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A Survey for Cervical Cytopathology Image Analysis Using Deep Learning

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ABSTRACT Cervical cancer is one of the most common and deadliest cancers among women. Despite that, this cancer is entirely treatable if it is detected at a precancerous stage. Pap smear test is the most extensively performed screening method for early detection of cervical cancer. However, this hand-operated screening approach suffers from a high false-positive result because of human errors. To improve the accuracy and manual screening practice, computer-aided diagnosis methods based on deep learning is developed widely to segment and classify the cervical cytology images automatically. In this survey, we provide a comprehensive study of the state of the art approaches based on deep learning for the analysis of cervical cytology images. Firstly, we introduce deep learning and its simplified architectures that have been used in this field. Secondly, we discuss the publicly available cervical cytopathology datasets and evaluation metrics for segmentation and classification tasks. Then, a thorough review of the recent development of deep learning for the segmentation and classification of cervical cytology images is presented. Finally, we investigate the existing methodology along with the most suitable techniques for the analysis of pap smear cells.

INDEX TERMS Cervical cancer, cytopathology, convolutional neural networks, deep learning, segmentation, classification, pap smear.

I. INTRODUCTION

Cancer is the deadliest disease of independent growth of body cells, which is accountable for around 9.6 million deaths each year [1]. This statistic fluctuates enormously among developing and developed countries. Approximately 70% of deaths from cancer occur in low- and middle-income countries [2]. As reported in the most recent world cancer statistics, cervical cancer is the fourth most common cancer (estimated 570000 new cases each year) worldwide and the second most common cancer in women, who are living in developing and

low-income countries with an annual death of 311000 women approximately, where 85% of these deaths are occurring in low- and middle-income countries [3], [4]. So, women with ages between 30 to 49, who are living in developing and least developed countries are at the highest risk for cervical cancer because of the lack of awareness and limited access to health services [5]. Research shows that human papillomavirus (HPV) is the main cause of cervical cancer [6].

HPV is the most prevalent sexually transmitted viral infection worldwide, and the most sexually active individuals of both sexes are usually affected with HPV in their lifetime [7]. There are around 200 types of HPV that have been identified so far. Among them, 13 are high-risk types, and HPV type

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16 and 18 account for roughly 70% of all cervical cancer [8], [9]. HPV type 16 has been detected in about 24% of women and type 18 has been detected in about 9% [8], [10], [11]. Pregnancy and first intercourse at an early age, having sex with multiple partners, weak immune system, smoking, use of oral contraceptives and improper menstrual hygiene are the common risk factors that are linked with cervical cancer. The common symptoms associated with cervical cancer include abnormal vaginal bleeding, vaginal discharge, and moderate pain during sexual intercourse [12]. Cervical cancer is treatable if it is detected timely and treated properly [13].

When the cervical tissue cells begin to grow and replicate abnormally, these infected cells are called cervical intraepithelial neoplasia (CIN). CIN is classified into low-grade CIN and high-grade CIN based on the cell intensity [14]. The most common ways of diagnosis to detect cervical malignancy is cervical cytopathology (pap smear or liquid-based cytology) because of its cost-effectiveness [13], [15]. These tests consist of a sample of cells that are collected from the patient's uterine cervix and analyzing the changes under a microscope by expert cytologists to check the HPV effects. However, manual screening is difficult, tedious, time consuming, expensive and subjected to errors because each slide contains around three million cells with different orientation and overlapping [16].

A. MOTIVATION OF COMPUTER AIDED DIAGNOSIS

For the past 60 years, the pap smear test has a significant effect of lowering the death rate due to cervical cancer [17]. Traditionally, the test is performed by collecting cells from the squamocolumnar terminal of the cervix by using brush or spatula and then smeared into glass slides [18], [19]. Next, the glass slides are examined under a light microscope by cytotechnologists to check the malignancy of the cell, which allows early and effective treatment. The screening processes usually take 5–10 minutes based on the difficulty of cell orientation. A cytotechnologist cannot analyze more than 70 samples a day [20]. This process also needs full attention all the time in order not to miss any cancerous cells. So, it is always a major concern to get an expert cytotechnologist to screen and diagnose the pap slides, which leads us to develop an automated computerized system that can analyze the pap slides efficiently and accurately [21]. Besides, to handle a large scale of image data sets, rigorous measurements of image features for clinical follow-up, comparative study, and personalized medicine, a computerized system is essential.

In comparison with manual assessment, digital pathology and microscope play a significant role in disease diagnosis by providing information for computer-aided diagnosis (CAD). Over the past few decades, there has been extensive research on the development of CAD systems, which can help doctors in tracking cervical cancer. This system can automatically detect and classify the abnormal cell form the cytology specimen [22], [23]. This automated system traditionally consists of three steps: Cell segmentation (cytoplasm and nuclei), feature extraction, and classification.

When training of data became possible at the end of the 1990s, an automated computer-assisted system began to develop. Active shape models, handcrafted feature extraction methods, pattern recognition, statistical classifiers started to grow very popular for the development of the new system. Later, the computer learned features based on the artificial neural network became very successful [24].

In a traditional CAD system, firstly, some preprocessing work is done by filtering methods to improve the image quality. Then, cell nuclei are extracted through segmentation method (k -means, clustering, super pixel, etc.) and post-processing work is done to correct the segmented nucleus. Next, features (morphological, color metric, texture) are extracted from each nucleus, and feature selection is applied to select the most discriminant feature. Finally, a classifier is designed to classify the cell [25].

The main limitation of the above method is that the features extracted for the classification are usually handcrafted that cannot guarantee the optimality of the classification stage. However, the deep learning approach reviewed in this paper is a kind of learning method that can directly process raw data (e.g., RGB images) and offers automated learning of features based on specific objective function such as detection, segmentation and classification [26]. Nowadays, deep learning techniques have significant contributions in the field of artificial intelligence and successfully applied to computer vision, natural language processing, image understanding, medical imaging, and computational biology [27], [28].

B. DEEP LEARNING IN CERVICAL CYTOPATHOLOGY IMAGE ANALYSIS

In this subsection, we will give a brief review about the importance of deep learning among other machine learning techniques and its development trend in the domain of cervical cancer.

Machine learning under a broad category of artificial intelligence (AI) is the science to develop algorithms that can autonomously learn from data and make predictions without being explicitly programmed. It is a tool that can be used to enhance human capabilities to solve problems. The learning style can be supervised, unsupervised, and semi-supervised. Despite the various learning styles, all combinations of machine learning algorithms consist of representation, evaluation, and optimization. Representation is a set of classifiers or languages like support vector machine, K-nearest neighbor, decision tree and a neural network that a computer understands. The evaluation function is needed to distinguish good classifiers from the poor one through finding accuracy, precision, and recall. Optimization is to find the highest accurate representation through evaluation [29], [30].

The performance of machine learning heavily rely on data representations (or features). In order to get a good illustration of data, a significant effort in data preprocessing and transformation is needed, which is labor-intensive and highlights the incompetence of automatic learning. In order to get an optimized learning process, a deep

learning (DL) approach can extract hierarchical features without human cooperation. Over the past decades, DL has made significant advantages over other machine learning algorithms by achieving state of the art results on challenging computer vision tasks such as image classification, segmentation, object recognition and face recognition [31], [32]. This model requires a labeled training set, from which it will learn the features. A critical thing about DL is that the features are not human-understandable though it affords more accurate outcomes [33]. Another compromise is that it typically requires a considerable number of labeled data sets compared with other machine learning approaches [34].

1) DEEP LEARNING IN CERVICAL CYTOPATHOLOGY

The acceptance of DL procedures in the medical image analysis is now the most repeatedly designed and successful type of machine learning algorithms, and analysis of cervical cytopathology images are no exclusion. A prevalent deep architecture in this field is convolutional neural networks (CNNs), which have obtained a great success in cell detection, segmentation, classification and extraction of the region of interest (ROIs) [27]. In supervised learning, the CNN model is determined to generate hierarchical data features from a given labeled image dataset to accurately classify the cells into normal and abnormal [35]. However, it demands a large number of annotated data, which is not apparent in the medical domain. On the other hand, unsupervised learning through a neural network for feature learning has produced an encouraging performance for the study of microscopic images [36], [37]. Autoencoder is one top-rated unsupervised neural network. Fig. 1 reports the popularity of deep learning overtime for the analysis of cervical cytology image.

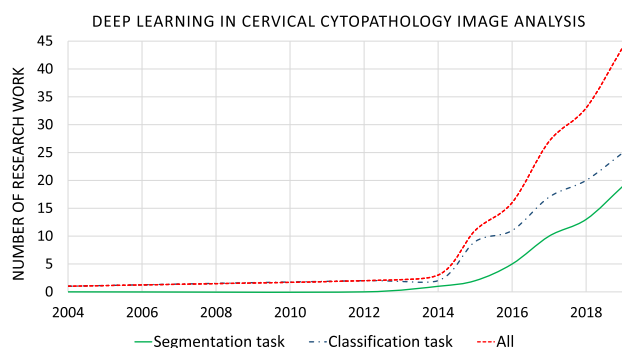


FIGURE 1. Development trend for the segmentation and classification of cervical cytopathology image analysis in deep learning.

2) DEEP LEARNING IN SEGMENTATION TASK

In medical image analysis segmentation is one of the most effective and extensive research fields. The main goal of segmentation is to partition the image into multiple regions to quickly analyze the cell [38]. A manual autopsy is challenging because each slide contains up to 300000 cells with different orientation and overlapping. Moreover, it also contains mucus, bacteria, blood, inflammation, and dust

particles, which prompt for automatic segmentation [16]. Accurate segmentation of nuclei and cytoplasm is vital since the nucleus carries reliable information for the detection of cancer. In the medical domain, automatic segmentation saves the life of a patient by providing fast, reliable, and accurate diagnosis of diseases. Because of the advantages, many researchers are performing segmentation task for cervical cancer using deep learning. Fig. 1 shows the increasing trend of segmentation of cervical cancer in deep learning.

