IDENTIFICATION OF BREAST CANCER FROM HISTOPATHOLOGICAL IMAGES USING DEEP CONVOLUTIONAL NEURAL NETWORKS

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This Report Presented in Partial Fulfillment of the Requirements for the Degree of Bachelor of Science in Computer Science and Engineering.

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APPROVAL

This Project/internship titled **"IDENTIFICATION OF BREAST CANCER FROM HISTOPATHOLOGICAL IMAGES USING DEEP CONVOLUTIONAL NEURAL NETWORKS"**, submitted by Rima Akter (ID No:163-15-1101), Sadia Tanzin Neela (ID No:163-15-1108) to the Department of Computer Science and Engineering, Daffodil International University has been accepted as satisfactory for the partial fulfillment of the requirements for the degree of Bachelor of Science in Computer Science and Engineering and approved as to its style and contents. The presentation has been held on *date* .

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DECLARATION

We hereby declare that; this project has been done by us under the supervision of **MD REDUANUL HAQUE**, **Senior Lecturer**, **Department of CSE**, Daffodil International University. We also declare that neither this project nor any part of this project has been submitted elsewhere for award of any degree or diploma.

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ABSTRACT

Breast cancer symbolizes the disease of uncontrolled growth of cells of the breast. There are 2 most common kinds of breast cancers we know about, (1) “Invasive lobular carcinoma” and (2) “Invasive ductal carcinoma”. There are almost 1.3-1.5millions of patients alone in Bangladesh, who are affected by breast cancer. Every year almost 0.2millions of patients, newly diagnosed with breast cancer. Among these two, 80% of cases are Invasive ductal carcinoma. In this work, a deep CNN approach is proposed to predict Invasive Ductal Carcinoma (IDC) from histopathological data using “Convolutional Neural Network” which is a state of the art machine learning algorithm. We use Breast Histopathology Images (198,738 IDC(-) image patches; 78,786 IDC(+) image patches) taken from Kaggle. We took 3 transfer learning approaches using VGG16, Inception V3, Inception ResNet V2 and one without transfer learning approach. Their final training accuracies are 77%, 89% , 88.5%, and 87% respectively.

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CHAPTER 1

Introduction

1.1 Overview

The diseases produced by uncontrolled cellular growth, known as one of the dangerous diseases, is called cancer. There are different kinds of cancers that are present on earth. Breast cancer is one of the top cancers for women and it is the second main reason for the deaths of women in Asian countries and the United States. Once the cells within the breasts start to spread out of control, then the breast cancer begins. These cells are one kind of tumor and we can detect them on x-ray [10]. Once the tumor becomes malignant, the cells will begin to start expanding into other tissues or other parts of the body.

Breast cancer in Bangladesh continues to be a leading terrible cancer among women. It has become an invisible burden accounting for 69 percent of women's deaths. The breast cancer rate in Bangladesh is assessed to be about 22.5 per 100,000 females of all ages; in Bangladeshi women between the ages of 15 and 44, breast cancer has the highest prevalence of 19.3 per 100,000 when compared to other cancers [17].

1.2 Problem Definition

Invasive Ductile Carcinoma (IDC), also referred to as Infiltration Ductal Carcinoma, is a special type of cancer that starts to grow in a milk duct and invades the breast's fibrous or fatty tissue outside the duct. IDC is the most prevalent type of breast cancer, accounting for 80% of all diagnoses of breast cancer [18].

The main target of this study is to identify Invasive Ductal Carcinoma (IDC) positive cells from histopathology images.

Many engineering feature-based methods are proposed for the purpose of the classification of histology images of breast cancer with pattern recognition and machine learning. Other studies focused on nuclei segmentation described in [1] - [2] [3]. The histology images of breast cancer are classified into malignant and benign by firstly identifying the area of

interest, then a feature set is extracted, and traditional classifiers are trained by feeding these features. Most of these researches were based on small size data sets containing around 590 images. Other researches have focused on the extraction of local or global features from the full images. Zhang et al. concentrated on the application of statistics from the gray level of the co-occurrence matrix, and curvelet transform, and local binary patterns. They used a scheme with random subspace ensembles with options for rejects. For the 1st step, the authors attempted to solve simple cases, complex pattern classification systems are used in later steps for harder cases. These studies classified the samples into invasive carcinoma, carcinoma in situ, and normal tissue. In another study [5], the same authors used the same data (361 images) [4] to evaluate the one-class kernel principal component analysis (KPCA). Different features were fed into the one-class KPCA model for training, then a product combining rule was used for achieving the expected result. In [6], BreaKHis, a database of histology images of breast cancer, was constructed by Spanhol et al. This helped to resolve the primary challenge in developing new methods of analysis as Veta el al. has pointed out. Also, the authors provided a baseline pattern recognition system performance. This system was built for distinguishing between malignant and benign tumors.

1.3 Motivation

As breast cancer is one of the main reasons for deaths related to cancer in women, the classification and detection of this disease have become one of the main topics of interest in medical informatics research in recent years. Generally, a breast cancer diagnosis is initially detected via palpation and regular check-ups using ultrasound imaging or mammography. Then, if the diagnosis indicates unnatural tissue growth, it is followed by breast tissue biopsy. The only way to identify if anyone has breast cancer is by studying the tissue under a microscope. This biopsy mostly depends on the qualification of the histopathologists. If a histopathologist is not well-trained, a test might end in the wrong diagnosis. Most of the time lack of expert histopathologists results in keeping the tissue sample on hold for up to two months, this situation happens mostly in developing countries

and underdeveloped countries. Being histopathology a subjective science, there is also a problem of reproducibility. We can receive different diagnoses especially if the pathologists are non-specialized. So, there can be seen increasing importance for computer-aided diagnosis.

The "Convolutional Neural Network" is viewed as one of the standard deep neural networks (DNNs). A special type of neural network is introduced in this variant that compromises of the so-called convolution and pooling layers rather than fully connected hidden layers. CNN was first implemented for solving known problems of fully connected deep neural networks while managing structured inputs (such as images or speech) of high dimensionality. CNN became the state of the art solution for detecting and classifying objects on a large scale. In [7], the authors separated the histology images into smaller batches to train CNNs for breast cancer classification. The patches were later combined for creating the whole image to obtain the classification result.

In [8], CNN was also used by Araújo et al. to group the histology pictures into four groups: situ carcinoma, normal tissue, benign lesion, and invasive carcinoma. For training "Support Vector Machines" (SVM), the authors fed the extracted feature sets from CNN into SVM. In order to classify breast histology images into malignant and benign Bayramoglu et al. used "Convolutional Neural Networks" in [9]. Two architectures were proposed, one was implemented for predicting the malignancy, named "single task convolutional neural network" and "multi-task convolutional neural network" was implemented for predicting the magnification factor and the malignancy.

The poor situation in our country for diagnosing cancer and the advantages of the Convolutional Neural Network has motivated us to implement a CNN base classification system for classifying breast histopathology images.

1.4 Objectives

The recent development in deep learning and image processing accelerated the usage of histology images in breast cancer classification and diagnosis. This has also increased the necessity of developing diagnostic systems based on pattern recognition to help the

specialists for improving the quality of diagnosis. In this paper, we have proposed a comparison between multiple neural network architectures to detect breast cancer from histology images and their accuracy. We trained different architectures of CNN like Sequential, “Transfer Learning” approach using VGG16, Inception ResNet-V2 and, Inception V3. The objectives of our project are: (a) Training different architectures of CNN, (b) Monitoring their outputs and accuracy. (c) To observe how image augmentation affects performances. (d) To find out the best architectures with the best accuracy for detecting breast cancer using histology images.

