International Research Journal of Engineering and Technology (IRJET) e-ISSN: 2395-0056
Volume: 06 Issue: 10 | Oct 2019 www.irjet.net p-ISSN: 2395-0072

Segmentation of Nucleus and Cytoplasm from Unit Papanicolaou Smear Images using Deep Semantic Networks

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Abstract - *Pap smear images require very efficient segmentation techniques to improve the prediction of carcinoma. Conventional techniques are not efficient for the entire dataset. The proposed technique, segmentation using semantic network, highlights the effective use of network architecture, available data, optimization algorithms and high- end computing; improving the efficiency in classifying cellular components, the nucleus and cytoplasm, in the unit pap image. High accuracy actually representing the human perception of vision has been achieved.*

Key Words: Semantic segmentation, highly accurate, ResNet, FC- Densenet, Image to image regression

1. INTRODUCTION

Cervical cancer is a cancer that affects the cervix which is the lower part of the uterus. Killing more than 288,000 women each year worldwide, cervical cancer is the second common cancer affecting women. It is more prevalent in developing countries. Cervical cancer, if detected at an earlier stage by the way of regular screening, can be prevented and treated. Pap screening or Pap test is one of the popular methods used for the early detection of cervical cancer. It has cut down the death rate successfully in developed countries by preventing the incidence of cervical cancer. One of the major setback of Pap test is that it requires human intervention for the examination of Pap smear. Analysis of hundreds of thousands of cells is very tiring and the accuracy may be decreased due to technical and human errors. [1]

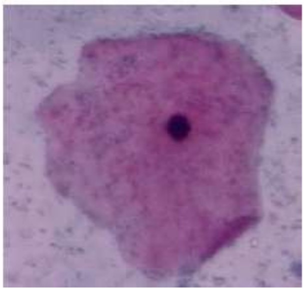


Fig 1: Pap smear cell

The process of divided images into meaningful parts is referred to as segmentation. The images usually have a background and a region on interest (ROI). Staining, poor contrast and overlapping of cells are some of the complexities that arise during the process of cell segmentation. Harandi et al [2] in his paper has segmented the nucleus of the pap cells using geometric active contour followed by thresholding. Marina E. Plissiti et al [3] applied morphological analysis in the detection of nuclei. Two types of classification algorithms namely unsupervised (Fuzzy C-Means) and supervised (Support Vector Machine) are being used and they have compared the results.

Yang – Mao et al [4] have segmented the nucleus and cytoplasm from the cervical smear cell image by adapting edge enhancement nucleus and cytoplast contour (EENCC). They have employed trim- meaning filter for the purpose of removing impulse and Gaussian noises while preserving the sharpness of the object and its boundaries.

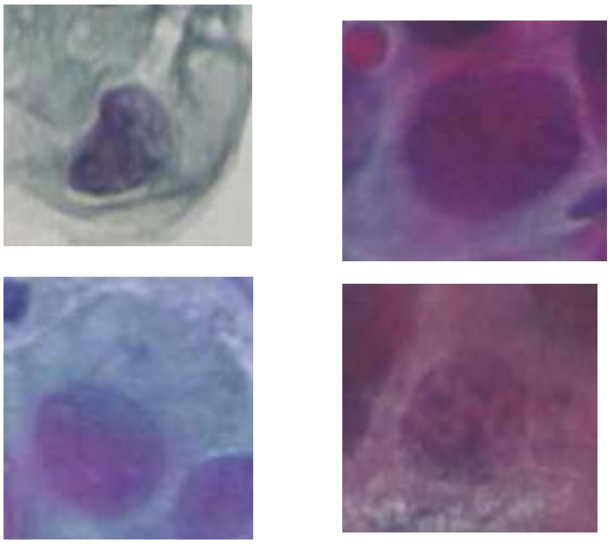
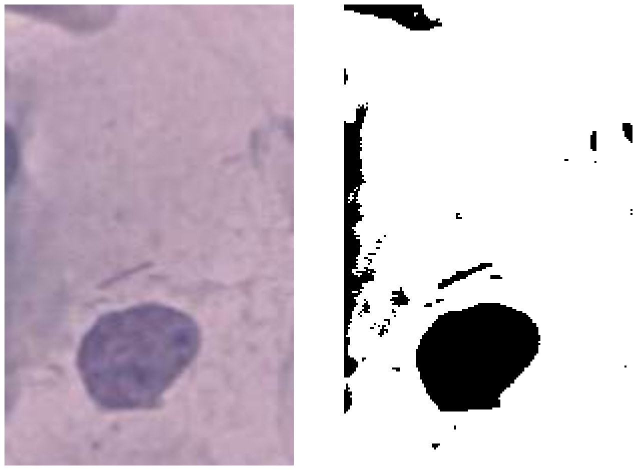


