. I also declare all unoriginal materials and conclusions have been cited in the text and all references mentioned in the Reference List have been cited in the text, and vice versa as required by the abovementioned rules and conduct.

Hussein Fadhil Abdulabbas ABEDI

Signature

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ABSTRACT

DEVELOPMENT AND EVALUATION OF A TRANSFER LEARNING-BASED FRAMEWORK FOR EARLY DETECTION AND CLASSIFICATION OF DIABETES MELLITUS THROUGH MEDICAL IMAGING AND BIOCHEMICAL DATA

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Diabetes mellitus, a complex metabolic disorder characterized by elevated blood glucose levels, has emerged as a global healthcare crisis of unprecedented magnitude. With its relentless increase in prevalence and the profound impact it exerts on individuals, healthcare systems, and societies worldwide, diabetes mellitus presents a multifaceted challenge that demands innovative and transformative solutions, this research seeks to enhance healthcare outcomes by contributing to a more efficient and effective diagnostic process for this chronic metabolic disorder. The overarching objective of this thesis is to pioneer the development and evaluation of a transfer learning-based framework designed explicitly for early detection and accurate classification of diabetes mellitus through the integration of medical imaging and biochemical data.

Keywords: CNN, AI, DM, DL, ML.

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ABBREVIATIONS

AI	:	Artificial Intelligence
FPG	:	Fasting Plasma Glucose
IDF	:	International Diabetes Federation
CT	:	Computed Tomography
MRI	:	Magnetic Resonance Imaging
ML	:	Machine Learning

1. INTRODUCTION

1.1 BACKGROUND

Diabetes mellitus is a global health epidemic with a profound impact on individuals and healthcare systems. This chronic metabolic disorder, characterized by elevated blood glucose levels, poses significant challenges in early detection and classification for timely intervention. The intersection of medical imaging and biochemical data offers a promising avenue for improving the accuracy and efficiency of diabetes diagnosis, as it can provide a comprehensive view of the disease's manifestations within the body. In recent years, the advent of transfer learning techniques in the field of machine learning has revolutionized the way we approach complex medical problems by harnessing the knowledge acquired from one domain and applying it to another. This thesis embarks on a transformative journey, aiming to develop and evaluate a transfer learning-based framework specifically designed for the early detection and classification of diabetes mellitus, leveraging both medical imaging and biochemical data.

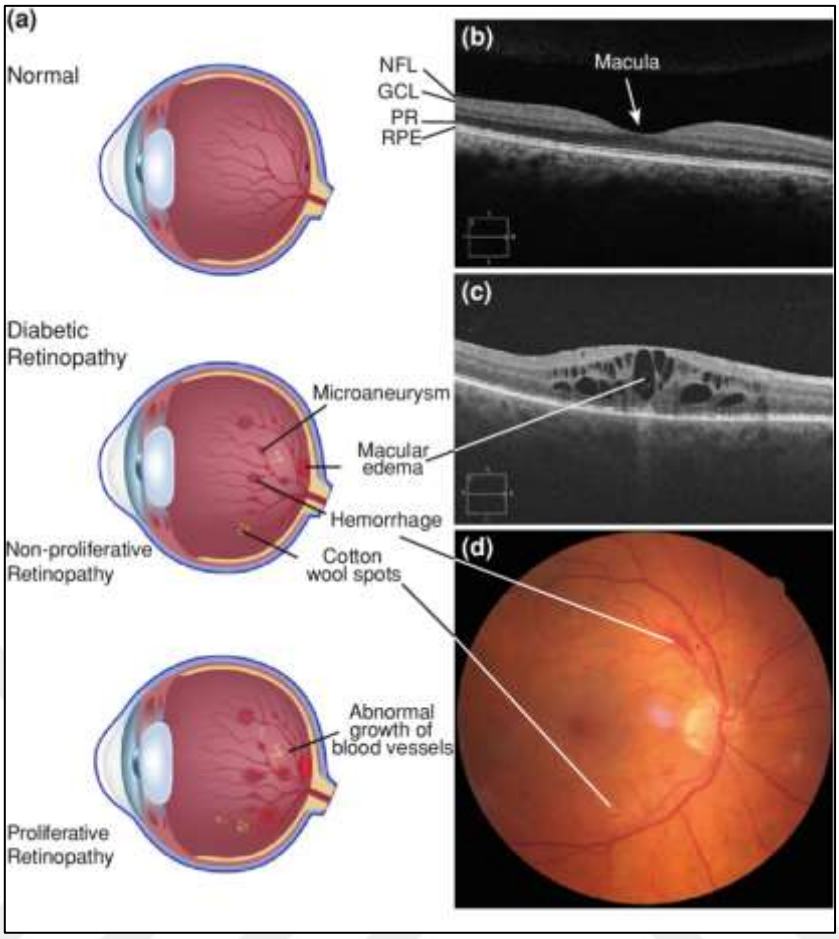

Figure 1.1: Diabetic Retina DR.

The significance of this research cannot be overstated, given the alarming rise in diabetes cases worldwide and the potential for transfer learning to enhance diagnostic capabilities. This introduction provides a glimpse into the broader context of diabetes mellitus, the role of medical imaging and biochemical data in its diagnosis, and the growing promise of transfer learning as a powerful tool in addressing this critical healthcare challenge. Over the course of this thesis, we will delve into the intricacies of this innovative framework, exploring its development, evaluation, and potential impact on the early detection and classification of diabetes mellitus.

Diabetes mellitus, a complex metabolic disorder characterized by elevated blood glucose levels, has emerged as a global healthcare crisis of unprecedented magnitude. With its relentless increase in prevalence and the profound impact it exerts on individuals, healthcare systems, and societies worldwide, diabetes mellitus presents a multifaceted challenge that demands innovative and transformative solutions. The chronic nature of the disease, coupled

with its potential to lead to severe complications such as cardiovascular diseases, retinopathy, neuropathy, and kidney dysfunction, underscores the critical importance of early detection and accurate classification. Timely intervention is not merely desirable but imperative in mitigating the disease's devastating consequences. Traditionally, diabetes diagnosis has relied heavily on fasting plasma glucose (FPG) measurements, oral glucose tolerance tests (OGTT), glycated hemoglobin (HbA1c) assessments, and the presence of clinical symptoms. While these methods have played a pivotal role in clinical practice, they are not without their limitations. They often fail to provide an early warning, necessitating a reevaluation of diagnostic paradigms to enhance their sensitivity and specificity. The landscape of medical diagnostics, particularly in the context of diabetes mellitus, has undergone a profound transformation in recent years. This transformation is marked by the intersection of medical imaging technologies and biochemical data, ushering in a new era of comprehensive disease assessment. Medical imaging modalities such as magnetic resonance imaging (MRI), computed tomography (CT), and positron emission tomography (PET) offer a non-invasive means to visualize the internal physiological changes associated with diabetes. Meanwhile, the wealth of biochemical markers available through blood tests provides valuable insights into the body's metabolic status. Together, these modalities furnish a rich source of information that can potentially revolutionize diabetes diagnosis. In parallel with these advancements, the field of machine learning and artificial intelligence (AI) has made remarkable strides. Machine learning models have demonstrated their capacity to analyze vast and complex datasets, including medical images and biochemical profiles, with remarkable accuracy and efficiency. The emergence of transfer learning, a technique that enables the transfer of knowledge from one domain to another, has been particularly transformative. This transfer of knowledge empowers machine learning models to generalize better and make more informed decisions, even when faced with limited data.

1.2 PROBLEM STATEMENT

The global burden of diabetes mellitus, a complex metabolic disorder characterized by hyperglycaemia, has escalated to pandemic proportions, posing a multifaceted and escalating challenge to individuals, healthcare systems, and society at large. According to the International Diabetes Federation (IDF), approximately 463 million people were living with diabetes in 2019, a number projected to surge to an alarming 700 million by 2045,

representing an undeniable public health crisis. Amidst this burgeoning prevalence, early detection and accurate classification of diabetes mellitus are pivotal for effective disease management, improved patient outcomes, and the alleviation of the associated socioeconomic burdens. The traditional paradigm of diagnosing diabetes has primarily relied upon fasting plasma glucose (FPG) measurements, oral glucose tolerance tests (OGTT), glycated hemoglobin (HbA1c) assessments, and clinical symptoms. These diagnostic methods, while established and clinically valuable, exhibit inherent limitations. The challenges encompass variations in individual metabolic responses, potential misdiagnoses, and the dependence on invasive and resource-intensive biochemical tests. Moreover, by the time overt clinical symptoms manifest, the disease often has already progressed to advanced stages, limiting the scope for preventive interventions. Simultaneously, advancements in medical imaging technologies have offered a non-invasive window into the intricate physiological changes accompanying diabetes. Imaging modalities such as magnetic resonance imaging (MRI), computed tomography (CT), and positron emission tomography (PET) have unveiled the subtleties of diabetic complications, ranging from microvascular changes in retinopathy to macrovascular lesions in cardiovascular diseases. However, the interpretation of these complex imaging data demands expertise and computational capabilities that often exceed the capacities of conventional diagnostic tools. In the contemporary era, the convergence of artificial intelligence (AI) and machine learning (ML) has fueled a revolution in healthcare, offering a promising avenue for addressing the diagnostic intricacies of diabetes mellitus.

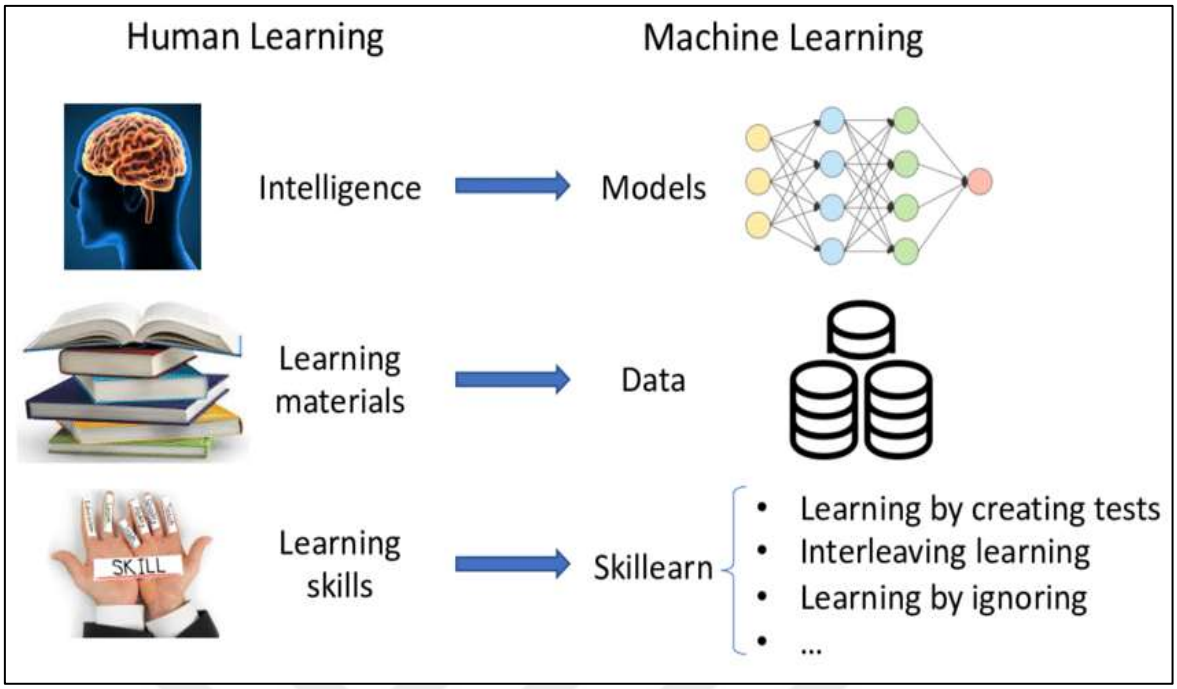

Figure 1.2: Machine Learning ML.

The deployment of ML models for the analysis of medical images and biochemical data has emerged as a transformative strategy, potentially circumventing the shortcomings of traditional diagnostic approaches. Nevertheless, the successful application of ML in this context hinges on the availability of large and diverse datasets, robust feature extraction techniques, and a deep understanding of the underlying biological processes, which continue to pose formidable challenges. One of the most notable breakthroughs in the realm of ML is the emergence of transfer learning, a technique that leverages knowledge acquired from one domain to enhance performance in another. Transfer learning embodies the promise of improved model generalization, reduced data requirements, and enhanced diagnostic accuracy. However, the adaptation of transfer learning methodologies to the intricate and multifaceted landscape of diabetes mellitus diagnosis, which involves integrating information from medical imaging and biochemical data, remains a relatively underexplored and complex endeavor. This multifaceted confluence of challenges forms the crux of the problem statement addressed in this thesis. The overarching problem is the urgent need for a novel, sophisticated, and efficient diagnostic framework that can harness the potential of transfer learning to integrate information from medical imaging and biochemical data for the early detection and accurate classification of diabetes mellitus. This framework must address

the limitations of conventional diagnostic methods, leverage the wealth of data available, navigate the intricacies of medical imaging analysis, and capitalize on the remarkable capabilities of transfer learning. the central issue at hand is to devise and rigorously evaluate a transfer learning-based framework capable of revolutionizing diabetes diagnosis, offering a transformative solution to the escalating global health crisis, and substantially improving patient care by enabling early intervention and personalized treatment strategies. In the subsequent chapters of this thesis, we embark on a comprehensive exploration of the development and evaluation of this framework, delving into its intricacies and potential ramifications for the field of healthcare, with a steadfast commitment to advancing our understanding and capacity to combat diabetes mellitus effectively.

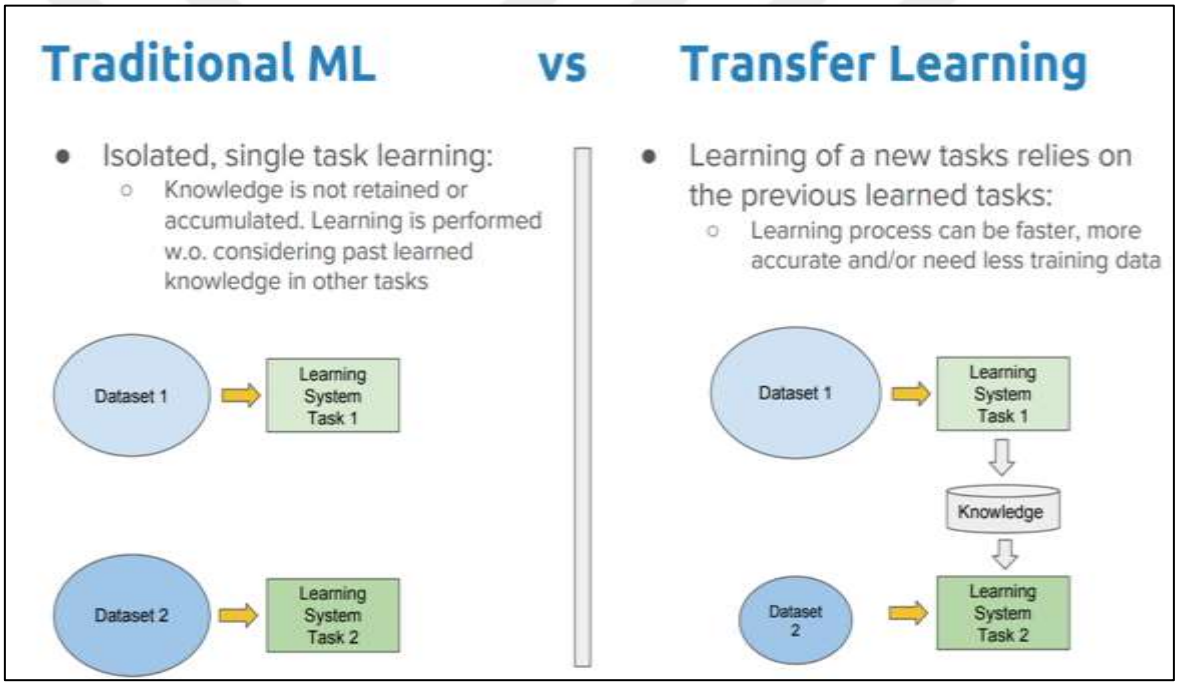

Figure 1.3: Machine Learning vs Transfer Learning.

