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Implementation of a faster R-CNN algorithm for identification of metastatic tissue using lymphoma histopathological images

Puja Aditya Winata[1], Isnaini Roysida[2]
[1,2]Department of Mathematics, Universitas Negeri Semarang, Indonesia

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ABSTRACT

Procedures for diagnosis of lymphoma includes blood tests, CT scan or MRI, and histopathological examination through a biopsy. Histopathological examination is the gold standard of diagnosis. Pathology diagnosis of lymphoma is challenging and difficult in the field of diagnostic pathology. This study aims to identify lymph node metastases using the Faster R-CNN algorithm using histopathological images of lymph nodes so that the Faster R-CNN system design can help the medical team to make diagnostic decisions. Identification carried out by Faster R-CNN is by classifying histopathological images into normal classes and metastatic classes. Loss values that are not indicated for underfitting and overfitting are shown from the 10th epoch to the 20th epoch. The optimizer and the number of epochs for the optimal value of 83.3% accuracy and 71.8% recall are ADAM with 20 epochs. The accuracy and recall results obtained are quite good. 1113 metastatic images and 1478 normal images were predicted correctly, while 437 metastatic images and 82 normal images were predicted incorrectly.

Corresponding Author:

Isnaini Roysida,
Department of Mathematics,
Universitas Negeri Semarang,
Sekaran, Semarang, 50229, Indonesia

Email: isnaini@mail.unnes.ac.id

1. INTRODUCTION

AI or what we know as artificial intelligence is the result of the development of computer technology. According to [1] AI is a subset of computer science derived from mathematics, logic, philosophy, psychology, cognitive science, and biology. AI and machine learning are two things that cannot be separated. According to [2] machine learning is just what is needed for a system to become AI. Machine learning is analogous to a machine or computer that can learn without having to be programmed explicitly first [3][4].

Deep learning is part of machine learning based on artificial neural networks. Deep learning is a process that involves a layered neural network architecture [1]. One of the popular deep learning implementations in computer vision is pattern recognition. Computer vision uses image features, such as color, shape texture to infer image content [5][6]. Image is a photo of a two-dimensional display that describes a visualization of an object. Meanwhile, a digital image is an array of numbers in two dimensions and stored in an array of digital numbers which is the result of quantification of the brightness level of each pixel that composes the image. Where pixels themselves are small elements that make up a digital image [7][8].

The implementation of deep learning as pattern recognition can be used in many fields, one of which is in the health sector, such as the research conducted by [6] regarding the diagnosis of cancer in images of histopathological examination results using the Convolutional Neural Network (CNN) approach.

Known approaches in deep learning that are used for classification and object detection include CNN, Regional Based CNN (R-CNN), Fast Regional Based CNN (Fast R-CNN), and Faster Regional Based CNN (Faster R-CNN). Faster R-CNN is an algorithm that is faster than R-CNN and Fast R-CNN in making predictions. In [10], it is shown that the speed of Faster R-CNN in image prediction is 0.2 seconds, faster than Fast R-CNN which is 2.3 seconds, and R-CNN is 49 seconds. Faster R-CNN yields impressive accuracy results, in the research [11] faster R-CNN provides 99% accuracy in tumor detection in brain. Although faster R-CNN is an algorithm used for object detection, this algorithm can also be used for classification purposes and produces better accuracy than CNN. The classification of nutmeg quality with faster RCNN produces an average accuracy of 93%, better than CNN with an accuracy of 86% [12]. In addition, [13] also used faster R-CNN to classify woven fabric patterns, and produced better accuracy than CNN with 82.14% accuracy for faster R-CNN and 76% accuracy for CNN.

Cancer of the lymph nodes (lymphoma) is a dangerous disease. [14] explained lymph node cancer or often known as lymphoma cancer is a cancer of the blood in the lymphatic system that causes enlarged lymph nodes.. Lymphoma (non-Hodgkin) was ranked the seventh type of cancer with the highest Indonesia national cases in 2020 [15]. In a study conducted by [16], identification of metastatic lymph nodes in MR imaging with faster region-based convolutional neural networks shows good accuracy results with 0.912 or 91.2%, but the research conducted is only from a radiological perspective because it uses MRI images, not pathologically. Histopathological examination or pathology is considered to be the gold standard procedure for arriving at the final diagnosis of various lesions on the human body [17]. Pathology diagnosis of lymphoma is a challenging and difficult in the field of diagnostic pathology [18]. Based on this, this study utilizes faster R-CNN algorithm to identify lymph node metastases by classifying images into normal and metastatic classes using lymph node histopathology images, to facilitate medical personnel in making decisions about lymphoma diagnosis quickly and easily.

