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Deep Learning Techniques For Breast Cancer Histopathological Images: A Pilot Study

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ABSTRACT:

On account of deep learning techniques, a drastic change is being experienced in the literature of medical image analysis. Application of deep learning in the field of medical image data develops sophisticated algorithms which enhance structural relationships within data. There is a rapid increase in the usage of electronic medical data and image diagnostics because of the incredible success of deep learning algorithms over image recognition tasks. Breast histopathological images take an active part in breast cancer diagnosis and its treatment. Automated histopathology image recognition tasks help in quickening the diagnosis and also improves error reduction. To obtain an agile, firm, judicial and significant result of medical images pathologists take the assistance of deep learning methods. Histopathological images have a current trend to develop as deep learning models acquired tremendous success when combined with computer vision applications.

INDEX TERMS: Histopathological Images, deep Learning, Computer Vision, Medical image analysis.

1. INTRODUCTION:

According to the International Agency for cancer research, breast cancer is often diagnosed among women, which even causes death [1]. In general, specimens collected from patients are initially stained by using several explicit chemical dyes that contain hematoxylin & eosin (H&E) stains in addition to immunohistochemical stains [2]. Preparation of biological tissue slide is a step by step process. Various steps that are incorporated in tissue slide preparation are chemical fixation, dehydration, embedding sample, sectioning and staining. Further pathologists check out cell structures and cell distributions using a microscope to identify state & stage of cancer. In the perspective of breast histological images, a wide variety of tissue components are visualized with the given specimen of biopsy by staining process [3]. H&E can be considered as poplar staining protocol that mainly stains nuclei structure as blue and cytoplasm as pink. WHO recommends the Nottingham grading system (NGS) to analyze breast histopathological images. These images act as a gold standard for cancer detection[4]. Pathologists examine the collected specimens under the microscope for tumour identification. As it is time tasking process, we digitalize this using whole side image (WSI) scanners. CAD systems extract essential features from given histopathological images. This computerization of histological samples with the help of WSI scanners provide several benefits such as easy storage, visualization and atomized analysis. Regular quantifiable examination of breast tissue components by applying WSI scanners incorporate nuclei analysis, tubule analysis, EP&ST analysis and mitotic activity analysis. Histopathology includes microscopic examination of stained histological slides that inquire knowledge about the existence and features of diseases [55].In general histopathological slide is comprised of tissue area with 15mm x 15mm

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dimensions. On staining tissue sections with different dyes leads to high spot variant tissue structures and cellular features[56]. According to morphological features and spatial arrangements of cells, detection of disease can be examined by pathologists. For diagnosing the presence, type and severity of disease such as cancer, histopathological analysis is considered as regular medical operation. Recent improvements in the field of biomedical engineering have led to the quantified evaluation of histological slides in diagnosing, grading and classifying carcinomatous diseases [46]. Histopathological CAD systems help in accurately extracting cellular structures. In the literature of breast histology, many tools have been used to diagnose breast carcinoma, which includes several image processing techniques. Breast Cancer constitutes of a wide variety of morphological structures that are classified as several histological subtypes [57]. The below table illustrates building blocks for the operation of CAD on histopathological images. According to the type of disease, the image processing steps may differ. Image de-noising [61, 62, 64, and 65] is the process of removing unwanted information from the image. In medical image unwanted information created by aging of devices and missed co-operation of patient.

Pre- Processing & Segmentation	**Feature Extraction & Selection**	**Disease Detection & Classification**
• ColorNormalization • Smoothening • Denoising • Enhancement • Thresholding • Edge-based Segmentation • Region-based Segmentation • Clustering	• Morphometry • Colour • Texture • Intensity • Linear & Nonlinear feature reduction	• Supervised • Unsupervised • Neural Networks • Fuzzy systems

Table 1: Overview of Histopathological Image Analysis

The grading system of Breast Cancer mainly relies on three factors, namely tubule formation, nuclei pleomorphism and mitotic count. Hence recent technologies are being developed to quantify the process of automatical nuclei detection, tubule segmentation and mitotic activity analysis. Deep Learning had provided an important breakthrough in the perspective of computer vision by accomplishing tasks of very tough image classification with progressive accuracy[5]. DL[66] based methods, when applied in histopathological images, gives more efficient results. DL Systems has the ability to learn the features automatically from WSI images[6]. Using DL methods helps in learning complicated models for data representation which performs effective information analysis[7]. Applying DL in Medical Image Analysis gives astonishing results in terms of disease diagnosis. DL can be considered as sub-class of representation learning techniques which has the ability to learn hierarchical feature representation from the raw images. Breaks can be considered as popular annotated data set used for breast cancer histopathological images[8]. It comprises of 7,909 microscopic images that are collected from 82 patients at P&D laboratory in Brazil. The below fig.1 gives a clear cut idea of histopathological images that belongs to BreaKHis dataset.

