Journal of Theoretical and Applied Information Technology
15th June 2023. Vol.101. No 11

ISSN: 1992-8645 www.jatit.org E-ISSN: 1817-3195

A SURVEY ON DETECTION OF SEVERITY IN DIABETIC RETINOPATHY USING MACHINE LEARNING MODELS

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ABSTRACT

Diabetes has rapidly become a leading cause of death globally. The metabolic irregularities and complications of diabetes, such as high blood sugar and insulin production, cardiovascular diseases, nephrological problems, neurological disorders, and diabetic retinopathy (vision loss), all have their origins in the disease itself. Diabetic retinopathy (DR) refers to a serious problem faced by diabetic affecting retina. It causes leakages in blood vessel walls within retina, thereby damaging it. It is considered the major cause of blindness because of its rapid onset and absence of symptoms. In order to properly intervene and treat DR, it is crucial to be aware of the early clinical indications of the disorder. Therefore, it's important to get your eyes checked often so you know whether you need to see an eye doctor right away so you can prevent any irreversible damage to your eyesight. The goals of this study are to provide a critical evaluation of many machine learning and deep learning methodologies and observe patterns to enhance strategies of current work, to highlight obstacles, and to recommend prospective future research directions. The results can help shape future research agendas, and the recommendations can help shape future models for diabetic retinopathy algorithms that have both high generalizability and high performance.
Keywords: *Diabetic Retinopathy; Machine Learning; Deep Learning; Blood Vessels; Taxonomy*

1. INTRODUCTION

When insulin production is inadequate, blood glucose levels rise, leading to the disease diabetes. High blood sugar and insulin production, heart disease, renal failure, neurological diseases, and diabetic retinopathy (vision loss) are all metabolic abnormalities and complications that stem from having diabetes. Early on in DR development, vision problems are uncommon. Most people don't notice any symptoms until the disease has progressed significantly. The effectiveness of treatment and the avoidance of disease consequences are both enhanced by early disease detection. Fundus image databases are produced as a result of developments in medical imaging technology.

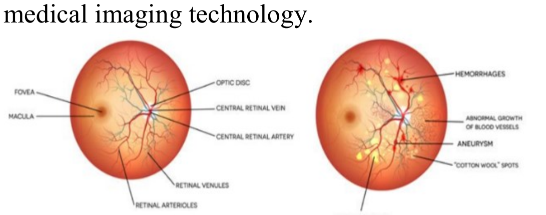

Figure.1.(a) Normal Retina (b) Diabetic Retinopathy

Color photographs of the eye's fundus are the starting point for most ophthalmologists. Trained doctors detect DR by examining retinal color fundus images that needs some time.

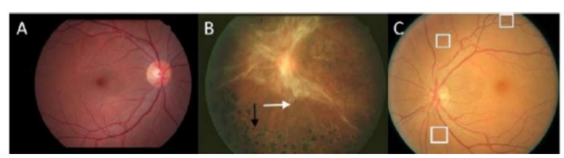

Figure 2: Different Stages of DR retinal images labeled as A-normal, B-Last phase, C-Starting phase.

Due to factors like the sheer volume of patients in a given hospital or the severity of a given patient's illness, quick clinical assessments and decisions are often required. Further, all patients should have access to treatment at an inexpensive price, but this is not the case in many underdeveloped nations. As a result, many low-income individuals face certain blindness due to a lack of adequate medical care [2].

1.1. Phases of Diabetic Retinopathy

DR can proceed through the following 4 distinct stages:

ISSN: 1992-8645 www.jatit.org E-ISSN: 1817-3195

- **Mild Non-Proliferative Retinopathy:** Microaneurysms are another term for these leaking blood vessel sacs that might lead to vision loss. Diabetic retinopathy's first stage is characterized by a ballooning out of blood vessels within retina [3].
- **Moderate Non-Proliferative Retinopathy:** Retinal blood vessels enlarge and may get clogged if therapy is delayed. Due to fluid buildup within retinal macula, diabetic macular edema can occur. [3]
- **Severe Non-Proliferative Retinopathy:** The retina's blood supply has been further compromised. The brain sends signals to the retina to initiate vessel growth, ensuring adequate blood flow to the retina at all times [4].
- **Proliferative Diabetic Retinopathy (PDR):** Detachment of the retina can be caused in case newer blood vessels grow inside retina, triggering the release of vitreous gel, which causes the retina to expand and become detached from the tissue beneath it. This is the ultimate stage of diabetic retinopathy, which can cause considerable vision loss as well as bright flashes and blurred vision [4].

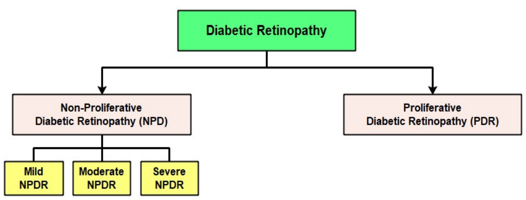

Figure.3. Hierarchy depicting diferent types of Diabetic Retinopathy (DR)

1.2. Kinds of Lesions

Microaneurysms (MA) appear as red patches with crisp boundaries and have a diameter of 125 microns or less. It is the primary clinical sign of DR and develops when there is a significant loss of blood pressure in the retinal blood vessels. Weakened walls eventually shatter, resulting in larger-scale hemorrhages (HMs)[5]. Dot and blot gets its name from the fact that its boundaries aren't perfectly even. Additional complications from bleeding include Splinter hemorrhage and the appearance of a yellow abnormality on the retina's surface due to capillary damage and exudates (EXs). Exudates (EXs) can be either hard or soft [6].

- **Hard exudates** (HEs) have a color scheme of white or white-yellow and angular shapes like blocks or circles for their borders. This disorder is brought on when retinal blood vessels leak proteins and lipoproteins. It is the layer of the retina that is situated in the most external position [7].
- **Soft exudates** cloud-like shapes or cotton-like patches that appear whitish grey (CWS) EX lesions are light, whereas MA and HM lesions are dark [8].

Neovascularization (NV) lesions develop when the brain sends signals to the circulatory system to find alternative blood channels due to the obstruction of the usual ones. Substances like sorbitol are produced to provide the necessary backdoors. Macular edema occurs when leakage occurs around the macula due to abnormalities in the retinal arteries (ME)[9].

