Short thesis for the degree of doctor of philosophy (PhD)

Predicting medical images using convolutional neural network

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Contents

1. Introduction

Cancer is one of the most lethal diseases in the world at the present time. Cancer itself is categorized as a non-communicable disease. Through a study, the World Health Organization (WHO) stated that cancer kills humans during productive age or before 70 years [1]. Cancer can be defined as hundreds of diseases with different characteristics from one another. Human cells, which are abundant, can reproduce and are dependent on one another. The human body can control these cells' proliferation in normal conditions to maintain their shape and size. However, cancer cells interfere with this growth by moving from one place to another and change shape and size beyond the control of the human metabolism [10].

Clinical diagnosis is necessary to be done by doctors predominantly before confirming whether a patient has cancer or not. Furthermore, the patient is advised to do a pathological examination by an expert using a microscope. Presently, with the availability of Whole Slide Image Scanner, there has been a significant improvement in the quality and quantity of the cancer diagnosis process due to its ability to detect variables in a more comprehensive histopathology image [7]. Another advantage of this tool is its ability to record appropriately all biological processes in the human body, such as apoptosis, angiogenesis, and metastasis [11]. The process of digitizing by the whole slide image scanner data resulted in an explosion of large amounts of data. Thus, the availability of sufficient data can be utilized to implement deep learning by developing a Convolutional Neural Network (CNN) model [9]

Understanding the fact that to distinguish histopathology images containing cancer cells and not containing cancer cells requires an expert's ability and supported by the fact that the development of machine learning methods have reported satisfactory achievements in classifying image data, this dissertation focused on implementing artificial intelligence such as a pathologist in classifying human histopathology images by utilizing machine learning methods, especially convolutional neural networks.

This dissertation's main idea has been published in both proceedings and journals in the form of articles [4, 5, 6] that will be discussed later. This work aimed to optimize the CNN model for predicting cancer cells in human histopathology images. The first experiment was run by developing a VGG module. The convolution layers in the VGG model were re-implemented with several adjustments, including the number of layers, convolution channels, filters, multilayer perceptron (MLP), and convolution blocks. The histopathology images in the dataset are then trained using a model developed to detect cancer cells.

The second experiment focused on ensemble-based CNN development. Ensemble-based CNN combines two or more sub-models in order to get better performance. The proposed ensemble model is a combination of three sub-models built from scratch by implementing three well-known CNN modules, namely the VGG module, the Inception module, and the ResNet module.

The last experiment focused on the efficiency of the ensemble model. If the previous work ensemble members were trained separately, and the final result was determined by voting, the ensemble members were trained simultaneously in an interconnected model in this work. Furthermore, in the first ensemble model, each sub-model weight is determined by the user, but in the second ensemble model, the weighting is part of the training process. The interconnected model determines the appropriate weight for each sub-model. Thus, the sub-model with better performance will possess a bigger weight than the other model.

2. Single CNN to Classify Medical Images

In the first experiment [6], the architecture was designed by adopting the VGG module. Referring to its architecture, VGG stacks convolution layers. Based on this idea, we stacked eight convolution layers, which were two 64 channels of convolution, two 128 channels of convolution, two 256 channels of convolution, and two 512 channels of convolution. Later, every two of these convolutions, a Max-pooling layer was inserted. Thus, four convolution blocks were formed, filled with two convolution layers and a max-pooling layer in each block. The next block was the MLP, a one-dimension vector. This requires the information that took shape multidimensional during the convolution process to be converted before entering the MLP block. This process involved a flatten layer which converts the multidimensional matrix to be a vector. After that, we installed two of the Dense layers with 64 channels and ended with the Dense layer two channels according to the problem in our dataset, the binary classification. We utilized the ReLu activation function on all layers except for the last layer that used the Sigmoid activation function. To avoid overfitting conditions, we also put two Dropout 0.5 after the 64 channels Dense layer. For more details, we show the architecture in Figure 2.1.

Hypothesis 1: The single CNN model built by implementing the VGG module can study the characteristics of the histopathological images on the PatchCam dataset.

