

Heinz 95-845: Image Classification for Colorectal Cancer Diagnosis with CNN Model Machine Learning and Health Care

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Abstract

The aim of this project is to implement a Convolutional Neural Network (CNN) to extract distinctive features from the images of HE stained colon tissue and predict the benign or malignant status for the sample. In this article, We will elaborate the ConvNet architecture which enabled an efficient training with an average accuracy nearly 70% on test samples. In our model, we also chose a very popular optimizer Adam algorithm to better control the learning rate and minimize memory usage.

1. Introduction

Image Classification is to assign an input image to a predefined fixed set of categories based on the identified representations. k-nearest neighbor (k-NN) and Support-Vector-Machine (SVM) are the most commonly adopted algorithms for classification. One of the most evident difference between these two approaches is that the former is a non-parametric classifier while the latter as learning-based classifier (Eli and O, 2008). Some research (J and BS, 2012)revealed that SVM outperformed k-NN on image datasets that have multiple attributes. One critical defect of k-NN is that it has a significantly high memory requirement to store all training images and high computation costs to compare test with all training images. SVM was considered to perform well on high-dimensional image datasets.

However, success in ImageNet competition in 2012 brought CNN in the spotlight and its substantially reduced top 5 error rate (15.4% vs. the second best entry at 26.2%) (A and SutskeverI, 2012)shocked the computer vision community. They began to realize the true value of CNN. Since then, CNN became increasingly popular and now as a state-of-art method to recognize objects, it has been widely applied in a variety of fields ranging from natural language processing to medical image analysis. As compared with other machine learning approaches, CNN is strong in extracting invariant image features through multiple stages, which enables CNN to learn representations of images more effectively.

In this work, we will implement a CNN model on HE-stained colorectal images and make a prediction on whether the glands in a given image indicate a benign or malignant colon tumor. In the model, we created the basic building blocks for a simple ConvNet and explored Adam algorithm instead of the more commonly used stochastic gradient descent (SGD) to train the model.

In Section 2, we provide background on colorectal cancer diagnosis based on histological image analysis and fundamental concepts to understand CNN architecture, such as convolutional layer, pooling layer, etc. In Section 3, we will deep dive into the model we built and go through each layer to understand how it works for classification. In the next

Section, we will cover the data description, pre-processing process, method comparison and evaluation criteria. In Section 5, we will visualize some quantitative metrics to show how well our method works. In the last section, we will comprehensively evaluate our project in the following aspects including the contribution to existing research work, the limitations of our project and implications for clinical decision-making on colon cancer.

2. Background

Colorectal cancer is the third most common cancer diagnosed in both men and women in the United States (Society, 2016). HE stained histological images are considered as one of the best ways to detect the morphological features of glands. Over ninety percent of colorectal carcinomas could be categorized as adenocarcinomas, which are characterized by glandular morphology (M and S, 2013). Glandular malformation, in particular, the degree of differentiation from the normal glands determines the colon cancer grading. Detection and visual interpretation of morphological features largely affect pathologists' decision-making on whether the colorectal tumor is benign and malignant. Currently, pathologists are still playing a key role in manually reading and evaluating the images of HE-stained slides. One aim of our project is to automate this process and build a ConvNet to accurately discriminate benign cases from malignant cases.

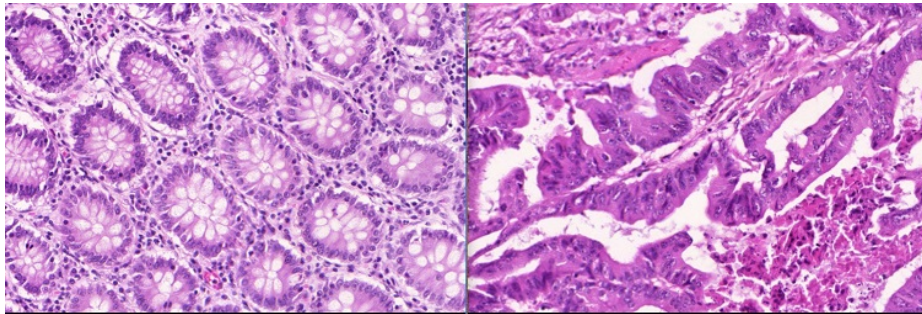


Figure 1: Comparison of the Benign Case (left) and Malignant Case (right)

Different from a regular Neural Network, a neuron in ConvNet has three dimensions (width, height, depth). For RGB image the depth would be 3, but in our project, we use RGBA images and therefore the depth would be 4. There are three major types of layers in a ConvNet - convolutional layer, pooling layer and fully-connected layer. Through multiple layers, a ConvNet could eventually transform 3D-array pixel values of an image into a class score.

