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DEEP LEARNİNG ARCHİTECHTURE FOR CLASSİFİCATİON OF BREAST CANCER CELLS İN FLUORESCENCE MİCROSCOPY IMAGES

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Abstract: Biological cell classification plays a significant role in the field of biomedical research. Cell classification is useful in different biomedical applications like identification of a normal and abnormal cell, cancer cell recognition, behavioural studies of cells to different drugs, etc. Automated cell classification techniquies would assist the radiologist for the disease diagnoses and to grasp the severity of the disease based on the intricate intracellular structures of the cells. In this work, a deep learning method based on EfficientNet is designed for automatic classification of human breast cancer cells from fluorescence microscopy images. More specifically, transfer learning is employed to take the advantage of the pretrained model and further improvising the performance of the network by fine tuning several of last layers for learning the specific classification task. The proposed deep learning method is evaluated on human breast cancer cells, which gave 98.15% accuracy, 98.33% precision, 98.15% recall and 98.14% F1 score. Comparitive analysis of the proposed method with the standard architectures is also performed to assert the efficacy of our model.

Keywords: deep learning; cell classification; microscopy images; EfficientNet

I. INTRODUCTION

According to GLOBOCAN 2020 estimation, there are approximately 19.3 million recently found cancer instances and almost 10.0 million cancer deaths in 2020. Also, the occurance of female breast cancer has increased with an predicted 2.3 million new instances[1]. Breast cancer occurs when the cells within grow erratically, leading to the development of a lump in a particular area of the breast. For malignant cells, the intracellular actin filaments are altered due to unusual growth of tumor cells and the ability of them to invade sorrounding tissues [2]. Hence classifying various types of cells based on their intracellular structure would pave the way to understand the various biological behaviours and aid as additional diagnostic marker. However, manually classifying intracellular cell structures is a difficult procedure and may not yield high accuracies due to certain challenges like varying cell topologies, difficult to identify different cell structures by a human eye, etc. This suggests the need for automatic cell classification algorithms. Hence in this article we explore the application of breast cancer cell categorization based on fluorescence microscopy images. Specifically these images are actin-labelled breast cancer fluorescence microscopy images so as to visualize the intracellular structures and hence they can be analysed. Currently deep learning models are giving excellent performance in computer vision, due to this reason in this work we investigate breast cancer cell classification task using contemporary deep learning models.

EfficientNet [3][4], is the more recent convolutional neural network(CNN) model which gave much higher performance than all its prior models in classification task. Hence we focus on utilizing the pretrained EfficientNet architechture and perform transfer learning(TL) for the task of effective classification of breast cancer cells. The significant addition of this experimentations are summarized below:

- Utilizing pre-trained EfficientNet deep learning model, we perform transfer learning for effective classification of breast cancer cells based on actin labelled fluorescence microscopy images.
- We perform the comparitive analysis of the proposed method with some standard methods and prove its efficacy.

The organization of the remaining article is presented in this manner. Section II depicts the related work. Section IIIpotrays the methodology, Section IV illustrates the results obtained. Section V mentions the conclusions which is followed by the references.

II. RELATED WORK

In article [5], they have demonstrated that at a fraction of the cost, classification based on imaging techniques enable morphological characterization and investigation of huge number of individual cells. Additionally, they have shown the statistical significance necessary to comprehend how cell heterogeneity affects many biological applications, such as the development and validation of drug candidates and cancer screening. They have designed a single cell classification framework with deep convolutional neural networks (DCNN). In [6], convolutional neural networks(CNN) and XGBoostare used for multi-class classification architecture for breast pathology images. In [7], they demonstrated an ensemble deep learning solution for the categorization of breast cancer images. They created a significantly more robust model by using an ensemble of improved VGG-16 and VGG-19 models. The article [8] is evaluation of several CNN architecture performance in the computerized automated Invasive Ductal Carcinoma (IDC) grading application. Using transfer learning, the Four-Breast-Cancer-Grades (FBCG) dataset was divided into the following four grades: fromgrade 0 to grade3. In [9], they offer adeep neural network model for the categorization of cell nuclei and non-nuclei in breast cancer cell histopathology

images. In [10] they have investigated multi-labelcategorization for breast cancer in histopathology images and introduced the class structure-based deep convolutional neural network (CSDCNN) model, which has achieved reliable and accurate recognition. In the article [2], a large collection of actin-labelled fluorescence microscopy images were collected and VGG-16 [11] based Deep Neural Network is trained using transfer learning to classify three types of breast cancer cell lines.