Result 1: From the training process of 50 epochs, it can be reported that the architecture seems to be well implemented by achieving an accuracy value of 0.80 on the first epoch and 0.91 on the fiftieth epoch. Likewise, the model's parameters can be appropriately implemented, evidenced by the validation value for the first epoch, which was 0.83, and at the last epoch, 0.92. It was a significant and consistent decrease in the loss

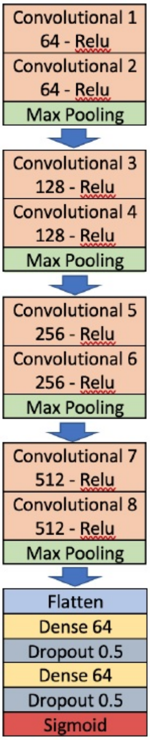

Figure 2.1: Architecture single CNN.

value during the training and validation. The initial loss value during the training was 0.45, then dropped to 0.22 at the fiftieth epoch. Simultaneously, the validation process had an initial loss value of 0.39 and ended with a loss value of 0.19 in the last epoch. The model's validation value and training accuracy were not incomparably indicated that the model was well implemented and did not experience overfitting.

Hypothesis 2: The single CNN model can predict cancer cells in Histopathology images.

Results 2: The model tested on 39,310 images that did not contain cancer cells, and 26,697 were images indicated to have cancer cells. As much as 37,058 normal images were correctly predicted as normal images, while 2252 normal images were incorrectly predicted as images containing cancer cells. On the other hand, 24,207 images indicated to have cancer cells have correctly predicted, and only 2490 images from this class were incorrectly predicted as normal images.

3. Ensemble CNN as a comparison for single CNN performance

In this experiment [4], we were using the VGG, Inception, and ResNet modules to design the ensemble model. To avoid very complex models, we designed a simpler architecture than the existing pre-trained models. Thus, the first model was the LT-VGG adopted from the VGG module. This architecture was a stack of thirteen layers consisting of ten Convolution layers and three Fully Connected layers. A Max Pooling layer was inserted in every two convolution layers to parse its dimensions. Then the Flatten layer changed the dimensions of the features to be passed on to the MLP. Within the MLP itself, there were three fully connected layers, each with two 64-neurons and a layer of two neurons. All activation functions in this architecture used the ReLu activation function except for the final layer used the Softmax activation function according to the dataset's problem.

The second model was the LT-Inception which adopted from the Inception module. The architecture in this model consisted of twelve convolution layers, divided into two levels. The architecture at both levels was identical, consisting of six convolution layers and ends with the Max Pooling layer. Afterward, the layers at each level were assembled. To reduce the number of dimensions of features, the Average Pooling layer was used. Finally, the feature was transmitted in an MLP consisting of two Fully Connected 64-neurons and a Fully Connected two neurons. The LT-Inception model used the ReLu Activation Function on almost all networks except the last layer, used Softmax two classes.

LT-ResNet was the last model we used in the designed ensemble. Using the ResNet module, we designed a total of 24 convolution layers. In detail, we installed eighteen convolution layers by inserting a residual layer on each of the three convolution layers. Like the previous model, LT-ResNet also used the Average Pooling layer and the Flatten layer before entering MLP. Furthermore, ended with the MLP consisted of three fully connected layers as in the two previous models.

The ensemble method is one of the popular techniques to improve CNN's accuracy, as described in [3, 8, 2]. In this work, we compared three single performances with the performance of the ensemble model. The ensemble method used was a voting system. Figure 3.1 is the design of our proposed model of the ensemble.

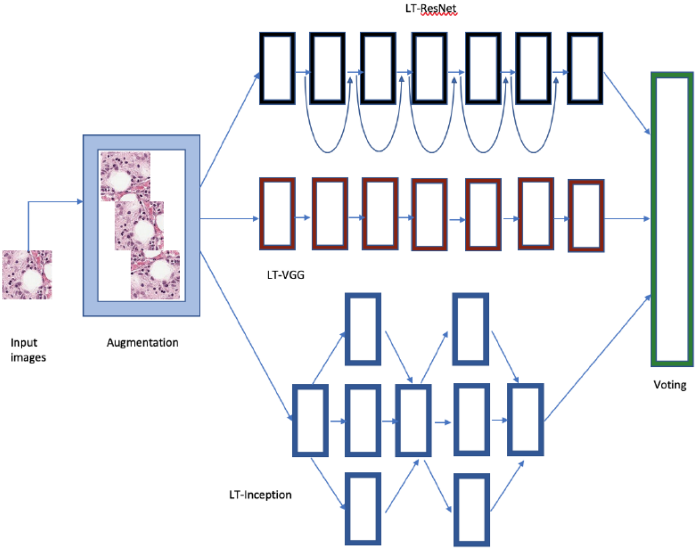

Figure 3.1: Architecture of the ensemble model.