1.3. Role of Machine Learning in Medical Research

Machine learning is one of the most significant and effective methods for deciphering extremely complex medical data. In order to develop healthcare and medicine on a worldwide basis, massive amounts of medical data must be collected and used properly. As more and more health records are collected, it is crucial to analyze this data. In the medical field, automating screening and diagnosis saves time and money for doctors by reducing the possibility of misdiagnosis [10]. As a result of the flood of new medical information being collected and stored, doctors are increasingly turning to electronic health records to keep track of patient records (EHRs). The use of machine learning algorithms makes it feasible to automatically glean useful information from massive datasets of patient records stored in electronic health records (EHRs). As a result, these models can aid in illness detection by monitoring data and forecasting likely diseases based on EHR features. Machine learning algorithms have advanced to the point where they can now analyze complicated aspects in medical data, resulting in rapid breakthroughs in automation. In ophthalmology, for retinopathy diagnosis and severity evaluation, such attempts have been undertaken to analyze retinal images and develop frameworks based on analysis [9] The overall framework for identifying and classifying DR includes an examination of the data analysis, pre-processing, and data augmentation; selection of an appropriate classification technique; and, ultimately, evaluation of the efficacy of the findings [11].

This study surveys the methods of ML applied to the creation of a DR diagnostic instrument. Also mentioned are the techniques that become necessary for the proper functioning of certain programs. In Section II, discuss the fundamental applications and algorithms of ML. The proposed systems are discussed in Section III. In Section IV, this work analyzes and contrasted results of literature review. The overall work's conclusion is presented in section V.

2. MACHINE LEARNING ALGORITHMS

Machine learning (ML) refers to process of encouraging machines to process data for accomplishing specific goals in the same way that humans do. Models for making predictions can be automatically constructed by ML algorithms using sample data (called "training data"). Learnings like supervised, semi-supervised, unsupervised, reinforcement, ensemble, transfer, instance-based, and deep refer to machine learning approaches that can be further subdivided into subcategories based on the model learning method. Among these techniques are supervised learning, semi-supervised learning, unsupervised learning, transfer learning, and instance-based learning [13][14].

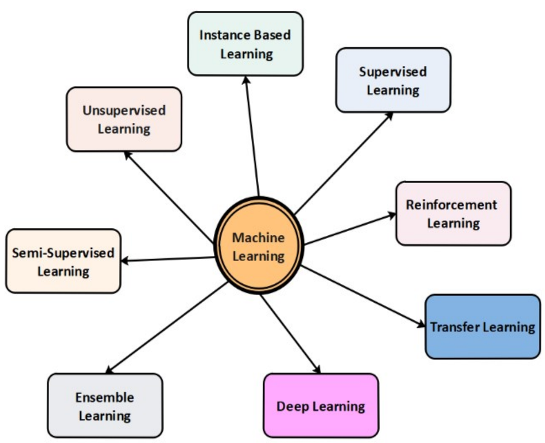

Figure.4. Different Machine Learning types for Diabetic Retinopathy Classification

2.1. Supervised Learning

Machine learning algorithms are considered to be supervised when they are unable to learn on their own and instead require supervision from a human being. The train dataset and the test dataset are the two varieties of input datasets that are available. The train dataset contains an output variable that must either be predicted or classified [15][16]. Every algorithm first studies the training dataset in order to acquire the knowledge necessary to predict outcomes or assign categories to data from the test dataset. Classification and Regression are the backbone operations of supervised learning.

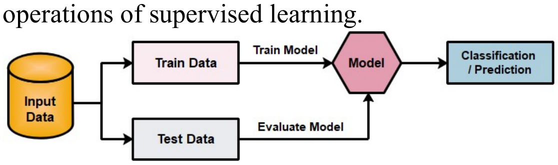

Figure.5. Supervised Learning Workflow

2.1.1. Classification

Classification methods are utilized in order to generate classification models based on the numerous input datasets that are available. Each classifier uses a different type of learning to find the most accurate correlation between characteristics and labeled data. The classifier's accuracy in predicting the labels of the unknown data stems from the fact that its roles are consistent with the input data. A highly generalizable classifier is the end goal of the learning algorithm. Mathematically speaking, what it does is map a function f, moving from input variables $\mathbf{X}$ to output variables $\mathbf{Y}$ as target, label, or category variables. The following are the common classification problems:

- **Binary Classification:** Classification assignments with two-way labels like "true" and "false" or "yes" and "no" are meant to illustrate this concept. For example, in a task requiring binary classification, "normal" could be one class and "abnormal" another. In the context of a medical test, for instance, the state "DR not detected" would be regarded normal and the state "DR discovered" would be considered problematic [16].
- **Multiclass Classification:** This is the standard notation for classification issues involving more than two groups. Multiclass classification tasks do not function based on normal and abnormal outcomes like binary classification tasks do. As an alternative, instances are assigned to one of a set of predetermined categories [17].

- **Multilabel Classification:** When an example has many labels, or classes, multilabel classification becomes an important factor in machine learning. In generalized multiclass classification, the classes within the problem have hierarchical formation. Additionally, each sample can be classified within multiple classes at every hierarchy, just as classifying multi-level text. This strategy was conceived as a means of resolving difficulties associated with the classification of enormous amounts of data. The classification of data is by far the most prevalent application of algorithms [18].

2.1.2. Models of Classification

- **Decision Tree:** represents potential effects of actions in a tree-like structure. The edges represent decision criteria, and the nodes represent events or choices. There are leaves and twigs on every tree. In a classification tree, a node represents an attribute of a class, and a branch represents a possible value for that attribute [19].

The most well-known choice tree algorithms are:

Journal of Theoretical and Applied Information Technology
15th June 2023. Vol.101. No 11

ISSN: 1992-8645 www.jatit.org E-ISSN: 1817-3195

- Chi-squared Automatic Interaction Detection (CHAID)
- Iterative Dichotomiser 3 (ID3)
- Classification and Regression Tree (CART)
- Conditional Decision Trees
- C4.5 and C5.0

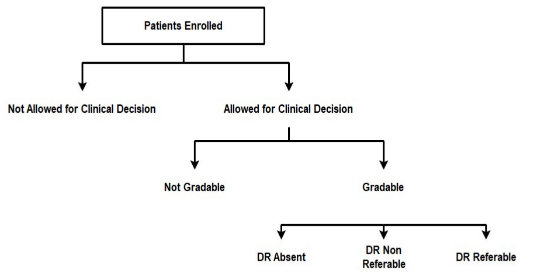

Figure.6. Example Decision Tree for DR Classification

- **Naive Bayes (NB):** Assuming that features are independent, Naive Bayes is an algorithm that applies Bayes' theorem. It specializes at a wide range of practical tasks, such as spam filtering, document classification, and more. The NB classifier may be used to categorize noisy occurrences efficiently and reliably in the data, which is necessary for building a reliable prediction model. One key benefit is that only a little quantity of training data is required to predict the required values quickly and reliably, in contrast to more complicated procedures. Its performance could be hampered by its heavy reliance on the assumption that qualities are unrelated to one another. Commonly used NB classifiers include the Gaussian, Multinomial, Complement, Bernays, and Categorical distributions [20].

$$P(H|E)=\frac{P(E|H)*P(H)}{P(E)} \qquad (1)$$

The most mainstream algorithms are:

- Averaged One-Dependence Estimators (AODE)
- Multinomial Naive Bayes
- Gaussian Naive Bayes
- Bayesian Network (BN)
- Bayesian Belief Network (BBN)

- **Linear Discriminant Analysis (LDA):** It refers to a linear decision boundary classifier that uses Bayes' rule and the fitting of class conditional densities to data. An improvement on Fisher's linear discriminant, this technique minimizes the complexity of the model and the amount of processing time needed to execute it when data gets mapped to lower-dimensional space. In simplest form of the LDA model, the covariance matrix between classes is assumed to be constant, and a Gaussian distribution is used to characterize the distribution of each class [21]. Like analysis of variance (ANOVA) and regression analysis, linear mixed models (LDA) allow expression of dependent variables in terms of linear combination of features or data.

