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RESEARCH ARTICLE

DEEP TRANSFER LEARNING BASE MODELSWITHOPTUNA HYPERPARAMETER OPTIMIZATIONON COLORECTAL CANCER IMAGES CLASSIFICATION

Ito Wasito[1] and Denny Saptono F.[2]

1. Department of Information Technology, Pradita University, Banten, Indonesia.
2. Department of Public Health, Universitas Muhammadiyah Surakarta, Surakarta, Indonesia.

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Abstract

Colorectal Cancer (CRC) is one of the forms of cancer and the second deadliest disease. Previously, some molecular tests, including next-generation sequencing has been used for this cancer classification. However, the required data do not always available to all cancer patients because of high cost and technical barriers. In recent development, Hematoxylin and eosin-stained (HE) biopsy slides are regularly available for colorectal cancer patients. Fortunately, rapid development has shown that objective biomarkers can be extracted from these images using Deep Learning (DL) approaches especially convolutional neural networks (CNN). This paper reports some experimental comparisons of transfer learning based on Deep Learning with CNN architecture as feature extractor to decompose nine classes of colorectal carcinoma slides images. The base of models of Transfer Learning includes MobileNet_V2, EfficientNet_b2, DenseNet201, Inception_V3, and Resnet18. All the base models were trained using Optuna hyperparameter optimization framework which has flexible, modular and easy to combined with transfer learning. This research has two main contributions, first, this research can contribute insight to medical expert and computer scientist related to the current state of development deep transfer learning approaches for histopathological images classification especially in colorectal carcinoma (CRC). The second contribution of this research is to recommend some CNN base models with hyperparameter optimization experimental framework development for decomposition of CRC feature extraction, parameter optimization and classification of slides images. The results show that highest accuracy is achieved by Resnet18 base models which has 99.99% on test data 1 and 98.16% on test data 2.

Introduction:-

As widely known that Colorectal Cancer (CRC) is the third most common form of cancer and the second deadliest disease (1). Furthermore, according to the American Institute of Cancer Research the cases for colorectal cancer

Corresponding Author:-Ito Wasito
Address:-Department of Information Technology, Pradita University, Banten, Indonesia.

world-wide are expected to rise by 60 percent over the next fifteen years, therefore, the required steps for diagnosis will also increase rapidly which would prove disastrous if pathologists only relied on manual examinations (2).
The Deep Learning based biomarkers could predict colorectal cancer patient outcomes comparably to gold standards. With the advancement in the field of Artificial Intelligence, including several Deep Learning approaches as part of AI, it has been applied to identify biomarker colorectal carcinoma cancer (3,4). The advantages of Deep Learning based approaches can be viewed as the powerful 'feature extractor' of slides of cancer composition. Then, those extracted features will be selected using a well-defined feature selection technique. Finally, a classifier will decompose slides images into their expected category of colorectal carcinoma (CRC) (6,7)
Various architectures of Convolutional Neural Networks (CNN) have been developed such as Deep Residual Networks (ResNet), Inception Networks, Densely Connected Convolutional Networks (Densenet), MobileNet and EfficientNet (13). Those architectures are usually implemented in images classification within transfer learning framework (12) in which knowledge learned from a task is re-used in order to boost performance on a related task. The applications of such approach simply use the "pre-trained weight" CNN based model architecture using related images data sets

This study has two contributions: first, this research can provide insight to medical expert and computer scientist related to the current state of development deep transfer learning approaches for histopathological images classification especially in colorectal carcinoma (CRC). The second contribution of this research to provide recommendation of the best deep transfer learning framework using parameter optimization for feature extraction, feature selection and classification of slides images in pathological applications.

This paper will be organized as follows. First, Deep Learning Architecture mainly in Deep Convolutional Neural Networks (CNN) will be reviewed. Next, transfer learning of the CNN based models which including Resnet18, Densenet201, Inception_v3, MobileNet_V2 and Efficientnet_b2 for classification of CRC will be explored. The Hyperparameter Optimization to the transfer learning will be reviewed. Then the experimental settings will be introduced. The results and discussions will show some findings from the experiments. The paper will be concluded by some recommendations the use of proposed frameworks for classification of Colorectal Carcinoma images.

Material and Methods:-

Data Description

Slides Images of Colorectal Carcinoma Data

The slides image data collected from in the following public website:
https://zenodo.org/records/1214456 (5) and https://zenodo.org/records/4024676 (17).

Data Training

Those downloaded colorectal carcinoma data sets are a set of 100,000, 89,100 and 105,100 non-overlapping image patches from hematoxylin & eosin (H&E) stained histological images of human colorectal cancer (CRC) and normal tissue. There 8 tissue classes are: Adipose (ADI), background (BACK), debris (DEB), lymphocytes (LYM), mucus (MUC), smooth muscle (MUS), normal colon mucosa (NORM), cancer-associated stroma (STR), colorectal adenocarcinoma epithelium (TUM). LYM, STR and TUM classes have important role in colorectal carcinoma cancer. Those classes will be our primary analysis. This data set will be used as training data. For the validation dataset we used external data set which has 7180 images slides of colorectal carcinoma.

Data Testing

Test 1 and test 2 were defined as two independent test sets. Those test sets were used to assess the classification performance of the trained CNN model. Dataset released with Kather et al. 's paper (5) was used to form the test set 1 and those randomly chosen from validation cohort were used to establish the test set 2 (22.5k patches from 48 slides) (17).