Fig 2. Pap Smear Images that are difficult to segment

The methods discussed above mainly focuses on nuclei segmentation and the cytoplasm is not given much importance. But the cytoplasm also contains features for distinguishing normal and abnormal cells. ImageJ is a Iava based image processing software. When ImageJ was used to segment the Pap smear images, the cytoplasm became less significant after segmentation. The nucleus was only prominent as shown in Fig. 3. The proposed method employs semantic segmentation to differentiate the nucleus and cytoplasm in the Pap smear image. In semantic segmentation, once the model is trained, it can be used to segment new Pap smear images whereas the conventional methods would require additional training. In semantic segmentation, efficiency of segmentation can be greatly increased since the model learns continuously.



a b

Fig 3. (a) Pap Smear Image (b) Pap smear image segmented using ImageJ software

2. PAPANICOLAOU SMEAR

A Pap (-anicoalau) smear is used to screen for cervical cancer. The presence of pre-cancerous or cancerous cells on the cervix can be detected using this test. A pre-cancerous cell is one in which the genetic information has been modified and exhibits abnormal cell division. A cancerous cell is one in which the cell is devoid of cytoplasm. This procedure is usually carried out in women who are in the age group of 21- 65 years. The pap cells are obtained from different areas of the cervix using cyto-brush, cotton stick or a wooden stick. The cells are mostly derived from columnar epithelium and the squamous epithelium. The cervix has two parts – the upper part the columnar epithelium and the lower part the squamous epithelium. The specimen is smeared onto a glass slide and is stained using Papanicolaou method so that the components of the cells are highlighted with specific colours [5].

The Pap smear database consists of 917 such microscopic images collected for different cases from different locations.

3. SEMANTIC SEGMENTATION

Semantic segmentation is the process in which each pixel of the image is associated with a class label. One of the algorithms used for semantic segmentation is the Fully Convolutional Network (FCN). FCN does not directly extract the region, instead, it learns a mapping from pixel to pixel in an image.

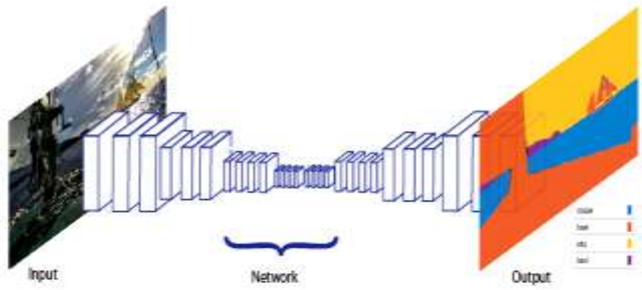


Fig 4. Representation of Semantic Network Flow

FCN first compresses the image to 1/32th of its original size by using various blocks of convolutional and max pool layers. It then predicts the class at the granular level (pixel wise). Then, sampling and deconvolution layers to resize the image to the original size. The semantic or contextual information is captured using down sampling and the spatial information is obtained using up sampling. The final and the original image are of same dimension.