In **convolutional layers**, a set of learnable filters (in tensorflow environment, it's also called kernel) slide across each small local regions of the input (or receptive field) and compute the dot product of the input and its weight to generate a 2D feature map (or activation map) (Stanford, 2016). Every time the filter slides, the number of pixels it skips is called stride. For example, if the filter moves by 2 pixels, the stride equals to 2. The size of the receptive fields is regarded as the spatial extent of the filter. When the filter moves to the border, a zero will be added to the input array and this is called zero-padding.

Pooling layers is added between convolutional layers to reduce volume size of the input. If we let the original size be $W0 * H0 * D0$, the number of filters be K , the spatial extent be F , the stride be S and the number of zero padding be P . Input volume would be:

$$InputVolume = W0 * H0 * D0$$

$$OutputVolume = W1 * H1 * D1$$

$$W1 = (W0 - F + 2P) / S + 1;$$

$$H1 = (H0 - F + 2P) / S + 1$$

$$D1 = K$$

In addition, we applied a max filter to each non-overlapped receptive field to lower the dimensionalities, which is called max pooling

Fully-connected layers is connected to activations of each layer and used to compute the class score. Each image get a score for each class. We also added nonlinear activation function after fully-connected layer and in our model, we use ReLU to speed up the training

$$relu(x) = \max(0, x)$$

Another concept to introduce is called **loss**. Take our project for example, if an image of a benign case gets a very high score for the label "malignant", it means it has a high (poor) loss. One of our aims is to minimize the loss and increase the accuracy.

$$loss = -\log(P_j)$$

The last component is the classifier. In our project, we used softmax function as the classifier, which generates the normalized probabilities. The function is written as:

$$f_i(z) = e^{z_j} / \sum_k e^{z_k}$$

3. CNN Model

We built seven layers to create the simple ConvNet architecture (Please refer to figure 3 on the next page). The architecture is as follows:

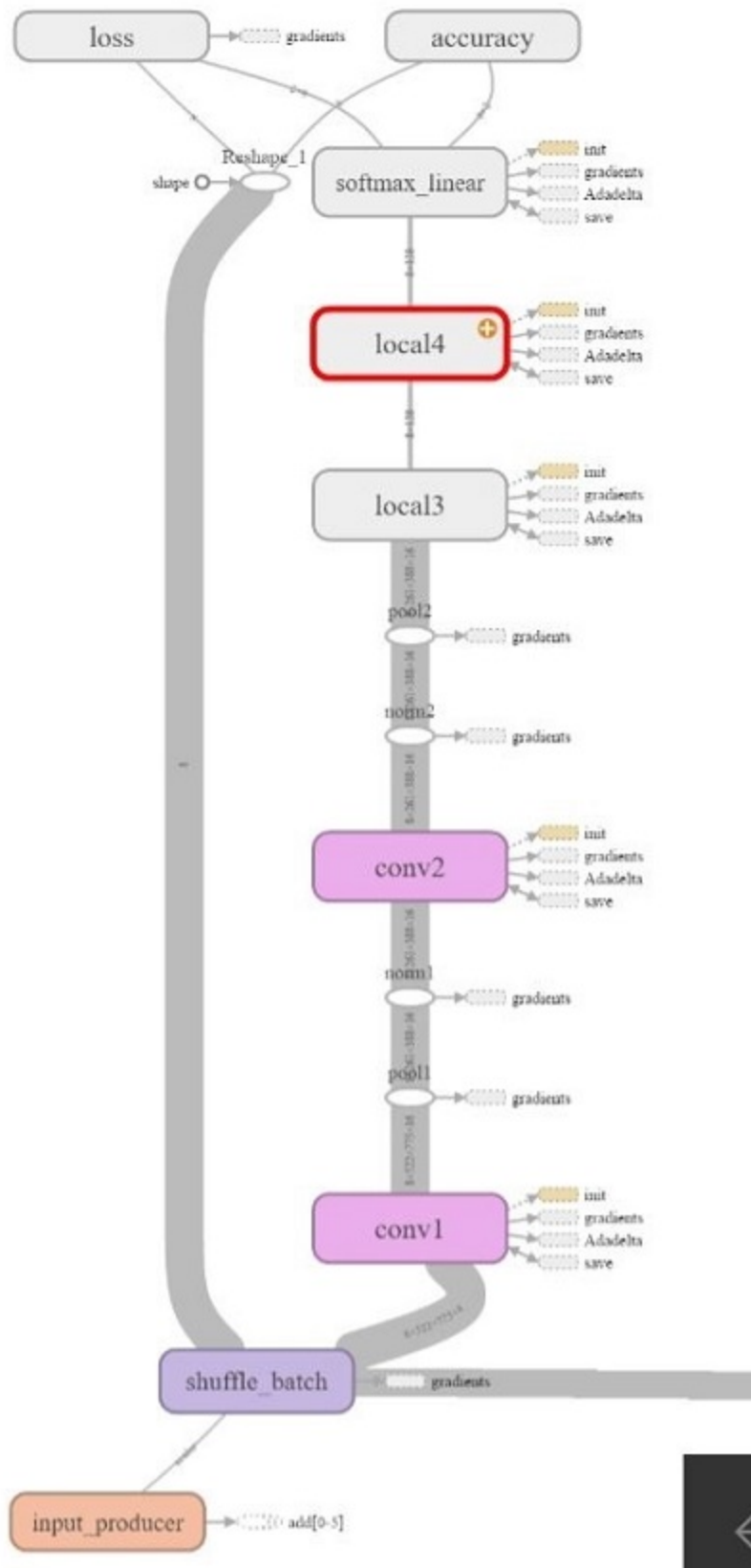
INPUT \rightarrow *CONV*(+*RELU*) \rightarrow *POOL* \rightarrow *CONV2*(+*RELU*) \rightarrow *POOL2* \rightarrow *FC*(+*RELU*)*2 \rightarrow *SO*