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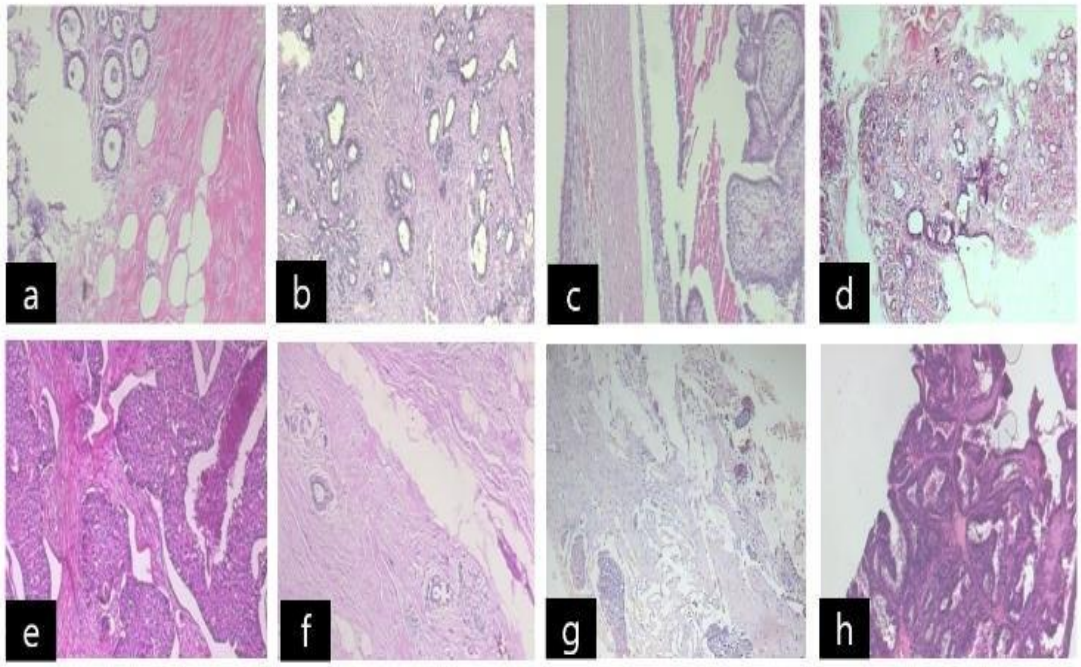

Fig.1 BreakHis dataset composed of benign and malignant images: benign [(a) : adenosis, (b) : fibroadenoma, (c) : phyllodes tumor, (d) : tubular adenoma], malignant [(e) : ductal carcinoma, (f) : lobular carcinoma, (g) : mucinous carcinoma, (h) : papillary carcinoma]

The structure of the paper is as described below.

i) SECTION II illustrates various DL concepts which are used for the analysis of histopathological images.

ii) Section III includes the survey of the papers which are essential for our study.

iii) Section IV describes various issues addressed by existing methods of DL techniques applied on Histopathological images. Then it is followed by possible future directions.

II. KEY CONCEPTS:

In this segment, a wide variety of Machine Learning concepts are described earlier. Further, we discuss deep learning techniques. Generally, Machine Learning [67, 68] concepts are categorized on the basis of trained data as supervised and unsupervised models. Methods build on DL are being permitted to be present in either of the above classification.

1. SUPERVISED LEARNING:

This model follows an assumption as particular training data is provided as a pattern of pair(x,y), such that $x \epsilon R^n$ can be considered as an example of training and y as its tag. Generally examples of the training set on distinct 'C' data classes. This process denotes y as binary vector residing in the class R^c, in such a way C^{th} coefficient as '1' if and only if x is belonging to the C^{th} class that leads to other coefficients as '0'. Finding the computational model μ with the assistance of training data is a major task of supervised learning. All imaginary data samples are referred to as data of test samples in ML leaflet. To learn a model that performs fruitful classification of test data, we make the formulation of our learning problem in the process of estimating of parameters of the model which minimarts a particular loss function $L(y,\hat{y})$.

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A forgiven test data frame, ŷ is described as a label vector estimated by the model. Then the cost of the predicted model is defined as the expected value of losses calculated for each and every data sample. DL learning framework provides learning model parameters that have the ability to obtain very low cost over huge data sets [7].

A.CONVOLUTIONAL NEURAL NETWORKS:

Convolutional Neural Networks (CNNs) [5], [9], [63] Fimparts a vital aspect in the relation of Deep Learning (DL) Techniques in the task of Medical Image Analysis. CNN contains three distinct layers as listed below: (a) Convolutional layers, (b) Pooling layers and (c) Fully connected layers.