Random Forest Classifier: It refers to a supervised learning technique that, like decision trees and support vector machines, may be used for both classification and regression. This algorithm applies available data samples in building decision trees, collects predictions from each tree, and then uses a voting mechanism to determine the optimal solution.

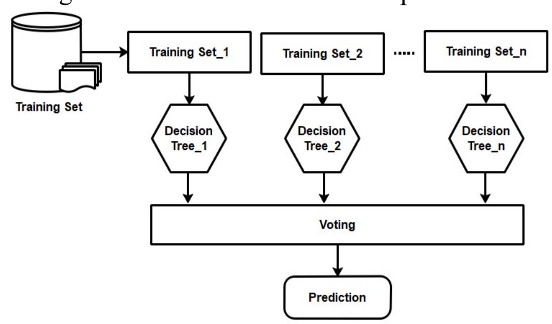

Figure.7. Random Forest Classifier

Support Vector Machine: When it comes to cutting-edge machine learning methods, Support Vector Machine is a popular choice (SVM). The primary function of this is for organizing information. The foundation of SVM is the calculation of margins. It establishes functional barriers between socioeconomic groups. To reduce misclassification, the margins are drawn to ensure a minimum distance between themselves and the classes [22].

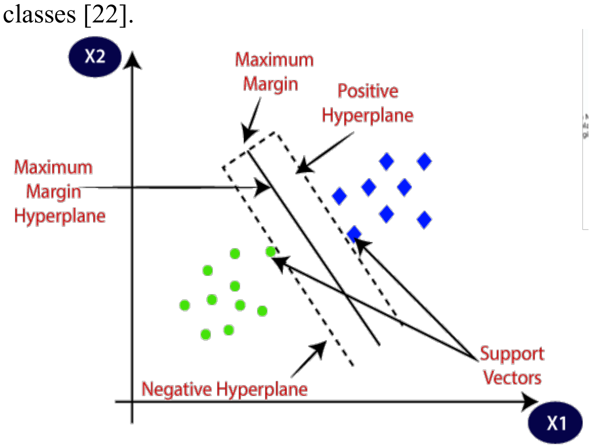

Figure.8. Support Vector Machine Classifier.

2.1.2. Regression

A new data prediction model can be created by regression algorithms using continuous variables to analyze the connection between input attributes and output class. Insight into this relationship is gained through examination of data. Real estate price forecasting, sales forecasting, and rating systems are three of the most prevalent uses of regression analysis. Regression techniques like Linear, trees,

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lasso and multivariate are some of known regression methods. In addition to logistic regression, linear regression is a popular option [24].

- **Linear Regression Algorithm**: It's a statistical method for figuring out why a given input feature x leads to a certain categorization. The x-factor was suggested by a user. The independent variables linearly combined as **x** will yield desired output **y**, which can be graphically demonstrated. This method is referred to as a simple linear regression with just one input feature **x**. When many features are supplied simultaneously, this statistical technique is referred to as multiple linear regression [25].

$$\mathbf{y}=\mathbf{a}+\mathbf{b}x+\varepsilon \qquad (2)$$

When a represents intercept value, b represents the line slope ϵ, representing error term.

- **Polynomial Regression:** It refers to a type of regression analysis that is used when the relationship between x and y is not linear, but rather the polynomial degree nth of dependence. This means that polynomial regression can be thought of as a more complex version of the traditional linear regression. This means that the relationship cannot be represented by a straight line. Polynomial regression can be represented by the following equation:

$$\mathbf{y}=\mathbf{b}_0+\mathbf{b}_1x+\mathbf{b}_2x^2+\mathbf{b}_3x^3+....+\mathbf{b}_nx^n+\varepsilon \quad (3)$$

- **Logistic regression Algorithm:** The primary domain of use for this algorithm is in manufacturing. In situations where only a yes or no answer will do, such as credit scoring, fraud detection, clinical trials, etc. Important advantages of this method include its applicability to a large class of dependent variables (including continuous and dichotomous ones) and the provision of a numeric value for gauging the strength of connections in comparison to other variables. By contrast, the insufficiency of robust technique and heavy reliance on the model are cited as weaknesses of this algorithm [26].

- **Lasso Regression Algorithm:** The objective of the method is identifying a predictor subset resulting in least amount of errors in predicting the quantitative response variable, and then to select just those predictors as candidates for further analysis. Using this method results in some regression coefficients being set to zero and limits the range of other model parameters. A zero-regression-coefficient variable is removed after applying the sectioning procedure. Non-zero regression coefficients on other variables are related to the reaction variable in a close way [27]. The variables used for explanation can be numerical, qualitative, or a mix of the two. Recession analysis via regression lets academics sort out the most important predictors.

Table.1. Literature-based Supervised Machine Learning

Author (Year)	Dataset	Features Extracted	Classifier	Performance
Zhang X. et al. (2014) [15]	e-Ophtha EX	HCF	Random Forest	AUC = 0.95
Liu et al. (2017) [16]	Additionally, e-Ophtha EX and DiaRetDB1	HCF	Random Forest	76% in sensitivity 75% in positive prediction value (PPV)
Badgujar et al. [17]	STARE	HCF	Classifiers k-NN, SVM, Naive Bayes, and a Decision Tree for the SMO-GBM	Average Accuracy 97.5%
Mahendran et al. (2015) [18]	Messidor	HCF	SVM, PNN	Average Accuracy SVM 97.89% and PNN 94.76%
Shailesh et al. (2020) [19]	DiaRetDB1, DiaRetDB0	HCF	RBF NN	Sensitivity 87% Specificity 93%
Du J. et al. (2020) [20]	Incorporating DiaretDB1, e-Ophtha-MA, and ROC	HCF	using RUSBoost and a decision tree for classification	FROC 0.516, 0.402 and 0.293
Najib Ullah. et al. (2022)	Kaggle dataset	HCF	Genetic Algorithm, SVM	Average Accuracy 96.4%

2.2. Semi - Supervised Learning

It bridges distance between fully supervised and fully unsupervised approaches. When labeled data is not readily available, this may prove useful for ML and DM purposes with many subfields within the larger topic of semi-supervised learning.

