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A Robust Deep Learning Approachto Detect Nuclei in Histopathological Images

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ABSTRACT: Automated cell detection in histopathology images is challenging due to large variations in size, density, and batch variations. Nuclei detection provides useful information for evaluating cancer progression and prognosis. The performance of most classical nuclei detection methods relies on appropriate data selection. These methods require experts to create useful features. On the other hand, deep learning can extract feature sets from the data automatically, not requiring the design of feature extractors by experts. In this work, a new enhancement for deep learning approach is proposed to learn a continuous mapping from H&E image patches centered around nucleus centroids to nuclear distance maps. Our approach formulates the problem as a continuous regression problem and builds a fully convolutional regression network. In this method, it handles partial detections and irregular-shaped, neighboring nuclei, and different nuclei sizes and color. We train the network with the colorectal dataset which is publicly available dataset. The work is evaluated with the human bone marrow dataset without re-training and superior results are achieved.

KEYWORDS: Deep learning; Nuclei detection;

I. INTRODUCTION

Nuclei detection and classification have a significant impact on the cancer diagnostics [1]. First step in quantitative analysis of histopathology images is accurate detection & localizationof cell/nuclei centers and boundaries as shown in Fig .1.

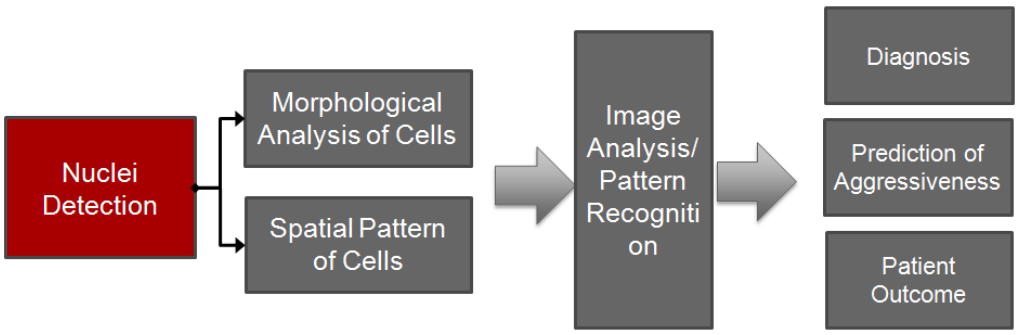

Fig.1. The importance of nuclei detection

Appearance of each nucleus, large variations of size, density and positions of nuclei are challenges to detect nuclei, Recently, a number of automated methods have been developed to detect nuclei in digitized histopathological images [2]. Thresholding, active contours, region growing, and K-means are the most widely used methods for cell or nucleus detection. Morphological features such as stability and symmetry of the nuclear region are used in [3] to identify nuclei in H&E images. Nuclei centers are localized using gradient directions in [4]. The above methods fail to detect irregular-

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shaped nuclei. Maximally stable extremal regions (MSER) method was used for detection as well, but this method is very sensitive to irregular chromatin texture or weakly stained nuclei [5].

There are number of studies that classify nuclei based on shape, color, and texture features. These studies need detection algorithms to locate nuclei in tissue images. Classical image analysis involves a series of steps including preprocessing, image segmentation, careful selection of features, learning, and classifies the output. The performance of these methods depends on the selected features. In this work, we propose a deep learning approach which can handle nuclei detection challenges and automatically extracting features. Since fully convolutional regression networks achieved state-of-art results in nuclei detection [11,13,16] that inspired us to use same concept with some changes and achieve results that are competitive with prior methods.

II. RELATED WORK

In recent years, deep learning methods have been successfully used in several biomedical image analysis challenges, as brain image segmentation [6, 7], and mitosis detection [8]. Deep learning provides methods that are automated learning of feature instead of hand-crafted methods. CNN is considered as one type of feed-forward artificial neural network. It is a learning network that allows multiple levels of representation and abstraction. CNNs have become a very effective and popular approach for nuclei classification [9].Moreover, fully convolutional regression networks have been proposed to work on different research areas such as face detection [10]. Moreover, fully convolutional regression networks have shown state-of-art results in nuclei detection [11, 13, 16].

