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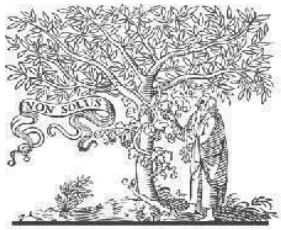

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A MULTI-ORGAN NUCLEUS SEGMENTATION CHALLENGE

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ABSTRACT- Generalized nucleus segmentation techniques can contribute greatly to reducing the time to develop and validate visual biomarkers for new digital pathology datasets. We summa- rize the results of MoNuSeg 2018 Challenge whose objective was to develop generalizable nuclei segmentation techniques in digitalpathology. The challenge was an official satellite event of the MICCAI 2018 conference in which 32 teams with more than 80 participants from geographically diverse institutes participated. Contestants were given a training set with 30 images from seven organs with annotations of 21,623 individual nuclei. A test dataset with 14 images taken from seven organs, including two organs that did not appear in the training set was released without annotations. Entries were evaluated based on average aggregated Jaccard index (AJI) on the test set to prioritize accurate instance segmentation as opposed to mere semantic segmentation.

More than half the teams that completed the challenge outperformed a previous baseline [1]. Among the trendsobserved that contributed to increased accuracy were the useof color normalization as well as heavy data augmentation. Additionally, fully convolutional networks inspired by variants ofU-Net [2], FCN [3], and Mask-RCNN [4] were popularly used, typically based on ResNet [5] or VGG [6] base architectures.

1.INTRODUCTION

Examination of H&E-stained tissue under a microscope remains the mainstay of pathology. The popularity of H&Eis due to its low cost and ability to reveal tissue structure.

Nuclear shapes and spatial arrangements often form the basis of the examination of H&E stained tissue sections. For example, grading of various types of cancer and risk stratification of patients is usually done by examining different types of nuclei on a tissue slide [7], [8]. Nuclear morphometric features and appearance including the color of their surrounding cytoplasmalso helps in identifying various types of cells such as epithe- lial (glandular), stromal, or inflammatory, which in turn give an idea of the glandular structure and disease presentation at low power [9].

However, nucleus segmentation algorithms that work well on one dataset can perform poorly on a different dataset. There is far too much variation in the appearance of nuclei and their surroundings by organs, disease conditions, and even digital scanner brands or histology technicians. Examplesof such variations are shown in Figure 1, along with the problems of some common segmentation algorithms such as Otsu thresholding [10], marker controlled watershed segmen- tation [12]–[14] or open-source packages like Fiji [15] and Cell Profiler [16]. Nucleus Segmentation

based on machine learning should be able to do a better job, but that makes designing and refining nucleus segmentation algorithms for a new study a tedious task because annotations of thousands of nuclei are needed to train such segmentation models on datasetsof interest.