Hypothesis 3: The three ensemble members, namely, LT VGG, LT Inception, and LT ResNet, performed well when trained separately.

Results 3: From the training results we found that the three single models did not experience overfitting, proven by the accuracy and validation values of the training process, which were not distant. In addition, the three single models showed a significant increase in accuracy and validation values from the first epoch to the last epoch. It also can be reported that the LT-ResNet model achieved accuracy and validation values of up to 0.95, the LT-Inception model achieved accuracy and validation values of up to 0.93, and LT-VGG reached accuracy and validation values of up to 0.95. Furthermore, the precision and recall values of every single network in each class were calculated. The results obtained was the LT ResNet achieved a precision score of 0.95 with a recall of 0.97 for normal category images and a precision score of 0.95, and a recall of 0.92 for images containing cancer cells. The LT-Inception model achieved a precision value of 0.92 and a recall of 0.96 for normal images, while for images containing cancer cells, 0.93 and 0.89, respectively, for the precision and recall scores. The VGG model showed excellent results with precision and recall values of 0.95 and 0.97, respectively for normal images, while for images containing cancer cells, the precision and recall values were 0.96 and 0.92, respectively. From the precision and recall calculations, it was clear that the LT-ResNet and LT-VGG models have slightly better capabilities than the LT-Inception model.

Hypothesis 4: Ensemble majority voting model can exceed the accuracy value of any single network model

Results 4: From the training results using the majority voting method, it was found that the ensemble model can correct the accuracy value of a single model up to 0.96, confirmed by the fact that the value of the precision and recall of the ensemble model was also better than the single network model. For normal im-

ages, the ensemble model achieved a precision value of 0.95 and a recall value of 0.98, while for images containing cancer cells, the ensemble model achieved precision and recall values of 0.96 and 0.93, respectively. After obtaining the training results for each single network, it was decided that the LT-ResNet and LT-VGG models each received a weight of 35%, while LT-Inception received a weight of 30% in the weighted voting process. The results of weighted voting also reported the same result as the majority vote method, namely an accuracy value of up to 0.96 as shown in Table 3.1. This confirmed that in our experiment, every single network received a suitable weight for the voting process.

x	LT-ResNet	LT-Inception	LT-VGG	MV	WMV
Pre 0	0.95	0.92	0.95	0.95	0.95
Rec 0	0.97	0.96	0.97	0.98	0.98
Pre 1	0.95	0.93	0.96	0.96	0.96
Rec 1	0.92	0.89	0.92	0.93	0.93
Acc	0.95	0.93	0.95	0.96	0.96

Table 3.1: Precision, Recall and Accuracy of the investigated models.

Hypothesis 5: Ensemble majority voting models predict cancer cells on histopathological images better than single network.

Results 5: We calculated the amount of the data either correctly or incorrectly predicted in the two classes. LT-ResNet was able to predict precisely 38,043 cancer images with 1653 images of errors. Meanwhile, the normal image that was predicted correctly was 24677 with an error rate of 2020. Furthermore, LT-Inception was able to predict accurately 37.657 images containing cancer cells with an error of 1653 images. As for normal *images, 23,634 images were predicted correctly with an error of 3063 images. LT-VGG correctly classified 38,186 cancer images and 1124 images misclassified. In the normal image class, 24,504 images were correctly classified, and 2193 images were misclassified. As previously, the ensemble model performed better than all single models. The results achieved by the majority voting system was 38,392 cancer images were successfully predicted with an error of 918 images. More than that, 24,773 normal images were predicted correctly with 1924 image errors. The majority voting results were confirmed by the results of the weighted majority vote, with 38,397 images predicted as images containing cancer cells and 913 images being misclassified. As many as 24,787 images were correctly predicted to be normal, with the error reaching 1910 images. Table 3.2 shows the comparison of the amount of data predicted correctly and incorrectly by all models.*

x	LT-ResNet	LT-Inception	LT-VGG	MV	WMV
TP	38043	37657	38186	38392	**38397**
TN	24677	23634	24504	24773	**24787**
FP	2020	3063	2193	1924	**1910**
FN	1265	1653	1124	918	**913**

Table 3.2: Confusion matrix of the investigated models.