Numerous works have been performed on automatic segmentation of cytoplasm and nucleus of a cervical cell. In this study, we briefly describe all those segmentation methods in Sec. IV. From the papers we have studied so far gives a general pipeline for cervical cancer image segmentation, which is shown in Fig. 2. This workflow includes image acquisition, pre-processing, deep learning methods, and application. From the general pipeline in Fig. 2, we can find that:

- The first step of segmentation is image acquisition. Most of the research work performed by collecting the images from some accessible public databases identified as Helev University database and ISBI challenge database. Herlev database contains single-cell images with ground truth. In the ISBI challenge database, there are images with overlapping cells. Few researchers used private databases collected from different hospitals or research institutes.
- The 2nd step of segmentation is image pre-processing. Here, image contrast enhancement, noise extraction, augmentation, and flipping operations are usually performed. Image enhancement may occur in noisy, blurred, or low contrast images. These challenges are not prevalent in laboratory pap smear imaging. Moreover, the pre-processing task is not apparent in some work where a hybrid segmentation algorithm is implemented.
- The 3rd step is the use of deep learning techniques for feature representation. There are three approaches in this section, which are supervised, unsupervised, and hybrid feature learning. In most of the reviewed articles, we have observed to use of supervised learning methods, where CNN's (VGG, ResNet, U-net) or custom-made CNNs are the most popular deep architecture. Patch-based CNN, super pixel-wise CNN, structured regression-based CNN, multiscale CNN and instant relation network are also employed. Under hybrid feature learning, one machine learning algorithm usually coupled with CNNs. For instance, fuzzy c means clustering is linked with backpropagation neural network, CNN is connected with the graph-based method, mask regional CNN is combined with fully connected conditional random field and so on. However, Unsupervised feature learning is not common in cervical cytopathology image analysis.
- The final step is the segmentation, where accurate nucleus segmentation is the primary goal because the nucleus carries vital information for the diagnosis of cancer. In some papers, cytoplasm, and background are

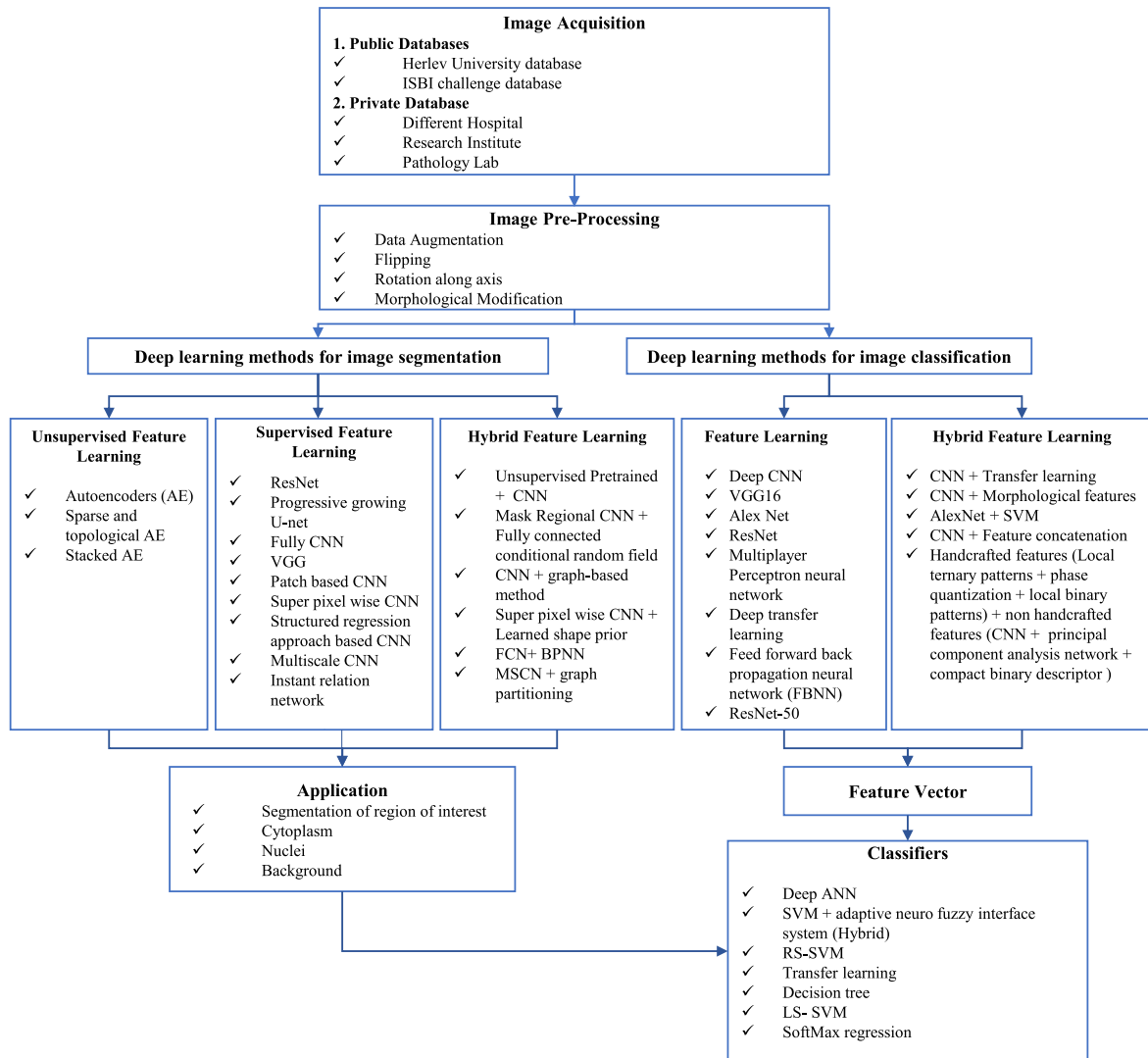


FIGURE 2. General deep learning algorithm for automatic cervical cytopathology image analysis. It includes (1) Image acquisition, (2) Image preprocessing, (3) Feature representation, (4) Application.

also segmented. It is observed that minimal effort has been made so far for the segmentation of overlapping cells. Most of the segmentation works are performed based on single-cell.

3) DEEP LEARNING IN CLASSIFICATION TASK

Image classification is a principal area of research in medical image analysis. In this area, a deep learning-based method made a tremendous contribution by providing state-of-the-art accuracies [39]. Image classification is a process in computer vision that takes multiple images as inputs and then classifies according to its visual content.

Generally, to train a neural network from scratch requires a considerable amount of data and computing power, which also result in longer training times. The solution to all these problems is transfer learning, which uses the pre-trained model from one task to solve a different task [40]. In medical imaging transfer learning benefits significantly,

since to arrange good quality imaging datasets is complicated, and the dataset is generally small (of an order of $10^2 - 10^4$).

Two popular techniques are identified for transfer learning. One is by using a pre-trained network as a feature representator, and two is by fine-tuning the pre-trained network on image data. The increasing trend of cervical cancer cell classification using deep learning, is displayed in Fig. 1, which indicates its popularity.

Many authors use different deep learning algorithms for the classification of cervical cells into normal, abnormal, and pre-cancerous cells. In Sec. V, we briefly describe all those classification methods. The general pipeline for the classification of cervical cancer exhibits in Fig. 2 after having prior knowledge and understanding of the papers we have studied.

- The stereotype image classification algorithm starts with image acquisition, then pre-processing of the data.

The first two steps are similar to the segmentation task, which we have already discussed in the previous subsection.

- The following stage is the feature extraction, which is the most important stage to get better classification accuracy. Most of the paper we studied are using supervised learning. VGGNet, pre-trained CNN using AlexNet, ResNet, multilayer perceptron neural network (MLPNN) are found to be the most commonly used feature extractor in the literature. Some authors use hybrid feature learning techniques, where they combine different machine learning algorithms with deep learning.
- Finally, the feature vectors are supplied to the classifiers. SVM, decision tree, deep ANN, fully connected layers, transfer learning, softMax regression are the leading classifiers in this stage. In some articles, segmentation tasks perform first, then the features of the cytoplasm and nucleus are extracted to perform the classification task.

C. MOTIVATION OF OUR REVIEW PAPER

The motivation of this article is to give a comprehensive overview of deep learning in cervical cytopathology image analysis as well as popular deep learning techniques, and their architectures with overview tables and figures are also presented for precise understanding. Besides, this paper also discusses potential techniques for the analysis of cervical cells in deep learning.

Cytology and histology both are the examinations of cells at a microscopic level. Histology examination is usually performed by investigating the sample of whole tissue, whereas cytology is the examination of cell samples [41]–[43]. The preparation of histology slides involves lots of stages compared to the preparation of cytology slides, which makes it costlier. Histology slide preparation involves fixing, preprocessing, embedding, sectioning, and staining. However, preparation of cytology slides does not involve any stages [44]. Cytology examination gives the best cellular details, which is an essential factor for the analysis of cervical cells. For cervical cancer screening, a cytology-based examination is preferred over histology and is performed traditionally [45].

In our study, we have obtained around ten survey papers related to machine learning in medical image analysis. Among those ten studies, one survey is based on an artificial neural network in cytopathology [46]. Other two documents focus on the detection of microscopic image analysis [47], [48], two papers concentrate on deep learning techniques in medical image analysis [24], [49], one gives priority on deep learning in microscopic image analysis [50]. However, four survey papers only concentrate on cervical cancer, and out of the four, one article directs on the classification tasks based on the neural network [51]. Additional two focus on the segmentation tasks for cervical cancer [52], [53], and

the final one presents a survey on automated machine learning techniques for cervical cancer image analysis [54].

Pouliakis *et al.* [46] publishes a research survey in 2016, focusing on the importance of employing ANN in cytopathology. He explored that ANN is a powerful field for the application of cervical cytopathology image. However, he explored all the related field in cytopathology but gave less priority of cervical cytology images. He summarized 31 papers in the summary table but no paper related to cervical cancer and deep learning.

Xing and Yang [47] in 2016 provides a comprehensive summary of the new state of the art cell segmentation approaches on different microscopic images. In that survey, we found about nine papers related to cervical cell segmentation, and among them, two articles are based on the neural network. He publishes another survey paper in 2017 by reviewing some popular deep learning methods in various tasks such as segmentation, detection, and classification in the microscopic image analysis [50]. This paper also explained the architecture and working principles of CNN, RNN, FCN, stacked autoencoders, deep belief networks. We detect over 65 summarized paper based on microscopic images, and among them, only one paper is related to cervical cancer.

Carneiro *et al.* [48] in 2017 summarizes current deep learning techniques in various tasks like segmentation, detection, and classification in different imaging modalities. In the summarizing table, we found around 28 papers on various imaging modalities. Among them, only one paper is on cervical cancer.

Litjens *et al.* [24] provides a very comprehensive review on deep learning in medical image analysis, and they summarized over 300 papers based on deep learning in the year of 2017. Among them, only three papers are on our topic.

Hu *et al.* [49], in 2018, give a review concentrating on deep learning in image-based cancer detection and diagnosis. In the study, he has explained some leading deep learning architectures (CNN, fully convolutional networks, autoencoders, and deep belief networks) for the detection of cancer and its diagnosis. Later, they provided a summary survey on studies exploiting deep learning for the determination of various types of cancer such as breast, lung, skin, prostate, brain, colonial, cervical, liver, and bladder. In the summary survey, we obtain three papers based on the topic of our interest among 76 documents that they have reviewed.

Devi *et al.* [51] in 2016 summarize 30 papers based on an artificial neural network for the classification task of cervical cancer. Among them, only one article is based on deep learning. Besides, a detailed description of ANN, Multi-layer perceptron, BPNN, Gene expression, Radial basis function network, CNN, feed-forward neural network, knowledge-based network, Modular neural network is provided. In the same year, she publishes another review article focusing on cervical cancer image classification algorithm based on SVM and fuzzy-based techniques [52]. This article does not include any paper centering on the neural network or deep learning among the 32 papers that they have summarized.

Sarwar *et al.* [53], in 2019, exhibits a very new survey article based on the segmentation of cervical cells. This review consists of a total of 78 papers in a period stats from 1997 to 2018. In this study mostly cover classical machine learning approaches for the segmentation of cervical cells. Among those 78 studies, mainly two papers employ deep learning techniques for cell segmentation.

William *et al.* [54] presents an overview of the state of the art in notable recent publications focusing on automated detection of cervical cancer from pap smear images in 2018. They reviewed 30 journal papers collected through four scientific databases, but among them, only three articles are on deep learning in cervical cancer.

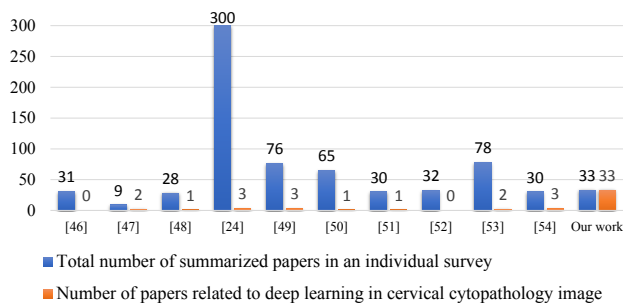


FIGURE 3. Comparative study among recent survey papers. Number of summarized papers found in the existing literature review in comparison to their contribution to deep learning in cervical cytopathology image analysis.

