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MACHINE LEARNING APPROACHES FOR CLINICAL DIAGNOSIS: LEUKEMIA

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Abstract

Leukemia is a cancer of blood cells that affects both children and adults. The morphological structure of leukemia cell and a normal cell is very similar thus posing a great challenge for the medical practitioner for an accurate diagnosis. Machine learning approaches can be applied to the classification of malignant cells.

I. Introduction

The term *"Machine learning"* was coined by "*Arthur Samuel" in* 1959 while working at IBM as "the field of study that gives computers the ability to learn without being explicitly programmed". ML discovers the new trends and algorithms can be developed that will be trained on the data to make the predictions models [1]. Machine learning approaches are becoming very popular in medical diagnosis and are widely used in the past for the prognosis of clinical disorders such as neurodegenerative disorders [2][3][4], cancer [5], diabetes [6], heart disorders [7], lung disorders [8], etc. The primary concern of ML is to develop AI systems in the field of medical science that can assert a medical practitioner in performing clinical diagnosis. These ML approaches by making use of various soft computational techniques find out the unseen patterns from the training data and these patterns can be used to classify the data into various categories. These systems depend on the various datasets obtained from the different clinical cases which can be used for the training of these systems. With the development in computer technology, ML along with many other Artificial Intelligence approaches has become the leading player in solving many complex problems of the healthcare industry [9]. In particular, ML provides the most promising solutions to various biomedical problems by creating the classifier systems that can aid medical practitioners in the diagnosis of medical disorders at early stages.

Leukemia is a hematological malignancy that develops in the bone marrow that affects white blood cells. Bone marrow is a gelatinous tissue inside some of the bones that makes blood cells and stores fats.

Figure 1

The cause of leukemia is the abnormal growth of white blood cells which spreads quickly into the blood and other organs like spleen, nervous system, etc. In general, leukemia is broadly grouped as either acute or chronic based on how quickly the number of malignant cells develops (fast or slowly) and the type of WBC affected.

The most common type of leukemia is Acute Myeloid Leukemia (AML), Chronic Lymphocytic Leukemia (CLL), Chronic Myeloid Leukemia (CML), Acute Lymphoblastic Leukemia (ALL) [10] [11][47].

Table 1: Common Leukemia Types [48]

	Lymphocytic leukemia	Myelogenous leukemia
Acute	Acute lymphoblastic leukemia (ALL)	Acute myeloid leukemia (AML)
Chronic	Chronic lymphocytic leukemia (CLL)	Chronic myeloid leukemia (CML)

Leukemia is the type of cancer mainly found in children whereas CML mostly affects adults and CLL is rarely seen in children. ALL and AML are the most fatal types of cancer if not diagnosed at the right time.

ALL also called acute lymphoblastic leukemia and acute lymphoid leukemia occurs due to the growth of leukemia cells (white blood cells) in the bone marrow [15][16]. ALL develops very fast by replacing healthy RBC which produces lymphocytes with immature abnormal cells (leukemia cells). Leukemia cells spread through the bloodstream to other parts of the body and organs namely brain, lymph nodes, liver, lungs where they multiply aggressively. There are two main subtypes of ALL, B-cell ALL and T-cell ALL. ALL may lead to anemia due to the

aggressive growth of white blood cells (WBC) [13]. ALL frequently occurs in people below 15 years of age and above 45 years of age. According to the American Cancer Society, it is estimated that there are 5930 new cases of ALL and 1,500 deaths due to ALL in America [14].

AML well known as acute myelogenous leukemia or acute myeloblastic is a malignant disease of bone marrow that grows very fast. In AML, bone marrow aggressively produces abnormal red blood cells and these leukemia cells suppress the normal healthy cells, RBC and platelets that the body requires. AML is categorized as M0 through M7 by FAB leukemia experts based on cells from where leukemia develops and maturity of the cells [17]. The occurrence of m0 - m5 starts in premature WBC whereas M6 is immature RBC while M7 starts in immature blood cells that form platelets.

