A Comprehensive Survey on Machine Learning Based Automated Detection of Blood Cancer

Anuja Pawar[1], Prof. Priyanka Prajapati[2]
[1, 2] Department of Computer Science and Engineering
[1, 2] Alpine Institute of Technology, Ujjain, India

Abstract- *Blood Leukemia is one of the most deadly diseases in the world with one of the most deadly mortality rates. The detection of blood leukemia at early stages is extremely difficult owing to the fact that leukemia's symptoms do not manifest themselves completely early. Off late, artificial intelligence is being used in several applications of healthcare which are complex to be handled by conventional or traditional techniques. One such domain is the automated classification of leukemia using artificial intelligence based techniques. The study of previous work in the domain shows the fact that the classification accuracy is an extremely important parameter related to automated leukemia classification and attaining high accuracy is a difficult task. Several approaches have their pros and cons in this regard. This paper presents a comprehensive analysis of the various machine learning based approaches employed for automated blood leukemia detection, highlighting the salient features of each approach.*

Keywords- Blood Leukemia, Microscopic images, machine learning, automated classification, classification accuracy.

I. INTRODUCTION

Blood Cander or Leukemia is one of the most dreaded diseases in the world with a high mortality rate. The incidence has been prevalent to a great extent and comes up with very common symptoms at the initial stage of the illness. It is seen that quicker detection of the disease leads to better treatment possibilities and success of the treatment [1]. There has been rampant technological advancement in the field of image processing and allied technologies that have led to improved medical image clarity and has aided in better diagnosis. Hence this domain of medical technology and classification of the cancer, the type i.e. benign or malignant etc have seen increase in in-depth research and study. The improved and efficient image services increases the accuracy and efficacy of diagnosis. Effective treatment can happen when the disease is detected quickly and accurately. This is possible with high end medical diagnosis and accuracy of diagnosis in less time. Consequently, modern techniques have become the go-to option for the evaluation and detection of this serious blood cancer cases that can predict it accurately and faster than other conventional methods [2].

Blood leukemia is form of cancer that exhibits uncontrolled growth of the white blood cells and is potentially very serious and life threatening form of blood cancer. For detection of the disease, images of the blood samples have to be evaluated by a hematologist for any other than normal feature. The images of blood samples are microscopic in nature and therefore correct diagnosis and identification is dependent on the accuracy and clarity of the images long with the expertise of the hematologist. Serious problem can arise if the images are erroneous because it can lead to incorrect line of diagnosis and incorrect treatments [3]-[4].. Hence this a major concern for accurate diagnosis and detection and proper identification of microscopic images of the blood samples. Time factor is also a major concern and the quicker is the diagnosis done, there is better treatment probability for the illness. Computer aided diagnosis system is an active tool used for early detection but 10%-30% of patients who have the disease and undergo diagnosis have negative classification. Two-third of these false negative cases was evident retrospectively. These mistakes in the visual interpretation are due to poor image quality, eye fatigue of the radiologist, subtle nature of the findings, or lack experienced radiologists especially in third-world regions. Nowadays the computer-aid systems play the main role in early detection and diagnosis of blood leukemia. Increasing confidence in the diagnosis based on computer-aid systems would, in turn decrease the number of patients with suspected blood cancer who have to undergo surgical blood biopsy, with its associated complications.

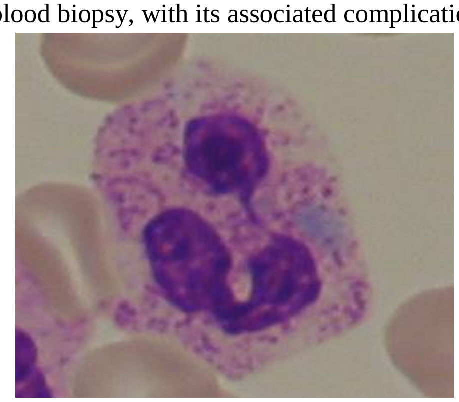


Fig. 1 A typical microscopic image [4].

Since detection of blood leukemia in extremely challenging, and yet critically important, hence the motivation of the proposed work is to detect blood leukemia cased with high accuracy. Since manual inspection and detection is prone to errors, automated detection is a strong alternative or at least can cast a strong second opinion. For this purpose, use of Artificial Intelligence and Machine Learning is proposed with an aim to detect blood leukemia cases successfully. The paper is divided into the following parts discussing different aspects of the automated detection mechanism.