By studying all the recent survey papers, we have identified that there is very little or no contribution at all, especially in the field of deep learning in cervical cytopathology image analysis. For a clear overview, we made a histogram diagram (Fig. 3) for a comparison purpose to show each of the present survey papers and their contribution to cervical cancer with our proposed studies.

D. STRUCTURE OF THIS REVIEW

The motivation of this review is to look extensively and specifically at the new state of the arts on the automated cervical cytopathology cell segmentation and classification. To prepare this comprehensive review, we looked for databases including PubMed, arXiv, Google Scholar, IEEE, ACM, Springer and Elsevier. Additionally, proceedings of the international conference on SPIE, ISBI, MBC and international conference on medical imaging with deep learning. We also checked the references in all the selected papers. We excluded papers that are not based on deep learning or cytopathology images. We considered the most important publications in the case of overlapping one. We set the cut off time of the search is February 10th, 2020, since new publications are coming out every month. We have considered research motivation, contribution, dataset, workflow, and results, while summarizing one paper. Considering the convenience of future researchers, this paper includes several

tables and a flowchart for quick access to the topic of their interest.

The structure of this review is as follows: we begin by introducing the deep convolutional neural networks and their popular architectures that have been used for cervical cancer cell analysis in Sec. II. Sec. III includes an overview of publicly available datasets and evaluation methods. It is followed by a comprehensive review of segmentation and classification work of cervical cytology image based on deep learning in Sec. IV and Sec. V, respectively. Then, a thorough methodology analysis of suitable segmentation and classification techniques and future potential methods are discussed in Sec. VI. Sec. VII summarizes the review and discusses prospective applications.

II. DEEP CONVOLUTIONAL NEURAL NETWORKS

After thorough studies, we have observed that CNN models are the most commonly used supervised machine learning models for the analysis of cervical cancer. CNN's are a distinct kind of supervised multilayer perceptron that requires minimal preprocessing to detect visual patterns. To obtain satisfying accuracies, CNN's demand a considerable amount of data. However, accumulating a well-annotated high-grade quality dataset is very challenging and costly, which leads to a larger but noisy dataset that is easy to obtain. Studies have shown that CNN's are robust to the noise until a certain label. Increasing noise reduces the batch size. Hence, increasing the batch size and lessening the learning rate can elevate the performance [55]. Besides, CNN's are invariant to translation, rotation, or size [56], [57]. Therefore, it can accurately analyze the objects even if it is placed in a different orientation. The architecture of CNN is composed of convolution, pooling, and fully connected layers. Convolution and pooling layers, mainly extract features from the image, whereas fully connected layers classify by mapping the extracted features [58].

Convolution layer is the primary building block of CNN architecture. It takes an image as input and extracts high-level features. The first layer usually extracts low-level features, and consequently, as the layer gets deep, it extracts high-level features and gives the network a good understanding of the image [59]. Then, there is a pooling layer after the convolution layer to reduce the size of the convoluted features. Max pooling and average pooling are the two popular types of the pooling operation. Max pooling extracts the maximum value, and average pooling returns the average of all values from the portion of the image covered by the kernel [60]. A fully connected layer serves the same principle as a multilayer perceptron (MLP). It connects every neuron of each layer to every neuron of another layer. The feature map goes through a fully connected layer to classify the image.

A. EVOLUTION OF CONVOLUTIONAL NEURAL NETWORKS

In the mid of the 20th century, Hubel and Wiesel [61] first proposed the concepts of "receptive field" in their experiments on cat's visual cortex cells, which later introduced

into the research work of CNNs. In the 1980s, the first artificial neural network called “neocognitron” is proposed by Fukushima and Miyake [62] to recognize the handwritten number and other pattern recognition tasks based on the receptive field, which served as a motivation for CNN’s [27]. Later, the researchers focused on studying computerized features using an MLP rather than hand-crafted features to train the network with back-propagation (BP) algorithm [63]. Next, in 1990, Y. LeCun stated and explained a back-propagation algorithm for the recognition of handwritten digits [64]. His advised CNN architecture is known as “LeNet-5” [65], which performs better than any other algorithm at that time. However, it encounters some problems such as local optimum, vanishing gradient, and overfitting with the increasing number of network layers. Hinton in 2006 uncovered that the neural network has excellent feature learning ability for image analysis, and the drawbacks can be alleviated by normalized initialization [66]–[69]. Since then, deep learning gained popularity.

With an ever-increasing number of image databases and computing power, it makes it easier to train deep learning for image classification and recognition problems. Starts from 2010, there is a global contest for object detection and classification known as the ImageNet Large Scale Visual Classification Challenge (ILSVRC). From 2012 till now, the algorithm based on CNN won the prestigious international contest, where tech giants like Google and Microsoft take part. Krizhevsky *et al.* won the ILSVRC-2012 competition by presenting a CNN model called AlexNet that reach a top 5 classification error of 15.31%. For comparison, the 2nd best entry that does not use CNN got a classification error of 26.1% [70], [71].

Following the path of AlexNet [70] later ZFNet [72], VGGNet [73], GoogLeNet [74], Inception-v2 [75], PReLU [76], Inception-v3 [75], ResNet [77], ResNeXt [78], DenseNet [79] and SENet [80] are proposed mostly by using ImageNet dataset or CIFAR-10 and showed the leading performance results in the top-5 (test) error rate starting from 15.31% to 2.251% [69].

B. POPULAR CNN ARCHITECTURE THAT ARE USED IN CERVICAL CYTOPATHOLOGY IMAGE ANALYSIS

AlexNet, VGG-16, and ResNet are found to be the most frequently used network architecture for the segmentation and classification tasks for cervical cancer. The work of [81] finds that ResNet is the preferable network for the classification problem compared with the VGG network. In this subsection, we will give a brief description of AlexNet, VGGNet, ResNet and Inception Net with their network architecture.

1) AlexNet

AlexNet is the first neural network to win the 2012 ILSVRC competition. The significance of AlexNet is that they use the Rectified Linear Unit (ReLU) as an activation function instead of the sigmoid or hyperbolic tangent function. Overlapping pooling, optimization for multiple GPU’s to speeding

up network training also introduced here. They solved the overfitting problem by data augmentation and dropout. The network architecture consists of eight hidden weight layers, five convolution layers, and three fully-connected layers. This network consists of 60 million parameters [70]. The architecture is given in Fig. 4-(a).

2) VGGNet

Simonyan and Zisserman from the University of Oxford proposed a CNN model called VGGNet that won the 2014 ILSVRC competition. The main idea of VGGNet is a deeper network with a smaller filter, and there can be 16-19 layers. The input of VGG is a fixed size of 224×224 RGB image. They use the smallest possible convolutional filters (3×3) with the stride of 1 pixel to preserve the spatial resolution after convolution. There is also a 1×1 convolution filter, which is a linear transformation of input followed by activation function ReLU. After convolution, pooling is performed by five max-pooling layers with a window size of 2×2 and stride 2. At the end, it has three fully connected layers. The first two have 4096 channels, and the 3rd has 1000 channels, 1 for each class. The last and final layer is a SoftMax layer.

The main discovery of the VGGNet is the application of 3×3 small convolution filters. The stack of three 3×3 convolutions layers has the same receptive field as one 7×7 Conv layer, which gives 55% less parameters. This small size of the receptive field allows VGG to have more weight layers, which results to improve performance. VGG-16 and VGG-19 comprise of 138 and 144 millions of parameters [73]. The network architecture is given in Fig. 4-(b).

3) ResNet

In the previous description, we have mentioned that AlexNet has eight weight layers, and VGG has 16 or 19 weight layers. So, increasing the depth or weight of a neural network can give better performance results. However, He *et al.* observed that with the increasing number of network depth accuracy gets saturated and then degrades rapidly [77]. They trained the CIFAR-10 data with 20 layers and 56 layers and observed that deeper network has higher training error and thus test error.

To solve the above problem, they introduced a novel approach pathway called skip connection (Identity mapping) so that network depth can increase for improved performance. In this way, there can be up to 1000 weight layers in ResNet [77].

If a convolution layer takes X (feature map) as input and residual function is denoted as $F(x)$. Then, input of the first layer (x) is copied to the output layer, $H(x)$. then, $H(x) = F(x) + X$ or $F(x) = H(x) - X$. Fig. 4-(d) shows the structure of residual learning block. So, the primary purpose of the residual network is that a deeper network can be made form a shallow network by copying weight layers in the shallow network and setting other layers in the deeper network to be

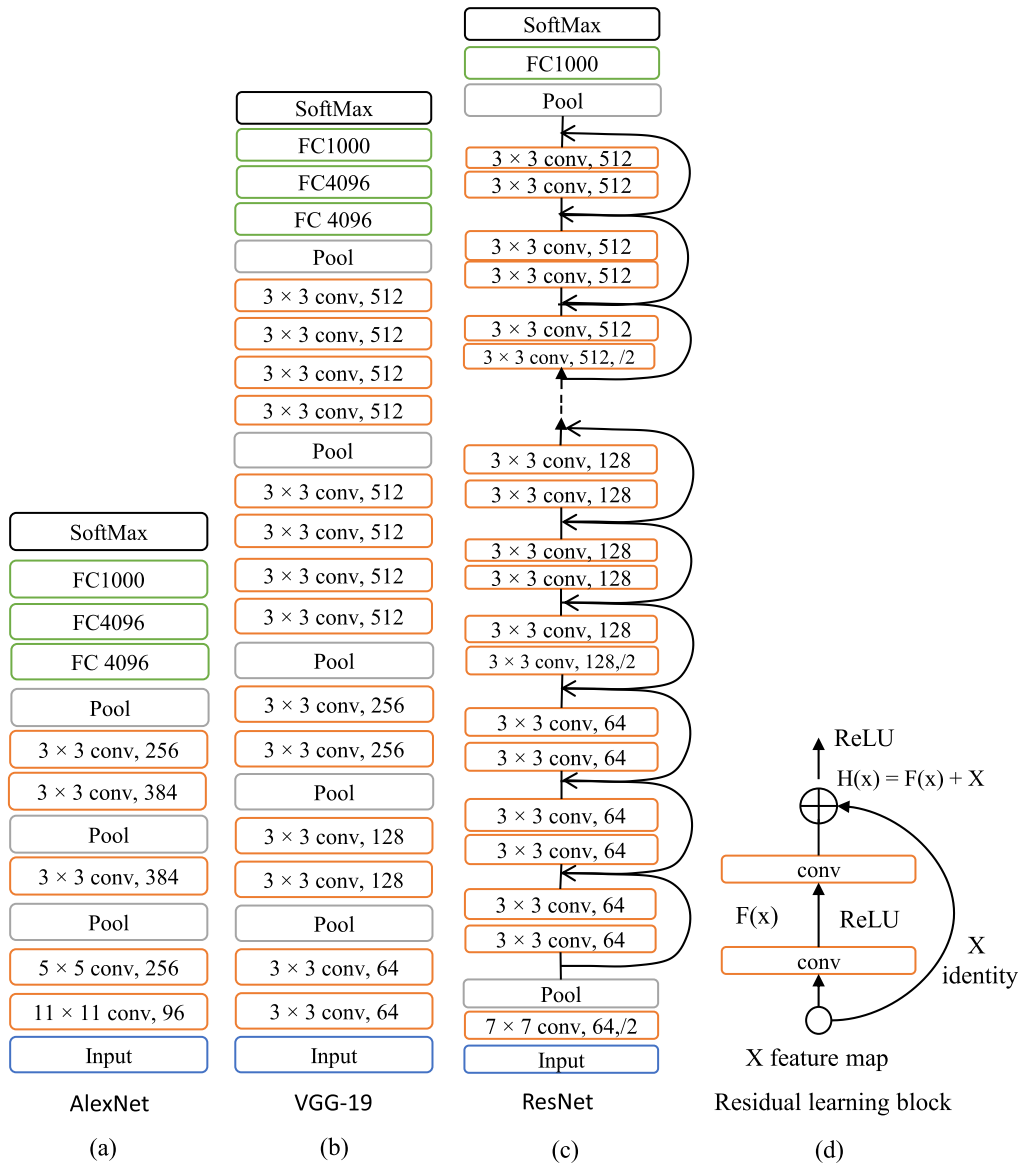


FIGURE 4. Network architectures of three commonly used CNNs. (a) is AlexNet, (b) is VGGNet, (c) is ResNet and (d) is the structure of a residual learning block.

identity mapping. ResNet won the 2015 image classification competition. The network architecture is given in Fig. 4-(c).

