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Automatic Brain Tumor Segmentation using Dense-Net

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Abstract - *Gliomas are commonly prevalent brain tumors that drastically decrease the life expectancy of the patient in their highest grade. Magnetic resonance imaging, used to gauge them, produces copious amounts of data that makes it very difficult to manually segment them in reasonable (MRI) is a widely used imaging technique to assess these tumors, but the large amount of data produced by MRI prevents manual segmentation in a practical amount of time. Reliable, automatic segmentation methods have become a necessity. But the large spatial and structural inconsistencies among glioma MRI scans make automatic segmentation a challenging problem. In this project, we propose an automatic segmentation method based on the Dense-Net architecture of Convolutional Neural Networks (CNN). The Dense-Net architecture has been proposed in recent years, and work on standard datasets has shown it to be substantially deeper, more accurate and efficient than most architectures. Its dense interconnections between layers is proposed to encourage feature reuse. But there are very few instances of this architecture being applied to medical automatic segmentation applications. So, in this project, we will test the performance of the Dense-Net architecture against that of U-Net, and draw analyses regarding its application to the BRATS dataset as compared to existing models.*

Key Words: **Dense-Network, Convolutional Neural Network, Segmentation, Gliomas, BRATS, ADAM Optimization, Stochastic Gradient Descent Optimization.**

1. INTRODUCTION

The task of Automatic Brain Tumor Segmentation can be achieved by using different models and approaches. This paper discusses one such method which involves the use of Dense-Net Model. Cancer can be defined as uncontrollable and unnatural growth and division of cells in the body. Mass occurrence of these cells in the brain tissue is termed as brain tumor. Brain tumors with the highest mortality rate are termed as GLIOMAS. Based on the grade these neoplasms (GLIOMAS) are classified into High Grade Gliomas (HGG) and Low Grade Gliomas (LGG) with former being more aggressive than the latter. On an average, even after treatment, patients do not survive more than 14 months from diagnosis. Presently available treatments include chemotherapy, radiotherapy, or a combination of these.

Analysis of MRI based medical images is mainly used in brain tumor studies for diagnosis, monitoring the patient and planning the suitable treatment. Moreover, it can also be used in clinical trials. The segmentation of tumor is crucial for analysing the growth of tumor and also the shrinkage in the tumor of the patient during the course of the treatment. Segmentation of the tumor is helpful in measuring the volume of the tumor and helps in outlining the different tumor regions as well as the healthy cells around the tumor. The segmentation helps in planning the treatment to be carried out for a particular patient with a particular tumor type. In present clinical practice the segmentation is still carried out manually with the help of radiologists. This process is very tedious, time consuming and prone to errors. The manual segmentation results in limited use of the images for objective and quantitative analysis.

The dataset utilized in this paper is MICCAI (Medical Image Computing and Computer Assisted Intervention.) BRATS 2017/2018 data set. All the multimodal scans available in BraTS are NIFTI files (.nii.gz). These scans describe four different modalities namely: T1-weighted(T1), Contrast enhanced T1-weighted(T1-ce), T2-weighted(T2) and T2 Fluid Attenuated Inversion Recovery(T2-FLAIR). In addition to these a ground truth image is provided for each patient. All the images are segmented manually by one to four raters following the same annotation protocols approved by experienced neuro radiologists. As described in the BraTS reference paper: Se'rgio Pereira, Adriano Pinto, Victor Alves, and Carlos A. Silva, "Brain Tumor Segmentation Using Convolutional Neural Networks in MRI Images", published in IEEE Transactions for Medical Imaging, the enhancing, non-enhancing, necrotic and the peritumoral edema are the composition of these annotations. The provided data are distributed after co-registering these images to same anatomical template and interpolating it to a resolution of $1mm^3$ and then followed by skull-strip.

This paper uses Dense Net Model as the basic structural unit for segmentation of the tumor. In deep learning Convolutional Neural Networks (CNN) are a class of deep neural networks used for analysis of visual images. CNNs can be considered as repetitive versions of multilayer perceptron. The fully connected network where each neuron is connected to every other neuron in the succeeding layer is called multilayer perceptron. The Dense Convolutional Network (Dense-Net), introduced in [2], is a convolutional network where every layer is connected to all the other layers in the network. The Dense-Net is used for an accurate image segmentation. The convolutional neural networks are typically used for classification tasks which gives output as an image with a single class label. However, in many visual tasks of medical imaging, the output should include a class label to every pixel of the image (i.e., localization). An important aspect to be noted is that large amount of training data (images) are not available for such biomedical tasks.

This Dense-Net model is described later in detail in the Section 2. The remainder of the paper is organized as follows. Section 2 is a detailed description about the method used. Section 3 is a discussion on evaluation and performance metrics. Results are presented in Section 4. Finally, a consolidated conclusion covering many topics of the paper as well as on future prospects in this study is presented in Section 5.

2. METHOD

Fig-1 provides an overview of the proposed method of Automatic Brain Tumor Segmentation and Fig. 2 represents the model. There are two phases viz., Training Phase and Testing Phase. In the training phase the Dense-Net model is fitted to the training examples provided to it. The trained model is. In the Testing Phase, the saved model is invoked to segment the unseen data examples. Patch extraction and pre-processing are implemented following this.

