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Analysis of blood samples for counting leukemia cells using Support vector machine and nearest neighbour

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Abstract: *analysis of blood samples for counting leukemia cells is discussed in this paper. support vector machine and nearest neighbour concept is presented in this paper. The identification of blood disorders, it can lead to classification of certain diseases related to blood. Several classification techniques are investigated till today. One of the best methods for classification techniques nearest neighbour and SVM (Support Vector Machine).By identifying and counting blood cell within the blood smear using classification techniques it's quite possible to detect so many diseases. If one of the new classifier is used i.e. nearest neighbour and SVM it is quiet possible to detect the cancer cell from the blood cell counting.*
Keyword: *Blood, Classification technique, Nearest Neighbour Network, SVM*

I. Introduction

In previous, there has been an exponential intensification in the classification of medical images by different classifiers and algorithm. Different algorithms have been used to classify the medical images. Effective medical image can play an important role in aiding in diagnosis for healthcare students by explaining with this image will help them in their studies as well. Data mining is the process of discovering meaningful new correlations. Pattern and trends by shifting through large amount of data stored in data base. From the beginning the algorithm are used for testing the existence or inexistence of a natural grouping tendency in data collection and most of them being based on arguments coming from mathematical statistics and heuristic graphical techniques. These systems enhance the classification process to be more accurate. Many techniques i.e. algorithms and classifies are used for the purpose of medical image classification fig. shows various approaches in Biomedical image processing [1]. Medical imaging has become one of the most important visualization and interpretation methods in biology and medicine over the past decade. This time has witnessed a tremendous development of new, powerful instruments for detecting, storing, transmitting, analyzing, and displaying medical images. This has led to a huge growth in the application of digital image processing techniques [2] for solving medical problems. The most challenging aspect of medical imaging lies in the development of integrated systems for the use of the clinical sector. Design, implementation, and validation of complex medical systems require a tight interdisciplinary collaboration between physicians and engineers. Main objective of analyzing through images is to gather information, detection of diseases, diagnosis diseases, control and therapy, monitoring and evaluation [3].At the moment, identification of blood disorders is through visual inspection of microscopic images of blood cells. From the identification of blood disorders, it can lead to classification of certain diseases related to blood. One of the most feared by the human disease is cancer. Leukaemia is a type of blood cancer, and if it is detected late, it will result in death. Leukemia occurs when a lot of abnormal white blood cells produced by bone marrow. When abnormal white blood cells are a lot, the balance of the blood system will be disrupted. The existence of abnormal blood can be detected when the blood sample is taken and examined by haematologists. Microscopic images will be inspected visually by haematologists and the process is time consuming and tiring [4], [5], [6]. The process require human expert and prone to errors due to emotion disturbance and human physical capability that is of course have its own limit. Moreover, it is difficult to get consistent results from visual inspection [4].

II. Background Of Leukemia

Cancer: The cells keep dividing and growing without normal control, causing an abnormal growth called a tumor. It can be classified two types. The tumour does not invade nearby tissues and body parts is called benign tumor or non-cancerous. If the tumor invades and destroy nearby cells and tissues is called malignant tumor or cancer.

Leukemia: leukaemia is a group of cancers that usually begins in the marrow and results in high numbers of abnormal white blood cells. These white blood cells are not fully developed and are called blasts or leukemia cells. Symptoms may include bleeding and bruising problems, feeling very tired, and an increased risk of infections. These symptoms occur due to a lack of normal blood cells. Diagnosis is typically by blood tests or bone marrow biopsy.

Symptoms of Leukemia:
Leukemia cells are abnormal cells that cannot do what normal blood cells do.
Systemic: weight loss, fever, frequent infections

- Psychological: fatigue, loss of appetite
- Lymph nodes: swelling
- Lungs: easy shortness of breath
- Muscular: weakness
- Bones or joints: pain or tenderness
- Spleen and/or liver: enlargement
- Skin: night sweats, easy bleeding and bruising, purplish patches or spots

Blood Component:

Blood is a highly specialized tissue composed of more than 4,000 different kinds of components. Four of the most important ones are red cells, white cells, platelets, and plasma. All humans produce these blood components--there are no population or regional differences.

