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CONVOLUTION NEURAL NETWORKS FOR DISEASE PREDICTION: APPLICATIONS AND CHALLENGES

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Abstract. More people are using Deep Learning techniques in the healthcare field as a result of the quick development in domains like Computer Vision, Graphics Processing Technology, and the accessibility of medical imaging datasets. Convolutional Neural Networks (CNNs), in particular, have quickly emerged as the preferred technique for processing clinical data. CNN-based designs have been embraced by the diagnostic imaging group to assist physicians with disease identification. Since AlexNet's enormous success in 2012, CNNs have indeed been employed more and more in the analysis of medical images to boost the effectiveness of physicians. This article summarises various CNN architectures for predicting medical diseases and their challenges. We examine the utilization of Deep Learning for the prediction of various diseases, including Brain diseases, Diabetic Retinopathy, and Lung cancer. This research also provides a survey of datasets available for analysis.

Keywords: Convolutional Neural Networks (CNNs), AlexNet, ResNet, Brain diseases, Diabetic Retinopathy, Lung disease, Alzheimer Disease

1. Introduction. Human lives are impacted by health complications. When a patient is receiving medical care, healthcare professionals gather clinical evidence about that individual and use information about the general community to decide how to treat that individual. Therefore, data is key to solving health problems, and better information is essential for enhancing clinical outcomes. Medical imaging is a crucial part of modern medicine. Because it allows for detailed exploration inside the human body in a non-invasive fashion. Deep Learning has reported promising results in medical image analysis. The major reason behind this is the advent of deep Convolutional Neural Networks (CNNs).

Huge phenotyping from observational data [78], autism subtyping [21] by clustering comorbidity, lymph node metastases from breast pathology [34], and the diagnosis of Diabetic Retinopathy [35] are just a few instances of the work being carried out in Deep Learning for healthcare. Deep Learning problems well adapted for healthcare [26], the requirement for visibility [115], also utilizing big data for targeted therapy [8] have been the focus of previous studies of deep learning in the medical field, that have focused entirely on biological applications [7]. In this paper, we review various CNN architectures and their application in disease prediction. Figure 1.1 explains the structure of the study.

The key contributions of this study are as follows:
- The study provides a thorough description of the different CNN architectures. Moreover, their complexity and challenges are also presented.
- The study reviews the literature pertaining to Diabetes diagnosis using CNN. Moreover, the literature on diagnosis of Diabetic Retinopathy using CNN is also reviewed.
- The study reviews the literature pertaining to diagnosis of brain diseases like Alzheimer's disease and Parkinson's disease using CNN.
- The study also presents a review on the diagnosis of lung cancer using CNN.

Image Analysis and Artificial Intelligence. Artificial Intelligence (AI) is not a novel idea. Renowned intellectuals like Leonardo Da Vinci [124] attempted to build automata that mimicked human actions. These days, it appears that this is already the case. Though there are many self-adjusting intelligent systems already, AI has grown exponentially, particularly in the field of health informatics [84]. AI in healthcare is indeed a rapidly expanding discipline that inspires enthusiasm and raises baffling concerns. AI is the capability of a machine to simulate biological mental capabilities. The term "AI" refers to a wide variety of technologies. One of the

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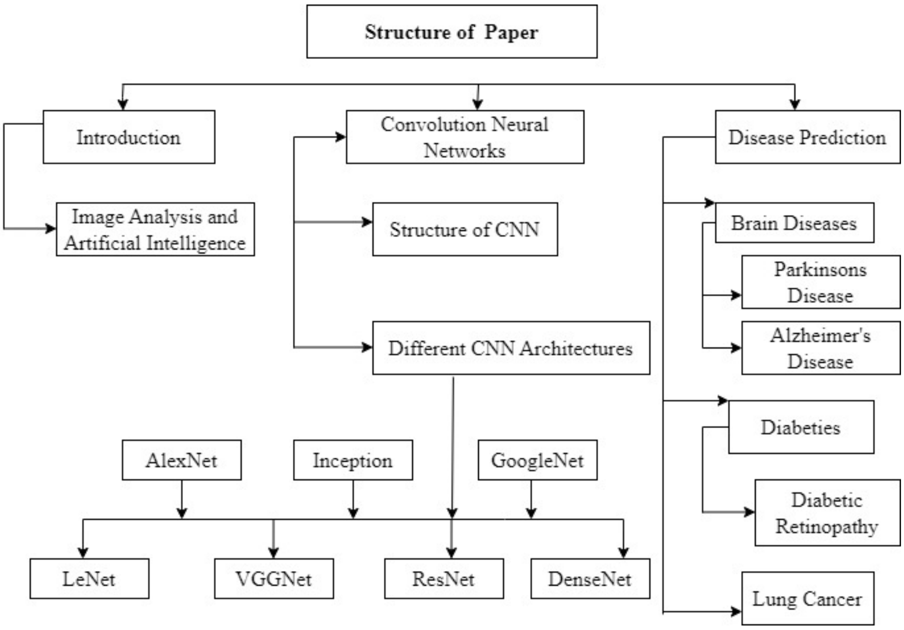

Fig. 1.1: Organizing and Visualizing Map of the Survey

most widely applicable methods in healthcare professionals among them is Machine Learning. Its techniques in medicine have been made possible by three overlapping technological advancements:

a) The emergence of ”big data” worldwide and analysis of exceedingly massive databases.
b) The extraordinary rise in CPU computational capabilities.
c) The invention of novel Deep Learning methods.

One of the most well-established sub-fields in Computer Engineering, Deep Learning, has improved performance in many areas, particularly in the analysis and categorization of pathological images. The revolutionary change towards Deep Learning systems, which most researchers find appealing due to the effectiveness and ”clarity” of the present models, is predominantly to blame for the expanding innovations. In practice, it is sufficient to think of Deep Learning systems as a black box toward which we supply data for input and output as a baseline for the intended training in most implementations (supervised learning) [95]. CNN, one of the Deep Learning techniques has latterly been proven to be an assuring approach in biomedical image analysis.

2. Convolutional Neural Network. The sub-field of the Machine Learning described as Deep Learning is focused on Artificial Neural Networks, a group of methods that are based on the composition and function of the brain. It is typically a neural network with three or more layers and belongs to the Machine Learning category. These Artificial Neural Networks attempt to replicate how the human brain functions but fall far short, allowing it to understand using enormous amounts of data. Various metrics could provide a response to the question, why Deep Learning? These are:

Commitment to Global Learning: Deep Learning is widely termed ubiquitous learning since it can function in nearly all application fields.

Robustness: In general, Deep Learning approaches do not need carefully planned features. However, the optimum attributes are automatically learned in connection with the task under consideration. However, robustness to the source data’s typical variations is gained.

Generalization: Different applications or types of data can employ the same Deep Learning method, known as transfer learning. Additionally, it is a beneficial method for issues in which the data is insufficient.

Scalability: Deep Learning is very extensible. ResNet [39], created by Microsoft, has 1202 levels and therefore is extensively used in high-performance computing environments. Deep Learning consists of a number

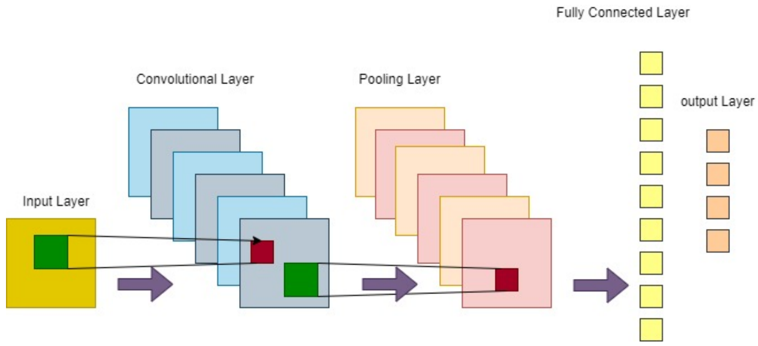

Fig. 2.1: Components of a CNN [69]

of architectures. These include; CNNs, Recurrent Neural Networks, Long-Short Term Memory (LSTM), Auto-Encoders (AEs), and Deep Belief Networks [88]. CNNs are one of the most widely used Deep Learning architectures [89]. Medical Images are one of the areas of Image Processing, where CNN, a subclass of Artificial Neural Networks [123] has gained leadership.