(a)Convolutional layer:

The main objective of the convolutional layer is learning weights of convolutional kernels/filters, which performs convolution operations upon images. According to Conventional Image analysis, using the fore mentioned filters results in the extraction of a wide variety of image features. Sobel filter, which is used for detecting edges in images, can be considered as the prototype of such filter [10]. These filters ought to be constructed manually by setting weights of the kernel incautious way before the existence of CNN. The convolutional operation is demonstrated in Fig.2.This indulges shifting a tiny window (Kernel) on a 2D grid, in case of 2D settings, for example, grey-scale images. For every transition, the interrelated elements of both grids are multiplied then summed to figure out a scalar. By adding above operation outputs in one more 2D grid is often termed as feature map in the context of CNN leaflet. When it comes to 3D settings, a similar process is implemented for distinct pairs relating to 3D volumes. Then the obtained activation maps are combined to figure out a 2D map as terminal output. The below equation [26] represents the output s(t) when the convolution operation is performed between the inputs I(t) and filter K(a). The * symbol denotes convolution operation.

$$s(t) = (I*k)(t) \quad (1)$$

From Fig 3, it is precise to perform the computation of activation a_1(2D grids) with the following simple equation[7].

$$a = f(w^T x + b) \quad (2)$$

$x, w \in R^9$ are vectors determined by the arrangement of $w_1, w_2, \ldots, w_9$ and $x_1, x_2 \ldots x_9$ as residing in the Fig2. This term of bias is regularly neglected in the convolution layers; hence we do not represent it in the Fig3. By using multiple kernels to form a volume, at the output, the same concept can be applied to 3D volumes. Every individual activation map derived from a filter, thus intrudes as a distinct channel in the volume of output in the given convolutional layer. From the above scenario, it is clear that convolutional layer is resembling standard perception layer, with dual asymmetries as listed below.

i. The similar kernel connects input features to its activation signal. This leads in the process of sharing of kernel weights, which is often termed as parameter-sharing. Therefore kernels struggle to fine-tune their weights such that they reproduce efficiently to preliminary patterns of the whole input signal.

ii. by reason of similar kernel connects each and every input features to the activation; convolutional layers have fewer parameters to learn in the representation of kernel weights. Thus Sparsity of connection leads to very profitable learning compared to densely connected perception layers.

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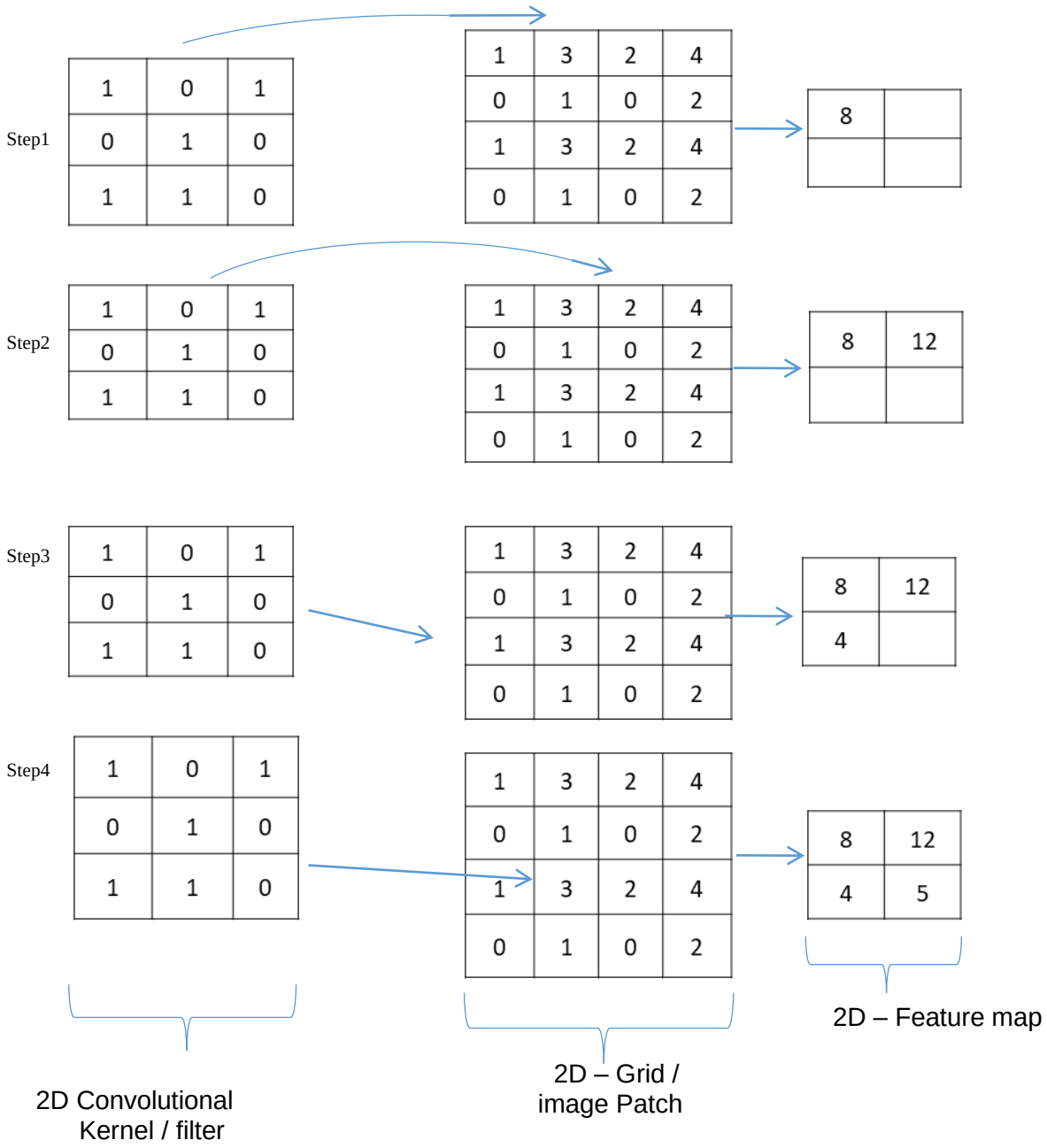