Convolution Layer We set the number of filters at 16, spatial extent at 3 and stride at 1. A total of two convolutional layers are implemented in this model for learning features.

Pooling Layer We added a local response normalization layer after pooling layer. The normalization layer works as a "lateral inhibition" to normalize the local neighbourhood of the excited neuron and better detect the features. In addition, 3*3 receptive fields are used for both pooling layers and 2*2 stride for the first one and 1*1 for the second one.

Full-connected layer Two full-connected layers are placed before the softmax function

ReLU layers ReLU is used as activation function throughout all layers



4
Figure 2: CNN Model used in this Project)

Training We chose Adam algorithms as the optimizer which requires less tuning parameter to perform well. Currently, it is recommended as the default optimizer to improve working efficiency and lower training costs (DP and J, 2014). The optimizer is used to minimize the loss function. In terms of setting learning rate, we set it at 0.0001. As a tricky hyperparameter, we cannot set it too high or too low.

Softmax We chose softmax instead of SVM as the classifier and assigned value 0 for benign case and value 1 for malignant case.

Layer Tyep	Configuration
Input	Size:775*522*4
Convolution	K =16, F =3, S=1, D= 4
Pooling	Max, F=3, S=2
Convolution	K = 16, F=3, S=1, D=4
Pooling	Max, F=3, S=1
CF	
SoftMax	
Loss	Negative Log-likelihood

Table 1: Architecture of Our Model

4. Experimental Setup

4.1 Cohort Selection

The dataset consists of 165 images of HE-stained colorectal adenocarcinoma in the format of BPM. All the datasets were acquired from the University of Warwickshire, UK. The table below shows the composition of the datasets in details.

Histologic Grade	Training Set (Width*Height)	Test Set A (W*H)	Test Set B(W*H)
Benign	1(574*433) 1(589*453) 35(775*522)	2(574*433) 4(589*453) 28(775*522)	4 (775*522)
Total(Benign)	= 37	=34	= 4
Malignant	1(567*430) 3(589*453) 44(755*522)	1 (578*433) 2 (581*422) 24 (755*522)	16(755*522)
Total(Malignant)	= 48	=27	=16

Table 2: Details of the Dataset

4.2 Data Preprocessing

As shown in the table above, it's easily observed that images are in different widths and heights. Therefore, we resized them to ensure they have consistent width and height. Given that the size of the majority images is 755*522 in pixels, we decided to set the target width

and height at (722,522). For those images with smaller size, we padded them evenly with zeros and then do normalization for each pixel. Different from the normal RGB images, we have to reset the shape of the images to ensure it has four channels.

