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Identifying Microscopic Augmented Images using Pre-Trained Deep Convolutional Neural Networks

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***Abstract* - Because of the success of deep learning in multiple sectors, it is gaining unquestionable acceptance in the therapeutic field also. The key challenge is determining how to construct a deep CNN model with an inadequate amount of training data. One key question is whether transfer learning and fine-tuning can be employed in biomedical image analysis to lessen the load of manual data labelling while still producing a complete deep representation for the task. In this paper, we compare the performance of transfer learning and machine learning for nuclei categorization to answer this question statistically. The used machine learning approaches are Decision Tree, Support Vector Machine, Quadratic Discriminant Analysis, K Neighbors, Ada-Boost, Gaussian Naïve Bayes, Logistic Regression, Extra Trees, Random Forest, Histogram Gradient Boosting. This paper shows how to recognize nuclei from microscope pictures using a deep learning model and an image processing-based processing flow. Convolutional neural networks and Inception Resnet V2 deep networks have been used to generate better results. The data augmentation is also done to address the paucity of data.**

Keywords: Machine Learning, micronucleus, nucleus, transfer learning, Supervised Learning, Object Identification, Deep Learning, CNN, Inception Resnet V2

I. INTRODUCTION

Scientific research has long been the topic of relevance to human brilliance in scientific-technological developments. Over the past few years, medical research has picked up speed and Artificial Intelligence (AI) has made a big leap forward[1]. Machine learning (ML), Artificial Neural Networks (ANN), and Deep Learning are a by- product of AI which is presently very active and these powerful techniques are being used in medical research. In a very short time, it is widely being used in all fields of biomedical sciences. This is primarily because the solution is not limited to linear form[2][3][29].

While the algorithms of machine learning have been around for a long time, the latest innovation is the capacity to significantly apply complicated mathematical computations to large-scale data[4-7]. Deep learning has emerged as an innovative technique of mankind, especially when the information is unstructured, noisy, and humungous[8][9]. In reality, artificial neural networks are regarded as universal function approximations because they can learn any function with just one hidden layer, no matter how ambiguous it is. For example, one can create many layers of neural networks, called deep neural networks, with more computing power and sufficiently large memory. The concept behind a DNN is to replicate with artificial neuron layers in a compatible structure[10][11].

Machine learning models are traditionally trained to conduct meaningful operations based on manually constructed characteristics obtained from raw data or characteristics learned from other basic models of machine learning. In deep learning, the computers automatically learn beneficial representations and characteristics from the raw data and bypass this manual and challenging step. Different versions of ANN are by far the most prevalent models in deep learning. The primary popular feature of deep learning techniques is their focus on learning features, i.e. automatically learning information representations. The curiosity in deep learning is commonly generated by convolutional neural networks[12][13]. It is one of the utmost fascinating development of the current era and is also an influential way to learn expedient representations of images and other organized data. The building blocks of CNNs are depicted in fig. 1.

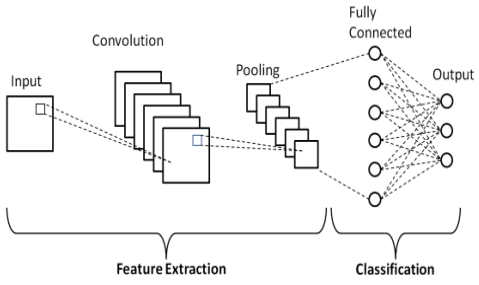

Figure.1. Building blocks of CNN

Diverse CNN designs such as Resnet-50[15], Googlenet [14], Inception-v3[16] and Inception-resnet-v2[17][18] have been created over the past few years.

Research in transfer learning focuses on storing knowledge gained from addressing one problem and applying it to a related but different scenario[19]. If one understands how to recognize vehicles, he may use that knowledge to identify trucks. Fig. 2 illustrates the transfer learning mechanism.

