Segmentation of Glands in the H&E Stained Histologic Images

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Introduction

Cancer is a class of diseases characterized by out of control cell growth. According to the American Cancer Society, Cancer is the second most common cause of death in the. Automated system of segmentation and classification of gland tissues has become a necessity of the hour provided the ever increasing rate of people suffering from cancer. In this work, we have proposed a novel technique of gland segmentation using deep learning.

Color Normalization

Due to the use of different microscopes/scanners or differences in tissue preparation, there might be color variations in the histologic images. As the CNN filters might also learn the color of the various entities in the slides, color normalization becomes an important technique in standardizing the color variations among the images.

Algorithm 1: Color normalization [11]

Input : source and target image, number of stains r, sparsity regularization parameter λ (default $\lambda = 0.1$)

Output: normalized source image

1. Convert source and target in to optical densities using eq.(4.2)
2. Source stain separation: $V_s = W_s H_s$ using eq.(4.5)
3. Target stain separation: $V_t = W_t H_t$ using eq.(4.5)
4. Adjust the dynamic range of H_s to be same as that of H_t to form the normalized source stains H_{snorm}. The dynamic range is robustly estimated with a pseudo maximum (99%).
5. Colour exchange: $V_{snorm} = W_t H_{snorm}$
6. Project the V_{snorm} into RGB colour space using eq.(4.2) to get the normalized source image

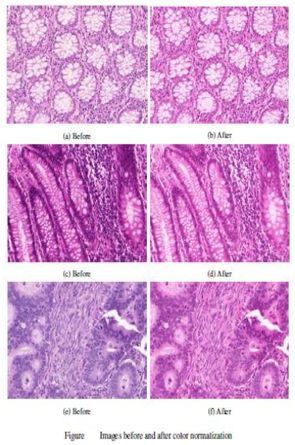

Figure Images before and after color normalization

Convolutional Neural Network

CNNs consists of multiple convolutional layers which are collection of small filters that take only a small portion of the original image as input and process over it. The outputs of these filters of a convolutional layer are pooled to have a better representation of the given image and passed as input to the next convolutional layer. The same set of weights of a filter is used over the entire image which reduces the training time and memory required. The complexity of the extracted features increases as the number of layers increases. These learned features can be passed through a hidden layer with a linear or nonlinear activation function. The output is used as input to a logistic regression model, multi-layer perceptron or other classifiers to solve binary or multi-class classification problems.

Post Processing

The predicted map was opened with a disk structuring element of size 4. The holes in the resulting image were then filled. Finally, the connected components which had fewer than 1000 pixels were removed.

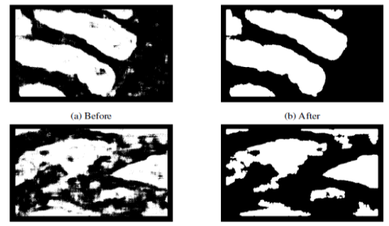

Figure Images before and after post processing

Proposed Methodology

We used the Warwick-QU Dataset consisting of 85 training and 80 test biopsy slides, both benign and malignant, of colon tissue. All the images were first color normalized. A fixed number of 51x51 sized patches were taken from the images such that the ratio of gland vs non-gland central pixels is 1:1. These were then fed into the CNN comprising of two alternating convolutional and max-pooling layers followed by a hidden layer and the final segmentation into gland or non-gland was done using logistic regression model. We played with the values of the different parameters of the CNN architecture to achieve high accuracy. Dropout and ReLU activation were also incorporated into the architecture to further improvise upon the results. After all the iterations, the weights corresponding to the minimum validation error were saved which were then used to segment the glands in the test images. The predicted binary maps were subjected to post processing. The efficacy of the proposed approach is computed using three evaluation metrics namely, F1-score, Dice index and Jaccard index, both at pixel level as well as object level.

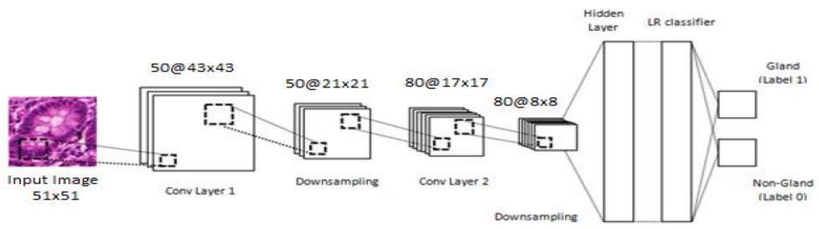

Figure CNN Architecture

Table Parameters used in the experiments on Warwick-QU Dataset

Patch Size	Convolutional Layer 1			Convolutional Layer 2			Hidden Layer		Learning Rate	Decrement in Learning Rate
	Number	Size	Dropout	Number	Size	Dropout	Dropout	Activation		
51x51	50	9x9	0.1	80	5x5	0.1	0.5	ReLU	0.01	0.4