- **Generative Models:** One of the earliest forms of semi-supervised learning, they take the form of $p(x,y)=p(y)p(x|y)$ where $p(x|y)$ is a mixed distribution e.g., Gaussian mixture models. Within the unlabeled data, the mixed components can be identifiable. One labeled example per component is enough to confirm the mixture distribution [28][29].
- **Self-Training:** This classifier training method uses only an example of labeled data. The classifier is then fed with unlabeled data. The unlabeled points and the predicted labels are added together in the training set. This procedure is then repeated further. Since the classifier is learning itself, hence the name self-training [30].
- **Transductive SVM:** TSVM are widely used in the field of Semi-Supervised learning to process data with incomplete labels. Due to unclear understanding into its relation to generalization, it offers challenges. In order to maximize the difference between the labeled and unlabeled data, it is applied to label the raw data. When using TSVM, arriving at a precise answer is an NP-Hard task [32].

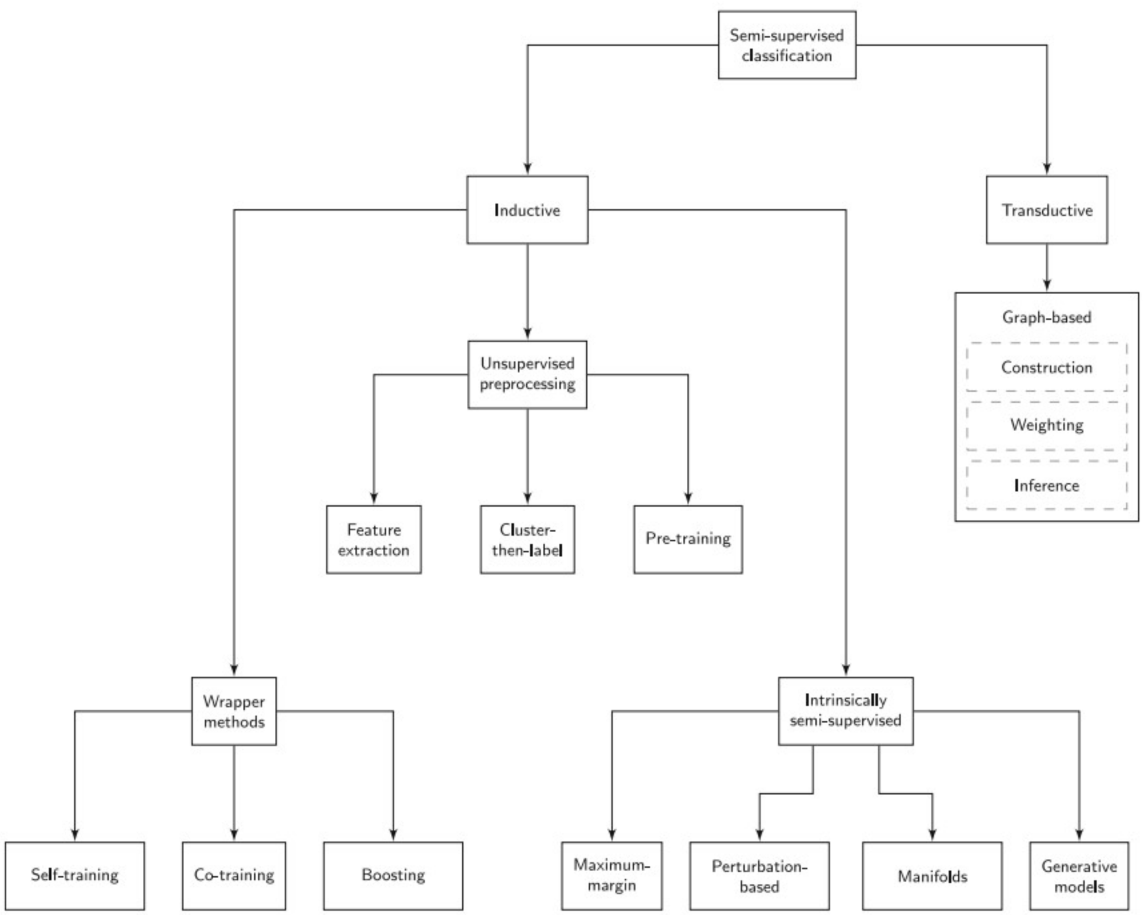

Figure.9. Semi-Supervised Machine Learning Classification

ISSN: 1992-8645 www.jatit.org E-ISSN: 1817-3195

Table.2. Literature-based applications of semi-supervised machine learning

Author (Year)	Dataset	Features Extracted	Classifier	Performance
Adal et al. (2014) [39]	ROC, UTHSC	Radial Feature, SURF Feature, and Scale-Space Feature	SVM, KNN, Naïve Bayes, RF	CPM Measure 0.364
Cao et al. (2018) [45]	Messidor	HCF	Multi-kernel Classifier	Accuracy 0.916% and Area Under the Curve 0.957%

2.3. Unsupervised Learning

Without labels, a learning algorithm in unsupervised learning must discover patterns in the data on its own. Unsupervised learning seeks to unearth latent patterns within a dataset such that a computational device can infer the representations necessary for classifying raw data on its own. Here, we'll go through the two most common methods for accomplishing this task: clustering and dimensionality reduction [31].

2.3.1. Clustering Algorithms

When it comes to data analysis and data mining, clustering is a crucial step. It's the process of classifying things into groups where members of the same group have stronger ties to one another than members of different groups do. A cluster is a ranked list of items that all share some commonalities. Cluster analysis is a method for organizing data by grouping together data elements that share common properties. You can find examples of the most well-known clustering algorithms in the figure [32].

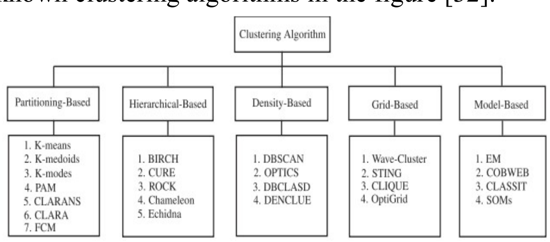

Figure.10. Taxonomy of Clustering Approaches

2.3. Dimensionality Reduction Algorithms

When dealing with data from the real world, like image data, you will often come across a large dimensionality of features. Increases in the amount of features may cause the induction process to take longer than it would have with a smaller feature subset, yet the end outcome may be the same. Reducing the dimensionality of data is necessary for working with such real-world data. Dimensionality reduction refers to the process of translating high-dimensional data into a meaningful representation at a lower dimensionality. Data dimensionality is the smallest number of components required to adequately characterize the data's properties. Techniques used to reduce the dimensions of a certain data set are a crucial solution to be confronted due to the large number of features that must be removed judiciously [35].