To handle data with a grid pattern, such as images, CNN is a Deep Learning model that is based on the structure of the animal visual cortex [47]. CNN is intended to be dynamic and is able to acquire spatial hierarchies of characteristics, from low-level to high-level structures. CNN for Deep Learning is well-liked for three key reasons:

a) CNNs do not require feature extraction manually because they understand the characteristics independently.
b) Outcomes from CNNs for identification are extremely precise.
c) It can be expanded on pre-existing networks by using CNNs that can be retrained for new recognition tasks.

CNNs are meant to automatically analyze and are able to adapt and learn spatial feature hierarchy by training algorithms that employ a wide range of construction blocks, such as pooling, convolution, and fully connected layers. The extraordinary outcomes have been disclosed in the object recognition contest considered as the ImageNet's Large Scale Visual Recognition Competition (ILSVRC) in 2012 [87], which is the most founded methodology among diverse Deep Learning Models. In several subjects, including medical technology, CNN has performed at an extremely high level. Deep Learning the prospect for diagnosing lymph node metastases, straining for diabetic retinopathy, and categorizing skin lesions, was founded by Gulshan et al. [35], Ehteshami Bejnordi et al. [9], and Esteva et al. [25] correspondingly. Knowing such cutting-edge approaches will benefit clinical radiologists as well as academics, which use CNN for their jobs in radiology and medical imaging as Deep Learning could soon impact clinical practice.

2.1. Structure of CNN. Comparable to a standard Neural Net, there are three layers in the CNN: input, hidden, and output. The distinction is that the image intake for CNN is the pixel matrix, and the image feature attained by the convolution estimation is the output [95]. The convolution kernel, from which the phrase "Convolution Neural Network" emanates, is the most crucial segment of CNN. Each pixel in the two-dimensional matrix n x n of the Convolution Kernel has a proportional weight. A CNN is a specific type of Artificial Neural Network with very few associations between the layers that strive to keep spatial relationships within the data. Every layer function in a CNN, on a small area of the preceding layer, with the input organized in a grid structure and handed through layers that preserve those relationships. CNNs are competent in creating a highly effective model for input data, making them intent for jobs involving images. A CNN is trained via backpropagation and gradient descent, just like classic Artificial Neural Networks. Figure 2.1 explains the layers of a CNN. These are:

a) Convolutional layers. The activations from the preceding layer are connected in the convolutional layers with several small parameterized filters, normally of size 3x3, and then kept in a tensor called W(J, I), where the filter number is represented by J and the layer number is represented by I. One drastically reduces the number of weights that need to be understood, i.e. translational equivariance at each layer.

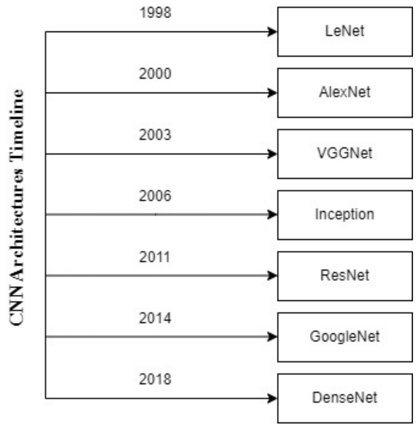

Fig. 3.1: CNN Timeline

This weight-sharing is necessary because characteristics that occur in one portion of the image will probably also occur in other areas. If a filter is competent in glimpsing horizontal lines, then it can detect them wherever they occur. A tensor feature map is generated after filters are applied at every input point in a convolution layer.

b) Activation layer. Nonlinear activation functions generate the feature maps from a convolutional layer. It enables nearly every nonlinear function to be approximately replicated by the neural network as a whole [62]. The extremely basic sigmoid, tanh rectified linear units or ReLUs, and its variations such as leaky ReLUs or parameterized ReLUs, are often the activation functions [38]. When the feature maps are fed through an activation function, new tensors—often also referred to as feature maps—are generated.

c) Pooling layer. CNNs use the pooling technique to generalize the features that the convolution filters have extracted, allowing the network to identify features regardless of where they are in the image. Small grid areas are indeed the input for pooling operations, which further yield single integers for every area. The max-pooling or average-pooling are commonly used to calculate the number. Utilizing convolutions having longer strides is another method for obtaining the pooling's downsampling impact. The network architecture can be clarified by eliminating the pooling layer without compromising production [101].

3. Different CNN Architectures. Different CNN architectures have already been presented over the past ten years [98]. A crucial component in improving the efficiency of many applications is model design. Since 1989 to the present, CNN's architecture has gone through a number of changes. These changes comprise regularisation, optimization techniques, and structural restructuring. On the other hand, it needs to be emphasized that major improvement in CNN effectiveness, is primarily the result of the rearrangement of the processing elements and the introduction of new blocks. The use of network depth was among the most innovative breakthroughs in CNN. Figure 3.1 gives the timeline of various CNN architectures.

3.1. LeNet. One of the inaugural CNNs, LeNet-5, contributed to the evolution of Deep Learning. In the year 1998 paper, "Gradient-Based Learning applied to Document Recognition," [61] introduced LeNet. For the image classification process from the MNIST dataset, they used LeNet-5 CNN. They were the first to use the backpropagation technique in real-world settings and thought that introducing limitations from the task's domain would significantly improve the capacity to learn complexity. The LeNet-5 CNN model has seven layers. This model's uncomplicated structure was the primary factor in its success.

Architecture of LeNet. The network is referred to as Lenet-5 because it comprises 5 layers with learnable parameters. It has 3 pairs of Convolutional Layers with an average pooling mixture. So have two fully connected layers succeeding the convolution and average pooling layers. Finally, a Softmax predictor arranges the images in the appropriate class. Figure 3.2 explains the architecture of Lenet.

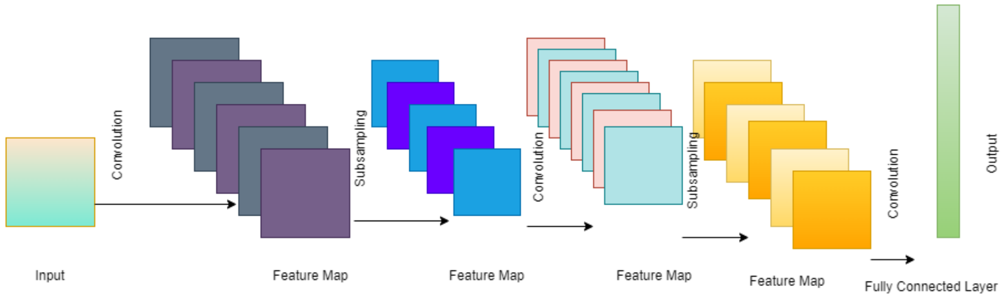

Fig. 3.2: Architecture of LeNet [61]

Complexity and challenges. This network is quite easy to grasp and served as a fantastic foundation for the field of neural networks. With character recognition images, it performs effectively. The system suffers to scan for all properties because it isn't very deep, resulting in simulations that perform poorly. It would be challenging for the neural network model to adapt and generate a precise model if it wasn't provided with just enough characteristics from the training images.