II. AUTOMATED DETECTION OF LEUKEMIA

The automated detection of leukemia is challenging due to the following reasons:

The disease is a very fatal one if it is not detected and treated in time. This form of cancer has many variants based on the type of cells showing improper behavior and function. Basically the lymphoid cells and the myeloid cells become affected in this illness resulting in the respective types of the disease [5].

Also based on how rapidly is the growth of cells, it can be classified into grades and also into chronic or acute. The chronic form of the illness, it progresses slowly and not very aggressively. But with the case of the acute version of the disease, it aggravates very fast and needs immediate treatment [6]. Hence a major aspect of this illness and solution is very fast line of action in terms of diagnosis as well as treatment.

The symptoms as discussed earlier are of very common types that cannot be guessed immediately. And many a times the illness is asymptomatic and does not show any symptom which is when the detection becomes even more difficult. Also as there are major symptoms that is observed, so the classification of the images of the blood samples also becomes improper and non conclusive.

The microscopic image of the blood has to have a lot of clarity and precision so that the medical expert can detect any tiny variation in the sample of the blood. This detection and evaluation phase is immensely important and has to be performed without any dint of error otherwise the entire thing could go wrong including the treatment. Therefore a mechanism is needed that can detect the images clearly and also the clarity of medical images has to be maintained so that the entire process is accurate and on point [7]-[8].

Based on the image processing and feature extraction, the classification is done. Automated classification requires training a classifier with the pre-defined and labelled data set and subsequently classifying the new data samples. Off late machine learning based classifiers are being used for the classification problems. Machine learning can be crudely understood as the design of automated computational systems which mimic the human behaviour and can be trained in the sense that they can learn from data fed to the system. Primarily machine learning is categorized into three major categories which are [13]-[15]:

1) Unsupervised Learning: In this approach, the data set is not labelled or categorized prior to training a model. This typically is the most crude form of training wherein the least amount of apriori information is available regarding the data sets.
2) Supervised Learning: In this approach, the data is labelled or categorized or clustered prior to the training process. This is typically possible in case the apriori information us available regarding the data set under consideration.
3) Semi-Supervised Learning: This approach is a combination of the above mentioned supervised and unsupervised approaches. The data is demarcated in two categories. In one category, some amount of the data is labelled or categorized. This is generally not the larger chunk of the data. In the other category, a larger chunk of data is un-labeled and hence the data is a mixture of both labelled and un-labeled data groups.

Some other allied categories of machine learning are:

4) Reinforcement Learning
5) Transfer Learning
6) Adversarial Learning
7) Self-Supervised learning etc.

While these learning algorithms can be studied separately, however they are essentially the modified versions of unsupervised, supervised and semi-supervised learning architectures. A more advanced and useful category of machine learning is deep learning which is the design of deep neural nets with multiple hidden layers.

Machine learning based classifiers are typically much more accurate and faster compared to the conventional classifiers. They render more robustness to the system as they are adaptive and can change their characteristics based on the updates in the dataset [16]. The common classifiers which have been used for the classification of pests are:

Regression Models: In this approach, the relationship between the independent and dependent variable is found utilizing the values of the independent and dependent variables. The most common type of regression model can be thought of as the linear regression model which is mathematically expressed as [15]:

$$y = \theta_1 + \theta_2 x \quad (1)$$

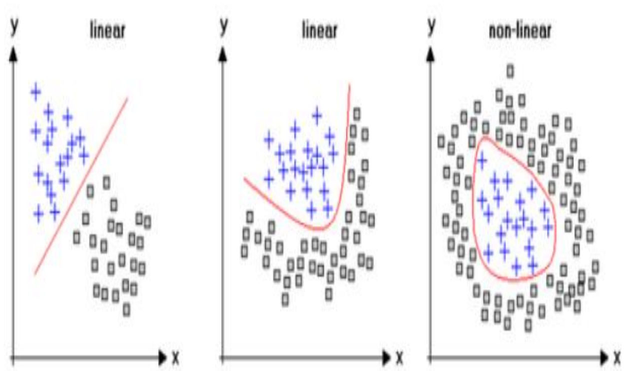
Here,
x represents the state vector of input variables
y represents the state vector of output variable or variables.
Ɵ1 and Ɵ2 are the co-efficients which try to fit the regression learning models output vector to the input vector.