Amidst the convergence of these transformative trends, a profound problem persists: the need for a robust, transfer learning-based framework that seamlessly integrates information from medical imaging and biochemical data to enable early detection and precise classification of diabetes mellitus. Such a framework must navigate the intricacies of two distinct domains, bridging the gap between the visual insights offered by medical imaging and the molecular information encoded in biochemical data. Furthermore, it must overcome the challenges posed by the inherent variability of biological systems and the diverse

manifestations of diabetes. The existing body of research in diabetes diagnosis has made significant strides in utilizing medical imaging or biochemical data individually. However, the true potential lies in their synergistic integration, a prospect that remains relatively uncharted in the current landscape. Challenges of feature extraction, data harmonization, and model generalization must be addressed to harness the full power of this integrated approach.

1.3 THESIS OBJECTIVES

1.3.1 General Objective

The general objective of this thesis is to advance the field of diabetes mellitus diagnosis through the development and evaluation of a transfer learning-based framework that integrates medical imaging and biochemical data, with the overarching aim of enabling early detection and accurate classification of diabetes mellitus. This research seeks to enhance healthcare outcomes by contributing to a more efficient and effective diagnostic process for this chronic metabolic disorder. The overarching objective of this thesis is to pioneer the development and evaluation of a transfer learning-based framework designed explicitly for early detection and accurate classification of diabetes mellitus through the integration of medical imaging and biochemical data.

1.3.2 Specific Objectives

a. To conduct a comprehensive review of the current state of diabetes mellitus diagnosis, encompassing traditional biochemical methods, medical imaging modalities, and emerging machine learning approaches.
b. To compile and preprocess a diverse and representative dataset of medical imaging and biochemical data related to diabetes mellitus, ensuring data quality, integrity, and ethical considerations.
c. To design and implement a transfer learning-based framework that can effectively leverage knowledge from related domains and modalities, integrating medical imaging and biochemical data for diabetes diagnosis.
d. To develop robust feature extraction techniques tailored to medical imaging data, optimizing their capability to capture intricate patterns and nuances specific to diabetes mellitus.

e. To explore novel approaches for feature engineering and selection, with a focus on biochemical data, to enhance the diagnostic capabilities of the proposed framework.
f. To rigorously evaluate the developed framework's performance against traditional diagnostic methods and state-of-the-art machine learning models, utilizing appropriate metrics, cross-validation techniques, and statistical analyses.

1.4 THESIS CONTRIBUTIONS

a. Innovative Framework for Diabetes Diagnosis: This thesis introduces an innovative transfer learning-based framework that integrates medical imaging and biochemical data for the early detection and accurate classification of diabetes mellitus. This novel approach represents a significant advancement in the field of diabetes diagnosis.
b. Enhanced Diagnostic Accuracy: The research contributes to improved diagnostic accuracy by harnessing the potential of transfer learning, effectively leveraging knowledge from related domains and modalities. By combining medical imaging and biochemical data, the framework offers a more comprehensive and precise understanding of the disease, enhancing early detection.
c. Robust Feature Extraction Techniques: The development of robust feature extraction techniques tailored to medical imaging data represents a substantial contribution. These techniques are optimized to capture intricate patterns and nuances specific to diabetes mellitus, improving the interpretability and performance of the framework.
d. Innovative Feature Engineering for Biochemical Data: The thesis explores innovative approaches for feature engineering and selection, particularly in the context of biochemical data. This contribution enhances the diagnostic capabilities of the framework, enabling it to extract valuable information from diverse biochemical markers.
e. Comprehensive Evaluation and Validation: Rigorous evaluation and validation of the framework against traditional diagnostic methods and state-of-the-art machine learning models contribute to the scientific community's understanding of its capabilities. This research provides empirical evidence of its effectiveness and reliability.
f. Interpretability and Practical Applicability: The assessment of the framework's interpretability, scalability, and computational efficiency is crucial for its practical

applicability in real-world clinical settings. This contribution ensures that the developed solution can be seamlessly integrated into healthcare systems.

g. Recommendations for Clinical Deployment: The research provides practical recommendations for the deployment of the developed framework in clinical practice. Considerations for data privacy, regulatory compliance, and integration into existing healthcare systems are outlined, facilitating its adoption in the healthcare industry.

1.5 THESIS STRUCTURE

This thesis is structured to provide a coherent and systematic exploration of the development and evaluation of a transfer learning-based framework for early detection and classification of diabetes mellitus through the integration of medical imaging and biochemical data. To facilitate a clear understanding of the research journey and findings, the thesis is organized into distinct chapters, each serving a specific purpose in the overall narrative.

Chapter 1: Introduction

The introductory chapter sets the stage for the thesis by providing essential background information, delineating the problem statement, establishing the research objectives, and outlining the contributions of this work. This chapter aims to offer a comprehensive context for the subsequent research endeavors.

Chapter 2: Literature Review

The literature review chapter offers a detailed examination of the relevant literature, covering key aspects of diabetes mellitus, current diagnostic methods, the role of machine learning in healthcare, and transfer learning techniques. It also reviews related research in diabetes diagnosis and transfer learning in healthcare, providing a foundation for the novel contributions of this thesis.

Chapter 3: Materials and Methods

This chapter delves into the practical aspects of data acquisition, selection, and preprocessing. It elucidates the datasets used in the study, their sources, and the ethical considerations governing data usage. Additionally, it discusses the data preprocessing steps undertaken to ensure data quality and suitability for analysis.

Chapter 4: Framework Development and Results

In this pivotal chapter, the transfer learning-based framework for diabetes detection and classification is designed and described. The architecture, feature extraction techniques, and innovative feature engineering methods are comprehensively elucidated, offering a deep understanding of the framework's core components.

Chapter 5: Conclusion

The concluding chapter summarizes the key findings, contributions, and implications of the research. It also offers insights into future directions and areas of potential expansion in the field of diabetes diagnosis.

2. LITERATURE REVIEW

2.1 INTRODUCTION

Diabetes affects around 422 million people all over the globe. Diabetes is a global epidemic. Over the course of the last several decades, the prevalence of diabetes has skyrocketed, reaching epidemic levels. Diabetes may result in a variety of consequences, including as impaired eyesight, kidney failure, nerve damage, limb amputations, an increased chance of stillbirth, and an increased risk of having a heart attack. Being diabetic may put a person at risk for a number of complications, one of the most frequent of which is diabetic retinopathy, sometimes referred to as diabetic eye disease. In the long run, around 30 percent of people who have diabetes will develop renal illness connected to their condition. In many parts of the globe, DR is one of the most important contributors to the onset of visual impairment or total blindness. Injury to the retina is one of the hallmarks of a condition known as retinal detachment. As a consequence of the damage, the blood vessels that are located in the retina either get clogged or begin to bleed blood. There are several instances in which the development of blood vessels in the retina might go in an unexpected direction. These veins have the risk of causing scarring or bleeding inside the retina if they are not treated. Patients who are in later stages of the disease may have visual loss or possibly total blindness [2, 3].

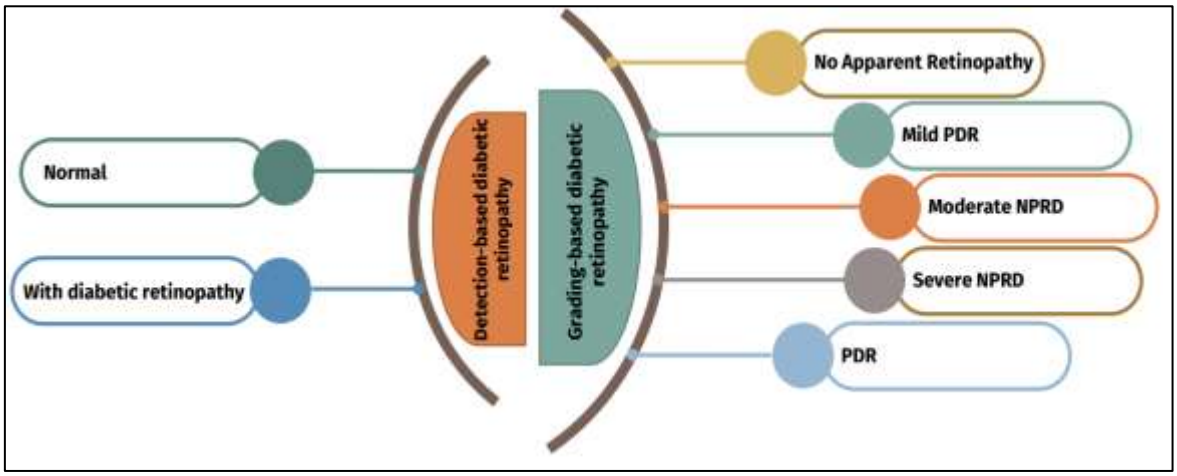

Figure 2.1: Types of Studies Related to DR.

It is very necessary to identify the DR as quickly as time permits. If diabetic retinopathy is recognized and treated in a timely way, there is a chance that blindness may be prevented. Patients with diabetes who see ophthalmologists are required to undergo routine examination

and monitoring in order to maintain good eye health. Ophthalmologists would benefit from having diagnostic tools at their disposal that are reliable and that can provide assistance in the process of analyzing fundus pictures. There has been a lot of progress made in the field of medicine thanks to the use of artificial intelligence. A diagnosis of an eye disease is one instance of this sort of activity being carried out. It is possible that the use of technologies that are based on artificial intelligence will be able to solve the issues that are brought about as a result of the constraints of DR treatment, and this is particularly true in countries that have a low income. Deep learning is a branch in artificial intelligence that refers to a number of distinct techniques to machine learning. Deep learning may be thought of as an umbrella term for these approaches. Deep learning models, on the other hand, in contrast to more conventional neural network (NN)-based models [4-6], have a large number of hidden layers and aim to explain the most significant features of the input. When it comes to picture datasets, the kind of deep learning model known as CNNs (which stands for convolutional neural networks) is currently the one that is used the majority of the time. Deep Neural Networks (NNs) and ordinary feed-forward Neural Networks (CNNs) are very comparable to one another in a number of different ways. Backpropagation may be used to assist fine-tune the settings of the network so that it functions optimally. CNNs are distinguished from feed-forward networks by four distinct properties: shared weights, local receptive fields, pooling operation, and aggregation across layers. The last feature is an aggregation that occurs across all of the levels. Convolutional layers serve as the basis for the construction of the deep CNN's first stage, which is subsequently followed by fully linked layer construction. CNNs perform very well in a diverse array of tasks, including image identification, the understanding of natural languages, voice recognition, automated video categorization systems, and autonomous driving [7]. CNNs were conceptualized after the visual cortex of the brain, which provided as a source of motivation for their creation.

2.2 RELATED WORKS

The procedure of diagnosing diabetic retinopathy may include the use of techniques for detecting or assessing the condition. Finding sick patches in the retina and giving one of three labels (mild, moderate, or severe) to them may be used to identify the severity of diabetic retinopathy. For the aim of diabetic retinopathy detection, binary classification is used. This classification serves the goal of determining if a patient has diabetic retinopathy

or a normal retina. During the experiments that pertain to the identification of DR, the input photographs are separated into two categories: healthy and DR. In light of this, the following discussion is going to center on deep-learning-based techniques, which have been proven to be the most effective approaches when contrasted with other machine-learning-based methods or traditional methods. A foundational convolutional neural network (CNN) was provided, for instance, by Kazakh-British et al. [10], with the intention of automatically classifying DR. Throughout the course of their investigations, they made use of the photos in both their unfiltered and their anisotropic diffusion-filtered forms. According to the findings of the study, the researchers came to the realization that using an anisotropic diffusion filter brought about the most successful results. By using a CNN architecture for binary classification, the authors [11-14] were able to identify diabetic retinopathy as a condition. Following the application of the Wiener filter to the fundus photos and the use of OTSU for the segmentation, the authors of [15] proposed a deep convolutional neural network (CNN) for the multi-class classification of fundus pictures into those with different vision-threatening disorders like DR and the normal fundus images. Following the application of the Wiener filter to the fundus pictures, this step was taken. Instead of employing basic convolutional neural networks, numerous authors have resorted to using pretrained models (backbones) for transfer learning or feature extraction in order to finish their techniques. This is done in place of using fundamental neural networks. Figure 3 illustrates them for you. By using InceptionV3, for instance, the authors of [16] were able to determine DR based on RGB and textural characteristics of the image. Umapathy et al. [17] identified DR data using a version of the InceptionV3 algorithm that has been trained in the past. The authors of the research [18] suggest making use of a binary convolutional neural network (BCNN) while classifying DR in order to cut down on the amount of memory that is required and to speed up the processing time. The authors of the research [19] decided to use the MobileNetV2 architecture to perform binomial and multinomial classification of fundus pictures due to the fact that it can be implemented in mobile devices and takes less time for training than other classification methods. [21] took use of transfer learning by applying EfficientNet-B0, EfficientNet-B4, and EfficientNet-B7 to perform the same thing as Saranya et al. [20], who were able to identify DR in fundus pictures by using the DenseNet-121 model. The classification of DR in [22] as either referable or vision-threatening was accomplished using conceptual frameworks quite similar to those utilized

here. When training a network, the author of the study [23] uses a fully connected layer network with a HE initialization and an EfficientNet-B3 backbone with ImageNet weights. This results in the formation of the network. The outcomes of the tests revealed that the EfficientNet model had performance that was comparable to the gold standard, demonstrating that the model was successful overall. During the course of their examination of diabetic retinopathy, Sudarmadji et al. [24] made use of a one-of-a-kind Backbone. The CNN-based model that was proposed to be constructed was done so with the assistance of the VGG network, which was employed for the purpose of feature extraction. Boral and Thorat [25] used a transfer learning technique to the DR classification problem. This strategy includes the application of SVM and InceptionV3. The scientists categorised DR into binary categories in a second piece of study that they conducted using the transfer learning models Xception, InceptionResNetV2, MobileNetV2, DenseNet-121, and NASNetMobile ([26]). DenseNet-121 is a method that is based on transfer learning, and the authors of [27] utilized it to identify DR in input photographs by distinguishing MAs, Exs, and hemorrhages. This was done in order to accomplish their goal of detecting DR. The creators of [28] used a variety of additional strategies, including transfer learning, VGG, AlexNet, Inception, GoogleNet, DenseNet, and ResNet, to name a few. Transformer-based networks, convolutional neural networks (CNNs), and multi-layered perceptrons (MLPs) were the three distinct architectures for deep learning-based DR classification that the researchers investigated and assessed in a different piece of study [29]. During the course of the inquiry, a broad range of models were used. Some of these models were EfficientNet, ResNet, Swin-Transformer, Vision-Transformer (ViT), and MLPMixer. It was discovered that the models that were built on the framework of the transformer were the ones that provided the most accurate results of these. The authors of the previous study [30] used a DR classification ensemble model that was constructed up of three separate CNN models. The foundation was laid using stack generalization, and it was constructed on top of it. Additionally, the ResNet-50 and VGG-16 neural networks were used. The authors of [31] examine several CNN topologies, preprocessing approaches, class imbalance, and finetuning as four of the most important aspects of employing CNN for DR classification. AlexNet, ResNet-50, and VGG-16 were the networks that we used in order to complete this challenge. The authors of the study [32] conducted an empirical comparison of the performance of twenty-eight distinct deep hybrid architectures in order to make a binary classification of DR into referable DR

and non-referable DR. For the purpose of evaluating this, complete deep learning (DL) architectures were used. Out of all the available choices, the hybrid architecture that made use of the SVM classifier and MobileNetV2 for feature extraction produced the highest quality work. The researchers that carried out the study [33] separated the fundus photographs that they analyzed into three unique groups: healthy eyes, eyes with glaucoma, and eyes with diabetic retinopathy. When it came to the DR labeling, we made use of a wide number of convolutional neural network (CNN) models, some of which are described below: MobileNetV2, DenseNet-121, InceptionV3, InceptionResNetV2, ResNet-50, and VGG-16. InceptionV3 is a variant of InceptionResNetV2, which is a variant of InceptionResNetV2.