3.2. AlexNet. A model as sophisticated as AlexNet is able to produce high precision on very difficult datasets. But taking out any of the convolutional layers will severely damage AlexNet's effectiveness. It is a well-known architecture for almost any object-detection task, and it may have numerous applications in the computer vision field of artificial intelligence problems. LeNet's [5] debut signalled the beginning of deep CNNs. Those CNNs could only be used for recognition of handwritten digits tasks, which are not easily scalable to all image classes. AlexNet is well-regarded in deep Network architectures [56] because it produced ground-breaking achievements in the areas of image recognition and classification. AlexNet was first introduced by Krizhevesky et al.[56], who then increased CNN's learning capacity by deepening it and adding a number of variable optimization algorithms. The technique developed by Krizhevesky et al. periodically runs across a number of structural units during the development phase to ensure that the features the algorithm learned are extra resilient. ReLU [120] could also be used as a non-saturating activation function to speed up converge [43] by lessening the gradient vanishing problem.

Architecture of AlexNet. The very first CNN to employ a GPU to optimize effectiveness was AlexNet. Five convolutional layers, three max-pooling layers, two normalization layers, two fully connected layers, and one softmax layer make up its architecture. Convolutional filters and then a nonlinear activation function called ReLU make up every convolutional layer. The pooling layers are used to carry execute Max Pooling. Due to the presence of fully connected layers, the intake size is set. The intake dimension is typically stated as 224x224x3, however, because of padding, it actually comes out to be 227x227x3. There are 60 million elements in AlexNet in total. Figure 3.3 explains the architecture of AlexNet.

Complexity And Challenges. A system as sophisticated as AlexNet is able to achieve highly accurate on really difficult datasets. But taking out any of the convolutional layers will negatively affect AlexNet's efficiency. For any object-detection operation, AlexNet is a prominent design, and it has numerous uses inside the field of computer vision of machine intelligence challenges. AlexNet may also be credited with introducing Deep Learning to related domains like Language processing and analysis of medical images as just a significant step toward rendering it more broadly usable.

3.3. VGGNet. Visual Geometry Group (VGG) is a complex CNN architecture that is typical and contains numerous layers. In 2014, scientists from the University of Oxford, Karen Simonyan and Andrew Zisserman, presented the VGGNet framework for CNNs [100]. The term "deep" refers to the number of layers, with VGG-16 or VGG-19 having 16 and 19 neural network layers, respectively. VGG architecture operates as the footing for innovative visual recognition techniques. The VGGNet, designed as a deep neural network, outperforms benchmarks on many tasks and databases outside ImageNet. It also remains among the most often used computer vision architectures today.

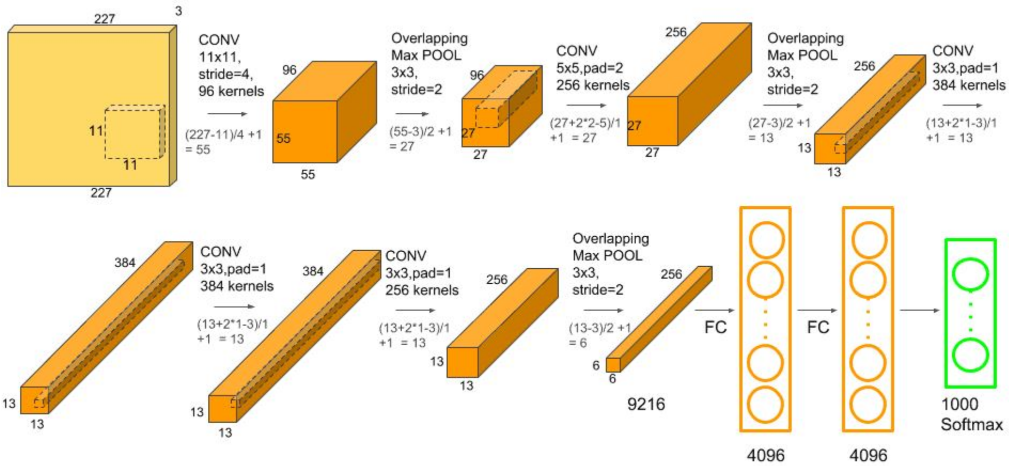

Fig. 3.3: Architecture of AlexNet [56]

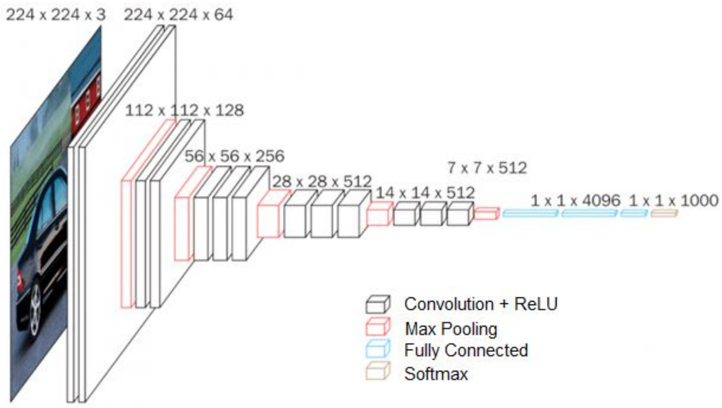

Fig. 3.4: Architecture of VGGNet [100]

Architecture of VGGNet. VGG's input is configured to an RGB image with a 224x244 resolution. The training set image's mean RGB values are determined, and the image is then used as an input to the VGGNet. The convolution phase is fixed, as well as 3x3 or 1x1 filters are employed. There are 3 completely connected layers and the number of convolutional layers plus fully connected layers determines their value, which ranges from VGG11 to VGG19. The minimum standard VGG11 consists of 3 fully connected layers and 8 convolutional layers. There are 16 convolutional layers in the maximal VGG19 plus three fully connected layers. The VGGNet also does not have a pooling layer following every convolution layer, a number of 5 pooling layers, spread behind convolutional layers. Figure 3.4 depicts the architecture of VGGNet.

Complexity and challenges. With each level of the convolution layer, the quantity of filters doubles. This fundamental idea underlies the architecture of VGG16. The VGG16 model is greater than 533MB due to its depth and quantity of completely connected layers. Because of this, building a VGGNet is a gradual task. Many Deep Learning image classification issues use the VGG16 model, however, simpler network topologies like GoogleNet and SqueezeNet are frequently chosen. In either case, the VGGNet is a wonderful basic foundation

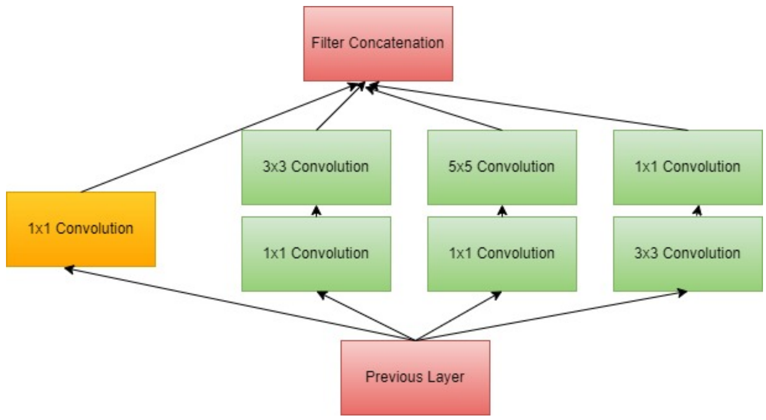

Fig. 3.5: Architecture of Inception Module [108]

for educational reasons since it is simple to set up.

3.4. Inception Network. A CNN with an organizational layout made up of repetitive elements known as Inception modules [108] is considered an inception network. Convolutional layers are enclosed within modules or blocks that are stacked as opposed to stacking convolutional layers themselves.

Architecture of Inception Network. Figure 3.5 depicts the architecture of the Inception module. It uses parallel processing and extracts the features concurrently. This is the prime characteristic of the Inception network that differs it from other CNN architectures. Figure 3.5 depicts that the Inception module simultaneously performs convolution operations of different sizes and then concatenates the outputs from all the operations and creates the next feature.