Transfer Learning Settings

CNN Base Models

Five CNN base models were deployed in transfer learning settings as follows:

1. Efficientnet_b2
2. Resnet18
3. Densenet201
4. Inception_v3
5. MobilenetV2

Hyperparameters
For each base models will be implemented using the following parameters:

1. **Optimizer**: determine between Adam or Stochastic Gradient Descent (SGD) optimization technique.
2. **Learning rate**: determine the number of learning rate to achieve the best accuracy.
3. **Batch size**: the size of image batch
4. **Weight Decay**: also known as L2 regularization, is a technique used in deep learning to prevent overfitting by penalizing large weights in the model.

Evaluation of Performances
The accuracy will used to determine the goodness of the based model of transfer learning. The pipeline of experiments is shown in Figure 3.

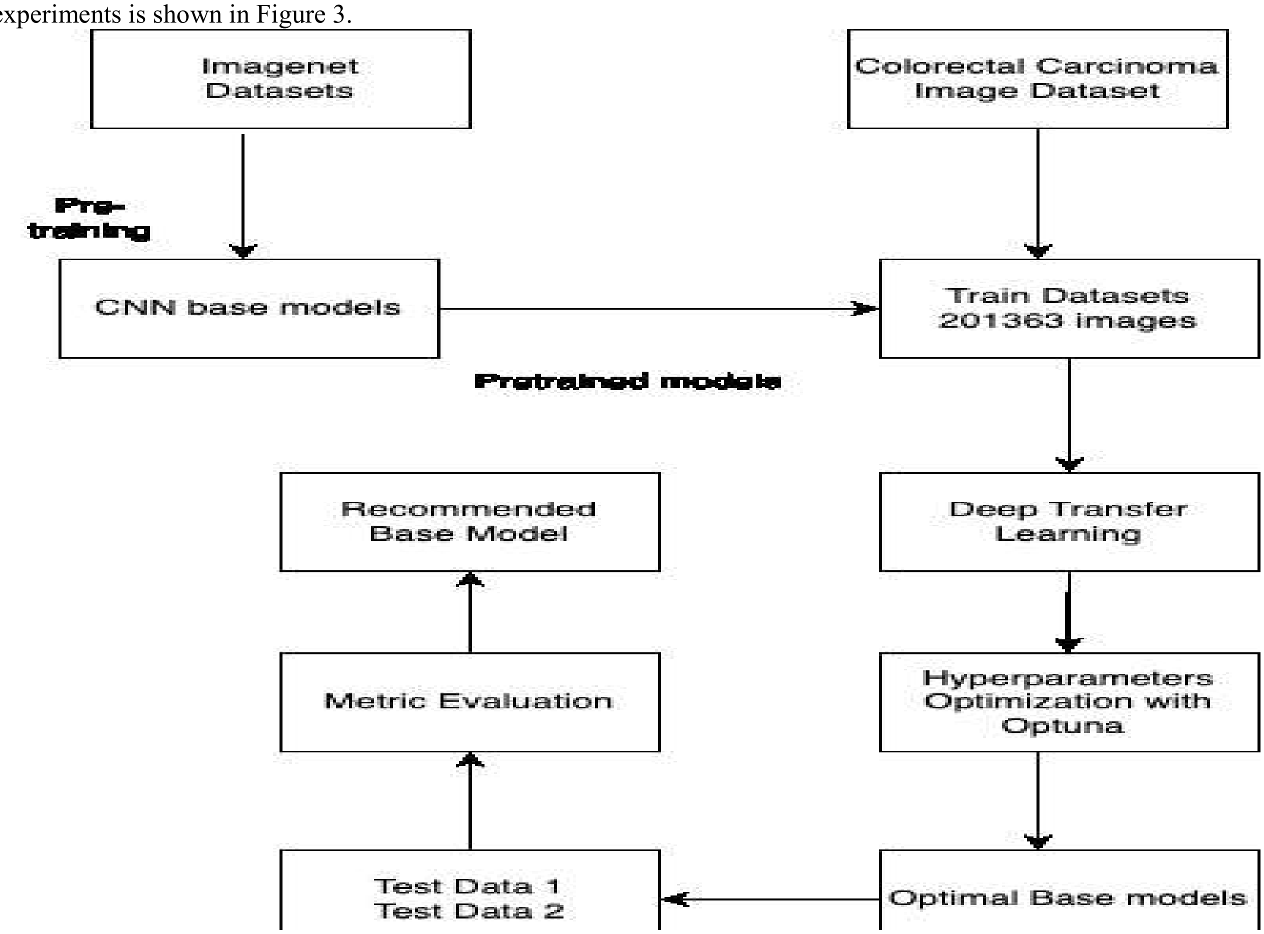


Figure 3:- The flow of experiments.

Methodology:-

Convolutional Neural Networks (CNN)
Convolutional Neural Network (CNN) is one of the Deep Learning models and general form of artificial neural networks (ANN) which is mainly used to extract the image features. CNNs have been frequently implemented in a range of different applications, including computer vision speech processing, Face Recognition etc (9,10). The structure of CNNs was inspired by neurons in human and animal brains, similar to a conventional neural network. The structure of CNN will be explored as follows.