Fig2. Convolution on 2D grids

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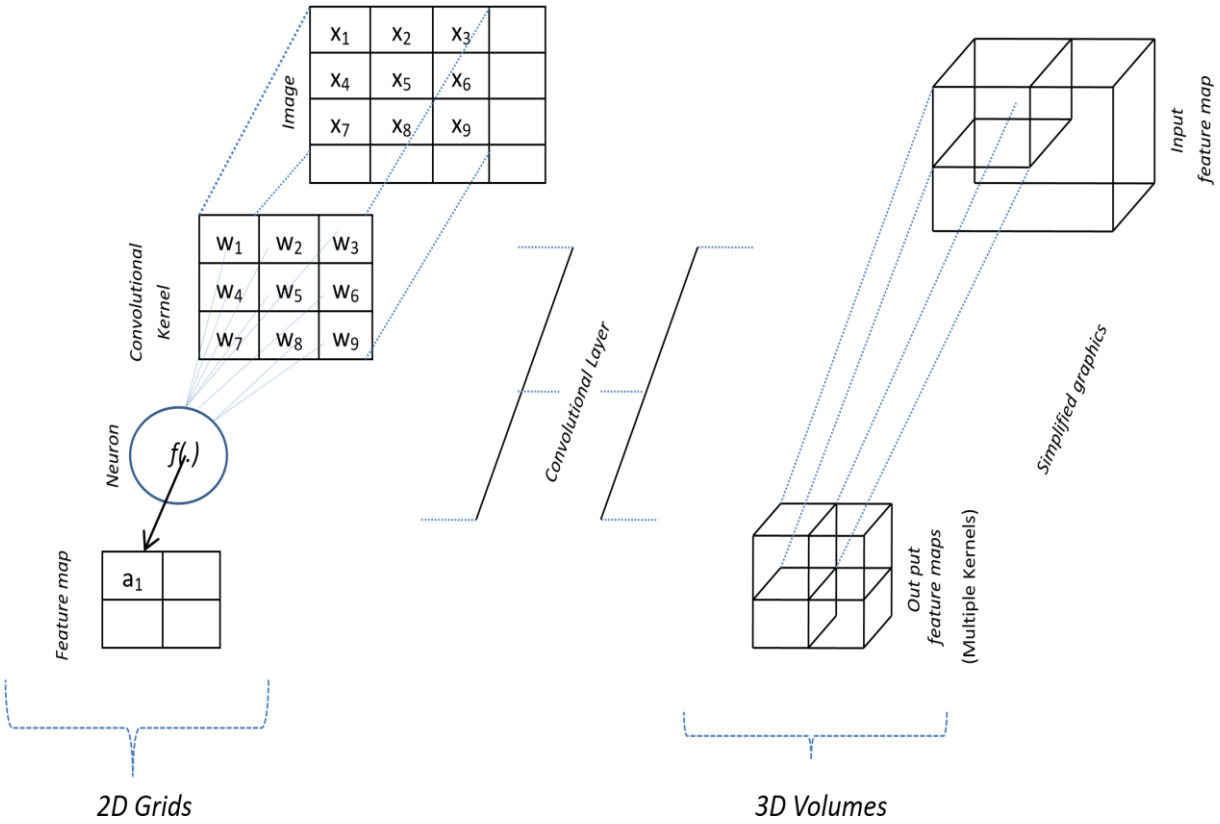

Fig 3. Working of Convolutional layer

(b) Pooling layers:

The Pooling layer works collectively to diminish the width and height of the activation maps residing inside CNN. For a minimal n_p x n_2 grid in the activation map, an individual output value 'v' is enumerated, v is nothing but maximum otherwise mean value of a particular grid in the respective activation map. According to the above operation performed, then the layer is termed as max-pooling or average pooling layer. For downsampling the detection of features in feature maps pooling layer is essential.

(c) Fully Connected Layers:

The terminal layer in a CNN is Fully Connected Layer; it defines that every neuron in the preceding layer is connected to every neuron in the FC-layers. Eventually, the feature maps from the deeper layer are refitted into the single vector, that is later fed to the FC-layer. The activation maps of FC-layers act on the point of better solid representations of the input signals.

