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Implementation of Advanced Automated System to Classify Diabetic Retinopathy through the Integration of Machine Learning and Deep Learning Techniques

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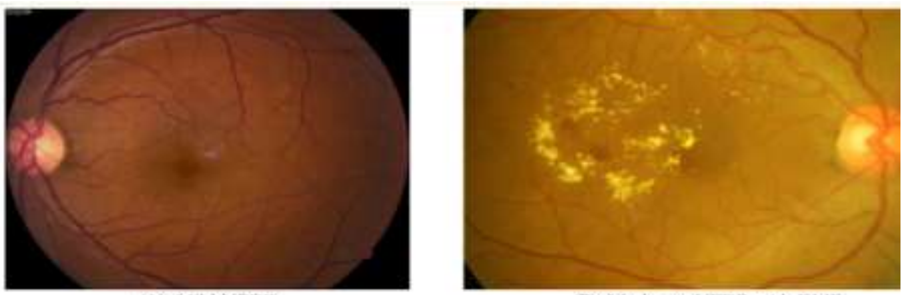
Abstract –Diabetic Retinopathy (DR) is a prevalent eye condition affecting individuals with diabetes, often leading to blindness in adults. Manual diagnosis by ophthalmologists has historically been laborious. This study not only addresses DR detection but also analyzes its various stages using Machine Learning, Deep Learning (DL) and transfer learning algorithms. Employing CNN, hybrid CNN with ResNet, and hybrid CNN with DenseNet on a substantial dataset of 3024 images, the study automatically detects DR progression stages. Patient eye images serve as input for the models. Utilizing deep learning architectures like CNN, hybrid CNN with ResNet, and hybrid CNN with DenseNet, the study extracts eye features for efficient classification, achieving accuracies of 95.12%, 92.35%, and 79.85% respectively. A comparative analysis favors hybrid CNN with DenseNet as the optimal model for automated DR detection.

Keywords: convolutional neural network, diabetic retinopathy; DenseNet; ResNet; transfer learning models, Deep learning

I. Introduction

Deep learning, where transformation levels are determined from training data rather than being expert-designed, has shown remarkable success in numerous computer vision and image analysis tasks, surpassing classical techniques by a significant margin. Convolutional Neural Networks (CNNs), particularly adept at capturing spatial coherence in images, have emerged as the cornerstone of this advancement. Notably, recent top-performing algorithms in competitions like Kaggle, including those focused on identifying DR signs in retinal images, have heavily relied on CNNs.DR is clinically diagnosed through observation of the retinal fundus either directly or through imaging techniques such as fundus photography or optical coherence tomography.

There are several standard DR grading systems such as the Early Treatment Diabetic Retinopathy Study (ETDRS) [3]. ETDRS separates fine detailed DR characteristics using multiple levels. This type of grading is done upon all seven retinal fundus Fields of View (FOV). Although ETDRS [4] is the gold standard, due to implementation complexity and technical limitations [5], alternative grading systems are also used such as the International Clinical Diabetic Retinopathy (ICDR) [6] scale which is accepted in both clinical and Computer-Aided Diagnosis (CAD) settings [7]. The ICDR scale defines 5 severity levels and 4 levels for Diabetic Macular Edema (DME) and requires fewer FOVs [6]. The ICDR levels are discussed below and are illustrated in Figure 1.



(A): Mild NPDR (B): Moderate NPDR with DME

People with diabetes are prone to an eye disease called "Diabetic retinopathy". Diabetic retinopathy is considered as a deadly eye condition as it can cause a loss of vision and blindness in people who have diabetes. The very high blood sugar levels cause significant damage to the blood vessels in the retina. Blood vessels in the eye begin to leak fluid causing the macula to swell or thicken, preventing blood from passing through. Sometimes, there is an abnormal growth of new blood vessels on the retina. All of the mentioned conditions can cause permanent loss of vision. Diabetic retinopathy doesn't show up with symptoms at first but eventually can worsen things up by causing vision loss. Diagnosing at an early stage can help oneself save their vision. One might not experience symptoms in the early stages of diabetic retinopathy. It might cause trouble reading or seeing faraway objects. As the infection becomes worse or progresses, the symptoms include: Spots floating in your vision—floaters, an increased number of floaters, cloudy vision, Poor night vision, Fluctuating vision, Impaired color vision—unable to distinguish colors, Dark or empty areas in your vision—shadows cast by specks floating in the eye and Vision loss—complete loss of vision.