III. METHODOLOGY

We propose a continuous formulation of nuclei detection problem where the input image is mapped into a continuous valued map and all background pixels are assigned zero but nuclei are assigned a positive value corresponding to their distance to the nuclei boundary as shown in Eq.1.

$$mask(x,y) = \begin{Bmatrix} 0 & if\ p\,(x,y)\ \notin nuclei \\ dist(p(x,y), border_{nuclei}) & otherwise \end{Bmatrix} \qquad (1)$$

We use Convolutional Regression Network architecture to learn this continuous mapping. The distance map serves as probability density function of nucleus. Thus, it does not only detect nuclei regions, but also localizes the center of each nucleus and can distinguish between full or partial nuclei. It also identifies clustered nuclei as shown in Fig.2. Our model maps the multi-channel input image to the output function exploiting full color information in H&E stained images. In addition, a pooling layer was added to improve the detection. We also add an up-sampling layer to maintain the size of features in the network [10].

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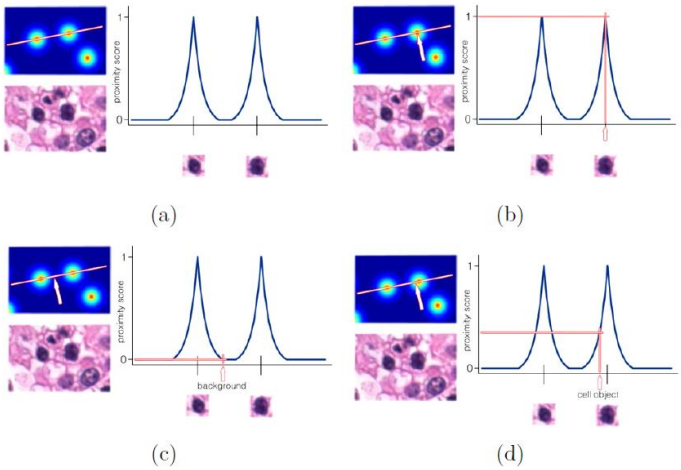

Fig.2. Fully Convolutional Regression ground truth (a) input patches and corresponding distance map, (b) nuclei center, (c) background, (d) nuclei body close to boundary).

The proposed model (Figure 3) was implemented using MatConvNet toolbox [12].Our model architecture consists of fourth types of layers: (1) convolutional, (2) pooling, (3) convolution prediction (FC), and (4) up-Sampling.

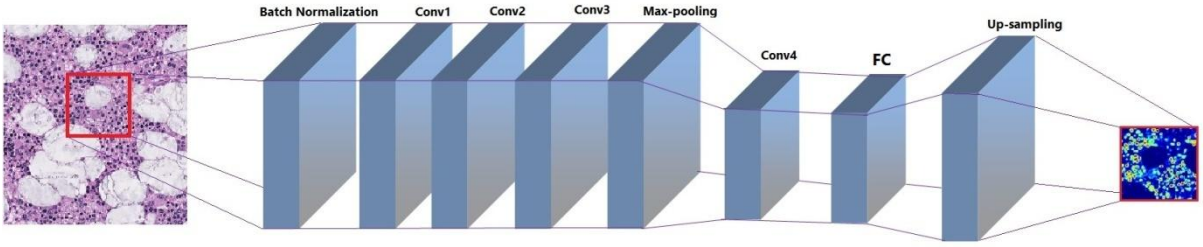

Fig.3. Network Structure

Training for nucleus center detection using the model (in figure 3) is implemented as follows. First, we have generated nucleus masks using ground-truth nucleus centers labeled by expert and expected nucleus radius. Then we implement Euclidean distance transform to these masks to produce continuous valued ground-truth values as shown in fig.4.

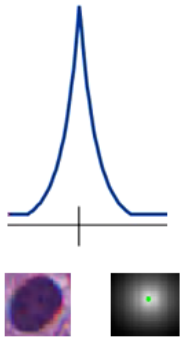

Fig.4. Ground Truth of FCRN

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Input image patches have been prepared by cropping patches centered around nucleus centers from original H&E stained specimen images and the corresponding distance transform masks. In this case, each input patch contents nucleus as shown in fig.5.