4) GoogLeNet/ INCEPTION Version 1 to 3

It is evident from the previous observations that Alexnet has 60 million, VGG-16 has 138 million, and ResNet-50 has 25.6 million parameters. However, GoogLeNet / Inception-v1 has only 7 million parameters. Lower parameters mean less computational cost. The inception model can describe the input data very thoroughly by expanding the depth and width of the model. The module has been regularly modernized since it first states in the 2014 ILSVRC image classification competition. Inception- v1 first introduces 1 × 1 convolutional kernel, which can reduce the network parameters. It also

employs kernel of 1 × 1, 3 × 3, and 5 × 5 that considerably improve the efficiency of the classification problem [69], [74]. Fig. 5 exhibits the network architecture and its block.

In the version 2 network, batch normalization is added, and two 3 × 3 convolutional kernels are employed instead of 5 × 5 to increase the network depth [82].

In version 3, different shapes of convolutions are introduced. In this module, 5 × 5 convolution is replaced by two 3 × 3. Moreover, 5 × 5 convolution is followed by 1 × 7 and 7 × 1, and 3 × 3 substitutes by 1 × 3 and 3 × 1 convolutions to make each of the block more deeper [75]. In inception- V4 residual learning block ideas has incorporated [83].

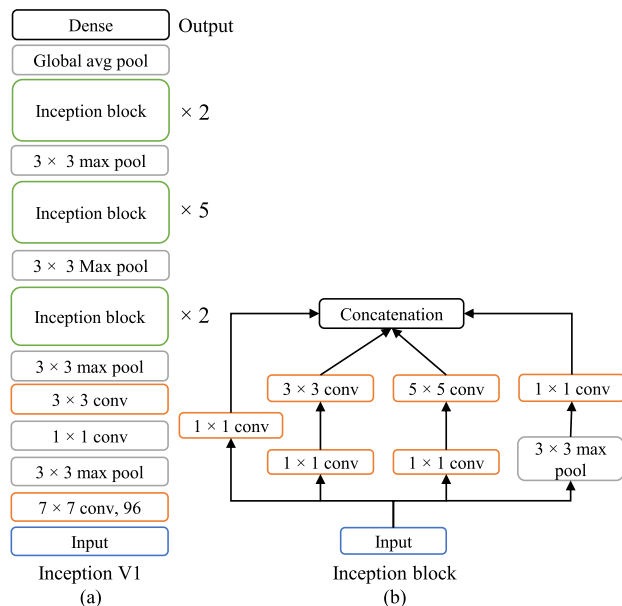


FIGURE 5. Network architectures of GoogLeNet/Inception. (a) is inception network and (b) is inception block.

III. DATASETS AND EVALUATION METHODS

In this section, we discuss some commonly used datasets and evaluation metrics for the segmentation and classification tasks.

A. PUBLICLY AVAILABLE CERVICAL CYTOLOGY DATASETS

In our study, we have found that the Herlev database and ISBI (International Symposium on Biomedical Imaging) challenge database are the most commonly used publicly available databases. Herlev and ISBI databases are mainly used for segmentation purposes. However, the Herlev database is mostly used for the classification task. We have found a new publicly available database named ‘‘SIPAKMED’’ that can be utilized for the classification task. Tab. 1 gives the download link for the databases, as mentioned earlier.

1) PAP SMEAR BENCHMARK DATABASE (Herlev DATASET)

The pap smear benchmark database was prepared and analyzed by the staff at Herlev University Hospital, Denmark. They prepared the database by using a commercially available software package CHAMP (Dimac) for the segmentation of images. They prepared two databases, the old one in 2003 and the new one in 2005 comprise 500 and 917 single cell images, respectively, with an average image size of 156×140 . The old database has 150 normal and 350 abnormal cell images, whereas the new database has 242 and 675 benign and malignant cells, respectively. The database has distributed into seven important classes: (a) superficial squamous epithelia, (b) intermediate squamous epithelia, (c) columnar epithelia, (d) mild squamous non-keratinizing dysplasia, (e) moderate dysplasia, (f) severe dysplasia, and (g) carcinoma in situ. Among those seven classes, the first

TABLE 1. Download link for the open access cervical cytology image databases.

Databases	Download Link
Pap smear benchmark database	http://mde-lab.aegean.gr/downloads
ISBI Challenge database	https://cs.adelaide.edu.au/~zhi/isbi15_challenge/dataset.html
SIPAKMED Database	http://www.cs.uoi.gr/~marina/sipakmed.html

three classes correspond to healthy cells, and the rest of the classes corresponds to the abnormal cells [84].

2) ISBI CHALLENGE DATABASE

The ISBI 2014 and 2015 are the publicly available database that contains overlapping cervical cells and their ground truth [85], [86]. The first dataset (ISBI 2014) contains 135 synthetic and eight real cervical cytology EDF (extended depth of focus) images in the training set, whereas, in the test set, there are 810 synthetic and eight real cervical cytology EDF images. The number of overlapping cells differs from 2 to 5 in the 2014 dataset. The ISBI 2015 dataset contains eight real cervical cytology EDF images in training set along with their volume images, whereas the test set has nine real cervical cytology EDF images along with their volume images [87]. The number of overlapping cells ranges here from 2 to 10.

3) SIPAKMED DATABASE

This database consists of 966 pap smear slide images and 4049 single-cell images. Based on the cell structure and morphology, the cells are classified into five distinct categories. They are intermediate, parabasal, koilocytotic, metaplastic, and dyskeratotic. The first two classes can be further categorized as normal cells. Then, the next two classes are considered as abnormal cells, where morphological changes of the nucleus start to appear. The final class (Dyskeratotic) is the malignant cells level, where cervical precancerous and cancerous conditions start to develop [88].

B. EVALUATION METHODS

In this subsection, we present the evaluation methods for segmentation and classification algorithms with all necessary equations.

1) EVALUATION OF SEGMENTATION METHODS

Choosing the appropriate evaluation metric can reduce the bias in the differentiation of algorithms. The automated segmentation algorithms for segmenting the region of interest is an exciting area of research. To evaluate the automated segmented images, we need ground truth images, which have been prepared by pathologists. As a result, there must have appropriate techniques to evaluate the results of the segmentation algorithm [89].

To evaluate the quality of segmentation, detection accuracy and segmentation accuracy are the most commonly

used measures. Detection accuracy is the ability to identify the region of interest by a segmentation algorithm. Segmentation accuracy measures how close or similar are the regions of interest obtained with comparison to the ground truth image by applying the automatic segmentation algorithm [89]. Precision, Recall, and F-measure are the extensively used detection accuracy metrics.

Precision is the number of correctly recognized pixels from all the detected pixels. A recall is the number of identified pixels from all the pixels in the ground truth. F1 score is the harmonic mean of precision and recall [90]. Mathematical expression for precision, recall, and F1 score is shown in table 2. In table 2 TP represents the number of correctly detected positive samples, TN is the number of correctly detected negative samples, FP indicates the number of negative instances that are misclassified as positive, FN denotes the number of positive instances that are misclassified as negative.

TABLE 2. Evaluation metrics.

Assessments	Formula
Precision, P	$\frac{TP}{TP+FP}$
Recall, R	$\frac{TP}{TP+FN}$
F1 score	$2 \times \frac{P \times R}{P+R}$
Sensitivity	$\frac{TP}{TP+FN}$
Specificity	$\frac{TN}{TN+FP}$
Accuracy	$\frac{TP+TN}{TP+TN+FP+FN}$
MCC	$\frac{TP \times TN - FP \times FN}{\sqrt{(TP+FP)(TP+FN)(TN+FP)(TN+FN)}}$

Now, to evaluate the segmentation accuracy Dice coefficient [90], [91], Zijdenbos similarity index (ZSI) [92], [93] are the most popular measures.

- 1) Dice co-efficient (D): let S denote the automatically segmented shape consisting of points $s_1, s_2, s_3, \dots, s_n$ and let G represents the ground truth shape with points g_1, g_2, \dots, g_n . Dice coefficient(D) measures the overlap between the two regions and is given by

$$D(S, G) = \frac{2|A \cap G|}{|A| + |G|} \quad (1)$$

where $D(S, G) \in [0, 1]$. A higher $D(S, G)$ value indicates better segmentation performance.

- 2) Zijdenbos similarity index (ZSI): ZSI considers TP, FP, and FN in all aspects. If the ZSI score is higher than 0.7, it indicates that the segmentation result is well-matched with ground truth [94]. It can be denoted as

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

2) EVALUATION OF CLASSIFICATION METHODS

After training a classifier with samples, an unknown test sample is provided to check whether the classifier can

classify the samples correctly or not [89]. Precision, recall, F1 score, sensitivity, specificity, and accuracy are observed as the most popular techniques to measure the classification results [95]–[99].

Precision, recall and F1 score we have discussed in Sec. III-B.1 and their mathematical expressions are given Tab. 2. Sensitivity can also refer to the correct positive rate or recall. Specificity indicates the percentage of negative labeled instances that are predicted as unfavorable. Accuracy identifies the proportion of correct predictions. Equations for sensitivity, specificity, and accuracy is exhibited in Tab. 2.

Though accuracy and F1 score are considered to be the most conventional standards for binary classification tasks, they can generate misleading returns on imbalanced datasets. The Matthews Correlation Coefficient (MCC), in that case, produce more authentic and informative scores. MCC returns a value between -1 and $+1$. A coefficient of $+1$ signifies a perfect classification, 0 is the expected value for arbitrary prediction, and -1 indicates perfect misclassification [100], [101]. The mathematical representation for MCC displays in Tab. 2.

IV. DEEP LEARNING FOR THE SEGMENTATION OF CERVICAL CYTOLOGY IMAGE

An overview of deep learning for cervical cytopathological image segmentation work is compiled in this section. We have summarized the proposed methodology, dataset, image pre-processing, and evaluation method of each paper in the reference review subsection. Next, we analyzed the suitable deep learning approach in the method analysis section. Finally, we concluded by summarizing the chapter.