CNN Architecture
The Convolutional Neural Network consists of several layers which basically consist of the four components; Input layer, Convolutional layer, Pooling and Fully Connected (fc) layers. The Convolutional layer uses filters to the input image to extract features of image. While the Pooling layer down samples the image to reduce computation, and the

fully connected layer will do the final prediction. The network learns the optimal filters through backpropagation and gradient descent (9,10). The structure of CNN can be seen as Figure 1.

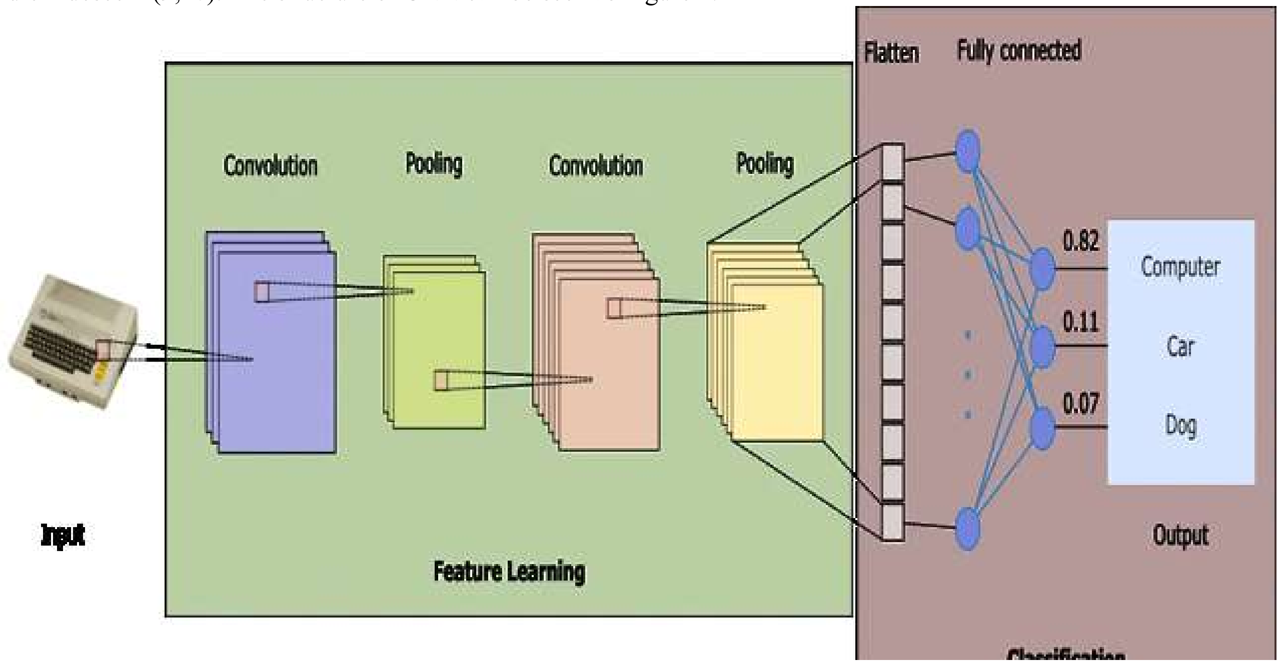


Figure 1:- CNN Architecture (9).

Transfer Learning

Transfer learning (**TL**) is a framework in Deep Learning in which knowledge learned from a task is re-used in order to boost performance on a related task (11,12). Transfer learning methods on deep learning aim to reduce the cost and training time, and the necessity of extensive training datasets which can be hard to harvest in some areas such as Colorectal carcinoma slides images. In this work, the five CNN base models which include Resnet18, Inception_v3, Desnet201, Efficientnet_b2 and MobileNetV2 will be explored and compared their performances using real Colorectal Carcinoma images data sets. The parameters of the models will be optimized using Optuna algorithm (Takuya Akiba et al, 2019). The transfer learning usually used weights from the pretrained model on Imagenet data sets (11,12).

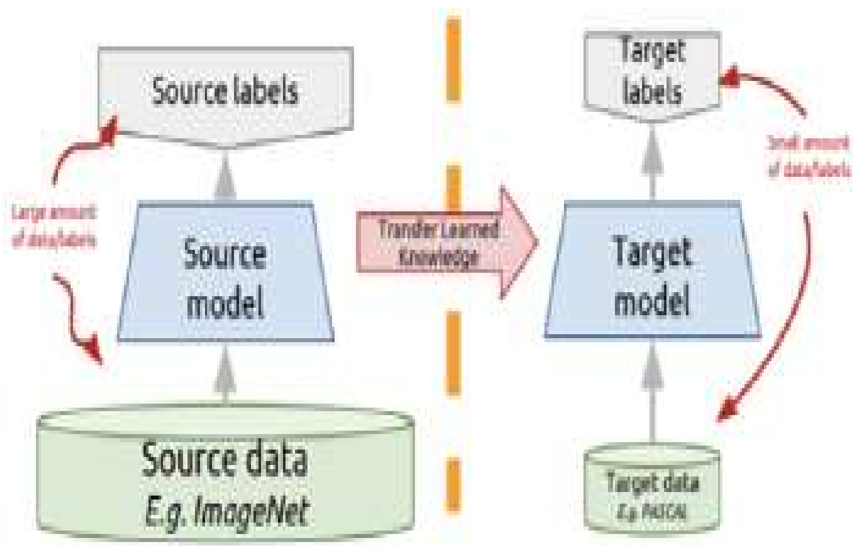


Figure 2:- Transfer Learning framework.