The purpose of this research is to determine the optimal hyperparameter to get the best accuracy value. Determination of hyperparameters is obtained by analyzing the validation loss and training loss values to determine the number of epochs that do not indicate underfitting and overfitting to be further selected and continued in the testing process to obtain the best accuracy results. The training process will use two different optimization methods. The optimization methods used are SGD and ADAM, so it will be analyzed which optimization method has the best accuracy. Since histopathology is the gold standard procedure for pathology to arrive at a final diagnosis [17] and previous studies [16] proposed Faster R-CNN which can only identify radiologically because it can only identify MRI images, the Faster R-CNN proposed in this study will later be able to carry out diagnostics pathology by identifying histopathological images. [18] explained that although current pathology diagnoses are based on combining results from ancillary techniques, the final diagnosis is still the subjective conclusion of a pathologist. Due to variations in training background and practical experience, pathologists sometimes draw different conclusions from the same objective specimen. These discrepancies can delay the proper treatment for patients, and in extreme circumstances can cause legal problems. Based on these problems, the Faster R-CNN proposed in this study can provide a fast and precise diagnosis to help integrate the diagnosis of pathologists.

2. METHOD

2.1 Data Source

The data source used in this study is secondary data on histopathological lymph node images from part of the dataset by [19] and [20]. Data collected by [20] is 399 whole-slide images and corresponding glass slides of SLNs during the first half of 2015. SLNs were retrospectively sampled from 399 patients that underwent surgery for breast cancer at 2 hospitals in the Netherlands: Radboud University Medical Center (RUMC) and University Medical Center Utrecht (UMCU). It consists of color (RGB) images (96 x 96px) extracted from histopathologic scans of lymph node sections. Each image is annotated with a binary label indicating presence of metastatic tissue. The data taken will be divided for data training, validation, and testing. Details of the amount of data used can be seen in Table 1.

An example of histopathological image data used in this study and their class distribution is shown in Figure 1 and Figure 2. The number of classes for this data is 2, namely metastatic and normal. The metastatic class represents a class with images that contain cancer while the normal class represents images that are not found to have cancer. In Figure 1 also show that the image with a yellow outline shows the image dataset for the mestastaic class, while the image with the blue outline shows the image dataset for the normal class.

Table 1. Amount of Data Used

	Training	Validation	Testing
Metastatic	6589	1658	1555
Normal	5911	1402	1555
Total Data	12500	3060	3110