4. Comparison of single, ensemble majority voting and, interconnected CNN performance in the medical images classification task

The interconnected CNN architecture is a combination of several CNNs. In this case [5], the three single networks were connected, which then trained together in a more extensive network to have a single decision. The purpose of connecting the three single networks was that even though the three single networks work independently, the results of training for every single network will determine how much this network affects the interconnected model. Thus, this training process will give the proper weight to every single network to influence the interconnected model in decision making.

In this work, we used three single networks, which were the pre-trained model. The three pre-trained models were VGG19 which consisted of 16-layer convolution; InceptionV3, which utilized 48-layer convolution; and MobileNet, which installed 18-layer convolution. After going through the convolution layer, the dimensions of the feature map need to be adjusted as required in the Multi-Layer Perceptron (MLP). For this reason, before the MLP section, a Flatten layer was installed to change the dimensions of the features. The MLP of each network was replaced with three fully connected layers to adjust to the problems in the dataset. Two of the fully connected layers used ReLu activation functions, while the other used the two-class Softmax function. In the next stage, the three single networks connected become one ensemble network. For this reason, the Concatenation layer was used to unite the three single networks into an Interconnected CNN model. After the three single networks were united, MLP consisted of two Fully Connected layers with a ReLu activation function and one final layer with two classes of Softmax was re-installed. The design architecture of the Interconnected model is shown in Figure 4.1.

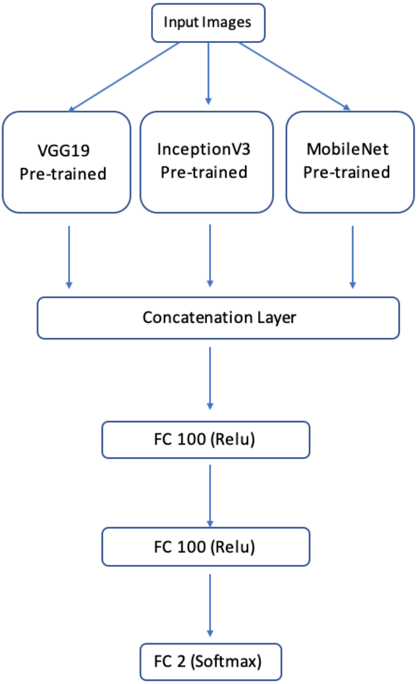

Figure 4.1: Architecture of the interconnected Model

Hypothesis 6:The interconnected model works better than the ensemble majority voting when predicting pneumonia in X-ray images.

Results 6: The predicting chest X-ray dataset shows that the accuracy values achieved were 0.91, 0.84, and 0.91, respectively, for the VGG19, InceptionV3, and MobileNet pre-trained models. In this case, although the Interconnected model cannot *exceed the accuracy value of the Majority Voting, the results of the two models can still be compared. In more detail, Table 4.1 provides a breakdown of the number of images that were predicted true or false in the two classes. From the values of Precision and Recall in Table 4.1, it was found that the ability of the Interconnected Model was slightly better than the majority voting. A total of 383 images indicated pneumonia could be predicted correctly and 7 images were mispredicted. Meanwhile, Majority Voting predicted images that indicate pneumonia as many as 370 images with 20 images were mispredicted. The number above was equivalent to the recall value of 0.98 for the Interconnected Model and 0.85 for the Majority Voting. Even so, the Precision values for the two models were still comparable, namely 0.91 and 0.87.*

Model	TP	FN	TN	FP	Acc	Pre	Rec
VGG19	361	29	206	28	0.91	0.88	0.88
InceptionV3	345	45	179	55	0.84	0.80	0.76
MobileNet	370	20	195	39	0.91	0.90	0.95
Majority Voting	370	20	198	36	0.91	0.91	0.85
Interconnected	383	7	177	57	0.90	0.87	0.98

Table 4.1: Confusion matrix and classification report of chest X-ray dataset.

Hypothesis 7: The interconnected model works better than the ensemble majority voting when predicting malaria on blood smear images.