In the early research that Paranjpe and Kakatkar [10] conducted on DR diagnosis, which relied on the manual extraction of features, they used techniques for blood vessel identification such as contrast augmentation, top-hat transformation, and morphological filtering. These techniques were performed manually. These techniques were used in an effort to increase the overall picture quality. In order to determine whether or not there were hard exudates present, several image processing techniques were used. Textural properties were recovered by the authors via the use of grey level co-occurrence matrices (GLCMs), which allowed for DR to be properly categorized. Inputs for Support Vector Machines included things like microaneurysms and blood vessels, as well as exudates. Harini and Sheela [11] used fuzzy C-means clustering in conjunction with a number of morphological image processing methods in order to retrieve these characteristics. Image transformation, top hat transformation, and Otsu's thresholding were the methods that Punithavathi and Kumar [12] used in order to pinpoint the location of the microaneurysm region. The writers also determined the mean and the entropy, which are two statistical evaluations of the overall quality of the texture. Both of these metrics were estimated by the authors. For the purpose of carrying out the categorization, an Extreme Learning Machine was used. In order to get morphological and textural information from retinal imaging, Colomer et al. [13] locally calculated granulometric profiles and local binary patterns by splitting the pictures into patches. In order to achieve our objectives, something needed to be done. In order to classify the data, a number of different classifiers, such as Support Vector Machines, Random Forests, and Gaussian Processes, were used and given the gathered characteristics as input. Utilizing CNN-based algorithms that perform admirably may allow for the successful

completion of the process of automatically extracting features from retinal pictures for use in DR classification tasks. Because training deep CNNs from scratch requires a substantial quantity of data, you will need to begin there in order to get started. Because there are so few photos of the retina that are accessible, transfer learning is an efficient way for classifying DR images. AlexNet was the technology that Johari et al. [14] used while they were working with the Messidor dataset. In order to discern between "normal" images and "exudates" photographs, the authors employed a binary classification technique as a research method. Takahashi et al. [15] constructed a GoogleNet model by making use of a dataset that was not readily accessible to the general public. The model had a random seed as a component of its initialization vector. A subset of the authors carried out an examination of DR making use of a variety of different networks. As an example, Choi et al. [16] used designs that were derived from the VGG19 and AlexNet networks. DenseNet169 and 201, in addition to ResNet50, were the feature extraction approaches of choice for Zhang et al. [17], who conducted their research. In order to accomplish their goal of feature extraction, Bodapati et al. [18] came up with a hybrid technique to use. The authors combined the qualities of Xception and VGG16 in their research. Nevertheless, a variety of designs, such as the CNN architecture that was created by Pratt and colleagues, have been presented in specific research [4]. When it comes to the categorization of images, the selection of features is just as important as the deep learning-based feature extraction that is carried out. The corpus of research that has been published provides a multitude of different feature selection methods that can be used to discover which characteristics work best with a given dataset. These algorithms may be used to determine which characteristics work best with a particular dataset. It is vital to take into account elements such as contributing to classifier performance, avoiding overfitting, and reducing the amount of time spent on training when selecting a method for feature selection [20–23]. Other important considerations include decreasing the amount of time spent on training. During the course of the process of selecting features, metaheuristics could prove to be helpful in solving certain problems. Canayaz [24] described in detail a method for determining the location of COVID-19 in radiological images that he had developed. The author made use of not just one but two different metaheuristic algorithms in addition to a deep learning model in order to choose which attributes should be extracted. According to the results of the study, BPSO was effective in improving classification performance while simultaneously reducing the total number of features. In

this investigation, we begin by using InceptionV3 to extract features from photos of the retina. Next, we make use of those features to build a binary classification of the images into nonreferable DR and referable DR categories. In order to evaluate how well the proposed model works in contrast to other techniques, we gathered a summary of previous research that has utilized the same testing dataset (Messidor-2), extracted features using the InceptionV3, and conducted a binary classification. Because of this, we were able to evaluate how well the suggested model worked in contrast to other strategies that are already in use. The procedure of feature extraction was carried out by Voets et al. [25] with the assistance of InceptionV3. The authors finished a two-way classification using ensemble learning, which is also known as NRDR-RDR. This classification method is more accurate. Training is accomplished via making use of an EyePACS dataset that may be accessed free of charge at any time. When the suggested model is used to analyze Messidor-2, the area under the curve (AUC) has been found to have a value of 85.3%. The final layers of Inception V3 networks were constructed by Li et al. [26] by using a dataset from Chinese Hospitals that included 19,233 retinal pictures. The dataset was used to build the networks. The neural networks were trained with the help of the dataset. They constructed a model that, when applied to the Messidor-2 RDR, has a diagnosis accuracy of 93.49 percent. The RDR was detected by Toledo-Cortés et al. [27] using the InceptionV3 diagnostic tool. The authors suggested making use of a deep learning Gaussian Process (GP) model, and then they assessed how well it performed using the EyePACS dataset. The area under the curve (AUC) for Messidor-2 was estimated to be 87.87% when using a GP regressor. Using the pre-trained weights of the InceptionV3 method, Gurcan et al. [28] were able to recover feature representations from pictures of the retina. During both the phase of the project devoted to development and the phase devoted to evaluation, the authors made use of Messidor-2. The XGBoost algorithm was able to obtain a classification accuracy of 91.40 percent on the Messidor-2 computer.

Table 2.1: Summary of Related Works.

Study	Methods/Approaches Used	Key Findings/Results
Paranjpe and Kakatkar [10]	Contrast enhancement, top-hat transformation, morphological filtering, texture features using GLCMs	Blood vessel detection, hard exudate detection
Harini and Sheela [11]	Fuzzy C-Means clustering, image processing operations (morphological), Support Vector Machines	Feature extraction from exudates, blood vessels, and microaneurysms
Punithavathi and Kumar [12]	Image transformation, top hat transformation, Otsu's thresholding, statistical texture properties	Microaneurysm area detection using Extreme Learning Machine
Colomer et al. [13]	Granulometric profiles, local binary patterns, Support Vector Machines, Random Forests, Gaussian Processes	Morphological and texture information extraction from retinal images
Johari et al. [14]	AlexNet architecture, Messidor dataset	Binary classification of normal vs. exudate images
Takahashi et al. [15]	GoogLeNet model, private dataset	Training GoogLeNet model for DR diagnosis
Choi et al. [16]	AlexNet, VGG19 architectures	Multiple networks for DR diagnosis

Table 2.1: Summary of Related Works "Table Continued".

Zhang et al. [17]	DenseNet169, DenseNet201, ResNet50	Feature extraction using various CNN architectures
Bodapati et al. [18]	Blended feature extraction from VGG16 and Xception	Fusion of features from different networks
Pratt et al. [19]	New CNN architecture	Development of a new CNN-based network
Canayaz [24]	Deep learning models, metaheuristic algorithms (BPSO)	Feature selection using BPSO in COVID-19 diagnosis
Voets et al. [25]	InceptionV3, ensemble learning	AUC of 85.3% on Messidor-2 for NRDR-RDR classification
Li et al. [26]	InceptionV3, Chinese Hospitals dataset	Accuracy of 93.49% on Messidor-2 for RDR diagnosis
Toledo-Cortés et al. [27]	InceptionV3, deep learning Gaussian Process (GP) model	AUC of 87.87% on Messidor-2 for RDR diagnosis
Gurcan et al. [28]	InceptionV3, XGBoost classifier	Accuracy of 91.40% on Messidor-2 for DR diagnosis

2.3 CONCLUSIONS

From this literature review, it is evident that researchers have explored a variety of methods and approaches for diagnosing diabetic retinopathy (DR) through the analysis of retinal images. Key findings and approaches include:

a. Traditional Image Processing Techniques: Some early studies relied on traditional image processing techniques, such as contrast enhancement, morphological transformations,

and texture feature extraction using grey level co-occurrence matrices (GLCMs) for detecting blood vessels and hard exudates.

b. Machine Learning Algorithms: Machine learning algorithms, such as Support Vector Machines, Fuzzy C-Means clustering, and Extreme Learning Machines, have been applied to extract features from retinal images and classify DR-related structures like exudates, blood vessels, and microaneurysms.
c. Deep Learning: Convolutional Neural Networks (CNNs) have gained prominence in DR diagnosis due to their ability to automatically extract features from retinal images. Transfer learning, using pre-trained CNNs like AlexNet, VGG19, DenseNet, and InceptionV3, has been particularly effective, especially when dealing with limited datasets.
d. Ensemble Learning: Some studies have employed ensemble learning techniques to improve classification accuracy, such as combining the features extracted from multiple networks.
e. Feature Selection: Feature selection techniques have been explored to identify the most relevant features for classification tasks, contributing to improved model performance, reduced overfitting, and shorter training times. Metaheuristic algorithms like Binary Particle Swarm Optimization (BPSO) have been applied for this purpose.
f. Dataset Utilization: Various datasets have been used for training and testing, with Messidor-2 being a common benchmark. Additionally, some studies have used datasets from specific hospitals or sources.
g. Performance Metrics: The studies report performance metrics such as accuracy, area under the curve (AUC), and binary classifications (e.g., normal vs. DR).
h. Architectural Innovation: Some studies have proposed new CNN architectures tailored for DR diagnosis.

this literature review reveals a broad range of methods and tools employed for the automated diagnosis of diabetic retinopathy, with a particular emphasis on deep learning and the significance of feature selection. Researchers aim to improve the accuracy and efficiency of DR diagnosis, especially given the challenges of limited datasets and the critical importance of early detection for patient care.]

3. THEORETICAL BACKGROUND

At this stage of the work, diabetic retinopathy will be discussed. Next, the object of study – the retina – will be briefly discussed and how the exam to obtain the diagnosis is currently performed. The second step is to understand what can be done to improve this whole procedure, using image processing and artificial neural networks, as well as evaluating the performance of the methods that can be used.

3.1 DIABETES MELLITUS

Diabetes Mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia (excess blood glucose) resulting from defects in insulin secretion or action [8]. The chronic hyperglycemia of diabetes is linked to long-lasting damage, dysfunction and failure in various organs and systems, especially the eyes, kidneys, heart and blood vessels.

Several pathogenic processes are involved in the development of DM. These range from the autoimmune destruction of pancreatic β cells, with consequent deficiency in insulin production, to abnormalities in the metabolism of carbohydrates, fats and proteins, which result in resistance to the action of insulin in its target. Deficient insulin action is a consequence of inadequate secretion and/or a decreased tissue response to insulin at one or more sites of hormonal action [8].

Long-term complications of diabetes include retinopathy with a high chance of vision loss; nephropathy leading to renal failure; peripheral neuropathy with risk of foot ulcers, amputations and Charcot joints; and autonomic neuropathy causing gastrointestinal, genitourinary, and cardiovascular symptoms. Patients with DM have a higher incidence of cardiovascular, peripheral arterial and cerebrovascular disease, as well as hypertension and abnormalities of lipoprotein metabolism [8].

The vast majority of DM cases fall into two categories: Type 1, the cause is β-cell destruction and usually a complete deficiency in insulin secretion, and Type 2, the cause is a combination of resistance to insulin action and a inadequate insulin secretory response, the second is the most recurrent.

Global estimates indicate that 382 million people live with DM (8.3%) [9], and this number could reach 592 million in 2035 [10]. It is also believed that approximately 50% of individuals with diabetes are unaware that they have the disease. The study also indicates

that the incidence rate of the disease grew 61.8% in the last ten years [10]. The focus of this work will be on two complications from DM, diabetic retinopathy and the risk of macular edema, both complications occur in the eye.

3.1.1 Diabetic Retinopathy

Diabetic retinopathy (DR) is a disease that affects the small blood vessels present in the retina. It is the most frequent cause of new cases of blindness in adults between 20 and 74 years [3]. During the first two decades of disease, almost all patients with type 1 diabetes and more than 60% of patients with type 2 diabetes have retinopathy [3].

The characteristics of the disease in its less advanced stage are the appearance of microaneurysms (small vascular dilations), hemorrhages and obstructed blood vessels, which means that several regions of the retina are without receiving oxygen and nutrients carried by the blood [11]. At a more advanced stage, there is an overgrowth of new blood vessels, the neovas, on the surface of the retina. This vessel growth is mainly due to the obstruction / rupture of old blood vessels.

The neo vessels do not cause any symptoms or loss of vision in the person, but they are very thin and fragile, which can cause them to rupture and end up causing hemorrhages and consequently lead to blindness [12].

The duration of DM in the patient is probably the most influential factor in the incidence of DR. A study in Wisconsin - USA [13] showed that in the group of patients with three years of DM, only 8% had retinopathy, 25% with five years, 60% with 10 years and the prevalence of the disease in patients with 15 years of DM was 80%.

There are treatment modalities that can prevent or delay the onset of diabetic retinopathy, as well as prevent vision loss in most patients with diabetes. Glycemic and blood pressure control can prevent and delay the progression of DR in patients with DM [14]. Timely laser photocoagulation therapy can also prevent vision loss in a large proportion of patients [14].

3.1.2 Macular Edema

Macular edema is a disease caused by the deposit of fluid and proteins (hard exudates) on or under the macula of the eye, making it thicker and swollen. It is considered the main cause of vision loss in patients with DM [6].

This occurs as a result of prolonged excess blood glucose from diabetes. This causes the blood vessels in the eyes to absorb more fluid, leading to swelling of the retina and loosening of the junctions between the cells in the blood vessel walls. Thus, there is an extravasation of blood and/or fat to the tissues around the retina, when this leakage is close to the macula, there is a greater risk of macular edema (REM) [15].

At the beginning of the disease, the patient may not experience any difficulty seeing, but over time blurring or distortion of vision may occur. Other symptoms are altered contrast sensitivity, change in color visualization, changes in the field of vision, as well as photophobia (sensitivity to light) [15]. The main treatment for macular edema is the drug ranibizumab, an inhibitor of the VEGF protein (Vascular Endothelial Growth Factor). This protein is responsible for the swelling of blood vessels in the presence of excess glucose. Another option is laser therapy, which involves cauterizing the broken blood vessels in the eye to stop the leak and reduce swelling. This method reduces the risk of disease progression, but does not restore lost vision.

3.2 EXAMINATION OF THE RETINA

Once the diseases that affect the retina are known, it is necessary to know how the exam is performed to verify if they are present, and this involves knowing the object of study – the retina, the medical devices involved, as well as the procedures. In this way, it is possible to indicate a way to facilitate the exams and the diagnosis.