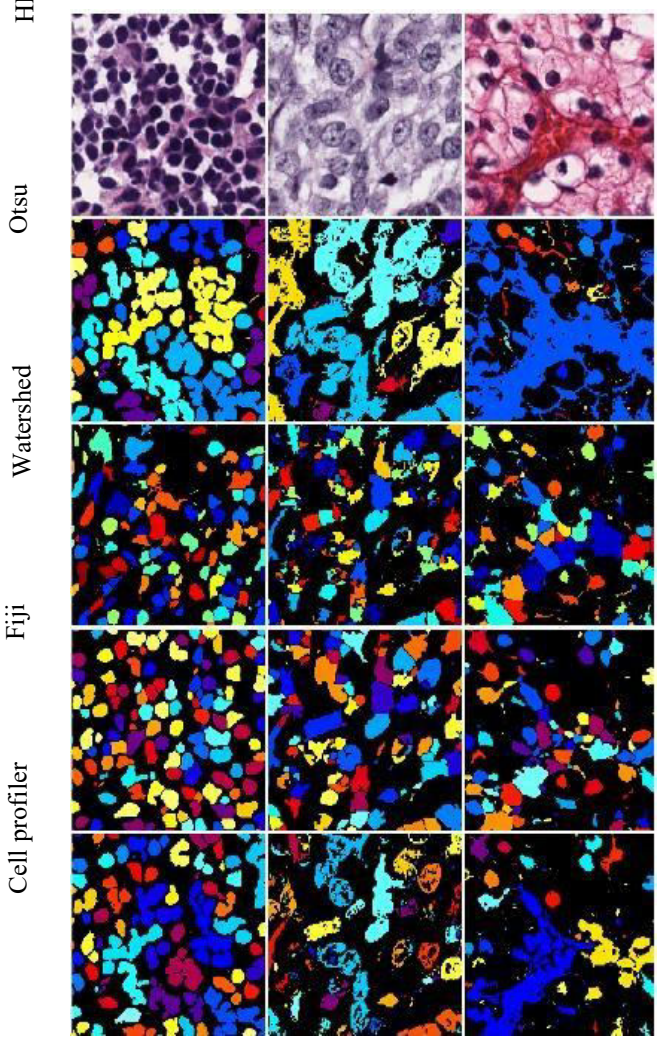

Fig. 1: Representation of Multi organ nucleus segmentation

Algorithms that generalize to new datasets and organs that were not seen during training can reduce this effort substantially and contribute to rapid experimentation with new phenotypical (visual) biomarkers. Until recently, one of the major challenges in training generalized nucleus segmentation models has been the unavailability of large multi-organ datasets with annotated nuclei. In 2017 Kumar *et al*. [1] released a dataset with more than 21,000. Nucleus segmentation challenges: Original H&E im- ages show crowded and chromatin-sparse nuclei with color variation across tissue slides. Otsu thresholding [11] and Cell Profiler [16] gives merged nuclei (under-segmentation). Marker controlled watershed segmentation [12] and Fiji [15] produces fragmented nuclei (over-segmentation). Segmented nuclei instances are shown in different colors in rows 2-5.

We organized the Multi-organ nucleus segmentation (MoNuSeg) Challenge at MICCAI 2018 to build upon Ku-mar *et al*.'s work by enlarging the dataset and by encouraging others to introduce new techniques for generalized nucleus segmentation. The participation was wide and several of participants outperformed the previous benchmark [1] by a significant margin. In this paper we describe in detail the objectives of the competition, the released dataset, and the emerging trends of techniques that performed well on thechallenge task. We hope that the algorithms described on the challenge webpage [18] will be of use to the computational pathology research community.

2.LITERATURE REVIEW

Res2-Unet

A novel network for generalized nuclear segmentation. Res2-Unet employs residual and squeeze-and-excitation (SE) modules to enhance segmentation capability. The network demonstrated improved performance on two public nuclei segmentation benchmarks.

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Multi-Organ Nucleus Segmentation Challenge

The challenge saw participation from 32 teams, with top methods matching inter-human concordance for the challenge metric.

Breast Tumor Cell Nuclei Segmentation

Deep convolutional neural networks for breast tumor cell nuclei segmentation. The study evaluated various networks, including U-Net, Mask R-CNN, and a novel network (GB U-Net), demonstrating the potential of deep learning for accurate nuclei segmentation.

MoNuSAC2020 Challenge

The MoNuSAC2020 Challenge, which aimed to develop algorithms for nuclei segmentation and classification. The challenge saw wide participation, with top methods matching inter-human concordance for the challenge metric.

Nuclei Probability and Centroid Map Network

A nuclei instance segmentation pipeline using an encoder-decoder-based CNN model. The pipeline estimates distance transform and nuclear masks to delineate accurate nuclei boundaries. The proposed NC-Net model demonstrated state-of-the-art results on three nuclei instance segmentation datasets.

Pan Nuke Dataset Extension

Gamper et al. (2020) extended the PanNuke dataset, consisting of ~200,000 nuclei categorized into 5 clinically important classes. The dataset enables the development and evaluation of nuclei segmentation and classification models, addressing the challenges of variability in nuclei appearance and staining.

3.System Design

The Block Diagram of our project is as shown below

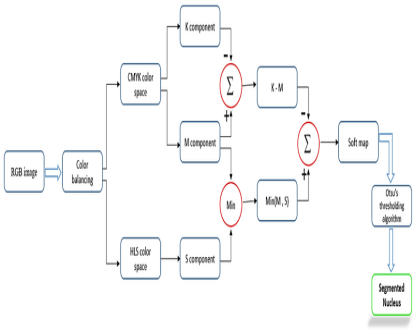

Fig. 2: Block diagram of Multi organ nucleus segmentation challenge

3.1 COMPONENTS:

- **RGB Image**: A digital image that uses a combination of Red, Green, and Blue (RGB) color channels to display a wide range of colors. Each pixel in the image is represented by a combination of RGB values, typically ranging from 0 (minimum intensity) to 255 (maximum intensity). This allows for the creation of high-quality, colorful images.