B. RECURRENT NEURAL NETWORKS:

In general, RNN has been used in the analysis of sequential data, for instance, words in a given sentence. As they are capable of generating text [15], RNNs are occupied in text analysis tasks such as machine translation, speech recognition, text prediction and image caption generation [16]. In a simple RNN, the output of the layer is combined to the next input, and this fed back into the layer that results in an incapacity for contextual memory. In the mathematical terminology, if i_t denotes current information of timestamp, h_{t-1} is the previously hidden output, then the transition function updates the current hidden output with the following equation [58].

$$h_t = \mathbb{H}\ (x_t, h_{t-1}) \qquad (3)$$

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Here $\mathbb{H}$ is nonlinear and differentiable transformation function. Different transition function leads to several RNN models. One of the common models used is vanilla RNN [55] that can be represented with the following equation [58].

$$h_t = \varphi(Wx_t + Hh_{t-1} + b) \quad (4)$$

Here W & H represent the transformation matrices, b is the bias vector, and φ is the non- linear activation function. Long Short-term memory (LSTM) and Gated Recurrent Units (GRUs) came into existence to avoid the problem of vanishing gradients. These are variants of RNN that helps in holding long term dependencies and forget a few amounts of acquired information. Segmentation task of Medical Image Analysis uses RNN concepts effectively.

2. UNSUPERVISED LEARNING:

In unsupervised learning, it assumes that data samples are not available. Here the prominent objective of the computational model is to cluster the data samples into distinct clusters on the basis of common features. Even Unsupervised Learning take privilege of minimization of the loss function. Coming to DL leaflet, the loss function is built such that the model learns rigorous mapping of an input signal to input itself. The computation of solid representations of data samples is possible after the process of mapping. Unsupervised learning has found to work progressively under DL frameworks.

A. AUTOENCODERS:

The basic concept behind autoencoders is to map an input signal to itself using a neural network. We determine a latent representation of the data that is more robust for a specific task than original data provided. This representation could achieve efficient results when compared to raw data. The motive behind autoencoders is that the output data must be the same as the input data as possible. With input 'x' and hidden layer 'h' encoder [58] performs a nonlinear mapping as follows:

$$h = \varphi(Wx + b) \quad (5)$$

To retain original data, the decoder uses the following equation [58] for Reconstruction.

$$Z = \varphi(W'h + b') \quad (6)$$

AEs have been broadly utilized for segmentation and detection tasks of Medical Image Analysis. Several Trivial models are defined in mapping a signal to itself. Different types of AEs are developed that are relied on the basis of the technique applied for mapping. Under Complete AEs assure that dimensionality of the latent representation is much lesser than the original data. Stacked autoencoders are provided with an ideal architecture with the phenomenon that middle = hidden layer. Some optimization principles have been utilized for training weights of decoding, encoding layers also training distinct subsets of AEs before stacking them together [11]. In sparse autoencoders [12], a definite amount of neurons in the hidden layers have been set to zero. Other trendy AEs are Variational AEs [13] and Contractive AEs [14].

B. DEEP BELIEF NETWORKS :

DBNs contains multiple layers of Restricted Boltzmann machine. DBNs could be trained in the process of layer-by-layer fashion [54] in such a way that lower layers learn low-level features whereas high-level features are learnt from hidden layers, reflecting practical data hierarchy. Visible and hidden layers are the components of RBM's network architecture. The layers residing in DBNs are assembled with RBMs that are connected to each other in a cascaded fashion. The prominent features of DBN are as follows: i) In the training phase, learning occurs in step-by-step fashion towards successive layers. After the training of initial RBM, the resulting output vector obtained in the hidden layer of RBM is given as training data

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Received 24 October 2020; Accepted 15 December 2020.

to next RBM. The same phenomenon is followed by the next layers. ii) Coming to the reconstruction phase, the data flow is implemented with the help of the last output vector in the last layer from the last RBM to initial RBM determines the reconstruction vector. The energy function utilized in RBM's is mathematically represented in the equations 7 & 8, where 'x' is the visible layer, and 'h' is the hidden layer, and 'w' is the connection weight between visible and hidden layers [46].

$$E(x, h; \phi) = -\sum_{i=1}^{p} b_i x_i - \sum_{j=1}^{q} a_j h_j - \sum_{i=1}^{p}\sum_{j=1}^{q} x_i w_{ij} h_i \quad (7)$$

$$E(x, h; \phi) = -b^T x - a^T h - x^T W h \quad (8)$$

The partition function Z is represented in terms of mathematics with the help of the following equation [46] where $\emptyset = \{b_i, a_j, w_{ij}\}$ in that b_i and a_j are bias terms, w_{ij} is the connection weight from visible layer i and hidden layer j.

$$Z(\phi) = \sum_{x,h} E(x, h; \phi) \quad (9)$$

According to this model, the probability density function is represented by the following equation [46].