3.2.1 Structure of the Eye

The eye is a photosensitive organ responsible for capturing images and perceiving light, that is, for vision. It is located inside a bone cavity and protected by the eyelid [16]. It consists of three layers: the outermost, formed by the sclera and the cornea; the middle layer, formed by the choroid and iris; and the innermost layer, which is made up of the retina (Figure 3.1).

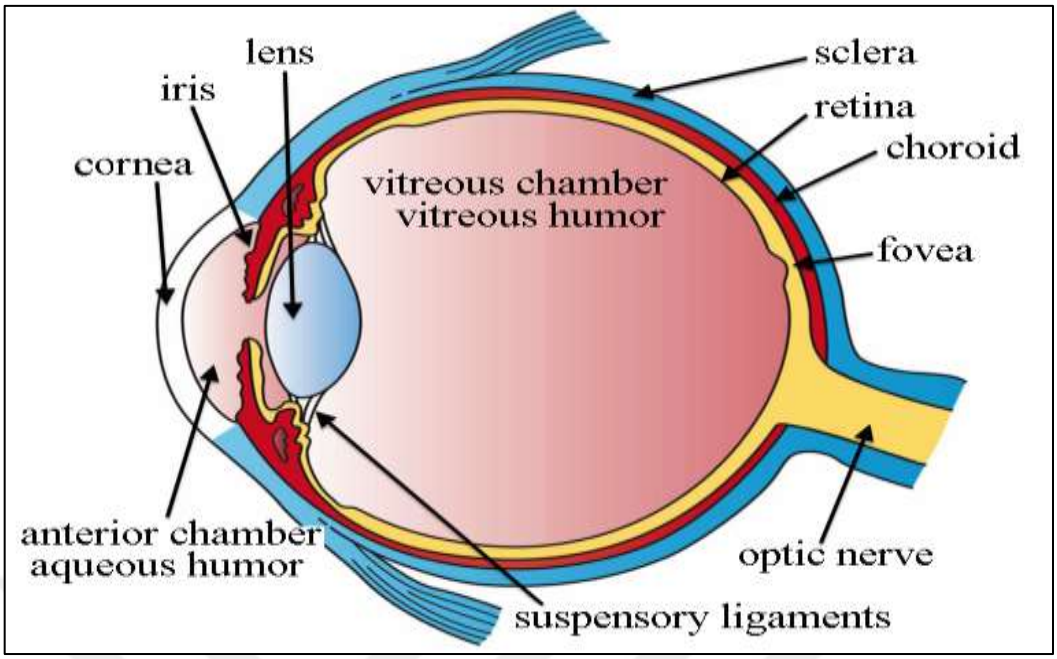

Figure 3.1: Schematic of the Human Eye.

The cornea is a transparent layer of tissue that sits at the front of the eye. It is a very thin layer. In addition to playing a role in the development of the eyeball, it also protects the spherical part of the eye from being damaged or polluted once it has already been formed. The sclera is a white covering that serves as a protective layer that surrounds the eye. It is also known as the sclerotic membrane. The function of this structure is to encircle the eye. In addition to its function as a site for the attachment of extraocular muscles, it also serves as a barrier to limit the loss of intraocular fluid. This function is performed in conjunction with the attachment of extraocular muscles. Collagen fibers make up the majority of its structure. Between the sclera and the retina lies a membrane called the choroid that is full with blood vessels. This membrane is made of membranous tissue. It may be found at the posterior region of the eye. They are in charge of supplying the retina with food in order to keep it healthy. The iris is the component of the eye that is placed behind the pupil and is an extension of the choroid that covers the lens. The color of the eye is determined by the iris, which is positioned in the back of the eye. Along with a central aperture, its structure also includes smooth muscles, which are responsible for controlling the quantity of light that is let into the eye. A hole in the eye known as the pupil, which is a circular aperture in the centre of the iris, is how light is allowed to enter the eye. Its diameter moves between about 2 and 4 millimeters as a result of variations in the light that is present in its environment. The

component that is responsible for controlling how light is focused is a structure that is known as a lens or crystalline. When combined, water, proteins, and minerals may generate a biconvex lens that is naturally elastic in its characteristics. It stands out due to the fact that its format shifts, which enables it to focus on items that are situated at a variety of distances from the camera. The optic nerve is the nerve that is responsible for sending visual information from the eye to the brain. It is located at the back of each eye. It is possible that there are around one million axons that make up the whole thing. The retina, which is an area located in the central section of the back of the eye, is where photoreceptor cells can be found. These cells are important for collecting visual information and are located in the rear of the eye. This is the region that receives the most light, and it is also the location where the nerve impulses that are sent to the central nervous system are generated. Due to the fact that the retina is the focus of the research presented in this paper, further information on the anatomy of the retina may be found below. adjusting their behavior in response to the changing light conditions. The component that is responsible for controlling how light is focused is a structure that is known as a lens or crystalline. When combined, water, proteins, and minerals may generate a biconvex lens that is naturally elastic in its characteristics. It stands out due to the fact that its format shifts, which enables it to focus on items that are situated at a variety of distances from the camera. The optic nerve is the nerve that is responsible for sending visual information from the eye to the brain. It is located at the back of each eye. It is possible that there are around one million axons that make up the whole thing. The retina, which is an area located in the central section of the back of the eye, is where photoreceptor cells can be found. These cells are important for collecting visual information and are located in the rear of the eye. This is the region that receives the most light, and it is also the location where the nerve impulses that are sent to the central nervous system are generated. Due to the fact that the retina is the focus of the research presented in this paper, further information on the anatomy of the retina may be found below. adjusting their behavior in response to the changing light conditions. The component that is responsible for controlling how light is focused is a structure that is known as a lens or crystalline. When combined, water, proteins, and minerals may generate a biconvex lens that is naturally elastic in its characteristics. It stands out due to the fact that its format shifts, which enables it to focus on items that are situated at a variety of distances from the camera. The optic nerve is the nerve that is responsible for sending visual information from the eye

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a. Retina:

The retina is a structure made up of light-sensitive cells (cones and rods), which capture the projected images, as well as neurons, which send what was captured to the brain through the optic nerve [18]. An extremely important region of the retina is the macula, as it contains a greater concentration of cones, which makes the images projected there have greater sharpness. Cones are specialized for daytime vision and color recognition. The fovea is a small depression present in the macula. The optic disc corresponds to the entrance zone of the optic nerve, that is, the point where the optic nerve expands into the retina. This point has the appearance of a small whitish disc, on which the blood vessels supplying the eye are clearly outlined (Figure 3.2). Rods are absent in the macula and are mostly concentrated at the periphery of the retina. In poorly lit environments, they are able to capture images, differentiate shades of light and dark, in addition to differentiating movements and shapes of images.

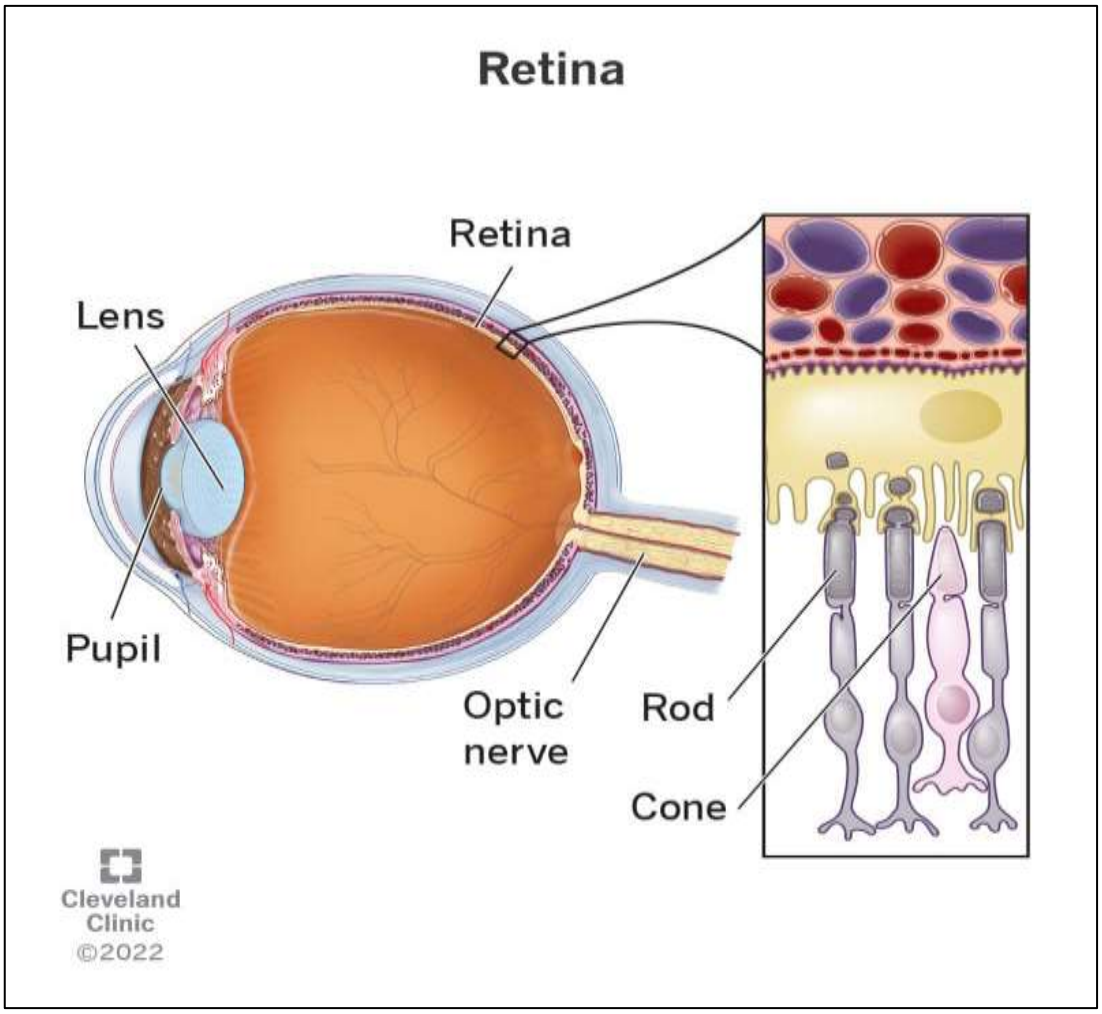

Figure 3.2: Retinal Structure.

Once the structure of tleadsetina is known, it is necessary to know how to take a picture so that an analysis of the pathophysiological state of the eye can be made, as obstructions and death of retinal cells lead a person to vision loss.

3.2.2 Fundoscopy

Fundoscopy is an imaging test that photographs areas of the back of the eye, such as the retina, choroid, optic nerve, and blood vessels [19]. Observation of the fundus of the eye is important to aid in the diagnosis and treatment of eye diseases, to document abnormalities and evolution of lesions, as well as to monitor the effectiveness of proposed treatments [20]. To perform the exam, the patient's pupil is usually dilated, then several pictures are captured through an ophthalmoscope. After somewhere around 7-10 minutes, the images are printed for evaluation. The ophthalmologist can also only use a suitable lens to look directly into the

back of the patient's eye, in this way he can make a quick diagnosis if the retina is healthy, but images are not recorded.

3.3 IMAGE PROCESSING

The images recorded for standard exams are sometimes noisy and with poor contrast, in addition to the lighting not being uniform [21]. Therefore, image enhancement techniques such as contrast and brightness enhancement are necessary. Standard contrast adjustment techniques have already been used by Sinthanayothin, et al. [22], Osareh, et al. [23] and Goldbaum, et al. [24] and were replicated in the way the author found most appropriate in this work. In addition to contrast and brightness, which affect the lighting of the images, two other image processing processes were tested, Equalization and Gray Scale, so that an analysis could be made considering certain characteristics. These two techniques were not found in any work until the date of publication of this dissertation. Some enhancement techniques for certain traits (eg, microaneurysms) are available in Walter's work [25], and can also be taken into account for some future work. Another proposal for processing is to work with image colors [26], because according to Patwari, et al. [27], each retinal lesion has its specific color.

3.3.1 Brightness

An image must have a good brightness so that it is easy to identify. Brightness refers to the overall amount of lightness or darkness present in an image. When the brightness of an image is too high, saturation of white pixels in the image occurs. If the brightness is too low, the saturation is from the black pixels. 3 Difference in brightness in an image, in (a) the original image, in (b) the image with high brightness and in (c) the image with low brightness.
Both images with a lot of brightness and with little end up having a loss of information in the areas where there is pixel saturation, so it is extremely important to correctly adjust the brightness level in a photo.

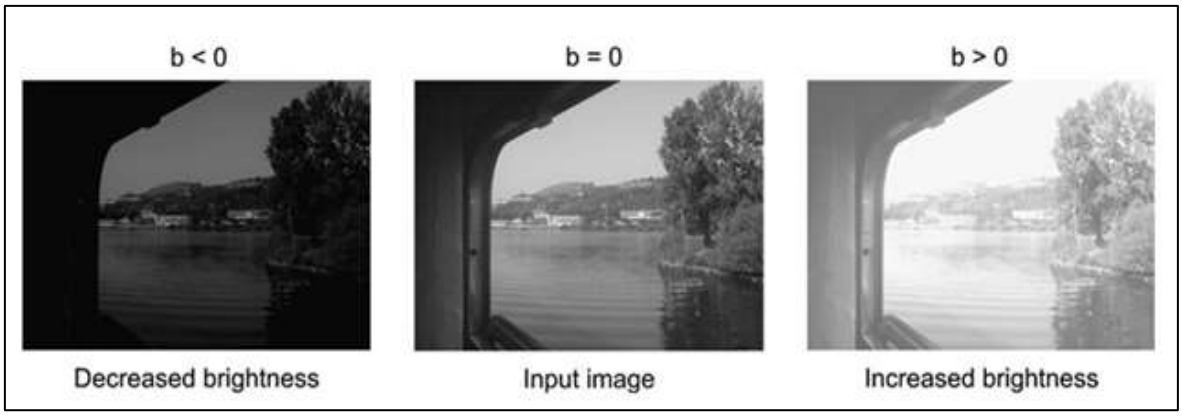

Figure 3.3: Brightness Adjustment in Image Processing.

3.3.2 Contrast

Contrast in an image is related to the brightness or darkness in the image between an area of interest and its background neighborhood [29].

Figure 3.4: Example of Contrast Variation in an Image. in (A) a Bear in the Snow, in (B) a Rabbit in the Snow.

In Figure 3.4 it is shown how the contrast can vary depending on this relationship between the optical densities of the object and the surroundings. It is easy to notice that the bear stands out much more in the snow due to its darker color, while the rabbit can even get confused in some part of the image. This difference makes it possible to visualize different structures. When there is little lighting at the time of image acquisition, short exposure time, insufficient opening of the camera diaphragm or other problems in image digitization, the images generated may have low contrast [30]. The low contrast in a scene can make it difficult to differentiate the elements that make up that image. When adjusting the contrast of an image,

what happens in the photo is that the shadows are very dark and the bright areas with more highlights [31].

3.3.3 Equalization

Equalization is nothing more than image normalization [32]. It redistributes the intensities of each pixel in the image so that their histogram (graphical representation of the number of pixels associated with each gray level present in an image) is as uniform as possible [33]. It often improves the visual quality of the image.