Complexity and Challenges. It is having the capacity to use different convolution filter sizes and extract features from input data at different scales. In order to improve the network's overall ability to extract features, 1x1 conv filters learn cross-channel patterns. And has effective utilization of computational resources with little rise in workload for an Inception network's outstanding performance output. Once the Inception section is split into its constituent parts, it is simple to break down and comprehend. The issue of overfitting, which happens when the quantity of input features is high throughout training, will be increasingly prevalent as our model grows in size (more layers). The total amount of layers will expand along with the number of variables, thus must also prepare to beef up our processing resources before we can execute the computation on these parameters. Therefore employing an Inception network will reduce computing costs while simultaneously expanding the width and depth of the system, instead of expanding the computing resource.

3.5. ResNet. ResNet (Residual Network), the ILSVRC 2015 winner, was created by He et al. [39]. In contrast to earlier systems, the goal was to create an ultra-deep network immune to the vanishing gradient problem.

Architecture of ResNet. The network employs a VGG19-inspired 34-layer plain network topology, to which the bypass link is introduced. The structure is subsequently changed into a residual network by these short-cut links. Figure 3.6 explains the architecture of ResNet. ResNet-34 was the initial ResNet architecture, and it included inserting shortcut interconnections to transform a simple net into an equivalent residual network [39]. In this instance, the CNN included 33 filters, whilst the simple network was influenced by VGGNets (VGG16, VGG19). ResNets, though, are simpler and require fewer filters than VGGNets.

Complexity and Challenges. ResNet is a significant advancement that altered the process of learning deep CNNs for tasks involving computer vision. Whereas the initial ResNet had 34 layers and 2-layer restriction blocks, more sophisticated models, such the Resnet50, used 3-layer restriction blocks to assure high efficiency and shorter training durations.

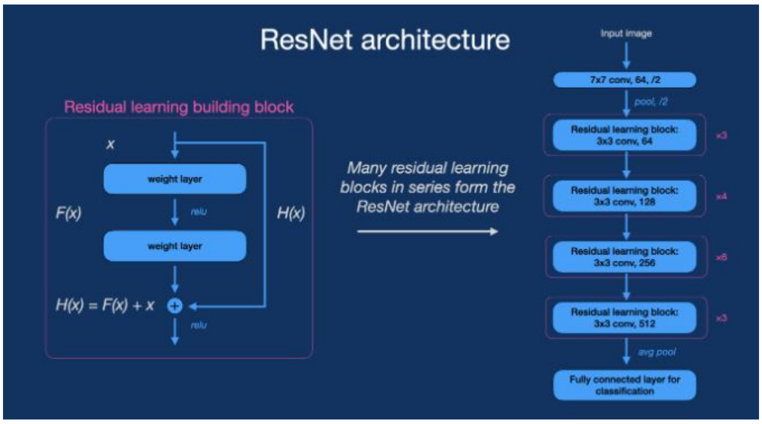

Fig. 3.6: Architecture of ResNet [11]

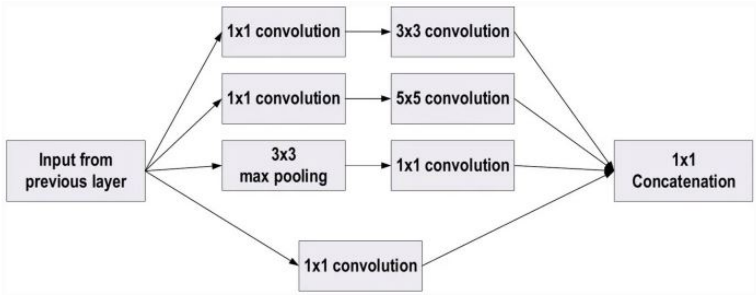

Fig. 3.7: Architecture of Googlenet Module [108]

3.6. GoogleNet. The winning entry in the 2014-ILSVRC competition was GoogleNet, also known as Inception-V1 [108]. The primary goal of the GoogleNet design is to achieve top-level precision with reduced processing expense. Since it combines multiple-scale convolutional transformations by using merging, modification, and splitter algorithms for extracting features, it suggested a new inception block (module) idea in the framework of CNN. In comparison to previous winners AlexNet (Winner of ILSVRC 2012) and ZF-Net (Winner of ILSVRC 2013), with a significantly lower error rate over VGGNet, it really has delivered a marked decline in the failure rate (2014 runner-up).

Architecture of GoogleNet. Figure 3.7 shows how the inception component architecture is organized. This design requires filters of various sizes including 5×5, 3×3, and 1×1 to record channel information as well as spatial information at various spatial levels of resolution. Small modules that implement the very same idea of Network-in-Network (NIN) architectures [65], that substituted every level with a micro-neural network, are used to substitute the common convolutional layer of GoogleNet.The GoogLeNet merge, transform, and split principles have been used, backed by focusing on a problem associated with various types of learning of variants present inside a class of multiple images that are comparable to each other. Figure 9 depicts the architecture of GoogleNet.

Complexity and Challenges. The goals of Google Learning Network were to increase learning ability and improve the efficiency of CNN characteristics. Additionally, it controls the processing by adding a blockage layer of a 1×1 convolutional filter before employing large-size kernels. Sparse connections were used by GoogleNet to solve the duplicate content issue. By skipping those useless channels, it reduces expenses. The number of interconnections was reduced by using a GAP layer as the end layer instead of an FC layer. The utilization of regularisation and RMSProp as an optimizer were 2 extra consistency considerations [17]. The primary

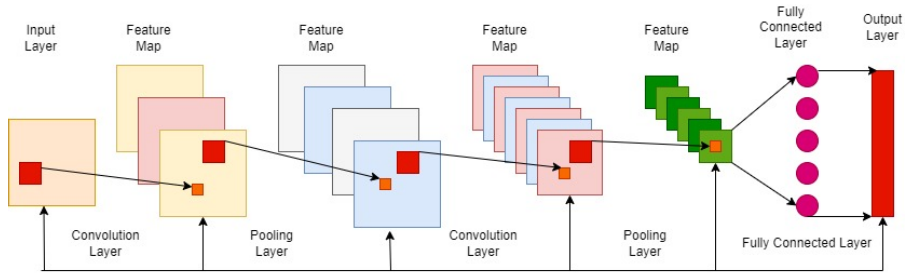

Fig. 3.8: Architecture of DenseNet [129]

drawback of GoogleNet, on the other hand, was its diverse architecture, which necessitates adaption from one component to the other. The representational jam, which significantly reduced the feature space in the layer below and sometimes led to the loss of critical info, is one of GoogleNet's major flaws.

3.7. DenseNet. DenseNet is among the most current revelations in neural networks for visual object detection. ResNet and DenseNet are roughly comparable, however, there are a few key distinctions. DenseNet, which Huang et al. citehuang2017densely designed to assure the greatest information flow between layers in the networks, earned the best paper prize at CVPR2017. Every level in DenseNet receives extra inputs from all layers that came before it and transmits its own extracted features to all layers that came after it. Huang et al. [45] presented CondenseNet as a solution to the issue of DenseNet's high memory utilization. The network structures are often gradually hierarchical. The input of the i^{th} layer in such a network structure is comprised of the feature maps from the $(i-1)^{th}$ layer. Every layer in the system is tied directly to the front layers, which is the fundamental concept behind DenseNet. Figure 3.8 depicts the architecture of DenseNet.

Architecture of DenseNet. The first convolutional layer, which receives the input, is the only one in a traditional feed-forward CNN that acquires the output of the convolutional layer before it. This convolutional layer then produces an output of extracted features, which is then passed on to the subsequent convolutional layer. As a result, there are L direct connections for each layer, one from one to the next. Figure 10 describes the architecture of DenseNet. Figure 3.8 explains the architecture of DenseNet.