CHAPTER 2

Literature Review

Kothari et al. [20] explored the effectiveness of biologically interpretable shape-based features for classifying histological pictures of renal tumors. Shape-based features were extracted that captured the tissue structure distribution in each image and then they employed these features within a multi-class classification model.

Doyle et al. [21] suggested an automated framework for separating between the high and the low grades of breast cancer from H&E-stained histology pictures. Together with spectral clustering, they employed a wide variety of image-derived features to decrease the feature space dimensionality. Subsequently, the feature set after reduction was used for training a "Support Vector Machine" classifier to differentiate among cancer and non-cancer images, and high and low breast cancer grades.

An award-winning deep learning system was suggested by Wang et al. [22] (at the International Symposium on Biomedical Imaging) for the purpose of whole-slide classification and cancer metastases in the lymph node pictures of the breast sentinel.

In another recent study [8], a "Convolutional Neural Network" based method was suggested to identify H&E-stained breast histopathology pictures into 4 types of tissue: benign, intrusive carcinoma, in situ carcinoma, and healthy tissue with a small number of training examples. The CNN-extracted features were then used to train a Support Vector Machine classifier. Accuracy of 77.8 percent was obtained for the classification of 4 classes. Also, the accuracy of 83.3 percent was obtained for the classification of non-carcinoma/carcinoma.

Litjens et al. [23], in their research used a deep network for delineating Prostate Cancer with 128*128 pixel histopathology image patches at 5x magnification.

CHAPTER 3

Methodology

3.1 Convolution Neural Network (CNN):

Deep learning is part of a larger machine learning family based on artificial neural networks with representational learning [11]. The working principle of artificial neural network or ANN is inspired from the structure and function of the neurons of the brain. A convolutional neural network (CNN) is a class of ANN or artificial neural network which is mainly used in visual imaging research. Biological processes in the animal visual cortex inspired the invention of convolutional networks. The way neurons are connected to each other in CNN, resembles the structure of the visual cortex in the animal body. Each individual cortical neuron only responds to stimulus in a small area of the field of vision known as the receptive zone. The receptive fields of various neurons partially overlap in such a way that they cover the whole field of vision [12].

A convolutional neural network (CNN) could be used for the gradual extraction of higher and higher-level image content representations. Rather than pre-processing the images in order to extract features such as shapes and textures, a CNN uses only the raw pixel data of the image as input and figures out how to derive these features and finally deduce what object they are. CNN takes an input image as a three-dimensional matrix where the first two dimensions represent the length and width of the images. The size of the third dimension is three (it represents 3 color channels: green, red, and blue). The CNN includes a stack of modules, each performing three types of operations [13].

In the convolution neural network, there are several types of layers. They are the Convolution layer, the Pooling layer, and the fully connected layer.

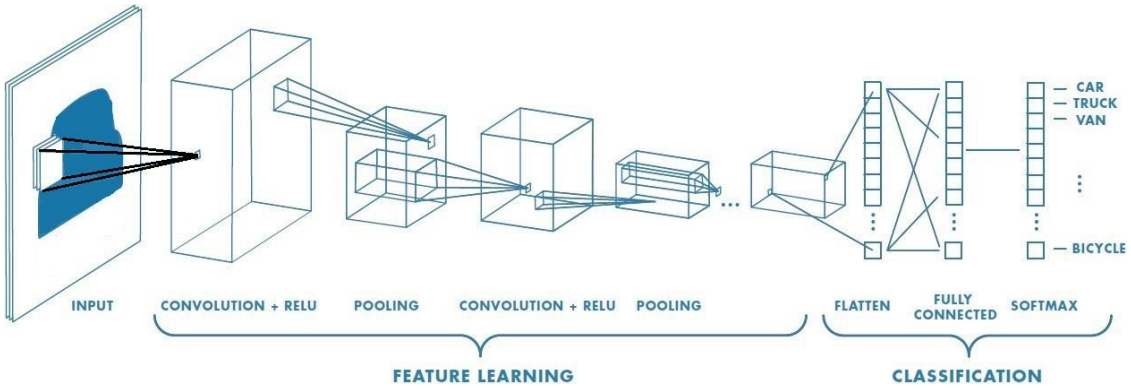

Fig 3.1: Basic Convolutional Neural Network

3.1.1 Convolution Layer: It is the Convolution Neural Network's main building block. This particular layer extracts different features such as edges, color, gradient, etc from input images.

Convolution is a simple mathematical operation. First, we start with a kernel matrix. This kernel matrix “slides” over the input matrix (image pixel data are represented as a matrix), and then an elementwise multiplication operation is performed with the part of the input matrix it is currently on, and then adding up the results into a single value which is the output pixel. The kernel keeps repeating this step for each position it slides over, converting the feature matrix into another feature matrix. An example of the convolution operation is shown in figure 3.1.2.

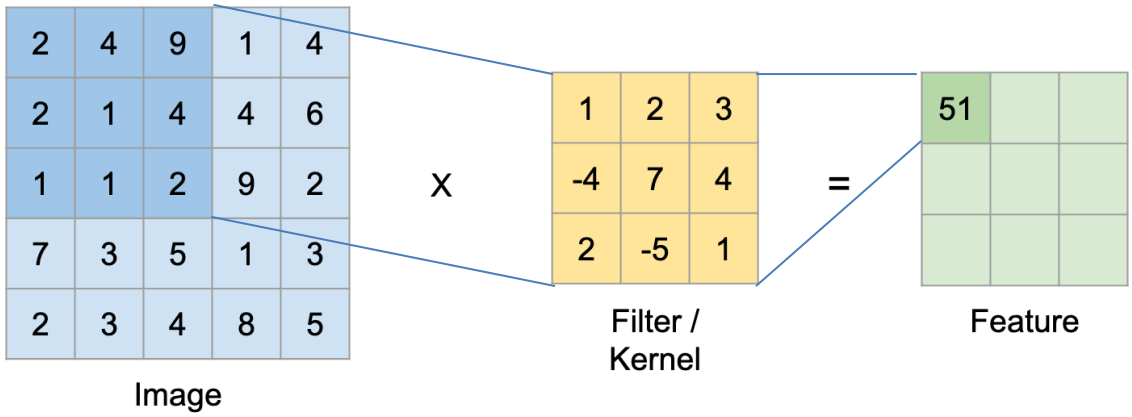

Figure 3.1.1: Convolution Operation

By changing the kernel, different features can be extracted. For example, an image can be focused, enhanced, blurred by applying different kernels.

The convolution operation is completed by moving the filter kernel into the input vector. In order to achieve the feature map, element-wise matrix multiplication is done and the result is computed.

There are three hyper-parameters are being used in the convolution layer.