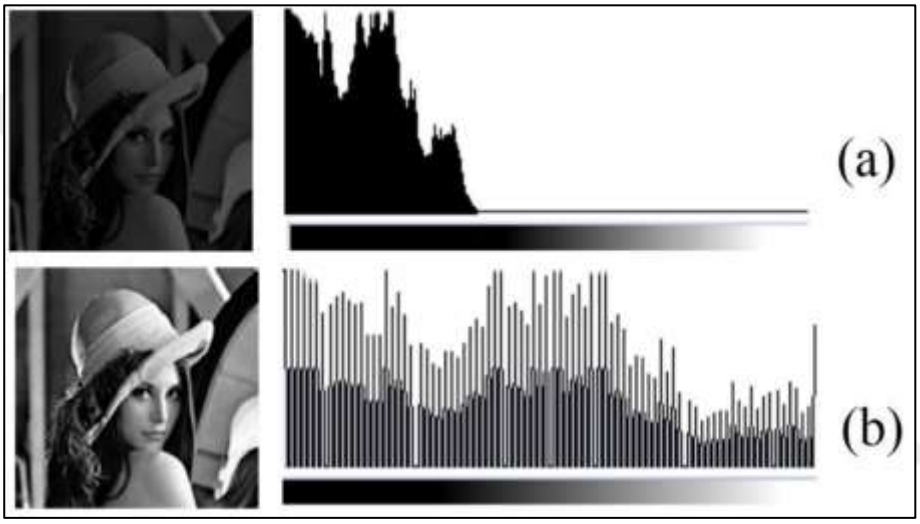

Figure 3.5: Example of Histogram Equalization on a Black and White Image. In (A) the Image and the Histogram are Observed Before the Equalization and in (B) After.

3.3.4 Black and White

Black and white processing is nothing more than transforming a color image into its equivalent without apparent colors, just different shades of gray [34]. The darkest possible tone is black, where there is no light, and the lightest possible tone is white, where all light is transmitted or reflected. The information contained in each pixel is then shifted from color to light intensity to some shade of gray. Considering an RGB (red-green-blue, or, red-green-blue) system and a CMY (cyan- magenta-yellow, or, cyan-magenta-yellow) system, it is possible to transform an image with these colors into a black and white image. removing the intensity of these pigments in each pixel. The scale used in the work was between -200 and

300, which means that if we define that all RGB and CMY levels are transformed to -200, the entire image will be black.

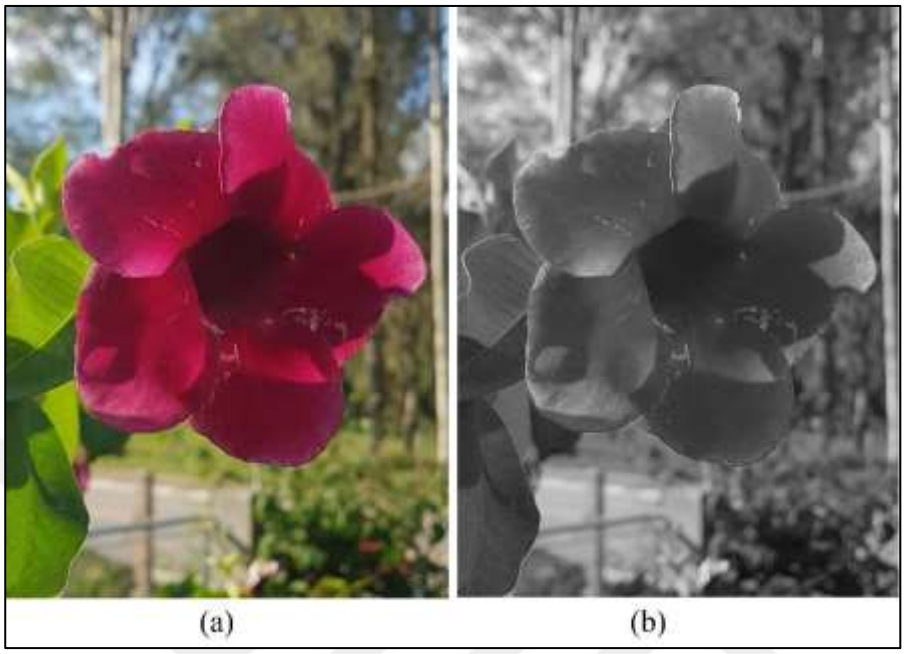

Figure 3.6: Example of Transforming a Color Image (A) into its Black and White Equivalent (B) Default Transformation Used.

3.4 ARTIFICIAL NEURAL NETWORK

Artificial neural networks (ANN) are computational techniques that present a mathematical model inspired by the neural structure of intelligent organisms and that acquire knowledge through experience. It is composed of several processing units, whose operation is quite simple. These units are usually connected by communication channels that are associated with a certain weight. It is possible to train an artificial neural network to perform a specific function by adjusting the connection weights. Usually artificial neural networks are trained so that a certain input leads to a specific result in the output. The units perform operations only on the inputs received by their connections. The intelligent behavior of an ANN comes from the interactions between the processing units of the network. They have a wide variety of applications, some examples are: Automatic Target Recognition; Character Recognition; Cars-autonomous; Medical diagnostic; Remote sensing; Voice Processing; Biometry; Data analysis (Data Mining).

3.4.1 The Neuron Model

In this section basic ANN concepts will be shown, starting with the simple neuron model, with only one scalar input; then three examples of activation functions; and finally, a neuron model that has an input vector.

a. Simple Neuron

A scalar input p is transmitted by the connection that multiplies its value by a scalar weight w, forming the product wp. In Figure 3.7(a) the input wp is just an argument of the activation function f, producing the output a. Figure 3.7(b) has a special scalar "bias" neuron b, which serves to increase the degrees of freedom, allowing a better adaptation, by the neural network, to the knowledge provided to it. The bias works similar to a weight, except that in this case its value is constant and equal to 1.

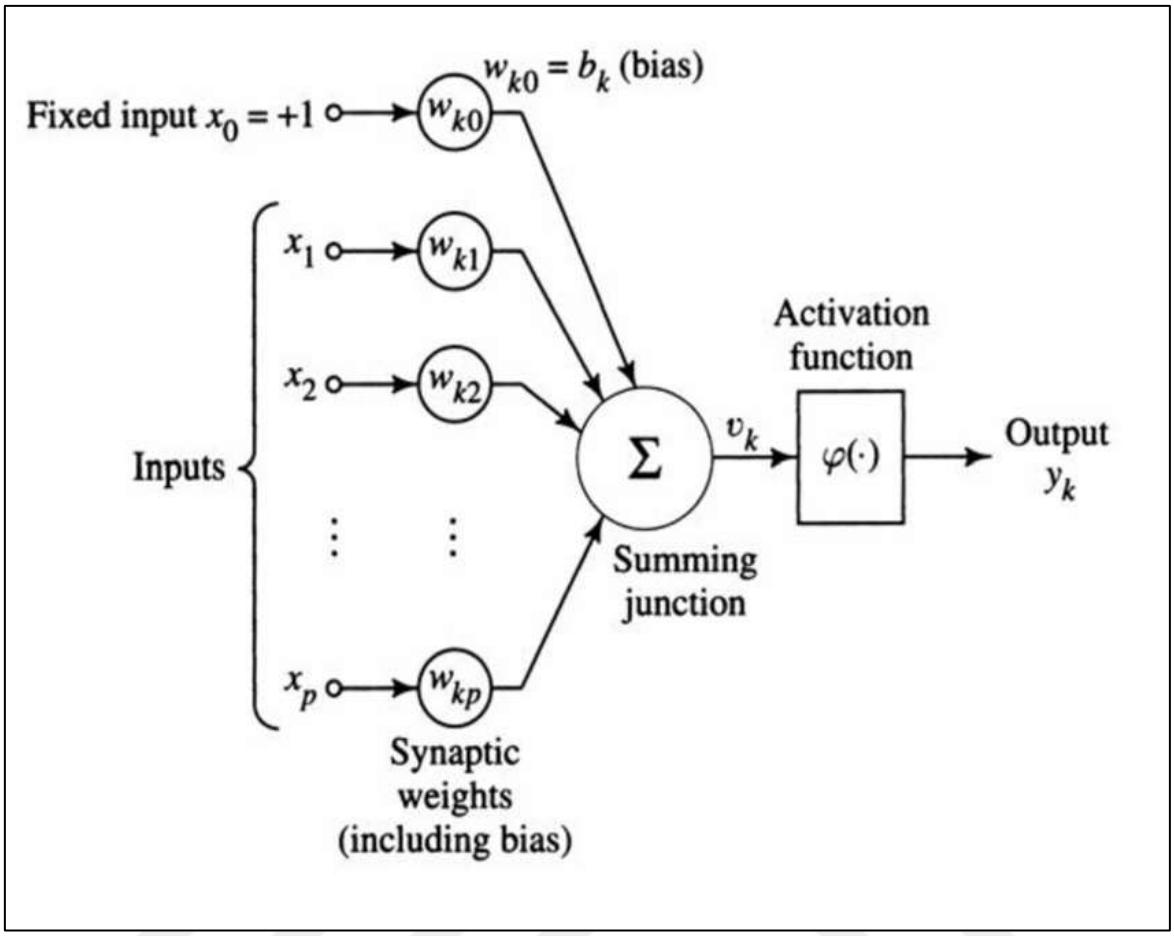

Figure 3.7: Simple Artificial Neuron. Where P is the Scalar Input, Wis the Scalar Weight, N is the Activation Function Argument, F is the Activation Function, a is the Output, and B is the Neuron Bias.

b. Neuron with an input vector

For an input vector with R elements, each of these elements will be multiplied by a weight w_(1, j), 1≤j≤R. The neuron has a bias b, which is added to the input weights (Wp) forming the network input n, which is the activation function argument.

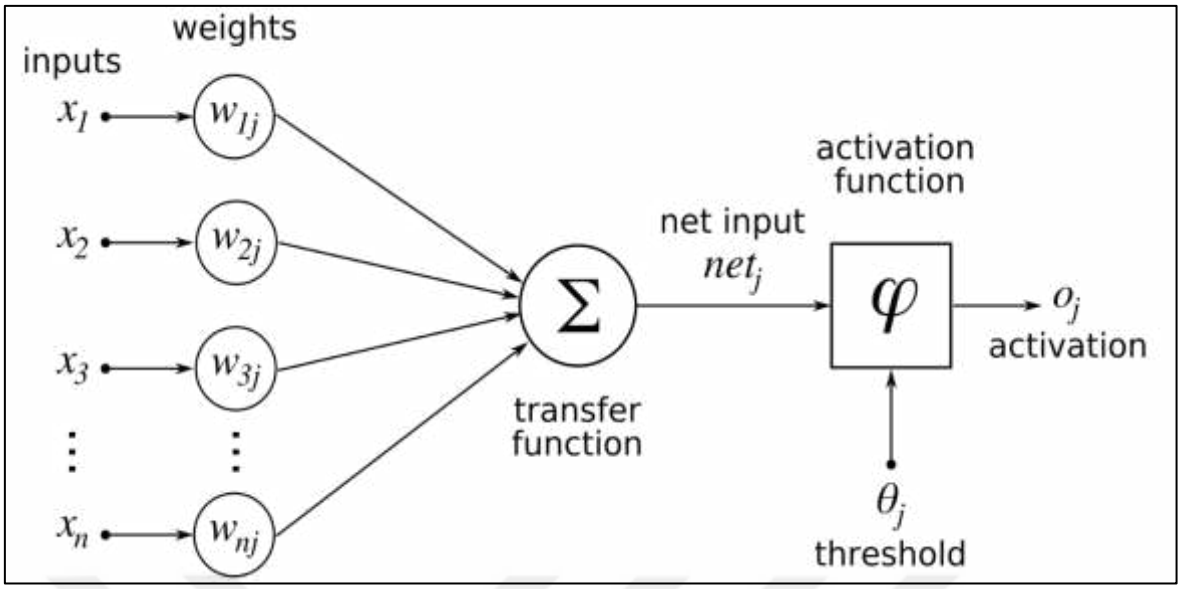

Figure 3.8: Neuron with an Input Vector. Where P_1…P_R are the Inputs, W_1,1…W (1,R) are the Weights, N is the Activation Function Argument, F is the Activation Function, A is the Output, B is the Neuron Bias and R is the Number of Input Elements.

3.4.2 Network Architecture

Two or more neurons can be combined in one layer, and a particular network can contain one or more layers. A one-layer network of neurons with R input elements and S neurons is shown in Figure 3.9.

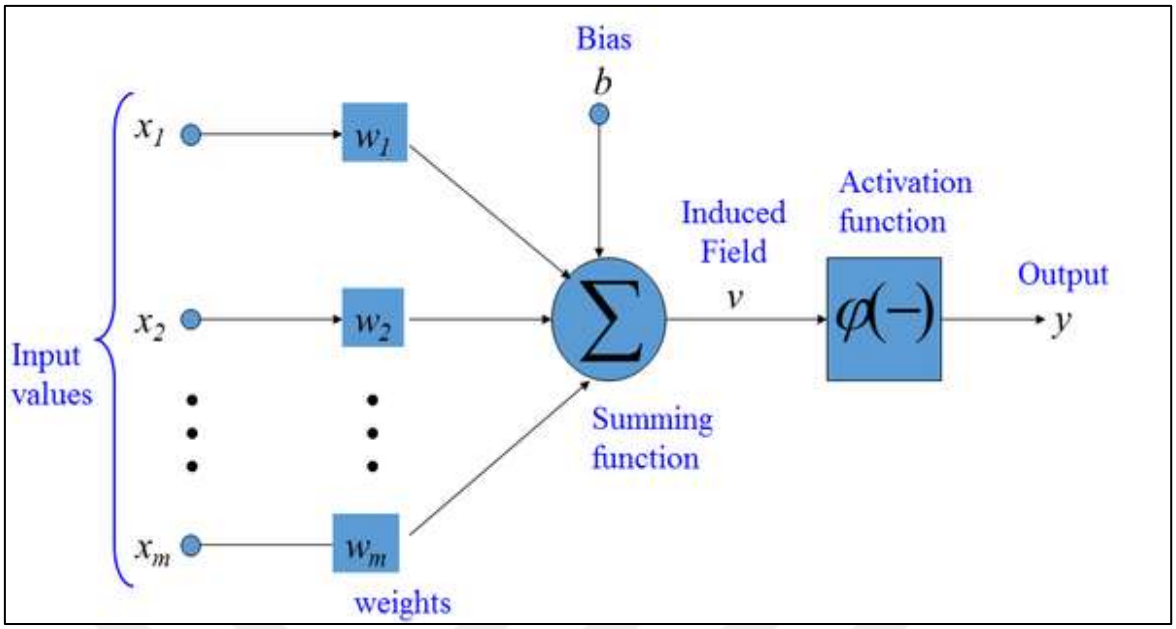

Figure 3.9: Network with One Layer. Where P_1…P_R are the Inputs, W_1,1…W_(S,R) are the Weights, N_1…N_S are the Arguments of the Activation Functions, F are the Activation Functions, A_1…A_S are the Outputs, B_1…B_S are the Bias Neurons, R is the Number of Input Elements.

In this case, each input element p is connected to each neuron input by the matrix weights W. The i-th input of the transfer function (n_i) is the multiplication of each element by the weight (Wp), added to the bias (b) of neuron i. The layer of output neurons will form a column a vector (Equation 1 and 2).

$$n_i = \sum_1^R p_R * w_{i,R} + b_i \tag{3.1}$$

$$ai = f(ni) \tag{3.2}$$

A multi-layer network will have a weight matrix W, a bias vector b and an output vector a for each layer. The network will then have R^1 inputs, S^1 neurons in the first layer, S^2 neurons in the second layer untilSineurons in the i-th layer. Since the superscript number represents which layer is being approached.