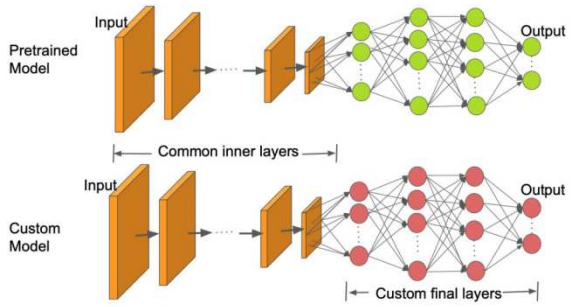

Figure. 2. Process of Transfer Learning

In our research, we probe the practicality of extracting significant features learned by pre-trained deep CNN models and further repurpose them for nucleus classification.

The remaining part of the paper is organized as follows: The second section is a brief overview of relevant literature. The proposed deep learning model and image processing are discussed in detail in Section 3. Our findings are summarized in Section 4. Section 5 concludes the paper.

II. Related Studies

In computational pathology, machine/deep learning-based methods have been extensively adopted in recent years[20]21]. Cells with defects in mitosis and micronuclei were detected by Su, H.H., et al.[22] using a method that automatically counts targets. Convolutional neural networks were used to identify normal cells, while colour layer signature analysis (CLSA) was used to identify cells with mitotic imperfections and micronuclei.

As inputs, Tarik Alafif et al.[23] fed the nucleus and micronucleus images through CNN models AlexNet, SqueezeNet, GoogLeNe, Dense Net-Mobile Net-v2, ResNet-101, ShuffleNet, and NASnetMobile. To assess the model's performance, a two-fold cross-validation was used. An investigational assessment revealed that GoogLeNet outperformed other models, with an average accuracy of 80.06 percent. Using a deep learning model Kemeng Chen et al. [24] detected and segmented nuclei in microscope images. As a result, they were able to isolate each nucleus. A multi-layer CNN based architecture was used to extract features from both spatial and colour information and build a grey-scaled picture mask. Images were then flattened and each nucleus was isolated individually using image processing techniques. H&E stained microscope images of seven diverse tissue samples were used to implement and test the suggested work. The average precision was 0.799, recall was 0.955, F-score was 0.86, and Intersection over Union (IoU) was 0.835 in the experiments. Mask R-CNN was used by Jung et al.[25] to segment nuclei. In addition, as a post-processing step, the authors used multiple inferences to improve segmentation performance. On two separate datasets, they tested their segmentation algorithm. The first dataset contains histopathology photos of several organs, whereas the second dataset has photographs of the same organ. The performance of their segmentation method was evaluated at the object and pixel levels in a variety of experimental scenarios.

III. Materials And Methods

A. Dataset

There are 148 nucleus images and 158 micronucleus images in the dataset used in this study [26]. The majority of these photographs are in RGB colour, with a handful in grayscale. The images come in a variety of sizes and resolutions. Images of nuclei and micronucleus vary in size and shape from one to the next. One or more nuclei or micronuclei may be present in each image. The creation of a strong computer-aided diagnostic (CAD) system is hampered by unbalanced and limited data sizes. Data augmentation is a technique for increasing the amount of a dataset to solve the problem of data scarcity. In this study, data augmentation techniques such as rotation, flipping, and zooming are used. We have used the augmentation technique to improve model accuracy, generalization, and to control overfitting. The immediate upshot of data augmentation is to create new samples without changing their sense.

B. Methodology

In this work, we apply Decision Tree, Support Vector Machine, Quadratic Discriminant Analysis, K Neighbors, Ada-Boost, Gaussian Naïve Bayes, Logistic Regression, Random Forest, Extra Trees, Histogram Gradient Boosting machine learning approaches on base dataset and augmented dataset. In conjunction with transfer learning approaches, we employed deep architecture CNN and InceptionResNetV2 models. The proposed framework is depicted in fig. 3. Each experiment was carried out using the Keras Python package's architecture for both the CNN and Inception-v2 networks [27][28]. The dataset was divided into two parts: 70% training data and 30% validation data. Using the Tensor flow v2.4.0 library, both training and validation data were loaded, augmented, and normalized as Batch Dataset objects, and then fed into the InceptionResNetV2 model.