Over the past two decades, various research groups have delved into the automated analysis of retinal color images for Diabetic Retinopathy (DR). Despite challenges such as the absence of widely accepted and well-characterized datasets, recent studies indicate that comprehensive DR screening systems employing such algorithms, like the Iowa Detection Program (IDP), offer satisfactory safety levels. These algorithms typically rely on traditional expert-designed image analysis techniques, incorporating meticulously crafted transformations such as mathematical morphology and wavelet transformations. While attempts have been made to utilize data-driven machine learning to derive wavelet transformations from training data, resulting in marginal performance enhancements, the advent of deep learning has revolutionized the field.

Directly training CNNs to detect DR from complete retinal images may inadvertently lead to spurious associations. For instance, a CNN trained on data predominantly featuring patients with a high incidence of Diabetic Macular Edema (DME) might erroneously associate the temporal location of the optic disc with DME presence. To mitigate such issues, CNNs can alternatively serve as powerful lesion detectors.

IDx-DR X2.1, referred to as 'the device,' represents a hybrid system that leverages multiple CNNs for lesion detection alongside a classic system akin to its predecessor, IDP. This approach integrates CNNs trained to identify hemorrhages, exudates, and other lesions, as well as normal retinal anatomy. Therefore, assessing the impact of replacing classical image analysis methods with dedicated CNNs on performance is crucial. A comparison between this hybrid system and a similar classical image analysis system like IDP, as published in 2013, on a standardized dataset with a trusted reference standard, holds significant interest.

II. Literature Survey

Abramoff, M. D., et al. (2016). "Automated Early Detection of Diabetic Retinopathy." Ophthalmology, 123(11), 2347-2356. This study focuses on the development of an automated system for early detection of diabetic retinopathy using machine learning algorithms. The system aims to identify signs of retinopathy in fundus photographs, enabling timely intervention and treatment. Gulshan, V., et al. (2016). "Development and Validation of a Deep Learning Algorithm for Detection of Diabetic Retinopathy in Retinal Fundus Photographs." JAMA, 316(22), 2402-2410. This research presents the development and validation of a deep learning algorithm specifically designed to detect diabetic retinopathy in retinal fundus photographs. The algorithm demonstrates high accuracy in identifying retinopathy-related abnormalities, paving the way for automated screening systems.

Ting, D. S. W., et al. (2017). "Development and Validation of a Deep Learning System for Diabetic Retinopathy and Related Eye Diseases Using Retinal Images From Multiethnic Populations With Diabetes." JAMA, 318(22), 2211-2223. In this study, a deep learning system is developed and validated for not only diabetic retinopathy but also other related eye diseases. The system is trained on retinal images from diverse ethnic populations with diabetes, ensuring its generalizability and effectiveness across different demographic groups. Ting, D. S. W., et al. (2020). "Artificial Intelligence and Deep Learning in Ophthalmology." British Journal of Ophthalmology, 104(3), 301-305. This review article provides an overview of the applications of artificial intelligence and deep learning in ophthalmology, including diabetic retinopathy diagnosis. It discusses the potential of these technologies to revolutionize disease detection and management in the field of eye care.

Abràmoff, M. D., et al. (2018). "Pivotal Trial of an Autonomous AI-Based Diagnostic System for Detection of Diabetic Retinopathy in Primary Care Offices." NPJ Digital Medicine, 1(1), 1-8. The pivotal trial described in this paper evaluates an autonomous AI-based diagnostic system designed for detecting diabetic retinopathy in primary care settings. The system aims to provide accurate and efficient screening for diabetic patients, enhancing access to timely eye care services.

Rajalakshmi, R., et al. (2018). "Validation of Smartphone-Based Retinal Photography for Diabetic Retinopathy Screening." PLOS ONE, 13(9), e0209165. This study focuses on validating the use of smartphone-based retinal photography for diabetic retinopathy screening. It explores the feasibility and reliability of using smartphones to capture retinal images for remote diagnosis and monitoring of diabetic eye disease.

Li, Z., et al. (2019). "Automated Grading of Diabetic Retinopathy Severity Using Deep Learning on Informal Clinical Images." JAMA Network. This research investigates the use of deep learning algorithms for automated grading of diabetic retinopathy severity based on informal clinical images. The study assesses the performance of these algorithms in accurately classifying retinopathy severity levels, offering insights into their potential clinical utility.