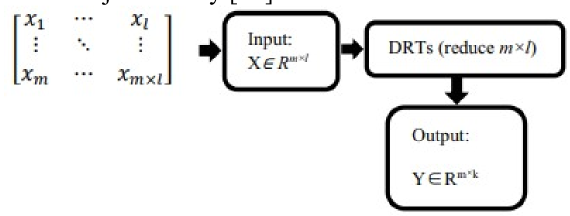

Figure.11. The general structure of DRTs steps

Figure.11. The general structure of DRTs steps

where $\mathbf{X}$ is the size of the input data set and the $\mathbf{m} \times \mathbf{l}$ dimension of the $\mathbf{Y}$ output space. Is the output corpus, where $\mathbf{m} \times \mathbf{k}$ the dimension is after DRTs have been applied. $\mathbf{m}$ has data points[36].

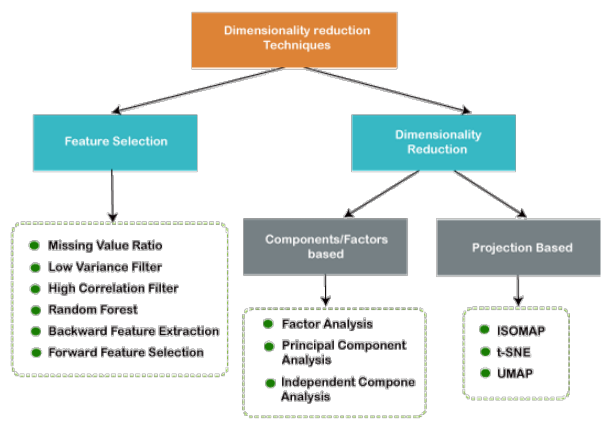

Figure.12. Taxonomy of Dimensionality Reduction Algorithms

ISSN: 1992-8645 www.jatit.org E-ISSN: 1817-3195

Table.3. Literature-based Unsupervised Machine Learning

Author (Year)	Dataset	Features Extracted	Classifier	Performance
Kaur et al. (2017) [6]	This includes the STARE, Messidor, DiaretDB1, and e-Optha EX telescopes.	Shape and Intensity features	k-means	Sensitivity 94.62% Specificity 98.64% Accuracy 96.74%
Akram et al. (2014) [14]	DRIVE, STARE, DiaretDB, Messidor	HCF	a classifier that is based on GMM and m-Mediods	Average Accuracy 82%.
Sopharak et al. (2009) [17]	DiaretDB1, Thammasat University Medical Center,	HCF	Fuzzy C-means (FCM) clustering	The PPV, PLR, sensitivity, and accuracy are all above 90%. The PPV is 87.28%, the PLR is -99.24%, the sensitivity is -224.26%, and the accuracy is -99.11%.
Huang C. et al. (2020) [18]	e-Ophtha EX and IDRiD	Intricate details on the pixel and super pixel levels	SLIC, CNN	Sensitivity 97.96%, Specificity 90.84%, Accuracy 97.58% AUC 0.9682

2.4. Ensemble Learning Approach

This approach seeks to identify an unknown image by combining the results of various models. Combining several canonical models yields the ensemble model. An ensemble can be categorized as either stacking, blending, bagging, or boosting depending on the method used to combine the individual components. The best answer was found by combining the results of the decision trees with a voting-based bootstrapping technique using RUSBoost.

- **Boosting:** Boosting is a technique that is part of ensemble learning, and its major goal is to reduce the negative impacts of bias and variation. It is possible to create a strong learner from a group of less capable learners by providing them with education. To put it another way, a strong learner is the inverse of a weak learner, which can be thought of as a classifier that cannot be associated to any specific classification [38].

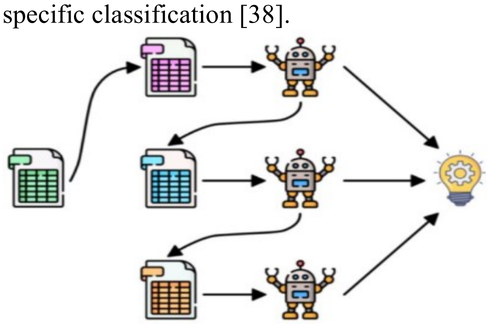

Figure.13. Boosting Ensemble Learning Method

- **Bagging:** When improving the precision and consistency of a machine learning algorithm, bagging or bootstrap aggregation is used. It can be used in the contexts of both classification and regression. Overfitting can be mitigated with the aid of bagging, which also reduces variance [39].

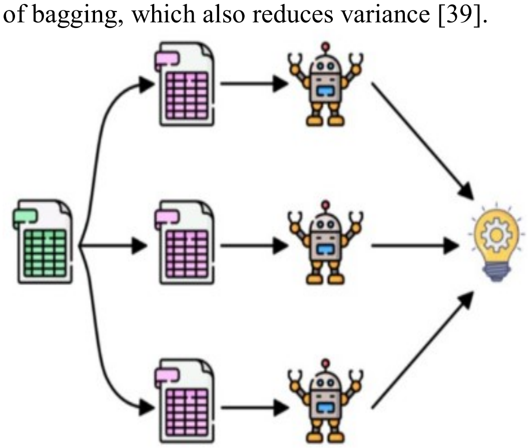

Figure.14. Bagging Ensemble Learning Method

ISSN: 1992-8645 www.jatit.org E-ISSN: 1817-3195

Table.4. Ensemble Learning has been literature

Author (Year)	Dataset	Features Extracted	Classifier	Performance
Orlando et al. (2017) [29]	DIARETDB1 in addition to e-ophtha	The HCF as well as Deep Features	Random Forest	AUC 0.9347
Du J. et al. [44]	The compounds DiaretDB1, e-Ophtha-MA, and ROC	HCF	Decision Tree	Final scores on the FROC metric are 0.516, 0.402, and 0.293, respectively.
Zhang W. et al. (2019) [47]	People's Hospital of Sichuan Province	HCF	Model that has been pre-trained and the standard Deep neural network	Sensitivity 98.1% Specificity 98.9%
Fraz et al. (2017) [46]	HEI-MED, e-Ophtha EX, and DIARETDB1 are known as Messidor.	Deep Features	Decision Tree	ROC as (0.8772, 0.8925, 0.9577, and 0.9836) Accuracy in Segmentation as (0.9310, 0.9403, 0.9842, and 0.9961)

2.5. Deep Learning-Based Methods

Deep learning, a subfield of machine learning, has recently demonstrated some very encouraging outcomes in a wide range of problem-solving applications. Deep learning methods often make use of a multilayered neural network structure. This is done so that generic features can be extracted from enormous datasets. Natural language processing, sentiment analysis, question answering, and language translation are just few of the areas where deep learning technologies have been shown to boost performance. In this chapter, we look at the many applications of deep learning to healthcare that have been documented in the academic literature.

Table.5. Use of Deep Learning in the literature.