Often when the data vector has large number of features with complex dependencies, linear regression models fail to fit the input and output mapping. In such cases, non-linear regression models, often termed as polynomial regression is used. Mathematically, a non-linear or higher order polynomial regression models is described as:

$$y = \theta_0 + \theta_1 x^3 + \theta_2 x^2 + \theta_3 x \quad (2)$$

Here,
x is the independent variable
y is the dependent variable
$\theta_1, \theta_2 \ldots \theta_n$ are the co-efficients of the regression model.

Typically, as the number of features keep increasing, higher order regression models tend to fit the inputs and targets better. A typical example is depicted in figure 2



Support Vector Machine (SVM): This technique works on the principle of the hyper-plane which tries to separate the data in terms of 'n' dimensions where the order of the hyperplane is (n-1). Mathematically, if the data points or the data vector **'X'** is m dimensional and there is a possibility to split the data into categories based on **'n'** features, then a hyperplane of the order **'n-1'** is employed as the separating plane. The name plane is a misnomer since planes corresponds to 2 dimensions only but in this case the hyper-plane can be of higher dimensions and is not necessarily a 2-dimensional plane. A typical illustration of the hyperplane used for SVM based classification is depicted in figure 3.

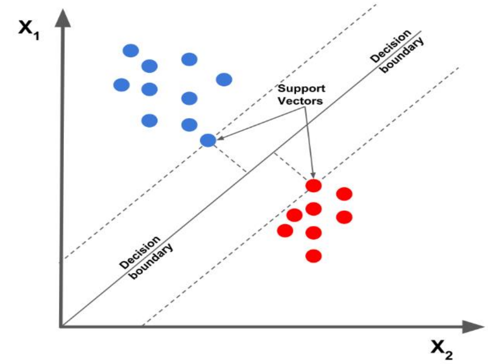


Fig. 3 Separation of data classes using SVM [15]

The selection of the hyperplane H is done on the basis of the maximum value or separation in the Euclidean distance d given by:

$$d = \sqrt{x_1^2 + \cdots \ldots \ldots . x_n^2} \quad (3)$$

Here,
x represents the separation of a sample space variables or features of the data vector,
n is the total number of such variables
d is the Euclidean distance

The (n-1) dimensional hyperplane classifies the data into categories based on the maximum separation. For a classification into one of 'm' categories, the hyperplane lies at the maximum separation of the data vector 'X'. The categorization of a new sample 'z' is done based on the inequality:

$$d_x^z = Min(d_{C1}^z, d_{C2}^z \ldots d_{C2=m}^z) \quad (4)$$

Here,
d_x^z is the minimum separation of a new data sample from **'m'** separate categories
$d_{C1}^z, d_{C2}^z \ldots d_{C2=m}^z$ are the Euclidean distances of the new data sample **'z'** from m separate data categories.

Neural Networks: Owing to the need of non-linearity in the separation of data classes, one of the most powerful classifiers which have become popular is the artificial neural network (ANN). The neural networks are capable to implement non-linear classification along with steep learning rates. The neural network tries to emulate the human brain's functioning based on the fact that it can process parallel data streams and can learn and adapt as the data changes. This is done through the updates in the weights and activation functions. The mathematical model of the neural network is depicted in figure 4.

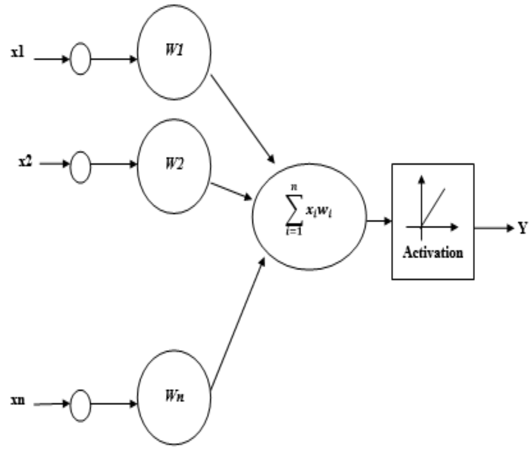


Fig. 4 Mathematical Model of Single Neuron [13]

The mathematical equivalent of an artificial neuron is depicted in figure 4 where the output can be given by:

$$y = f(\sum_{i=1}^{n} x_i w_i + b) \quad (5)$$

Here,
x denote the parallel inputs
y represents the output
w represents the bias
f represents the activation function