Complexity and Challenges. By altering the typical CNN architecture and streamlining the connection among layers, DenseNet addresses the challenge of Vanishing Gradient. Each layer in a DenseNet architecture is connected to each other layer directly, giving rise to the densely connected CNN. There are $L(L+1)/2$ close links among both L layers as shown in Figure 10. DenseNets, as opposed to its regular CNN or ResNet equivalents, has acquired state-of-the-art capabilities and improved results among comparable datasets because they require fewer parameters and permit feature reuse, resulting in more compact models.

4. Disease prediction and analysis. Modern people suffer from a range of illnesses as a result of both their environment and lifestyle habits. Therefore, predicting disease sooner has become a crucial challenge. The most difficult challenge is to predict disease accurately. Deep Learning is crucial in predicting the disease in order to solve this issue.

4.1. Diagnosis of Diabetes. Diabetes is a metabolic condition that affects a lot of individuals all over the world. Each year, its incidence rates are frighteningly rising. Diabetes-related problems in several of the body's major organs could be lethal if not treated [107]. Early diabetic diagnosis is crucial for prompt treatment that can prevent the condition from escalating to severe problems. Deep Learning techniques have shown promising results in diagnosing diabetes at its onset.

Diabetes occurs in Cardiac Autonomic Neuropathy (CAN), a total neural system disturbance that reduces heart rate variation. Consequently, Heart Rate Variability (HRV) is a sign to detect the presence of diabetic neuropathy[77]. To achieve a more objective evaluation and diabetes diagnosis employing iris images, a combined Deep Learning and image processing technique has been proposed by Onal et al.[71]. The proposed methodology initially recognized the iris boundary in the iridology chart, after which it automatically identified

Table 4.1: Summary of research works corresponding to CNN for Diabetes diagnosis

Work	Method	Accuracy
[107]	LSTM, CNN and its combinations	95.7%
[71]	Hybrid method + VGG16	80%
[106]	CNN + CNN-LSTM + heart rate signals	90.9% using CNN-LSTM, 93.6% using 5 fold cross-validation, 95.1% using CNN-LSTM
[50]	SVM + CNN-LSTM + IF-CNN	96.26%
[68]	CNN-Bi-LSTM	98%
[33]	CNN	97.3%
[111]	AlexNet+VGG-16+SqueezeNet	AlexNet 93.46%, VGG-16 91.82% and SqueezeNet 94.49%

the pancreatic region. CNNs were then used to diagnose diabetes on images, and the outcomes were contrasted with other CNN models. It was determined that an efficiency of 80% was achieved using the suggested strategy in conjunction with the VGG16 architecture and automatic pancreatic area partitioning. Wang et al.[117] proposed a model for forecasting improvements in diabetic symptoms using an enhanced CNN technique. The model can aid doctors to forecast the probability of recurrence in patients after discharge and use case records of inpatient diagnosis and treatment to rate the patient's effectiveness of the treatment. Pal et al. [75] give an overview of the current Deep Learning methods that are used to forecast diabetes in its beginning stages. It can help researchers in this field by giving them knowledge of the most advanced techniques for earlier diabetes detection. Fufurin et al.[27] proposed a technique for detecting type 1 diabetes using infrared imaging spectrometry of exhaled human breath. The strategy can be employed in everyday clinical practice, but the results need to be confirmed on a bigger database and in subsequent biomedical studies. Swapna et al. [106]employed Deep Learning networks of CNN-LSTM and CNN combination to automatically identify the irregularity. Approaches to Deep Learning do not need feature extraction, in contrast to the standard analytical techniques that have been used up to this point. Kamalraj et al.[50] proposed the Pet Dog-Smell Sensing (PD-SS) method and Interpretable Filter-based CNN (IF-CNN) prediction model, that could effectively diagnose diabetes using PIMA Indian diabetes databases. This could improve the general approach to disease forecasting in the patient database, perhaps handling difficulties with older Deep Neural Network-based algorithms. Leveraging the publicly accessible PIMA Indian diabetes database, Madan et al.[68] developed a continuous monitoring hybrid Deep Learning-based model to detect and diagnose Type 2 diabetes mellitus. The research provided four contributions. Initially, they conduct an evaluation of various Deep Learning algorithms. In order to identify (and diagnose) Type 2 diabetes, they subsequently proposed integrating two models, CNN-Bi-LSTM. The proposed approach proved better than previous approaches. Goel et al. [33] provided a comparison of the CNN model's effectiveness in predicting sugar levels by employing the four non-linear activation functions sigmoid, tanh, ReLU, and ELU. According to the research observations, CNN offers a maximum accuracy of 97.3% when used in conjunction with the ELU activation function. Table 4.1 gives a summary of research works on Diabetes diagnosis using CNN variants.

Diagnosis of Diabetic Retinopathy. Diabetic Retinopathy (DR) is a common complication of diabetes mellitus that harms vision. It can lead to blindness, if not detected early. It is not a reversible process, and treatment only sustains vision. Early detection and treatment can remarkably diminish the risk of vision failure. The hand-operated diagnosis process of retinal images by doctors is time, energy, cost-consuming, and prone to misdiagnosis, unlike automated diagnosis using AI. In recent years, DR classification and detection have made extensive use of Deep Learning. Even with the integration of numerous diverse sources, it can effectively acquire the properties of the provided data [13]. There have been numerous Deep Learning-based approaches, including AEs, CNNs, Restricted Boltzmann Machines, and Sparse coding that have been used for the diagnosis of DR [37]. Unlike Machine Learning approaches, the effectiveness of these approaches improves as the amount of training data rises [20] because the variety of discovered attributes expands.

Gayathri et al. [29] demonstrate a new CNN model to automatically extract from retinal fundus images for enhanced classification results. In the proposed approach, different machine learning classifiers are fed the CNN output characteristics as input. The evaluation findings demonstrate that the J48 classifier and the recommended feature extraction approach surpass all other learners. Kwasigroch et al.[58] suggest a Deep Learning strategy to simplify the detection of DR. The most widely used class of Deep Learning algorithms, deep CNNs, succeeded at image recognition and analysis. Qomariah et al. [81] presented a support vector machine-based Deep Learning algorithm for feature extraction and categorization. As input features for classification utilizing the support vector machine, they utilize the high-level attributes of the final fully-connected layer depending on transfer learning via CNN. By employing this technique, it was observed that the classification process using CNN with fine-tuning required less computation time. Gayathri et al. [30] offer a technique for computerized DR grading in which characteristics from fundus images may well be retrieved and classified according to seriousness by employing Deep Learning and Machine Learning technologies. The identification of global and local characteristics from visuals is accomplished using a Multipath-CNN (M-CNN).To investigate fundus images and automatically differentiate among controls (i.e., no DR), moderate DR (i.e., a combination of mild and moderate Non-Proliferative DR (NPDR)), and severe DR (i.e., a group of severe NPDR, and Proliferative DR), a deep CNN of 18 convolutional layers as well as 3 fully connected layers is proposed by Shaban et al.[96]. The suggested method dramatically improves the availability of retinal care by eliminating the requirement for a retina expert and precisely diagnosing and evaluating diabetic retinopathy. Chen et al. [12] findings demonstrate that deep CNN-based algorithms are successful in facilitating autonomous DR detection by identifying patients' retinal images. To support their CNN learning, similar methods generally rely on an extremely large dataset made up of retinal images with predetermined categorization labels. Comparing the proposed approach to contemporary representative integrated CNN learning models, the classification accuracy can be increased by 3%. Hemanth et al. [40] suggest a different, hybrid method of using retinal fundus images for the diagnosis of DR. The hybrid approach, particularly, is built on combining both image processing and Deep Learning for better outcomes. Zeng et al.[128] By categorizing color retinal fundus images into two grades, a computer-aided diagnosis methodology development of deep learning algorithms is suggested by Zeng et al.[128] to accurately diagnose the referable DR. This study uses a transfer learning technique to create a distinctive CNN model with such a Siamese-like structure. The proposed method achieves an Area Under the receiver-operating characteristic curve (AUC) of 0.949 using a training dataset of only 28104 images as well as a test set of only 3510 images. Gangwar et al. [28] use pre-trained Inception-ResNet-v2 with transfer learning, and construct a customized set of CNN layers on top of Inception-ResNet-v2 to create the hybrid version. The model outperformed other results that have been reported. Automated identification of the DR stage is presented by Qureshi et al. [83] using a novel multi-layer framework of Active Deep Learning (ADL). The CNN model was used to develop the ADL system to dynamically feature extracted as contrasted to manually created attributes. CNNs are recommended by Wu et al. [119] as an automated clinical tool for identifying five stages of DR seriousness categories as a hierarchically Coarse-to-Fine network (CF-DRNet). The CF-DRNet greatly improves the categorization effectiveness of five-class DR grading while adhering to the hierarchical character of DR marking. Liu et al. [66] offer a novel approach driven by ensemble learning, the WP-CNN, which incorporates several weighted pathways into CNNs. Backpropagation is used in WP-CNN to optimize various path weight coefficients, and the return features are averaged enabling quick convergence. Pao et al. [76] proposed that the green element of a retina image was utilized to compute the entropy image. They trained this network on the publicly accessible Kaggle dataset that used a high-end graphics processing unit (GPU), and showed outstanding results, especially for a high-level classification problem. Figure 4.1 gives us the sample of a severe non-proliferative DR (NPDR) fundus image that shows the severity and likelihood, of the presence of microaneurysm, hemorrhage, and exudate. Figure 4.2 outlines the general measures taken by a CNN model to categorize fundus images into 5 severity categories. Table 4.2 presents the summary of research works corresponding to DR diagnosis using CNN. Table 4.3 presents the datasets available for DR diagnosis.

