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CANCER DETECTION IN HISTOPATHOLOGY OF LYMPH NODES

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Abstract: Cancer is one of the main diseases around the world. Many cancer patients die every year due to late diagnosis and treatment. Hence, lately, early cancer recognition frameworks dependent on histopathology slides are sought after. With the advancements in technology, deep learning has rooted its applications in various domains. In this project, a comparison between pre-trained models with customized models is performed, which adapts the CNN model and ResNet for feature extraction to the problem at hand. The convolutional neural network which is known as profound learning architecture has accomplished amazing outcomes in numerous applications. Working on histopathology images requires high tuning while pre-processing images to obtain high accuracy while classifying. While using CNN, due to the increase in parameters the model might get highly complex. Hence, we experiment using ResNet to overcome these problems and evaluate the models. Broad examinations on a freely accessible histopathologic cancer dataset of lymph nodes are completed and the precision scores are determined for execution assessment on the two models.

Keyword: CNN, ResNet, Histopathology, Cancer.

I INTRODUCTION

In this generation, many people suffer from many diseases, out of which the most common one happens to be cancer. The most basic and easiest approach for the identification and detection of the cancer is the naked eye observation by the laboratory experts through microscopes. A person gets cancer due to many reasons ; It maybe is genetic, maybe due to some other internal factors, or maybe due to constant exposure to certain external factors the number of cancer patients is increasing, detection of such disease is essential in the field of medicine. In a few growing countries, laboratory experts are comparatively expensive and they are nit easily available as a person requires extreme knowledge in this specific field.The automatic detection of cancer is needed to instantly detect the infected area and start with the treatment. The objective of this paper is to implement image analysis and classification techniques for the detection of cancer in lymph nodes. Lymph nodes are little glands that channel the lymphatic framework liquids. These lymph nodes are the initial and first place cancer starts spreading. Lymphoma is the name given to cancer in lymph nodes. To automate the process of testing, our project aids the process of easy and quick detection of cancer. The Project utilizes a grouping- based strategy to isolate pixels into different classes utilizing distinctive arrangement techniques. Out of many, Bayesian grouping is the most utilized by specialists, it's the place where the pixels are contrasted and a pre- determined model and classified as defected or healthy. This project has been proposed then experimentally simulated using two classifiers and made into a comparative study. Convolutional Neural Network (CNN) as the first classifier and Residual Neural Network (ResNet) as the second.

II LITERATURE REVIEW

Previous methods and papers include Breast Cancer Detection Extreme Learning Machine Based on Feature Fusion with CNN Deep Features: They proposed a system using an eight-layered Convolution Neural Network with an Unsupervised Extreme Learning Machine for breast cancer detection. Convolution Neural Network with High-throughput adaptive sampling for whole-side histopathology image analysis(HASHI): Application to invasive breast cancer detection: This paper deals with the detection of invasive cancer on whole side images (WSI). The Histopatholoic Review of Lymph Nodes in Metastatic Breast Cancer Using the Impact of Deep Learning Assistance: This paper is about deep learning assistance helps in improving the accuracy and efficiency of digital pathology. The experiment shows an accuracy of 80% in detecting can Neural Networks for Lung Cancer Detection through Radiomic Features: The proposed system uses 30 radiomic features**.**

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III METHODOLOGY

In this evolving generation, many automated gadgets work just like the human brain. This is possible due to a certain study called machine learning. Machine learning is a piece of Artificial Intelligence that empowers the framework to adapt consequently. It studies the algorithm and changes concerning the data or the information inputted.To put it in simple words, it is the work of getting a computer to learn and execute as humans do. Now, why do people go for machine learning? The most appropriate answer for this would be its ability to process a huge amount of data and the time taken. Unlike manually operating a machine and processing the data, which would consume a huge amount of time, machine learning makes it easier for anyone to save time and money as it is automated.