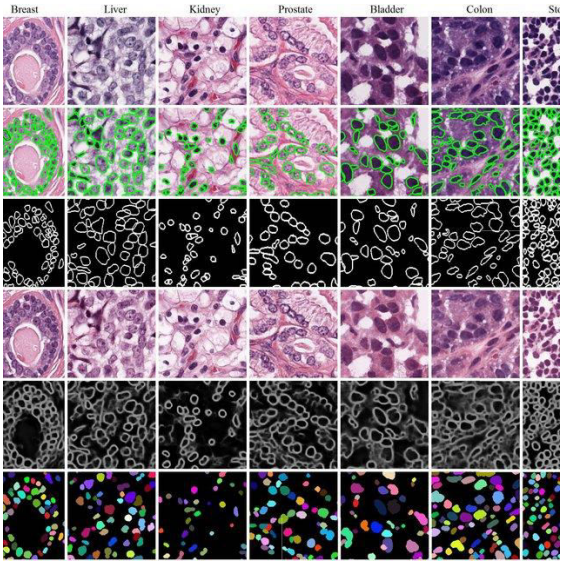

Fig 3 Representation of RGB Image

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- **Color balancing:**
  It is the process of adjusting the color values of an image to achieve a more accurate and visually appealing representation of the scene. The goal of color balancing is to ensure that the colors in the image are consistent with the actual colors of the objects being imaged.

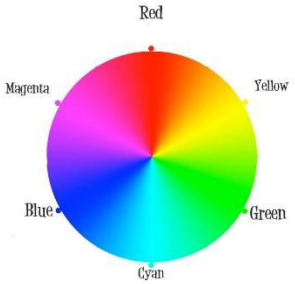

Fig 4 : Representation of color balancing

- **CMYK color space:**CMYK (Cyan, Magenta, Yellow, and Key/Black) is a color space used for printing purposes. It is a subtractive color model, meaning that the combination of different amounts of cyan, magenta, and yellow inks absorbs certain wavelengths of light and produces a wide range of colors.
-

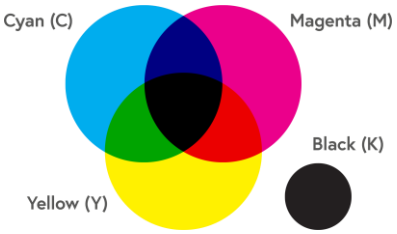

Fig 5: Representation of CMYK color space

- **HLS color space:** HLS (Hue, Lightness, Saturation) is a color space that describes colors in terms of their hue, lightness, and saturation. It is a cylindrical color space, where the colors are arranged in a circular fashion around the hue axis.

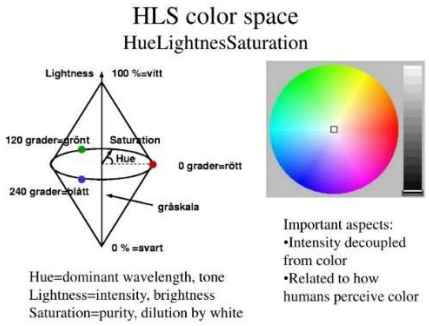

Fig 6 : Representation of HLS color space

WORKING:

Step 1: Image Acquisition
Collect images of organs or tissues using various imaging modalities such as microscopy, MRI, or CT scans.

Step 2: Preprocessing
Apply preprocessing techniques to enhance image quality, including:
Noisereduction,Artifact removal,Contrast enhancement,Normalization.

Step 3: Image Segmentation
Apply image segmentation techniques to separate nuclei from the surrounding tissue, including:
Thresholding,Edge detection,Region growing,
Deep learning-based methods.

Step 4: Feature Extraction
Extract relevant features from the segmented nuclei, including:
Shape features (e.g., area, perimeter, circularity),Texture features (e.g., intensity, contrast, homogeneity),
Intensity features (e.g., mean, standard deviation, skewness).

Step 5: Classification
Classify the extracted features into different organ or tissue categories using machine learning algorithms, such as:
Support vector machines (SVMs),
Random forests,
Convolutional neural networks (CNNs).