This work relies on deep network models trained on Image Net datasets in a specific domain D_s for a specific task T_s. The source domain $D_s = \{(x_{s1}, y_{s1}), (x_{s2}, y_{s2}), \dots, (x_{sn}, y_{sn})\}$. The target domain is denoted as $T_s = \{ , f(\cdot)\}$. The task domain is denoted as $D_t = \{(x_{t1}, y_{t1}), (x_{t2}, y_{t2}), \dots, (x_{tn}, y_{tn})\}$. The task target is denoted as $T_t = \{y_t, (\cdot)\}$.

Here, x is an instance of input data, y is a target label, and (.) is the objective predictive function. Transfer learning is defined mathematically as a method for improving the result in the target task T_t given the base knowledge from the source domain D_s and the target domain, on the condition of $D_s \neq D_t$ or $T_s \neq T_t$. We examine the efficiency of a pre-trained network when used solely as a feature extractor and when

migrating the network (part of its weights) to the medical imaging domain.

To quantitatively measure the performance of machine learning models, seven metrics: accuracy, precision, recall, and F-score, Mathew's coefficient and Kappa Coefficient as defined below have been used. Here, True positive is TP, false positive is FP, and false negative is FN. We defined TP as when our model correctly detects nuclei in our assessment measures. When our model finds a nuclei /micronuclei that is actually background, we call it FP. When our model fails to detect genuine nuclei/micronuclei, we call it FN.

$$Accuracy = \frac{Number\_of\_Correct\_Predictions}{Total\_Predictions}$$

$$Accuracy = \frac{TN + TP}{TN + TP + FN + FP}$$

$$Precision = \frac{TP}{TP + FP}$$

$$Recall = \frac{TP}{FN + TP}$$

$$F1\ Score = \frac{2}{\frac{1}{recall} + \frac{1}{Precisionl}} = 2 \times \frac{recall \times precision}{recall + precision}$$

$$\text{Mathew's Coefficient} = \frac{TP \times TN - FP \times FN}{\sqrt{(TP + FN)(TP + FP)(TN + FN)(TN + FP)}}$$

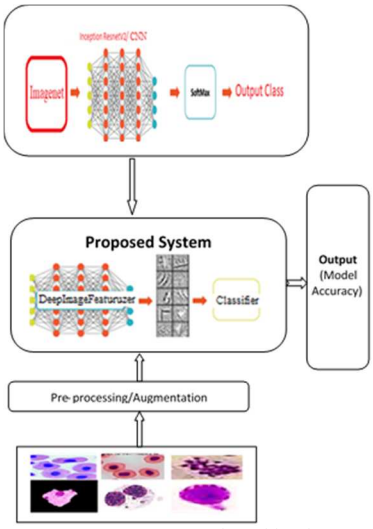

Figure 3. Proposed workbook

IV. RESULTS

A. *Analysis of Machine learning algorithms with base and augmented dataset*

Preliminary for comparison purposes as mentioned in table 1 and table 2, machine learning and ensemble learning algorithms were implemented on base data and augmented dataset. Here, with both base and augmented dataset Extra Trees and random forest classifiers performed best with accuracy 78 percent along with stable precision, recall and F1-score. Similarly, Mathew's coefficient and Kappa statistics were also highly identified in Extra Trees and random forest classifiers in comparison to other mentioned algorithms.

TABLE I. MACHINE LEARNING WITH BASE DATA

Algo	ACC	PRE	REC	F1	MC	KS
DT	0.65	0.65	0.65	0.65	0.29	0.29
SVM	0.63	0.7	0.63	0.59	0.32	0.26
QDA	0.55	0.71	0.54	0.43	0.19	0.09
KNN	0.64	0.65	0.64	0.63	0.28	0.28
AB	0.62	0.62	0.62	0.62	0.23	0.23
GNB	0.52	0.53	0.52	0.5	0.05	0.04
LR	0.55	0.56	0.56	0.55	0.11	0.11
RF	0.78	0.78	0.78	0.77	0.55	0.55
ET	0.78	0.78	0.78	0.78	0.56	0.55
VC	0.67	0.71	0.67	0.65	0.37	0.34
HGB	0.74	0.74	0.74	0.74	0.48	0.48