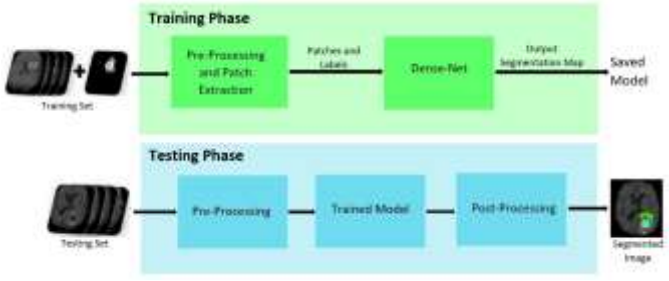

Fig-1: System level block diagram

- Patch Extraction and Pre-Processing:

This refers to extracting the given regions of interest and removing any inconsistencies that may be contained in the MRI image like bias field distortions in intensities of same tissue type. This is done by N4ITK correction [10], which filters the images which removes unwanted distortions. However, inconsistencies occur among MRI images of same tissue in different patients and even same patients when taken at different times. So we do intensity normalization using histogram transformation on a set of MRIs to extract parameters and then apply it to individual images (Fig-2).

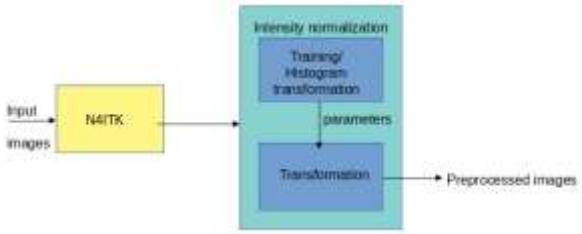

Fig-2: Pre-processing block

- Dense-Net Model

This model as shown in Fig-3 takes the pre-processed image and feeds it into a feed forward network that connects each layer in the network to every other layer (hence the name Dense-Net). In this model, there are 2 stages each made of a dense block and a transition block.

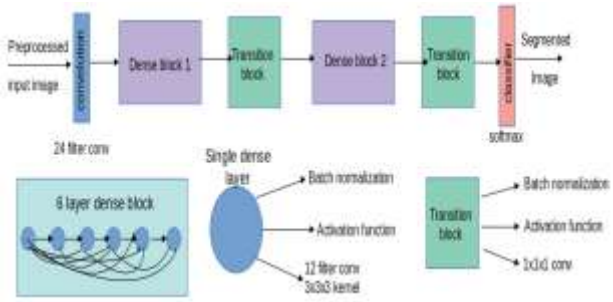

Fig-3: Dense-Net Architectural block

Input pre-processed image is given to 24-filter convolution layer. Each dense block consists of 6 layers that are densely interconnected, where each layer does 3 operations:

- Batch Normalization
- Activation
- Convolution

ReLU activation is used, and the convolution layer is made of 12 filters with a 3x3x3 kernel. The transition block, which follows the dense block, is also made of the same 3 operations except that this is a 1x1x1 convolution with no repetitions. Finally, a softmax classifier is used to classify the various regions of the image.

- Post-processing:

In the segmented image, small clusters may be incorrectly labelled as tumor region. To correct this, we apply volumetric constraints so as to

remove groups that are smaller than a predetermined threshold. We use connected component labelling (Fig. 4), also known as blob extraction, to achieve this. It is an algorithmic graph theory application where subsets of connected elements are distinctly labelled based on a given heuristic. After this is achieved, gamma correction is applied to the image to correct its luminance and enhance its contrast. Finally, the various regions of the image are colored (Fig. 5) as: RED for necrotic and non-enhancing tumor, YELLOW for enhancing tumor and GREEN for peritumoral edema. The rest of the image is untouched. This post-processed image is saved as a .png file. This is shown in Fig-4.

Fig-4: Post-Processing block

- Optimization

During training and test phases, optimization techniques play a pivotal role in improving performance of overall CNN. In this implementation, we have used 2 techniques, Stochastic Gradient Descent and ADAM (Adaptive Momentum estimation).

- Stochastic Gradient Descent (SGD):

After seeing only a single or a few training examples, cost issue is addressed by SGD [4] by computing the negative gradient of the objective. In the CNN, the use of SGD is motivated by the high cost of running back propagation over the full training set. This cost can be overcome by SGD and still lead to fast convergence.

$$\emptyset = \emptyset - \alpha \nabla_{\emptyset} \mathrm{E}[J(\emptyset)]$$

Where the E is the expectation in the above equation and is approximated by evaluating the cost and gradient over the full training set. Stochastic Gradient Descent (SGD) simply does away with the expectation in the update is simply done away by SGD and the gradient of the parameters is computed using a few or a single training example. The new update is given by,

$$\emptyset = \emptyset - \alpha \nabla_{\emptyset} J(\emptyset; x^{(i)}, y^{(i)})$$

- ADAM:

The Adam optimization algorithm [21] is an extension to stochastic gradient descent. This optimizer combines the advantages of RMSProp and AdaGrad, which are 2 subsets of SGD optimizer. The main difference between ADAM and SGD is that SGD performs computations over small subsets, whereas ADAM performs computations over the entire dataset. However, the disadvantage with this optimizer, is its poor convergence rate, which increased the amount of training time.