In semantic segmentation the model can be trained to segment new images. Once the model is trained it can segment new images thus reducing the time complexity. Also it can learn continuously thereby increasing its efficiency greatly. Watershed Algorithm is usually used for medical image segmentation. The disadvantage in watershed algorithm is that the boundaries are not retained after segmentation. Sematic segmentation, on the other hand, segments the images while retaining the boundaries. Also semantic segmentation can clearly discriminate overlaying structures which proves to be useful in the segmentation of nucleus and cytoplasm in a Pap smear cell image.

Fully Convolutional Networks (FCNs) were an extension of CNN introduced to overcome the problems associated with per pixel prediction. FCNs differ from CNN in such a way that they add upsampling layers to recover the spatial resolution of the input image at the output layer. This makes FCNs able to process images of arbitrary size. Resolution is lost in pooling layers and this is compensated by the FCNs by introducing skip connections between their downsampling an upsampling paths. The fine- grained informations from the downsampling layer can be recovered with the help of skip connections.

ResNet (Residual Network) is a superior neural network when it comes to image classification. ResNets makes the training of very deep neural networks easier. It is very deep network having 152 layers. It is a collection of multiple deep neural networks with identical structures but different depths. ResNet are extended to work as FCNs and they have additional skip connections which increases the segmentation accuracy and results in faster convergence of the training. In this work, 56 layers are used for training.

DenseNets which are built from dense blocks and pooling layers can be considered as an extension of ResNets. Dense block is the iterative concatenation of previous feature maps. DenseNets induce skip connections and multi-scale supervision which makes them more suitable for semantic segmentation [6].

4. PROPOSED METHODOLOGY

4.1 Pre- Processing

The segmentation of cells from the Pap smear is difficult even for trained cyto- technicians. A new database created from the smear images using the Champ software was also used as the target images. The Pap smear images have three classes: nucleus, cytoplasm and background. Three different colors, red, blue and black were assigned to these classes respectively. One of the important requirements in semantic segmentation is that the input and the output images should be of the same dimension. Hence to achieve this, zero- padding of images has been done and it was ensured that all images are of the size 128 x 128.

The available database is enlarged by means of horizontal and vertical flipping of images. At the end of pre-processing, the enlarged datasets of the input and the target images were available for the training process.

4.2 Neural Network Architectures

The parameters of the trained DL are

- Batch Size:

  Batch size is usually chosen based on the computing source available. It depends on the computing power of CPU, GPU, RAM and VRAM. The optimal batch size is usually around 8 to 32 in powers of 2 during the initial stages of training. In later stage after significant training, the batch size is ended with 2 or 1 depending upon the data size. By doing so, accuracy can be improved.

- Learning Rate:

  Learning rate or step size is the amount of weights that are updated during training. The learning rate used in this model is 0.0001 which corresponds to higher resolution. This helps in convergence.

- Decay:

  Decay refers to the shutting out of neurons randomly to prevent over-fitting of data. The decay here is 0.995 i.e. one neuron per layer per epoch is shut down.

- Number of epochs:

  The number of epochs indicate the total number of epochs the model should be trained for.

- Checkpoint Step:

  Checkpoint step determines how frequently the check points should be saved i.e. the epochs should be saved.

- Validation Step:

  The validation step determines how often the validation of the trained model should be performed. The number of images used for validation can also be decided.

4.2.1 ResNet – classifier

The proposed methodology employs Resnet -101 for classification of pixels within the same image into the number of classes required. This residual network consists of convolutional layers for reducing dimensionality of images and increasing the depth by higher order fielders, max pooling to extract the important information from the image and batch normalization is employed to extract relative content of multiple images within the same batch. A batch is a group of images simultaneously trained on the model for the model to learn.