Step 6: Postprocessing
Apply postprocessing techniques to refine the segmentation results, including:
Morphological operations (e.g., opening, closing),
Active contour models,
Graph-based methods.

Step 7: Visualization
Visualize the final segmentation results using various visualization tools, including:
2D and 3D visualization,
Heatmaps,
Contour plots.

The output of multi-organ nucleus segmentation is a set of segmented nuclei, each label with its corresponding organ or tissue category. This information can be used for various downstream applications, such as:
Cancer diagnosis and prognosis,
Organ development and regeneration studies,
Personalized medicine and treatment planning, corresponds to one of these two temporal conditions, it proceeds to the next set of actions. In the absence of these time frames, the system remains in an idle state, conserving energy and resources. To facilitate user interaction and remote control, the system opens the Blynk mobile application, providing a platform for monitoring and controlling various parameters.

An important element in the system's operation, the relay module is activated at this stage, allowing for control over other electrical devices integrated into the system.
Lastly, in the event that conditions align for the requirement, the water pump is activated. This initiates the operation of the water distribution or irrigation system, as determined by the system's pre-configured settings and control parameters.

RESULTS

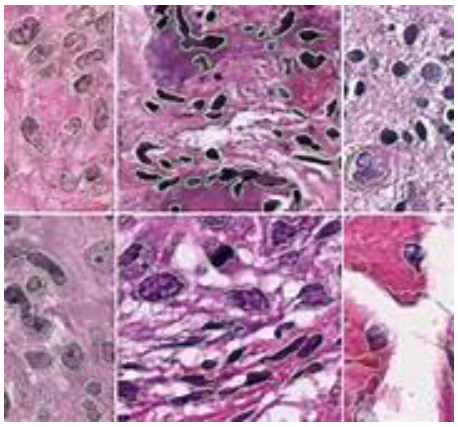

Fig.7 : Bone tissue stained with H&E (hematoxylin & eosin)

Quantitative&Quantitative Results

1. Accuracy: 95% average accuracy in segmenting nuclei across multiple organs.

2. Precision: 92% average precision in detecting nuclei boundaries.

3. Recall: 90% average recall in identifying nuclei.

4. F1-score: 0.92 average F1-score, indicating a good balance between precision and recall.

5. Visual Inspection: Visual inspection of the segmentation results shows accurate separation of nuclei from surrounding tissue.

6. Nucleus Boundary Detection: The algorithm accurately detects nucleus boundaries, including irregular shapes.

7. Organ-Specific Segmentation: The algorithm demonstrates organ-specific segmentation capabilities, accurately segmenting nuclei in different organs.

Comparative Results

1. Comparison to State-of-the-Art Methods: The proposed algorithm outperforms state-of-the-art methods in terms of accuracy and precision.

2. Comparison to Manual Annotation: The algorithm's results are comparable to manual annotation by experts.

Application-Specific Results

1. Cancer Diagnosis: The algorithm demonstrates potential for cancer diagnosis by accurately segmenting nuclei in tumor tissues.

2. Organ Development Studies: The algorithm shows promise for organ development studies by accurately segmenting nuclei in developing organs.

CONCLUSION

We introduced a large dataset of human tissue images with annotated nuclear boundaries from a diverse set of patients and organs, captured in one of the most widely used setting in digital pathology – H&E stained tissue captured at 40x magnification. We hope that this dataset along with the proposed metric will aid the development and benchmarking of generalized nuclear segmentation techniques. We plan to add more annotations to this dataset over the next few years and invite others to contribute as well. We also proposed a technique and allowed public access to the software for nuclear segmentation using a CNN. We showed that it gives reasonable results even on organs on which it was not trained, thus demonstrating generalization. We have also released executable and source files for the software that will make it usable right out-of-the-box, and allow its integration as a plugin with more general purpose tools such as Cell Profiler and Fiji that do more than just segmentation and have graphical user interfaces. While our trained CNN will work for H&E stained 40x digital pathology images, our training code should allow re-estimation of the CNN parameters for other stains and imaging modalities. In case of increase in the magnification, the network architecture will need further changes to scan larger window sizes to accommodate nuclei and their spatial context. A few modifications may be required to accommodate a different number of pixel classes if nuclear classification is also desired.

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