Distance representation with boundary refinement for clustered nuclei segmentation: a solution to CoNIC2022 challenge

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Abstract—Nuclei instance segmentation within histology images enables the extraction of interpretable cell-based features that can be used in downstream explainable models in computational pathology (CPath). However, two major challenges exist in this task. One lies in the overlapping/clustered nucleus while another lies in the varying size of different objects. In this paper, we employ distance representation and boundary refinement network to achieve robust nucleus instance segmentation. Firstly, we extend Hover-Net's horizontal and vertical distance representation into multi-directional distance representation, which is utilised to separate clustered nuclei, resulting in an accurate segmentation, particularly in areas with overlapping instances. Secondly, we further employ a boundary refinement network to get more accurate boundary for each segmented instance. Five-fold cross validation procedure is employed to evaluate the method. Overall, the PQ is 0.692 and the mPQ of six types of nucleus is 0.58 in CoNIC2022 challenge dataset.

Index Terms—clustered nuclei segmentation, instance segmentation

I. INTRODUCTION

Nucleus segmentation is a crucial task in computational pathology, as it provides rich spatial and morphometric information regarding nuclei. However, automatic nucleus segmentation remains challenging. Firstly, nucleus are often clustered together. Secondly, the size, shape of different nucleus varying greatly. These two challenges make it difficultly for models to accurately detect the boundary of each instance.

Existing approaches mainly focus on contour detection. One popular scheme is to segment the contours first and then subtract contours from predicted foreground to obtain final instance segmentation. In order to segment contour accurately, chen et al [1] adopted two independent decoders for U-Net, one for foreground segmentation and another for contour segmentation. Since there is no interactions between these two decoders, inconsistency may exist between segmented foreground and segmented contour. In order to make use of the correlation between two decoders, BES-Net [2] , CIA-Net [3], BRP-Net [5] further introduced uni-directional and bi-directional information transmission, respectively, which means one decoder obtains extra features from the other one.

TABLE I
FIVE CROSS-VALIDATION RESULTS

	PQ	mPQ+
HoverNet Fold 0	**0.642**	**0.510**
Ours Fold 0	**0.706**	**0.578**
Fold 1	0.684	0.594
Fold 2	0.676	0.562
Fold 3	0.700	0.568
Fold 4	0.693	0.583
Mean	0.692	0.58

Another popular scheme for nuclei segmentation is to employ distance information to separate clustered nucleus. Hover-Net [4] employ horizontal and vertical distance representation for cluster object separation, which achieved state-of-the-art results on multi-type nuclei segmentation.

In this paper, we propose a novel solution for CoNIC2020 challenge [6], which is an extension of effective Hover-Net [4] and BRP-Net [5]. For instance egmentation, similar to BRP-Net [5], proposed method also comprises two stages: one stage to obtain instance proposals and another for boundary refinement. In the first stage, we implement the distance representation to separate clustered nuclei. In the second stage, a boundary refinement network is employed to get more accurate boundary for each segmented instance. Besides, a simple generic U-Net with densenet121 as backbone is used for classification.

II. METHODS

Our method consist of two parts, one for clustered nuclei segmentation and another for nucleus classification.