TABLE II. MACHINE LEARNING WITH AUGMENT DATA

Algo	ACC	PRE	REC	F1	MC	KS
DT	0.74	0.74	0.74	0.74	0.48	0.48
SVM	0.69	0.75	0.65	0.64	0.39	0.33
QDA	0.56	0.65	0.6	0.53	0.24	0.18
KNN	0.51	0.5	0.5	0.5	0.01	0.01
AB	0.66	0.66	0.65	0.65	0.31	0.31
GNB	0.45	0.48	0.49	0.43	0.03	0.02
LR	0.57	0.57	0.57	0.57	0.14	0.14
RF	0.71	0.71	0.7	0.7	0.42	0.41
ET	0.71	0.71	0.71	0.71	0.42	0.42
VC	0.58	0.62	0.61	0.58	0.23	0.2
HGB	0.68	0.67	0.67	0.67	0.34	0.34

B. *Analysis of CNN on Available and Augmented Dataset*

As per the objective of this paper, an efficient classification model was implemented and analyzed using a deep neural network approach on the same datasets. Table 3 and table 4 depicts the results CNN applied on base and augmented dataset. CNN with base dataset obtained average training accuracy and average validation accuracy 96% and 66.11% respectively. With the augmented dataset average training accuracy and average validation accuracy was found 98.22% and 86%.

C. *Analysis of Deep Learning Classification Algorithm Inception-ResnetV2 on base and Augmented Dataset*

Table 5 and Table 6 depicts the results obtained when the deep learning model InceptionResNetV2 from pre-trained CNN networks was applied on base and augmented dataset. With base dataset average training accuracy and average validation accuracy were 99.33% and 77.33% respectively.

With the augmented dataset average training accuracy and average validation accuracy were found 99.88 and 97.22% respectively.

Further abbreviations in tabular results utilized as Accuracy-ACC, Precision–PRE, Recall-REC, F1Score-F1, Mathew's-Coefficient-MC, Kappa Statistics-KS, Area under Curve-AUC, Training-TR, Validation-Val, Decision Tree - DT, Support Vector Machine -SVM, Quadratic Discriminant Analysis -QDA, K Nearest Neighbors (KNN), Ada Boost Classifier (AB), Gaussian Naïve Bayes (GNB), Logistic Regression (LR), Extra Tree (ET), Random Forest (RF), Voting Classifier (VC), Histogram Gradient Boosting (HGB).

TABLE III. CNN WITH BASE DATA

Epoch's	TR-ACC	VAL-ACC	TR-Loss	VAL-Loss	TR-PRE	TR-REC	TR-AUC	VAL-PRE	VAL-REC	VAL-AUC
1	0.52	0.55	1.87	0.67	0.52	0.52	0.54	0.55	0.55	0.56
10	0.69	0.52	0.55	0.80	0.69	0.69	0.77	0.52	0.52	0.65
20	0.80	0.66	0.33	0.52	0.80	0.80	0.92	0.66	0.66	0.76
30	0.89	0.66	0.24	1.80	0.89	0.89	0.96	0.66	0.66	0.68
40	0.99	0.59	0.05	1.44	0.99	0.99	1.00	0.59	0.59	0.73
50	0.96	0.59	0.10	0.99	0.96	0.96	0.99	0.59	0.59	0.76
60	1.00	0.66	0.00	1.91	1.00	1.00	1.00	0.66	0.66	0.71
70	1.00	0.69	0.00	3.03	1.00	1.00	1.00	0.69	0.69	0.73
80	1.00	0.69	0.00	2.82	1.00	1.00	1.00	0.69	0.69	0.74
90	1.00	0.72	0.00	3.83	1.00	1.00	1.00	0.72	0.72	0.72
100	1.00	0.69	0.00	4.53	1.00	1.00	1.00	0.69	0.69	0.71