4.2. Brain Diseases. The operations center of our body is the brain. The brain is impacted by a wide range of conditions and abnormalities. The buildup of aberrant proteins in our brain is a prevalent trigger of neurodegenerative illnesses. They comprise, among others, ALS (Amyotrophic Lateral Sclerosis), Parkinson's disease, Alzheimer's disease, and others.

4.2.1. Parkinson's Disease. A neurological condition that affects voluntary muscle movement is Parkinson's Disease (PD). Identifying PD and its root causes is essential for developing its treatment and prevention plan. Traditional PD diagnostic techniques suffer from subjectivity as they rely on the evaluation of movements

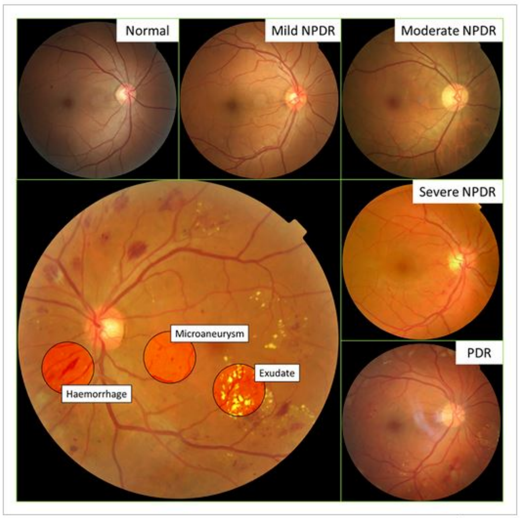

Fig. 4.1: Sample of a severe NPDR fundus image that shows the severity and likelihood, the presence of microaneurysm, hemorrhage, and exudate [109]

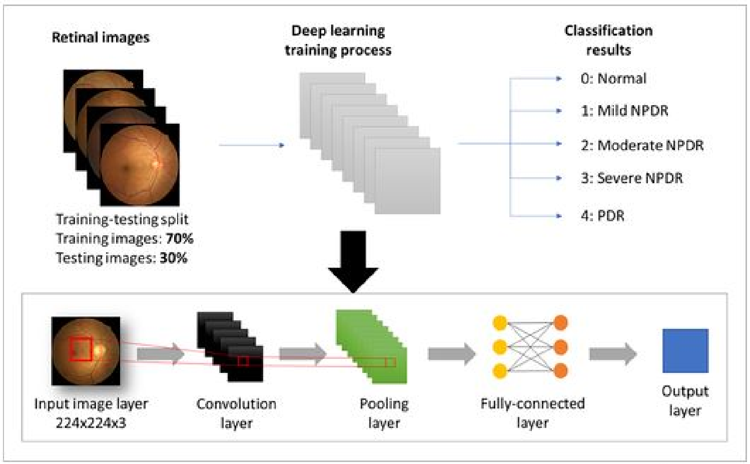

Fig. 4.2: Deep Learning process for classifying images to 5 severity levels [109]

that are sometimes subtle to human eyes and therefore make the correct classification difficult. This makes early diagnosis of PD challenging. To combat this challenge, Deep Learning has been identified as the potential solution. Several researches have reportedly been conducted to analyze the potential of Deep Learning in PD diagnosis. Taleb et al. [110] investigated how various Deep Learning architectures, such as the CNN and the CNN-BLSTM, can be utilized to diagnose PD via time series analysis. Hire et al.[42] presented a group of CNNs for the detection of PD using speech recordings from 50 patients suffering from the condition and 50 healthy people from the PC-GITA database. Kurmi et at.[57] proposed a collection of Deep Learning to diagnose PD utilizing DaTscan images. To begin with, they categorized PD by applying four DL models: VGG16, ResNet50, Inception-V3, and Xception.To improve the classification model's overall effectiveness, they used a fuzzy fusion logic-based ensemble technique in the subsequent steps. Yousif et al.[125] proposed a global standard for the diagnosis of PD utilizing voice signals and/or handwritten drawings. To diagnose PD using handwriting images,

Table 4.2: Summary of research works corresponding to DR diagnosis using CNN

Work	Dataset	Method	Accuracy
[58]	88000 retina images(own dataset)	CNN	82%
[81]	Messidor	SVM+CNN	95.83%
[30]	IDRiD, Kaggle, and MESSIDOR	M-CNN	99.62%
[40]	MESSIDOR	image processing + deep learning	94%
[28]	APTOS+Messidor-1	transfer learning+Inception-ResNet-v2	72.33% for Messidor-1 and 82.18% for APTOS
[83]	Own dataset(54,000 images)	ADL-CNN	98%
[66]	-	WP-CNN	94.23%
[80]	Kaggle (80,000)	CNN	75%
[121]	Kaggle (80,000)	CNN	94.5%
[23]	Kaggle (35000)	CNN-ResNet34	85%
[116]	Kaggle (35,126)	CNN (AlexNet, VggNet, GoogleNet and ResNet)	95.68%
[1]	DiaretDB0 (130), DiaretDB1 (89), and DrimDB (125)	CNN	99.17 (DiaretDB0), 98.53 (DiaretDB1), 99.18 (DrimDB)
[52]	MESSIDOR (1200)	CNN (AlexNet, VggNet16, custom CNN)	98.15%
[130]	Own dataset	CNN (ResNet50, InceptionV3, InceptionResNetV2, Xception and DenseNets)	96.5%
[113]	HRF (45) and DRIVE (40)	CNN	93.94%

8 pre-trained CNNs using transfer learning were optimized by Aquila Optimizer. Features from the MDVR-KCL dataset are extracted numerically for the speech signals using 16 feature extraction methods and fed to four different machine learning models tuned by the Grid Search algorithm, as well as pictorially utilizing five different methods and fed to eight pre-trained CNN frameworks. Vyas et al.[114] presented two cutting-edge methods that make use of Deep Learning approaches. CNNs in 2D and 3D that were learned on axial-plane MRI data are employed. Alissa et al.[4] proposed a technique focusing on using drawing tasks to identify patient movement abnormalities. Additionally, their research examines the superiority of the spiral pentagon over the wire cube as a categorization tool. Zhao et al. [131] proposed greedy methodology, integrates the concepts from different regions into a sophisticated one. Every region was trained and tested for this prototype. To categorize the presented participants into PD and healthy utilizing neuroimaging (T1 weighted MRI scans and SPECT) and biologic (CSF) parameters as the database, two frameworks—feature-level and modal-level—are proposed by Ahuja et al. [74]. All of these parameters are combined in the feature-level framework to produce a heterogeneity database that is later provided to two Deep Learning models to diagnose PD. A summary of such research used for PD diagnosis using CNN is presented in Table 4.4.