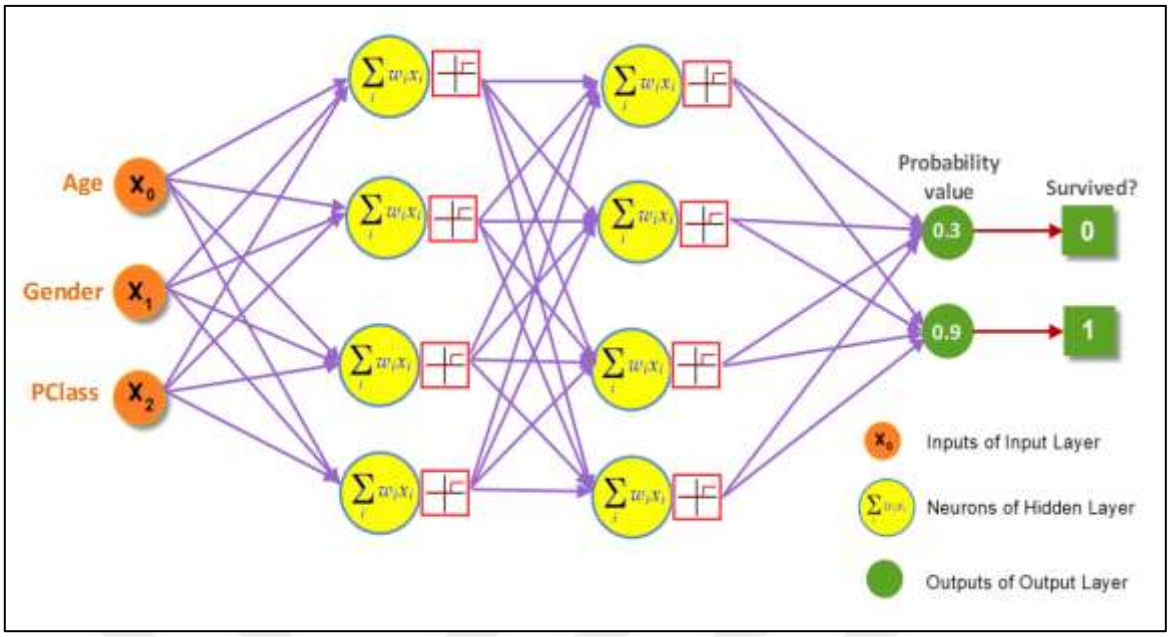

Figure 3.10: Network with Several Layers.

Where the inputs are represented by the letter p, the weights by w, n are the arguments of the activation functions, f are the activation functions, a are the outputs, b are the bias neurons, R is the number of input elements and S is the number of neurons.

The output of each intermediate layer is the input of the next layer. Then layer two can be analyzed as a one-layer network with S^1 (number of neurons in the first layer) inputs, S^2 (number of neurons in the second layer) neurons, and a matrix of weights W^2 (weights in the second layer). second layer) with dimensions S^2xS^1, that is, the weight matrix varies from W_1,1^2 to W_(S^2,S^1)^2. The second layer inputs are a^1 (first layer outputs) and the outputs are a^2 (second layer outputs). It is possible to treat all layers of a multi-layer network as a one-layer network, just identify its elements in the same way as the elements of the second layer.

The layers of a multilayer network have specific names. The layer that produces the network output is called the output layer and the others are called hidden layers. In Figure 3.10, for example, layer three is the output layer and layers one and two are the hidden layers.

The architectures shown in this theory are the basics for the formation of a neural network, from which other associations and multiplications in the layers can happen, such as a concatenation, which is when several outputs form only one, or some feedback loop, when an output goes to the entry itself, as well as many other possible combinations within a network.

3.4.3 Supervised Learning

One of the learning methods of a neural network is supervised. It is a process that consists of providing as much information as possible about what is for the network to classify. A ready database is delivered to a learning algorithm and a person (supervisor) tells this algorithm which class each of these data belongs to [36]. From this, a learned model is generated, the artificial neural network.

To exemplify, imagine that a database has 300 images of dogs and 300 images of cats, the objective is to create a model that knows how to classify between dog and cat. These images are then delivered to a learning algorithm with the information of which class each image belongs (Dog or Cat), in this way the network will remove the characteristics of each image during its training, with the purpose of discovering what is only in the images of dogs and what is present only in cats, creating your own model. So when you want to find out if a photo is a dog or a cat, you just need to present it to the created model, which, based on the characteristics of the image, will classify it.

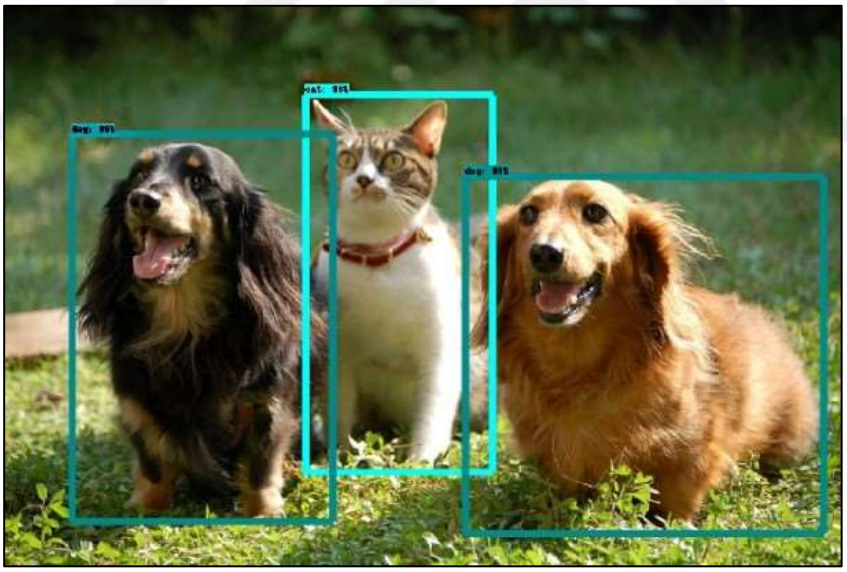

Figure 3.11: Example of a Neural Network Classifying Between Dog and Cat.

3.5 PERFORMANCE EVALUATION

Performance evaluation is an important step in the analysis of biomedical systems and should always be considered before any algorithm can be used to aid medical diagnosis. In this case, performance can be evaluated from the ability of neural networks to correctly

classify patients in their different degrees of diabetic retinopathy and risk of macular edema. The indicators in Table 3.1 are True Positives (TP), False Positives (FP), False Negatives (FN) and True Negatives (TN).

Table 3.1: Confusion Matrix.

		actual condition		
		Positive	Negative	Total
Condition predicted	Positive	TRUE Positives (TP)	False Positives (FP)	Positives (TP + FP)
	Negative	False negatives (FN)	TRUE negatives (TN)	Negatives (FN + TN)
	Total	Positives (TP + FN)	negatives (FP + NV)	

For the case of Diabetic Retinopathy, the number associated with TP represents how many images were classified as grade 1, 2 or 3 by the neural networks when in fact the patient has the disease; FP represents how many images were classified as grade 1, 2 or 3 by the neural networks, but the patient has a healthy retina; FN are how many images of grade 1, 2 or 3 that were considered without the disease; and TN is the number of grade 0 images that were actually classified as a patient with a healthy retina.

For the risk of Macular Edema, the number associated with PV represents how many images of risk 1 or 2 were classified by the neural networks when in fact the patient was at some degree of risk; FP represents how many images were classified as risk 1 or 2 by the neural networks, but the patient is not at risk for macular edema; FN are how many images of grade 1 or 2 that were considered as patients without grade of risk; and TN is the number of grade 0 images that were actually considered as a patient without this risk.

The most common performance indices are calculated using data related to patients and the results of tests performed, represented in the contingency table. These indices are sensitivity, specificity, positive predictive value, negative predictive value and accuracy, as well as the ROC curve to evaluate these indices.

3.5.1 Sensitivity

Sensitivity is an important index of diagnostic tests. It indicates the ability of a test to detect the disease when it is present. A low sensitivity rate demonstrates that the test is not capable of detecting the disease in a truly sick subject. Sensitivity is calculated through Equation (3).

$$\text{Sensitivity} = \frac{TP}{TP+FN} \tag{3.3}$$

3.5.2 Specificity

Like sensitivity, specificity is also an important index of diagnostic tests. It refers to the ability of a test to indicate as not sick subjects who are actually not sick. A test that has low specificity indicates a disease present in non-diseased subjects. Specificity is calculated by Equation (4).

$$\text{Accuracy} = \frac{TP+TN}{TP+FP+TN+FN}$$

$$\text{Sensitivity} = \frac{TP}{TP+FN} \tag{3.4}$$

$$\text{Specificity} = \frac{TP}{TP+FN}$$

3.5.3 Positive Predictive Value (PPV)

The Positive Predictive Value indicates the probability that a positive result is a True Positive, that is, it shows the probability of the disease being present when the test result is positive for the disease. The VPP is calculated by Equation (5).

$$VPP(\%) = \frac{VP}{VP+FP} * 100 \tag{3.5}$$

3.5.4 Negative Predictive Value (VPN)

The Negative Predictive Value indicates the probability that a negative result is a True Negative, that is, it shows the probability of the disease not being present when the test result is negative for the disease. The VPN is calculated by Equation (6).

$$VPN(\%) = \frac{VN}{FN+VN} * 100 \tag{3.7}$$

3.5.5 Accuracy

Accuracy is the ability of a measurement to be correct. Indicates the union of TP and TN results in individuals with and without the disease. The accuracy index is calculated by Equation (7).

$$Accuracy = \frac{TrueNegatives + TruePositive}{TruePositive + FalsePositive + TrueNegative + FalseNegative} \tag{3.8}$$

3.5.6 ROC Curve

ROC is the acronym for "Receiver Operating Characteristic", or efficiency of the signal reception operator. It indicates the ability of an observer, in this case artificial neural networks, to correctly classify data.

Sensitivity and specificity are probabilities that measure the diagnostic accuracy of a classifier, therefore, a value between zero and one. Both are part of the criterion known as validity, the degree to which the test or procedure identifies what it was designed to identify. Any test or procedure must be validated in order to be reliable, and this is based on comparing it with previously classified samples with great precision.

The validity of a diagnosis lies in the ability of the operator to detect the greatest possible number of hits (true positive results) and minimize errors (false positive results). In other words, maximizing sensitivity and minimizing false positive diagnoses. This is conveniently evaluated using the ROC curve, plotting all sensitivity values (the proportion of true hits) on the y-axis, against the values corresponding to the proportion of false hits (calculated as 1 - specificity), on the x-axis.

Area Under Curve (AUC) ROC is an important indicator because it provides a measure of overall accuracy independent of a particular threshold. It is a measure of the discriminative ability of a test, that is, the ability of a test to correctly classify those with and without the disease. In other words, if we draw at random one case with the disease and one without the disease from the population, the area under the curve gives us the probability of correctly classifying this pair. If the AUC is less than 0.5, the test is not valid, as the correct answers and errors enter in the same proportion, that is, they happen by chance.

It is not necessary to compare one test with another to assess whether a procedure is reliable or not, just use the following estimate to assess the ability to correctly identify a condition using the AUC of the ROC curve

[39]:

a. Above 0.9 = Excellent
b. 0.8 - 0.9 = Good
c. 0.7 - 0.8 = Regular
d. 0.6 - 0.7 = Bad

0.5 - 0.6 = Failed

4. METHODOLOGY

Automatic diagnosis of DR would help clinicians in screening for the disease, by introducing computer vision tools. However, there is no clinically deployed solution yet.
In this chapter, we detail the methods used to carry out this diagnosis. First, we discuss the fundus image quality assessment model. Then, we present the algorithms realized to perform the automatic screening. Finally, we investigate the importance of quality in training and testing screening models.

4.1 IMAGE QUALITY

The objective of this section is to establish an algorithm for evaluating the quality of fundus images. This algorithm is inspired by SGDRS and the way clinicians assess fundus images. These images can be divided into two categories, usable for screening or not depending on their quality. A good quality image contains the macula as well as the blood vessels around the fovea. The goal of the algorithm is to segment these two regions of interest and thus to give an interpretable score on the quality of the image. First the macula and vessel segmentation is performed independently, then a score is calculated on a region around the macula in the image where the vessels are segmented.
Two different U-Nets [14] are used for macula and vessel segmentation in the fundus image. These two models are trained independently and have different architectures.
Algorithm 1 and Figure 3.1 present the entire image quality evaluation method.
An article published in the ICIAR 2020 conference presenting this method is available in appendix A.

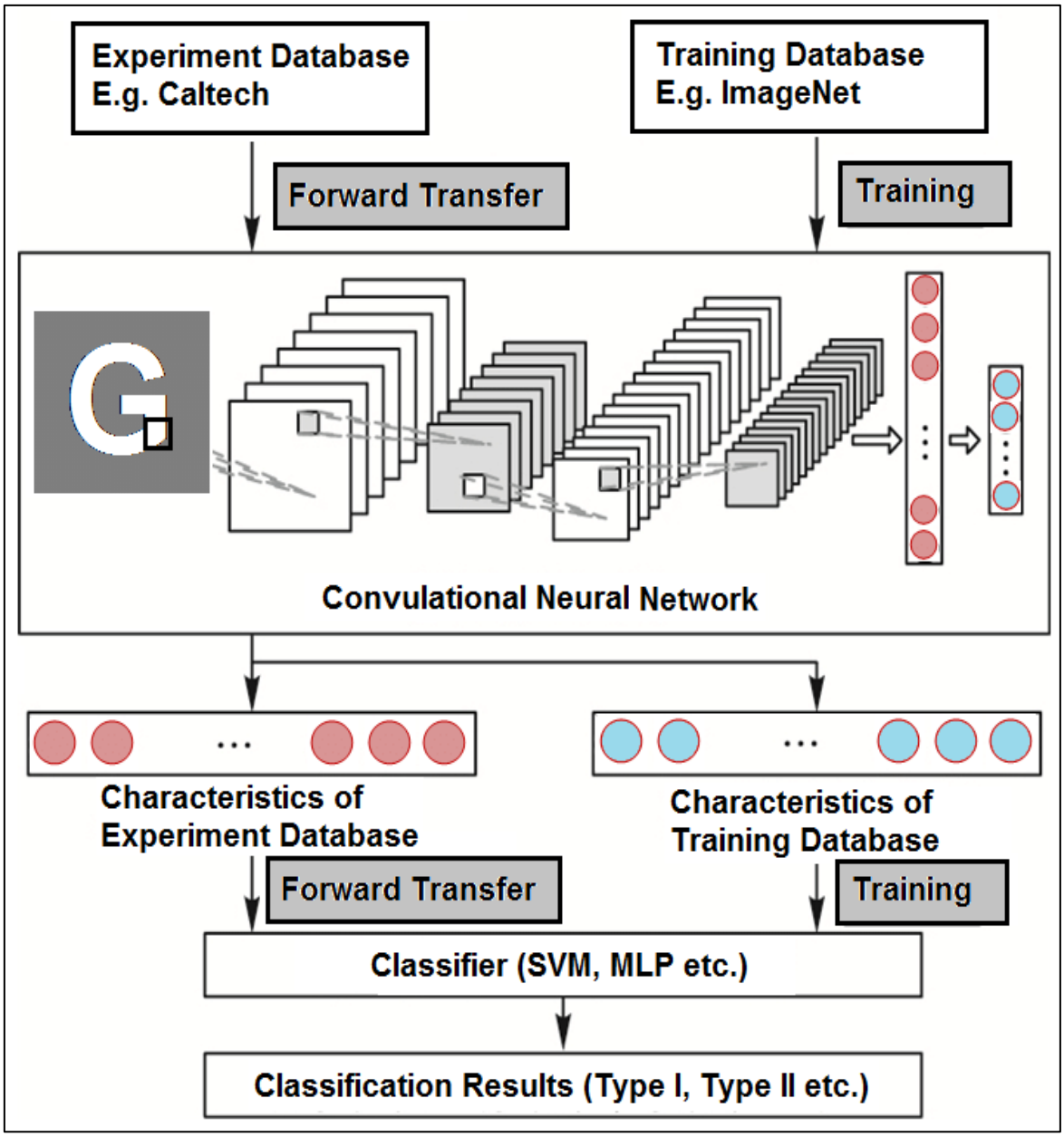

Figure 4.1: Flow Chart Detailing the Complete Process of the Fundus Image Quality Assessment Method.