A. REFERENCE REVIEW

In [102], a super-pixel and CNN based segmentation methods are proposed for cervical cell segmentation. The author performs the cytoplasm segmentation first since the background, and cytoplasm contrast is not evident. Then CNN is applied here to detect the region of interest. In this experiment, they acquire the data privately. They use 1200 cell samples to train the network and 200 cell units for testing. For performance evaluation, they use 21 images (15 images have abnormal, and six have normal nuclei). Image size is 1024×1360 pixels. Pre-processing is done to reduce the noise of the image by the trimmed mean filter. They achieved an F1 score above 0.89.

In [103], the author has developed a deep learning method via a multiscale convolutional neural network (MSCN) for feature extraction and graph partitioning for nucleus segmentation. The MSCN and graph partitioning algorithms can separate cytoplasm, nuclei, and background. However, to solve the overlapping nucleus in the cell image, a new robust nuclei clump algorithm is introduced. They privately collect the dataset, which consists of 21 images (15 abnormal and six normal) for this experiment. By using MSCN and graph partitioning, they got cytoplasm and nucleus segmentation accuracy of 90% and 85%, respectively.

An automated CAD system is proposed in [90]. The author in this study improves the existing Fuzzy c -means clustering algorithm for nucleus segmentation by finding the optimum number of clusters instead of fixed clusters. Moreover, BPNN is used to extract the shape features to match the regions as a nucleus or non-nucleus. Publicly available Herlev University database is used in this experiment. Pre-processing work is done by using Perona-Malik diffusion (an isotropic diffusion) filter to reduce noise. They obtained a precision, recall, and ZSI value of 0.86, 0.90 and 0.85, individually.

In this experiment [104], the author proposed a unique deep CNN-based framework that can accurately segment the cervical cells from overlapping clumps. This proposed method has three parts. The first part is the cell component segmentation. The second part is multiple cell labeling, and the final part is cell boundary refinement and inference. For the evaluation of the segmentation method, they use two datasets: ISBI 2015 challenge dataset and one privately acquired dataset. ISBI dataset consists of 8 cervical cytology images, and the private dataset has 21 cervical cytology images. 5650 background, 8590 cytoplasm, and 8560 nucleus pixels are taken from eight images in the SZU dataset to establish our training set. For testing, they have used 1200 cells. Pre-processing has been done by rotating the cell images from 0 to 180 degrees with a step of 15 degrees. They transform the training sample color into YUV to enhance performance. Figure 6 shows the segmentation outcome of both of the datasets. They achieved the dice coefficient (DC) value 0.91 for cytoplasm and 0.93 for nucleus in the ISBI challenge dataset and 0.90 and 0.92 for cytoplasm and nucleus respectively in the private dataset.

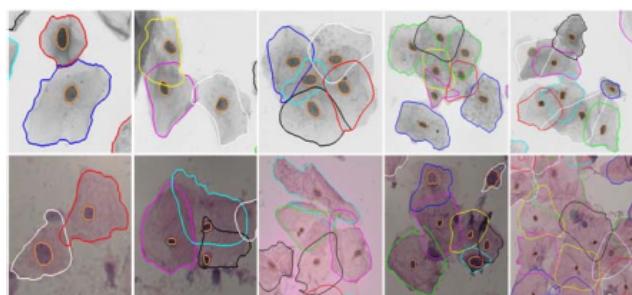


FIGURE 6. Samples of the segmentation result for qualitative evaluation of proposed approach. The upper row is from ISBI 2015 dataset, while the bottom row derives from the private dataset [104].

Segmentation of the nucleus is essential because it carries vital information about the cells. Considering that fact, [105] in his paper proposed an automated cervical nucleus segmentation method. Usually, there are two methods for automatic nucleus segmentation, one is initial segmentation, and the other is fine segmentation. For initial segmentation, a fully convolutional network (FCN) image-patch based classification method is suggested, which does not need any pre or post-analysis. For fine segmentation, a graph-based method is proposed that can detect the nucleus boundary as a globally optimal solution. For FCN training, VGGNet architecture

is deployed. Herlev dataset has utilized in this experiment. ZSI value is calculated to check the performance of the proposed algorithm. The ZSI value of 0.92 demonstrates the outstanding performance of this experiment.

The author in [106] presents a robust variational segmentation framework based on pixel-wise CNN and a learned shape prior, that can successfully segment nuclei and cytoplasm from densely overlapping mass. The proposed method first classifies the cellular components into the background, nuclei, and cytoplasm using CNN. Later, individual cytoplasm segmentation work is performed with Voronoi segmentation and dynamic shape prior based level set evaluation. Figure 7. shows the detailed workflow of the proposed method. In this work, they used two datasets from ISBI 2014. The first one is the preliminary version of the baseline method of the ISBI 2014 challenge. The 2nd one is the ISBI challenge dataset. Two datasets contain a total of 159 cervical cytology images with 870 cells in total. For quantitative pixel-level nucleus segmentation, the proposed method achieved precision, recall, and ZSI index is 0.94, 0.95, and 0.94, respectively, on the 2nd dataset. Moreover, they achieved ZSI value 0.90, TP value 0.95 for cytoplasm segmentation. The workflow of this work is shown in Fig. 7.

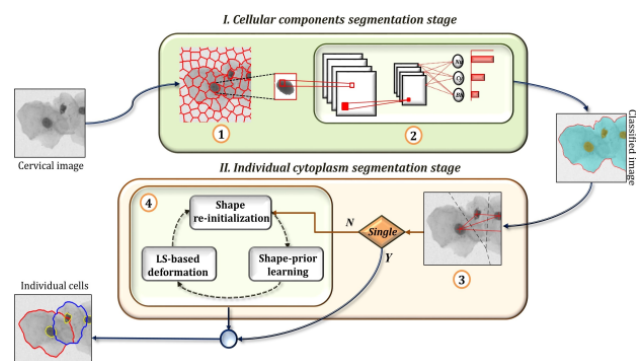


FIGURE 7. The workflow of the proposed learning methodology. (I) is the 3-class cellular components classification stage, including (1) cellular patches generation and (2) CNN-based classification. (II) is the individual cytoplasm segmentation stage, including (3) Voronoi segmentation and (4) learned shape prior-based evolution [106].

The author presents a CNN based approach for the detection of nuclei from overlapping cervical cytology images in [107]. They used a Lightweight library called Lasagne to construct CNN that is written in python and is build and trained in Theano. The trained network can classify each pixel to one of the classes: Nucleus, cytoplasm, or background. Pixel that belongs to the nucleus is used for training. Then, they apply the rectified linear unit as an activation function to all convolutional and fully connected layers. ISBI 2014 challenge dataset is used in this experiment. Among 945 images, 45 images are used for training, 90 is for testing, and 810 is for evaluation. The proposed system yielded a precision and recall value of 0.929 and 0.917, respectively, for nucleus detection.

In this paper [108], the author proposes a patch-based CNN approach using selective pre-processing for nuclei segmentation. VGGNet has used as CNN architecture to extract features. Herlev dataset is employed to evaluate the performance of the proposed method. 70% images of each class are used for training, 15% for validation and 15% is for testing. Contrast enhancement has been performed for small and compact nuclei as pre-processing. Their proposed method achieved a similar ZSI and F1 value of 0.90.

In this study [93], the author suggests a unique method to segment cervical cancer cell nuclei. They merge a mask regional convolutional neural network (Mask-RCNN) for coarse segmentation and local fully connected conditional random field (LFCCRF) to refine the nuclear boundary. ResNet based on feature pyramid network uses as a foundation of Mask-RCNN. Herlev dataset is used to evaluate the performance of the proposed method. The suggested study obtained 0.96, 0.96 and 0.95 for the precision, recall, and ZSI value, respectively.

The author in [109] presents an approach to segment the whole cervical cell image by using Mask R-CNN and transfer learning. ResNet10 is the backbone of Mask R-CNN. In the beginning, the cell areas are partitioned by using MASK R-CNN. Later, the cell areas are classified into nucleus and cytoplasm. The network is pre-trained using the COCO dataset consisting of 25, 00, 000 labeled objects with 91 categories. The introduced technique is evaluated using the Herlev dataset. In the preprocessing stage, images are resized into 200 pixels, then the data augmentation technique is performed. The proposed algorithm produced a precision, recall, and ZSI value of 92%, 91%, and 90%, respectively.

Deformable Multiple Ensemble Model(D-MEM), a unique computerized segmentation technique based on deep neural networks, is addressed in [92], for the segmentation of cervical cell nuclei. U-net is the backbone of the ensemble model. The deformable convolution can segment objects with various appearances and dimensions. Moreover, they introduce dense blocks to overcome the information vanishing problem. The recommended methodology reached ZSI, Precision, and Recall value of 0.933, 0.946, and 0.984 on the Herlev dataset.

A cell segmentation method from a special resolution of the pap smear image is proposed in [110]. This approach is composed based on fully convolutional neural networks (FCN-8 and FCN-16) and classical(superpixel-based) segmentation approach. VGG-16 is the backbone of FCNs. A high resolution of 6 digitalized images, each with $94,000 \times 84000$ pixels are taken to monitor the performance of the proposed algorithm. Those large images are split into sub-images with a resolution of 2000×2000 pixels. Seven hundred sixty-seven images are considered for training, and 315 images are considered for testing. The data augmentation measure is implemented to increase the volume of the dataset. They reached a segmentation accuracy of 86.67% by combing all the three techniques.

In [111], the author suggests a deep learning algorithm based on LeNet architecture to segment both free-lying and

overlapping clumps of the abnormal cell from conventional digitized pap smear images and rank those images according to their level of abnormalities. A preprocessing system eliminates images before segmentation if it only holds background or inadequate information, which improves the computational cost. They created two different datasets, specifically training and test datasets contains 26 (24 abnormal and two normal) and 168 (84 abnormal) images respectively from Brazilian Health System (BHS). They used those datasets to evaluate the performance of the proposed methodology. Mean average precision (MAP) is used to evaluate the ranking quality of the abnormal images. They achieved F score, precision, recall, and MAP value of 0.69, 0.73, 0.65, and 0.936, individually.

A progressive growing U-net model (PGU-net+) introduces in [112] to segment the nucleus of a cervical cell. Two modifications are made to the classical U-net model. Firstly, residual learning blocks attach to the different scales of U-net. Secondly, a continuous developing training model is selected, where the most inferior part with the downsample images are trained first and then following to the finer part for training until the full model is incorporated. Four sets of measures are conducted to investigate the performance of the recommended design on the Herlev dataset. It is explored that among the classical U-net, U-net+, PGU-net, and PGU-net+, PGU-net+ gives the highest segmentation accuracy of ZSI, precision, and recall value of 0.926, 0.901, and 0.968 sequentially.

In [113], A novel Instant Relation Network (IR-Net) is advised to segment the overlapping cervical cell. ResNet-50 is the backbone of the IR-Net. In this system, firstly, object candidates are formed by the region proposal network (RPN). Then the characteristics are obtained by the RoIAlign layer and passed into two branches for the detection and segmentation of the cell. Cervical pap smear (CPS) dataset consisting of 4439 cytoplasms and 4789 nuclei is adopted to evaluate the performance of the suggested method. 70% of the dataset is accepted for training, 10% is for validation, and 20% is testing. They achieved Average Jaccard Index (AJI) and F1 value of 0.7185 and 0.7497 for cytoplasm and 0.5496 and 0.7554 for nucleus segmentation.