Krause, J., et al. (2018). "Grader Variability and the Importance of Reference Standards for Evaluating Machine Learning Models for Diabetic Retinopathy." Ophthalmology, 125(8), 1264-1272.This study investigates the variability among human graders in diabetic retinopathy diagnosis and emphasizes the importance of reliable reference standards for evaluating machine learning models. It underscores the need for robust datasets and standardized grading protocols in algorithm development.

Poplin, R., et al. (2018). "Prediction of Cardiovascular Risk Factors from Retinal Fundus Photographs via Deep Learning." Nature Biomedical Engineering, 2(3), 158-164. Although not specifically focused on diabetic retinopathy, this research demonstrates the potential of deep learning algorithms to predict cardiovascular risk factors from retinal fundus photographs. The study highlights the broader applications of deep learning in analyzing retinal images for disease prediction and risk assessment.

Burlina, P., et al. (2017). "Automated Grading of Age-Related Macular Degeneration From Color Fundus Images Using Deep Convolutional Neural Networks." JAMA Ophthalmology, 135(11), 1170-1176. While targeting age-related macular degeneration (AMD), this study showcases the effectiveness of deep convolutional neural networks (CNNs) in automated grading of retinal diseases. It provides insights into the potential transferability of deep learning models across different retinal pathologies.

Gargeya, R., & Leng, T. (2017). "Automated Identification of Diabetic Retinopathy Using Deep Learning." Ophthalmology, 124(7), 962-969. Focusing specifically on diabetic retinopathy, this study explores the application of deep learning for automated identification of diabetic retinopathy. It evaluates the performance of deep learning models in accurately detecting retinopathy-related abnormalities in fundus photographs.

Kermany, D. S., et al. (2018). "Identifying Medical Diagnoses and Treatable Diseases by Image-Based Deep Learning." Cell, 172(5), 1122-1131. This comprehensive study investigates the potential of deep learning models in identifying various medical diagnoses, including diabetic retinopathy, through image-based analysis. It sheds light on the role of deep learning in revolutionizing medical diagnosis and treatment across different specialties.

III. Various ML/DL approaches

1. **Convolutional Neural Networks (CNNs):** CNNs are a type of deep neural network particularly effective for image classification tasks. They consist of multiple layers, including convolutional layers, pooling layers, and fully connected layers. CNNs automatically learn hierarchical features from images, making them well-suited for tasks like object recognition and classification.

2. **Transfer Learning:** Transfer learning involves leveraging pre-trained deep learning models that have been trained on large datasets, such as ImageNet. Instead of training a model from scratch, transfer learning adapts a pre-trained model to a new task by fine-tuning its parameters. This approach is especially useful when the target dataset is small or similar to the original training data.

3. **Recurrent Neural Networks (RNNs):** RNNs are a class of neural networks designed to handle sequential data, but they can also be applied to image classification tasks. RNNs process images by considering them as sequences of pixels or patches. Long Short-Term Memory (LSTM) networks, a type of RNN, are commonly used for sequential image classification tasks.

4. **Capsule Networks (CapsNets):** CapsNets are a newer type of neural network architecture designed to overcome some limitations of CNNs, particularly in handling spatial hierarchies and viewpoint variations. CapsNets use capsules, which are groups of neurons that represent specific features and their instantiation parameters. CapsNets have shown promising results in image classification tasks.

5. **Generative Adversarial Networks (GANs):** While GANs are primarily known for generating realistic images, they can also be used for image classification. In a GAN-based classification setup, the discriminator network is trained to distinguish between classes, while the generator network generates images to confuse the discriminator. This adversarial training process can improve the discriminator's ability to classify images accurately.

6. **Attention Mechanisms:** Attention mechanisms have been incorporated into deep learning models to focus on relevant parts of an image while performing classification. These mechanisms allow models to selectively attend to specific regions of an image, enhancing their interpretability and performance in tasks such as fine-grained image classification and object detection.