4.1.1 Pre-Processing

Both U-Nets use the same pre-processing of fundus images. This pre-processing consists of the application of a Contrast-Limited Adaptive Histogram Equalization (CLAHE) function in the LAB color space. This is an effective and commonly used method to increase the quality of retinal images [41]. Indeed, the presence of noise from uneven illumination in fundus images can affect model performance. The CLAHE function reduces the effect of

this noise by improving the contrast of the image. This makes it possible to better perceive important characteristics of the fundus images, such as blood vessels for example.

4.1.2 Segmentation of the Macula

A U-Net is used to segment the macula on the image after pre-processing. The architecture and the strategy used are identical to those used by Ronneberger et al. in [14]. This model is then trained on 2000 images from the manually annotated Kaggle 2015 database.
A mean shift algorithm then makes it possible to locate the center of the macula and reduce segmentation errors. This algorithm groups the pixels activated by the U-Net according to their location. The pixels corresponding to the macula are therefore grouped together and the center of this group is calculated. This mean shift algorithm also makes it possible not to hold Algorithm 1: The complete process of the method.
Result:Image Score image = Image.open(fundusImage)
preprocessed_image = preprocess(image)
unet_macula = load_unet(model_macula) unet_vessels = load_unet(model_vessels)
macula_segmented = unet_macula(preprocessed_image) x, y = mean_shift(macula_segmented) vessels_segmented = unet_vessels(preprocessed_image)
patch = extract_patch(vessels_segmented, x, y)
skeleton = skeletonize(patch) score = sum(skeleton) return score.
account of U-Net segmentation errors in the calculation of the center of the macula because these errors will not be grouped with the macula. If the macula cannot be segmented, the image is automatically classified as unusable. Figure 3.2 presents the results of the algorithm on a few macula segmentation images.

4.1.3 Segmentation of Vessels

The model performing the vessel segmentation is also a U-Net but with a different architecture from the original. Compared to the model presented in [14], this model has:

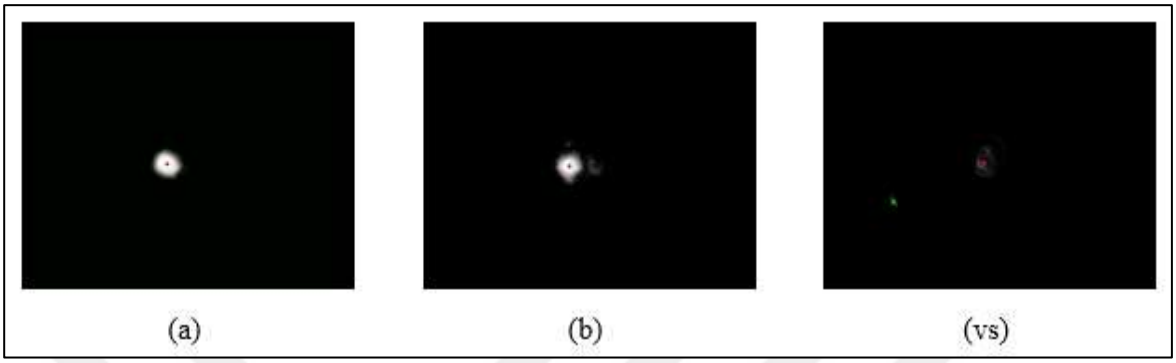

Figure 4.2: Mean Shift Algorithm for Locating the Center of the Macula. in Red, the Center of the Spot Found in the Images in Green, the Center of Groups of Pixels that are not the Macula.

twice as many layers and half as many features per layer. This reduces overfitting and widens the receptive field. This U-Net model is trained on 20 images from the DRIVE database [42] and on 100 images from the Messidor database [43]. This model is trained on 100 epochs with the ADAM optimizer [44]. Also, the following data augmentations were used: rotations of the image following a uniform law between -180 and +180 degrees, horizontal flips of the image with probability 0.5, random selection of a region centered on a pixel of vessel with a size of 516x516 pixels, change of contrast according to a normal law of standard deviation 0.4 and change of gamma according to a normal law of standard deviation 0.15. This template is used to segment the vessels on the original image after pre-processing. The results can be seen in Figure 4.3(c).

4.1.4 Image Quality Assessment

The coordinates of the center of the macula are utilized as a starting point in order to isolate the region of the image that contains the vasculature. This region is concentrated on the macula and contains the minuscule vessels that are seen in the area around the fovea. The macula is not visible in this photo because just the vessels have been segmented rather than both the vessels and the macula.

According to the SDRGS, the distance that this region should span from the center of the macula should be equivalent to the diameter of one optic disc. This recommendation was made to ensure that patients have the best possible vision. In order to reach a judgment on the size of the area, we carried out an examination by hand to determine the average diameter of the optic disc shown in the fundus photographs. We have discovered that there is very little change in the size of the optical disc; hence, it is possible to keep a constant value for the diameter of the optical disc. This was discovered as a result of our findings that there is extremely little fluctuation in the size of the optical disc. This number corresponds to about 12.5% of the overall dimensions of the picture when they were initially measured out. In order to cover a distance that is equivalent to the diameter of the optic disc from the center of the macula, the size of the extracted region is thus 25 percent of the height and 25 percent of the breadth of the original image. This is done in order to ensure that the extracted area is of sufficient size. As a result, the dimensions of the extracted area are one quarter of the height and one quarter of the breadth of the original picture. There is a possibility that an increase in the propagation of errors may occur if an additional way to segment the optical disc in order to get a number that is more accurate than this constant value was implemented. This is because making a mistake while segmenting the optical disc would lead to making a mistake when establishing the size of the region, which would then lead to making a mistake when computing the overall image quality rating. The results may be seen here, and they are shown in Figure 4.3(d), which can be found here.

After that, a skeletonization of the region is performed, and it includes the smaller vessels that are close to the fovea. This has the effect of lessening the impact that really large ships have and shifting the attention more toward the total number of ships that can be seen as well as the length of those ships. Additionally, an explanation for this is provided by Hunter, et al. in reference (19). As a direct consequence of this, the number of false positives has reduced, which is advantageous considering the frequency with which artifacts are incorrectly classified as vessels. The skeletonization process leads to a considerable reduction in the weight that those criteria have in determining the final score. Finally, the number of remaining white pixels is used to obtain the final score.

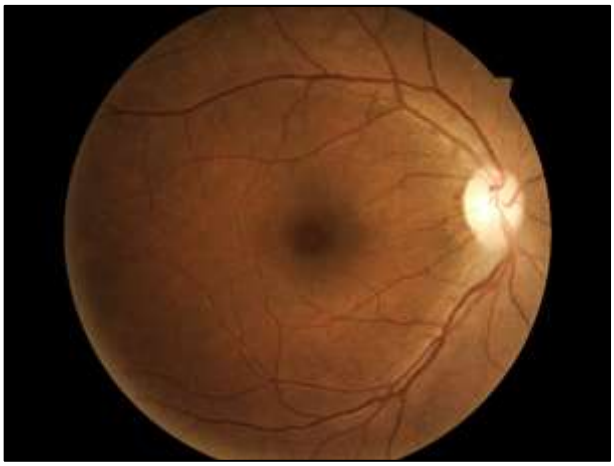

Figure 4.3: Details of the Quality Detection Algorithm on a Good Quality Image.

This score is an interpreted indication of the image's overall quality that may be found here. If you obtain a score of zero, it means that the macula was not segmented by the first U-Net or that there is not a vessel present in the region that is focused on the macula. Both of these possibilities are possible depending on whether or not the area was segmented. In any of these two possible outcomes, the image lacks the necessary level of detail to be utilized in the DR screening procedure. If you have a high score, it implies that a considerable number of long vessels have been segmented around the fovea. If you have a low score, it shows the opposite. This indicates that the picture quality is sufficient enough to assess the degree to which the dynamic range (DR) of the image has been increased. In point of fact, in order to help diagnosis, the image quality around the fovea has to be acceptable.

After that, we will need to settle on a cutoff point before we can assign letter grades to the images based on the quality of the shot as a whole. The amount of blood vessels that ought to be seen in the region around the fovea is not discussed in the SDRGS. This parameter's value is believed to be subjective since it seems to vary not only from one image to the next but also from one clinician to another. In order to ascertain what the appropriate level of this threshold should be, we had a medical professional review a database including fifty different images. After that, we determined the cutoff point that provided the most accurate reflection of the evaluations provided by the medical professionals by utilizing this test database. The value of 500 white pixels was maintained as the threshold in the picture of the skeleton of the vessels in the region around the fovea. This was done so that the image could be properly analyzed.

The threshold might cause an increase in the number of false negatives while at the same time causing a decrease in the number of false positives. Because we have access to several images of the same patient, determining the degree to which the DR has shown itself only requires a single image of appropriate quality. As a result, accuracy is the measure that is the most important for us to take into consideration because it allows us to achieve our goals. It is not as important to find every picture of exceptional quality as it is to determine with complete assurance that the photos that have been discovered are of high quality.

4.2 IN CONNECTION WITH THE CATEGORIZATION

Image categorization is a problem that has to be solved in order to automatically identify DR. In point of fact, the problem is in establishing a connection between the severity of the illness and the way it is portrayed. Table 4.1 presents information on the severity of the condition. These values will be referred to as ranging from 0 (indicating that there is no detectable DR) to 4 (indicating that there is a proliferation of DR) for the purpose of brevity and clarity. In the next section, we are going to study the process of developing a deep learning model that is capable of screening fundus images for diabetic retinopathy (DR). In order to do this, we will first present a summary of the several models that were constructed for the Kaggle 2019 competition, and then we will proceed to provide a full explanation of the approaches that were studied.

4.2.1 DATASET

We trained different networks in the Kaggle APTOS 2019 competition [31]. A training database of 3662 images with labels was provided. Figure 4.4 illustrates the distribution of classes in this database. We notice that the base is not balanced, the prevalence of class 0 is important.

During this Kaggle competition, a public and private ranking system has been implemented. A team could submit up to 5 submissions per day and a public score was revealed for each submission. This public score is calculated on 15% of the test database. The remaining 75% is used to calculate the private score which is revealed only at the very end of the competition, corresponding to the final score. The public score could therefore be used as validation of the models throughout the competition. After the competition ended, the

private scores of all submissions were revealed. These scores will be used to compare the different models used.

4.2.2 Model

a. Pre-treatment

During this competition, we studied the importance of pre-treatment in diagnosing DR. The pre-processing used is described by a member of the competition on the Kaggle site [45]. This is a pre-treatment inspired by that of the winner of the 2015 competition, Benjamin Graham [46]. This pre-processing consists of subtracting the local average color using a Gaussian blur filter. The images are also cut to keep only the eye and they are resized to have the same size. Figure 4.5 shows examples of images after pre-processing.

b. Data increase

The transformations that we have applied are the following: horizontal and vertical flipping of the image, horizontal and vertical translation, rotation and enlargements. Figure 4.6 shows examples of the different types of increases used in training. Data augmentation is used to generate new data from a database. In general, the performance of a model can increase with the number of different data, so different databases can also be merged to create a larger database. These databases must be similar for the merger to be beneficial. The 2019 Kaggle Eyepacs competition training base [30]

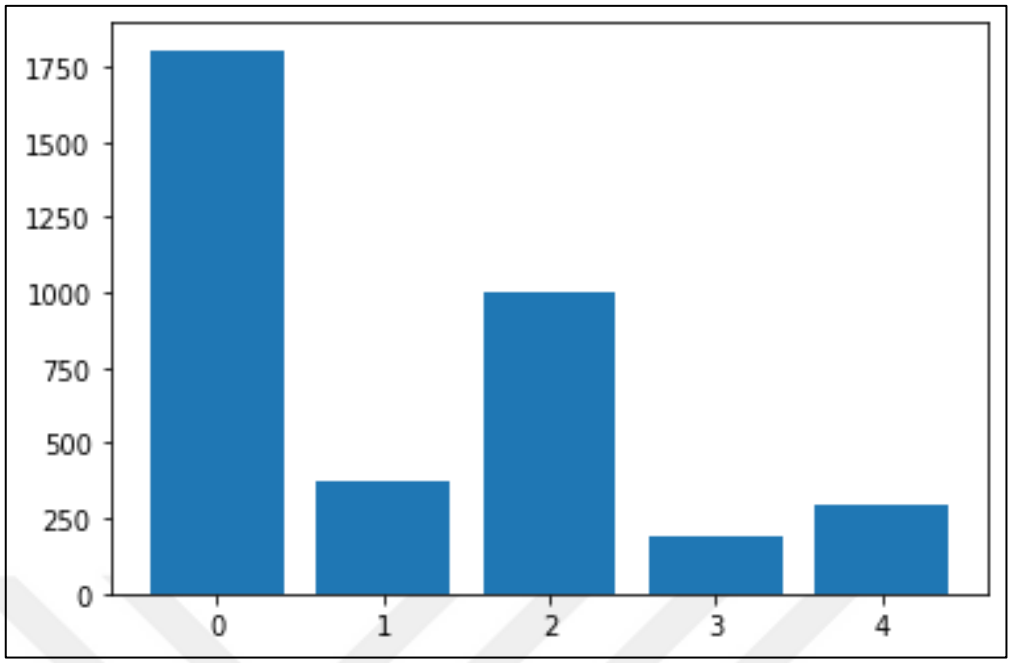

Figure 4.4: Distribution of Images According to DR Severity in Images From the 2019 Kaggle Training Database. the Proportion of Images is not Balanced, Class 0 is in the Majority.

has more than 30000 fundus images similar to those of APTOS 2019 competition. Moreover, the level gradation system is identical, which makes base merging possible. Increasing the size of the training database as well as performing data augmentations allows the model to generalize better and thus achieve better results.

c. Regression and Classification

This competition presents a classification problem, since it involves dividing the images into different discrete categories defined by the level of DR in the images. However, a regression approach can also be approached. Regression is all about predicting a real number. Unlike discrete classification prediction, regression prediction is continuous. Here, DR is classified into 5 levels. The levels are progressive (0 to 4) and the regression aims to make this progression continuous.