The neural network is a connection of such artificial neurons which are connected or stacked with each other as layers. The neural networks can be used for both regression and classification problems based on the type of data that is fed to them. Typically the neural networks have 3 major conceptual layers which are the input layer, hidden layer and output layer. The parallel inputs are fed to the input layer whose output is fed to the hidden layer. The hidden layer is responsible for analysing the data, and the output of the hidden layer goes to the output layer. The number of hidden layers depends on the nature of the dataset and problem under consideration. If the neural network has multiple hidden layers, then such a neural network is termed as a deep neural network. The training algorithm for such a deep neural network is often termed as deep learning which is a subset of machine learning. Typically, the multiple hidden layers are responsible for computation of different levels of features of the data. Several categories of neural networks such as convolutional neural networks (CNNs), Recurrent Neural Network (RNNs) etc. have been used as effective classifiers [17] .

III. PREVIOUS WORK

This section cites the various contemporary approaches employed for automated leukaemia classification. The salient features of each approach is also presented in the work.

Denny et al. showed that acute lymphoblastic leukemia is a condition that occurs in the bone marrow. Most cases of Acute Lymphoblastic Leukemia (ALL) develop from cells that would turn into white blood cells (other than lymphocytes), but some cases of ALL develop in blood-forming cells of various kinds. Anything begins in the bone marrow (the soft inner part of some bones, where new blood cells are made), yet it moves rapidly into the blood by and large. The proposed approach uses imaging processing techniques to detect irregular blood cells in the microscopic images of the blood. Using the training data collection, the program is trained using DCNN and is uploaded into HDFS Hadoop framework.

Tuba et al. proposed a method for automatic detection of one type of leukemia, acute lymphoblastic leukemia, by classifying white blood cells into normal cells and blasts. The proposed method uses shape and texture features as input vector for support vector machine optimized by bare bones fireworks algorithm. Based on the results obtained on the standard benchmark set, ALL-IDB, our proposed method shows a competitive accuracy of classification comparing to other state-of-the-art method.

Kumar et al. proposed that leukemia is kind of blood cancer in which white blood cells are triggered to grow uncontrollably and also in an immature way. It is a leading cause of loss of lives. The detection of this illness is done using the microscope images of the affected blood samples. presents an algorithm for automated image based acute leukemia detection systems. The method implemented uses basic enhancement, morphology, filtering and segmenting technique to extract region of interest using k-means clustering algorithm. The proposed algorithm achieved an accuracy of 92.8% and is tested with Nearest Neighbor (kNN) and Naïve Bayes Classifier on the dataset of 60 samples.

Rawat et al. did their study on the computer based classification methods that have been employed for the accurate classification of the different forms of serious blood cancer that is leukemia. The CAD system is an efficient mechanism using which the forecasting and classification of the illness can be smoothened and made effective. As the disease is of a complex form and also shows very intricate symptoms. It is important to detect is correctly as the treatment depends on it. The proposed technique firstly segments the nucleus from the leukocyte cell background and then computes features for each segmented nucleus. A total of 331 geometrical, chromatic and texture features are computed. A genetic algorithm using support vector machine (SVM) classifier is used to optimize the feature space. Based on optimized feature space, an SVM classifier with various kernel functions is used to eradicate noisy objects like overlapped cells, stain fragments, and other kinds of background noises.

Mao et al. used DCNN approach and methodology to train samples for the cancer detection. The CTC in the blood can play a significant role in evaluating the cancer detection procedure. These markers are very necessary as they can signal the tumor response in the blood. The deep convolutional neural network is an advanced methodology that can help with training with the input data set very swiftly. This is a streamlined course of action that can help in the overall progress of the process. The microscopic image of the blood has to have a lot of clarity and precision so that the medical expert can detect any tiny variation in the sample of the blood. This detection and evaluation phase is immensely important and has to be performed without any dint of error otherwise the entire thing could go wrong including the treatment. Henceforth this technique was a good method to increase the quotient of accuracy.

Shankar et al. showed that the field of image processing has seen a lot of advancement and progress over the last few years. The application of image processing in the field of disease detection and medical diagnosis is immense. As the medical images form the basis of clinical resource for the disease evaluation. These images need to be very accurate and free from any kind of error. The microscopic image of the blood has to have a lot of clarity and precision so that the medical expert can detect any tiny variation in the sample of the blood. This detection and evaluation phase is immensely important and has to be performed without any dint of error otherwise the entire thing could go wrong including the treatment. So this process very robust and effective with good accuracy.