$$P(x, h; \phi) = \frac{e^{-E(x,h;\phi)}}{Z} \quad (10)$$

C. GENERATIVE ADVERSARIAL NETWORKS:

GANs [17] are widely used in natural image Analysis in the modern DL frameworks. GANs are addressed to simulate the distribution of generated data that is designed as a variant of AEs. The generator facilitates to generate a sample and discriminator categories it as fake or real. If the sample comes from training data, set it is considered as real. There is a requisite of gameplay between generator (G) and discriminator (D), where the generator keeps its effort to fool the discriminator through the generation of more and more real samples. The loss function [59] of GAN can be mathematically represented as follows.

$$\mathcal{L}_{GAN} = \mathbf{E}_{x\sim Pdata}(x)[\log D(x)] + \mathbf{E}_{z\sim Pz}(z)[\log (1 - D(G(z)))] \quad (11)$$

Henceforth generator keeps adjusting its parameters to outcome better samples inducing realism in synthetic images [18], domain adoption [19] and data completion [20] are applications of GANs, Implementing GAN for progressive Medical imaging domain has been discussed in the recent surveys [21], [22],[23].

III.DEEP LEARNING IN BREAST HISTOPATHOLOGICAL IMAGES:

Application of DL in Medical Image Analysis leads to the following pattern recognition tasks 1. Classification 2. Detection 3. Registration 4. Segmentation. For a detailed study, we can refer to the following articles [24], [25], [26]. These pattern recognition tasks are further sub-classified according to the component of the human body on which it is applied. Coming to breast histopathology images, we perform detection, segmentation and classification tasks.

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Received 24 October 2020; Accepted 15 December 2020.

1) DETECTION:

To determinate a specific Region of Interest in a particular image, we draw a bounding box around it is the main objective of detection. Coming to Leaflet of Medical Image Analysis detection is generally represented as Computer-Aided Detection. To identify the preliminary signs of abnormalities in patients, CAD systems have been used.

Xipeng et al. [27] proposed multi-scale Fully CNN approach for regression of density map that efficiently detects the nuclei of pathology and microscopic images. This method has been categorized into three components, namely Data Pre-Processing, Multi-Scale FCNN and Image Post Processing. In the process of training, they cropped patches from big size breast cancer histopathological images. To evaluate the performance, they have selected 160 images randomly out of 265 images as training sets to provide optimization of the detection algorithm. They have determined the relationship between the detection performance and the number of feature maps in FCNNs. The performance of the proposed 4-layer Multi-Scale CNN is relatively high when compared to 3- layer Multi-Scale CNN. Jun Xu et al. [28] developed Stacked Sparse Auto Encoder for progressive nuclei detection that works on high-resolution histopathology images of breast cancer. The principle subscription of his work is explained below.
(i) SSAE framework can convert the input pixel intensities into nuclei or non-nuclei representations. Hence this model is able to learn high-level structure information from a large number of unannotated image patches. Therefore, its entirely different from handcrafted methodologies that are based on low-level image information like color, texture and edge cues.
(ii) Since SSAE classifier is trained with unlabeled instances, the proposed framework used a hierarchical architecture that converts original pixel signal intensities into equivalent high-level structural information. This helps out in the evaluation of image patch in the classification stage denoting nuclei or non-nuclei patches. The proposed model has suggested that SSAE + SMC performs efficiently in learning favorable high-level features for growth nuclei representations. This framework, when compared to other prominent models like Expectation Maximization, Blue ratio Thresholding, CNN based nuclei detection methods, proves its efficiency in terms of accuracy. The developed model implements exact seed points or vertices in the development of cell-by-cell graph features that has the ability to describe features of cellular topology in the literature of tumor histology [29]. Nadia Brancati et al. [30] developed a DL approach for two different use case, namely Detection of Invasive Ductal Carcinoma in breast histopathological images and classification of lymphoma subtypes. Detection of IDC on WSI plays an active-active part in diagnosis and estimating tumor grading according to its aggressiveness. This methodology used the following synopsis 1. Classification by Reconstruction, and 2. Supervised Classification. A deep learning technique termed Supervised Encoder Fusion Net (SEF) had been used for learning histopathology images. This model has been developed on the basis of Residual CNN and SoftMax classifier. As they constrict the drawback of vanishing gradients SEF method is the fruitful derivation for detecting small cellular structures in histology images. When SEF method is compared with DNNs like Fusion Net, UNet it gives a significant improvement in IDC Detection.

2) SEGMENTATION:

The process of splitting an image into distinct substantial segments through automatic or semi-automatic outlining of boundaries within the image is referred to as segmentation. Generally, these segments are compatible with different types of tissues classes, pathologies, organs or any other biological structure [31] in the literature of MIA. DL techniques based on segmentation has become more robust since deep networks have the ability to learn very complicated functions that are essential for the tasks.