TABLE IV. CNN WITH AUGMENT DATA

Epoch's	TR-ACC	VAL-ACC	TR-Loss	VAL-Loss	TR-PRE	TR-REC	TR-AUC	VAL-PRE	VAL-REC	VAL-AUC
1	0.54	0.58	0.96	0.65	0.54	0.54	0.57	0.58	0.58	0.69
10	0.82	0.79	0.37	0.41	0.82	0.82	0.91	0.79	0.79	0.89
20	0.94	0.83	0.16	0.52	0.94	0.94	0.99	0.83	0.83	0.90
30	0.98	0.76	0.06	1.59	0.98	0.98	1.00	0.76	0.76	0.82
40	0.98	0.88	0.07	0.74	0.98	0.98	0.99	0.88	0.88	0.94
50	0.98	0.88	0.08	1.41	0.98	0.98	1.00	0.88	0.88	0.92
60	0.98	0.88	0.06	2.18	0.98	0.98	1.00	0.88	0.88	0.90
70	1.00	0.88	0.01	1.70	1.00	1.00	1.00	0.88	0.88	0.93
80	0.99	0.88	0.06	0.86	0.99	0.99	1.00	0.88	0.88	0.93
90	1.00	0.86	0.05	1.57	1.00	1.00	1.00	0.86	0.86	0.90
100	0.99	0.89	0.07	1.29	0.99	0.99	1.00	0.89	0.89	0.92

TABLE V. INCEPTION RESNET V2 ON BASE DATASET

Epoch's	TR-ACC	VAL-ACC	TR-Loss	VAL-Loss	TR-PRE	TR-REC	TR-AUC	VAL-PRE	VAL-REC	VAL-AUC
1	0.68	0.48	1.41	1489.10	0.68	0.68	0.74	0.48	0.48	0.48
10	0.99	0.85	0.12	0.32	0.99	0.99	0.99	0.85	0.85	0.94
20	0.98	0.73	0.13	2.99	0.98	0.98	0.99	0.73	0.73	0.67
30	1.00	0.82	0.00	0.67	1.00	1.00	1.00	0.82	0.82	0.92
40	1.00	0.58	0.00	48.35	1.00	1.00	1.00	0.58	0.58	0.63
50	1.00	0.85	0.00	0.65	1.00	1.00	1.00	0.85	0.85	0.91
60	0.99	0.85	0.06	0.73	0.99	0.99	1.00	0.85	0.85	0.92
70	0.99	0.64	0.03	3.55	0.99	0.99	1.00	0.64	0.64	0.67
80	1.00	0.79	0.00	71.39	1.00	1.00	1.00	0.79	0.79	0.87
90	0.98	0.82	0.15	1.44	0.98	0.98	0.99	0.82	0.82	0.80
100	1.00	0.88	0.01	0.48	1.00	1.00	1.00	0.88	0.88	0.94

TABLE VI. INCEPTION RESNET V2 ON AUGMENT DATASET

Epoch's	TR-ACC	VAL-ACC	TR-Loss	VAL-Loss	TR-PRE	TR-REC	TR-AUC	VAL-PRE	VAL-REC	VAL-AUC
1	0.85	0.80	0.65	0.45	0.85	0.85	0.89	0.80	0.80	0.90
10	0.99	0.92	0.03	0.25	0.99	0.99	1.00	0.92	0.92	0.97
20	1.00	0.97	0.00	0.11	1.00	1.00	1.00	0.97	0.97	0.99
30	0.99	0.94	0.05	0.99	0.99	0.99	1.00	0.94	0.94	0.97
40	1.00	0.93	0.00	0.49	1.00	1.00	1.00	0.93	0.93	0.95
50	1.00	0.99	0.00	0.06	1.00	1.00	1.00	0.99	0.99	0.99
60	1.00	0.99	0.02	0.02	1.00	1.00	1.00	0.99	0.99	1.00
70	1.00	0.99	0.00	0.08	1.00	1.00	1.00	0.99	0.99	0.99
80	1.00	0.99	0.00	0.07	1.00	1.00	1.00	0.99	0.99	0.99
90	1.00	0.99	0.00	0.03	1.00	1.00	1.00	0.99	0.99	1.00
100	1.00	0.96	0.00	0.42	1.00	1.00	1.00	0.96	0.96	0.97

D. Comparison

Fig. 4 depicts the comparative analysis of CNN an inceptionResnetV2 on base and augmented datasets in terms of training accuracy, validation accuracy, AUC, precision and recall.