Chronic myeloid leukemia (CML) is a slow-growing cancer where genetic change takes place in immature myeloid cells which are responsible for the formation of RBC, platelets, and other types of WBC. Abnormal gene BCR-ABL develops due to this change which transforms the cells into a CML cell. CML mostly affects the adults but very rarely occurs in children, too. Chronic lymphocytic leukemia (CLL) develops in normal cells that turn into abnormal WBC. In CLL, leukemia cells develop slowly and with time, spread into the parts of the body through the bloodstream.

Machine learning algorithms are applied on medical datasets to diagnose the disease based on the previous knowledge of the disorder, however, retrieving relevant information from histopathological data is challenging due to its complex nature. Leukemia, if diagnosed at the initial stage is curable and increases the lifespan of the patient. Since the morphology of malignant cells and normal cells are very similar making it difficult for medical practitioners to identify. Therefore, the development of a robust system for the classification of leukemia cells is required for early treatment.

II. Literature Review

The literature associated with the proposed topic of the research is available from different sources. Some indispensable sources that contribute to a review of the literature regarding this research topic include articles, research papers, and books. The abstract of some research papers based on ML approaches and medical diagnoses are as follow:

Sharma et al., 2019[18] presented a novel PCA based ABC-BPNN for the classification of leukemia cells which gives better results than GA-BPNN and reduces the computation time. Jothi et al., 2019[19] applied BSA- based clustering for image segmentation and reduced the dimension of features using STRSPSO-QR, STRSPSO-RR and STRSFF-QR.proposed that Jaya algorithm when applied to standard classification techniques like Naïve Bayes, decision tree, SVM, KNN, ensemble random under-sampling boost increases the accuracy but gives better

accuracy when used SVM and decision tree. Acharya et al., 2019[20] proposed an automated algorithm with K-medoids for predicting the stages of ALL-1, ALL-2, AlLL-3. A three-stage model including nucleus segmentation, splitting of touching nucleus, and segmentation K-medoid give better accuracy as compared to KNN, Naïve Bayes and decision. Mishra et al., 2019[21] proposed an LDA based PCA model for predicting leukemia by making use of DOST for feature extraction of microscopic images. Tuba et al., 2019 [22] applied GAO for fine-tuning the parameters of SVM for the classification of lymphocytes and achieve higher accuracy when compared with ANN, KNN, SVM, and Naïve Bayes. Naz et al., 2019 [23] applied 8 layer CNN model for the classification of leukemia cells on LISC and Druv's and achieve accuracy of 96.9% and 81.9% respectively. Al-jaboriy et al., 2019[24] developed an automated leukocyte cell segmentation process using ANN and applied GA to extract the features. Promising results were shown compared to watershed and MBS techniques.

Ramya et al., 2019 [25] assessed a few most available techniques of leukemia classification and suggested that better accuracy is obtained for ALL and AML rather than on its subtypes classification. Jha et al., 2019 [26] developed novel chronological SAC based deep CNN for the segmentation and leukemia identification and evaluated its performance based on state of art ML techniques with TPR and TNR. Jung et al., 2019 [27] proposed a CNN based W-Net architecture for the classification of five types of white blood cells (WBC). Pansombut et al., 2019 [28] experimented with CNN classifiers to identify the lymphocytes that deliver better performance to identify normal WBC and pre-B cells. Boldu et al., 2019 [29] experimented LDA classifier with the novel color clustering segmentation framework for the recognition of blasts and different types of acute leukemia. Alférez et al., 2019 [30] developed a color clustering segmentation framework that separates the nucleus, cytoplasm and other zones from the cell and applied the same for the classification of malignant lymphoid.

Moraes et al., 2019 [31] proposed a Decision-tree approach for the diagnosis of various lymphomas and Lasso algorithm was used to avoid overfitting and regularization. Liu et al., 2019 [32] proposed a two-stage bagging ensemble approach for the classification of ALL cells and HEM cells. Kutlu et al., 2019[33] examined different CNN architecture for the detection of WBC based on deep learning and transfer learning. Resnet50 CNN showed better efficiency than AlexNet, GoogleNet, and VGG16. Kumar et al., 2018[34] devised an automated method for leukemia detection by applying K-mean clustering for feature extraction and segmentation. It shows the promising result when used with kNN and Naïve Bayes.