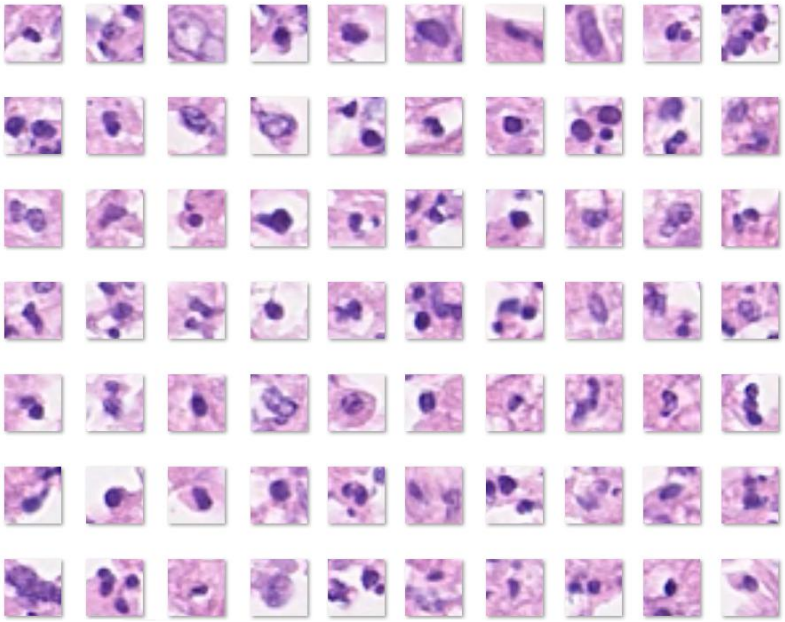

Fig.5. Samples of input patches.

We have trained our model with these sets of image patches. As a challenging dataset, colorectal dataset [13] is used for training and the network has been trained for 1000 epochs. Convolutional layer convolves the result of previous layer with a set of learnable filters where the weights specify the convolution filter. In order to evaluate the performance we test the model using full image labeling scheme described in [14, 15].In this technique, the full image size is directly fed to the network without dividing into blocks and equivalent of sliding window class labels are obtained all at once. Applying the convolutions over the whole image reduces the redundant repeated convolutions for overlapping regions of sliding windows. We tested the network on human bone marrow dataset [16].

IV. EXPERIMENTAL SETUP

In this section we describe datasets used, evaluation methods, and experimental results.

A. Datasets

1. The colorectal dataset [13] has 100 images of H&E stained colorectal adenocarcinoma specimens. This dataset is one of the most challenging datasets due to shape and size variations of the cells. This dataset has been used to train the network.
2. The human bone marrow dataset [16] consist of 11 images of H&E stained healthy human bone marrow from eight diff erent patients. This dataset has been used to test the network because the size of the images is 1200 ×1200 pixels. Ground-truth nuclei centers are provided for all nuclei in 11 images.

B. Evaluation Measures

We assessed the results in terms of precision (Eq.2), recall (Eq.3) and F-measure (Eq.4) where TP is true positives, FP is false positives, FN is false negatives.

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$$Precision = \frac{TP}{TP + FP} \quad (2)$$

$$Recall = \frac{TP}{TP + FN} \quad (3)$$

$$F_{measure} = 2 \times \frac{Precision \times Recall}{Precision + Recall} \quad (4)$$

C. Experimental Results

We have trained our model with the colorectal dataset [13] and tested on the human bone marrow dataset [16]. We have achieved 85.5% precision, 94.7% recall, and 89.9%F-measure. Table 1 shows comparison of our results to another approach in [11]. [16] hadnot reported qualitative results on The human bone marrow dataset.

Approaches	Precision%	Recall%	F-measure%
FCRN [11]	82.5	93.4	87.6
Our approach	**85.5**	**94.7**	**89.9**

Table .1.Nuclei detection performance comparison

It is important to notice that we tested on different dataset without re-train. Our approach handled partial detections andirregular-shaped, neighbouring nuclei,and different nuclei sizes and colour.