Model	**Technique**	**Datasets**	**Features**	**Performance Methods**
CNN-Based Methods[41]	Ensembles of patch-based CNN models	DRIVE	HCF and Deep features	AUC=0.9283 Achievable Roughly 94.7 Percent Accuracy
	Patch-based CNN	DRIVE	HCF and Deep features	Sensitivity=98.07% Specificity equals 78.11 percent AUC=0.9790 The accuracy is 95.35%
		STARE	Pixel and Super Pixel Level Features	Sensitivity=85.54% 99.62% specificity AUC=0.9928 97.29% accuracy
	A classifier based on patch-based CNN/PCA and vessel tracking.	DRIVE	HCF and Deep features	AUC=0.9701
AE-Based Methods[3]	SDAE/RF utilizing a patch	DRIVE	HCF and Deep features	AUC equals 0.9195 Accuracy equals 93.27%
	SAE based on patches	STARE	HCF and Deep features	AUC=0.92
	SDAE based on patching	DRIVE	HCF and Deep features	Sensitivity=75.60% 98.04% specificity AUC=0.9738 95.27% accuracy
		STARE	Consisting of both HCF and Deep characteristics	Sensitivity=77.26% Specificity equals 98.79 percent

ISSN: 1992-8645 www.jatit.org E-ISSN: 1817-3195

				Precision equals 96.27%
		CHASE (28 images)	Pixel and Super Pixel Level Features	Sensitivity=75.07% The value of specificity is 97.94% AUC=0.9718 Accuracy=95.84%
RNN-Based Methods[42]	RNN incorporating patch-based CNN/CRF	DRIVE	Consisting of both HCF and Deep characteristics	The specificity value is 76.03% Accuracy=95.23%
		STARE	Consisting of both HCF and Deep characteristics	The specificity value is 74.18% Accuracy=95.85%
		CHASE	Functionality on the Pixel and Superpixel Scales	Specificity equals 71.30 percent Accuracy=94.89%
DBN-Based Methods[3]	Training was done using a DBN, while classification was done with a multiclass support vector machine. ,	ARIA	HCF and Deep features	Accuracy was measured at 96.73%, while sensitivity was measured at 79.32%.
AE Based Methods[3]	SSAE that is based on patches	DIARETDB	HCF and Deep features	Specificity=91.62% Accuracy=91.38%
AlexNet[3]	Classification Using AlexNet/SVM	Kaggle	HCF and Deep features	Sensitivity=100% Specificity=93.79% Accuracy =97.97%
ResNet[43]	Gradient tree learning with ResNet	MESSIDOR-2	HCF and Deep features	AUC=0.9418

2.5. Transfer Learning Approach

Learning that can be transferred from one context to another is called transfer learning. It's utilized to create model-based strategies and is thus characterized as a pre-trained model

Table.6. Literature-based Transfer Learning.

Author (Year)	Dataset	Features Extracted	Classifier	Performance
Samanta et al. (2020) [19]	Kaggle dataset	Deep Features	Inception Xception, ResNet-50, DenseNet, and AlexNet Networks; Inception Xception, ResNet-50, and AlexNet Networks	Accuracy 84.10 %.
Saxena et al. (2020) [20]	EyePACS, Messidor1, Messidor2	Deep features	Inception V3 and Inception, ResNet	AUC of 0.92 Sensitivity 81.02% Specificity 86.09%
Sugeno et al. (2021) [51]	Diabetic Retinopathy Dataset, Small Eye Research and Treatment at Multiple Eye Centers (STARE), Electronic Ophthalmology Records and Results (ROC), and the Little Flower Hospital	Deep features	Inception V3 and Xception	Accuracy 98.05%. Specificity and Sensitivity Values ≳ 0.98%
Khojasteh et al. (2018) [52]	E-Ophtha EX, and DiaretDB1	Deep features	ResNet50	Accuracy 98% Sensitivity 0.99%

2.6. Reinforcement Learning

The field of machine learning known as "Reinforcement Learning" investigates the best ways to guide the actions of software agents toward maximizing a reward. Reinforcement learning is one of the three fundamental pillars that support machine learning. The other two are supervised learning and unsupervised learning.

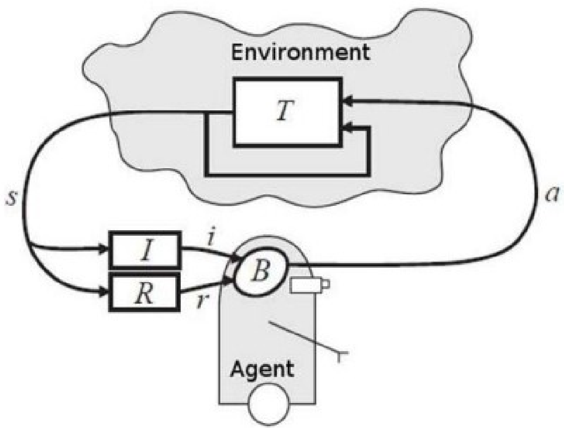

Figure.15. Model of Reinforcement Learning.

As shown in Figure.14, the agent's input consists of data from its environment about its present state, its ability to change that state, and its input function. The agent then produces a behavior and acts upon it, producing an outcome based on the inputs.

2.7. Instance-Based Learning

A collection of classification and regression techniques, "instance-based learning" determines a query's prediction or label by examining its relationship to other instances in the training set. Instance-based learning algorithms can't generalize from specific instances, unlike other methods like decision trees and neural networks. Instead, they compile everything and, when receiving a query, look at the records immediately around the one being queried in order to determine its answers.

- K-Nearest Neighbor (KNN): The k-nearest neighbor (KNN) learning algorithm is non-parametric and time-consuming. KNN uses a data set to classify a test case into one of several possible groups. Based on the information available, a KNN model is built. Because no assumptions are made about the distribution of the input data, this algorithm cannot be considered parametric. Unfortunately, the facts in many real-world contexts does not match the theoretical expectations. To categorize data in this situation where no prior knowledge of the data distribution exists, KNN is the most natural choice.

3. CHALLENGES OF THE EXISTING MODELS

Challenge 1: Degraded Image Quality

The efficacy of Machine learning models is proportional to the quality of the data they use. However, environmental, and non-invasive acquisition conditions frequently decrease the visual and qualitative quality of retinal fundus images employed in ophthalmological diagnosis. As a result, the predictive accuracy of the models suffers, and the learning of feature representations is hampered. A bent retina, a moving patient, or improper camera settings are just a few of the many causes of blurry retinal photos. If the earliest symptoms of an illness are obscured by a low-quality photograph, a wrong diagnosis may be made, delaying treatment.

Challenge 2: Lack of a Standard Pre-Processing Approach

When dealing with brilliant intensity structures with non-homogeneous intensity characteristics, such as EXs, which are sometimes misunderstood for OD, it might be challenging to detect salient features amidst noise, low contrast, uneven lighting, and color fluctuation. Standardizing the pre-processing of retinal fundus pictures can be achieved by the development and implementation of a single pre-processing method. Such a system would make it possible to compare results more accurately.