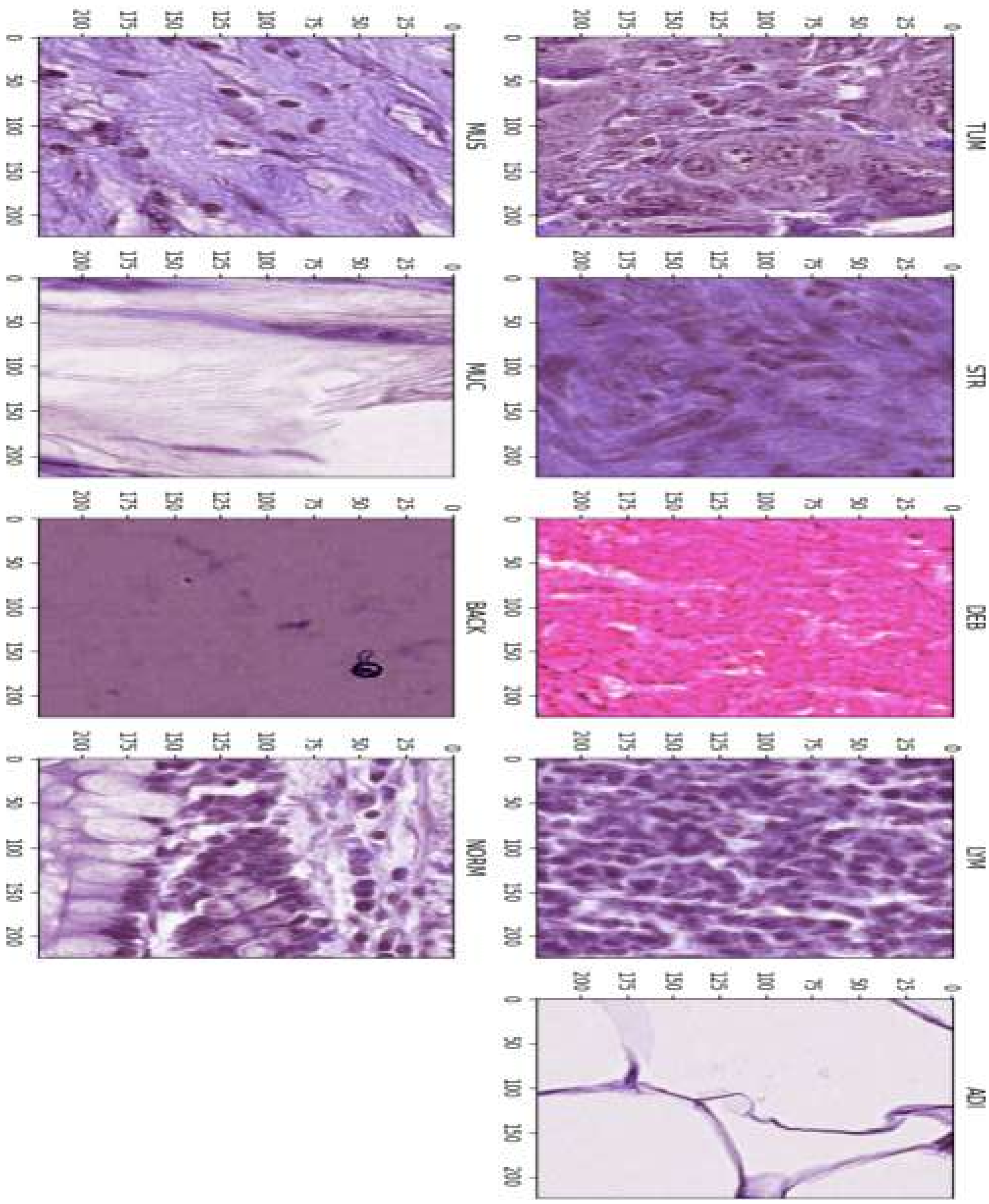


Figure 4:- Sample of each class of slide images which consists of Adipose (ADI), background (BACK), debris (DEB), lymphocytes (LYM), mucus (MUC), smooth muscle (MUS) normal colon mucosa (NORM), cancer-associated stroma (STR), colorectal adenocarcinoma epithelium (TUM).

Hyperparameter Optimization (HPO)

Despite Deep Learning achievement in various applications, the design and training of Deep Learning are still challenging and uncontrolled processes that have been alleged to uncertainty. To minimize the technical thresholds for naive users, automated hyper-parameter optimization (HPO) has become a trend topic in both academic and industrial areas. Currently, there are four main approaches in hyper-parameter optimization implementation which including: Grid Search , Random Search, Bayes Optimization and Optuna framework. The approaches will be briefly explored as follows:

Grid Search

Grid search is one of the most widely implemented hyperparameter optimization approaches. It deploys by intensively searching through all possible combinations of hyperparameters in a given grid. This guarantees that every candidate combination is considered, so you are guaranteed to find the best set of hyperparameters within the defined grid.

