CANCER METASTASIS DETECTION IN LYMPH NODE

Bharti Munjal[⋆]*, Amil George*[⋆]*, Shadi Albarqouni*[⋆]*, Nassir Navab*[⋆†]

[⋆]Chair for Computer Aided Medical Procedure (CAMP),
Technische Universität München (TUM), Munich, Germany.
[†] Johns Hopkins University, Baltimore, MD, United States.

ABSTRACT

Automated detection of metastasis in lymph node sections is of great value as lymph node metastasis occur in most cancer types. Our approach uses two Convolutional Neural Networks to detect metastatsis regions in lymph node sections.

***Index Terms*—** Breast cancer, histopathology, deep learning, object detection.

1. INTRODUCTION

Pathology image analysis is a tedious process and requires an expert pathologist for the job. Often more difficult diagnosis tasks require review by more than one pathologist as diagnosis is based on the subjective opinion of pathologists. There is also clearly a need to reduce the workload of pathologists. The use of computer aided methods will not only reduce the work of pathologist but also has the potential to improve the quality of diagnosis. Classifying histopathology images is difficult due to large variations caused by different chemical stainings (e.g hematoxylin and eosin) and different source scanners. As part of the CAMELYON16 [1] challenge, we worked on the whole slide images of lymph node sections to automatically detect metastasis regions. This task is highly challenging as tissue samples from normal and tumorous slides have very similar structures.

2. BACKGROUND

In recent years Convolutional Neural Networks have been used extensively in Computer Vision and Medical Image Analysis. Convolutional Neural Networks have gained interest of the researchers as they provide an automated feature extraction method and have also shown promising results when applied to pathology data. In ICPR 2012 and AMIDA 2013, the work by Jurgen Schmidhuber [1] uses a two staged deep Neural Network for mitosis detection in breast cancer histology images and outperforms other approaches based on handcrafted features. Many different flavors of Neural Networks have been proposed for pathology images over the last few years. Recent works by S. Albarqouni [2] that is based on a Multi Scale Convolutional Neural Network shows how the results of different scales can be combined to improve the accuracy of Mitosis Detection. Our approach for CAMELYON16[1] dataset also uses CNN.

3. METHODOLOGY

A whole slide image (WSI) contains data in multiresolution pyramid structure with Level 0 being the highest resolution. We chose to work on Level 6 and Level 3 of the WSI keeping in mind the computational requirements. We have trained two CNN based pixel classifiers, Level3Net and Level6Net for Level 3 resolution and Level 6 resolution of the WSI respectively. The classifier classifies by taking a square patch of the raw RGB image around a point on the image. For any point p in the WSI, the classifier outputs the probability that the patch is centered around a metastasis region.

3.1. CNN Architecture

For both the networks, we have employed the same network architecture appeared in [2]. Each network consists of 3 subsequent convolutional and max-pooling layers followed by 3 fully connected layer. Dropout regularization was added to the fully connected layers to prevent overfitting.

3.2. Training the classifier

The CNN was trained using Adaptive gradient descent and minimizes the logistic loss function. The training data is prepared by taking patches of fixed size around ground truth pixels. Our training data for the network consists of 1 million metastasis patches and 1 million normal patches sampled from the training set. Since the training set has images from two separate scanners 3D Histech scanner and the Hamamatsu scanners, we keep a uniform distribution of samples from both scanners. At the slide level, we cannot sample uniformly from the available slides as some slides have too small metastasis region while some have large regions. The patches from slides having too few samples were augmented

B. Munjal and A. George contributed equally towards this work
[1]http://camelyon16.grand-challenge.org/

with their rotated and flipped versions so that their contribution to the training data is not too less. Our validation data for the network consisted of 200,000 metastasis patches and 200,000 normal patches sampled from the validation set.