4.2.2. Diagnosis of Alzheimer's Disease. The seventh largest leading cause of death in the world is cognition, including Alzheimer's Disease (AD) [118]. The most widespread form of dementia, accounting for 60% to 80% of cases, is AD. A condition known as dementia is characterized by a decline in mental capacity that goes beyond what may be anticipated with the aging process. It impairs consciousness and damages memory, reasoning, orientation, understanding, computation, learning ability, communication, and the capacity to distinguish. Synapse weakness, synaptic loss, and neurodegeneration are all brought on by alterations in Amyloid Precursor Protein (APP) breakage and synthesis of the APP component beta-amyloid (A), as well as hyperphosphorylated protein aggregation. Key elements of the disease include metabolic, vascular, and inflammatory alterations as well as associated conditions. A healthy brain and an AD-affected brain are contrasted in Figure 4.3.

Table 4.3: DR Datasets

Dataset	No. of Images	Resolution	Comments
Kaggle	88,702 high-resolution images	433 × 289 pixels to 5184 × 3456 pixels	Many of the images on Kaggle are of inadequate grade and have erroneous labels [63, 59, 82, 121, 22, 116]
DIARETDB1	89 publicly available retina fundus images	1500 × 1152 pixels	It has 5 normal images and 84 DR images with annotations from four medical professionals [51, 82, 72]
E-ophtha	463 images	-	The E-ophtha EX and E-ophtha MA are included in this publicly accessible dataset [18, 15]
DRIVE	40 images acquired at 45-degree	565 × 584 pixels	It includes images of a max normal retina images, and there are only seven mild DR images [103]
DDR	13,673 fundus images acquired at a 45-degree	-	757 images of DR lesions [63]
Messidor	1200 fundus color images	-	Images are acquired at a 45-degree FOV [19]
Messidor-2	1748 images	-	Images are acquired at a 45-degree FOV [19]
CHASE DB1	28 images	1280 × 960 pixels	Images acquired at a 30-degree FOV [73]
STARE	20 images	700 × 605 pixels	The freely accessible dataset is used to segment blood vessels [44]
Indian Diabetic Retinopathy Image Dataset (IDRiD)	516 fundus images	-	Contains images of normal retinal structures and diabetic retinopathy lesions [79]
ROC	100 publicly available retina images	768 × 576 to 1389 × 1383 pixels	There are just training reality on the ground [16]
DR2	435 publicly available retina images	857 × 569 pixels	98 images are classified as references [53]

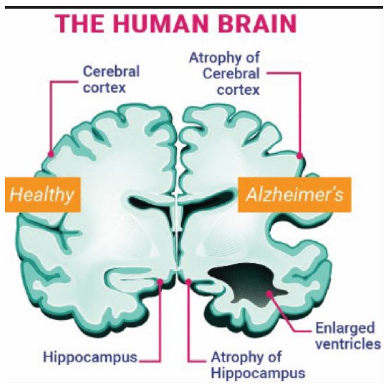

Fig. 4.3: Difference between healthy brain vs severe AD [92]

AD has no cure, however, early diagnosis of AD is crucial to inhibit its progression. The advanced neuroimaging strategies combined with Deep Learning have the potential to diagnose AD in the early stages. Non-invasive neuroimaging techniques are available to understand the pharmacology, function, or structure of the brains [41]. The two categories of imaging technology are typically structural imaging and functional imaging. The anatomy of the brain, including its neurons, synapses, glial cells, etc., can be learned through effective segmentation [41]. The following are the neuroimaging methods more frequently in use for AD:

Magnetic Resonance Image (MRI): The medical imaging technique described as magnetic resonance imag-

Table 4.4: Summary of research works corresponding to PD diagnosis using CNN

Work	Dataset	Method	Accuracy
[110]	HandPDMultiMC	CNN-BLSTM	97.62%
[42]	PC-GITA, a publicly available database	Ensemble of CNNs	99%
[57]	Parkinson's Progression Markers Initiative (PPMI)	VGG16, ResNet50, Inception-V3, and Xception	98.45%
[125]	NewHandPD, MDVR-KCL	VGG19, KNN, SVM	99.75% using the VGG19, 99.94% using the KNN, 100% using the combined the mel-specgram graphical features + VGG19
[114]	318 MRI scans	2D-CNN and a 3D-CNN	3D-CNN 88.9%, 2D-CNN 72.22%
[4]	drawing task	CNN	93.5%
[131]	Three retrospective investigations included 305 Parkinson's patients (aged 59.9–9.7 years) and 227 healthy control individuals (aged 61.0–7.4 years)	CNN	94.1±3.2%
[74]	SPECT	CNN	93.33%
[55]	NTUA	CNN-RNN	98%
[24]	PPMI	3D-CNN	100%
[97]	NIMHANS	CNN	80%
[54]	NTUA	CNN-RNN	98%

ing (MRI), which creates exact images of human tissues and organs, uses a magnetic field and radio waves generated by the computer. Ogawa et al.[70] discovered that operational knowledge about the brain can be obtained via MRI in 1990.

Positron Emission Tomography (PET): FDG-PET is extensively and frequently used in the examination of persons with possible neurodegenerative illnesses, notably AD, to confirm the diagnostic accuracy [90]. It stands for impaired neural function or synaptic degeneration. It was once believed that lower FDG-PET values were really a symptom of neuronal hypo-metabolism caused forward by neuro-degeneration. Instead of reflecting neurons' glucose absorption, it has been discovered to correlate with astrocytes. However, there is proof that anomalies in blood-brain barrier (BBB) transport could be detected by PET by decreased FDG brain absorption.

According to [36], the hippocampal, cortex, and ventricle are the three key brain regions associated with AD. They used layered AEs using a patch-based and ROI-based approach and utilized CNN to diagnose AD. In order to evaluate the proposed CNN model, various image morphological operations and datasets were used. The outcomes of such studies point to the significance of early AD diagnosis utilizing image processing and Deep Learning methods. Suk and Shen [105] suggest a hybrid model for identifying AD built on CNN and Sparse Regression Networks. Multiple Sparse Regression Networks were employed by the model to produce different targeted images. Next, CNN merged these target-level descriptions best determined the output label. The 16-layered VGGNet was altered by Billones et al. [10] for dividing the patients into three categories according to structural MRI: AD, MCI, and HC scanning. Testing carried out for the study showed that the researchers were successfully carrying out categories accurately. According to the writers, this was accomplished. without doing MR image segmentation. Sarraf and Tofighi used LeNet architecture [94] to distinguish AD patients from healthy ones using functional MRI. The findings showed that because of CNN has vast potential in relation to a shift-invariant and scale-invariant feature. Imaging in medicine [67] surpassed a patch-based and voxel-based DBM hybrid [104]. Sarraf and Tofighi [93] used LeNet and GoogleNet architectures in another experiment for diagnosing AD based on both architectural and operational MR images. These suggested and placed-into-use pipelines show a substantial increase in categorization performance over other investigations.