3. METRICS USED

In our implementation, we have made use of 4 metrics, DSC (Dice Score coefficient), PPV (Positive Predictive Value), Sensitivity, Hausdorff distance and Dice Loss.

- Dice Score coefficient:
Dice score coefficient is a statistical parameter that measures the spatial overlap between 2 sets, in our case images. This tells us whether the given tumor region is located in the correct position. One set represents trained data and another set represent test data. This was introduced by Fleiss [19].

$$DSC(M,N) = 2 * \frac{M \cap N}{M + N}$$

Where, M represents trained data and N represent test data.

- Positive Predictive value:
In medical sciences, this metric measures the probability of whether the given patient tests positive [18] or not for any disease/cancer. This metric is measured by taking ratio between true positives and false positives.

$$PPV = \frac{P}{P + P'}$$

Where, P is number of true positives and P' is number of false positives.

- Sensitivity:
Sensitivity is one of the most important parameters in all machine and deep learning techniques. It measures the ratio of true positives with respect to false negatives. This measures how likely whether the given data has been misclassified or not.

$$Sensitivity = \frac{P}{P + N'}$$

Where, P is number of true positives and N' is number of false negatives.

- Hausdorff distance:
This measures the maximum distance between 2 subsets M and N. In the case of segmentation, the distance between 2 tissues [11] i.e. between enhancing and necrotic tumor or peritumoral edema and enhancing tumor.

$$H(M,N) = \max\left(h(M,N), h(N,M)\right)$$
$$h(M,N) = max_{m\in m} min_{n\in n\|m-n\|}$$
$$h(N,M) = max_{n\in n} min_{m\in m\|m-n\|}$$

Where, M and N are the subsets between which the Hausdorff distance is calculated.

- Dice Loss:
  Dice Loss specifies the amount of non-overlap between two sets, in our case images. Here one set represents trained data and other set represents test data. It can be calculated by subtracting the obtained DSC from unity.

$$Dice\ Loss = \frac{(M \cap N)'}{M + N}$$

Or it can be written as,

$$Dice\ Loss = 1 - DSC$$

4. RESULTS

In this implementation, input patch size defined is 38x38x38x2, which was randomly sampled and fed into the Dense-Net model for training, the model parameters are saved in .meta file extension. For testing, first, the images are passed through pre-processing block, then trained model and finally images are saved.

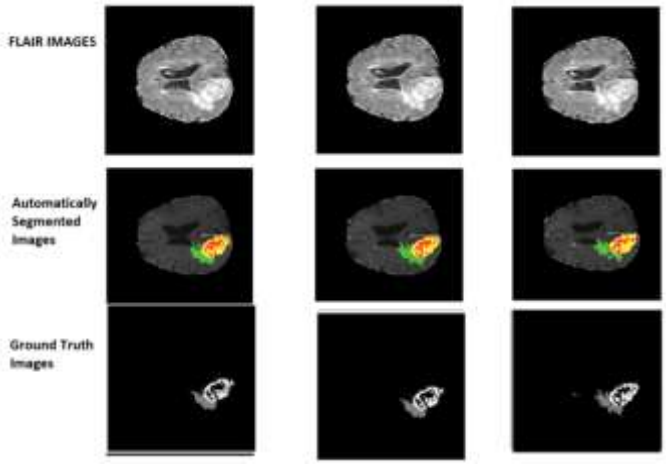

Fig-5: Final output images

The Fig-5 shows 87th, 88th and 89th slide of a particular Patient's T2-FLAIR data and the corresponding Nifty predicted image and the ground truth. As can be seen from the Fig-5 the final colored segmented image is superimposed on the flair image for better clarity about the position and spread of the tumor in the brain image given as input.

Table 1: Results

Optimizer	DSC	PPV	Sensitivity	Hausdorff distance	Dice Loss
ADAM	0.98	0.99	0.9	2.5	0.02
SGD	0.99	0.98	0.99	2.7	0.01

Table 2: Results with percentile normalization method

DSC	PPV	Sensitivity	Dice Loss
0.61	0.59	0.6	0.39

The Table 1 and Table 2 indicate the results obtained for valuation metrics for different optimization methods.

5. CONCLUSION

Brain Tumor segmentation using Dense-Net is surely interesting. The fact that the number of filters reduce substantially improves speed and accuracy of the model in comparison with models such as U-Net, and Res-Net [1]. The depth can be as much as the user wants it to be. Also, pooling though effective but a costly operation, can be optional in the case of Dense-Net. Whereas in U-Net, the architecture includes pooling and a depth is specified. Beyond a certain point, the depth cannot be extended. ADAM optimizer by itself, is a very good optimizer, however, due to late convergence, it slowed down the process of training, whereas the SGD algorithm improved the convergence in the network, resulting in a faster implementation. The overall time taken to train this network went from 4 days to 1 week.

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