Secondly, CNN performs better on a large-scale dataset and given that we only have 85 images in the training set, we did the data augmentation to improve its performance. In this model, we use random flip function to horizontally and vertically flip the images.

In addition, because tensorflow3.5 is applied to build the CNN model, we need to use a pipeline to read image files and convert input data into a 4-d tensor which has a shape of [batch, height, width, channels].

4.3 Feature Choices

The format of images is BMP which could not be decoded or processed by tensorflow and therefore we converted them into BNP format. Another important feature is that our images have four channels, indicating that if we want to leverage existing well-trained model like VGG16, we may have to convert them into RBG images.

4.4 Comparison Methods

We use a classic LeNet-5 architecture to build a seven-layer ConvNet. In vision4GlaS' model(Kainz et al., 2015), they also used a seven-layer architecture to do a classification but they had three convolutional layers and only one fully connected layer. The table below shows key performance metrics for their model

Dataset	Precision	Recall
Training	0.97 (0.09)	0.67(0.21)
Test A	0.83 (0.22)	0.60(0.24)
Test B	0.70(0.35)	0.48(0.30)

Table 3: Performance Metrics of vision4GlaS' Model

4.5 Evaluation Criteria

To fine-tune our hyperparameters, we conducted a 5-fold cross-validation (ratio = 0.2). We split the training dataset into 5 equal folds and use 1 fold for validation.

Accuracy: orange line represents the training set and green line represents the validation set

Loss Reduction: orange line represents the training set and green line represents the validation set (see figure 4 on the next page)

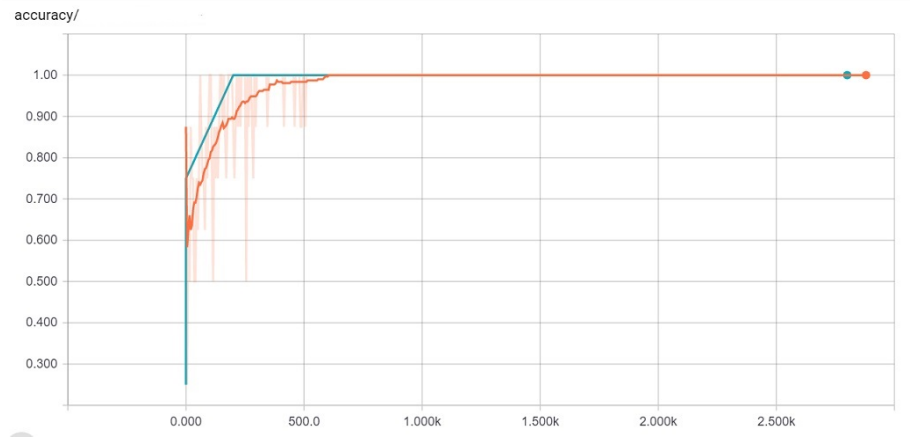


Figure 3: Evaluation on Accuracy for Training and Validation Datasets)

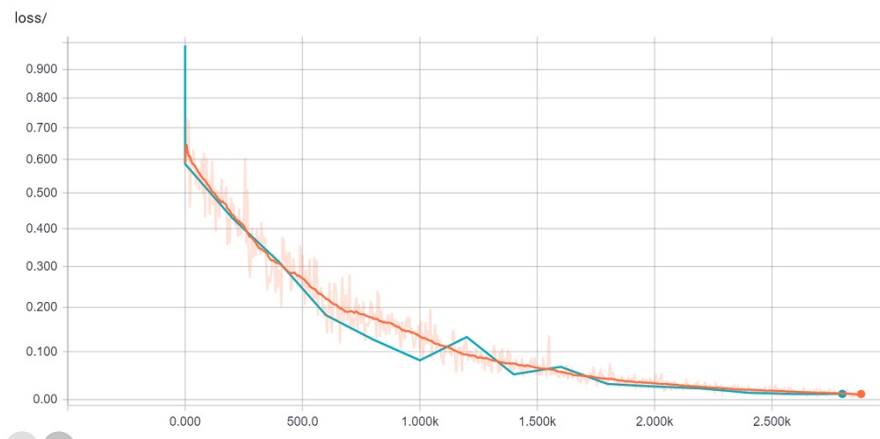


Figure 4: Evaluation on Loss Reduction for Training and Validation Datasets)

5. Results

We employed confusion matrix to measure the performance of current model on test samples.