Following presents the datasets available for AD diagnosis:

OASIS: Information from the data sets from neuroimaging called the Open Access Series of Imaging Studies (OASIS) is accessible to the general public for analysis and research. The current MRI data set is made up of a longitudinal collection of 150 participants, ranging in age from 60 to 96, all of whom were recorded employing the same machine and the same procedures. A total of 373 imaging examinations were performed on each patient over the course of at least 2 sessions separated by at least one year [33].

DARS: The Virginia Department for Aging and Rehabilitative Services (DARS) has been compiling information on people with AD as well as other forms of dementia and their carers since 2012 in collaboration with employees from other State Health and Human Resources (HHR) departments [34].

ADNI: The ADNI collection can be used to detect AD, which is typically seen in senior citizens [49], which contains details of MRI scans for 843 subjects with scanner intensity fields ranging from 1.5 T to 3 T. It has been noted that people with mild cognitive impairment(MCI) tend to have reduced intellectual capabilities, particularly reasoning, and loss of memory

IBSR: Brain image features extraction methods are tested and developed using the IBSR dataset [48]. In addition to the MRI data, the dataset additionally includes expert segmentation findings that were carefully supervised. The ground Truth is made up of 20 actual T1-Weighted (T1-W) MRI scans with an expert segmented image that was carefully steered.

MICCAI: The MICCAI-2012 dataset [60] was received via Neuromorphometrics, Inc., Scotts Valley, California, USA, it comprises 35 T1-w MRI volumes and manual segmentation of 134 features. It is mostly employed to segment tissues, tumors, and formations. In 2012, this dataset began with 80 authentic and artificial examples. The quantity of training and testing data has grown over time. Subcortical structure segmentation is done using the MICCAI 2012 task in multi-atlas labeling.

MCSA: MCSA [85] is a population-based controlled trial with the goal of determining the prevalence of MCI along with its causes and risk factors, also include dementia. On October 1, 2004, Olmsted Counties, Minnesota's inhabitants aged 70 to 89 were tallied using the Rochester Epidemiology Survey. The original study participants were randomly selected from among the eligible subjects.

4.3. Diagnosis of Lung Cancer. Among the most prevalent malignancies, Lung Cancer accounts for approximately 3 million cases, more than 1 million fatalities, and 12$ billion in annual spending on health care in the United States [14]. Being one of the fatal tumors, just 17 percent of those diagnosed with lung cancer in the United States remain five years following detection, and life expectancies are worse in emerging economies. Anyone can develop pulmonary cancer, particularly people who smoke or breathe in hazardous, toxic components [46]. Smoking can cause lung cells to mutate. Lung-threatening development [31] was the second-leading death cause in 2015, and it is now the fifth scenario in 2017, as determined by the World Health Organization (WHO) evaluation.

In comparison to the trained radiologists, the latest cyber-physical technologies and computer-aided detection with Deep Learning has shown promising results in lung cancer diagnosis [127, 126, 32]. Many different types of Deep Learning [102] architectures have been studied to understand better how to diagnose lung illness. In [102], a 3D multipath VGG-like system with two setups is suggested.

The two groups are kind knobs and dangerous knobs, and lung knobs and non-knobs, respectively. So various architectural designs are suggested and evaluated in various studies. CNN [100, 112] and its derivatives were primarily covered. CNNs can be used to analyze both 3D and 3D data referred to as 3D CNN/ConvNet and C3D/3D ConvNet, respectively [86]. In blockchain material using extended CNN[102], the lung knobs could be categorized and arranged using lung CT imaging, but their hazard level may also be determined. Although ECNN has time complexity and accuracy limitations, its development is much less sensitive than that of earlier approaches. In [91], CNN was used for lung cancer diagnosis. In [3], 3D-CNNs were used for classifying the CT scans as true (lung cancer) or false (no lung cancer), a result of 86.6 % accuracy was produced on the test set. Lin et al. [64] suggested using a 2D-CNN using the Taguchi optimization procedure to detect lung cancer using CT scans automatically. To increase the accuracy rate of lung cancer using the Taguchi technique, the appropriate parameters for the 2D-CNN architecture were found through the selection of 36 experiments and 8 control factors of varied levels. Sibille et al. [99] proposed that it is possible to

Table 4.5: Summary of research works corresponding to Lung Cancer diagnosis using CNN

Work	Method	Accuracy
[102]	Blockchain + extended CNN	96.88%
[91]	CNN	Recognize and detect the lung cancer
[3]	3D-CNN	86.6%
[64]	2D-CNN with Taguchi parameter optimization	6.86% and 5.29% more accurate than the original 2D CNN on the two datasets
[99]	Deep-CNN	96.4%
[6]	3D-Deep Learning	94.4%
[122]	Deep Learning on CT images	95% Confidence Interval (CI)
[2]	AlexNet	93.548%

achieve high diagnostic productivity when both CT and PET images are being used, to automate anatomic identification and categorization of fluorine 18-fluorodeoxyglucose PET accumulation pattern in foci suggestive and non-suspicious for cancer in lung tumor patients and lymphoma. Table 4.5 Summarizes research work on Lung Cancer using CNNs.

5. Discussion. Although there are numerous encouraging findings from earlier investigations, there remain a number of challenges to be addressed before Deep Learning can be implemented in diagnostic imaging. Initially, the degree of learning dataset's quality and quantity, as well as its propensity for overfitting and bias, must be taken into account. A Deep Learning generalization should be given, considering the variations in illness occurrence, diagnostic techniques, and medical centers around the world. Therefore, developing assessment methods to measure each technique's effectiveness is necessary. Additionally, as the effect would be strongly influenced by the information quality, there may be legal and ethical concerns around the use of clinical images acquired for marketing. Furthermore, it is crucial to consider the Deep Learning's black-box character. While the Deep Learning-based approach produces outstanding results, it is often complicated or even unattainable to articulate the reasoning behind the judgment. Finally, if we deploye a Deep Learning system in a particular clinical practice process without the instruction of a doctor, legal liability concerns would arise. The inherent constraints of Deep Learning, implementation logistics, and evaluation of acceptance hurdles as well as required socio-cultural or route adjustments are major obstacles to the application of AI systems into healthcare. The following are the main challenges of Deep Learning in medical imaging:

- Low accuracy is sometimes the result of inadequate data. Deep Learning models need ample amount of data to attain high accuracy. In medical imaging, there is dearth of labeled data and this poses a challenge.
- Disease-specific information about rare disorders is limited. This limits the use of Deep Learning in the diagnosis of such dis-orders.
- Small modifications to the input samples can easily fool Deep Neural Network, leading to misinterpretation.
- Heterogeneity of data is another challenge. Nowadays, one barrier to widespread Deep Learning usage in medical imaging is the variety of data. Thousands of handwritten documents scanned combined with broken, redundant, and incomplete information can produce insufficient conclusions and impair decision-making.
- The lack of skilled data scientists and modelers is yet another obstacle to utilizing Deep Learning in medical imaging.

6. Conclusion. Medical imaging is possibly the most appropriate and attractive topic for AI technologies in the biomedicine and healthcare systems sectors. We provided a thorough overview of Deep Learning architectures and reviewed the applications of CNN in medical imaging. It was observed that Deep Learning techniques based on CNNs are becoming more widely accepted in all areas of early disease detection including DR, lung cancer, AD, etc. Data augmentation and transfer learning are examples of methods used to solve problems with Deep Learning methods caused by inadequate data and labels. Improved Deep Learning architectures and much more computation power are making it possible to function better on massive datasets. This achievement could eventually lead to enhanced computer-assisted detection and treatment systems. Given the recent achievements, Deep Learning approaches would significantly advance clinical disease analysis. However, there are a number of challenges that are yet to be resolved in order to utilize the full potential of Deep Learning techniques in medical diagnosis.

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