3.1.2 Stride: During convolution, the filter is slide over the image. Stride is the number of pixels, the filter slides each time. Usually, the filter slides one pixel at a time. But when said 2 strides, the filter slide two-pixel at a time. For 1 stride, the effect is shown in fig:3.1.3

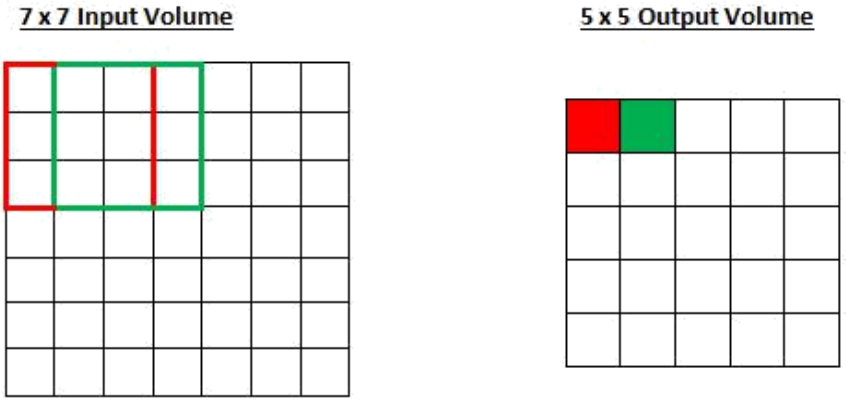

Fig: 3.1.2: Effect of stride 1

3.1.3 Depth: In Convolutional Neural Network, convolution is done in a 3D region. In the case of an image, 3D represents height, width, depth. Depth is the color channel in an image. For color images, the color channels are red, green, and blue. For a grayscale image, it is a 2D image that doesn't comprise of depth. Neurons of the input region in a convolutional layer produce the depth of the output volume within the same layer. The total number of inputs of the network can be minimized by decrease the depth.

3.1.4 Zero Padding: During convolution operation, the edges of the matrix get trimmed off. A feature matrix with a dimension of 7*7 becomes a matrix of 5*5. The edge pixels

are never at the center of the kernel because the kernel does not have anything to extend beyond the edge. This is not ideal, as the output size is often needed to equal the input. A clever solution is padding. The technique is to pad the edges with extra zero value "fake" pixels. This is why it's called "Zero Padding". By padding, the output size becomes as same as the input size.

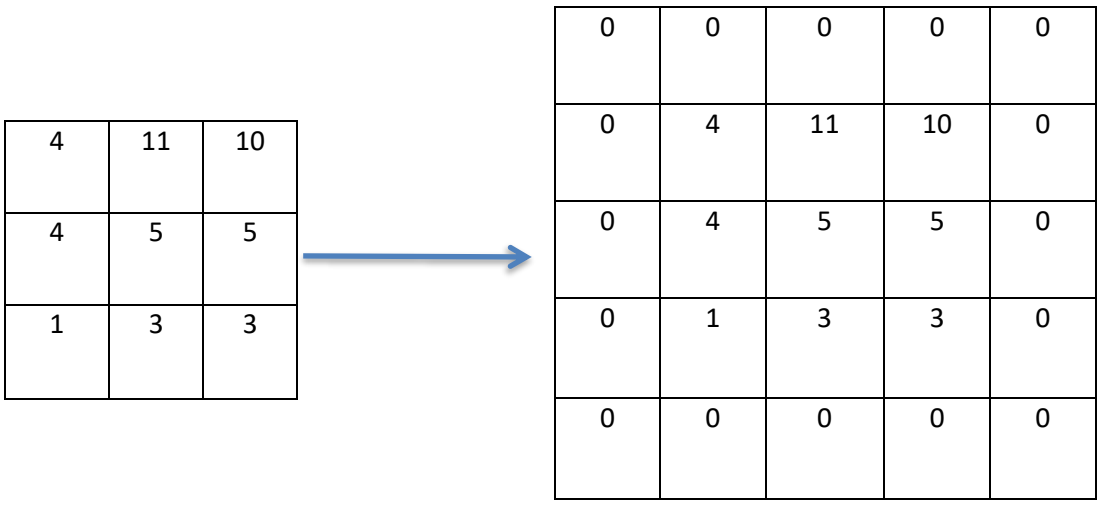

Fig3.1.4: Example of Zero Padding

3.1.5 Rectified Linear Unit(ReLU):

ReLU stands for "Rectified Linear Unit". The rectified linear unit is an activation function. It is a non-linear activation function. In the field of deep learning, it has achieved popularity.

In a neural network, when using ReLU, if the input is less than zero the neuron stays deactivated. A neuron will only activate when the input value is higher than or equal zero.

ReLU can train faster than other activation functions. ReLU solved the 'vanishing gradients' problem caused by sigmoid and tanh function.

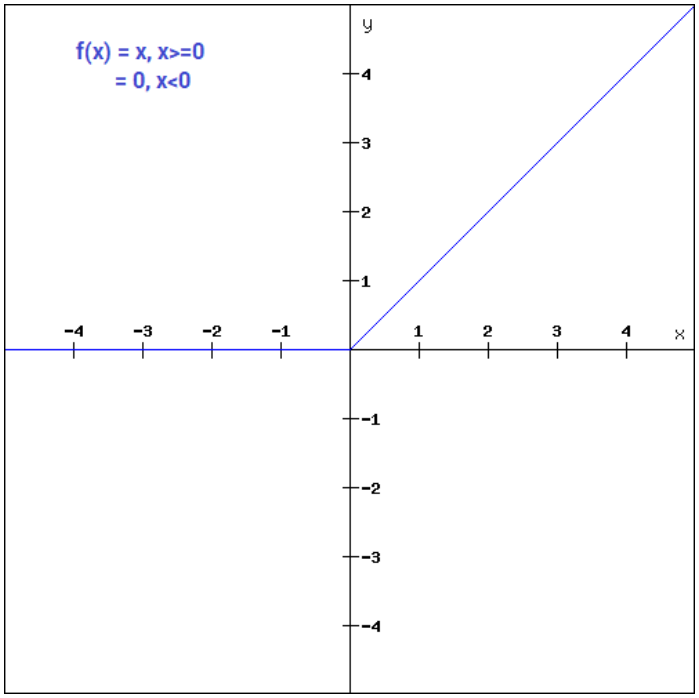

Fig3.1.5: ReLU Function Illustration

The main benefit of the ReLU activation function instead of using other activation functions is that it doesn't activate all neurons at the same time.

The disadvantage is it makes some neurons dead neurons. These neurons never active again.

3.1.6 Pooling Layer:

One important building block of CNN is the pooling layer. It effectively reduces the size of the image. Thus, reducing the parameter and size of the networks. There are mainly two types of pooling layer. One is max pooling and another one is average pooling. Max pooling is more popular.

An example of pooling is given in the following figure-3.1.6 and figure-3.1.7.