Rawat et al. proposed that automated technical classification methods were studied under this paper. The blood smar method becomes very easy and the identification task also becomes less tedious for the pathologist when such technology allied methods are utilized. In this microscopic analysis, the review of classification of the leukocytes is carried out very efficiently. However, the nonspecific nature of white cell with symptoms of Acute Lymphoblastic Leukemia (ALL) often leads to erroneous identification. It is important to detect is correctly as the treatment depends on it. The microscopic samples need to have great clarity and this diagnostic assessment must be free of any errors or glitches.

Goutam et al. proposed that blood leukemia is form of cancer that exhibits uncontrolled growth of the white blood cells and is potentially very serious and life threatening form of blood cancer. For detection of the disease, images of the blood samples have to be evaluated by a hematologist for any other than normal feature. The images of blood samples are microscopic in nature and therefore correct diagnosis and identification is dependent on the accuracy and clarity of the images long with the expertise of the hematologist. The concept of classifier approach was implemented for this that yielded good accuracy of the classification.

Agaian et al. proposed that leukemia is kind of blood cancer in which white blood cells are triggered to grow uncontrollably and also in an immature way. It is a leading cause of loss of lives. The detection of this illness is done using the microscope images of the affected blood samples. The pathologists carryout analysis of the samples and bring out conclusions of the diagnosis. In this paper, the proposed methods used the blood smear samples for an automated screening and classification scheme. Segmentation based on unique features has also been added to this process and hence it gives very coherent output.

Talukda et.al. proposed that the field of image processing has seen a lot of advancement and progress over the last few years. The application of image processing in the field of disease detection and medical diagnosis is immense. As the medical images form the basis of clinical resource for the disease evaluation. These images need to be very accurate and free from any kind of error. The cancer is very serious form of disease that calls for immediate diagnosis and treatment. Any delay can be very fatal. Also a very robust detection measure should be in place for proper and glitch free diagnosis. In this approach the author has proposed an automated detection scheme based on the image processing method using the fuzzy concept. Fuzzy logic is a very useful idea that has increased the efficiency of the system considerably.

Sharma et al. put forth the a novel idea of using the quantum dots based approach that could speed up the classification and detection very well. Using this quantum approach along with the fuzzy concept implements the sun processing unit. The process is quite similar to the detection based mechanism where in the blood smear images are pre processed for the classification. It is a very useful approach used by the researchers that gave 95% accuracy and also very good performance. Effective treatment can happen when the disease is detected quickly and accurately. This is possible with high end medical diagnosis and accuracy of diagnosis in less time. Consequently, modern techniques have become the go-to option for the evaluation and detection of this serious blood cancer cases that can predict it accurately and faster than other conventional methods.

Vendrell et.al. proposed the enhanced raman concept was introduced for the cancer detection and imaging purpose. The microscopic samples need to have great clarity and this diagnostic assessment must be free of any errors or glitches. Several sort of morphological characteristics are used for the same. They include the shape, size, change in color, texture etc. The computer assistance has greatly improved the accuracy and effectiveness. Errors in the visual images due to various factors such has lack of clarity, poor image quality, lack of expertise of the expert etc can prove to very serious and problematic. As the detection phase is very crucial stage, henceforth this process must be very accurate and fast. The motivation is thus, to design an efficient system. The proposed process was very effective and coherent in nature.

Koestler et.al proposed that medical field is being flooded with a lot of medically intricate cases and challenges in today's time. One of such challenging case is the case of blood cancer and its effective detection and treatment. These cases of illness have seen a significant surge over the past few years. So a proper evaluation method is required to deal with such important cases. The detection is primarily based on the images for microscopic level. So it is important that these medical images are clear and precise that can make the identification and evaluation of images free form any mistakes.. Effective treatment can happen when the disease is detected quickly and accurately. This is possible with high end medical diagnosis and accuracy of diagnosis in less time. So this was a good implementation instance of the method in hand and also worked quite well. It was a novel concept and very reliable method.

Madhloom et al. proposed that image processing of the digital image applications have increased manifold. In this work, the authors have used the image processing idea for the localization and segmentation based classification of the blood smear images for cancer detection. The disease is a very fatal one if it is not detected and treated in time. This form of cancer has many variants based on the type of cells showing improper behavior and function. But with the case of the acute version of the disease; it aggravates very fast and needs immediate treatment. Hence a major aspect of this illness and solution is very fast line of action in terms of diagnosis as well as treatment. Therefore it's a very good concept for the structured segmentation part and also well in sync with the image clarity and accurate feature selection.