Results 7: The model was also tested on a malaria test set that had never been used before in the training process. Table 4.2 shows slightly different results where two of the single models achieved good results while one model had lower performance than the previous two models. Models VGG19 and InceptionV3 *achieved an accuracy value of 0.87, while MobileNet achieved an accuracy value of 0.72. MobileNet's ability was not optimum due to the significant errors when predicting images containing malaria. Thus these results brought out two dominant models in the voting process. So that the accuracy value of Majority Voting can still be maintained at a reasonably good value, namely 0.86. On the other hand, the Interconnected model worked adequately well by assigning precise weights to every single network, raising the accuracy value to 0.88. This can be seen in detail in Table 4.2 where the Interconnected Model reached a recall value of up to 0.82 compared to the Majority Voting, which only reaches 0.74. These values were obtained from the number of images that the two models can predict accurately. The Interconnected Model accurately predicted 823 malaria images with 177 errors compared to the Majority Voting, which could only accurately predict as many as 737 malaria images with 263 prediction errors. Even so, the Precision value of all models was above 0.93.*

Model	TP	FN	TN	FP	Acc	Pre	Rec
VGG19	798	202	938	62	0.87	0.93	0.80
InceptionV3	776	224	963	37	0.87	0.95	0.78
MobileNet	443	557	997	3	0.72	0.99	0.44
Majority Voting	737	263	988	12	0.86	0.98	0.74
Interconnected	823	177	942	58	0.88	0.93	0.82

Table 4.2: Confusion matrix and classification report of Malaria dataset.

Model	TP	FN	TN	FP	Acc	Pre	Rec
VGG19	6692	2199	12400	709	0.87	0.89	0.75
InceptionV3	6638	2253	8838	4271	0.70	0.61	0.75
MobileNet	2696	6195	11882	1227	0.66	0.69	0.30
Majority Voting	5902	2989	12342	767	0.83	0.88	0.66
Interconnected	6721	2170	12316	793	0.87	0.89	0.77

Table 4.3: Confusion matrix and classification report of PatchCam dataset.

Hypothesis 8:The interconnected model works better than the ensemble majority voting when predicting cancer cells on histopathology images.

Results 8: The final evaluation process involved the PatchCam test set, which has never been used before by all models in the training process. From Table 4.3, it can be seen that this experiment only shows one dominant model, namely the VGG19 model with an accuracy value of 0.87. Meanwhile, the other two models achieved accuracy values of 0.73 for InceptionV3 and 0.66 for MobileNet. This result influenced the voting process, which could only reach a score of 0.83. Concurrently, the Interconnected Model achieved an accuracy value of 0.87, proving that the Interconnected Model can find the correct weight for every single model in the training process. It was also verified by the Precision and Recall value of the Interconnected model, which was better than the Majority Voting value, namely, 0.89 compared to 0.88 for the Precision value and 0.77 compared to 0.66 the recall value.

Publications

Journal publications related to this dissertation:

1. Oktavian Lantang, Gyorgy Terdik, Andras Hajdu, and Attila Tiba. "Comparison of single and ensemble-based convolutional neural network for cancerous image classification". In: *Annales Mathematicae Et Informaticae* 54 (2021), pp. 45-56.
2. Oktavian Lantang, Gyorgy Terdik, Andras Hajdu, and Attila Tiba. "Investigation of the efficiency of an interconnected convolutional neural network by classifying medical images". In: *Annales Mathematicae et Informaticae* 53 (2021), pp. 219-234.

Conference and proceedings related to this dissertation:

1. Oktavian Lantang, Attila Tiba, Andras Hajdu, and Gyorgy Terdik. "Convolutional Neural Network for Predicting The Spread of Cancer". In: *Proceedings of the 2019 10th IEEE International Conference on Cognitive Infocommunications (CogInfoCom)*. Naples, Italy: IEEE, 2019, pp. 175-180.

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[5] Oktavian Lantang, Gyorgy Terdik, Andras Hajdu, and Attila Tiba. “Investigation of the efficiency of an interconnected convolutional neural network by classifying medical images”. In: *Annales Mathematicae et Informaticae* 53

(2021), pp. 219–234. DOI: https://doi.org/10.33039/ami.2021.04.001.

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List of publications related to the dissertation

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1. **Lantang, O.**, Terdik, G., Hajdu, A., Tiba, A.: Comparison of single and ensemble-based convolutional neural networks for cancerous image classification.
   Ann. Math. Inform. 54, 45-56, 2021. ISSN: 1787-5021.
   DOI: http://dx.doi.org/10.33039/ami.2021.03.013
2. **Lantang, O.**, Terdik, G., Hajdu, A., Tiba, A.: Investigation of the efficiency of an interconnected convolutional neural network by classifying medical images.
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Foreign language conference proceedings (1)

3. **Lantang, O.**, Tiba, A., Hajdu, A., Terdik, G.: Convolutional Neural Network For Predicting The Spread of Cancer.
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