A subset of the above happens to be Deep learning. Deep learning is similar to the working of a human brain in processing and recognizing many things such as objects, information, etc. This can be done with or without supervision depending on the purpose. It comes under an artificial neural network. Artificial neural networks are computing systems, which simulate the same way how the human brain processes and analyses data. The artificial intelligence basis is ANN. The basic parts of an ANN are nodes which are known as artificial neurons. These are modeled the same way as the neurons in the human brain. A deep learning algorithm runs data through many layers. The output of each is simplified in that specific layer and then passed on to the next layer where it is again simplified. The interaction is rehashed until the last layer is reached and afterward the output will be acquired. It mainly extracts high-level features from the given input. Deep Learning Algorithm consists of many classifiers. Classifiers consist of algorithm that executes classification. Naive Bayes, K-Nearest Neighbour, Logistic Regression, etc., are some of the classifiers. The training time for the mentioned is quite high. These give the same output for the data loaded repeatedly unlike ANN. Convolutional Neural Network is one among the many classifiers. The processing of images using CNN is done more accurately as well as the accuracy of the output. CNN functions on pre-training and so it saves memory space and training time. Complexity is also less in CNN when compared to other classifiers.

Another classifier is the Residual Neural Network. ResNet is built as similar to the pyramidal cells' formation in the cerebral cortex. It was first brought to use in 2015 by Kaiming He, Xiangyu Zhang, Shaoqing Ren, and Jian Sun. It secured first place in the 2015 ImageNet Large Scale Visual Recognition Challenge (ILSVRC). The ImageNet Large Scale Visual Recognition Challenge is an annual computer-based competition, which uses the ImagenNet data to come up with various problem-solving algorithms. The well-recognized CNN architecture that won this competition is the AlexNet (2012) which was found by Alex Krizhevsky in collaboration with Ilya Sutskever and Geoffrey Hinton. AlexNet is made up of 3 convolutional layers,2 normalization layers, 3 max-pooling layers, 2 fullyconnected, and a softmax layer.Then came the most famous Google Net Model (2014) by Christian Szegedy. This happens to be a 22 layered network. The next was the VggNet. VggNetiscategorized based on the number of layers. The most common ones are the Vgg16 and Vgg19. With all the above types of architecture present, why do we go for ResNet?

ResNet has a special feature known as skip connection. These skin associations help tackle the vanishing gradient problem. When a large input space is squeezed into a tiny input space, a huge change in the function's input will lead to a changed output; this is known as the vanishing gradient problem. Skip connections prevent this. It skips a few layers, which increases efficiency. This project has makes use of a Convolutional Neural Network and Residual Neural Network which are deep learning algorithms.

3.1 Dataset

The collection of the dataset is vital for training in machine learning. For this project, histopathology images of lymph nodes are used. The dataset is contributed from Patch Chameleon and can be obtained in Kaggle and GitHub. This dataset consists of around 3,27,680 images of size 96x96 as shown in fig 1. The pictures can be isolated dependent on their marking. A positive label indicates cancerous tissues and a negative label indicates non-cancerous tissues. This dataset can be further separated into training, testing, and validation data for training the models.

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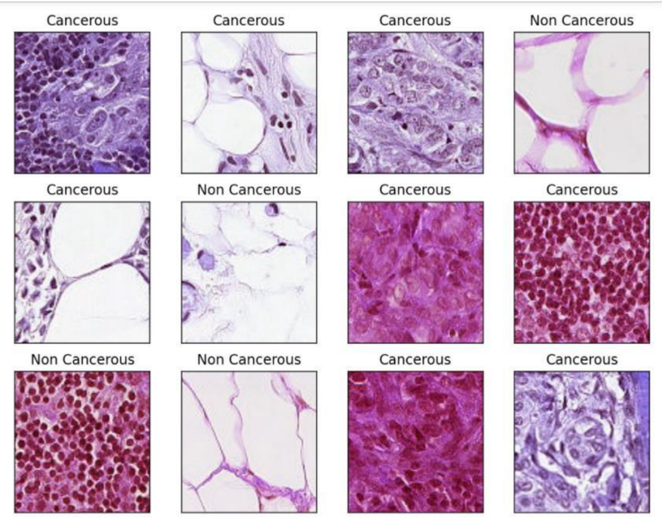