B. METHOD ANALYSIS

It is observed from the reference review that most of the research work has been conducted using the publicly available databases, which we have discussed in section III. The research group that employs Herlev datasets is the only one to perform nucleus segmentation. Zijdenbos similarity index (ZSI) is a trendy method to evaluate the segmentation result. The higher ZSI value symbolizes more reliable exactness. In [90], the author implements a backpropagation neural network for feature extraction and fuzzy *c*-means clustering to segment the nucleus. They obtain a ZSI value of 0.85. However, in [93], the author proposes a combine Mask-RCNN and LFCCRF to segment the nucleus and achieve a ZSI value of 0.95. So, it is clear that the following approach

TABLE 3. Summary of reviewed works for the segmentation of cervical cytology image. (Multiscale convolutional neural network (MSCN), Back propagation neural network (BPNN), Fully convolutional neural network (FCN), Regional convolutional neural network (RCNN), Local fully connected conditional random field (LFCCRF), Accuracy (Acc), Precision (P), Recall (R), Zijdenbos similarity index (ZSI), Dice coefficient (DC), Deformable Multiple Ensemble Model (D-MEM), Mean average precision (MAP), progressive growing U-net model (PGU-net+), Instant Relation Network (IR-Net), Cervical pap smear (CPS), Average Jaccard Index (AJI)).

Year	Ref	Segmented region	Method	Data	Pre-processing	Result
2014	[107]	Cytoplasm and nucleus	Superpixel based CNN	Private dataset	Denoising and color conversion	$P = 0.91, R = 0.87, F1 = 0.89$.
2015	[108]	Cytoplasm and nucleus	MSCN & graph partitioning	Private dataset		Acc = 90%, 85% for cytoplasm and nucleus.
2016	[95]	Nucleus	Improved fuzzy <i>c</i> -means clustering & BPNN	Herlev dataset	Denoising	$P = 0.86, R = 0.90, ZSI = 0.85$.
2016	[109]	Overlapping cell	MSCNN with robust shape priors	ISBI 2015 dataset and one private dataset	Color transformation, rotation of cell	DC = 0.91, 0.93 on 1st dataset, DC = 0.90, 0.92 on 2nd dataset for cytoplasm and nucleus.
2017	[110]	Nucleus	FCN image-patch based & graph based method	Herlev dataset		ZSI = 0.92.
2017	[111]	Overlapping cell	Super-pixel wise CNN & learned shape prior based method	ISBI 2014 dataset		ZSI = 0.94, 0.90 for nucleus and cytoplasm.
2017	[112]	Nucleus	CNN	ISBI 2014 dataset		$P = 0.929, R = 0.917$.
2018	[113]	Nucleus	Patch based CNN	Herlev dataset	Contrast enhancement	ZSI = 0.90, F1 = 0.90.
2018	[98]	Nucleus	Mask-RCNN & LFCCRF	Herlev dataset		$P = 0.96, R = 0.96, ZSI = 0.95$.
2019	[114]	Cytoplasm and nucleus	Mask R-CNN (ResNet10) & transfer learning	Herlev dataset	Image resize and augmentation	$P = 0.92, R = 0.91, ZSI = 0.90$.
2019	[97]	Nucleus	D-MEM (U-net)	Herlev dataset		$P = 0.946, R = 0.984, ZSI = 0.933$.
2019	[115]	Cervical cell	FCN-8 (VGG-16) & FCN-16 (VGG-16) & super pixel	Private dataset	Data augmentation	Acc = 86.67%.
2019	[116]	Overlapping cell	LeNet	Private dataset	Eliminate images with inadequate information	$P = 0.73, R = 0.65, F1 = 0.69, MAP = 0.936$.
2019	[117]	Nucleus	PGU-net+	Herlev dataset		$P = 0.901, R = 0.968, ZSI = 0.926$.
2019	[118]	Overlapping cell	IR-Net (ResNet-50)	CPS dataset		AJI = 0.7185, F1 = 0.7497 for cytoplasm, and AJI = 0.5496, F1 = 0.7554 for nucleus.

is more accurate for the segmentation of cervical cancer cell nuclei.

Studies that are performing the segmentation of overlapping cervical cell employs private datasets or CPS or ISBI challenge datasets. For the overlapping cells, segmentation of cytoplasm and nucleus are both carried out. Segmentation work, which combines pixel-wise CNN and a learned shape prior, obtain the highest precision, recall, and ZSI value for the overlapping cytoplasm and nucleus [106]. Besides, one task is recognized for the segmentation of the CPS dataset based on IR-Net [113]. So these are the preferable approaches for the segmentation of overlapping cervical cells.

C. SUMMARY OF SEGMENTATION METHOD

A summary of the deep learning method for the segmentation of cervical cancer cell is exhibited in table 3. This table comprises of some essential attributes of any research paper.

Each row indicates publication year, reference, segmented region, segmentation techniques, dataset, data pre-processing, and result of an individual paper. From the table, it can be perceived that most of the work reached an exactitude of over 85%. Thus, it delivers a direction to the new researchers to utilize the most suitable algorithm for the segmentation of cervical cancer cells.

V. DEEP LEARNING FOR THE CLASSIFICATION OF CERVICAL CYTOLOGY IMAGE

An overview of deep learning for cervical cytopathological image classification practice is compiled in this section. We summarize the proposed methodology, dataset, image preprocessing, and evaluation method of each paper in the reference review subsection. Next, we examine the suitable deep learning strategy in the method analysis subsection. Finally, we conclude by summarizing the chapter.

A. REFERENCE REVIEW

In [96], the author introduces a deep learning-based computerized vision system that is capable of classifying pap smear cells into normal and dysplastic. The proposed architecture has two steps for extracting the hierarchical data features, which is supervised by independent neural agents. ANN is pre-trained with a distinctive reticle pattern to develop a prominent ability to recognize the unseen pap cells. Herlev dataset is employed in this research. Images are resized into 100-by-100 pixels. Noise balanced training set has been utilized for training the dataset. One hundred images of each class have been used for training, and 150 images of each class are used for testing. The proposed method yielded a sensitivity of 97% and specificity 96%.

A general-purpose (GP) system is stated in [114] to check the performance of different classifiers on twenty-five datasets, among them, 14 are image datasets. Since our review is based on cervical cytology images. Therefore, we only consider the performance on cervical cytology images and the best performing algorithms. The GP system can take care of multiple datasets and a large number of problems. Local Ternary Patterns (LTP) and Local Phase Quantization (LPQ) are the two-texture descriptors that have used to extract features for the image datasets. This experiment compares the result of several classifiers (Gaussian process classifier (GPC), RS of AdaBoost (RS AB), RS of rotation boosting (RS RB), RS of support vector machine (RS SVM) and deep learning (DL)) with LibSVM library. The area of the ROC curve (AUC) evaluates the performance of the GP system. Ensemble four (E4) comprised of GPC, RS AB, RS RB, RS SVM, and DL obtained the highest performance for all the image datasets. On the Herlev dataset, E4 achieved an AUC value of 0.92.

In [97], the author proposes an automatic CAD system for the detection of cervical cancer from pap smear images. They introduce a hybrid classifier by combining SVM and neural network-based adaptive neuro-fuzzy interface system (ANFIS). GLCM, Local binary pattern features, grey level features, histogram features wavelet features, and laws texture features are extracted. Herlev dataset was used to test the proposed algorithm. Images are resized to 256×256 pixels, and RGB to grey level color conversion has executed in the preprocessing step. The proposed method has reached an accuracy of 99.1% in a 2-class classification problem.

A neural network-based automated system is developed to classify the cervical cytology images into non-cancerous, low-grade, and high-grade in [98]. MATLAB image processing toolbox is used to extract features to train the back-propagation neural network algorithms. A private dataset consisting of 38 images (12 high-grade, 10 low-grade, 16 non-cancerous cells) and 228 single cells are used to evaluate the performance of this algorithm. In the preprocessing step, RGB to grey color conversion, morphological operation, edge detection, and labeling work has performed. The accuracy is obtained 79%, with sensitivity and specificity of 94% and 68.2%, respectively.

In order to get much higher classification accuracy, the author in [115] suggests a hybrid ensemble technique for the screening of cervical cancer from pap smear. The proposed ensemble technique combines 15 different classification algorithms such as Random subset space, Radial basis function network, Multiclass classifier, Random forest, Bagging, Rotation Forest, J48 graft, Ensemble of Nested Dichotomies (END), Decorate, PART, Random Committee, Filtered Classifier, Decision Table, Multiple back propagation artificial neural network, and Naïve Bayes. To test the proposed methodology, the Herlev dataset (2003 and 2005 version) has considered. 75% of 1417 images are granted for training, and rest are kept for testing. For the 7-class classification problem, the proposed technique achieved an efficiency of 78%, and for the 2-class problem, the hybrid ensemble has an efficiency of about 98%. The hybrid ensemble technique performs better than any individually applied algorithm.

A deep convolutional neural network-based classification algorithm is recommended in [116]. In this experiment, deep features are extracted by using CNN, and later an unsupervised feature selection task is accomplished. AlexNet architecture is used as a base of CNN. After that, the feature vectors are fed into two classifiers, namely a least-square version of the support vector machine (LSSVM) and SoftMax regression, to check the performance of these two classifiers. Privately acquired single-cell image database containing 1611 images and Herlev dataset consisting of 917 images are considered to check the performance of the proposed study. 70% of instances are accounted for training, and rest are counted for testing. Study has found that after the application of feature selection, the accuracy has improved to 90 – 95% from 84 – 87%. On the private database, SoftMax regression achieved an accuracy of 93.1%, whereas LSSVM achieved 92.24% on a 3-class classification problem. For a 2-class problem, LSSVM and SoftMax yielded 98.88% and 99.32% of accuracy independently. On the Herlev database, the accuracy is 89.97% and 88.88% by LSSVM and SoftMax respectively on a 3-class classification problem. Moreover, for 2-class classification, the accuracy is 94.61% and 91.81% by LSSVM and SoftMax individually.

In [117], the experimenter's design and train a CNN and machine learning classifiers-based model to classify the cervical pap images into normal and abnormal. A privately acquired pap smear dataset consisting of 71344 images are used to evaluate the performance of the proposed method. VGG16 has used to extract features. In preprocessing work, the actual image is divided into several pieces, since VGG can take input of an image size of 224×224 . 80% of images are used for training, and 20% is for testing. They explored that SVM performs better compared to logistic regression, random forest, and adaboost and achieved a 78% F1 score.

In [99], the author proposes a pre-trained CNN architecture rather than designing and training from scratch to extract the in-depth features to train an SVM classifier. AlexNet architecture has used in this experiment.

The proposed method achieved precision, recall, specificity, and accuracy of 99.51%, 99.5%, 97.67%, 99.19% independently on Herlev dataset on a 2-class classification problem. 70% of the images are used for training, and rest are used for testing.

In order to investigate the effectiveness of the artificial neural network, a multilayer perceptron based neural network (MLP-ANN) has proposed in [118] to classify cervical pap image into benign and malignant. A privately acquired database consisting of 416 liquid-based cytology images used for this experiment. 50% of the datasets are used to train MLP-ANN, and the other 50% is used to evaluate the performance and stability of ANN. The percentage classifier gives an overall accuracy of 95.91%, compared to 90.87% in the simple numeric classifier.