Random Search
Instead of intensively searching through every possible combination of hyperparameters, random search collects a fixed number of random combinations from the search space. This allows random search to determine the hyperparameter space more efficiently, often showing good results with fewer iterations**.**

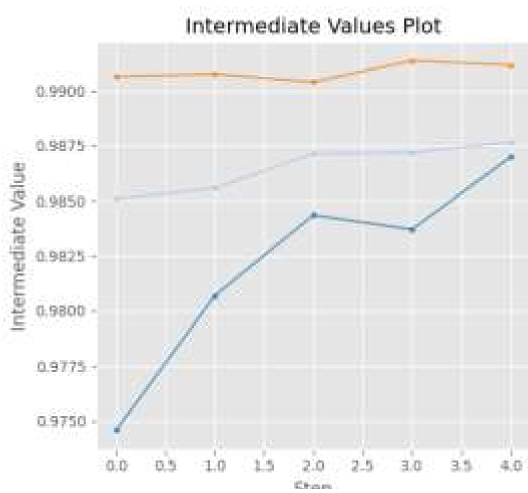
Bayes Optimization
Bayesian Optimization is an advanced and efficient method that determines the probabilistic relationship between hyperparameters and the objective function using, usually a Gaussian Process (GP) model. The objective is to search the optimal hyperparameters by choosing the next set of hyperparameters to learn based on the results of previous evaluations.

Optuna: A hyperparameter optimization framework
More recent approach in hyperparameter optimization which is called Optuna which is basically defined as an automatic hyperparameter optimization software framework (18). It features an imperative, define-by-run style user Application Program Interface (API). The program written with Optuna takes benefits high modularity, and the user of Optuna can dynamically develop the search spaces for the hyperparameters. The paper will use this approach based on some considerations in flexibility, modularity and easy to combine with transfer learning framework (10).

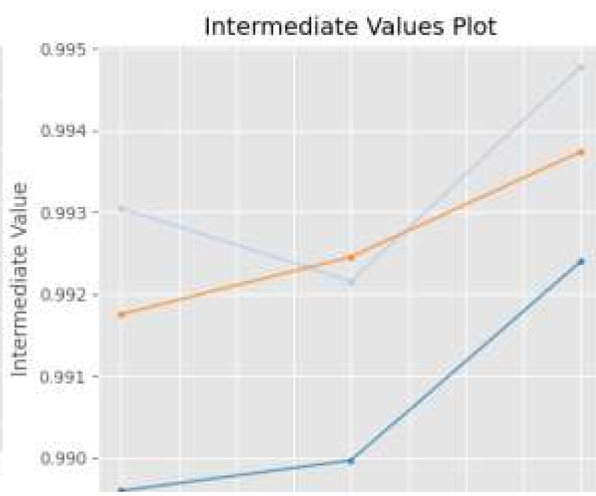
Results and Discussion:-

Sample of Colorectal Carcinoma Classes
The figure 1 shows the sample of classes of Colorectal Carcinoma which consist of Adipose (ADI), Background (BACK), Debris (DEB), Lymphocytes (LYM), Mucus (MUC), smooth muscle (MUS), normal colon mucosa (NORM), Cancer-Associated Stroma (STR) and Colorectal adenocarcinoma epithelium (TUM). The next steps, those pretrained base models transfer learning using Optuna optimization will be used to train model of Colorectal Carcinoma patient images to the correct classes.

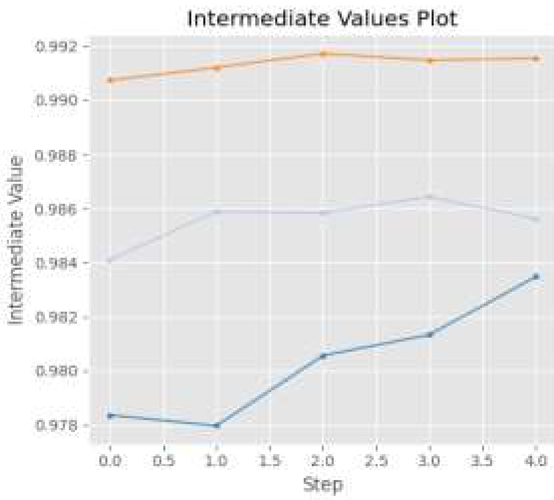
CNN Based Models Training
Five base CNN model which including: Resnet18, Densenet201, Inception_v3, Efficient_b2 and MobilenetV2 were trained on training data sets. The training process used Optuna hyperparameter optimization 20 epochs and 3 trials. Figure 5 shows that the accuracy of five based models. Overall, the Resnet18 and Inception_v3 produced consistent and stable in the last trial. Despite Densenet201 produced highest accuracy in the trial 1, however in the last trial it produced lower accuracy than trial 2. Efficientnet_b2 produced the highest accuracy in the trial 2. And the Mobilenet_v2 shows the lowest accuracy.