Fig 1 Collected Dataset

3.2 Architecture of CNN

Convolution Neural Network comes under the above. CNN takes an image as an input; it then assigns important weights to various parts/objects/pixels in the input image and would be able to differentiate one from the other. CNN consists of many layers [shown in Fig 2]; the number of layers depends on us and the purpose of use. The basic layer of CNN is the Convolutional layer. The Convolutional layer receives the input, transforms it in some way, and then passes it onto the next layer. The transformation that happens here is Convolution. Convolution blends one function with the other. CNN's can detect patterns, more specifically the number of filters that the convolutional layer has does this.

Pool happens to be a non-linear layer where downsampling occurs. It gets the contribution from the past layer. The output will rely upon the window size utilized here. What this does is, decreases the size of the info. The above two layers are repeated depending on our purpose of use. The final layer is the hidden layer, which is also known as the fully connected layer. It consists of the number of hidden convolutional and pool layers. This is used to detect the final output category.

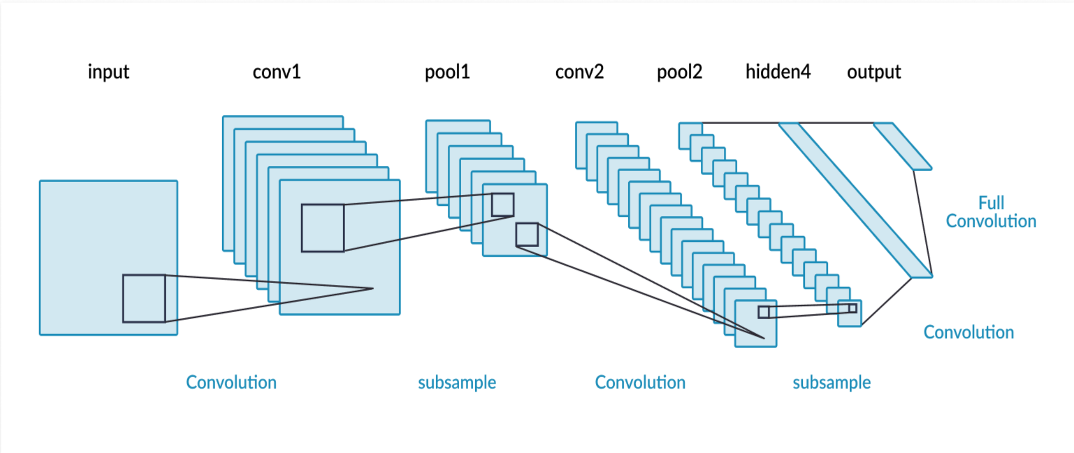

Fig 2 Architecture of CNN

3.3 Architecture of ResNet

Residual Neural Network is built using blocks known as Residual block as shown in fig 4. They are the base of a ResNet. A single residual block is made up of two convolutional layers and an activation function as shown in fig 3. ResNet starts with a convolutional and pooling step, after which the residua blocks follow. The input goes into the first block (i.e., the first convolutional layer) and output as the input of the next block.