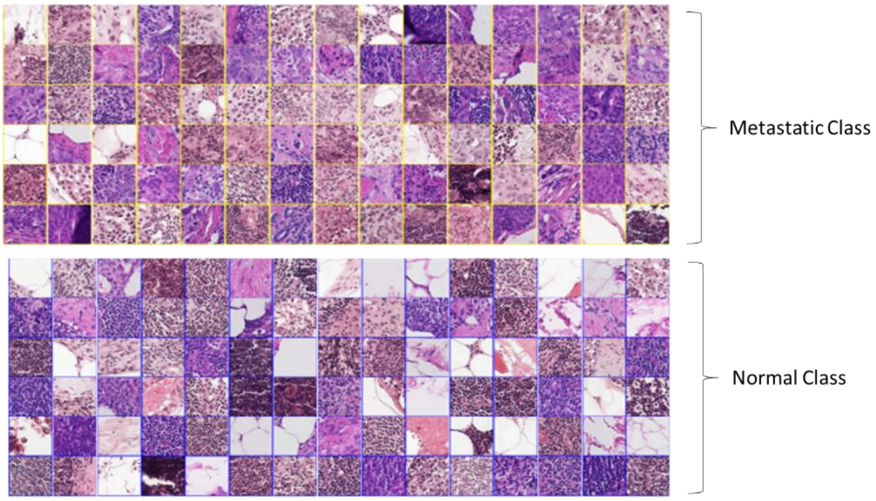

Figure 1 Examples of histopatological images

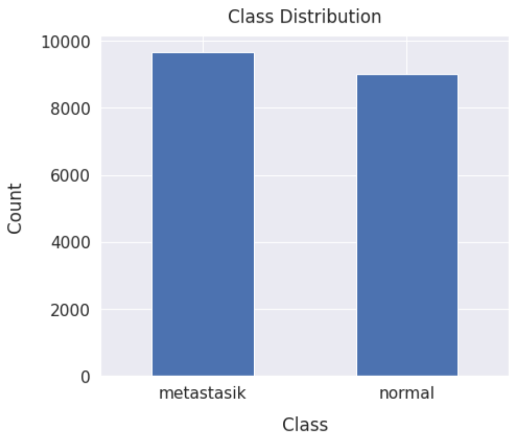

Figure 2 Class Distribution

2.2 Faster Regional-based Convolutional Neural Network (Faster R-CNN)

Faster R-CNN algorithm will be used to learn histopathological image pattern in training data to identify images for normal and metastatic classes. Faster R-CNN is the next generation of object selection developed from fast R-CNN where faster R-CNN shows impressive results in object detection [21][22]. In [23] the object detection system called faster R-CNN consists of two modules. The first module is a deep fully convolutional that proposes regions, and the second module is a fast R-CNN detector that uses the proposed region. The whole system is a single and unified network for object detection as can be seen in Figure 3. Using neural network terminology with an "attention" mechanism, RPN module tells fast R-CNN module where to look or it is this RPN that proposes a region (which part of an image needs to be "looked at" further).

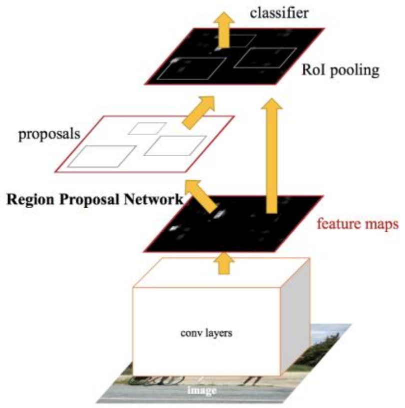

Figure 3. Faster R-CNN architecture [23]

2.3 Experimental Scenario

The experiment that will be carried out is to determine the maximum number of epochs as much as 20 for each different optimizer selected. The selected optimizers are Stochastic Gradient Descent (SGD) and Adaptive Moment Estimation (ADAM). According to [24]–[26] optimization function is a function that is useful for improving the training (learning) process on the system. Optimizer is an algorithm for process optimization, and optimization itself is an artificial intelligence process to find the value of a function (usually called a fitness function).

The validation method in this study is used as a process to see in what epochs the model does not indicate underfitting and overfitting. After the training and validation processes have been carried out, the models that are not indicated for underfitting and overfitting will be seen through the loss value and then selected to enter the testing process.

The data preprocessing process carried out is as follows.

1. Checking and eliminating missing values, data duplication, and checking the balance of the number of classes from each class. Figure 1 shows that there is no class imbalance because the number of classes from each class is not much different.
2. Make augmentation on the image. This process aims to provide variations to each image so that the faster R-CNN can understand image patterns with various image variations. The augmentation performed is vertical and horizontal rotation of the image as shown in Figure 3.