Table Results on Warwick-QU Dataset

Input	Error (in %)		F1-score				Dice Index				Jaccard Index			
			Pixel Level		Object Level		Pixel Level		Object Level		Pixel Level		Object Level	
	Validation	Test	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation
RGB	11.97	14.28	0.836	0.087	0.633	0.187	0.836	0.087	0.707	0.149	0.727	0.119	0.595	0.171
H&E	12.31	16.37	0.826	0.119	0.605	0.223	0.826	0.119	0.676	0.185	0.718	0.147	0.565	0.260
RGB+H&E	12.03	15.12	0.841	0.0857	0.622	0.191	0.841	0.085	0.704	0.159	0.734	0.120	0.594	0.185

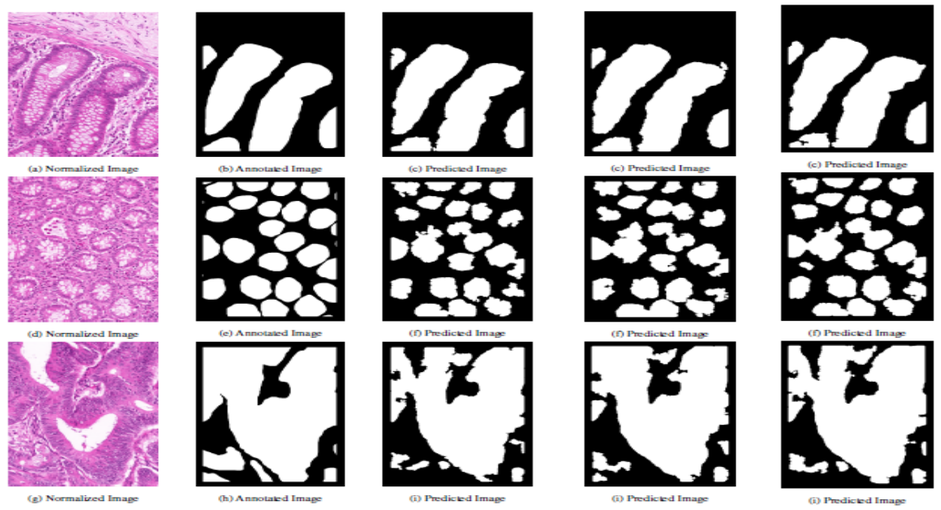

Figure : Segmentation results using RGB , H&E, RGB + H&E channels

Table Results on non-normalized benign and malignant data

S.No	Convolutional Layer 1 Filters		Convolutional Layer 2 Filters		Convolutional Layer 3 Filters		Learning Rate	Decrement in Learning Rate	Error (in %)	
	Number	Size	Number	Size	Number	Size			Validation	Test
1.	50	3x3	80	5x5	-	-	0.001	0.00025	19.27	26.55
2.	20	3x3	40	5x5	-	-	0.001	0.00025	20.08	27.49
3.	120	3x3	80	5x5	-	-	0.001	0.00025	21.78	27.81
4.	150	3x3	80	5x5	-	-	0.001	0.00025	20.09	27.38
5.	50	3x3	80	5x5	-	-	0.01	0.0025	14.69	23.83
6.	50	3x3	80	5x5	-	-	0.01	0.1	14.00	21.00
7.	40	3x3	60	5x5	-	-	0.01	0.1	13.00	23.00
8.	50	3x3	80	3x3	50	3x3	0.01	0.001	18.00	27.00

Table Results on color normalized benign and malignant data

S.No	Convolutional Layer 1 Filters		Convolutional Layer 2 Filters		Learning Rate	Decrement in Learning Rate	Error (in %)		Remarks
	Number	Size	Number	Size			Validation	Test	
1.	50	5x5	80	5x5	0.001	0.00025	20.09	27.38	-
2.	80	3x3	100	3x3	0.001	0.00025	24.60	27.40	-
3.	120	3x3	80	3x3	0.001	0.00025	21.78	27.81	-
4.	50	5x5	80	3x3	0.01	0.1	15.00	23.00	Dropout and ReLU added
5.	50	5x5	80	3x3	0.01	0.1	7.09	20.30	Input patch size of 51x51
6.	50	5x5	80	3x3	0.01	0.1	6.80	21.75	Equal Training and test data