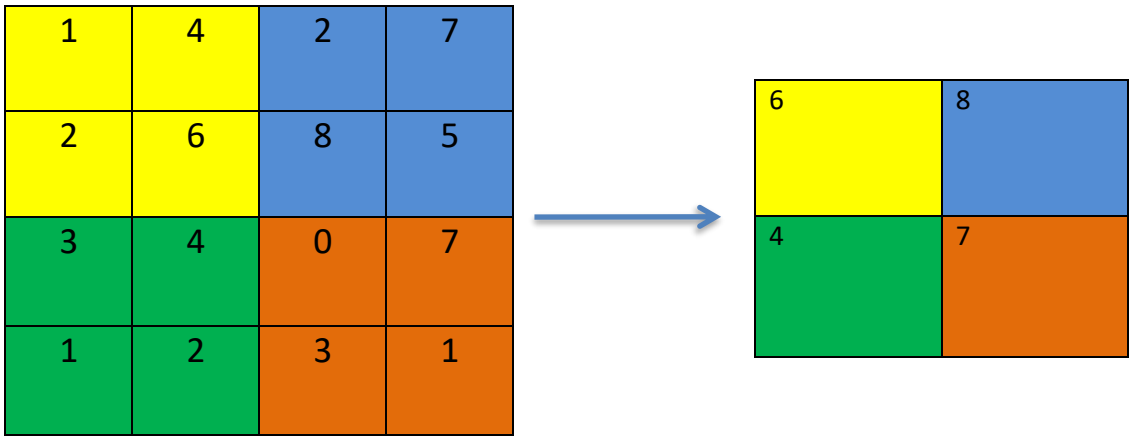

Figure 3.1.6.1: Example of max pooling for 2x2 filter and stride 2

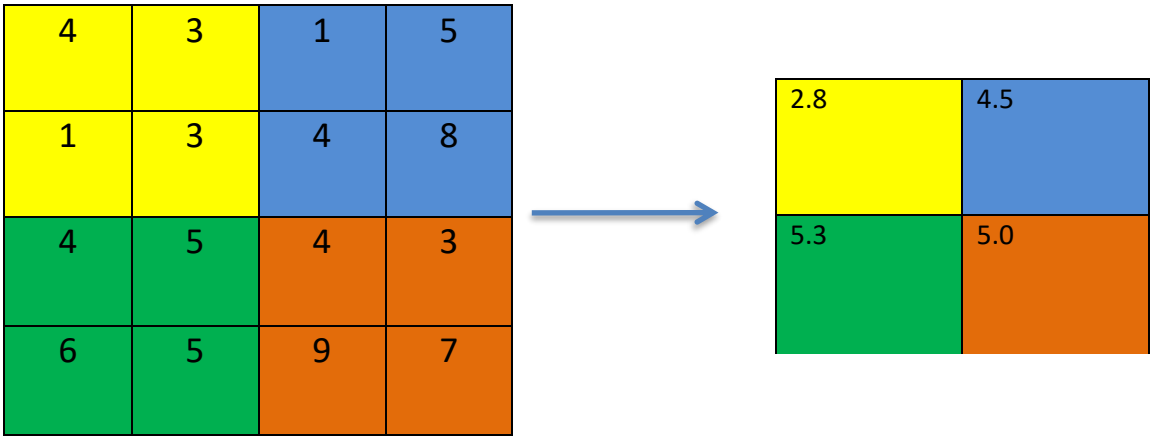

Figure 3.1.6.2: Example of Average Pooling for 2x2 filter and stride 2

3.1.7 Fully-Connected Layer:

In CNN, the end layer is a fully connected layer. In a fully connected network, each neuron of one layer is linked to each neuron of the subsequent layer. This layer is essential for classifying and recognizing images. The following figure-3.1.7 represents the fully connected layer structure.

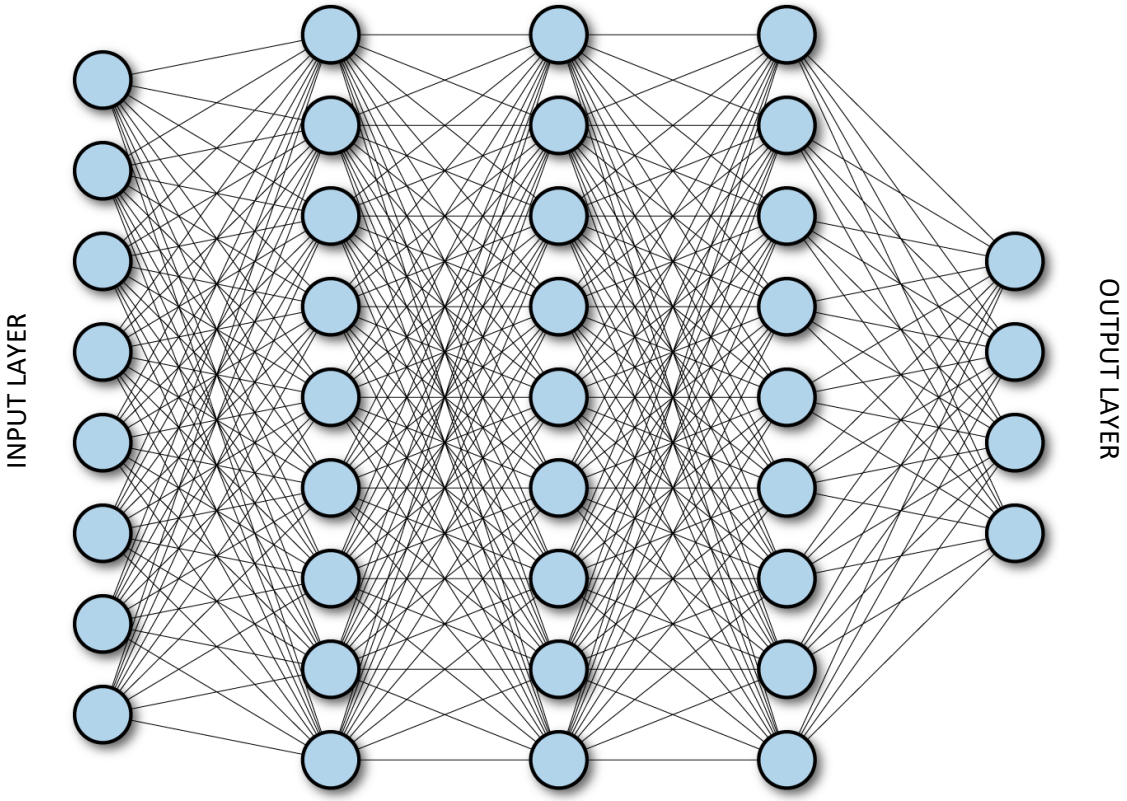

Figure 3.1.7: Fully Connected Deep Neural Network

In the last output layer, for binary classification, the sigmoid activation function is used. The softmax activation function is used in the case of multi-class classification.

3.2 Transfer Learning:

Transfer learning is a research area in the field of machine learning(ML) which emphasizes on the gained knowledge stored while finding the solution of one problem and apply it to another problem but related to the previous one [14].

In transfer learning, at first, a base-network is trained on a base dataset and task, and then the features learned from the task were repurposed or transferred to another network to be trained on a different dataset and task. The method will work if the features are common for both cases, which means that the features are suitable for both the basic and the target tasks, rather than the base task-specific. [15].

There are many pre-trained neural networks. Such as VGG16, VGG19, ResNetv2, Inception V3, etc. These models are trained on millions of images. These models are capable of extracting different features that are almost impossible if we train a new network from scratch. Also training a neural network is a time-consuming and heavy computational work. Ordinary computers are not fast enough to train large networks quickly and suitably.

Using transfer learning can solve this problem. A pre-trained artificial neural network(ANN) can be used for extracting features from images. So, using a pre-trained model with our classifier can result in an effective classifier.

Different pre-trained neural networks are described below.

3.2.1 VGG 16

VGG-16("Visual Geometry Group"- University of Oxford) was first proposed by K.Simonyan and A. Zisserman. Mainly it has 16 layers with 13 convolutional and 3 fully connected layers. About 138M parameters are used in this architecture. The most significant things are the accuracy of this architecture was 97.2% in imageNet.