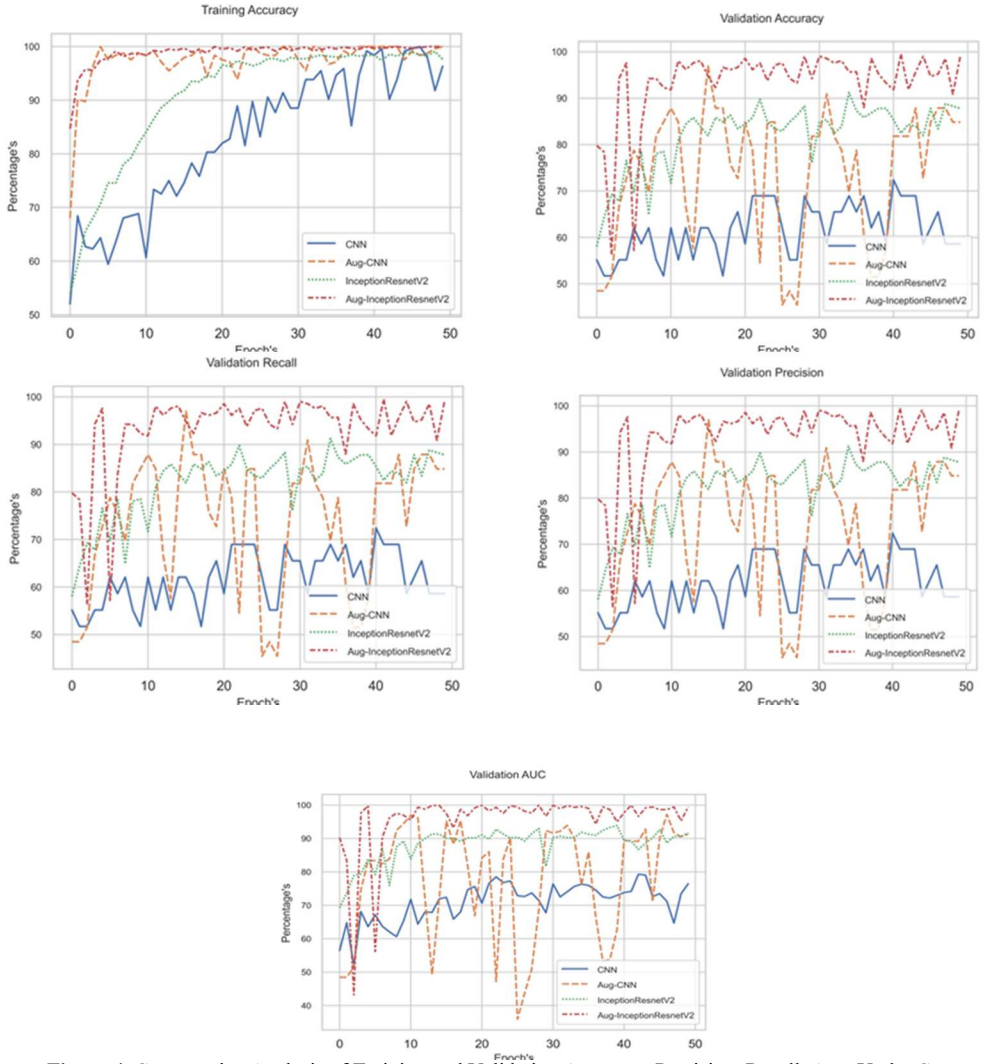

Figure 4. Comparative Analysis of Training and Validation Accuracy, Precision, Recall, Area Under Curve

V. CONCLUSION

To automate the recognition of nucleus and micronucleus from microscope pictures, we first use traditional machine learning algorithms and deep transfer learning. Microscopy image retrieval and classification are useful but difficult undertakings. The nucleus and micronucleus pictures are fed into Convolutional Neural Network (CNN) models that have been pre-trained. When compared to traditional machine learning approaches, both a feature extractor and a transfer learned network were able to improve classification accuracy. Our tests reveal that the pre-trained model outperforms traditional machine learning methods. InceptionRasnetV2 offers 99.98% average training accuracy and 97.22% average validation accuracy.

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