Classification and regression methods obtain similar results, despite their different approaches. It is difficult to interpret these results, arguments support both methods. The classification method follows the approach of clinicians and SDRGS by classifying images according to 5 categories. The regression method takes into account the order of the classes and has a loss function more suited to the measurement of the quadratic kappa Indeed, the

root mean square error and the root kappa measure a distance between the solution and the prediction. If a class 4 is predicted by the

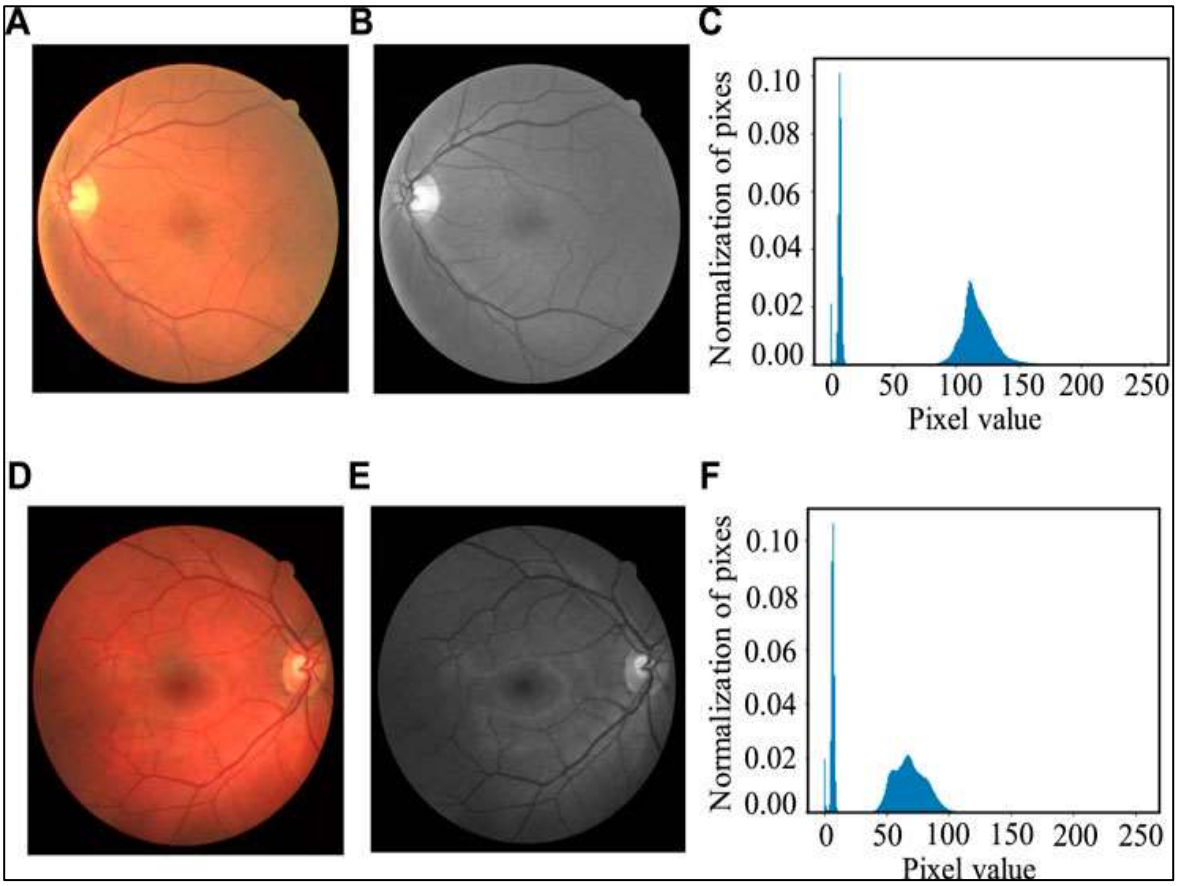

Figure 4.5: Example of Data Augmentation on an Image From the Kaggle 2019 Database the Following Augmentations are Performed: Horizontal and Vertical Flips, Enlargements, Rotation, Translation.

regression model when the expected value was 0, the error will be greater than if the prediction was 1. This notion of distance is not present in the loss function used by the classification However, the prediction of the regression method has no real clinical interpretation since this prediction is a real number which must then be rounded to an integer value between 0 and 4. Both methods seem to be adapted to the problem, these approaches will then be grouped in a set model for their complementarity.

d. Architecture

Several types of ResNets [10] and EfficientNets [11] were trained during this competition. These convolutional networks are used for the classification of natural images, on databases such as ImageNet for example. This allows us to use transfer learning. It involves using the

weights from the pre-trained networks on ImageNet and modifying them to perform a different task. Indeed, networks trained on ImageNet learn certain representations and characteristics of natural images. These features can also be useful for DR classification, so training a model from the learned weights on ImageNet can improve the results.

The different architectures used are as follows: EfficientNet-B3, EfficientNet-B4, EfficientNet-B5, EfficientNet-B6, ResNet-50, ResNet-101.

e. Learning

We used the ADAM optimizer for learning, along with a learning rate planner. The latter makes it possible to modify the learning rate when the model no longer improves its validation score. It is therefore a question of reducing the learning rate to allow the network to make more precise modifications and thus improve the results.

Also, we have developed a learning strategy which consists in first training the network on the Kaggle 2015 training database composed of approximately 30,000 images for 20 epochs. The validation during this first learning phase is the Kaggle 2019 database. The best network on this first training phase will then be used as the start of a second training on the Kaggle 2019 training database. This method allows the network to learn on a large database while specializing in the images of the competition in question.

f. Transfer methods

We first carried out the learning of the different networks. Then we applied the data augmentation method during the test phase to some networks. Then, we grouped four networks to create an ensemble model. This model performs the prediction of an image by calculating the rounding of the average of the predictions of the networks which constitute it. In order to increase the variability, we grouped networks with different architecture (EfficientNet-B3, B4 and B5), different objectives (classification and regression) and different input image resolution (300, 380 and 456) .

First, we filtered the poor quality images in the Kaggle 2015 training database to compare the training of two identical models on the original database and the database containing only good quality images. We used models that have proven their effectiveness during the Kaggle 2019 competition summarized in the previous part. This is why the architecture chosen for this experiment is an EfficientNet-B5 model. The objective of the model is classification and it is trained on 25 epochs with an ADAM optimizer. We decided to vary certain parameters of the learning method in order to better understand which factor allows

the quality to impact the results. These variable parameters are the pre-treatment and the increases.

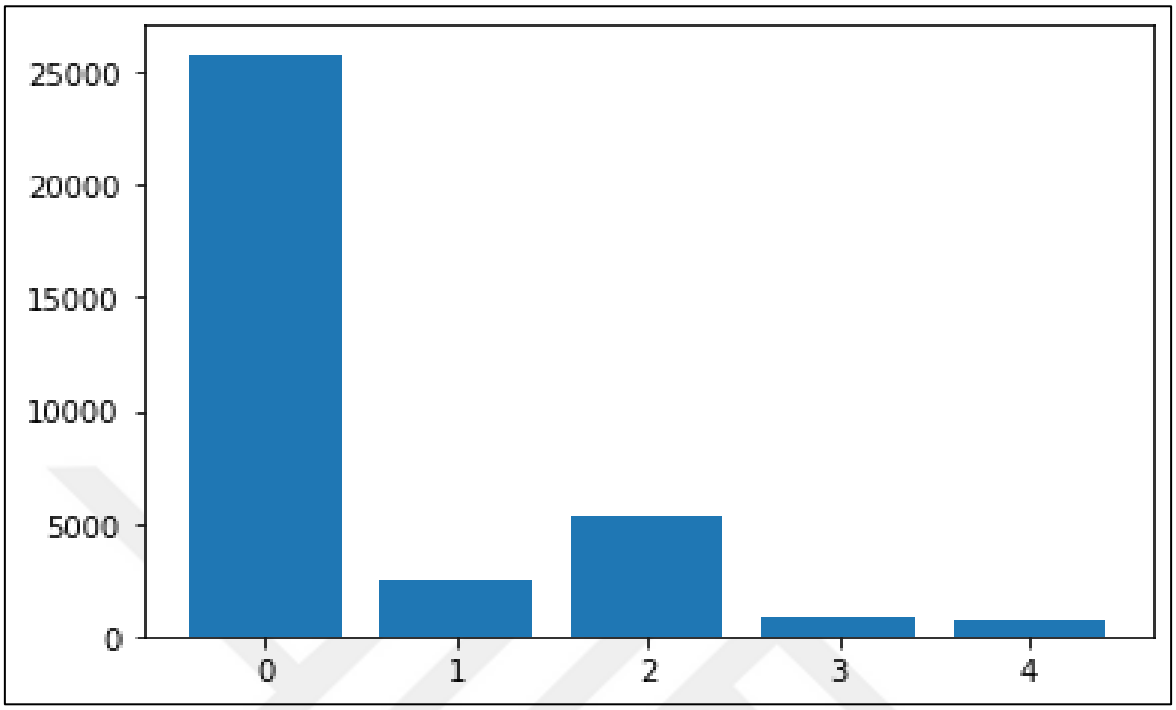

Figure 4.6: Distribution of Images According to DR Severity in Images From the 2015 Kaggle Training Database.

The proportion of images is not balanced, class 0 is in the majority data, in addition to the training database.

4.2.3 Test Phase

The performance of different models is measured on the test database images based on their quality. The architectures tested here are the same as those of the previous section, as well as those presented in the set method of the Kaggle 2019 section, ie EfficientNet-B3, EfficientNet-B4 and EfficientNet-B5. B3, B4 and a B5 networks have a regression objective while a B5 network has a classification objective. All networks are trained for 25 epochs with the ADAM optimizer on the Kaggle 2015 training database. some networks are trained only on the good quality images from the database. Some networks are trained with the pre-processing of B. Graham [46].

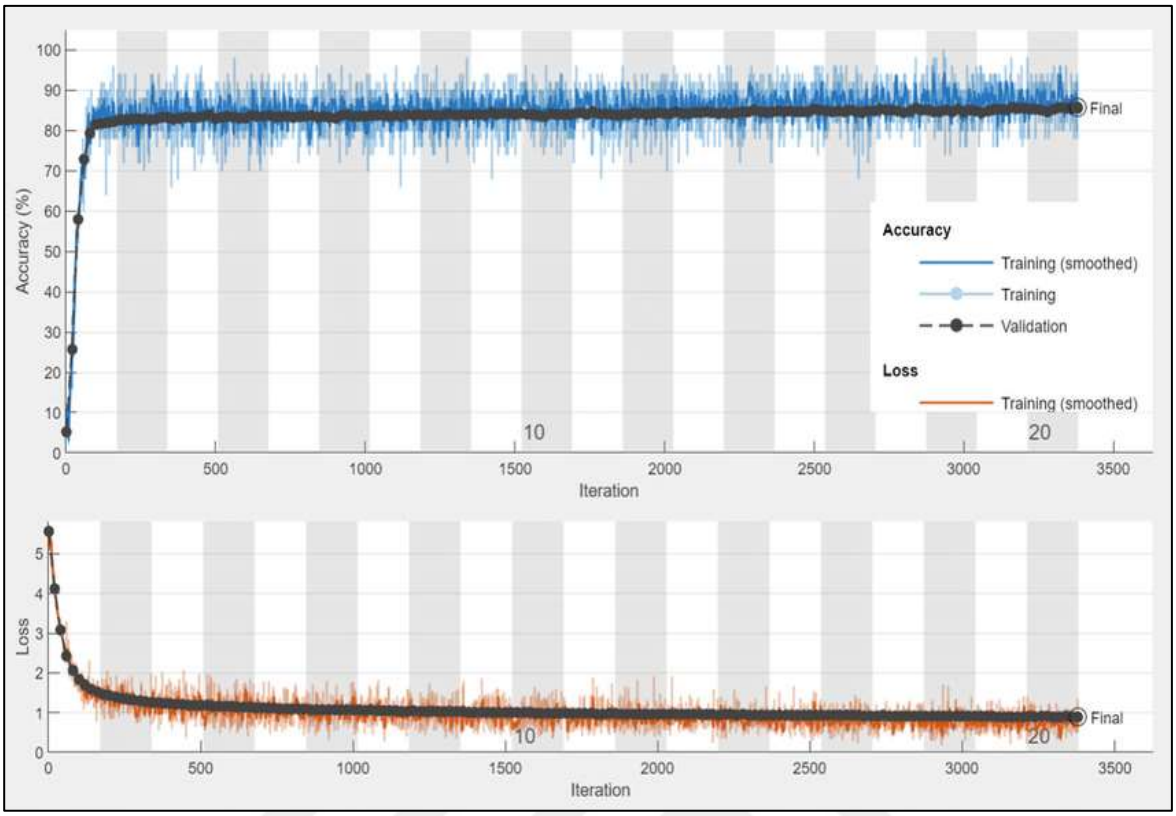

Figure 4.7: Transfer CNN Accuracy.

Table 4.1: Comparing the Accuracy and ROC to Other Methods in the Literature.

Study	Algorithm	Dataset	Accuracy (%)	ROC (%)
Voets et al. [25]	InceptionV3 CNN	EyePACS (35,617)	Not given	91.20
Li et al. [26]	InceptionV3 CNN	Custom (17,253)	93.49	90.03
Toledo-Cortés et al. [27]	InceptionV3 + GP Regressor	EyePACS (53,527)	Not given	85.88
Gurcan et al. [28]	InceptionV3 + XGBoost	Messidor-2	91.40	91.58
Proposed Model	Transfer CNN	Messidor-2	98.35	97.22

5. CONCLUSION AND FUTURE WORK

5.1 CONCLUSIONS

In this thesis, we have conducted a comprehensive review of the existing literature on the diagnosis of diabetic retinopathy (DR) using various imaging and machine learning techniques. Our analysis reveals several key insights and findings:

Diverse Approaches: The research landscape in DR diagnosis is characterized by a rich diversity of approaches, ranging from traditional image processing techniques to state-of-the-art deep learning models. Each approach offers unique advantages and challenges.

Deep Learning Dominance: Deep Convolutional Neural Networks (CNNs) have emerged as a dominant force in the field, demonstrating impressive performance in feature extraction and classification tasks. Transfer learning, where pre-trained CNNs are fine-tuned for DR diagnosis, has proven especially effective, mitigating the need for large, labeled datasets.

Feature Selection Significance: Feature selection methods, including metaheuristic algorithms like Binary Particle Swarm Optimization (BPSO), have been recognized as crucial in enhancing model performance, reducing overfitting, and expediting training times. These techniques have the potential to further refine DR diagnosis models.

Benchmark Datasets: The adoption of benchmark datasets like Messidor-2 has facilitated consistent evaluation of DR diagnosis models. However, there remains a need for larger and more diverse datasets to enhance the generalization and robustness of these models.

Ensemble Learning: Ensemble learning techniques have demonstrated promise in boosting classification accuracy by leveraging multiple feature extraction models. Further exploration of ensemble methods could yield even more reliable diagnostic systems.

5.2 FUTURE WORK

Building upon the insights gained from this thesis, several avenues for future research in the field of DR diagnosis are worth exploring:

Enhanced Feature Selection: Investigate advanced feature selection techniques, including novel metaheuristic algorithms, to identify the most informative features from retinal images effectively. Optimization of feature subsets can lead to more compact and discriminative representations.

Large-Scale Datasets: Collaborate with healthcare institutions and organizations to gather larger, more diverse datasets. These datasets should encompass various populations, ages, and ethnicities, improving model generalization and applicability.

Explainable AI: Develop interpretable deep learning models that provide insights into the decision-making process. Understanding how models arrive at diagnoses can enhance trust among healthcare professionals and patients.

Real-Time Diagnosis: Focus on the implementation of real-time DR diagnosis systems, which can assist ophthalmologists during patient screenings and examinations.

Clinical Validation: Conduct clinical validation studies to assess the real-world impact of automated DR diagnosis systems. Evaluate the performance of these systems in conjunction with human experts to determine their clinical utility and reliability.

Global Access: Ensure that developed DR diagnosis systems are accessible and affordable, particularly in underserved regions, to democratize access to early detection and treatment.

Integration into Healthcare Systems: Collaborate with healthcare institutions to seamlessly integrate automated DR diagnosis tools into existing healthcare systems, ensuring that they are used effectively in routine clinical practice.

In conclusion, the field of diabetic retinopathy diagnosis continues to evolve rapidly, with opportunities for innovation, scalability, and improved patient care. Future research endeavors should strive to enhance the accuracy, accessibility, and real-world impact of automated DR diagnosis systems.

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