Dataset	Precision	Recall	F1 Score
Training	0.60	0.83	0.69
Test A	0.53	0.88	0.66
Test B	0.80	0.75	0.77

Table 4: Performance Metrics of Our Model

6. Discussion and Related Work

In this project, we implemented a typical ConvNet model to classify the images of HE-stained adenocarcinoma and achieved an accuracy over 80%. However, there are many areas to be improved.

Firstly, I may explore more advanced or novel CNN model. In H Chen, XJ Qi, et al (Chen et al., 2015) (who is the winner of the competition)’s model, they used fully convolutional networks to conduct the image segmentation which achieved an F1 score of 0.9116 on test set A and 0.7158 on test set B. Their model contains two modules - down-sampling path and up-sampling path. The former includes convolutional layer and pooling layers and the latter includes convolutional layers and deconvolutional layers. Secondly, in terms of data pre-processing, I should do more testing to select the best target width and height. Some studies applied an equal target width and height at 480,480. Moreover, the size of training dataset is too small and current precision and recall values revealed that the model was over-fitting, indicating that we may need to improve the data augmentation algorithm. Thirdly, due to the limitation of my computer’s computational and storage capability, I could not add more layers to build a more complicated structure. Fourthly, the ultimate goal of this project is to use advanced machine learning algorithms to perform gland segmentation and depict gland contours. Tensorflow has released a new package TF-slim which is specialized in conducting image segmentation. Other computer vision packages like openCV could also be used to match the representative gland structure on the image and do the segmentation.

This project enables the automatic detection of a malignant colorectal tumor with a relatively good accuracy. This would help reduce the workload of clinical pathologists and serve as an auxiliary tool to improve diagnosis accuracy.