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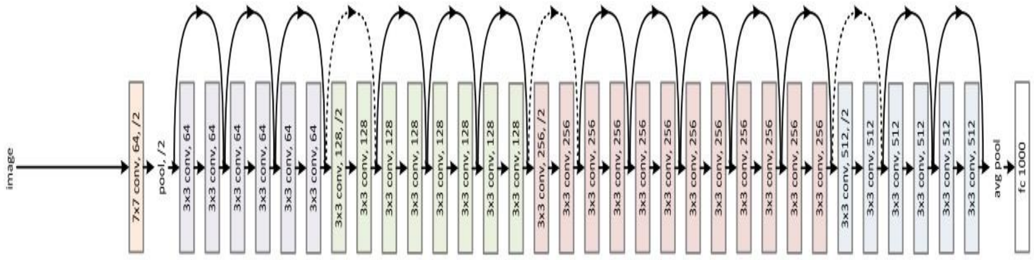

Fig 3 ResNet Architecture

Rectified Linear Unit (reLu) is the activation function used here.On the off chance that the info is positive, the output will be the specific information else the output will be zero. At the end of the first block, we have the output of that specific block added with the input of the block. The dotted lines represent the change in the dimension of the input (due to convolution). This interaction is continued relying on the number of layers we use.

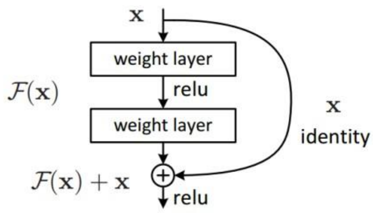

Fig 4 Residual Block

3.4 Software Implementation:

The project has been carried out using Python, and it has been executed in Google collab and Jupyter Notebook. Tensorflow is the software library used for the entire project. The premise of TensorFlow is information stream graphs that have edges and nodes. As the mechanism of execution is in the form of graphs, the TensorFlow code is easy to execute across many computers using GPU. The acceptable data are in the form of multi-dimensional arrays called tensors. With Tensorflow, Keras can be accessed. It is a high-level, open- source library that operates over TensorFlow. It's an interface for TensorFlow Library. Since it is easily approachable and has high iteration velocity it is used widely among researchers.

3.4.1 CNN Model

Three different CNN model has been trained and tested for the given dataset. The model was customized based on convolutional layers. The convolutional layer was stacked to increase the performance of the model. Each convolutional layer was given a ReLU filter. This filter ensures that only positive value of weights get passed on to the next layer and it is represented by

$$f'(z) = \begin{cases} 1, & for\ z \geq 0 \\ 0, & for\ z < 0 \end{cases}$$

Here z denotes the weight of the image. After the stacking block, the input image passes onto the max- pooling layer where downsampling takes place. A window size of 2 x 2 was chosen. Following this, the dropout layer of the value 0.3 was passed between each stack to prevent overfitting of the model. Usage of optimizers is vital to decrease loss. One can instantiate the optimizer before compiling or passing it with its string identifier. There are many optimizers available; a few are SCG (Stochastic Gradient Descent), RMSprop, Adadelta, etc. ADAM optimizer is used to run the model. It is based on the adaptive estimation of first and second-order moments.

3.4.2 ResNet Model

In contrast to the previous model, which had to be built from scratch, a transfer learning method was used to compare the model performance. ResNet has already been trained on a huge dataset 'ImageNet'. It uses the weights obtained from training and this reduces the time to build the model from scratch. ResNet50 is a fifty-layered model which follows

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CNN and is made up of residual networks that forming a deep network. As the classes trained in ImageNet are different from the dataset used, the last layers had to be separately declared as shown in fig 8. For fine-tuning of the model, all the layers are frozen except the last few layers. The model is trained for 10 epochs with continuous monitoring of the training; the learning rate gets reduced when there is no improvement seen.ResNet101 model has 101 layers split into five blocks each block of 20 layers. The last few layers are declared to tune the classification model. To improve the performance the last block is freeze. The model is trained for 10epoch, if there is no improvement the training will stop at that epoch.

IV RESULTS AND DISCUSSIONS

The dataset was separated into three categories of training, testing, and validation. The training and validation data were used for training the models, which consisted of 1,40,000 and 16,000 images respectively. The model's performance was evaluated with the help of testing datas. It was found that while using CPU the training time was very high, so GPU Nvidia P100 was used as an accelerator which significantly reduced the training time. The CNN models were trained for 20 epochs and the ResNet model was trained for 10 epochs which were stopped at the 6 epoch stage as there was no increase in performance after that stage.