The input image size of VGG16 is 224*224 and the image is RGB. [16]

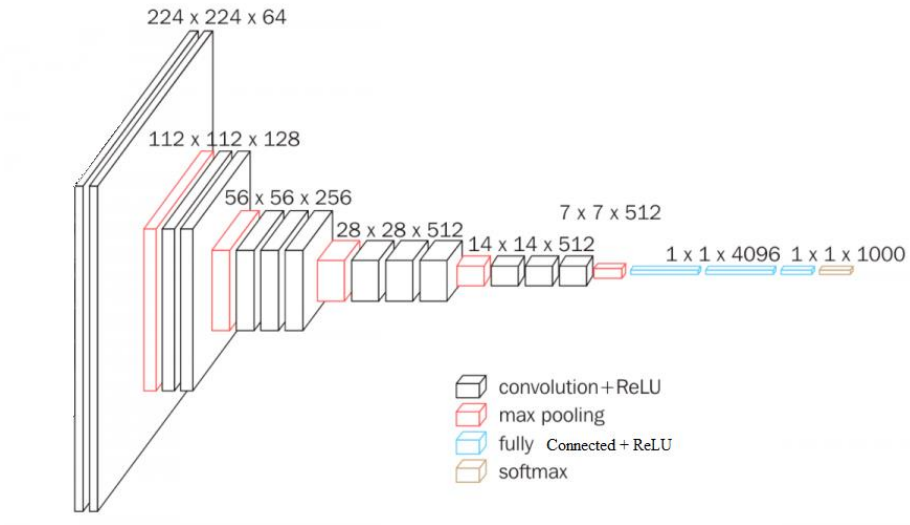

Figure 3.2.1: VGG16 Architecture

3.2.2 VGG19

VGG-19 is a trained Convolutional Neural Network developed by **V**isual **G**eometry **G**roup, Department of Engineering Science, University of Oxford. The number 19 stands for the number of layers with trainable weights. 16 Convolutional layers and 3 Fully Connected layers. Millions of images were used in order to train the VGG-16 neural networks.

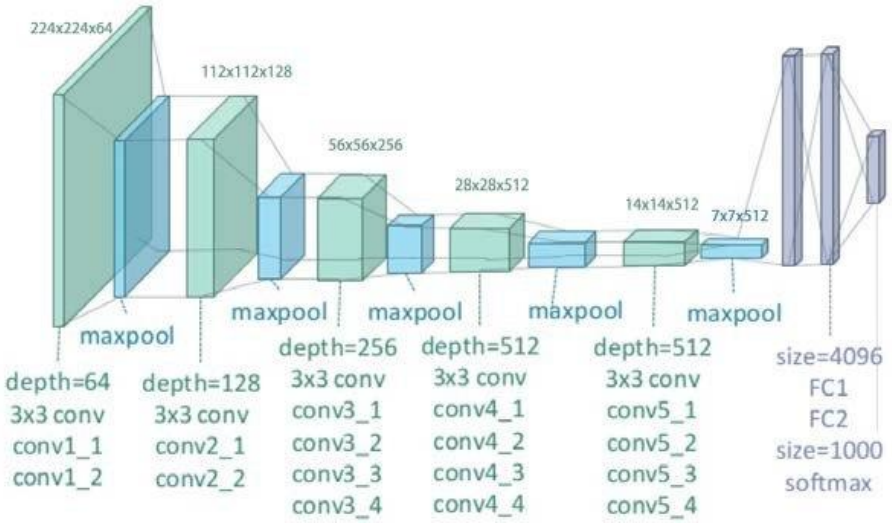

Figure3.2.2: VGG19 Architecture

Both VGG-16 and VGG-19 is trained for classifying 1000 different types of object. Their accuracy is pretty good. But they soon became obsolete as more computing efficient and better neural networks such as inception v3, ResNet, etc. were introduced.

3.2.3 Inception V1

Inception V1 also known as GoogleNet is a convolutional neural network with 22layers(27 including the pooling layers) and 5M parameters. It is a very deep classifier. As with other very deep neural networks, the vanishing gradient problem is a key weakness.

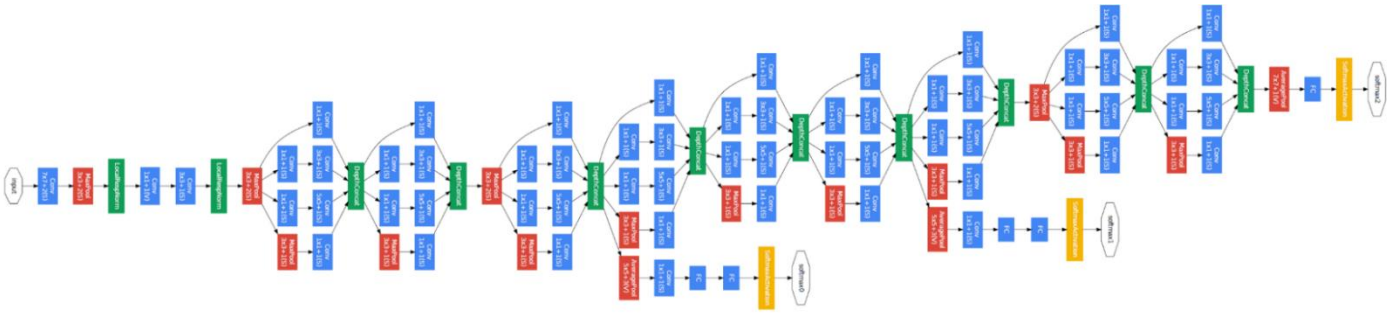

Figure 3.2.3: Inception V1 Architecture (left to right)

Inception V1 has 9 stacked inception module. Its top-5 error rate is 6.67%.

Inception V1 also requires less computation power. Its total network parameter is 7M which is much lesser than AlexNet with 60M parameters and VGG16 with 138M parameters and VGG19 with 144M parameters and ResNet50 with 25.6M parameters.

3.2.4 Inception V3

Inception V3 is an improvement over Inception V1. About 24M parameters are used here. In Inception V3, factorized 7x7 convolution is used.

Though the Inception V3 has a depth of 42 layers, the computation cost is about 2.5 times higher than that of GoogLeNet. Inception V3 has an efficiency that is better than that of VGGNet. It's top 5 error is 5.6% and the Top-1 error is 21.2%.

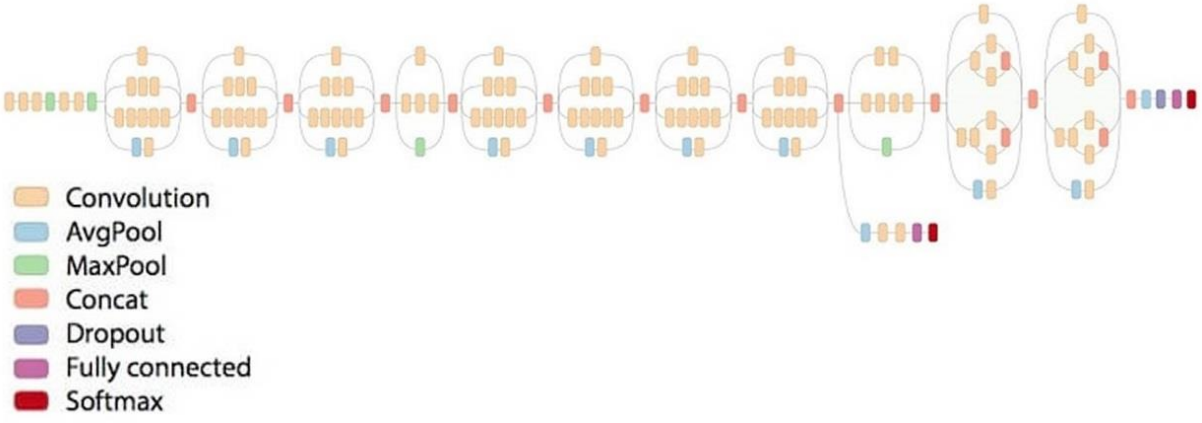

Figure 3.2.4: Inception V3 Architecture

3.2.5 ResNet-50

ResNet-50, A very deep network is 50 layers deep with 26M parameters. Trained on millions of images from the ImageNet dataset, it can classify images into 1000 categories. It has an input image size of 224*224.