Vogado et al., 2018 [35] applied three pre-trained CNN architectures for feature extraction and used SVM without the segmentation process for leukemia classification on the hybrid database. Rehman et al., 2018 [36] contributed a robust segmentation technique applied with Alexnet-CNN for the classification of L1, L2, L3. Thanh et al., 2018 [37] used 7 layer CNN on the augmented dataset of leukemia cells for their classification. Moshavash et al., 2018 [38] designed an

effective segmentation technique based on background reduction and developed two ensemble classifiers with SVM for the classification of malignant and healthy leukocytes. Tosta et al., 2018[39] analyzed the fitness function of GA for unsupervised segmentation algorithm and identified Renyi entropy is most suitable for the classification of CLL and FL nuclei. Abdeldaim et al., 2018 [40] implemented the classification model by applying the Zack technique for segmentation followed by data normalization techniques for feature extraction. Applied different classifier methods and concluded that kNN achieves the best classification accuracy. Abinash et al., 2018 [41] analyzed the leukemia gene dataset using correlation and wrapper based SVM for the classification of malignant cells.

Mirmohammadi et al., 2018[42] presented a model for the classification of ALL and its subtypes using SVM, Multi-SVM and feature reduction by PCA. Umamaheswari et al., 2018[43] applied a customized kNN approach for the recognition and detection of ALL. Agaian et al., 2016[44] presented a whole image classification approach for detecting ALL by using a new cell energy feature with SVM. Mohapatra et al., 2016[45] discussed the use of ensemble classifiers for the characterization of ALL subtypes from peripheral blood samples (PSB) based on FAB. Rawat et al., 2071{46] experimented kernelized methods with GA for detecting leukemia subtypes M2, M3, M5 and L1, L2, L3 based on FAB classification.

III. **Image classification steps of malignant cells**

Image processing and ML techniques are widely used in the field of medical science for the analysis of hematological images. The standard steps applied for the efficient classification of leukemia are:

1) **Data Acquisition:** It is the process of acquiring the cell images of both healthy and leukemia patients from the various pathological sources. The tissue cells are obtained using the fine needle aspiration (FNA) method from the bone marrow of the patient and smeared on a slide followed by the standard staining methods. Then, the cell images are generated by the expert medical practitioner using the microscope under different magnification and illumination conditions.

2) Pre-Processing: The pre-processing task aims to enhance the image data by suppressing the unwanted distortions generated by the microscope. Image quality can be further enhanced by applying geometric transformations. Artificial images can be created through image augmentation such as random rotation, flips, shear, etc to increase the dataset.

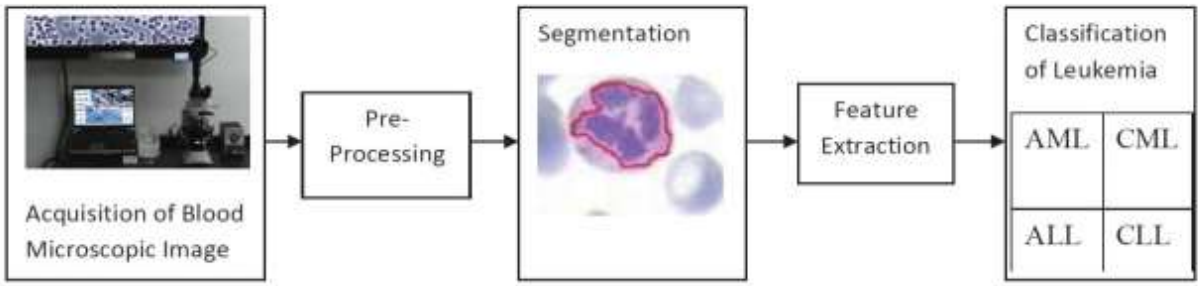

Figure 2

3) Image Segmentation: The main task of image Segmentation is to create the multiple partitions of a digital image and is used to identify the region of interest. Clustering, threshold, edge detection, region growing, and histogram-based methods, etc of segmentation techniques can be used to obtain leukemia cells from the microscopic image.

4) Feature Extraction: It is applied to reduce the dimensionality of the data set into manageable groups for further processing. Here, the texture, contours, geometrical and statistical characteristics of the leukemia cell are extracted from the sub-images which are suitable for the classification process.