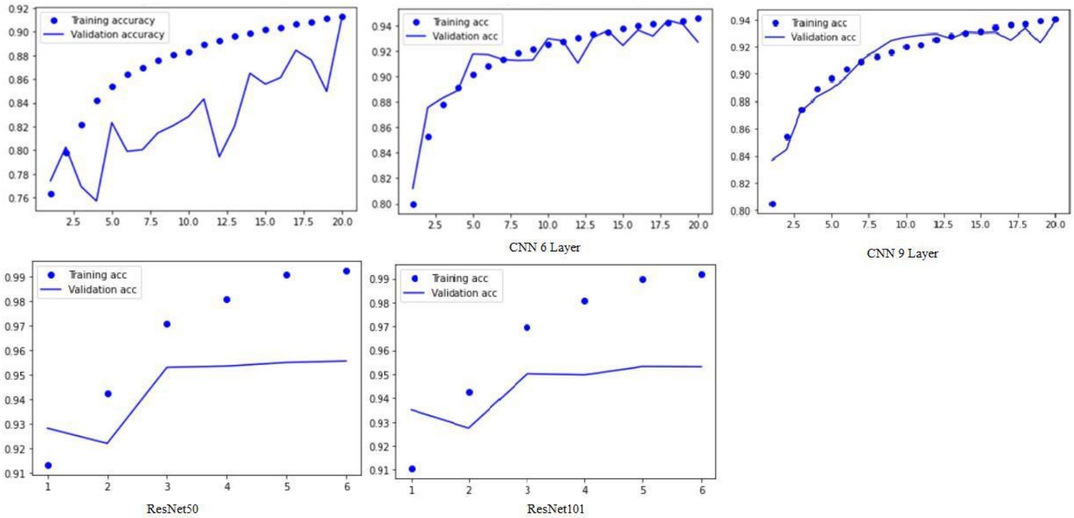

Fig 9 Accuracy Graph

Various parameters were considered to evaluate these models. Fig 9 shows the accuracy graph for the models. It has been seen that there is a remarkable expansion in accuracy. In this evaluation, it is found that the CNN 3-layer model and ResNet50 model exhibit similar underfitting as the value of training accuracy is greater than validation accuracy in both cases. CNN 6 layer and CNN 9-layer exhibit perfect model training.