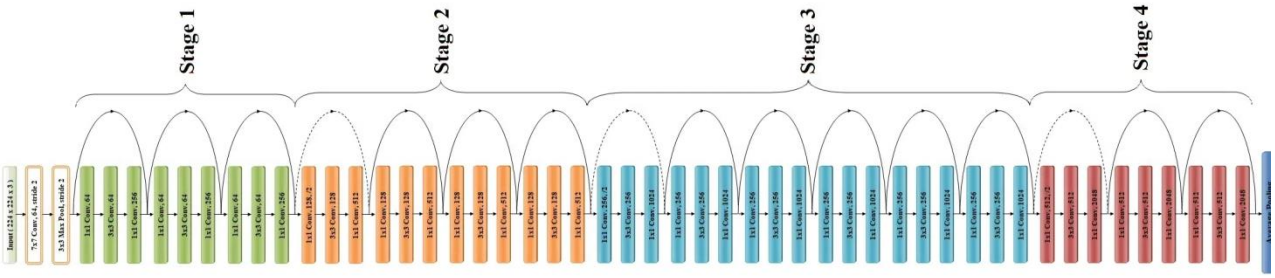

Figure3.2.5: ResNet-50

3.2.6 Inception V4

InceptionV4 is a more uniform simplified architecture with more inception modules than Inception-v3. It has 5% top-5 error and 20% top-1 error. The architecture of Inception-V4 is described below.

Schema of the inception V4 is

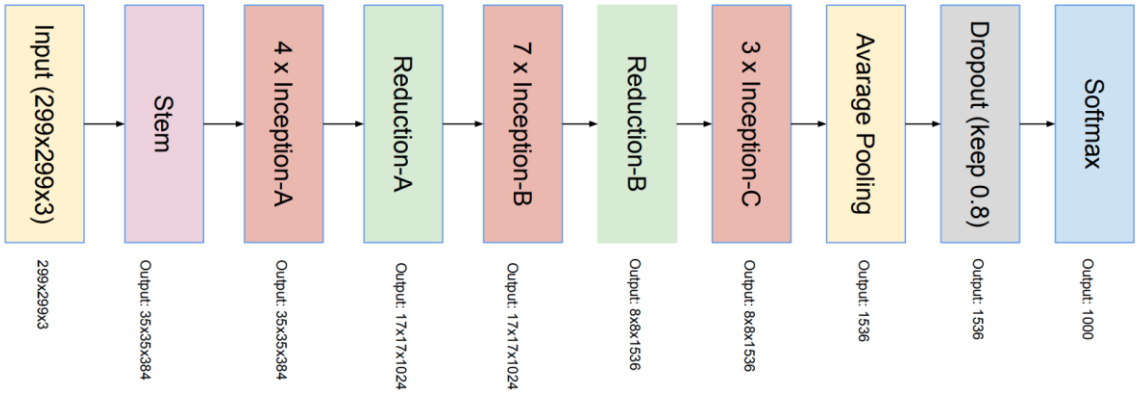

Figure 3.2.6.1: Schema of the inception V4

The schema for stem in inception V4 is

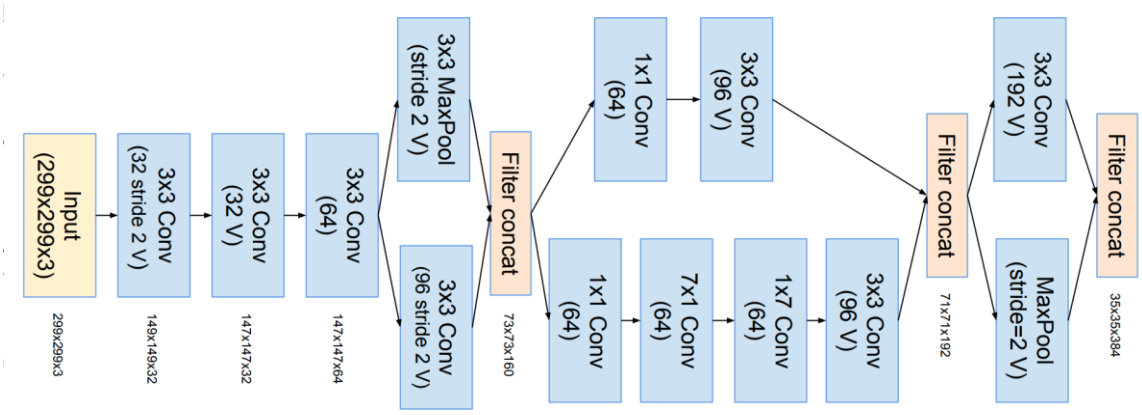

Figure 3.2.6.2: The schema for stem in inception V4

The schema for Inception A,B and C module:

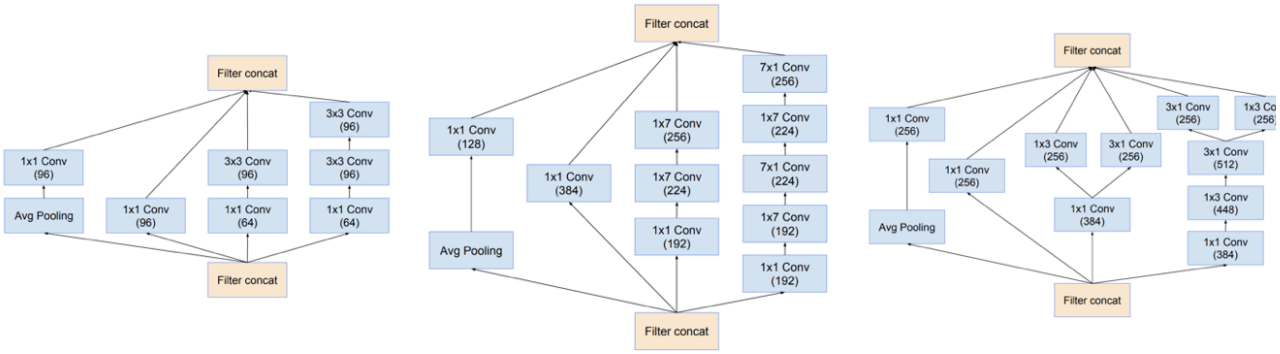

Figure3.2.6.3: The schema for inception A , B , C modules of Inception V4

Reduction module of Inception V4

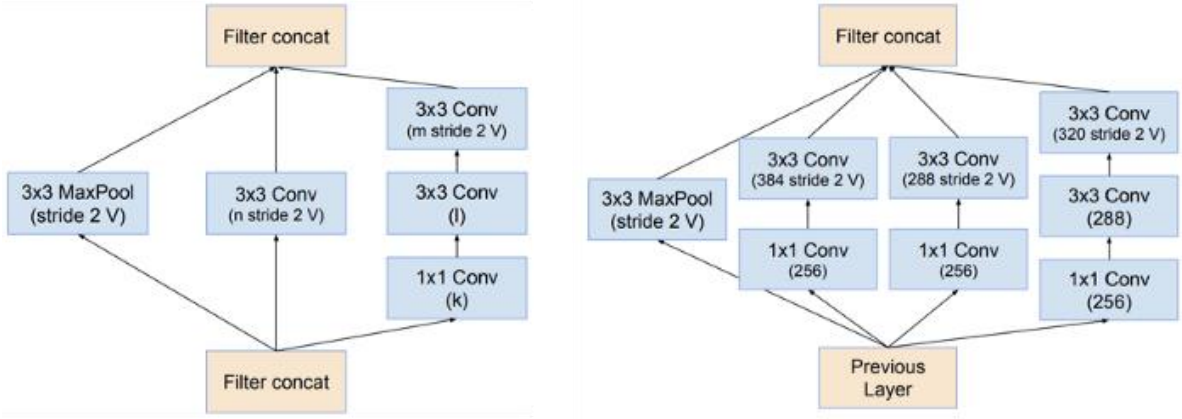

Figure3.2.6.4: Reduction Module of Inception V4

3.2.7 Inception Resnet-V2

It is another deep neural network with a Top-5 error of 4.9% and a Top-1 error of 19.9%. Inception ResNet-V2 is computationally similar to Inception-V4 but achieved higher accuracy in lower epoch. It has 56M parameters. Its training cost is less than Inception-V4.