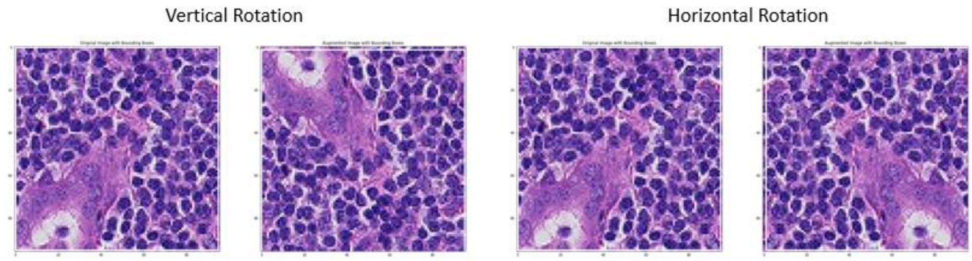

Figure 4 Augmentation of histopatological image

3. Define training parameters of Faster R-CNN. The training parameters used in this study are shown in the following Table 2. In this study the GPU used for this research is the Tesla P100. In this study all experiments have been implemented using PyTorch library in Google Colab. Based on the flowchart in Figure 5 below, we used the pretrained Faster R-CNN with ResNet50 backbone as object detection model. Based on [27] ResNet50 are less demanding to optimize and can obtain high accuracy as the dept increases. ResNet50 has 50 layer deep-CNN and

ResNet-50 model was trained on 1.28 million training images in 1000 classes and reaching an average of 5.25% of top-5 error [28]. The architecture of ResNet50 is shown in Figure 6.

Table 2 Training Parameters

Pre-Trained Weight	Optimizer	Optimizer parameters	Epoch Maximum	Batch Size	Num_classes	Dimention Input
ResNet 50 (COCO Pre-trained Dataset)	SGD	γ = 0.0001, $\mu = 0, \lambda = 0, \tau = 0$	20	4	2	96 x 96 px
	ADAM	γ = 0.0001, β_1= 0.9, β_2=0.999, $\epsilon = 10^{-8}, \lambda = 0$				

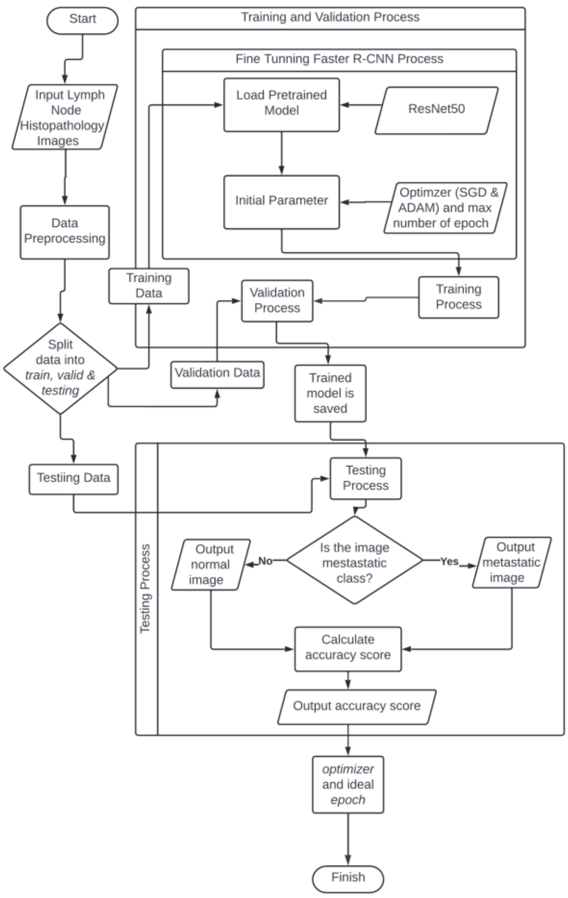

Figure 5. System Flowchart

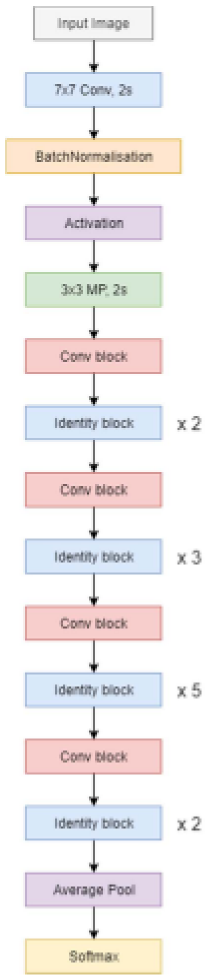

Figure 6 ResNet50 Architecture [27]

3. RESULTS AND DISCUSSIONS

3.1 The Loss Value of the Training Process and the Accuracy of the Testing Process

The calculation of the loss value in the training and validation process uses the PyTorch Cross-Entropy Loss Function. The PyTorch Cross-Entropy Loss Function formula equation is defined as follows.

$$\ell(x, y) = L = \{l_1, \dots, l_N\}^\top, \; l_n = -w_{y_n} \log \frac{\exp(x_{n,y_n})}{\sum_{c=1}^{C} \exp(x_{n,c})} \cdot 1 \qquad (1)$$

Figure 3 shows the value of training loss and validation loss of the two models using the SGD and ADAM optimizers starting close to each other and approaching stable at epochs 10 to 20. This shows the model with epochs 10 to 20 does not indicated underfitting and overfitting. So that the model that will be chosen to be used in the testing process is a model with number of epochs 10 to 20.