Accuracy of Resnet18

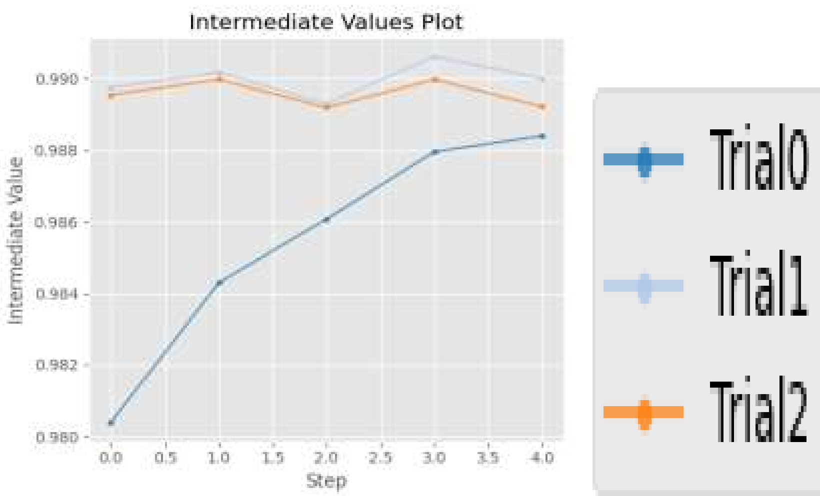


Accuracy of Densenet 201



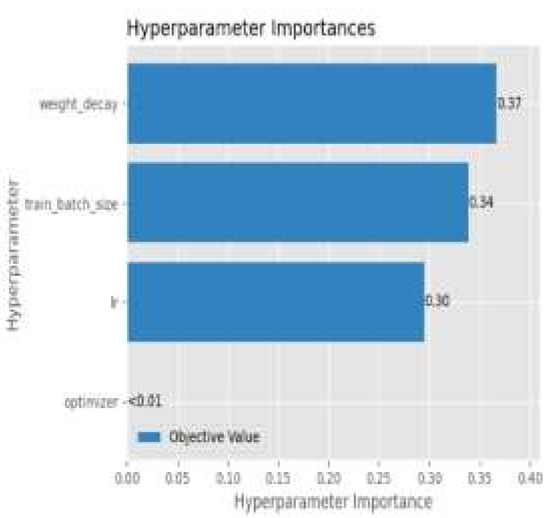
Accuracy of Inception_v3

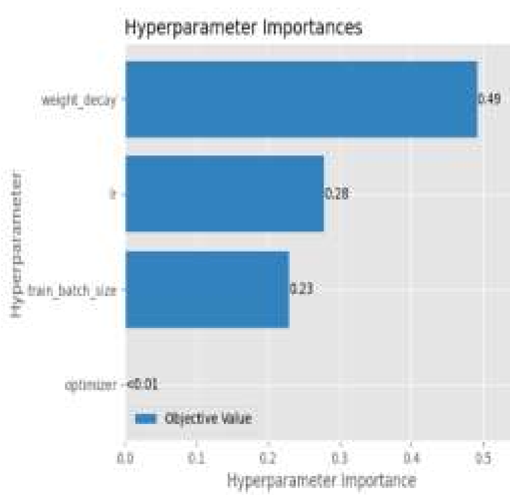
Accuracy of Efficientnet_b2



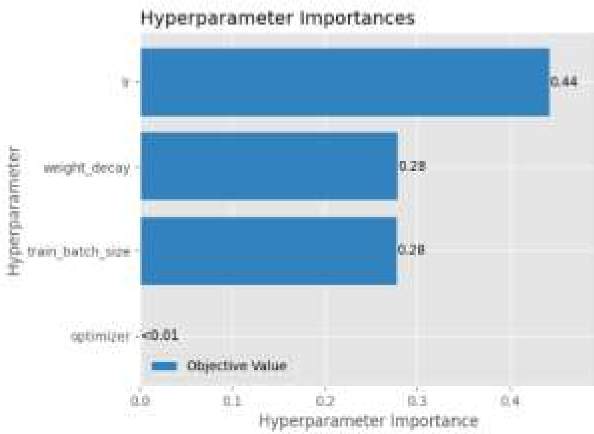
Accuracy of MobilenetV2

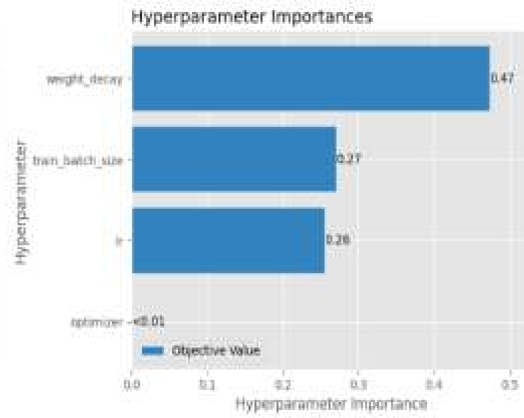
Figure 5:- Accuracy of training of based models Resnet18, Densenet201, Inception_v3, Efficientnet_b2 and Mobilenet_v2



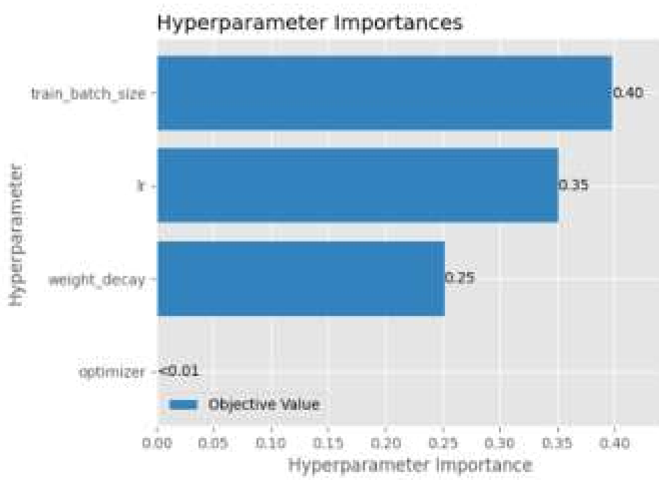


Hyperparameter Importance of Resnet18Hyperparameter Importance of Densenet 201





Hyperparameter Importance of Inception_V3Hyperparameter Importanceof Efficientnet_b2



Hyperparameter of Importance of Mobilenet_v2

Figure 6:- The Hyperparameter importance on base models Resnet18, Densenet 201, Inception_v3,Efficientnet_b2 and Mobilenet_v2.