The architecture is described below.

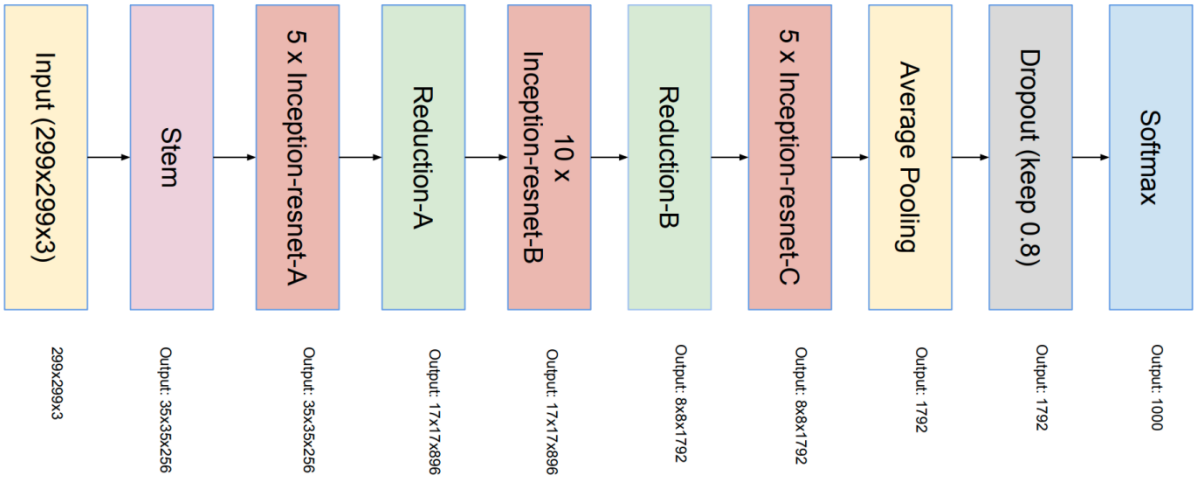

Figure 3.2.7.1: Schema of the Inception ResNet-V2

Schema of the stem module of Inception ResNet-V2

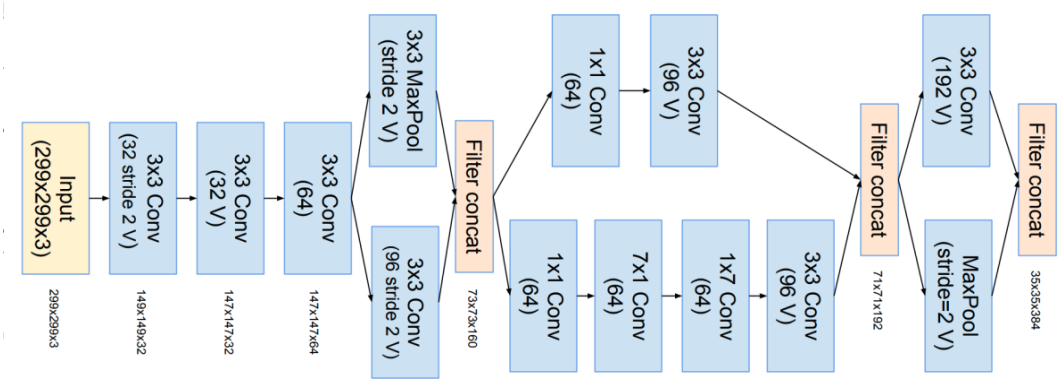

Figure 3.2.7.2: The schema for stem in inception ResNet-V2(Similar to Inception V4)

Schema of Inception-Resnet A, Inception-Resnet B and Inception-Resnet C modules

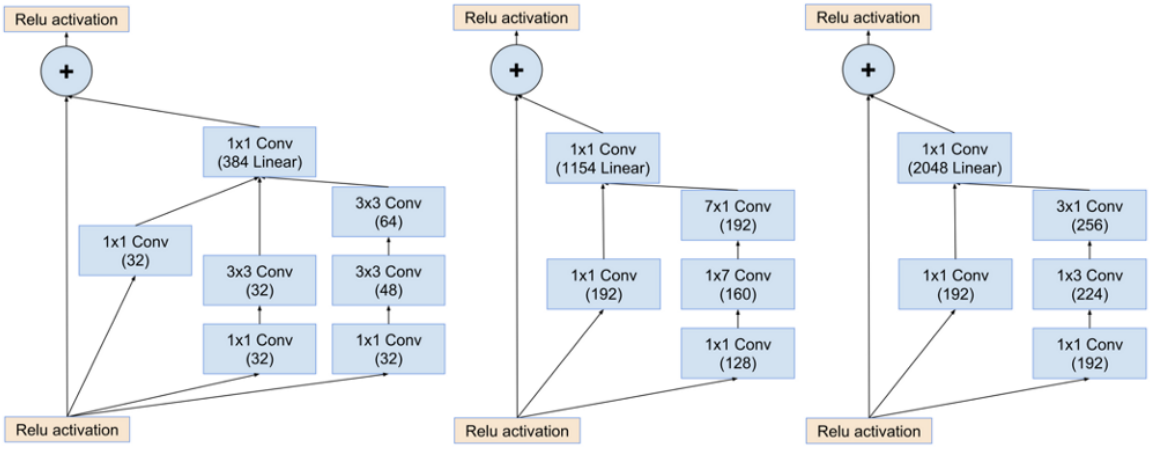

Figure 3.2.7.3: Schema of Inception-Resnet A, Inception-Resnet B and Inception-Resnet C modules

Reduction Module A and B

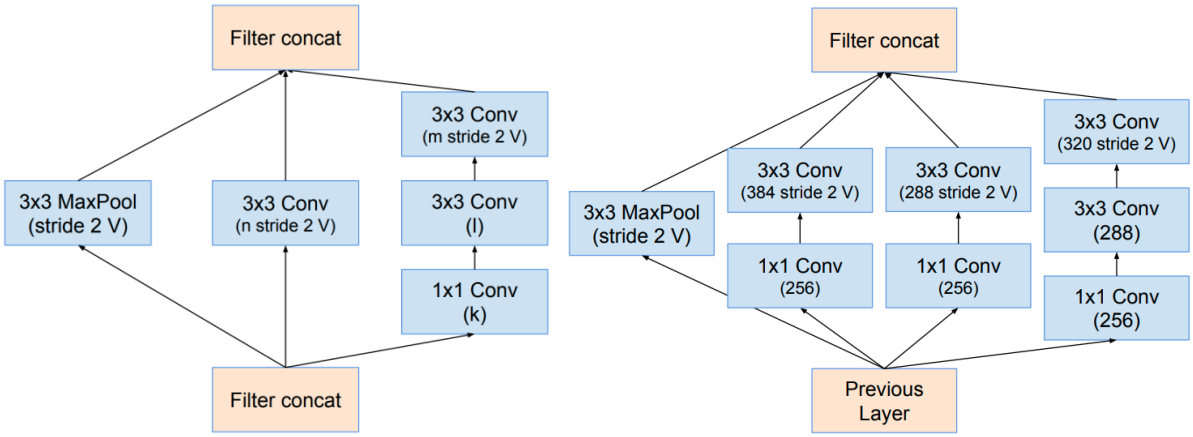

Figure 3.2.7.4: Reduction Module A and B of Inception ResNet-V2

CHAPTER 4

Implementation and Result Analysis

4.1 Dataset Description:

The original dataset has 162 whole mount slide images of Breast Cancer Specimens. These images were scanned at 40x zoom. From these images, 277,524 patches of size 50 x 50 were extracted (78,786 IDC positive and 198,738 IDC negative). The dataset is downloaded from kaggle[19]. It is published under "CC0 1.0 Universal Public Domain Dedication" license. So the dataset can be used for any purpose without asking permission.