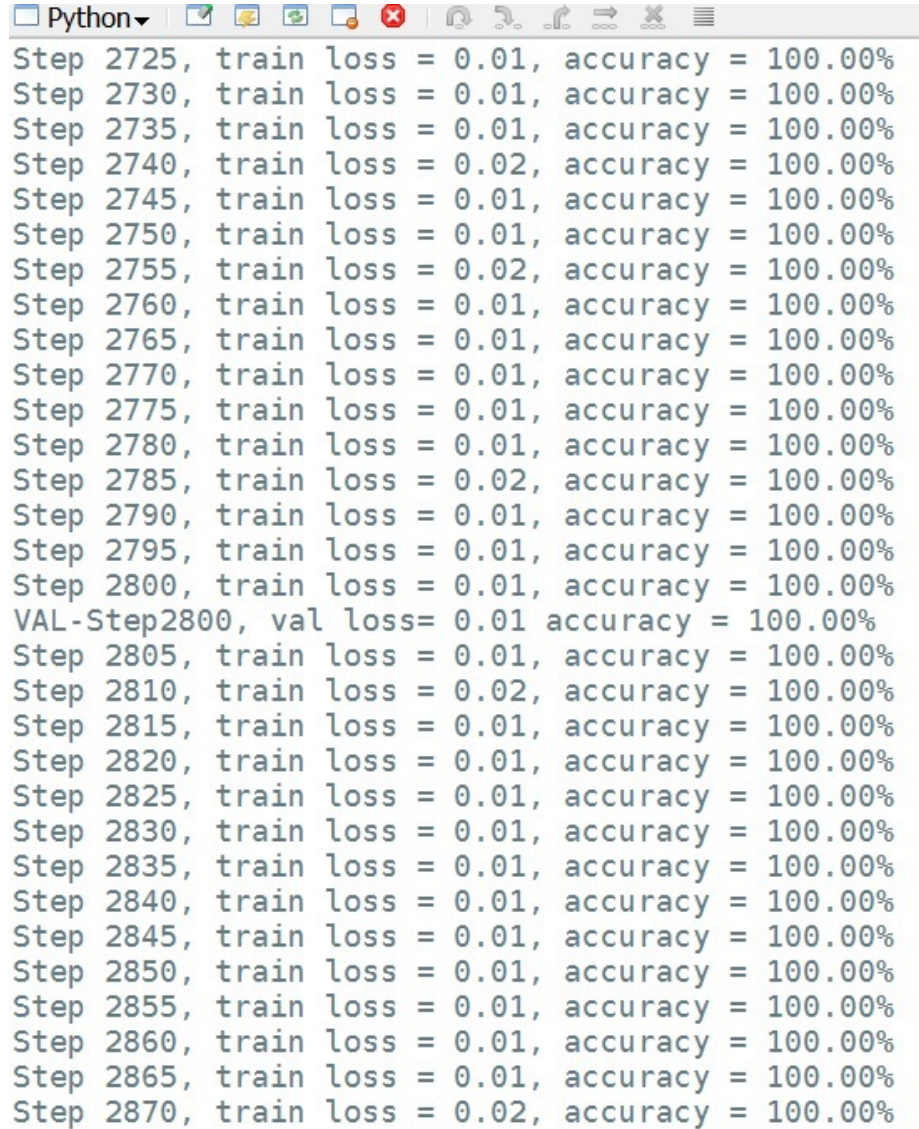
7. Conclusion

This project implemented a classic CNN model to distinguish benign colorectal adenocarcinoma from the malignant. We used seven layers to build the architecture and achieved a good accuracy on test samples. In future work, we will further optimize the method and investigate more novel algorithms to perform gland segmentation.

References

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Appendix A.



```

Python
Step 2725, train loss = 0.01, accuracy = 100.00%
Step 2730, train loss = 0.01, accuracy = 100.00%
Step 2735, train loss = 0.01, accuracy = 100.00%
Step 2740, train loss = 0.02, accuracy = 100.00%
Step 2745, train loss = 0.01, accuracy = 100.00%
Step 2750, train loss = 0.01, accuracy = 100.00%
Step 2755, train loss = 0.02, accuracy = 100.00%
Step 2760, train loss = 0.01, accuracy = 100.00%
Step 2765, train loss = 0.01, accuracy = 100.00%
Step 2770, train loss = 0.01, accuracy = 100.00%
Step 2775, train loss = 0.01, accuracy = 100.00%
Step 2780, train loss = 0.01, accuracy = 100.00%
Step 2785, train loss = 0.02, accuracy = 100.00%
Step 2790, train loss = 0.01, accuracy = 100.00%
Step 2795, train loss = 0.01, accuracy = 100.00%
Step 2800, train loss = 0.01, accuracy = 100.00%
VAL-Step2800, val loss= 0.01 accuracy = 100.00%
Step 2805, train loss = 0.01, accuracy = 100.00%
Step 2810, train loss = 0.02, accuracy = 100.00%
Step 2815, train loss = 0.01, accuracy = 100.00%
Step 2820, train loss = 0.01, accuracy = 100.00%
Step 2825, train loss = 0.01, accuracy = 100.00%
Step 2830, train loss = 0.01, accuracy = 100.00%
Step 2835, train loss = 0.01, accuracy = 100.00%
Step 2840, train loss = 0.01, accuracy = 100.00%
Step 2845, train loss = 0.01, accuracy = 100.00%
Step 2850, train loss = 0.01, accuracy = 100.00%
Step 2855, train loss = 0.01, accuracy = 100.00%
Step 2860, train loss = 0.01, accuracy = 100.00%
Step 2865, train loss = 0.01, accuracy = 100.00%
Step 2870, train loss = 0.02, accuracy = 100.00%