Challenge 3: Heterogeneity in the Retinal Blood Vessel Morphological Structure

Noise introduced by differences in lighting and structural behavior makes retinal vascular segmentation all the more important. Therefore, better detection of DR lesions requires background subtraction to remove anatomical components of the retina. However, when OD and RBVs are subtracted from one another, it can mask anomalous OD behavior and NVs and IRMAs in RBVs. Possible approaches to these problems include picture analysis and backdrop subtraction. Due to this, the relevance of preprocessing methods is increased, and the computing cost is increased in a roundabout way.

Challenge 4: Class Imbalance

When taking a snapshot of the retinal fundus, the region of interest (the blood vessels) is quite small (known as the background, i.e., non-blood vessels). Because the classes of pixels to be categorized aren't distributed evenly, class imbalance becomes an issue. There is a risk that the network will unfairly prioritize the more numerous user group because of this imbalance. Addressing the problem of label distribution imbalance more effectively can be done by the use of dice, targeted, weighted class balancing, and well-designed joint loss functions (i.e., blood vessel and non-blood vessel).

Challenge 5: Multiclass Classification Limitation of Deep Learning Models

ISSN: 1992-8645 www.jatit.org E-ISSN: 1817-3195

When fully linked layers are added into the architecture, many deep learning models excel at binary classification problems over multi-classification ones. By swapping out the completely linked layers for a convolution layer and employing SoftMax functions at the output layer, we may solve the problem of a CNN model's limited ability to produce numerous classifications.

4.Proposed Computer aided Diabetic Retinopathy Detection Model

Here are the measures that make up the created computer-aided model system for the diagnosis of diabetic retinopathy. First, we'll work to improve image quality. Deep learning and other AI advancements have led to vastly improved general image enhancing results. However, natural image enhancement approaches cannot be utilized directly to resolve low-quality concerns in fundus images because of the structure of the retina and the special characteristics of the ophthalmoscope imaging process. Both incident and reflected imaging beams have to pass through the pupil because of the retina's structure, which prevents internal illumination. In addition, the eye's spherical geometry can lead to substantial inter-reflection, which in turn can produce unwanted shading artifacts. Pathological characteristics such as hemorrhages, microaneurysms, and drusen are usually few pixels wide and appear in circular forms, making them readily misconstrued as artifacts and noises, so it's vital to improve the appearance of these structures throughout the correction process. Pre-processing the photos with sufficient and effective methods is thus crucial for improving image quality. Higher order reflectivity features that are identifiable during the second phase are isolated. In the final step, a global diagnosis is reached by first classifying each layer based on the extracted feature, and then using majority voting on the layer classification outputs.

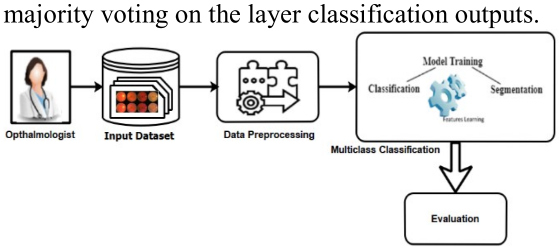

Figure.16. Proposed Computer aided Diabetic Retinopathy Detection Model

5. Performance Metrics

Evaluation of the aforementioned algorithms is conducted through the lenses of true positives (TP), false positives (FP), and false negatives (FN). In order to determine the output of a binary classifier, the metrics shown in Table 7 must first be defined.

Table.7. Retinal Feature Classification Measures

Measures	Retinal Feature	Non-Retinal Feature
An algorithm for identifying characteristics of the retina	True Positive (TP)	False Positive (FP)
A computational algorithm for identifying non-retinal characteristics	False Negative (FN)	True Negative (TN)

Sensitivity: How many true positives were identified is what this metric tracks.

$$\textbf{Sensitivity(SE)}=\frac{\textbf{TP}}{\textbf{TP+FN}} \tag{4}$$

False Negatives (FN) are the opposite of True Positives (TP).

Specificity: The most crucial element of a diagnosis is categorizing patients who do not have the condition.

$$\textbf{Specificity(SP)}=\frac{\textbf{TN}}{\textbf{FP+TN}} \tag{5}$$

For this purpose, we make use of the terms True Positive (TP) and False Negative (FN).

Accuracy: It's due to a combination of random and deliberate mistakes. Considering how important accuracy is, it follows that its precision should also be quite high. For each image under consideration, it determines how many are truly positive and how many are truly negative.

$$\textbf{Accuracy (Acc)}:\frac{\textbf{TP+TN}}{\textbf{TP+FN+TN+FP}} \tag{7}$$

Positive Predicted Value (PPV): An estimate of how reliable a given pixel's depiction of a detected retinal feature is.

$$\textbf{Positive Predicted Value(PPV)}=\frac{\textbf{TP}}{\textbf{TP+FP}} \tag{8}$$

False Detection Rate (FDR): When there's a good chance that an identified retinal characteristic is false positive.

$$\textbf{False Detection Rate(FDR)}=\frac{\textbf{FP}}{\textbf{TP+FP}} \tag{9}$$

6. Publicly Available Diabetic Retinal Databases

Tables 8--11 describes each database by name and provides a summary of them in a table.

Table.8. Popular datasets for DR diagnosis and lesion segmentation

Name of Dataset	Images Number	Image acquisition	Description
DIARETDB0	130 (110 DR, 20 Normal)	Camera settings for fundus digital cameras with a field of view of 50 degrees are currently unknown.	https://www.it.lut.fi/project/imageret/
DIARETDB1	89 (84 DR, 5 Normal)	The 50-degree viewing angle of both the Nikon F5 digital camera and the ZEISS FF 450 plus fundus camera (FOV).	https://www.it.lut.fi/project/imageret/
Retinopathy Online Challenge	100	The field of vision (FOV) is circular on the Topcon NW 100 and Topcon NW 200, however it is rectangular on the Canon CR5 45NM.	http://webeye.ophth.uiowa.edu/ROC/
Messidor	1200	Color video, 3CCD camera, and a 45-degree field of vision are just some of the features of the Topcon TRC NW6 non-mydriatic retinograph.	http://www.adcis.net/en/third-party/messidor/
Messidor-2	1748	The Topcon TRC NW6 fundus camera offers a 45-degree field of vision and does not employ mydriasis.	https://www.adcis.net/en/third-party/messidor2/
e-ophtha EX	47 with exudates, 35 healthy	-	http://www.adcis.net/en/third-party/e-ophtha/
e-ophtha MA	148 with MA, 233 healthy	-	http://www.adcis.net/en/third-party/e-ophtha/
DeepDR	2256	TOPCON , Optomap P200Tx (Optos, Dunfermline, UK)	https://isbi.deepdr.org/data.html