To automatically detect the morphology and chromatin-associated changes of the cervical cell nucleus, a CNN based approach has been developed in [81]. VGG16 and ResNet architecture is used as CNN. CerviSCAN and Herlev dataset is used to evaluate the performance of the proposed method. CerviSCAN is a private dataset consisting of 9809 healthy and 2234 abnormal single-cell images. In the preprocessing work, the variance of Laplacian was used to find the image with the best focus. Then, they resize the image into 100×100 pixels, and images are augmented to expand the dataset. For the CerviSCAN dataset, both of the network architecture achieved an accuracy and F score of over 84%. Herlev dataset yielded an accuracy of 86% on both network architectures, and F1 scores 82% on VGGNet and 83% on ResNet. They explored that for the cervical cell classification task, ResNet is more suitable over VGG.

A very first application of deep learning and transfer learning methods for the classification of the cervical cell into normal and abnormal is proposed in [119]. Herlev and HEMLBC (private) datasets have utilized to evaluate the proposed method. HEMLBC dataset consists of 989 abnormal and 1381 normal cells. Patch extraction and data augmentation are performed in the preprocessing work. On Herlev dataset sensitivity, specificity, accuracy and F1 measure are 98.2%, 98.3%, 98.3% and 98.8%, separately. On the HEMLBC dataset, they yielded sensitivity 98.3%, specificity 99%, and accuracy 98.6%.

A few general-purpose (GP) systems are available that can provide results comparable with the state of the art system. Some researchers build a GP system that can operate up to 16 datasets, but no system has developed so far that can work well across all the dataset. In [120], the author has developed a better performing GP ensemble model by comparing and combining state of the art handcrafted features with non-handcrafted features that can handle an extensive range of image classification problems. Deep transfer learning features based on CNN, principle component analysis, and compact binary descriptor are considered to extract the non-handcrafted features. Local ternary patterns, local phase quantization, and so on are examined to extract the handcrafted features. Among 18 different image datasets,

the Herlev dataset is reviewed to evaluate the performance of the suggested system. They explored that performance of the transfer learning is more excellent than the standard approach. Besides, a combination of handcrafted with non-handcrafted features performs better than their individual. They obtained an accuracy of 95.1% with transfer learning, whereas 91.4% by standard approaches on the Herlev dataset.

In [121], the author proposes a deep learning-based cervical cell analysis system—detection, segmentation, and classification. Based on the purpose of our study, we only focus on the classification approach. Feature level analysis using transfer learning on AlexNet has proposed for the classification of the Herlev dataset. They proved that accurate segmentation is not necessary for classification. For a 2-class problem, they achieved an accuracy of 99.3% and 93.75% for the 7-class classification problem on the Herlev dataset.

In [122], a unique cervical cell study is presented by connecting morphological and appearance-based characteristics with in-depth features. They examined that the combination of appearance and morphology-based CNNs provides more positive classification accuracy than their individual. CNN models such as AlexNet, GoogLeNet, ResNet, and DenseNet Image are pre-trained on the ImageNet dataset and later fine-tuned on the cervical cell dataset. Herlev dataset is utilized to test the performance of the recommended model. patch and cell morphology extraction, along with data augmentation task is executed in the preprocessing step. Among the four CNN's, GoogLeNet obtains the highest classification accuracies of 94.5%, 71.3%, and 64.5% for 2-class, 4-class, and 7-class classification problems. It is to be remarked that the segmentation of the nucleus and cytoplasm are pre-required to employ this method.

In [109], pre-segmented cervical cell images are fed into the VGG-like network to perform the classification task. The VGG-like network is the compact version of its original consists of 7 layers to reduce the computing costs. Segmented images are resized, augmented, and copied to specific folders for 2 and 7-class classification cases in the preprocessing step. For a binary classification problem, they achieved 96.7% sensitivity, 98.6% specificity, and 98.1% accuracy. Similarly, for 7-class problems, they achieved 96.2% sensitivity, 99.3% specificity, and 95.9% accuracy on the Herlev dataset.

A comparative analysis of the cervical cytopathology image in deep learning is introduced in [123]. Five deep learning models, such as ResNet101, DenseNet161, AlexNet, VGG19_bn, and SqueezeNet1_1 are assessed to compare the performance on the Herlev dataset. 70% of pap images are accepted for training, 20% is for validation, and 10% is for testing. They investigate that DenseNet161 is the best DL model among those 5 DL models to provide the maximum accuracy of 94.38% and 68.54% in binary and 7 level classification problem.

In [124], a mask regional convolutional neural network (Mask R-CNN) is recommended to identify the nucleus of pap smear slides and organize it into healthy and irregular. One hundred seventy-eight images from the pap smear slides

TABLE 4. Summary of reviewed works for the classification of cervical cytology image. (Sensitivity (S_n), Specificity (S_p), Efficiency (Eff), Area of the ROC curve (AUC), Precision (P), Recall (R), General purpose (GP), Accuracy (Acc), Gaussian process classifier (GPC), RS of AdaBoost (RS_AB), RS of rotation boosting (RS_RB), RS of support vector machine (RS_SVM), Deep learning (DL), Multilayer perceptron (MLP), Variance of Laplacian (VL), Mean average precision (mAP)).

Year	Ref	Method	Class problem	Data	Pre-processing	Result
2015	[101]	Deep ANN	2 class	Herlev dataset	Resize	$S_n = 97\%$, $S_p = 96\%$.
2015	[119]	GPC & RS_AB & RS_RB & RS_SVM & DL	2 class	Herlev dataset		$AUC = 0.9164$.
2015	[102]	SVM & ANFIS	2 class	Herlev dataset	Resize, color conversion	$Acc = 99.1\%$.
2015	[103]	BPNN	3 class	Private dataset	Color conversion, morphological operation, cell labeling	$S_n = 94\%$, $S_p = 68.2\%$, $Acc = 79\%$.
2015	[120]	Hybrid ensemble	2 and 7 class	Herlev dataset		$Eff = 78\%$, 98% for 2 and 7 class problem.
2016	[121]	AlexNet & LSSVM/SoftMax Regression	2 and 3 class	Herlev and private dataset		Herlev : $Acc = 89.97\%$, 94.61% , Private: $Acc = 93.1\%$, 99.32% on 3 and 2 class problem.
2017	[122]	VGG16 & Logistic regression/ Random forest/ Ada boost/ SVM	2 class	Private dataset	Resize	$F1 = 78\%$ (SVM).
2017	[104]	Pretrained AlexNet & SVM	2 class	Herlev dataset		$P = 99.51\%$, $R = 99.5\%$, $Acc = 99.19\%$.
2017	[123]	MLP-ANN & Case classifier (Numeric/percentage)	2 class	Private dataset		$Acc = 95.91\%$, 90.87% on percentage and numeric.
2017	[84]	VGG16 & ResNet	2 class	Herlev and private dataset	Resize, augmentation and VL	$Acc = 84\%$, 86% on private and Herlev dataset.
2017	[124]	CNN & transfer learning	2 class	Herlev and private dataset	Patch extraction	$S_n = 98.2\%$, 98.3% , $S_p = 98.3\%$, 99.0% , $Acc = 98.3\%$, 98.6% on Herlev and Private dataset.
2017	[125]	CNN & transfer learning	2 class	Herlev dataset		$Acc = 95.1\%$.
2018	[126]	AlexNet & transfer learning & decision tree	2 and 7 class	Herlev dataset	Augmentation	$Acc = 99.3\%$, 93.7% for 2 and 7 class problem.
2019	[127]	Morphological & CNN's (AlexNet, GoogLeNet, ResNet, DenseNet)	2, 4 and 7 class	Herlev dataset	Augmentation, patch and cell morphology extraction	$Acc = 94.5\%$, 71.3% , and 64.5% for 2, 4, and 7 class problem on GoogLeNet.
2019	[114]	VGG-like network	2 and 7 class	Herlev dataset	Segmentation, resize, augmentation	$S_n = 96.7\%$, 96.2% , $S_p = 98.6\%$, 99.3% , $Acc = 98.1\%$, 95.9% for 2 and 7 class.
2019	[128]	Resnet101, Densenet161, AlexNet, VGG19_bn, and squeezeNet1_1	2 and 7 class	Herlev dataset		$Acc = 94.38\%$, 68.54% for 2 and 7 class problem on Densenet161.
2019	[129]	Mask R-CNN (ResNet-50)	2 class	Private dataset	Resize, augmentation, mean subtraction	$mAP = 57.8\%$, $Acc = 97.1\%$.
2019	[130]	Feature concatenation & CNN's (Inception-v3, Resnet152, Inception-Resnet-v2)	2 class	Herlev dataset		$Acc = 93.04\%$.

are collected from Thammasat University hospital to check the performance of the recommended algorithm. 20% of the datasets are used for testing, and the rest are considered for training and validation. ResNet-50, which is pre-trained on the ImageNet dataset, is used as a backbone network for the feature pyramid of Mask R-CNN. During the training process, the images are preprocessed by resizing, augmentation, and mean subtraction. The mean average precision (mAP)

value represents the performance of a combined detection and classification task. They achieved an mAP value of 57.8% and an accuracy of 97.1% per image.

In [125], a feature concatenation and ensemble approaches are suggested by coupling several CNNs (Inception-v3, Resnet152, and Inception-Resnet-v2) with different depths and structures to classify biomedical images. Three publicly available datasets such as the 2D Hela dataset, PAP

smear dataset, and Hep-2 cell image datasets have considered checking the performance of the introduced method. It is noticed that an ensemble of different models obtain more reliable results than individual ones. Ensemble of Inception-v3, Resnet152, Inception-Resnet-v2, and feature concatenation of those three achieved 93.04% accuracy on the Herlev dataset.

B. METHOD ANALYSIS

It is apparent from the reference review that openly accessible databases have been examined widely to check the performance of the recommended model. Out of eighteen studies, 14 of them utilize the Herlev dataset to check the performance of their introduced algorithms and compare the outcome with others.

Some researchers employ hybrid ensemble techniques, where they combine lots of classification algorithms along with different image datasets. However, they could not accomplish a state of the art accuracy on any specific dataset. Most of the contributors utilize CNN to extract the deep features and then manage classifiers like SVM to analyze the cell images. The author in [81] compares the results obtained from ResNet and VGGNet and verify that ResNet is more suitable for the classification of the cervical cytology images. Most of the researchers achieve accuracies over 80%. The highest classification accuracy achieved for 2-class is 99.3% and 93.7% for 7-class problems on the Herlev dataset by using the algorithm combination of deep learning and transfer learning [121]. Moreover, a VGG-like network reaches the highest correctness of 95.9% on 7-class problem [109].

C. SUMMARY OF CLASSIFICATION METHOD

A summary of the deep learning methods for the classification of the cervical cytopathological image is presented in Tab. 4. The given index is composed of all the key attributes of any research paper. Each row designates publication year, reference, proposed method, types of classification problem, dataset, preprocessing, and result. From the table, it can be noticed that most of the work achieves an accuracy of over 80%. Thus, it provides a direction for new researchers to pick the most suitable algorithm for the classification of cervical cells.

VI. METHODOLOGY ANALYSIS

Various deep learning-based algorithms have been designing for the segmentation and classification of the cervical cytological image. Among them, few algorithms have shown tremendous results. Thus, a corresponding in-depth analysis of the best performing algorithms is given in the subsection below.