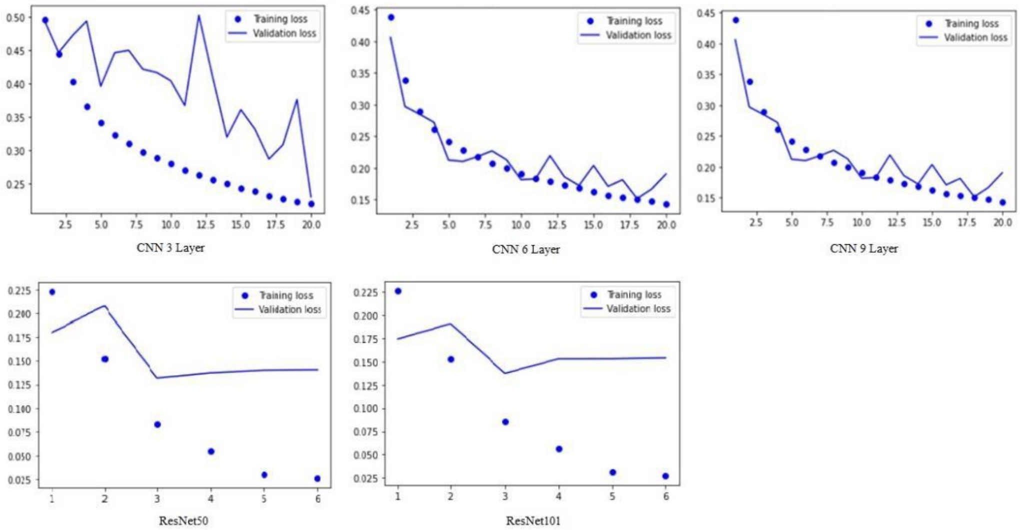

Fig 9 Loss Graph

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From the above graph, the training and validation loss for the different layered models is plotted. For CNN 3 Layer model, the training loss curve is under the validation loss curve. Hence, this model is the underfitting model. Similarly, ResNet50 and ResNet101 model is underfitting, as the training curve is under the validation curve in the graph. For CNN 6 Layer and CNN 9 Layer, the training curve and validation curve remains in similar approximately. Thus these two models are considered to be perfectly fitted.
Using the confusion matrix, the value of true positive, true negative, false positive, and false negative has been calculated as shown in Table 1. These values are useful for further evaluation of the model as shown in Table 2. The values have been plotted for test data of 16,000 images for which the model has made predictions.

Table 1 Model's Performance Classification

Model	True Positive	True Negative	False Positive	False Negative
CNN 3 Layer	7549	7046	954	451
CNN 6 Layer	7625	7205	795	375
CNN 9 Layer	7381	7630	370	619
ResNet50	7273	7243	757	727

Accuracy is the number of predictions that have been correctly classified by the model and it can be calculated by
Accuracy = (TP + TN)/ (Number of test dataset) (4.1) Precision denotes out of all the predictions from True positive, how many are accurate. *Precision = (TP)/(TP+FP)*
(4.2) Recall gives the value of how many among True positive is accurate
Recall =(TP)/(TP+FN) (4.3) The average of recall and precision gives F1 Score
F1 = 2 x (Recall x Precision)/(Recall + Precision) (4.4) Table 2 Evaluation Parameters

Model	Accuracy	Precision	Recall	F1 Score	Roc – AUC score	Time(sec)
CNN 3 Layer	0.91	0.89	0.88	0.91	0.97	2450
CNN 6 Layer	0.93	0.90	0.90	0.92	0.983	3303
CNN 9 Layer	0.94	0.95	0.95	0.94	0.984	3397
ResNet50	0.95	0.90	0.90	0.90	0.99	2328

ROC – AUC score is a widely used evaluation parameter for binary classification. It is calculated with a true positive rate (TPR) and a false positive rate (FPR). A value near or equal to 1 is considered to be an excellent classification model, whereas a score below 0.5 indicates that the model is not able to classify between the classes.

As the number of layers increases, the time complexity of the model has also increased, All the CNN model has been trained for 20 epochs, but he ResNet model has been trained only till 6 epoch. When compared to the number of epoch ResNet has taken more time for training. The time complexity of these models is given by $O(n^4)$.

V CONCLUSION AND FUTURE SCOPE

This paper is about the comparison of different layered models based on CNN that has been analyzed and evaluated in various stages. From the above result, it is concluded thatthe ResNet50 model provides a better result in comparison with ResNet 101. The result from the CNN 9 layer is almost similar to the ResNet50 model. It is that increase inthe layer can provide better results whereas in this case CNN 9 layer and ResNet50 model differ with many layers but the result provided in both models is similar. From this, CNN 9 Layer trained model can provide a similar result as ResNet50 pre-trained model. Thus, few changes in the parameter of the model can provide complete accuracy of 1.0 is possible.Therefore, CNN 9 Layer properly trained model can be used to get a better result.

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The models generated will be of good use in faster and accurate prediction of Lymphoma in histopathological images. This will be useful for the medical purpose of early detection and diagnosis of cancer. It can be further improved by training it with the additional dataset, making it perform categorical predictions as there are more than seventy subcategories of lymphoma found. It could be made to predict and classify the type of cancer is present in the given slide. This project can also be extended for other medical-related predictions. With the development of a user-friendly application with the trained model, the usage of this project can be easily accessed around the globe.

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