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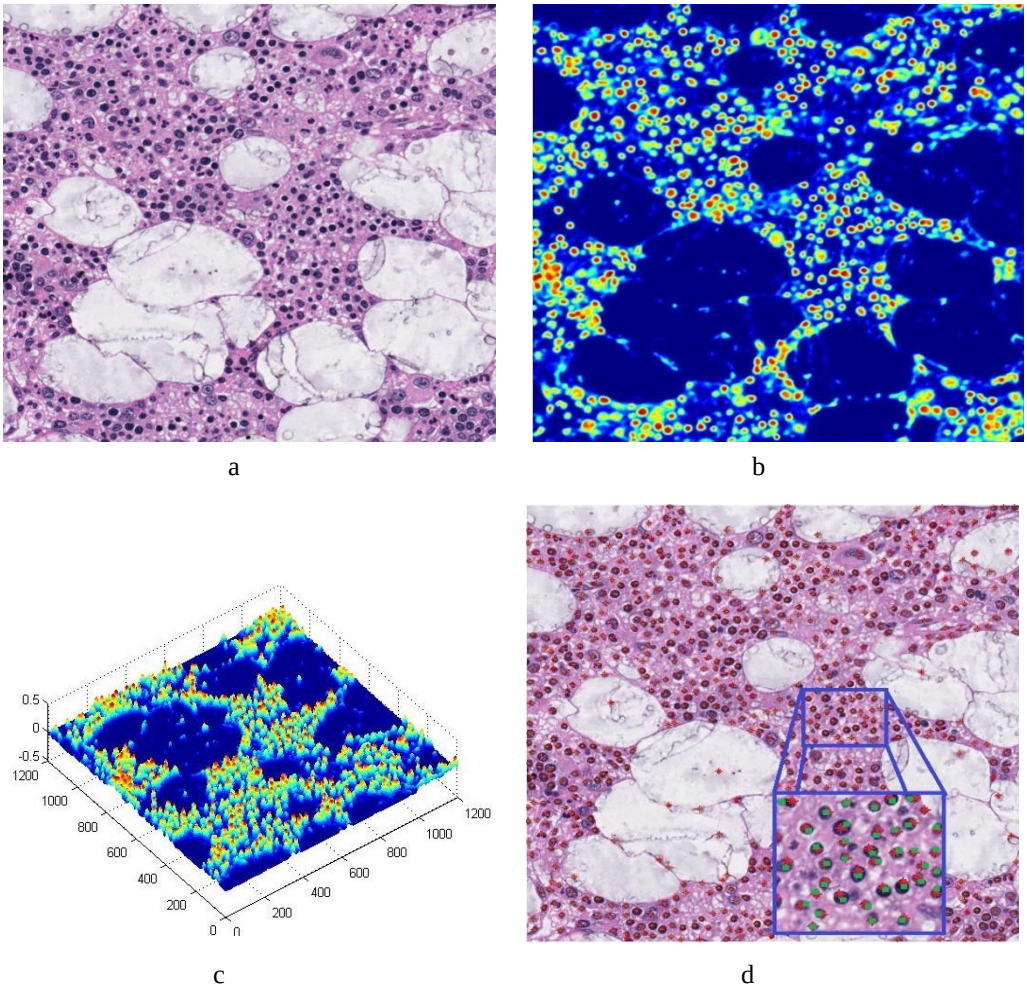

Fig.6. Output of the proposed approach. (a) Original image, (b) Output of our approach, (c) Output shown in 3D, (d) Detection results are red stars and expert annotated manual nuclei centers are green dots marked on original image.

IV. CONCLUSION

In this work, we have presented a deep learning approach to detect nuclei centers in images of H&E stained. We have used deep learning approach that enables automated learning of feature sets instead of hand-crafted features .Our approach learned an equivalent of probability density functions of centroid locations from H&E image patches. We trained the proposed model with the colorectal dataset then we tested on the human bone marrow dataset without retrain. Our method handled most nuclei detection's problems (merged cells, size, and color). Experimental results obtained on the human bone marrow dataset showed improved accuracy presented by [11] on same dataset.