Hyperparameter Importance

To gain the high training accuracy the base models used Optuna hyperparameter optimization based on learning rate (lr), batch size, optimizer types which including Adam and stochastic gradient descent (SGD) and weight decay (L2 regularization). Figure 6 shows that The Resnet18, Densenet201 and Efficientnet_b2 were influenced by weight_decay (L2regularization) meanwhile Inception_V3 rely on the learning rate and finally mobilenetV2 depends on batch size. The overall, the results show better performance compare to the results from previous results in (16).

CNN based models Testing

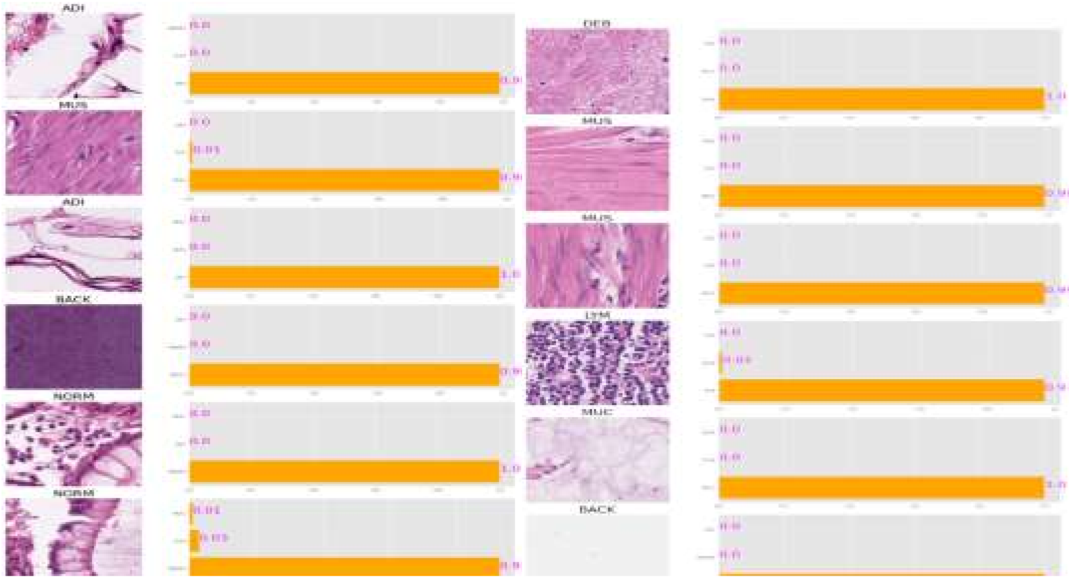
The five CNN base models will test using test-1 and test-2 datasets. The Table 1 shows that results of experiments. Overall, the Resnet 18 produced highest accuracy and the fastest computation based on batch size and learning rate are 44 and 0.00004, respectively.

Tabel1:- Test Accuracy of Based Models of Resnet18, Densenet 201, Inception_V3, Effecientnet_b2 and Mobilenetv2 using Optuna Hyperparameter optimization.

Base Model	Test1-accuracy(%)	Test2-accuracy (%)	Learning rate	Batch Size	Weight Decay	Optimizer	Time(Min)
Resnet18	99.99	98.16	0.00004	44	0.000008	Adam	53.57
Densenet201	99.99	97.23	0.00003	27	0.000001	Adam	156.25
Inception_v3	99.99	98.12	0.00002	16	0.000002	Adam	79.38

Efficientnet_b2	99.99	98.13	0.00008	29	0.000003	Adam	67.57
MobilenetV2	98.98	96.12	0.00006	24	0.000003	Adam	61.67

Therefore, for the next analysis the Resnet 18 will be further processed to estimate probability of correct classes prediction.



Test Data 1 **Test Data 2**

Figure 7:- The probability of Resnet 18 model to classify the test data 1 (left) and test data 2 (right) in thecorrect classes.

Having determine of the probability of Resnet 18 model on test data 1 and test data 2 to classify the colorectal carcinoma patient images, then the confusion matrix will be used to show how accurate the Resnet 18 models to assign images on correct labels of classes which including ADI, BACK, DEB, MUC, MUS, STR and TUM. The figure 8 shows the confusion matrix of Resnet 18 models on test data 1. Overall, the results show that Resnet 10 model provide very good performance which the predicted classes are almost 100% classify the images in the actual classes.