III. METHODOLOGY

A. *Dataset*

The dataset for the current research is available in [2]. The dataset consists of a singlenon-cancerous human breast epithelial cell line (MCF-10A, nonaggressive) and two harmful cancerous epithelial cell lines of human breast (MCF-7, less aggressive and MDA-MB-231, more aggressive). The entire dataset consists of confocal immune fluorescence microscopy image consisting of larger than 1500 cells with visible actin filaments network. Studies in[12] reveal that modifications in actin filaments are related to the cause of cancer. Therefore, the organization of actin filaments could be a leading source of insight into biological behaviour of cell. The three different cell lines of the dataset is shown in Figure 1, which clearly indicates the difference in the cell structures for the three classes.

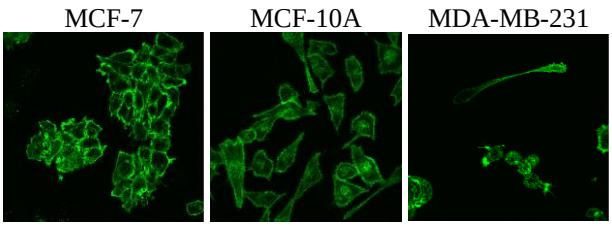


Figure 1: Sample images from breast cancer cell dataset

B. *Data Preprocessing*

The original images are resized to 224 x 224 pixels. Image normalization is done by dividing each pixel value in each channel by 255, so that pixel value in each channel is in the range 0 to 1. Data augmentation is done by using Keras ImageDataGenerator module. By increasing the quantity of training data, data augmentation helps to boost the model's training accuracy and decrease over-fitting. To expand the dataset size, data augmentation techniques such as flipping, zooming, shearing, width shift, height shift, and rotation are applied to the source images.

C. *Proposed Model*

The proposed system workflow is depicted in Figure 2. In this work pre-trained EfficientNetV2-B0 [4] from Keras applications module is utilized. This network is trained on ImageNet [13] image classification challenge dataset which consists of 1000 classes.

D. *Model Architecture*

This work focus to use the pre-trained EfficientNetV2-B0 architecture. EfficientNet is a family of models which consists of EfficientNet-B0 to EfficientNet-B7 having increasing number of layers and complexity. EfficientNet utilizes compound-scaling technique for building an effective deep learning architecture.In this technique, width of the network, depth of the network and resolution of the image is scaled up in a systematic way to obtain improved model accuracy and efficiency. EfficientNet model is based on neural architecture search [14], where the ideal architecture is found inside a given space. EfficientNetV2 [4] overcomes certain limitations of EfficientNetV1[3] with smaller amount of parameters and faster training. EfficientNet-B0 is shown in Figure 3. EfficientNet is a state-of-the-art model which gave significant improvement in the performance than all the previous models.

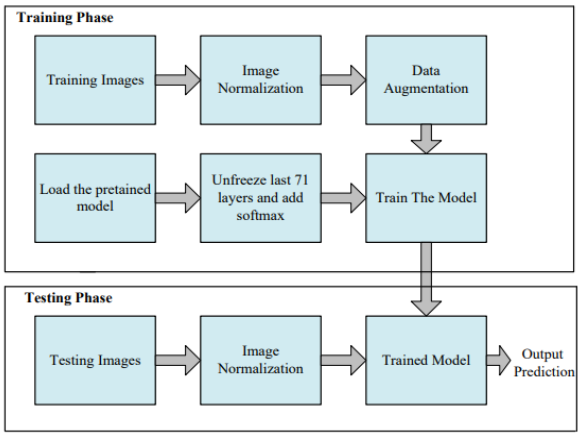


Figure 2:Deep Learning Framework used in our work.

E. *Transfer Learning*

Transfer learning (TL)uses a pre-trained model, trained using a huge, labelled dataset before applying the learnt weights to newsimilar tasks inside the similar architecture. It eliminates the need of training the model from initial point with random weights, by treating the model as a beginning point in the training of the objective task. In TL, the final layers needto be adjusted to the desired number of categories before being fine-tuned on the desired dataset. According to literature, using TL increases performance when compared to building a model from initial random weights on a limited dataset. Additionally, TL improves generalisation, cuts down

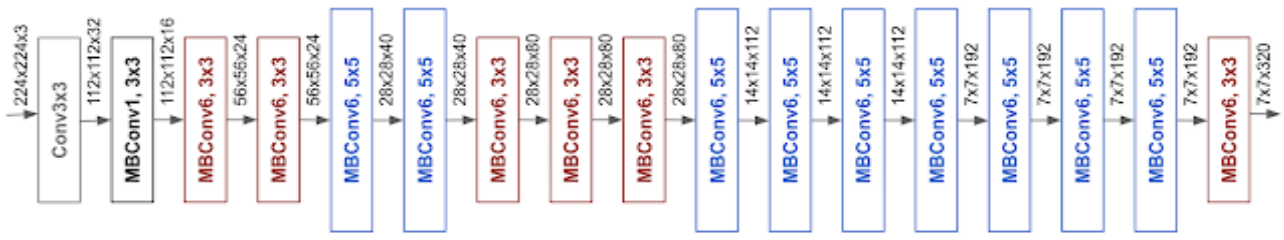


Figure 3: Architecture of Baseline EfficientNet-B0 [15]

on overfitting, training time, and requires less labelled data. Recent years have seen extensive use of TL in computer vision[8][16][17].