The architecture of Resnet used is denoted below:

Layer Name	Output Size	No. of Layers	Mask Size	No. of filters
conv1	128x128	1	7x7 (CNV) stride 2	64
conv2_1	56x56	6	3x3 (max pool) stride 2	960
conv2_3	56x56	3	3x3 (max pool) Stride 2	192
conv3_1	28x28	8	1x1,128 (x4) 1x1, 512 (x4)	2560
conv3_3	28x28	4	3x3, 128 (x4)	512
conv4_1	14x14	46	1x1,256 (x23) 1x1,1024 (x23)	29440
conv4_3	14x14	23	3x3,256 (x23)	5888
conv5_1	7x7	6	1x1,512 (x3) 1x1,2048 (x3)	7680
conv5_3	7x7	3	3x3,512 (x3)	1536

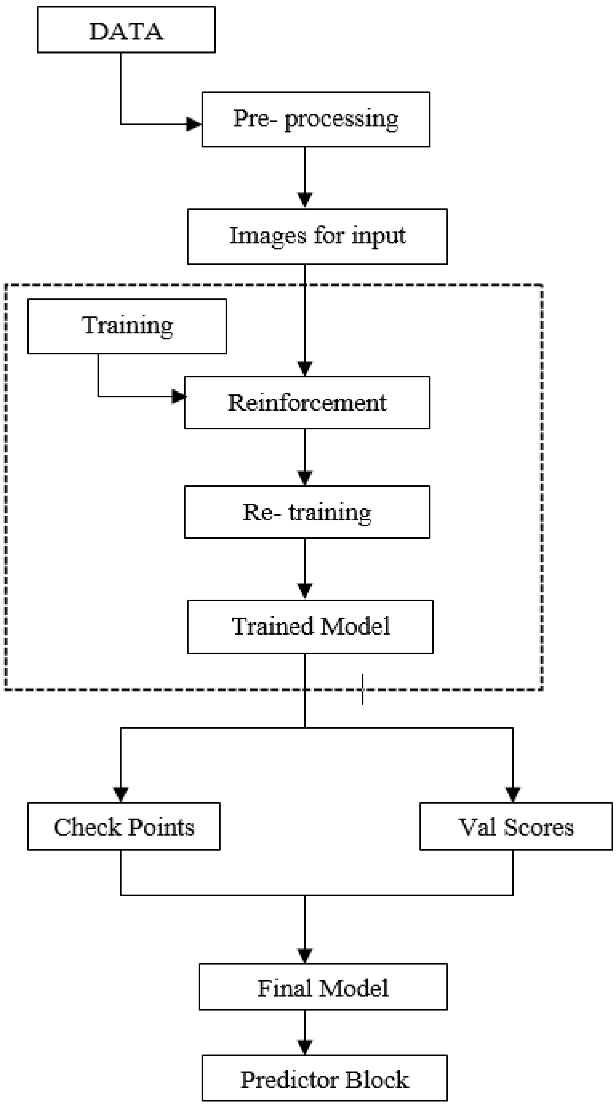
Table:1 Architecture of Resnet- 101

4.2.2 FC-DenseNet Estimator

The architecture of this network resembles an infinity loop. It pools down the image, extracts important info and then flushes it back to its original size by up convolution across the transition up path. The network comprises of only convolutional layers, fully-convolutional. It consists of multiple dense blocks. The entire transition down and transition up through both the front end and backend models is a complete path for an input to cross through the entire path. The dense net is most suitable in rendering images than for classification because of the extensiveness brought into picture by the use of dense neurons.

This is essential to generate the image after the Resnet is able to classify the groups within. The architecture of the network in figure 5

Overall process flow is shown below: Reinforcement mentioned below is achieved by varying batch size and randomizing data trained.