Jun Xu et al. [32] proposed a DCNN based feature learning which is helpful for automatic segmentation and classification of EP & ST regions from computerized tumor tissue arrays[TMA]. By applying DCNN as a feature extractor EP & ST tissues are directly learned from intensity values of the raw pixel in a data-

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driven fashion. Classifying EP & ST patches out of IHC stained images is a plain task that concentrates on allotting a single label to the corresponding patch. But the task of segmenting EP & ST areas is comparatively complicated as it objects to find the ROIs and further attach the label to the respective ROI. The architecture utilized for this study constitutes of two convolutional layers, max-pooling layers, two fully connected layers and final classifier layer, when this approach is compared to other handcrafted features-based methods, DCNN based architecture gives more accurate results. Nuh Hatipoglu [33] compared the outstanding DL architectures like CNN, SAE and DBNs with familiar ML techniques SVM and RF in the leaflet of histopathological cell segmentation. In consideration of cell structure that is spatially coherent in local regions of images [34], [35], this study added spatial relationships. For obtaining progressive accuracy rate in segmentation spatial data would be much helpful. The proposed model tells that segmentation accuracy is directly proportional to window size. With the incorporation of spatial and contextual data into larger local windowing, the obtained features of cellular and extracellular patches grow into highly selective type in the aspect of pattern recognition and ML. In the design of CAD, the task of segmentation acts as a principal work. The proposed study used spatial and contextual alignments of cellular and extracellular pixels in the process of cell segmentation which has been applied on digital images by developing a window structure that accommodates neighbors of the pixel in discrete window sizes. It also determines that the application of DL methods provides encouraging CAD methods in evaluation of histopathological images

3) CLASSIFICATION:

Image Classification has been considered a persistent problem in the field of MIA. In the leaflet of Medical Imaging, Classification is an intrinsic task for CAD. Medical Image Classification helps doctors to identify and distinguish the image recognition area. DL models have been widely used in various medical image classification tasks.

Xing Li [36] developed a model that mines dissimilar patterns separating normal and malignant images, then procreate a probability map with abnormalities to validate its interpretation. In this study, he used Fully Convolutional Autoencoder to learn prevalent structural patterns presented on the regular image patches. With the help of One-Class SVM and one-layer Neural Network, patches which do not claim the features of these normal images are detected. The developed model used a new Convolutional AE based contrast mining technique to identify invasive segments of malignant breast epithelial growth in normal H&E stained histopathology images. It also strived hard to solve the problem of Self-Interpretability in breast cancer diagnosis. This method obtains a probability map to figure out traces of abnormalities of an image through the mining of prevalent patterns in images. To simplify local characteristics learning, this method splits an image into tiny patches. The model initially performs Reconstruction of image patches by utilizing loss functions SSIM and MSE. Then the generated features are visualized via contrast pattern mining. As the developed model is not much reliable on particular malignant image samples, it achieves Generalizability. Suspicious regions of malignant cell clusters in a particular image can be detected by the proposed method with the help of contrast mining amidst normal and malignant images. Compared to Spanhol's method [37] and Ajuro's method [38], the proposed method improves its efficiency in terms of practicality, Generalizability, classification accuracy and self-interpretability. P.J.Sudarshan et al. [39] developed a MIL benchmark which provides a better improvement in tasks of patient and image classification. The task of data annotation is very pricey. This problem has been solved by classic MIL framework by arranging instances into bags, which removes the necessity of labelling for each and every instance. This study propagates how MIL corresponds to the CAD system by analyzing breast histology images. MIL can be interlinked with specific application and provided dataset in two distinct scenarios (i) Image as a bag: Splitting images into sub-images or patches then ponder image as a bag, where the instances are patches. (ii) Patient as a bag: With the instances correlated with the number of images or piece of images termed patches, the patient is referred to as a bag. General Assumption of MIL is that positive bag comprises of at least single positive instance whereas negative bag comprises of only

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negative instances. When compared to Diversity Density (DD) methods, SVM based approaches the proposed method gives more efficient classification accuracies through Non-Parametric MIL approach. Thus the developed MIL framework contributes to improving Computer-Aided Diagnosis through classification and analysis of digital histology images. Sana Ullah Khan et al. [40] proposed a deep learning model that used transfer learning in the detection and classification of breast images. To reduce contrasting noises in tissue images, it is necessary to perform a pre-processing step. In this study, H&E stains are normalized with the method in [41]. Using the familiar CNN architectures like GoogleNet[42], VGGNet[43], and ResNet[44] the proposed model obtains different low-level features. Also, the developed model applied data augmentation in order to boost up the dataset and diminish the problems of over-fitting [5], [45]. The aforementioned architectures of CNN are utilized to distribute their characteristics on transfer learning and fine-tuning. The developed robust architecture yields more efficient results in terms of accuracy when compared to other methods.

Table 2. Different DL methods used in Breast Cancer Histopathological Images.