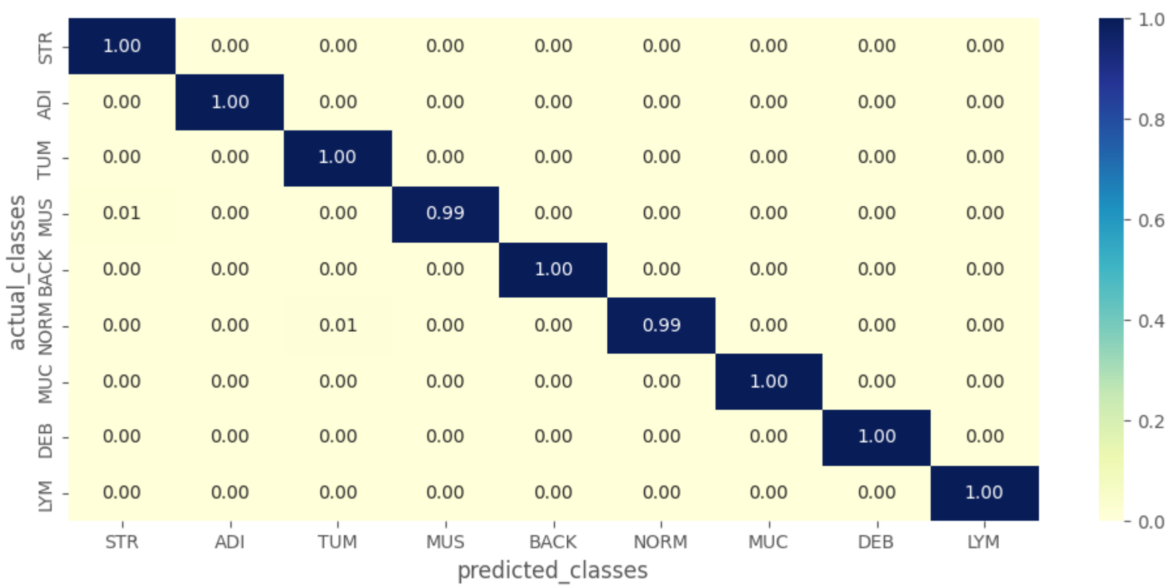


Figure 8:- The Confusion matrix of Resnet18 model between predicted classes and the actual classes on test data 1.

The confusion matrix of Resnet18 model on test data 2 shown in figure 9. Overall, the results show that test data 2 is more complex than test data 1 and the Resnet 18 model produced lower accuracy than on test data 1. Furthermore, the Stroma (STR) class has the lowest accuracy. The stroma class has important role to determine biomarker of colorectal carcinoma.

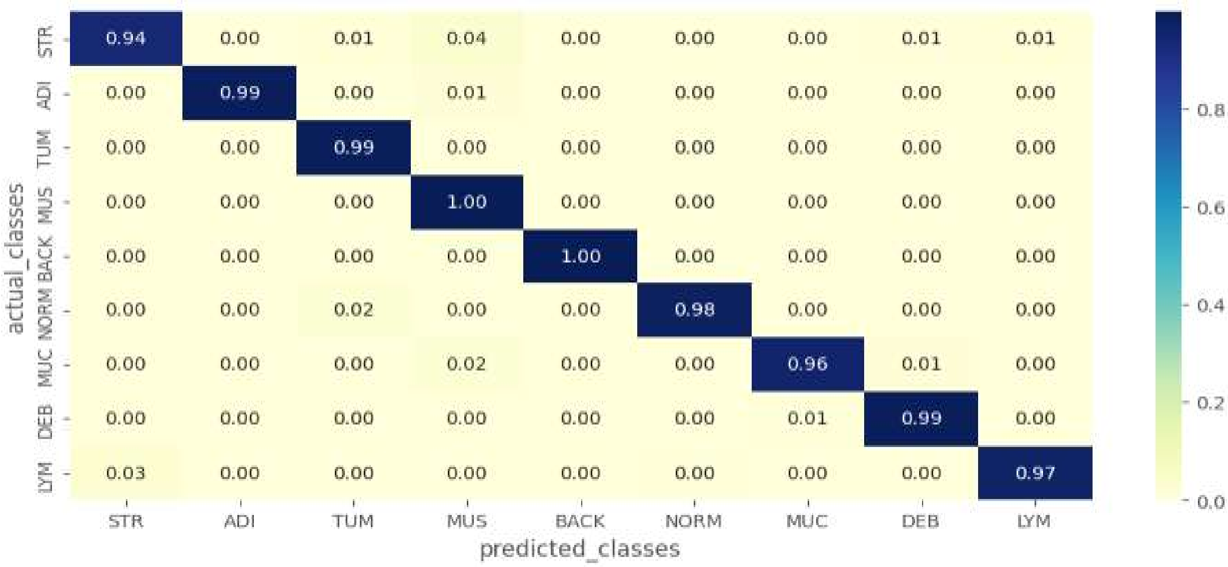


Figure 8:- The Confusion matrix of Resnet18 model between predicted classes and the actual classes on test data 2.

Conclusions:-

This paper reports the experimental comparisons five well-known based models which including Resnet18, Densenet201, Inception_v3, Efficientnet_b2 and MobilenetV2 on Colorectal Carcinoma patient images classification. This study has two contributions: first, this research can provide insight to medical expert and computer scientist related to the current state of development deep learning based approaches for histopathological images classification especially in colorectal carcinoma (CRC). The second contribution of this research can be used as a recommendation to select suitable CNN based models using Optuna hyper optimization for decomposition of CRC feature extraction, feature selection and classification of slides images.

Overall, the five CNN based models performs well on training data sets. However, Resnet18 and Innception_v3 shows stable and consistent performances. Densenet18 shows unstable results for 3 trials. The effcientnet_b3 produced the highest accuracy and Mobilenet_v2 shows the lowest accuracy.

CNN based models tested on two tests data: test data 1 and test data 2. Overall, Resnet 18 shows the highest on test data 1 and test data 2 with the highest speed. Therefore, further analysis on Resnet based models to find probability the correctness of classification and accuracy of predicted classes compare to the actual classes. From the results of Confusion matrix on test data 1 and test data 2, Resnet18 shows very good performances.

Acknowledgement:-

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