In this work EfficientNetV2-B0, consisting of 271 layers, pre-trained on ImageNet dataset is utilized. Weights of the first two hundred layers are frozen, whereas the next 71 layers are unfrozen. In the final layer three neurons followed by a softmax activation function is utilized to categorize the input image in three output classes. Thereafter the network is re-trained on the target dataset (Breast Cancer Classification dataset). Various experiments were performed to select the best hyperparameters empirically. The model with the highest performance is selected. Test images are given to the trained model for prediction.

IV. Results and Discussion

This section discusses the specifics of the evaluation metrics used to rate the success of the suggested model, as well as its execution, classification results, and comparison to cutting-edge methodologies.

A. *Evaluation Metrics*

Accuracy, Precision, Recall and F1-score were utilized to evaluate the classification performance of our proposed model on the testing set. These performance measures are shown in Eqs (1) - (4),

$$\text{Overall Accuracy} = \frac{TP+TN}{TP+TN+FP+FN} \quad (1)$$

$$\text{Recall} = \frac{TP}{TP+FN} \quad (2)$$

$$F1-\text{score} = \frac{2*\text{Precision}*\text{Recall}}{\text{Precision}+\text{Recall}} \quad (3)$$

$$\text{Precision} = \frac{TP}{TP+FP} \quad (4)$$

where, TP is True Positive, FP is False Positive, FN is False Negative, and TN is True Negative.

B. *Implementation Details – Model Training and Testing*

We executed the experiments for this work using TensorFlow open-source library and Python programming language in Google Colab Pro+ environment. After data augmentation, the entire data is partitioned into 80% training data, 10% validation data and 10% test data. The breast cancer dataset consists of three classes consisting of non-aggressive, less aggressive, and aggressive cell images. Image normalization is performed so that pixel values lie in the range 0 to 1. Pre-trained EfficientNetV2-B0 trained on ImageNet dataset from Keras library is loaded. This model consists of a total of 271 layers. The weights of first two hundred layers are frozen and the next seventy-one layers are unfrozen or will be trained and last layer consists of three neurons to classify into three classes by softmax activation function. This network is retrained for 70 epochs with batch size of 16 and categorical cross entropy loss function. Stochastic gradient descent algorithm and ADAM is used for network optimization. Since it is transfer learning, we are using pre-trained weights therefore the initial learning rate is set very small i.e., 0.00005 to prevent overfitting. Several experiments were carried out to choose the best hyperparameters. Details of the hyperparameters used while training are given in Table I.

The training and validation metrics are displayed in Table

***Table I*: Hyperparameters used in this work**

Hyperparameter	*Value*
Input size	224 x 224 x 3
Number of epochs	70
Batch size	16
Initial learning rate	0.00005
Loss function	Categorical Cross Entropy
Optimizer	ADAM
Metric	Accuracy, Precision
Train-validation-test split ratio	80:10:10
Activation function in output layer	SoftMax

II. As observed validation metrics for the proposed TL with EfficientNet is higher than the methods. This method is not overfitting and Training and Validation accuracy increased over epochs and stabilized after 60epochs.

***Table II*: Training and Validation Metrics**

Architecture	*Dataset*	*Accuracy*	*Precision*
Inception V3 [18]	Training	0.9726	0.9746
	Validation	0.9608	0.9608
NasNet Mobile [19]	Training	0.9979	0.9935
	Validation	0.8627	0.8648
TL with EfficientNet (Proposed)	Training	0.9916	0.9915
	Validation	0.9804	0.9804

The proposed work is compared with two state-of -the-art architectures Inception v3 [18] and NasNet [19]. All the training and validation curves for the three networks for accuracy and loss is shown in Figure4. These curves show that