REFERENCES

1. Kazuhiro Katahira, Taro Takahara, Thomas C Kwee, SeitaroOda, Yasuko Suzuki, Shoji Morishita, KosukeKitani, Yasuyuki Hamada, MitsuhikoKitaoka, and Yasuyuki Yamashita,"Ultra-high-b-value diff usion-weighted mr imaging for the detection of prostate cancer",*European Radiology*, 21(1):188–196, 2011.
2. Xiaowei Chen, Xiaobo Zhou, and Stephen TC Wong,"Automated segmentation, classification, and tracking of cancer cell nuclei in time-lapse microscopy",*IEEETransactions on Biomedical Engineering*, 53(4):762–766, 2006.

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3. MitkoVeta, Josien PW Pluim, Paul J van Diest, and Max A Viergever," Breast cancer histopathology image analysis", A review. *IEEE Transactions on Biomedical Engineering*, 61(5):1400–1411, 2014.
4. MitkoVeta, Paul J van Diest, Robert Kornegoor, André Huisman, Max A Viergever, and Josien PW Pluim,"Automatic nuclei segmentation in H&E stained breast cancer histopathology images,"*PloS One*, 8(7):e70221, 2013.
5. Carlos Arteta, Victor Lempitsky, J Alison Noble, and Andrew Zisserman," Learn-ing to detect cells using non-overlapping extremal regions", In *International Con-ference on Medical Image Computing and Computer-Assisted Intervention*, pages348–356. Springer, 2012.
6. Dan Ciresan, Alessandro Giusti, Luca M Gambardella, and Jürgen Schmidhuber," Deep neural networks segment neuronal membranes in electron microscopy im-ages," In *Advances in Neural Information Processing Systems*, pages 2843–2851, 2012.
7. Wenlu Zhang, Rongjian Li, Houtao Deng, Li Wang, Weili Lin, ShuiwangJi, and DinggangShen," Deep convolutional neural networks for multi-modality isointense infant brain image segmentation,"*NeuroImage*, 108:214–224, 2015.
8. Dan C Ciresan, Alessandro Giusti, Luca M Gambardella, and Jürgen Schmidhu-ber," Mitosis detection in breast cancer histology images with deep neural net-works", In *International Conference on Medical Image Computing and Computer-assisted Intervention*, pages 411–418. Springer, 2013.
9. Spanhol, Fabio Alexandre, et al., "Breast cancer histopathological image classification using Convolutional Neural Networks" *Neural Networks (IJCNN), 2016 International Joint Conference on*. IEEE, 2016.
10. Yuan, Jun, Bingbing Ni, and Ashraf A. Kassim. "Half-CNN: a general framework for whole-image regression." *arXiv preprint arXiv:1412.6885* (2014).
11. Alzubaidi L, Ersoy I, Shin D and Bunyak F (2016), *"Nucleus Detection in H&E Images with Fully Convolutional Regression Networks"*, IEEE First International Workshop on Deep Learning for Pattern Recognition (DLPR2016)., Dec, 2016.
12. Matconvnet,toolbox, http://www.vlfeat.org/matconvnet/.
13. KorsukSirinukunwattana, Shan E Ahmed Raza, Yee-Wah Tsang, David RJ Snead, Ian A Cree, and Nasir M Rajpoot," Locality sensitive deep learning for detection and classification of nuclei in routine colon cancer histology images", *IEEE Transactions on Medical Imaging*, 35(5):1196–1206, 2016.
14. Jonathan Long, Evan Shelhamer, and Trevor Darrell," Fully convolutional net-works for semantic segmentation", In *IEEE Conference on Computer Vision andPattern Recognition*, pages 3431–3440, 2015.
15. Hai Su, Fujun Liu, YuanpuXie, Fuyong Xing, SreenivasanMeyyappan, and Lin Yang," Region segmentation in histopathological breast cancer images using deep convolutional neural network", In *2015 IEEE 12th International Symposium onBiomedical Imaging (ISBI)*, pages 55–58. IEEE, 2015.
16. Philipp Kainz, Martin Urschler, Samuel Schulter, Paul Wohlhart, and Vincent Lepetit," You should use regression to detect cells", In *International Conference onMedical Image Computing and Computer-Assisted Intervention*, pages 276–283.Springer, 2015.