A. ANALYSIS OF THE SEGMENTATION METHOD

The segmentation of cervical cancer cells can be divided into two parts. One is overlapping, and the other is non-overlapping. Cytoplasm and nucleus segmentation tasks have performed in the case of an overlapping cell. Segmentation of

cytoplasm from an overlapping cell is always challenging. MS-CNN, along with shape priors-based methods, are found to have more prominent result [104], over others [92], [106], [107], [109]–[113]. MS-CNN has some advantages over conventional CNN. Small size inputs of a regular CNN provides below standard observations, whereas large dimension inputs not only expands the network parameter but also add noise, which is challenging to manage. On the other hand, multi-scale CNN takes an input size of 32×32 pixels and can offer an observation of 128×128 pixels, which can eliminate noise and also merge the network parameters. Multiple cell labeling model is also proposed in this algorithm since MS-CNN cannot predict the specific cell that gives the pixels of cytoplasm and nucleus. Moreover, the portion of overlapping regions can have multiple cell labeling. Therefore, a multi-template deformation model is proposed to recover the weak boundary of an overlapping cell. This proposed template yielded the dice coefficient value of 0.91 and 0.93 for the segmentation of the cytoplasm and nucleus independently on the ISBI 2015 challenge dataset [104]. Super pixel-wise CNN and a learned shape prior, based model have shown superior performance for the segmentation of overlapping cytoplasm and nucleus on the ISBI 2014 challenge dataset. However, the overlapping cell ratio is higher in the 2015 challenge dataset than in 2014. So, we can say that MS-CNN, along with shape priors, is preferable for the segmentation of overlapping cells.

Among non-overlapping cells, the nucleus segmentation task has been conducted widely because the nucleus of a cell sustains essential diagnostic information for cervical cancer. A MASK-RCNN merged with a LFCCRF gives superior performance [93] over other methods [90], [105], [108]. MASK-RCNN performs the coarse segmentation of the nucleus. It is composed of feature extraction, region proposal network (RPN), and prediction. In the first step, a feature pyramid network (FPN) based on ResNet along with feature extraction layer work as a foundation of MASK-RCNN. Then, RPN uses the feature map provided by FPN to create the proposal for the objects. Finally, in the RoIAlign layer, the features from RPN are converted into small feature maps with a fixed dimensional scale ($H \times W$), which leads to the accurate deployment of the nuclear boundary. In the LFCCRF part, coarse segmentation results from Mask-RCNN, intensity, and pixel-level information has employed to refine the nuclear boundary. This proposed approach yielded the highest precision, recall, and ZSI value of 0.96, 0.96, and 0.95 on the Herlev dataset.

For overlapping cell segmentation, publicly available ISBI 2014 and 2015 datasets have been utilized widely. Herlev dataset has considered for the evaluation of non-overlapping cervical cells. A detailed explanation of the dataset has been given in Sec. III.

B. ANALYSIS OF THE CLASSIFICATION METHOD

We have observed that more than 90% of studies have utilized the Herlev dataset to check the performance of their

classification algorithms. This dataset is divided into seven classes. However, most of them further categorized these seven classes into two classes as normal and abnormal. So far, it is observed that in the proposed algorithm 2-class classification problem achieves higher accuracy than the 7-class classification problem.

The heterogeneous GP ensemble system has been developed in [114], [120] to classify various types of microscopic images. The result they produce is comparable with the state-of-the-art systems. In [114], deep learning, RS_SVM, RS_AB, and GPC are merged to examine on 25 datasets. On the Herlev dataset, the proposed GP system got an AUC value of 0.92, which is very promising. Similarly, in [120], a combination of CNN with transfer learning is introduced to create a general-purpose system that can classify 18 different types of image datasets and yield an accuracy of 95.1% on Herlev dataset.

It is discerned that a combination of two or three algorithms has a better recognition ability than the individual one. [81], [96], [98] proposes classification algorithm based on single classifiers, for instance, Deep ANN [96] or BPNN [98] or CNN [81]. Those algorithms need multiple data preprocessing operations, such as data resize, augmentation, edge detection, and cell labeling. Moreover, they failed to give state of the art accuracies. On the other hand, studies [99], [116]–[119], [121] that combined CNN with SVM, transfer learning, or decision tree performed out of the box for the classification of cervical cancer with a little or no preprocessing. A combination of CNN (AlexNet) along with transfer learning and decision tree-based algorithm [121] provides superior performance over others [99], [116]–[119], [122]–[125]. AlexNet is considering to have a smaller architecture with efficient performance. Since there is a more inadequate availability of annotated cells in the medical domain, so the use of transfer learning is beneficial in this regard. It also reduces training time. Besides, for the multiclass classification problem, a decision tree-based algorithm is proposed. This advanced combined technique yielded an accuracy of 99.3% for 2-class and 93.75% for 7-class classification on the Herlev dataset [121]. Moreover, a compact version of the VGG-like network, consisting of only seven layers, has employed on pre-segmented images of the Herlev dataset and reaches an accuracy of 95.9% on 7 class classification problems [109].

C. POTENTIAL RELATED FIELDS FOR THE APPLICATION OF SIMILAR SEGMENTATION AND CLASSIFICATION METHOD

Segmentation algorithms that have been discussed in this review are not only applicable for cervical cytopathology images but also in some other medical fields such as pleural effusion images, breast cytology images, sperm cells, and microorganisms. A cytological pleural effusion has been examined by pathologists because of its simplicity, cost-effectiveness, and less invasive over X-ray, ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI). There are many CAD systems developed

for the detection or segmentation of the nucleus of pleural images. Most of them are based on machine learning techniques. Particular examples are automated cell nuclei segmentation [126], detection of cancer cells [127], [128], segmentation, and isolation of touching nuclei [129]. Next, the nucleus segmentation of breast fine-needle aspiration cytology (FNAC) images will be a handy field in this regard [130]–[133]. For a more precise diagnostic, FNAC is performed by a patient. Then, the same segmentation technique can be applied for the sperm cell segmentation, detection, tracking, and counting [134]–[137]. Moreover, the discussed segmentation algorithms also have potential applications in the microorganism. Microorganisms are significant for our ecosystem, and the segmentation of microorganisms is essential in order to find the harmful and useful one. In the literature, there are many classical [138]–[142] and machine learning [143]–[148] based segmentation methods that has been applied for the segmentation of microorganisms. Furthermore, the discussed deep learning algorithms can find significant use in segmentation of microorganisms.

Similarly, the deep learning-based classification algorithm discussed in this paper also has potential in some other medical fields such as cytology of the gastrointestinal system, thyroid gland, breast, and effusion system. First of all, the gastrointestinal system incorporates all organs in between mouth and anus. Based on the morphometry of the nucleus, they classify the smears into cancer, gastric, and ulcer [149]–[152]. Secondly, FNAC based on thyroid examination is another potential field for application. Depending on the classification result, it can be found out whether the patient needs surgery or not [153]–[158]. Thirdly, many efforts have been made for the classification of cells form malignant ones [159]–[162]. Finally, in the field of effusion cytopathology, to differentiate the reactive lymphocytosis from malignant lymphoma [163] and classify the benign cases from malignant ones [164] is another potential research area.

D. OTHER POTENTIAL METHODS FOR THE SEGMENTATION AND CLASSIFICATION OF CERVICAL CYTOPATHOLOGY IMAGE

In this subsection, we introduce some potential deep learning methods that have been successfully implemented in some other medical imaging fields and have potential in cervical cytopathology image analysis as well.

1) POTENTIAL SEGMENTATION METHODS

Lack of training data is a big challenge in biomedical image segmentation. Considering the fact CNN based U-Net architecture has been developed by combining the low- and high-level features through skip connections for biomedical image segmentation [165]. To the best of our knowledge, there is no previous work using the U-Net structure on cervical cytopathology image segmentation.

Rift Valley virus segmentation work is proposed in [166], based on U-Net architecture. Even though there were insufficient data and minimal annotated images, they achieved a promising result of the dice coefficient value of 0.90.

Similarly, leishmania parasite segmentation work has performed in [167], depending on U-Net architecture. Thirty-seven images are used to train the algorithm. Outstanding performance has achieved with 82.30% recall value.

Both of those microscopic image datasets share some similar segmentation challenges with pap smear images like noise, debris, poor contrast, and scarcity of dataset. So, we believe that U-Net can show outstanding performance for the segmentation of cervical cytopathology images.

2) POTENTIAL CLASSIFICATION METHODS

Generative Adversarial Networks (GANs) is one of the most recent discoveries of deep learning. It is a particular type of neural network that can train two networks at the same time. One of them focuses on image generation, and the other is for discrimination. A discriminative model distinguishes features of the input image by providing labels, whereas the generative model does the opposite. Rather than giving labels based on features, they give features on individual labels [168]. With the addition of a new class parallel with generated images, discriminator can be used as a classifier [169]. Some notable applications of GANs for image classification problems are introduced below.

A combination of Wasserstein-GAN(WGAN) and information maximizing GAN (InfoGAN) is proposed in [170] for unsupervised cell level feature representation that can be further used for cell-level classification, nuclei segmentation, and cell counting. The proposed system yielded an outstanding performance on bone marrow cellular components. Moreover, the dermoscopy image classification algorithm is proposed in [171] by adding WGAN and categorical GAN(catGAN) in an unsupervised and semi-supervised feature learning manner. The proposed model yielded an average precision value of 0.424, with only 140 labeled images. Furthermore, traditional feature extraction practices such as histogram of oriented gradients (HOG) [172], a combination of K-means with fuzzy c-means clustering [173], and a fusion of textual and statistical information [174] are potent procedures in analyzing the pap cell. However, they fail to produce the state of the art accuracies. Therefore, a mix of traditional and deep features can deliver a more effective result in examining the pap cells. These instances demonstrate the potential of the proposed method, which can be applied for the cervical cytopathology image classification problem where limited labeled data is available.

VII. CONCLUSION AND FUTURE WORK

In this paper, we examined studies related to cervical cytopathology image segmentation and classification based on deep learning techniques. Besides, major deep learning concepts and their popular architectures are also explained. The review showed that cervical cytopathology image analysis in deep learning is an increasing topic of interest. Most of the state-of-the-art methods that have been proposed for the segmentation and classification are applied to the same dataset. Thus, it is obvious to distinguish which algorithm is better than others. The Herlev dataset and

ISBI challenge dataset are the publicly available benchmark datasets. MS-CNN, along with shape prior based method and MASK-RCNN merged with LFCCRF give superior performance for the segmentation of overlapping and non-overlapping cervical cell respectively. For the classification work, the combination of CNN(AlexNet) along with transfer learning and decision tree-based algorithm has better recognition ability. So, it is observed that compound algorithms can improve the performance of a classifier. AlexNet, VGGNet, and ResNet are found to be the most popular CNN architecture for feature extraction in this field.

It is perceived that CNN has achieved outstanding performance in the task of segmentation and classification, which will help the patient for the early detection, diagnosis, and treatment of cervical cancer. However, there is still room for improvement. First of all, texture feature is a significant low-level feature that can describe the content or region of an image very adequately. Hence, concatenation of some novel texture descriptors such as hybrid color local binary patterns (HCLBP) [175], moment invariant features, wavelet features, local binary pattern (LBP) [176] and elongated quinary pattern (EQP) [177] with deep features can lead to a superior performance of network model. Secondly, researchers can develop entirely new CNN architecture for the analysis of cervical pap smear cells. Thirdly, the analysis of overlapping cells is still a big challenge. Fourthly, designing an algorithm that can analyze whole slide images, which may contain millions of cells, is still an open challenge. Fifthly, to the best of our knowledge, there are only three open sources pap smear database is available with a significantly imbalanced ratio of positive and negative, so to create a public dataset will be beneficial for future researchers. Finally, attempts have been made to create deep learning enhanced mobile phone microscopy [178]. So to develop a mobile phone application that can use the mobile phone microscopy to automatically analyze pap slides would be extremely useful.

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