A. Clustered nuclei segmentation

Proposed clustered nuclei segmentation approach consists of two stages. In the first stage, a base segmentation model extended from Hover-Net is employed to roughly segment instances. In the second stage, a boundary refinement model is employed to further refine the prediction from previous stage, where predictions with varying size are processed using a same scale.
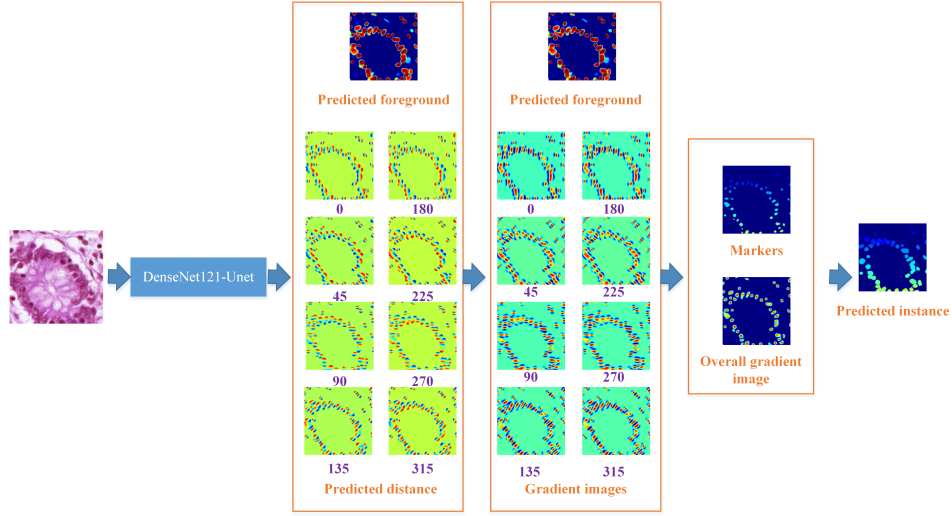
Fig. 1. Schematic diagram of the proposed base instance segmentation model.

1) Base segmentation model: The base segmentation model, Densenet121-Unet, is a fully convolutional neural network(FCN), which consists of a encoder and a decoder. The input to base segmentation model is the histology image(H×W×3) and the outputs include the predicted foreground (H×W×1) and predicted eight-directional distance image (H×W×8). Once we get the predictions from the model, we firstly use 8 sobel kernels with different directions to obtain gradient images from predicted distance image. Then, predicted markers and overall gradient images are generated by merging and thresholding these gradient images and predicted foreground. Finally, marker-controlled watershed algorithm is employed to get final predicted instance.

As for model architecture, we employ densenet-121 as the encoder. Compared to the standard densenet implementation, we reduce the total down-sampling factor from 32 to 8 by using a stride of 1 in the first convolution and removing the subsequent pooling operation. A series of consecutive dense units is denoted as a dense block. The number of dense units within each dense block is 6, 12, 24, and 16 that are applied at down-sampling levels 1, 2, 4 and 8 respectively.

The up-sampling path is employed to gradually recover the resolution of feature images and generate a high-resolution predictition. The decoder block mainly consists of repeated up-sampling layers, skip concatenations, 3×3 convolution layers, BN layers, and ReLUs. In order to obtain richer details, the encoder layers with {1, 1/2, 1/4} of the original image size are passed to the decoder block by skip concatenations since earlier high-resolution feature images from encoder can help refine the information of locations. We adopted trilinear scaling followed by 3×3 convolution layers to up-sample the features images. Based on the decoder module, feature images are gradually up-sampled to the original resolution, and the predicted distance images and predicted foreground are generated after 1×1 convolution layers.

2) Boundary refinement model: We crop one square 48 × 48 patch containing each segmented instance. If an instance larger than 48, it will be resized to 48 × 48.Inputs to the model include the patch, and the probability maps that are predicted by the semantic segmentation in the clustered nuclei segmentation model. To relieve the influence of background, elements in the probability maps that fall outside of the dilated proposal are set to zero. We use a tiny small 4-stage U-Net model for this part.

B. Nucleus classification

Since we mainly focus on clustered nuclei segmentation, a simply U-Net use the same Densenet121 as backbone is employed for nuclei classification task.

C. Loss function

For clustered nuclei segmentation, we used the same loss functions as Hover-Net. For boundary refinement model, we use Batch dice loss and CE loss for optimization. Besides, we use an additional classification branch with CE loss for deep supervision. For classification task, we also use Batch dice loss and CE loss for optimization.

D. Training details

We use SGD with Stochastic Weights Averaging (SWA) to train all the models. The base learning rate is 0.01 and adapted following 2k warmup and 120k cosine annealing scheduler. The optimization procedure is stopped at 122,000 iterations. All models are implemented using a single 3090 GPU with 24 GB memory. It takes around 25 hours to train a single fold.

III. RESULTS

We do five cross-validation on CoNIC challenge dataset and the results are show in Table 1. As we can see that proposed method shows significant improvement than Hover-net baseline.

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