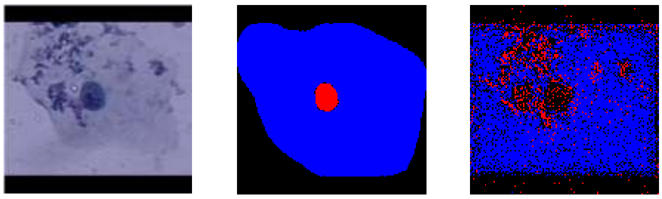
Architecture
Input, $m = 3$
3×3 Convolution, $m = 48$
DB (4 layers) + TD, $m = 112$
DB (5 layers) + TD, $m = 192$
DB (7 layers) + TD, $m = 304$
DB (10 layers) + TD, $m = 464$
DB (12 layers) + TD, $m = 656$
DB (15 layers), $m = 880$
TU + DB (12 layers), $m = 1072$
TU + DB (10 layers), $m = 800$
TU + DB (7 layers), $m = 560$
TU + DB (5 layers), $m = 368$
TU + DB (4 layers), $m = 256$
1×1 Convolution, $m = c$
Softmax

Fig. 5 Architecture details of FC-DenseNet103 model

5. Results:

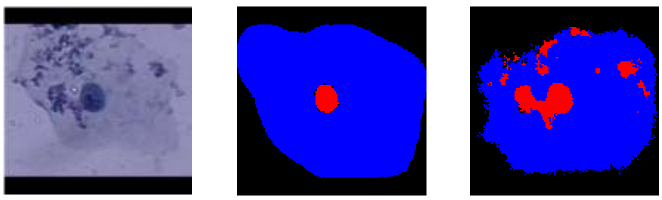
The following is representation of how the deep learning network has been established over the entire training period. Various images, their target and their performance is analyzed. Results from analysis is described below.

EPOCH – 0



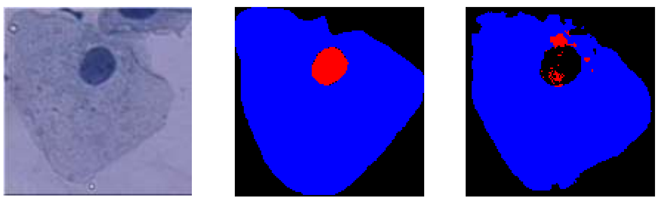
Original Image **Target Class Image** **Predicted Image**

EPOCH – 10



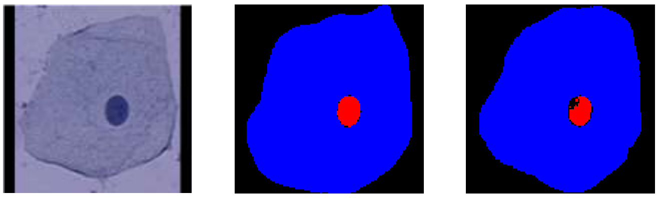
Original Image **Target Class Image** **Predicted Image**

EPOCH – 50



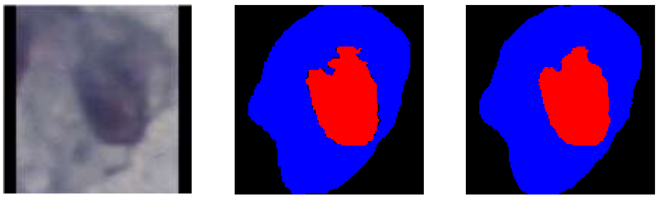
Original Image **Target Class Image** **Predicted Image**

EPOCH – 100



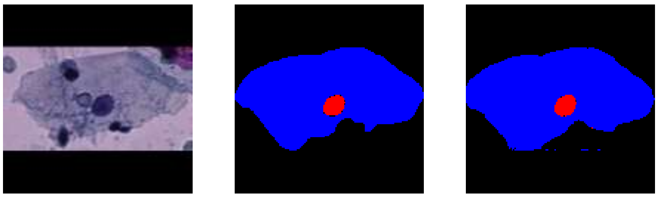
Original Image **Target Class Image** **Predicted Image**

EPOCH – 1000



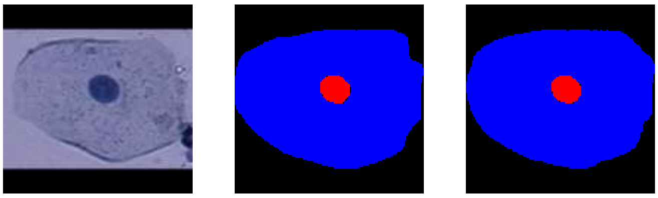
Original Image **Target Class Image** **Predicted Image**