Figure 7. Training Loss and Validation Loss from Each Optimizer

Table 2 is the result of accuracy and recall of the model that has been previously selected in the validation process. Calculation of the value of accuracy and recall using the confusion matrix showed in Figure 7. Equation (2) and (3) below are the formula of accuracy and recall. The metric values for measuring the performance of the model used are accuracy and recall because the number of classes is close to symmetrical and this study is a medical case that wants more false positives than false negatives.

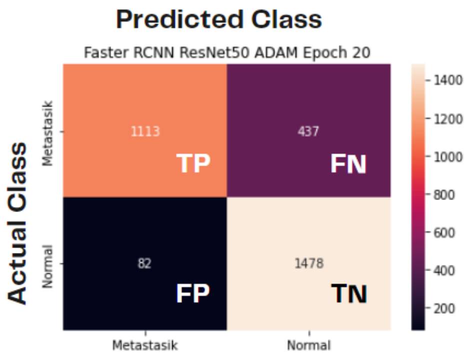

Figure 8 Example output of confusion matrix

$$Accuracy = \frac{TP+TN}{(TP+TN+FP+FN)} \quad (2)$$

$$Recall = \frac{TP}{(FN+TP)} \quad (3)$$

3.2 Optimal Optimizer and Epoch Number

From Table 2, the model with the SGD optimizer has an optimal value of 0.807 or 80.7% for accuracy and 0.639 or 63.9% for recall. This value is achieved by the model with 20 number of epochs. The model with the ADAM optimizer had an optimal value of 0.833 or 83.3% for accuracy and 0.718 or 71.8% for recall. This value is achieved by the model with 20 number of epochs. So the faster R-CNN model with the ADAM optimizer shows better performance than the faster R-CNN model that uses the SGD optimizer, and the optimal model in classifying metastatic tissue is the faster R-CNN model using the ADAM optimizer with a total of 20 epochs. The optimal model accuracy value is 83.3%, the optimal recall value is 71.8%, and the precision value is 93.1%. Based on the results of the 83% accuracy, the designed Faster R-CNN model can identify as many as 2591 images correctly out of total 3110 images. The results achieved indicate that the model has been able to identify metastatic and normal images quite well.

3.3 Image Classification Result

Table 3 shows the classification results for normal classes are higher than the results for metastatic class classification. These results indicate that the faster R-CNN system recognizes normal histopathological image patterns better than metastatic histopathological images. For the ADAM optimizer with the number of epochs of 20 that has optimal accuracy and optimal recall values, successfully predict 1113 metastatic images correctly, and 1478 normal images correctly. While the wrong predictions are 437 for metastatic images, and 82 for normal images.

Table 3. Accuracy, Recall, and Precision Testing Process

Optimizer	*Epoch*	**Precision**	**Accuracy**	**Recall**	**Prediction Time (in seconds)**	**Prediction Time Each Image (in seconds)**
SGD	10	0,961	0,768	0,557	279,454	0,0899
	11	0,959	0,778	0,580	279,650	0,0899
	12	0,964	0,774	0,568	279,459	0,0899
	13	0,963	0,775	0,571	279,151	0,0898
	14	0,965	0,779	0,577	279,517	0,0899
	15	0,965	0,780	0,580	279,447	0,0899
	16	0,969	0,765	0,546	278,323	0,0895
	17	0,972	0,772	0,559	279,204	0,0898
	18	0,966	0,780	0,579	279,354	0,0898
	19	0,970	0,785	0,586	279,527	0,0899
	20	0,959	0,807	0,639	284,056	0,0913
ADAM	10	0,961	0,791	0,606	278,363	0,0895
	11	0,958	0,805	0,637	278,733	0,0896
	12	0,969	0,810	0,639	278,935	0,0897
	13	0,969	0,810	0,639	279,027	0,0897
	14	0,967	0,787	0,592	279,966	0,0900
	15	0,934	0,830	0,708	279,721	0,0899
	16	0,966	0,769	0,555	280,052	0,0900
	17	0,970	0,807	0,632	283,165	0,0910
	18	0,965	0,813	0,648	284,277	0,0914
	19	0,965	0,813	0,647	284,923	0,0916
	20	0,931	0,833	0,718	284,977	0,0916