Table.9. Vessel Segmentation datasets that are used a lot

Name of Dataset	Images Number	Image acquisition	Description
DRIVE	40 (33 healthy, 7 moderate early DR) (33 healthy, 7 mild early DR)	Canon CR5 camera that does not have mydriasis and has a 3CCD sensor with a field of vision of 45 degrees	https://drive.grand-challenge.org/Download/
STARE	A total of 400 (40 labels for vessel segmentation and 10 for A/V)	Fifty of the Best Con TRV Fundus Cameras with a Field of View of 35 degrees	http://cecas.clemson.edu/%20ahoover /stare/
CHASE DB1	28	-	https://blogs.kingston.ac.uk/retinal/chasedb1/
HRF	Among the 45 participants, 15 were classified as healthy, 15 as having DR, and 15 as having glaucoma.	fundus camera Canon CR1 with 45 degree field of view	http://www5.cs.fau.de/research/data/fundus-images/

Table. 10. Popular datasets for glaucoma diagnosis and segmentation in both OD and OC

Name of Dataset	Images Number	Image acquisition	Description
ONHSD	100	Fundus Camera, Canon CR6 45MNf, 45 Field of View	http://www.aldiri.info/Image%20Datasets /ONHSD.aspx
Drishti GS	101	camera able to capture images of the fundus with a field of view of 30 degrees	http://cvit.iiit.ac.in/projects/mip/drishti-gs/mip-dataset2/Home.php
Drions DB	110	a colour analogical fundus camera	https://www.researchgate.net/publication/326460478 _Glaucoma_dataset_-_DRIONS-DB
RIGA	750	various field-of-view (FOV) fundus cameras	https://deepblue.lib.umich.edu/data/ concern/data_sets/3b591905z/
RIM ONE	169	This particular camera is a Nidek AFC 210 fundus camera	Not available online

Table.11. Widely used datasets for A/V classification

Name of Dataset	Images Number	Image acquisition	Description
DRIVE A/V	40 in total (33 healthy, 7 with mild to moderate early DR), 33 healthy, 7 with moderate early DR	Canon CR5 wide-angle camera with a non-mydriatic 3CCD lens and a 45-degree viewing angle	http://reviewdb.lincoln.ac.uk/
HRF A/V	Among the 45 participants, 15 were classified as healthy, 15 as having DR, and 15 as having glaucoma.	fundus camera Canon CR1 with 45 degree field of view	https://github.com/rubenhx/av-segmentation
IOSTAR	30	An Easy Scan camera	http://www.retinacheck.org/datasets

7. Traditional Machine Learning Based Methods

One subfield of artificial intelligence known as "machine learning" (ML) is capable of analyzing data in order to derive conclusions. The techniques presented here can be used to construct truly autonomous systems. Speech recognition, controlling robots, bio surveillance, product recommendations, and computer-aided design are just few of the many fields that have benefited from machine learning (CAD). In the next section, we'll discuss the many machine learning approaches that have been applied to the DR problem in the past. Per Quellec et al. [30]. provided evidence that their CBIR-based discriminant response identification method can be utilized to offer a second view to aid inexperienced graders. In this study, 1176 different types of ocular fundus photographs were used to draw conclusions. Cohen's kappa statistics were used to evaluate the algorithm's accuracy in comparison to that of a human grader with two years of experience. The ground truth was developed by an expert grader with seven years of experience, and it showed far greater consistency with the results of the algorithm.

Table.12. Traditional Methods from the Field of Machine Learning

S.No	Types	Technique	Datasets	Performance Methods
1	Detection of Blood Vessels	options for betterment [5] such as the Tyler Coye algorithmic and the enhanced Hough line transformation	Stare Drive	Absolute sensitivity: 100% Species-level accuracy: 66% Accuracy: 92%
2	Detection of Microaneurysm	Hessian operator for microaneurysm detection utilizing multiple candidate extractors[13]..	DIARETDB1 e-Ophtha HEI-MED MESSIDOR	Accuracy 87.72%, 95.77%, 89.25% 98.36%
		The SVM classifier and the KNN classifier[13].		
		Ensemble based MA detector[31]		
		An assortment of bagged decision tree classifiers[32].		
3	Detection of Hemorrhages	should incorporate techniques such as (CLAHE), Smoothing+ HMBF, SIF+ KNN[33], and Gradient-Based Neural Network[34].	ROC e-Ophtha DRIVE STARE CHASE_DB1	Sensitivity 37.6% 57.3% Accuracy 92.30%
		Multi-layered Feed-Forward Neural Networks trained with feature descriptors.[34]		
		Visual features of potential hemorrhages were extracted using a 2D Gaussian fit[2].		
4	Detection of Macular Edema[35]	Applying Convolutional Neural Networks with Blind Cross Validation Techniques to Detect Age-Related Macular Edema[35]	Kasturba Medical Hospital DIRETDB1	Level of sensitivity: 92.66 % 96.43 % Specificity88.56% 93.75 % Accuracy 91.17% 95.45 %
		Ten-fold cross-validation techniques in a CNN[35].		
5	Detection of Exudates	This includes (SDMM+ Kullback-Leibler kernel), "(SDMM+ Bhattacharyya kernel)," and "(SDMM+ Fisher kernel)". [33]	DRIVE MESSIDOR DIRETDB1	Accuracy 90.87% 91.33%. 100% 100%. 94% 99.18%
		Methods for Detecting Exudates Using Support Vector Machines, Kernel Naive Bayes, and the Random Forest Classifier[17].		
		Through the application of the Circular Hough Transform[17].		
6	Detection of Optic Disc	Histogram Equalization with Multi-Level 2D Wavelets[36]	HRF Messidor DIARETDB0 DIARETDB1 DRIVE STARE Kasturba Medical College	Accuracy 95.61% 99.58% 97.4% 100% 95.7% 92.1%
		Methods for OD localization include those based on histograms and cluster analysis[37].		
		Circularly transforming line operator [38]		
		Snake using Atanassov Intuitionistic Fuzzy Histon (AIFSH), Gradient Vector Flow (GVF), and Otsu[39].		
		Binary vessel masks can be made with VAMPIRE software. [40].	HRIS VDIS	

8. CONCLUSION

This article presents a survey of contemporary approaches and frameworks for diagnosing diabetic retinopathy using machine learning techniques. Diseases associated with DR may be prevented or their progression halted if they are diagnosed and treated promptly once they are first suspected. The objective of this work is to pique the attention of aspiring scientists, researchers, and practitioners in DR detection and classification. This paper lays out the state-of-the-art in identifying diabetic retinopathy, covering topics such as the most widely used databases, performance metrics, DR classification algorithms, and the increasing success of machine and deep learning. To save space, we've provided a brief overview of the various approaches that have come before us, which should help shed light on the various methodologies currently in use and the development of related research. The results of this study demonstrate that deep/machine learning can greatly enhance the automatic identification performance of problems related to diabetic retinopathy throughout the diagnostic procedure.

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