EPOCH – 1350



Original Image **Target Class Image** **Predicted Image**

EPOCH – 1660



Original Image **Target Class Image** **Predicted Image**

Fig 6. Predicted Image for Various Epochs

One of the important characteristics observed along the course is that, changing the data that is trained over the period of training with respect to the knowledge possessed by the learned model. At this time step we changed the no of data points validated proportionally to the no of data trained at the rate of 1:3.

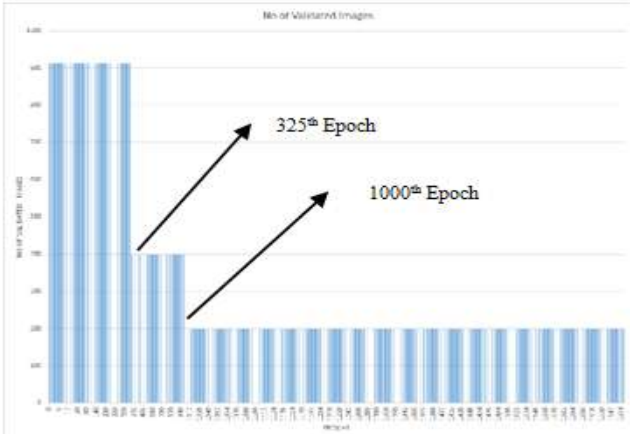


Fig 7. The epochs through which the validation images were altered

For the changes made we observed the following results in the accuracy of the model.

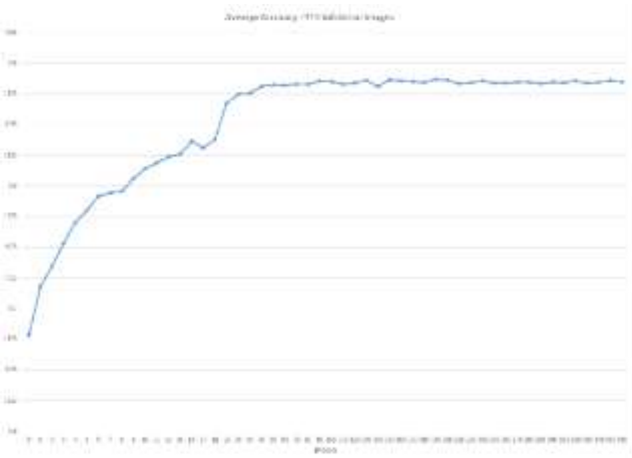


Fig 8. Accuracy for 913 validation images that is total data points of 2793 split at 32.68% for validation.

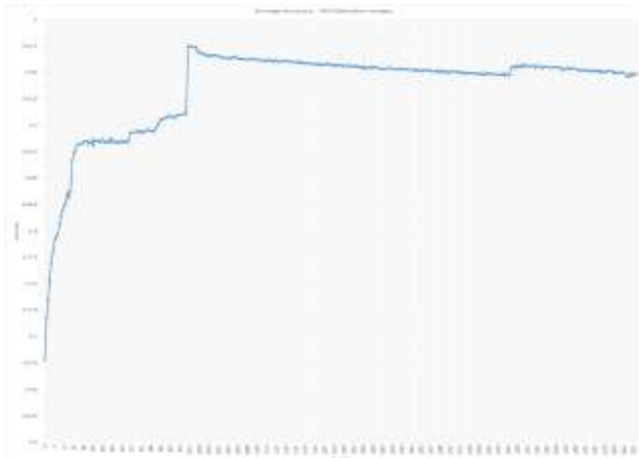


Fig 9. Accuracy for 400 validation images that is total data points of 2793 split at 14.3% for validation.

The graph below indicates how much the accuracy has varied amongst varies classes within an image. The following table shows the final metrics achieved at the end of the 1660 epoch.