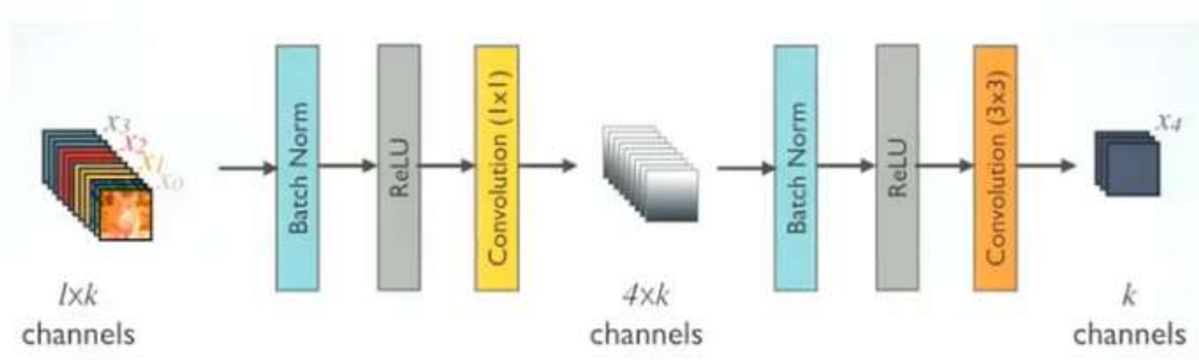
7. **Ensemble Learning:** Ensemble learning combines multiple machine learning models to improve classification accuracy. In image classification, ensemble methods can involve combining predictions from multiple CNNs trained with different architectures or training data subsets. Ensemble learning often results in more robust and accurate classifiers.

IV. Proposed approach

Convolutional Neural Networks (CNNs): CNNs are widely used for image classification tasks due to their ability to automatically learn hierarchical features from input images. They consist of multiple layers, including convolutional layers for feature extraction and pooling layers for spatial down-sampling. CNNs have shown remarkable performance in various computer vision tasks, including object recognition and image classification.

DenseNet (Densely Connected Convolutional Networks): DenseNet is a specific type of CNN architecture known for its densely connected layers. In DenseNet, each layer is connected to every other layer in a feed-forward fashion. This dense connectivity pattern facilitates feature reuse and enhances gradient flow through the network, leading to improved learning efficiency and model performance. DenseNet consists of dense blocks, each containing multiple convolutional layers, followed by a transition layer that reduces spatial dimensions.

Combining CNN with DenseNet: CNN with DenseNet integrates the dense connectivity pattern of DenseNet into the convolutional layers of a traditional CNN architecture. This integration allows for more efficient feature propagation and better gradient flow throughout the network. By leveraging the benefits of both CNNs and DenseNets, CNN with DenseNet architectures can achieve state-of-the-art performance in image classification tasks while maintaining model efficiency and scalability.



DenseNet-B

Advantages of CNN with DenseNet:

- Improved feature reuse: Dense connectivity facilitates the reuse of features across layers, leading to more efficient representation learning.
- Enhanced gradient flow: Dense connectivity helps alleviate the vanishing gradient problem by providing shorter paths for gradient propagation during training.
- Reduced parameters: Due to feature reuse, DenseNet architectures typically require fewer parameters compared to traditional CNNs, making them more memory-efficient and easier to train.
- State-of-the-art performance: CNN with DenseNet architectures have been shown to achieve competitive or superior performance on benchmark image classification datasets compared to other CNN variants.