90%of the images from the dataset is used for training and 10% is used for the purpose of validation.

Sample images from the dataset:

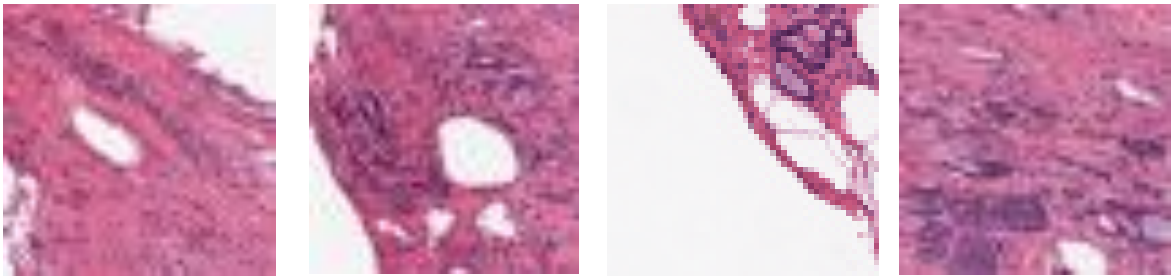

Figure4.1.1: IDC negative images from the dataset

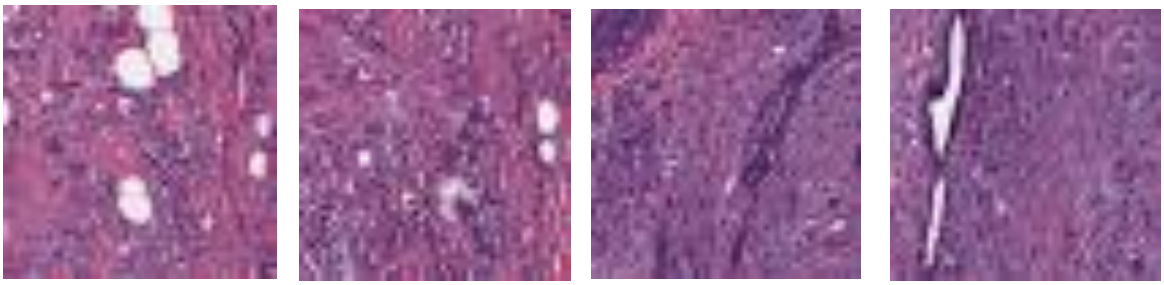

Figure4.1.2: IDC positive images from the dataset

4.2 Experimental Results and Discussion:

We developed our own neural network as well as we used the transfer learning approach. We proposed three different architectures for transfer learning. They are VGG16, Inception V3, InceptionResNetV2. In the case of transfer learning, we trained all the models from scratch as we have sufficient data. We also used Image augmentation to increase data.

The final training accuracy comparison of different models is compared in the following Table-4.2.1.

Table 4.2.1: Training Accuracy comparison of different models

Architecture	**Accuracy**
VGG16	77%
Inception V3	89%
InceptionResNetV2	88.5%
Without transfer Learning	87%

In our experiment, we have seen that the model without transfer learning and transfer learning with VGG16 performs very poorly. We tried to tune different hyper-parameters. But these models have shown clear signs of over-fitting during training. But Inception ResNet-V2 and Inception V3 performs quite well. Further comparative analysis of the accuracy of all the models is given in Table 4.2.2.

Table 4.2.2: Comparative analysis of All proposed model(For detecting Invasive Ductile Carcinoma(IDC))

		Precision	Recall	F1-Score	Accuracy
Inception V3	IDC_NEG	0.87	0.96	0.91	0.87
	IDC_POS	0.87	0.63	0.73	
Inception-ResNet-V2	IDC_NEG	0.90	0.94	0.92	0.88
	IDC_POS	0.83	0.73	0.78	
VGG-16	IDC_NEG	0.78	0.95	0.86	0.78
	IDC_POS	0.72	0.34	0.46	
Without Transfer Learning	IDC_NEG	0.72	0.73	0.72	0.60
	IDC_POS	0.29	0.28	0.28	

The confusion matrices of all the models are given below.

Table 4.2.3: Confusion matrix of Inception-V3(For detecting Invasive Ductile Carcinoma(IDC))

Confusion matrix of Inception-V3			
		Predicted	
		IDC_NEG	IDC_POS
Actual	IDC_NEG	19128	746
	IDC_POS	2913	4966

Table 4.2.4: Confusion matrix of Inception-ResNet-V2(For detecting Invasive Ductile Carcinoma(IDC))

Confusion matrix of Inception ResNet-V2			
		Predicted	
		IDC_NEG	IDC_POS
Actual	IDC_NEG	18712	1162
	IDC_POS	2155	5724

Table 4.2.5: Confusion matrix of VGG-16(For detecting Invasive Ductile Carcinoma(IDC))

Confusion matrix of VGG-16			
		Predicted	
		IDC_NEG	IDC_POS
Actual	IDC_NEG	18819	1055
	IDC_POS	5187	2692

Table 4.2.6: Confusion matrix of Without-Transfer-Learning(For detecting Invasive Ductile Carcinoma(IDC))

Confusion matrix of Without-Transfer-Learning			
		Predicted	
		IDC_NEG	IDC_POS
Actual	IDC_NEG	14413	5455
	IDC_POS	5704	2175

From the confusion matrix, we can see that InceptionResNetV2 performs better when detecting cancer positive images. When compared to Inception-V3, ResNet-V2 is less biased towards IDC negative images. Other models perform very poorly.

Chapter - 5

Conclusion and Future Scope

5.1 Conclusion:

We have implemented multiple transfer learning approaches in our problem. The performance of each model was evaluated. Their performances were then compared. At first, their accuracy was measured. All of them were further evaluated. Inception-V3 and InceptionResNet-V2 were the most promising ones. The Inception-V3 has higher accuracy. But the confusion matrix showed that it is biased towards IDC negative images. Inception ResNet-v2 produces a much better result in this regard. It is less biased and more generalized model. The other 2 models perform quite poorly.

5.2 Limitation

The main limitation is the lack of a high-performance computer. Though "Google Colaboratory" is used for training purposes, it is not sufficient. It took over 8 hours for each training. And each of these models requires many training, sometimes 20 or more training for tuning hyperparameters. That means a single model requires at least 160hours of training. The training 5 model was very difficult because of this.

5.3 Future Scope

The future endeavor of this research is to improve the accuracy of this model as well as collecting data on other types of breast cancers and include those in these models. Also implementing this model in software that can be easily used by an operator with limited knowledge to diagnose IDC in the laboratory for rapid detection of breast cancer is also another research scope.

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