The results are taken for the test data samples which has not been included in the training data.

Epoch Number	1660
Avearge Accuracy	0.949079
Precision	0.950182
Recall	0.949079
F1_Score	0.948729
Mean_IOU	0.898314
Class - Nucleus Accuracy	0.975541
Class - Cytoplasm Accuracy	0.928534
Class - Background Accuracy	0.948887
No of Validated Images	200

Table:2 Performance metrics for the tested data.

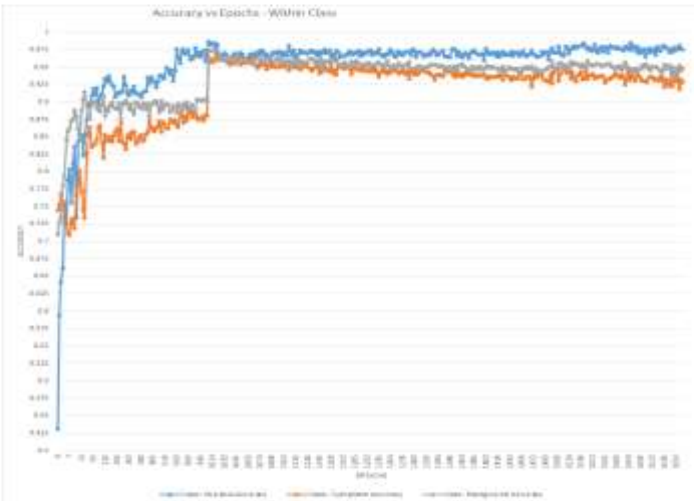


Fig 11. Accuracy of individual classes within the image

Overall from the observations made, using a meagre amount of around 900 samples, a deep learning approach was possible only because of the efficient way the data was managed and it directly correlates to the way the deep learning network has learnt the images. It was astonishing to realize that the deep learning has performed better than what the initial labelling manually created. Moreover, the accuracy metrics were tested as a measure directly against the created label images and not with the original image. So, the accuracy metric achieved was not the actual value. The actual value should be theoretically around 97.75% to 98.25%.