Mohapatra et al. showed that the case of blood leukemia is a very serious form of illness and needs effective and quick treatment. Quality of treatment depends on the quality and efficacy of the detection and diagnosis and that also very quickly. The detection of the disease form the microscopic images is still an area that needs to more advanced and effective. So the authors herein presented a fuzzy concept based image segmentation idea that could detect the blood cancer in an automated manner. This was a very novel and robust concept that worked well for the overall systematic performance for the accuracy factor. This is a part of the digital image processing principal. It showed improved outcomes and could very well classify the images. It is a very robust approach used by the researchers in this domain. The classification is to be done in a better manner and approach. The performance of the system has been evaluated in terms of the accuracy of classification. It is worth mentioning that a comparative analysis is done based on the common and overlapping dataset of the different methods.

Noteworthy Contributions and Future Work:

The following are the contributions in the previous work can be summarized as

1) The use of an ANN based on training rule generally used for time series predictions or otherwise may be used for classification problems but generally tend to render degraded results since there is no clear boundary for the classification problem. [1], [3]
2) The use of K-means clustering can be used to find the features in the specific set of data. By ding of mathematics, statistics tells us that no matter how large the data set, there is only 5-6 specific clusters which are highly correlated. This approach may yield good results for some data sets but would falter for others. [2].
3) The use of the DCT is useful for image pre-processing but generally renders lesser accurate feature values due to symmetric division of images of the data set into sub-frequency bands. A similar approach is seen in. [5], [6].
4) The approach used in [8], [11] and [15] use the fuzzy inference machine or fuzziness for final classification of the images. The idea is to render crisp values at the output of the system given the features. However, this may lead to erroneous results if the expert views do not coincide with the data set.
5) Another approach used is the Convolutional neural network with the maxpool in [5]. In this approach the separate approach for feature classification is ditched which may often result in lower accuracy.
6) In [8], the supervised learning approach is used for the training of the neural network without assigning relative weights.

The future work can be aimed or directed towards the design of deep learning algorithms which can address the following issues:

1. Separate out the region under interest from the composite leukaemia image.
2. Mitigate the possibility of vanishing gradients in case of deep learning algorithms.

3. Avoid overfitting for staggeringly large datasets.

The performance metrics of the classifiers are generally computed based on the true positive (TP), true negative (TN), false positive (FP) and false negative (FN) values which are used to compute the accuracy and sensitivity of the classifier, mathematically expressed as:

$$Ac = \frac{TP+TN}{TP+TN+FP+FN} \quad (6)$$

Sensitivity: It is mathematically defined as:

$$Se = \frac{TP}{TP+FN} \quad (7)$$

$$Recall = \frac{TP}{TP+FN} \quad (8)$$

$$Precisiosn = \frac{TP}{TP+FP} \quad (9)$$

$$F - Measure = \frac{2.Precision.Recall}{Precision+Recall} \quad (10)$$

The aim of any designed approach is to attain high values of accuracy of classification along with other associated parameters. The computation complexity of the system often evaluated in terms of the number of training iterations and execution time is also a critically important metric which decides the practical utility of any algorithm on hardware constrained devices.

IV. CONCLUSIONS

It can be concluded that It can be concluded that AI based techniques can prove to be a strong supporting tool to medical practitioners aiming to detect blood leukemia. Development of such techniques are not aimed at replacing doctors, rather supporting and augmenting them. Several AI and ML based techniques have been proposed with their own strengths and limitations. Different stages of the data processing and segmentation have been enlisted. The significance of different image features and extraction techniques have been clearly mentioned with their utility and physical significance. Various machine learning based classifiers and their pros and cons have been highlighted. The mathematical formulations for the feature extraction and classification gave been furnished. A comparative analysis of the work and results obtained has been cited in this paper. It can be concluded that image enhancement and feature extraction are as important as the effectiveness of the automated classifier, hence appropriate data processing should be applied to attain high accuracy of classification.

Some of the future directions of work can be separate image enhancement and data optimization to avoid both over fitting and under-fitting, moreover, employing separate image denoising to extract features more accurately. Solely computing feature based on deep learning architecture can be compared with statistical feature extraction. This would make the system application to a large variety of datasets. Moreover, classifiers which do not saturate in terms of performance with increasing sat size can be employed.

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