3.3. Testing WSI for Metastasis

The whole slide images are large and a significant portion of WSI are white background region. We start at the lower resolution level that is Level 6 of the WSI. First, we eliminate such background regions and select our area of interest i.e the stained regions of the slide by thresholding. Then for each pixel p_{L6}, in the stained region of Level 6 of the WSI, a square patch is taken and evaluated using Level6Net to create the response map R_{L6}. Next, all pixel locations with response less than threshold T_{L6} are rejected. For all locations with responses greater than the threshold T_{L6}, the corresponding pixel locations p_{L3} of the Level 3 resolution of the WSI are calculated. Since the resolution at Level 3 is greater than the resolution at Level 6 there is more than 1 pixel location at Level 3 corresponding to each pixel location at Level 6. We then evaluate all the locations p_{L3} using Level3Net to obtain our final response map R_{L3} as shown in Fig. 1. We then process the response map to get probable locations of metastasis region.

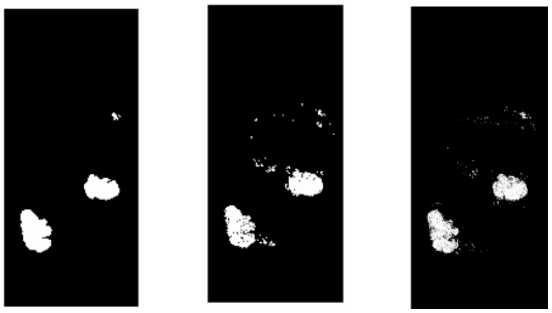
The response map R_{L3} obtained can be very noisy. Therefore we smooth the response map using a disk filter of radius r. Then we apply non-maximal supression and choose maximas such that each selected maxima is at a distance threshold of d pixels from any other selected maxima. The intensity and location of the maxima gives us the probability and location of metastasis region. The probability that an entire slide contains metastasis is empirically chosen as the mean of top n probabilities of metastasis regions in that slide.

4. EXPERIMENT AND RESULTS

4.1. Dataset

Our dataset consists of 270 WSIs of lymph nodes released as the training dataset of the CAMELYON16 challenge. Out of the 270 WSIs, 170 WSI were scanned using the 3D Histech scanner and the remaining 100 WSI using the Hamamatsu scanner. Among the first set of 170 WSIs scanned using the 3D Histech scanner 70 WSIs contained metastasis and the remaining 100 WSIs were normal. In the second set of 100 WSIs scanned using the Hamamatsu scanner, 40 contain metastasis and 60 are normal.

There is significant appearance variation among the two sets of slides from the 3D Histech scanner and the Hamamatsu scanner. Rather than trying to normalize appearance of staining we chose to partition our data and build the training set for our network taking into account such considerations. First, we partition the available WSIs into two disjoint sets: training set and validation set. We randomly select and set aside 10 WSIs containing metastasis and 15 normal WSIs from each of WSI sets from 3D Histech scanner and Hamamatsu scanner making a total of 50 WSIs in our validation set. The remaining 220 WSIs constitute our train set.



(a) Ground Truth (b) Level 6 (c) Level 3

Fig. 1: (a) The ground truth mask showing actual tumor regions. (b) The response map R_{L6} obtained after Level6Net. (c) Response map R_{L3} obtained after Level3Net

4.2. Evaluation

There were two separate evaluation criterion as per the challenge: Slide based evaluation and Leison based evaluation. For Slide Based Evaluation, the performance of the method is measured using ROC curve. The final score is calculated as the area under the ROC curve.

For Lesion based evaluation, the performance is measured using the FROC curve. The final score is computed as the average sensitivity over 6 predefined false positives rates of 1/4, 1/2, 1, 2, 4, 8.

4.3. Results

We calculated the ROC and FROC for 50 slides using the discussed approach. We obtained an area of approx. 0.90 under the ROC curve. An average sensitivity of approx. 0.35 at the 6 predefined false positive rates.

5. DISCUSSION AND CONCLUSION

CNN based classifiers were built and trained to identify metastasis regions in WSIs as part of the CAMELYON16 Challenge. Future work would involve improving the accuracy of the network by making use of higher resolutions in WSI.

6. REFERENCES

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