5) Diagnosing and classification of Leukemia: Leukemia and its sub-types can be identified using various ML algorithms. These algorithms will classify the malignant cells and non-malignant cells.

IV. **Conclusion**

In this paper, various ML approaches for the diagnosis of leukemia and its subtypes were studied. Few most normal ML techniques have been used by different authors on the public dataset giving promising results. Natured inspired computing algorithms when applied with existing and novel ML techniques enhance the efficiency of the system. Larger leukemia dataset should be developed to avoid overfitting.

V. Table 2- Representation of ML approaches

Author	**Dataset**	**Methodology**	**Accuracy**

Author	Dataset	Methodology	Accuracy
Sharma et al., 2019 [18]	UCI database having 85 samples of leukemia	PCA based ABC-BPNN	98.72%
Jothi et al., 2019 [19]	ALL-IDB with 300 images	Hybrid classification method using Jaya algorithm and existing classification techniques	99% Jaya + SVM 98% Jaya + decision tree
Acharya et al., 2019 [20]	ALL- IDB 600 Images	K-medoids algorithm	98.6%
Mishra et al., 2019 [21]	ALL- IDB1	DOST+PCA+LDA model for feature extraction	99.66%
Tuba et al., 2019[22]	ALL- IDB2 260 images	GAO based methods	93.84%
Naz et al., 2019[23]	LISC and Dhruv's	CNN	96.9% 81.9%
Al-jaboriy et al., 2019[24]	ALL-IDB1 108 images	GA and ANN	97.07%
Ramya et al., 2019[25]			
Jha et al., 2019[26]	ALL-IDB2	SCA based deep CNN	98.7%
Jung et al., 2019[27]	6562 images CU, Korea	CNN based W-Net	97%
Pansombut et al., 2019 [28]	ASH image bank, ALL-IDB1	CNN based ConVnet	81.74%

Author	Dataset	Methodology	Accuracy
Boldu et al., 2019[29]	442 Smears	LDA classifier with a novel automated segmentation framework	85.8% and 94%
Alférez et al., 2019[30]	4578 images	Color clustering segmentation framework	92.24%
Moraes et al., 2019[31]	283 Smears	Decision-tree approach	95%
Liu et al., 2019[32]	C_NMC 2019 10661 images	Two-stage bagging ensemble approach	88%
Kutlu et al., 2019[33]	BCCD and LISC 652 images	SVM with pre-trained CNN	99%
Kumar et al., 2018[34]	60	K-mean clustering algorithm wit kNN and Naïve Bayes.	92.8%
Vogado et al., 2018[35]	Heterogeneous database ALL-IDB1, ALL-IDB2 1268 images	Pre-trained CNN with SVM without segmentation	99%
Rehman et al., 2018[36]	Amreek Clinical laboratory Swat KP Pakistan 330 images	Novel segmentation method with Alexnet-CNN	97.78%
Thanh et al., 2018[37]	ALL-IDB1 108 images	CNN	96.6%

Author	Dataset	Methodology	Accuracy
Moshavash et al., 2018[38]	ALL-IDB1, ALL-IDB2, Dr. Juan Bruno Zayas Alfonso Hospital, Santiago de Cuba.	Two ensemble classifier with SVM	89.81%
Tosta et al., 2018[39]	74 images	Unsupervised segmentation algorithm with GA	98.14%
Abdeldaim et al., 2018[40]	ALL-IDB2 260 images	kNN	
Abinash et al., 2018[41]	UCI	Wrapper basedSVM	94.26% 97.13%
Mirmohammadi et al., 2018[42]	21 Blood smears	SVM with PCA	
Umamaheswari et al., 2018[43]	ALL-IDB2 80 images	Customized kNN	96.25%
Agaian et al., 2016 [44]	ALL-IDB1 98 images	Cell Energy Feature with SVM	94%
Mohapatra et al., 2016[45]	SCB Medical College, Cuttack, India	Ensemble classifier	97.37%
Rawat et al., 2071{46]	ASH 420 images	GA with SVM	97.1% ALL 98.5 % AML

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