Table 4. Classification Result Each Class

Optimizer	*Epoch*	**Accuracy**		**Number of Correct Predictions**		**Number of Wrong Prediction**	
		Metastatic	**Normal**	**Metastatic**	**Normal**	**Metastatic**	**Normal**
SGD	10	0,557	0,978	864	1525	686	35
	11	0,580	0,976	899	1522	651	38
	12	0,568	0,979	880	1528	670	32
	13	0,571	0,978	885	1526	665	34
	14	0,577	0,979	894	1528	656	32
	15	0,580	0,979	899	1528	651	32
	16	0,546	0,983	847	1533	703	27
	17	0,559	0,984	867	1535	683	25
	18	0,579	0,979	898	1528	652	32
	19	0,586	0,982	909	1532	641	28
	20	0,639	0,973	991	1518	559	42
ADAM	10	0,606	0,976	939	1522	611	38
	11	0,637	0,972	988	1517	562	43
	12	0,639	0,979	991	1528	559	32
	13	0,639	0,979	991	1528	559	32
	14	0,592	0,980	918	1529	632	31
	15	0,708	0,950	1098	1482	452	78
	16	0,555	0,981	861	1530	689	30
	17	0,632	0,981	980	1530	570	30
	18	0,648	0,977	1005	1524	545	36

Optimizer	Epoch	Accuracy		Number of Correct Predictions		Number of Wrong Prediction	
		Metastatic	Normal	Metastatic	Normal	Metastatic	Normal
	19	0,647	0,977	1003	1524	547	36
	20	0,718	0,947	1113	1478	437	82

4. CONCLUSION

The number of non-underfitting and non-overfitting epochs was shown from 10 to 20 epochs for the each optimizer. As a result, the SGD optimizer had an optimal accuracy of 80.7% and an optimal recall of 63.9%, while the ADAM optimizer has an optimal accuracy of 83.3% and an optimal recall of 71.8%. The ADAM optimizer had a higher optimal accuracy and recall value than SGD, with a total epoch of 20. The classification results showed that the faster algorithm model R-CNN recognized normal histopathological image patterns better than the metastatic class. For the ADAM optimizer with the number of epochs of 20 that had optimal accuracy and optimal recall values, successfully predict 1113 metastatic images correctly, and 1478 normal images correctly. While the wrong predictions were 437 for metastatic images, and 82 for normal images.

The results achieved by the proposed Faster R-CNN model with the ADAM optimization method are 83.3%. This means that the model successfully identified correctly 2591 images out of total 3110 histopathological images. The results show that the proposed model has been able to identify lymphoma metastatic tissue quite well. Compared to research conducted by [29] regarding the Classification of Colorectal Cancer Lymph Node where the optimal accuracy results with the AlexNet pre-trained model are 75%, the proposed model has better accuracy. However, the model still needs furthert raining to improve the recall value even better. The limitation in this study was that the maximum number of epochs used is only 20 because of the limitation of Google Colab runtime, therefore further research is needed by setting a higher number of epochs using other software such as MatLab or other software to get a higher optimal value, and due to the limitations of the available datasets only having a binary label without a bounding box by a pathologist, the identification made is only in the form of a classification so that for further research, the faster R-CNN algorithm is expected to be developed as an object detection for identification of lymph node metastatic tissue in real time. Compared to [13], this study proposed a model using the Faster R-CNN with ADAM optimization method because in this case, ADAM optimization has a better accuracy value than SGD. Since this model can carry out a pathological diagnosis by classifying histopathological images, this model can be used as a gold standard pathology diagnosis compared to radiological diagnosis.

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