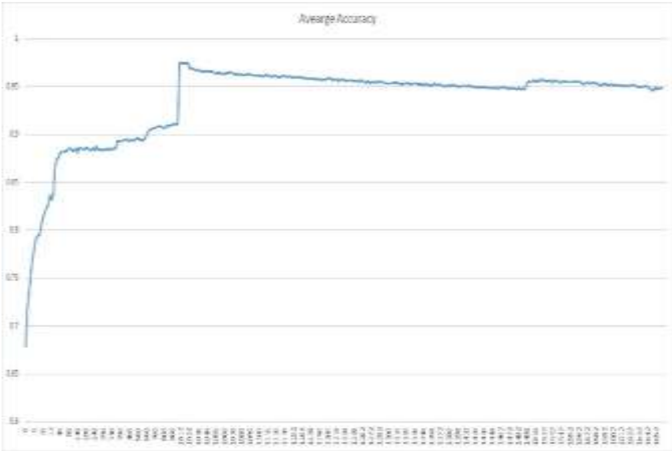


Fig 12. Accuracy trend across the 1660 epochs

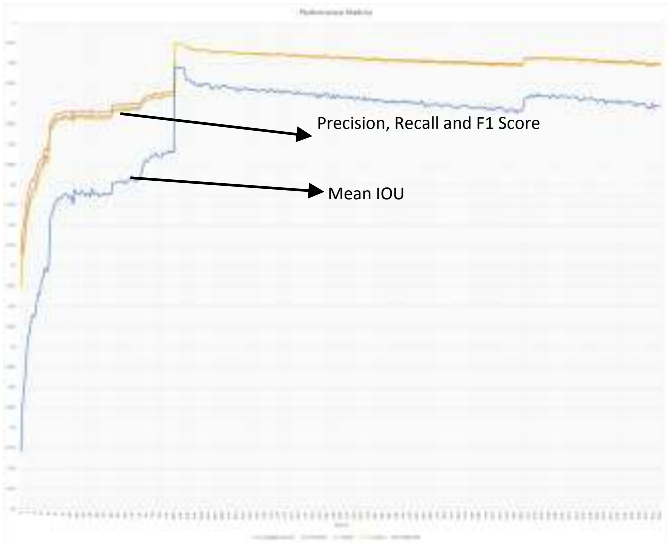


Fig 13. Other Performance Metrics over the 1660 epochs

ACKNOWLEDGEMENT

We have taken efforts in this project. However, it would not have been possible without the kind support and help of many individuals and staff. We would like to extend our sincere thanks to all of them. We would also like to extend our thanks to Dr. R. Vidhyapriya, HOD, Biomedical Engineering. We would like to express our gratitude towards the members of The Department of BIOMEDICAL ENGINEERING, PSG College of Technology for their kind co-operation and encouragement which helped us in completion of this project. Our thanks and appreciations to people who have willingly helped us out with their abilities.

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BIOGRAPHIES

Abhinaav Ramesh - Aspiring Biomedical Engineering student currently pursuing final year in PSG College of Technology. Currently exploring through various technologies and vast opportunities in the field of research for Biomedical Engineering using Artificial Intelligence. Stepping up over the path to a respectful place in the society of Engineers perfecting the art of Research and Development. Specializes in the domain of Artificial Intelligence and its various possibilities and applications focused on Healthcare. Strength in programming reflects the confidence shown in writing new algorithms and the efficiency and robustness of my work. Ardent perfectionist. Has Research experience in the field of AI for the past 2 years. Projects are mainly oriented towards the possibilities of effective software writing and developing algorithms. Research work on the use of Machine learning for the Papanicolaou image classification was published by IEEE. Currently working on Effective Signal Information extraction and using it as a tool for predictive analysis of blood.

Dr. Padmapriya. B – She has completed Ph.D in the area of medical image analysis with "Urinary Bladder Volume Measurement and PCOS Classification". She has subject expertise in Biomedical Image analysis, ICU and Operation theatre equipment, Sensors in Medical applications, Therapeutic Equipment and Biomedical Instrumentation. Currently researching in the areas of Biomedical Image Analysis and Biomedical Instrumentation. She has published 14 papers in International Journals, 1 paper in National Journal, 5 papers in International conferences and one paper in a national level conference. She holds two patents in Testing machine for structural analysis and System and method for auto immune disease diagnosis.

Akshaya Sapthasri M - Enthusiastic student with a strong knowledge over electronics and has a superior verbal jargon to bolster her way through critical situations. Domain of interest orients towards embedded systems and product design. Interest in Biology exceeds programming intent and serve as a pseudo medical specialist giving suggestions completely towards hardships and ideologies faced in prototype development. Good management skills and articulated presenting forte.

Anusha V - Highly skilled in multiple verticals and fast learner for newer technologies. Energetic and motivating in the team and successive feedbacks provided will reflect on the improvement in the overall team performance in net development. Combined knowledge of both biology and programming expertise helps in device fail proof technologies and succeed further Overall will be able to come up as a skilled professional well suited to the industry.

Nivetha Sivakumar - Strength primarily orients towards enormous confidence in work done and support towards prototype development. Skilled in analysing technical information and extracting data which acts as crucial inputs towards the entire phase of brainstorming. Constant participation and learning providing a far more deserving technical outlook. Stress free attitude towards work help maintain and balance harmony and workflow in the team. Domain of interest focusses toward device design and marketing techniques. Research experience in the project helps grasp techniques and increase skillset.

Pujithagiri G – Ardent and honest student with a proficient background in biological sciences. She has a lucid understanding of subject content she deals in. Moreover, she has experience in biomedical image processing too. If given a task, she works with extreme diligence in completing it and also makes sure that it is perfect. Overall she has good oratory skills and puts strenuous efforts in her tasks.