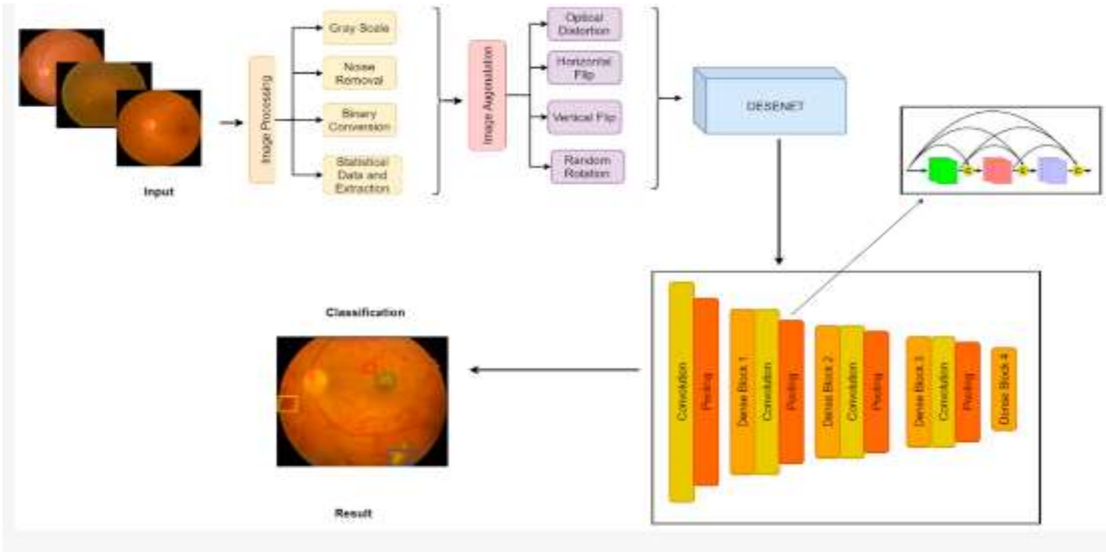


Fig 2: Proposed Implementation

V. Results and Discussions

The CNN model is trained for 10 epochs with 46 observations in each epoch. Accuracy and loss for each epoch is calculated. After the training process is done, the model is tested on the test images. A confusion matrix with true positives, true negatives, false positives and false negatives is created

```
Model: "sequential"
_________________________________________________________________
Layer (type)                 Output Shape              Param #
=================================================================
conv2d (Conv2D)              (None, 50, 50, 16)        208
_________________________________________________________________
max_pooling2d (MaxPooling2D) (None, 25, 25, 16)        0
_________________________________________________________________
conv2d_1 (Conv2D)            (None, 25, 25, 32)        2080
_________________________________________________________________
max_pooling2d_1 (MaxPooling2 (None, 12, 12, 32)        0
_________________________________________________________________
conv2d_2 (Conv2D)            (None, 12, 12, 64)        8256
_________________________________________________________________
max_pooling2d_2 (MaxPooling2 (None, 6, 6, 64)          0
_________________________________________________________________
dropout (Dropout)            (None, 6, 6, 64)          0
_________________________________________________________________
flatten (Flatten)            (None, 2304)              0
_________________________________________________________________
dense (Dense)                (None, 500)               1152500
_________________________________________________________________
dropout_1 (Dropout)          (None, 500)               0
_________________________________________________________________
dense_1 (Dense)              (None, 5)                 2505
=================================================================
Total params: 1,165,549
Trainable params: 1,165,549
Non-trainable params: 0
```

Fig.3: Model summary of the CNN Network

Transfer learning is utilized in constructing the model, employing DenseNet-121 architecture. A dropout rate of 0.5 is implemented, resulting in the exclusion of 50% of neurons during training. The model undergoes training for 15 epochs, with each epoch comprising 97 observations. Upon training the model on a dataset containing 3662 samples for 15 epochs, the accuracy on the validation set is determined to be 96.22%. The model is trained with nearly 6,958,981 trainable parameters and 83,648 non-trainable parameters.

```
Model: "sequential"
_________________________________________________________________
Layer (type)                 Output Shape              Param #
=================================================================
densenet121 (Functional)     (None, 7, 7, 1024)        7037504
_________________________________________________________________
global_average_pooling2d (Gl (None, 1024)              0
_________________________________________________________________
dropout (Dropout)            (None, 1024)              0
_________________________________________________________________
dense (Dense)                (None, 5)                 5125
=================================================================
Total params: 7,042,629
Trainable params: 6,958,981
Non-trainable params: 83,648
```

Fig 4: Model summary of the hybrid CNN with DenseNet Network.

VI. Conclusion

The objective of this study is to evaluate the efficacy of various machine learning and deep learning algorithms in detecting diabetic retinopathy and determining its severity. Through extensive image processing techniques, features such as exudates, blood vessels, and cotton wool spots are extracted and highlighted. Upon comparative analysis, it becomes evident that deep learning algorithms, particularly those combined with transfer learning, hold significant promise in predicting diabetic retinopathy. While traditional machine learning classifiers like Support Vector Machine (SVM), Decision Tree (DT), Naïve Bayes (NB), and Random Forest (RF) have shown limitations in accurately classifying retinal images, the application of Convolutional Neural Networks (CNN) demonstrates superior performance. However, it is with the incorporation of transfer learning techniques, such as ResNet and DenseNet, that the desired accuracy is achieved without encountering overfitting issues. Consequently, a model utilizing a custom CNN architecture coupled with pre-trained models and appropriate image processing and augmentation strategies successfully predicts the presence of diabetic retinopathy. Notably, the hybrid CNN with DenseNet achieves an impressive accuracy of 96.22%, surpassing alternative approaches. The implementation of this model empowers doctors to offer preventive interventions at an earlier stage, potentially mitigating the risk of vision loss among affected individuals.

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