Segmentation of Nuclei in Digital Pathological Images

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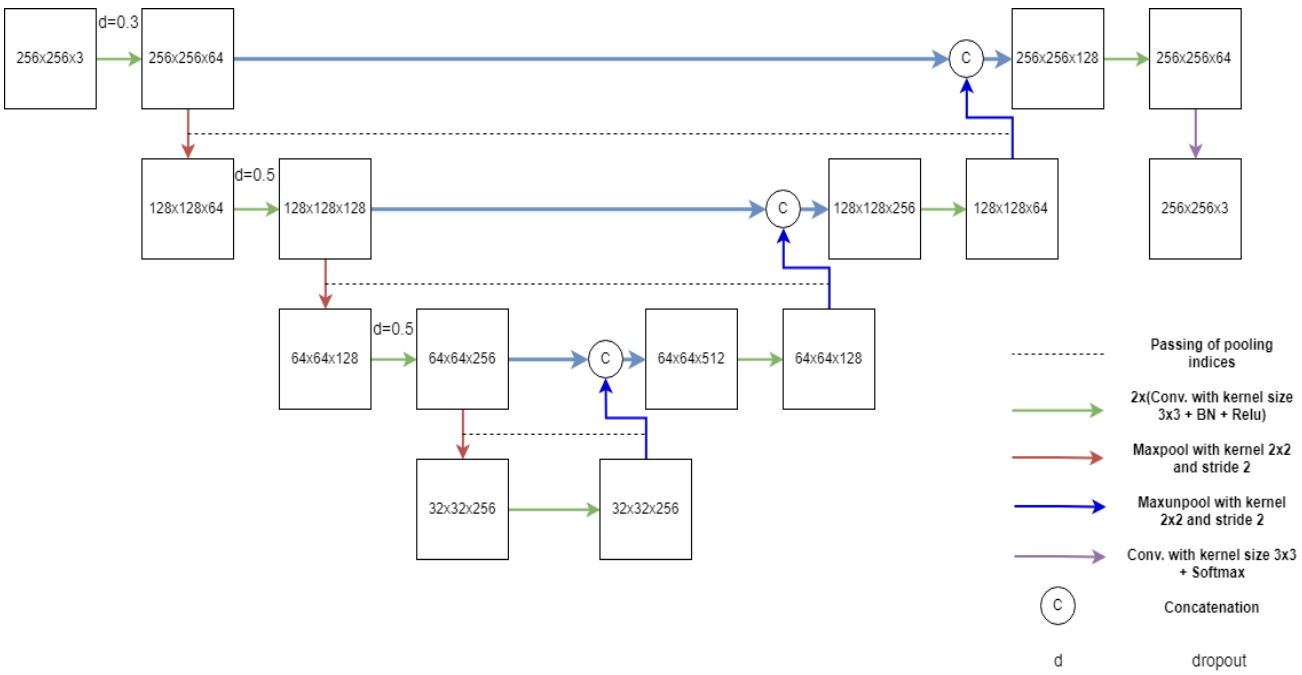
Introduction

Diagnosis and analysis of tumors in cancer patients is traditionally done by examining tissue specimens under a powerful microscope by expert pathologists. This type of manual segmentation is a painstaking task, thus requiring efficient and reliable computer aided segmentation methods. In this project, we have used Convolutional Neural Networks (CNN) for nuclei segmentation in image tiles which are rectangular regions extracted from a set of Glioblastoma and Lower Grade Glioma whole slide tissue images. The main challenges faced during this task were segmenting overlapping nuclei and heterogeneity in the test images. Apart from these, the training dataset available was not very large.

Network Architecture

We implemented three different network architectures – Segnet, Unet and Relaynet. Out of these, Relaynet was producing the most accurate results. Relaynet combines both the features of Segnet and Unet, i.e., passing of Maxpool indices to subsequent Unpooling layers and conveying low level feature maps from the encoder channels to the subsequent decoder channels. Being motivated from Unet, we tried to increase the channels during convolution, keeping in mind the maxpool indices and the concatenation of previous channels to subsequent channels. Inclusion of dropout layers in the encoder part significantly reduced overfitting.



NETWORK ARCHITECTURE

Method

Pre Processing: We implemented colour normalisation on the input RGB images.

Training: We used Adam optimiser on the network, with a learning rate decaying with every 4 epochs for better convergence. The output layer consisted of 3 channels- Nuclei mask, Background and Nuclei boundary.

As loss function, we used Binary Cross Entropy with Logits Loss with weight maps. The weight maps were computed from the labelled masks using morphological operations. The pixel weights were computed as follows:

$$\boldsymbol{w(x) = w_c(x) + w_o(x).exp\left(-\frac{(d_1(x) + d_2(x))^2}{2\sigma^2}\right)}$$

where the first term in the RHS takes care of difference in class probabilities and the second term provides more weight to closely packed borders, so that the network learns small separation borders efficiently. $d_1(x)$ and $d_2(x)$ denote the distances of a background pixel from the two nearest cells.

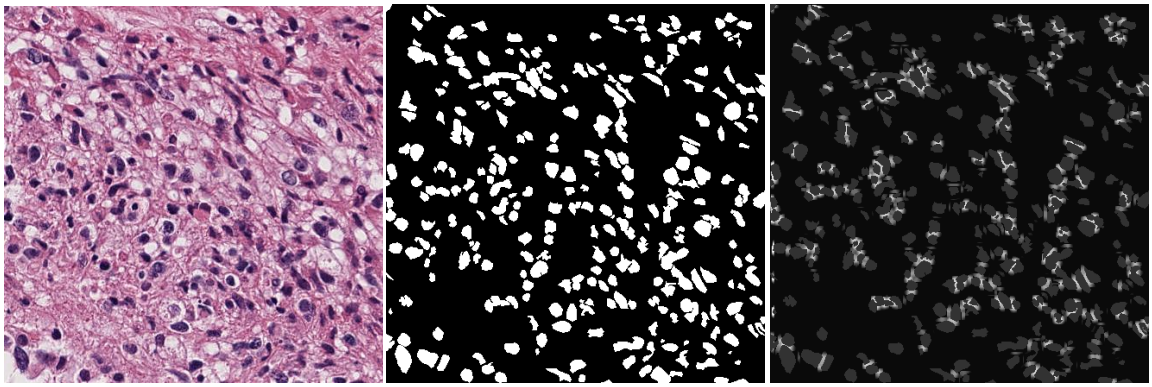


Image Ground Truth Mask Weight Map

Post Processing: The output masks of the test images were thresholded with a threshold level of 0.5. Unnecessary small fragmented masks (with size less than 15 pixels) were removed. The individual nuclei of the final output masks were then labelled.

Evaluation Metric

We implemented the Aggregated Jaccard Index (AJI). It computes an aggregated intersection cardinality numerator, and an aggregated union cardinality denominator for all ground truth and segmented nuclei under consideration. For each ground truth nucleus *Gi* in an image (or a dataset), after associating a segmented nucleus *Sj*, we add the contributions to the aggregated Jaccard index by adding the pixel count of *Gi* ∩ *Sj* to AJIs numerator, and that of *Gi* ∪ *Sj* to the denominator. It incorporates both pixel level and object level errors, thus proving to be a more relevant metric than normal Jaccard Index and Hausdorff distance.

Result

We obtained a score of 0.702 (combined DICE 1 and DICE 2 loss as per the metric of the challenge).

The result on test images have been illustrated below: