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An Effective Multi-Patch Deep Learning Method for Mitosis Detection in Breast Histopathology

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Abstract

Within the realm of computational pathology, the detection of mitotic cells poses a formidable challenge. Many existing approaches rely on hand-crafted features, which often result in poor generalization, as their performance degrades across different tissue types, staining processes, and the various scanners used for digitizing whole slide images. The Multi-Patch Mitosis-Detect (MPMD) framework is suggested in the proposed work to detect mitosis from histology images. To identify mitotic reference regions, the proposed MPMD framework uses the detection module for segmentation by utilizing the Recurrent Residual Convolutional Unit (RRCU). The classification model then employs Inception Recurrence Residual Convolutional Neural Networks (IRR-CNN) to validate the mitotic regions. Furthermore, a novel confidence analysis and the MPMD technique are combined to improve the performance of the detection in the testing phase. The novelty of the proposed multi-patch approach is that: (a) Mean Squared Error (MSE) loss is used instead of Dice Coefficient (DC) loss for both training and testing; (b) Global Average Pooling is used in place of fully connected layers in the classification model to reduce the number of network parameters. Experimental findings demonstrate the performance improvement of the proposed approach compared to existing state-of-the-art methodologies.

Keywords: Breast cancer detection, Mitosis detection, Multi patch similarity scheme, Recurrent Residual Convolutional Unit, Pathological images, Deep neural network.

1. Introduction

As per the 2018 publication by the International Agency for Research on Cancer, there was an estimation of 1 crore 81 lakhs novel instances of cancer along with 96 lakhs related demises. Breast cancer stands out as one of the prevalent malignancies in females globally, ranking high among the leading causes of mortality. Both the World Health Organization and the Nottingham Grading System identify three important features for evaluating breast cancer: the formation of tubules, the presence of abnormal nuclei, and the mitosis count. These data are highly essential for understanding, diagnosing, and treating breast cancer. Pathologists analyze High-Power Fields (HPFs) within Total Slide Images (TSI) to identify and count mitotic cells. The manual visual examination of histology slides by pathologists is characterized by tedium, susceptibility to errors, and time consumption. Consequently, there is a need for automatic approaches to mitotic cell detection within clinical settings. The detection of mitotic activity in E&H (Eosin and Hematoxylin) stained histopathological images poses

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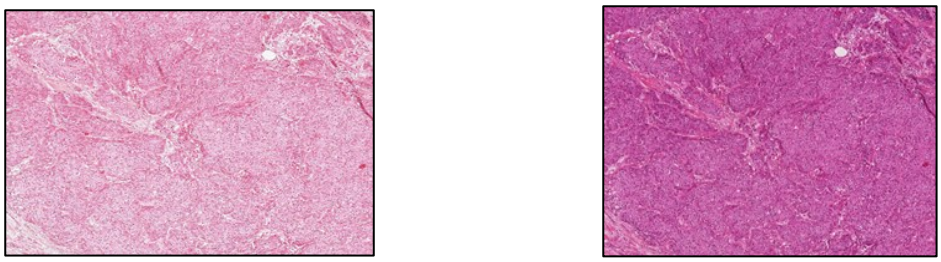
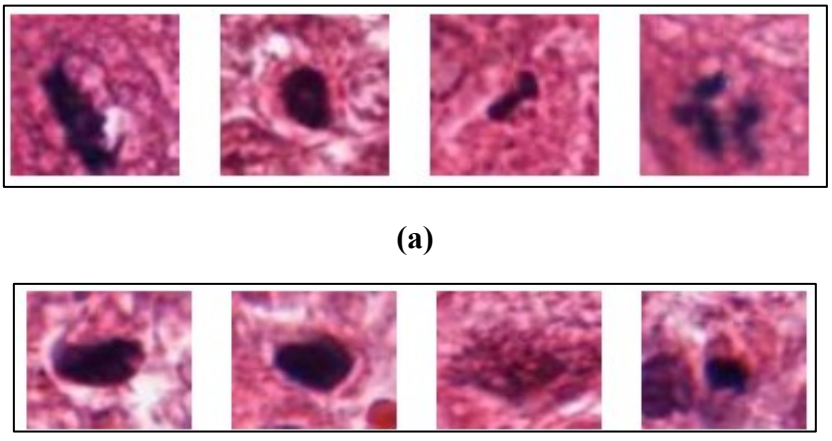
challenges due to various factors like subtle differences between different kinds of images, cell overlapping, heterogeneity of nuclei, and nuclei overlapping. Mitosis nucleus undergoes diverse transformation through four distinct phases, each phase exhibiting unique morphology and texture which complicates the detection. Further, mitosis detection becomes challenging because some cells may not be in focus. Accurate detection of mitotic cells is complicated due to certain cell types. Because there are so many HPFs in a Whole Slide Image (WSI), the process is laborious and error-prone. Assessing mitotic cells is subjective and not easily reproducible, making it hard for pathologists to conclude on the mitotic count. Early detection techniques are required to satisfy the needs of clinical applications. The histopathological images captured using an A-type and an H-type scanner are displayed in figure 1.



(a) **(b)**

Figure 1. Histology Images Captured using Both A Type and H Type Scanner: (a) Captured by the A-level Scanner (b) Captured by the H Scanner

Given the critical nature of cancer severity determination, there has been a surge in research activity aimed at developing efficient methodologies for automatic mitotic cell detection in pathological images. Recent advancements in deep learning techniques have led to the emergence of numerous automatic mitosis detection systems, demonstrating markedly superior performance when compared to traditional machine learning approaches. One of the primary hurdles encountered in deep learning pertains to the acquisition of a sufficient volume of samples with labeling required for training significant neural network frameworks. Mitotic detection is a challenging task as seen in competitions like ICPR 2012, AMIDA 13, MICCIA 2013, ATYPIA MITOSIS 2014 and TUPAC-16. Mitotic cells and non-mitotic cells are shown in figure 2.



(a)

(b)

Figure 2. (a) Patches of Cells with Mitosis (b) Patches of Cells with no Mitosis

However, simple CNNs by themselves do not have cell-level monitoring, which frequently necessitates restricting the size of the input image. The size of the images is reduced to concentrate on localized areas of the image instead of the entire image context. Due to this, both objects and non-objects can be used to learn the sub- image features. Furthermore, in medical applications, accurate localization or object recognition is actually a more frequent challenge than full-image categorization. Therefore, deep learning techniques like R-CNN, Faster R-CNN, and Mask R-CNN were first created for object detection and have been adapted to target particular areas of the image referred to as ROI (Region of Interest).

Selecting particular features to identify mitotic cells is challenging due to the complex and diverse areas of mitotic cells as well as the presence of confused cells. Consequently, in recent years, several mitosis detection systems employing deep learning techniques have been presented. These methods have improved accuracy compared to traditional methods [2]. The mitosis detection systems face two types of problems. Firstly, the classification problem involves extracting non-overlapping slides (patches) and employing Convolutional Neural Networks (CNNs) to classify whether the patch corresponds to a mitotic or non-mitotic region. [3]. However, the drawback is it is that not certain that the mitotic region will align with the central areas of the patches. Secondly, there are instances where patches only partially contain mitotic regions, leading to the model's failure in detecting mitotic cells.

Alternatively, the problem in a segmentation task involves pixel-level classification to delineate mitotic regions rather than classifying patches [3]. Despite its potential, this method disregards regional context and is unsuitable for weakly annotated samples, such as single-pixel annotations typical in datasets like the Atypia Mitosis 2014 dataset [4]. Recently, an article addressed the challenge of mitosis detection using a Faster Recurrent Convolutional Neural Networks (R-CNN) model. This model employs a fully connected Region Proposal Network for generating the target regions, followed by classification using a classifier. The system comprises two distinct models: firstly, a segmentation model to estimate the bounding boxes using a Fully connected Convolutional Network (FCN). Secondly, a detection model to enhance the classification of detected patches using ResNet based Recurrent Convolutional Neural Networks. However, there are issues with this detection model. The mitosis detection in openly available datasets lacks bounding box labels, posing a challenge for the detection model. This is addressed by applying a previously trained FCN model from the 2012 mitosis dataset on the 2014 mitotic dataset in order to create bounding boxes. Segmentation model output images are labeled. It is challenging to train the deep learning model to define accurate boundaries because the mitosis regions exhibit variations in size and appearance. In this paper, introduce a Multi Patch Mitosis Detection (MPMD) system based on multiple tasks, leveraging different models for classification, detection and segmentation. We simultaneously employ a segmentation model for region based annotated images and a detection model for pixel annotated images. By combining the output images of the segmentation and detection models, we extract the regions of interest areas for mitotic cells. Subsequently, a classification method is utilized to classify mitotic and non-mitotic cells. The following sections constitute the remaining manuscript as: Section 2 consists an overview of the literature. Section 3 describes the proposed method, the results and discussion are presented in section 4 and Section 5 shows the concluding part.

2. Literature Review

With the availability of WSI over glass slides [5-7], automatic detection of mitotic activities in Hematoxylin and Eosin (H&E) examinations of stains has gained significant attention. In the past, handcrafted features were utilized to define morphologies, textures, and statistics-based attributes in regions of mitosis. However, these methods require extensive validation efforts and suffer from poor generalization due to insufficient representation of mitotic region features or characteristics, consequently yielding subpar accuracy. Recently, methodologies based on deep learning [8] have gained popularity among researchers for segmenting, detecting, and recognizing activities across various medical imaging modalities. Notable strides have been made in computational pathology over the past few years, along with the development of various deep learning methods specifically designed for detecting mitosis [9]. Groundbreaking advancements have occurred in pixel-based classification for histology images by applying deep neural networks in mitosis detection. These techniques are complemented by post-processing techniques to obtain better results. Experimentation conducted on the 2012 ICPR MITOSIS challenge yielded remarkable results, achieving the highest performance with an F1-score of 78.2%, marking a substantial improvement over existing feature-based method. The deep CNN methods demand computational resources and are time consuming.

In 2016, a methodology [10] was introduced that utilized both coarse and fine approaches, employing a cascading framework involving two CNN models. Initially, candidate regions were extracted using the first CNN model, referred to as the framework for retrieving coarse information. Recognizing the challenge posed by the availability of labeled samples for training Deep CNN (DCNN) models, a CNN augmented with an additional crowdsourcing layer (AggNet) was proposed in 2016 to address this issue. Subsequently, a new framework was employed for classification purposes, distinguishing mitotic and non-mitotic regions exhibiting similar appearances [11]. For the classification model, a transfer learning technique was employed, involving training deep CNN frameworks over a vast dataset comprising naturalized images. Evaluation of frameworks had been conducted over both the 2012 ICPR MITOSIS and 2014 MITOS-ATYPIA examinations [4], yielding F1-scores of 78.8% and 48.2%, respectively. Notably, the system's limitation lies in its evaluation and reporting solely on samples obtained from an A-type scanner.

The detection process has been enhanced by Deep Regression Networks (DRNs) with fully convolutional kernels [12]. In a single forward propagation, these networks can generate a dense score map matching the original input size. Moreover, we've leveraged knowledge transfer from diverse domains to augment their generalization capabilities. The performance evaluation of DRN on the MITOSIS 2012 dataset exhibits an F1score of 78.9%. In 2018, another study was conducted for mitosis detection, presenting coarse and fine-based models [13]. The 37 distinct features were extracted based on color, texture and size. The Random forest classifier is used to select primary candidate regions. This study reported F1-scores of approximately 78.4% and 42.7% for the ICPR MITOSIS 2012 and ATYPIA MITOSIS 2014 datasets respectively. They conducted experiments on only A-type scanners.

In early 2018, the DeepMitosis framework [14] was introduced, comprising segmentation, detection, and verification networks. The detection task utilized a Faster R-CNN, an area-based framework for detecting ConvNets incorporating totally convolution-based Networks of Proposals or Region or RPN for suggestion generation along with subsequent classification. The experimental evaluation was restricted to samples obtained from an Aperio

type, yielding F1 scores of 83.2% 2012 43.7% for the 2012 and 2014 datasets, respectively. In 2019, a CNN based on a transfer learning approach [15], with random forest classifiers, was proposed for better feature extraction in mitotic detection. These methods were performed on the ATYPIA MITOSIS 2014 dataset and dataset prepared by cancer affected areas in Thiruvananthapuram, South Asia. This method shows a 15 percent performance improvement in mitosis detection.

In 2022, an advanced deep learning framework Residual Cascaded Networks [16], was proposed to enhance the existing method for mitosis detection. This method discussed three improvements: Firstly, to reduce erroneous detection by relocating predictions around window borders to new windows for re-evaluation. Secondly, to enhance overall accuracy by adjusting the center of objects by improving consistency and subsequent classification. Thirdly, to identify informative example an active learning integration is performed by leveraging discrepancies between the two pipeline stages. This method achieves an F1 score of 0.82.

In 2023, FoCasNet [17], an enhanced two-stage nuclei detection method, was introduced. It comprises two components: the initial stage is Mdet for detecting mitosis to capture as many instances as possible. The second stage is Mclass, which classifies the results from the previous stage by eliminating false positives. This method achieved state-of-the-art performance with an F1-score of 0.88 on the ICPR 2012 dataset.

The classification issue involves identifying whether the non-overlapping regions match mitotic tissue or non-mitotic tissue. A disadvantage is that there is no guarantee that the mitotic region will always line up with the center regions of the patches. The issue with segmentation identifies mitotic areas using pixel-level classification as opposed to patch classification. The disadvantage is that it may not be appropriate for datasets with pixel annotations, such as MITOSIS ATYPIA 2014. To address these problems, a novel approach based on multi-tasking with a multi-patch mitosis detection technique is proposed in this paper.

3. Proposed Methodology

The existing CNN based networks are used to extract features by training on images. These methods are extended to medical images to identify the locations of mitotic regions. For recognizing mitotic figures both hand-crafted and CNN features are employed. Later, to recognize the mitotic figures within the patches of images, a sliding window approach is used to avoid the need for hand-crafted features. A two-stage pipeline for detecting mitosis called Cascade Neural Networks [13] is initiated, where a semantic segmentation network first coarsely proposes mitotic cell locations, followed by refinement using a classification network for detailed prediction. DeepMitosis [14] shows significant improvement in performance by enhancing the detection algorithm in first stage where semantic segmentation is transformed into object detection. But the bounding boxes are estimated with the help of semantic segmentation networks for datasets that lack pixel-level annotations.

The proposed method, MPMD, innovatively tackles the problem in the first stage by multi-patch based learning, training both segmentation and detection models concurrently. In both training and testing the Dice Coefficient loss is replaced with the Mean Squared Error loss in the proposed method. In the segmentation model to differentiate mitosis from non-mitosis regions, Gaussian density surfaces are generated with respect to the center points of the mitotic figures. Due to the mean squared error loss, the model is trained based on density surfaces instead of pixels. Because patches are applied as input to the model, it focuses on localized

features instead of focusing on entire context of the images. The model effectively detects mitotic and non-mitotic regions and improves the F1-score compared to other methods. In the proposed architecture, two distinct models are utilized for the detection phase, addressing detection and segmentation tasks, as illustrated in figure 3.

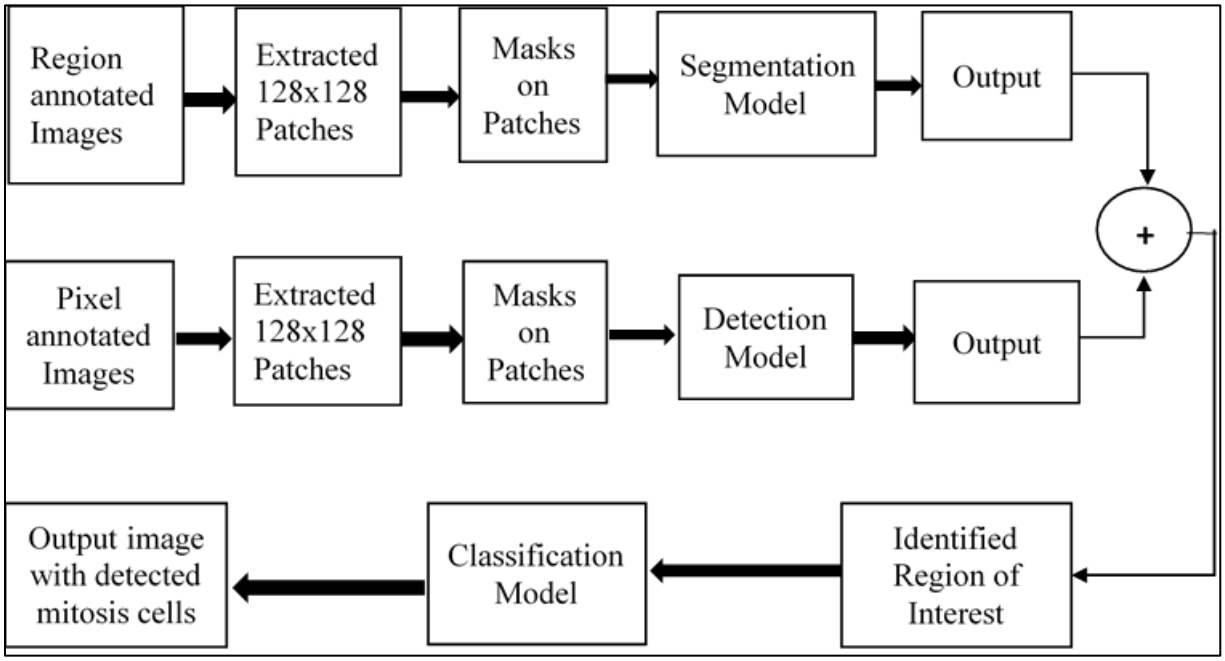


Figure 3. Block Diagram of Multi Patch Mitosis Detection System

For datasets featuring region-based annotations, the mitosis segmentation task employs the Recurrent Residual U-Net (R2U-Net) framework, while a regression model-based R2U-Net is employed for datasets with single point annotations, facilitating mitosis detection. Patches are extracted from the input images in sizes of 128x128 non-overlapping sections for detecting the regions of interest. Patches are generated from each method and combined to create merged masks for the final prediction mask. Subsequently, a blob detection technique is employed over the merged masks to obtain the centers of the blobs. An integrated multi-patch reference scheme is then utilized for cropping patches measuring 64 x 64 pixels centered on the translated blob centers. Finally, the validation of cells that have undergone mitosis and non-mitosis activities, including nearby candidates to cells that have undergone mitosis, is conducted utilizing Inception Recurrence Residual Convolutional Neural Networks IRR-CNN.

3.1 Segmentation and Detection Models

The segmentation framework architecture employed in the R2U-Net model shown in figure 4 follows the sequence: 128×128×3 → (64×64×32) → (32×32×64) → (16×16×128) → (8×8×256) → (8×8×512) → (8×8×256) → (16×16×128) → (32×32×64) → (64×64×32) → 128×128. In each R2U net, M×N is the size of the input image or feature maps in the notation (M×N×K) and the number of filters is represented with K. Each convolutional layer employs 3×3 kernels.

Recurrent Residual Convolutional Units (RRCUs) consist of a combination of two ideas: recurrence and residual learning. This method is best suited for segmenting and differentiating mitotic and non- mitotic regions accurately. RRCU applies the same

convolutional layers repeatedly with shared weights to create deeper representations without expanding the number of parameters.

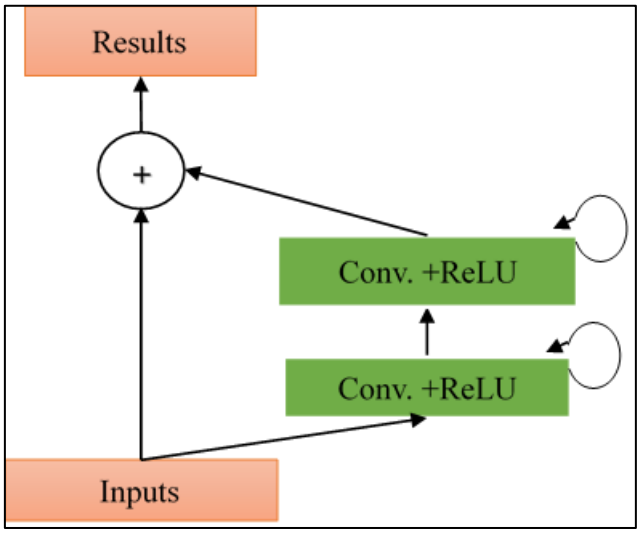


Figure 4. Segmentation Model-Recurrent Residual Convolutional Unit

The very important advantage of RRCUs is that they make it easy to train deeper networks and solve the vanishing gradient issue. Due to the integration of residual connections, they maintain significant lower layer weights integrated with the higher layer produced by recurrence. This fusion is essential for the input to avoid the recurrent convolutional block in the residual path. To enable the segmentation model in detection tasks, the mitotic cell center coordinates are used to construct a Gaussian density surface. At least one mitotic cell can be observed in most input data, resulting in matching Gaussian distributions, since learning the density surface is the final goal, Mean Squared Error (MSE) loss is used for both training and testing rather than Dice Coefficient (DC) loss.

3.2 Classification Model

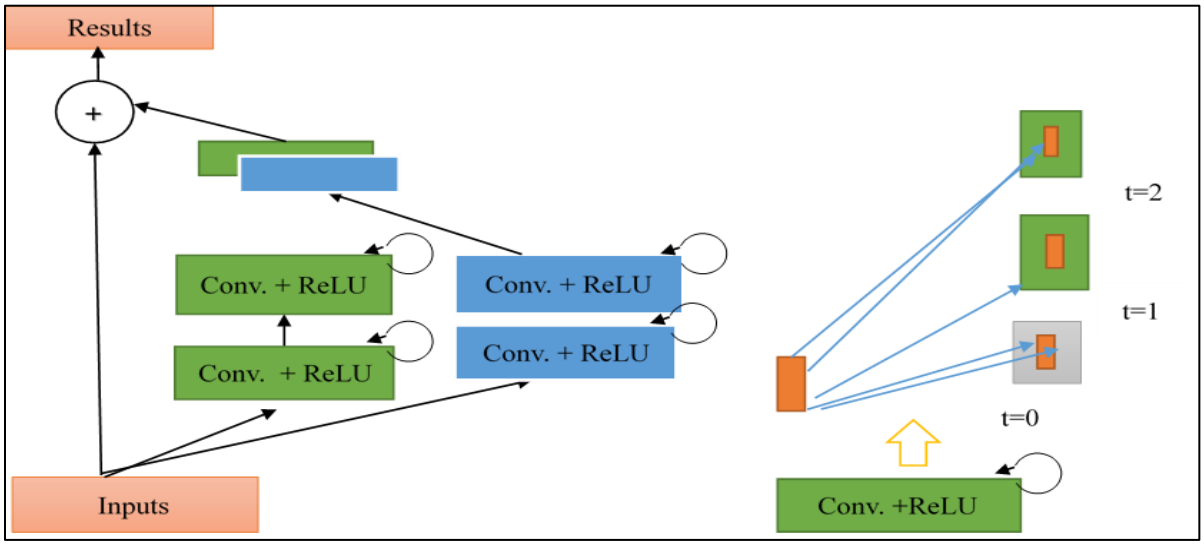


Figure 5. Classification Model-Inception Recurrent Residual Convolutional Neural Networks (IRRCNN)

The IRRCNN architecture consists of both inception recurrent residual units (IRRU) and transition units. A softmax layer at the output, transition blocks, IRRUs, and many convolutional layers make up the architecture. Figure 5 shows a graphic illustration of the IRRU. The IRRU consists of inception units, recurrent convolutional layers, and residual layers. For different kernel sizes, recurrent convolution operations are applied to the inception units. The repeated structures in the convolutional layer are formed by combining the output of the present time step with the output of previous time steps.

The classification model uses the positive and negative mitotic samples that were obtained from the segmentation and detection model's output. The inception model utilizes different dimensional filters, such as 3x3 and 1x1 in size. An inception unit followed by average pooling and then a 1x1 convolutional layer is used. When it comes to computer vision and medical imaging applications, our model performs noticeably better than other deep learning models. In the classification model, the number of network parameters is reduced by using global average pooling in place of fully connected layers. Finally, to calculate confidence probability, a softmax layer is used for separating mitotic and non-mitotic figures.

4. Results and Discussion

We implemented the MPMD method with the TensorFlow deep learning framework on GPU. Evaluation of the system was conducted across two distinct datasets, encompassing the 2012 ICPR MITOSIS dataset and the 2014 MITOSIS-ATYPIA dataset. We used 450 images from ICPR MITOSIS 2012 and 340 images from ATYPIA 2014 with both A-type and H-Type of size 2084x2084. Patches of size 128x128 were extracted from these images and with the help of augmentation technique a greater number of images were generated by flipping, rotating and scaling. The dataset is split into 80% for training and 20% for testing. The methodologies described in this section are evaluated against the latest findings. Most of the existing methodologies solely present results derived from A-type scanners, whereas the proposed approach utilizes training and testing with samples from either H or A type scanner. The regions indicating mitosis are identified with varying confidence scores: 1.0, 0.8, 0.6, 0.2, or 0. The model has been trained specifically on mitosis regions with confidence values equal to or greater than 0.6.

4.1 Segmentation and Detection Results

The Adam optimizer was used with default parameters: $\beta1 = 0.9$, $\beta2 = 0.999$, and $\varepsilon = 10\text{-}8$. The segmentation model was trained using the cross-entropy loss function. The model experienced 300 epochs with a batch size of 16 during the training procedure. Figure 6 shows the segmentation model's accuracy throughout training and validation. At first, the model's training and validation accuracy fluctuated, but eventually, it stabilized and ended up with a validation accuracy of 97.78% DC score. For later use, the weights that showed the best validation performance during training were retained. With the exception of the loss function used, the detection model underwent the same training process. The detection model used the Mean Squared Error (MSE) as its loss function rather than the DC. The DC for two sets X and Y can be mathematically given as follows:

$$Dice\ Coeff. = \frac{2|Y \cap Z|}{|Y| + |z|} \quad (1)$$

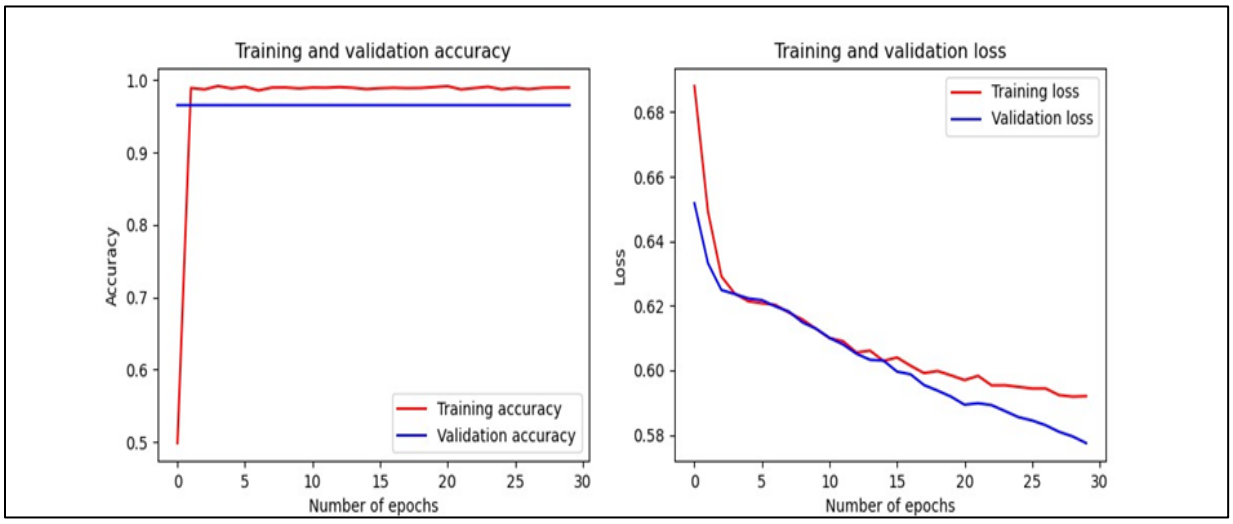


Figure 6. Accuracy Plots for Segmentation Model During Training and Validation

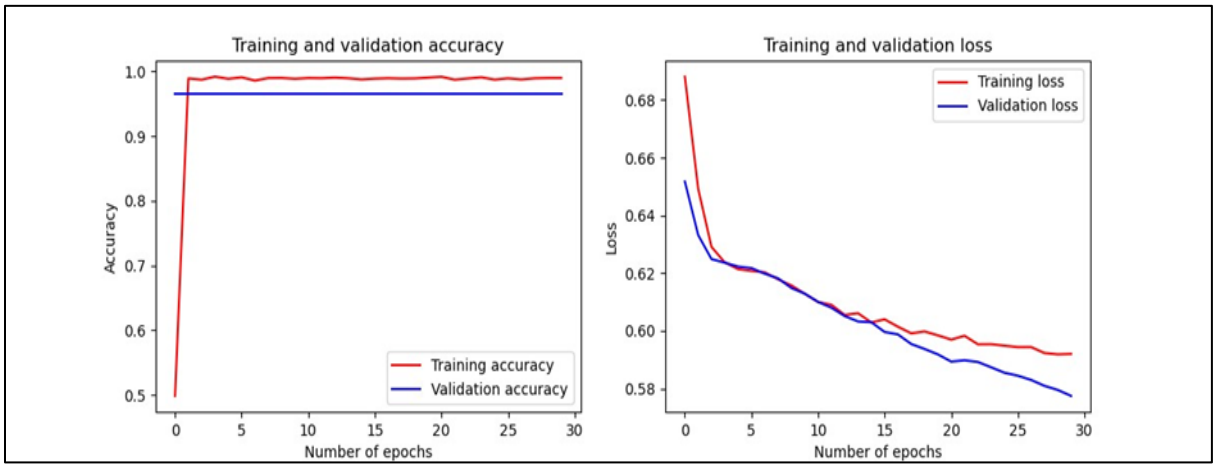


Figure 7. Accuracy Plots During Training and Validation for Classification Model

With a categorical cross-entropy loss function, a momentum of 0.9, and an initial learning rate of 10-2, the segmentation model is trained using the Stochastic Gradient Descent (SGD) method. For every 100 epochs, the learning rate drops by a factor of 10 according to a predetermined schedule. Training of the classification model uses a batch size of 16 and covers 300 epochs. A graphical representation of the training and validation accuracy for the classification model is depicted in figure 7. The figure illustrates a validation accuracy of approximately 98 percent during the training phase of the classification model. Since the model is trained based on patches, the size of the images was reduced the segmentation model focuses on local features and separates the mitotic regions effectively.

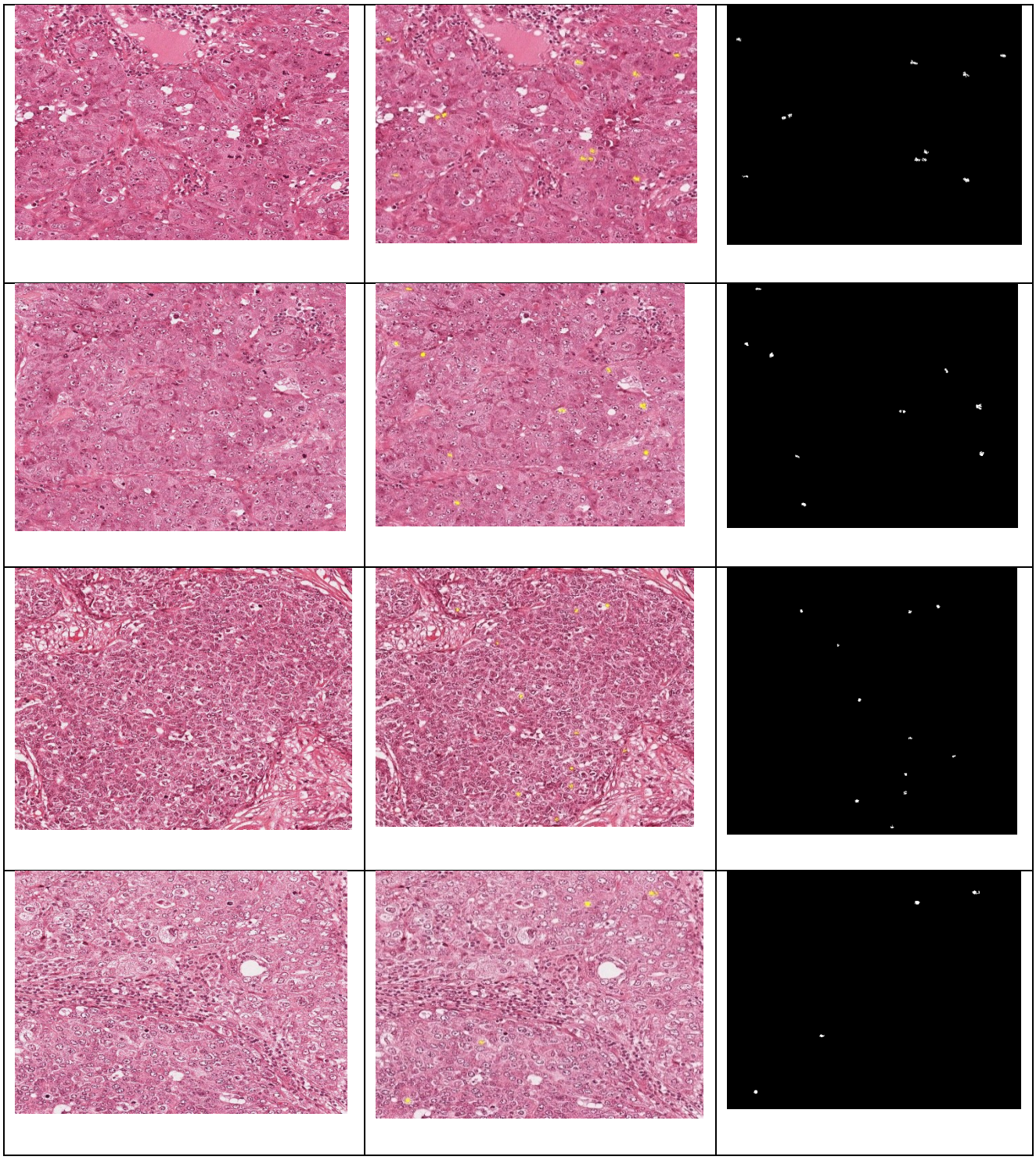


Figure 8. Results Detecting Regions of Interest for Mitosis using the Dataset 2012 MITOSIS (a) Input Images (b) Masked Images (c) Output Images of Detection Model

Visual representations of incoming patches and results from the frameworks for detecting and segmenting have been showcased in Figure 8. Figure 8(a) shows the input images given to the model, 8(b) shows the masked images based on density levels, and 8(c) shows the output images of the detection model. The initial rows depict accurate detection of mitotic events by the model, a typical outcome observed in the proposed model. The following row shows outputs from the region of interest detection, focusing on extreme cases and emphasizing

the need for frameworks that adapt to specific requirements in cases where detection and segmentation are successful. Consequently, a combined mask is generated for blob detection using these outputs.

4.2 Classification Results

The outputs of quality-based frameworks on mitotic activity detecting procedures that are under proposition across the ICPR MITOSIS 2012 dataset have been visually depicted in Figure 9. The top row images of Figure 9 are the results of the classification model for the A-type scanner, and the bottom row images are the results of the classification model for the H-type scanner. In these illustrations, bluish circles signify ground truths, while greenish circles, having associated magnitudes of confidence, represent these terminal predictions from the framework under proposition.

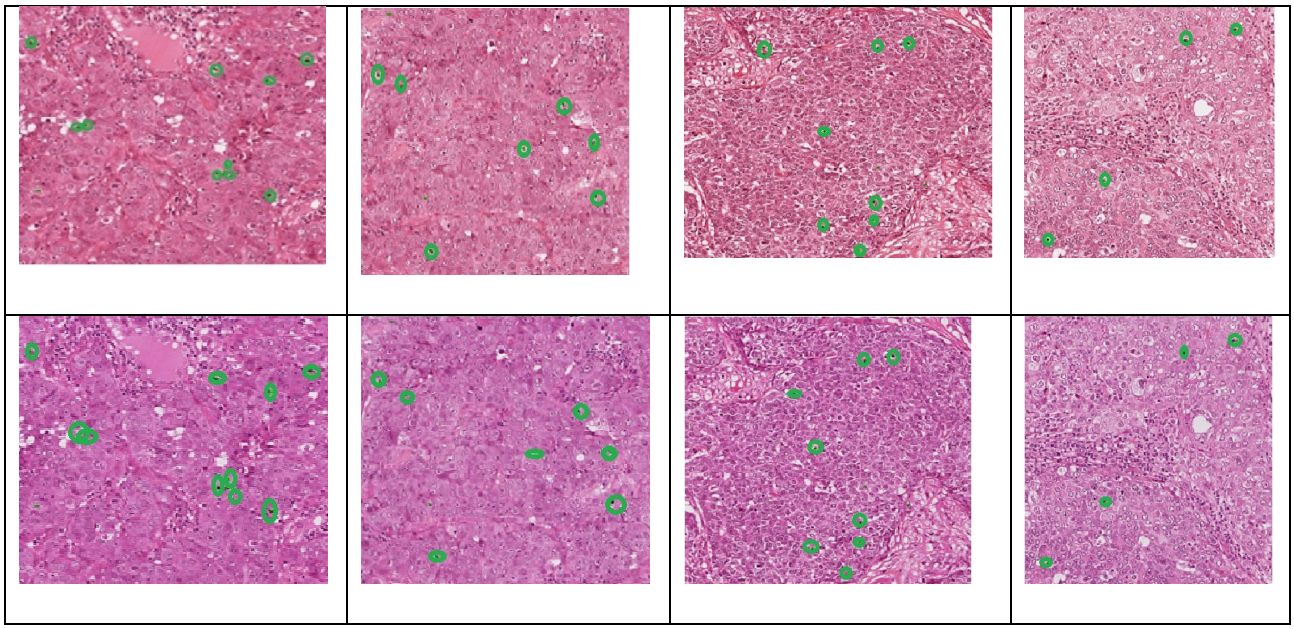
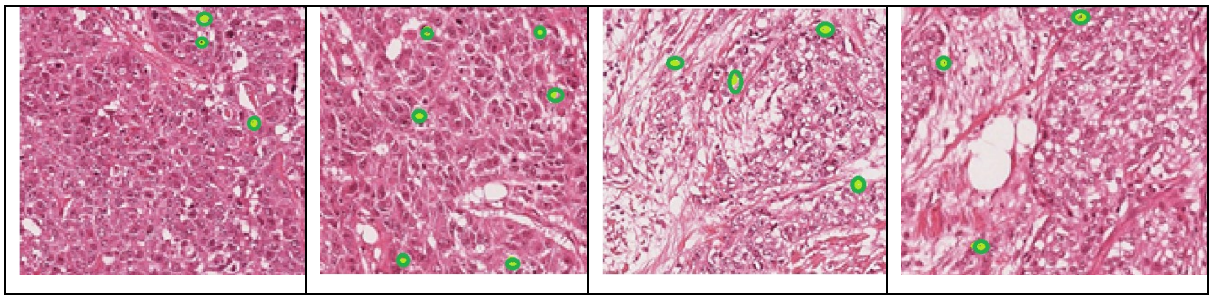


Figure 9. Classification Results of Experiment on Dataset of 2012MITOSIS: Top Row: Results of Type-A Scanners. Bottom Row: Results of Type-H Scanners. Greenish Circles Demonstrate Detection of Mitosis for the Framework

Usually, the overlapping of blue circles and green circles represents the detection of mitosis. Within the markings, the yellow writing indicates the confidence values. The frameworks' false detections are represented by green circles with confidence values. Conversely, false negative events from the model are indicated by blue circles that lack confidence values.



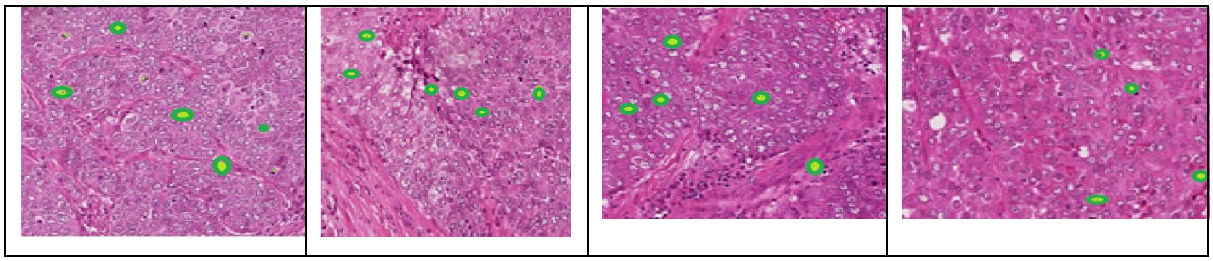


Figure 10. Result of Experiments on Dataset of 2014 MITOSIS Top Row: Result of HPF in Type-A Scanners. Bottom Row: Result of HPF in Type-H Scanners. Greenish and Yellowish Rounds Demonstrate Ground Truths and Detection of Mitosis for the Framework

Detecting mitotic cells in the MITOSIS 2014 dataset poses greater challenges in comparison to the Databases of 2012-MITOSIS because of various factors. Initially, the appearance of the remaining muscle is more complex, and there is more variation in patterns and colors when it comes to mitotic cells, as shown in Figure 10. The images in the top row of Figure 10 are results of the classification model for the MITOSIS 2014 dataset using the A-type scanner, while the bottom row images are results of the classification model for the H-type scanner.

4.3 Performance evaluation

In order to create integrated binary masks of the same size as the HPFs, the system first ingests HPF images, after which mitotic region segmentation and detection techniques are performed successively on non-overlapping patches. The performance of the model to detect mitotic cells is assessed using the following performance metrics precision, recall and F1-score given in equations 2,3,4.

$$Precision = \frac{TP}{TP+FN} \tag{2}$$

$$Recall = \frac{TP}{FN+TP} \tag{3}$$

$$F1 - Score = \frac{2\times preciseness\times Recalls}{(Preciseness+Recalls)} \tag{4}$$

Table 1. Comparisons of MPMD with Similar Different Methods for Mitosis 2012

Citation	Methodology	F1-Score	Recall	Precision
[13]	Cas-NN(FCN+DCNN)	0.788	0.772	0.804
[12]	DRN+FCN+knowledge transfer	0.790	0.802	0.779
[18]	CNN	0.611	0.591	0.752
[19]	CLBP+SVM	0.712	0.73	0.71
[20]	Colour channels+ Laplacian of Gaussian +threshold +morphology +decision tree	0.719	0.75	0.699
[8]	DNN	0.783	0.702	0.887

[21]	Light weight RCNN	0.785	0.792	0.789
[22]	RRF	0.824	0.813	0.834
[14]	DEEPER-MITOSIS(RPN+R-CNN)	0.833	0.813	0.542
[23]	Seg-mitosis (FCN+Gaussian filter+concentric loss function)	0.803	0.763	0.847
[17]	FoCasNet	0.881	0.823	0.856
Proposed	MPMD (R2UNet + IRR-CNN)	0.891	0.893	0.887

Table 1 tabulates these quantity-based results within frameworks on the 2012 MITOSIS dataset, providing a comparison with current approaches. The best results in identifying mitotic activity were reported by competitors in the 2012 ICPR competition. Since then, different techniques for handcrafted features and convolutional neural networks have surfaced. With an F1 score of 0.824, notable segmentation strategies include REMSS (Relativity-Entropies Maximum Scales Spaces) in conjunction with RF (Randomized Forests) classification. Numerous mitosis detection techniques based on convolutional neural networks, including CNNCas, SEGMITOSIS, and DeepMitosis, have been presented. In 2014, a technique that combined the features of CNNs and HCFs was also suggested. In order to detect mitosis and achieve an F1 score of 0.834, DeepMitosis, which was first presented in 2018, uses segmentation, detection, and validation models with an area-based convolutional neural networks, or CNN-R framework. The suggested MPMD, which uses a multi-patch-based methodology, shows a noteworthy F1 score of 0.891 for A-type scanners, which is a 4.6% improvement over the most recent results. MPMD experimental results on the MITOSIS 2012 dataset obtained F1 scores, precision, and recall of 0.891, 0.887, and 0.893, respectively. Furthermore, during testing, MPMD produces an F1 score of 0.840 for H-type scanners; no other published findings are available for comparison. Figure 10 shows the qualitative results of the 2014 MITOSIS-ATYPIA in the situations of H-type and A-type scanners. Greenish circles indicate forecasts, while bluish circles indicate ground truth. The suggested model is able to identify mitotic areas in the majority of cases.

Table 2. Comparisons of MPMD with Similar Different Methods for Mitosis 2014

Citation	Methodology	F1-Score	Recall	Precision
[13]	FCN+DCNN	0.451	0.482	0.417
[14]	DEEPERMITOSIS(RPN+R-CNN)	0.452	0.458	0.447
[23]	Seg-mitosis (FCN + Gaussian filter+ concentric loss function)	0668	0.786	0.496
[21]	Light Weight RCNN	0.667	0.671	0.663
proposed	MPMD (R2UNet+IRR-CNN)	0.771	0.799	0.753

Apart from these, samples in the MITOSIS-2014 datasets have been narrowly annotated through unitary point annotations, where a unitary pixel represents the full region of mitosis. Consequently, the magnitudes of F1 in these experiments indicate reduced levels compared to those obtained through the 2012-MITOSIS datasets. However, the examination of the

performance in the proposition of MPMD, along with different present methodologies, is presented in Table 2. MPMD achieves an F1-score of 0.771, precision of 0.753, and recall of 0.799 in the case of multiple patches methodologies based on references. LRCNN, or Lightweight CNN, introduced in 2018, reported F1-scores of 0.427 and 0.658 for outward and inward groups, respectively. DeepMitosis has notably not performed well in the 2014 MITOSIS dataset. Although it doesn't work as effectively as two other methods on these datasets, it still offers many advantages over existing approaches. Figure 9 shows qualitative outputs for both H and A types of scanning, demonstrating highly accurate detection of mitotic cells.

5. Conclusion

This paper presents a deep learning-based multi-patch approach for mitotic identification through detection, classification, and segmentation. While the classification model divides regions into mitotic and non-mitotic groups, the segmentation and detection models are used to select regions of interest. To improve overall testing accuracy, we also provide a novel confidence analysis approach and an integrated multi-patch reference method. Popular publicly available datasets, such as MITOSIS 2012 and MITOSIS 2014, with the Aperio (A) and Himamasthu-Tx (H) scanners were used to evaluate our suggested mitosis detection algorithm. When compared to recently published data, experimental results show higher performance. In summary, the effectiveness of the mitosis detection system is not solely reliant on robust training methodologies but also hinges on the efficiency of the testing strategy to enhance overall accuracy in identifying mitotic cells. MPMD is designed to tackle these issues by analyzing multiple neighboring patches during testing. Though the proposed method exhibits improved performance compared to state-of-the-art methods, there is room to improve the performance of the model when applied to unlabeled datasets like TUPAC 2016 and real-time clinical datasets.

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