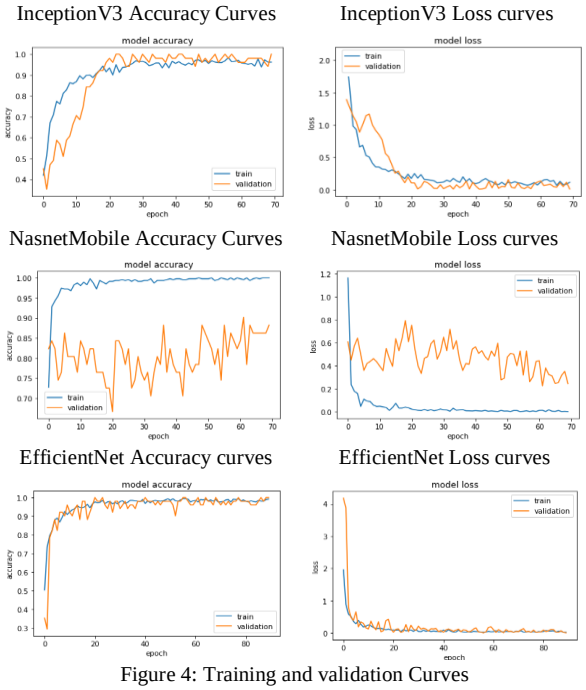
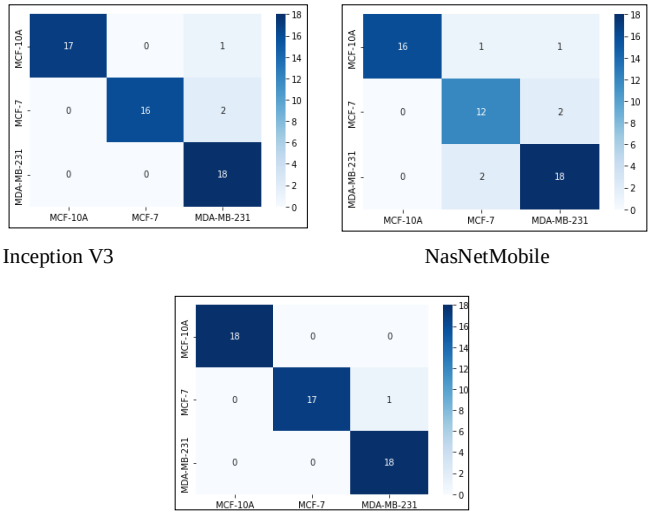


Figure 4: Training and validation Curves

the proposed model has higher accuracy and lower loss than the other two methods. Once the architecture is trained, the model is generated. Test images are given as input for model prediction.

C. Analysis of the Results

The confusion matrix for the three methods is shown in Figure 5.



Inception V3 NasNetMobile

EfficientNet

Figure 5. Confusion Matrix for all the three architectures

Evaluation metrics on the three methods are shown in TableIII. As can be seen in the table the best metrics are shown in bold which is obtained for the proposed method.

Table III*: *Results for Test Data

Architecture	*Accuracy (%)*	*Precision (%)*	*Recall (%)*	*F1 Score (%)*
Inception V3	94. 44	95. 24	94. 44	94. 52
NasNet Mobile	88. 46	89. 12	88. 46	89. 63
TL with EfficientNet (proposed)	**98. 15**	**98. 33**	**98. 15**	**98. 14**

This proves that EfficientNet is one of the best architectures for classification. Moreover, the performance of the proposed model is high since pre-trained EfficientNet which was trained on ImageNet dataset is taken as the initial point. Later, due to retraining a part of the network with the target dataset further improved the performance.

D. Comparison with Existing Techniques

The proposed method's performance is compared with the existing work[2], which is based on VGG-16. The corresponding results are shown in Table IV. As can be seen the suggested method is much more effective in classifying the dataset and reaches accuracy of 98.15% in only 70 epochs in contrast with the existing method with accuracy of 97.20% in 1000 epochs. This is since EfficientNet is a muchmore efficient architecture due to compound scaling and also due to retraining a part of the network with the target dataset. This clearly indicates the power of transfer learning and efficacy of EfficientNet.

Table IV*: *Comparision with existing techniques

Architecture	*Test Accuracy(%)*	*Number of Epocs*
VGG-16, model b [2]	97. 20	1000
TL with EfficientNet (Proposed)	**98. 15**	**70**

V. Conclusion and Future Scope

A deep learning technique for categorization of three types of human breast cancer cells of actin labelled fluorescence microscopy images is proposed. EfficientNetV2-B0 trained on ImageNet dataset is considered for TL of target dataset. The suggested method gave 98.15% test accuracy in classification of the target dataset in just 70 Epochs. This method outperformed other deep learning Models like InceptionV3, NasNetMobile and VGG16. This clearly proves that EfficientNet combined with TL is an efficient architecture for classification. In future this method may be explored for other kinds of microscopic images of biological cell classification.

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