REFERENCE	YEAR	TASK	DATA SET	DL ARCHITECTURE
Brancati et al. [6]	2019	IDC Detection & Lymphoma Classification	Lymphoma & IDC dataset (Public Available)	SEF method
Radulovic et al. [36]	2019	Classification	Breast Cancer Benchmark dataset	Fully Convolutional AE
Hatipoglu et al. [46]	2016	segmentation	Harvard dataset; UCSB dataset	CNN SAE DBN
Wang et al. [47]	2019	Classification	BreakHis Dataset	Deep Learning Active Framework
Xiang et al. [28]	2015	Detection	Anonymous	SSAE, SMC
Gilmore et al. [32]	2016	Classification & Segmentation	Acquired from ANKI, VGH.	DCNN
Sudharshan et al. [39]	2018	Patient & Image Classification	BreakHis	MILCNN

Annals of R.S.C.B., ISSN:1583-6258, Vol. 24, Issue 2, 2020, Pages. 117 - 132
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Khan et al. [40]	2019	Detection & Classification	BreakHis	GoogleNet, VGGNet, ResNet
Wan et al. [48]	2016	Nuclei Segmentation Feature & Extraction	Anonymous	Multi-class SVM; CNN
Bardou et al. [50]	2018	Classification	BreakHis	CNN
Li et al. [49]	2019	Classification	Bioimaging 2015	CNN, ResNet50

The below figure illustrates the performance comparison of different deep learning techniques applied to histopathological images of breast cancer.

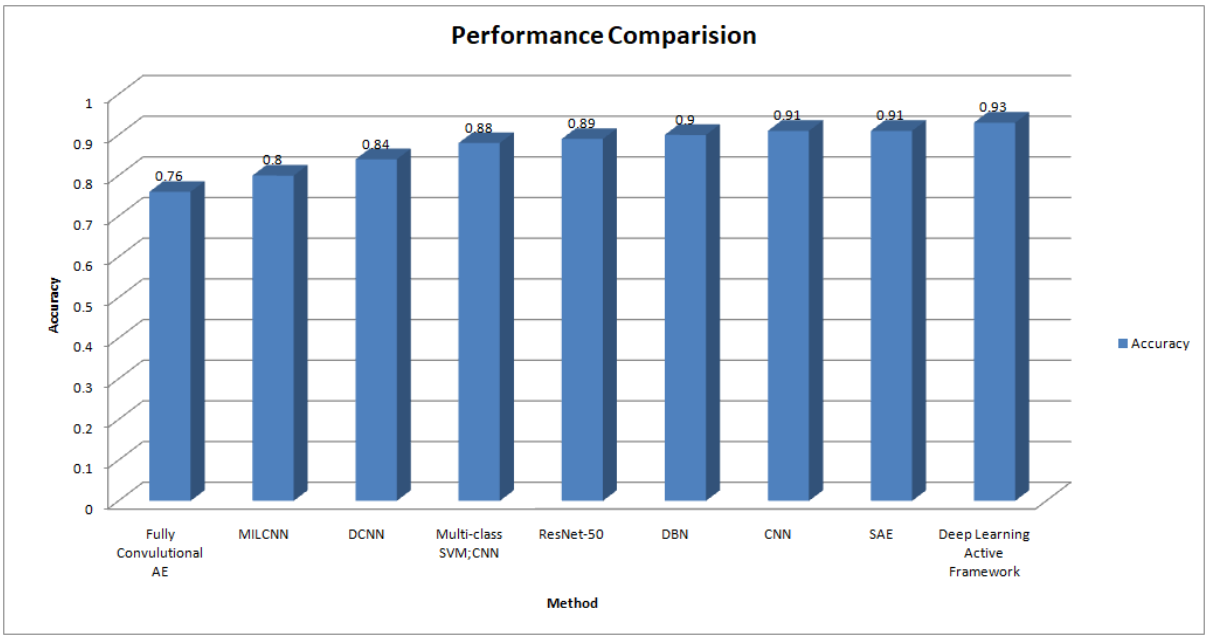

Fig4: Performance comparison of DL techniques.

IV.CONCLUSION:

In the medical imaging domain, the available public datasets are not massive, though it is needed specification for training efficient deep learning [51]. The regular clinical practice could not assign proper essential annotations for DL Frameworks. DL that works on lesser amounts of data could be able to solve the above-mentioned issues. Concurrently making the available public datasets to large scale could also make the DL work efficiently. Imbalanced data could be another issue faced by any medical imaging data that is trained on deep networks. Balancing out the original data will become a difficult task if the recurrence of positive samples is less. By keeping effort on CAM [52] and grad – CAM [53] it will be helpful to interrogate on future deep diagnosis system. By combining SSAE and cell-graph based methods helps in improving the feature extraction of breast histological images [29]. After undergoing mammographic screening [60], some doubtful malignant abnormalities are further performed a biopsy to have detailed information. Most of the cases it was observed that the biopsy was useless, to reduce

unnecessary biopsies, a novel algorithm could be developed which can provide a biological association between histology & mammography. This model could be worked out with the help of DL frameworks which would provide more efficient results.

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