```

Figure 5: Screenshot of Accuracy Evaluation

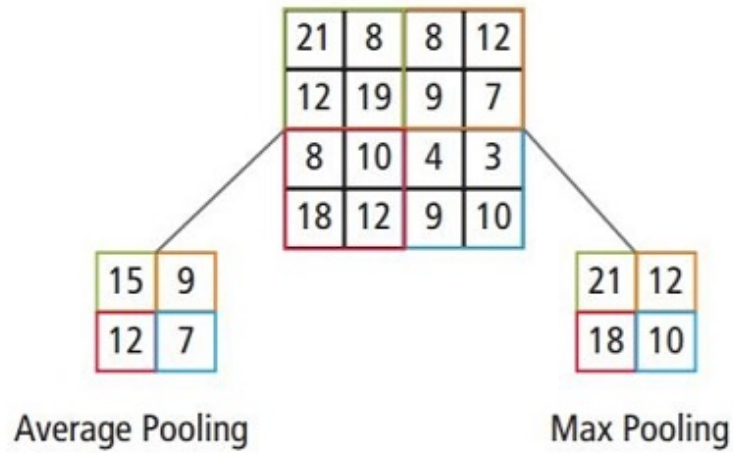


Figure 6: Max Pooling vs. Average Pooling

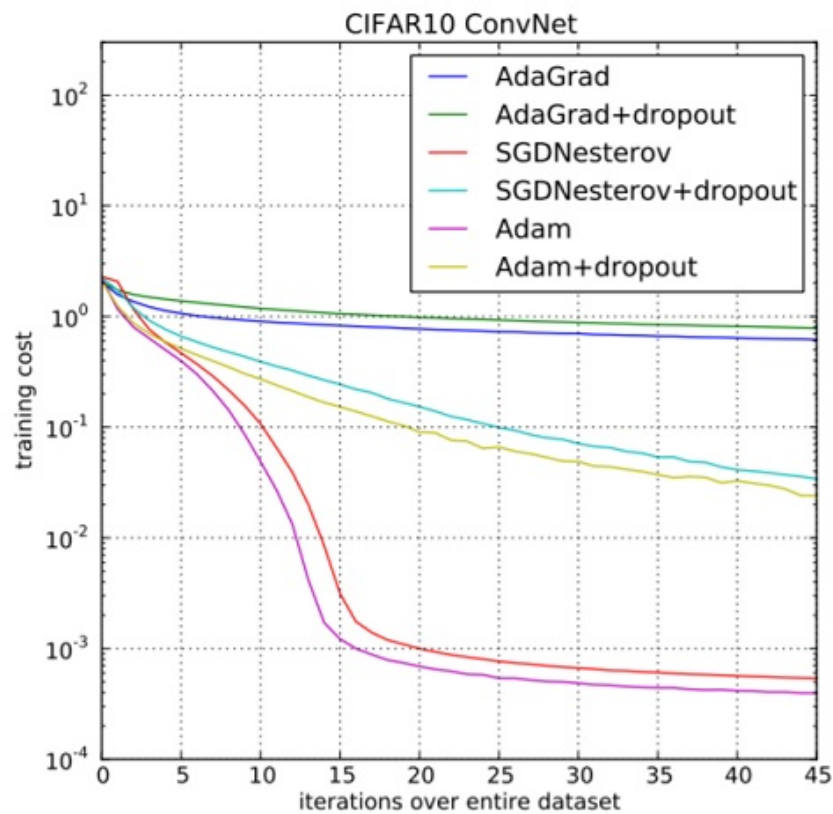


Figure 7: Comparison of Different Optimizer in Reducing Training Costs

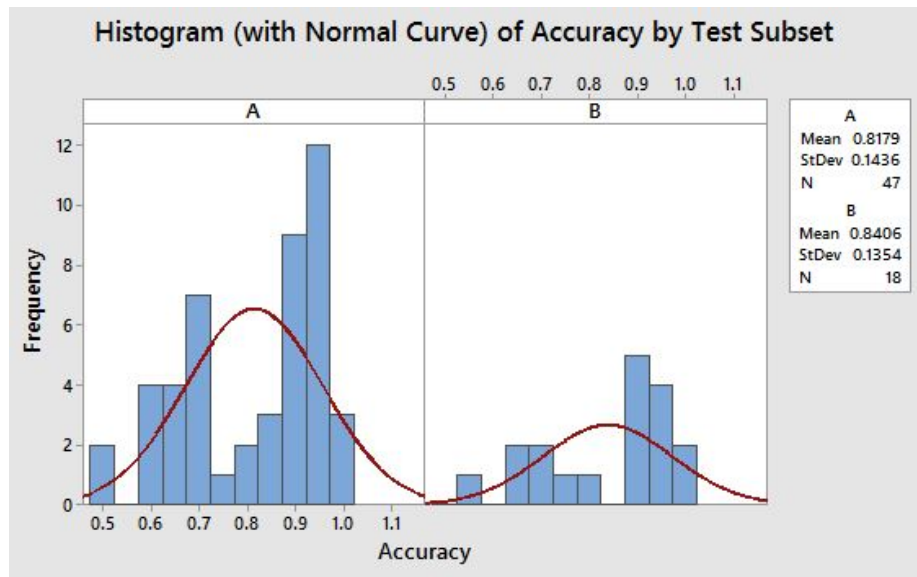


Figure 8: Evaluation on Accuracy on Test Samples