- **Red cells or erythrocytes:** It can carry oxygen to tissues and back to the lungs with carbon dioxide.
- **White cells or leukocytes:** Defending the organism from infection. There are several types of white blood cells.
- **Platelets or thrombocytes:** It can helps blood clotting to control bleeding.
- **Plasma:** The fluid in blood containing dissolved ions needed for cell function and consists of sodium, potassium, chloride, hydrogen, magnesium and iron.
  While blood cells are older or spoil, the cells will die and new cells will replace it [7].

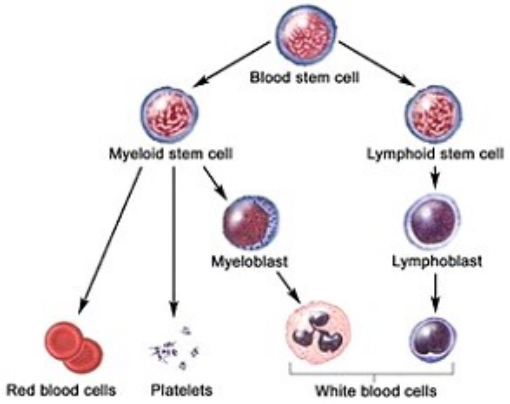


Figure 1: Production of Blood Cell [7]

Figure 1 shows that how stem cells became mature and evolve into several components of blood. They evolve into either myeloid stem cell or lymphoid stem cell. Myeloid stem cells eventually mature and became myeloid blast. This blast will form red blood cell, platelet and several types of white blood cell. Lymphoid stem cells also will mature and can form lymphoid blast and this blast will eventually form several types of white blood cells. White blood cells from myeloid blast are differs from lymphoid blast. The study will focus on leukemia because the disease is dangerous and can lead to death. For someone who has leukemia, bone marrow produces abnormal white blood cell. Compared with normal cells, abnormal white blood cell will not die when they should. Thus the number of abnormal white blood cell become numerous and interfere normal white blood cells to carry out their duties. This also causes an imbalance of blood system in the human body. Leukemia can be grouped based on how quickly this disease develops and become severe. Leukemia is either Chronic or Acute.

- **Acute leukemia** involves an overgrowth of very immature blood cells.
- **Chronic leukemia** involves an overgrowth of mature blood cells.

Four major kinds of leukemia can be divided by following. [8]

Cell type	Acute	chronic
Lymphocytic leukemia (or "lymphoblastic")	Acute lymphoblastic leukemia (ALL)	Chronic lymphocytic leukemia (CLL)
Myelogenous leukemia ("myeloid" or "nonlymphocytic")	Acute myelogenous leukemia (AML or myeloblastic)	Chronic myelogenous leukemia (CML)

- **Acute lymphoblastic leukemia (ALL)** is the most common type of leukemia in young children. This disease also affects adults, especially that age 65 and older. Standard treatments involve chemotherapy and radiotherapy. The survival rates vary by age: 85% in children and 50% in adults. Subtypes include precursor B acute lymphoblastic leukemia, precursor T acute lymphoblastic leukemia, Burkitt's leukemia, and acute biphenotypic leukemia.

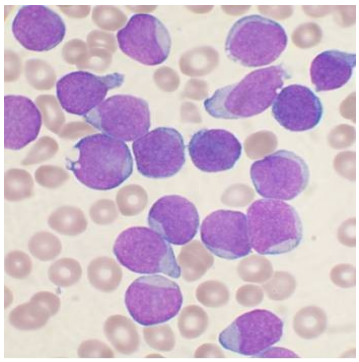


Figure 2: Acute Lymphocytis Leukemia (All) [8]

- **Chronic lymphocytic leukemia (CLL)** most often affects adults over the age of 55. It sometimes occurs in younger adults, but it almost never affects children. Two-thirds of affected people are men. The five-year survival rate is 75%. It is incurable, but there are many effective treatments. One subtype is B-cell prolymphocytic leukemia, a more aggressive disease.

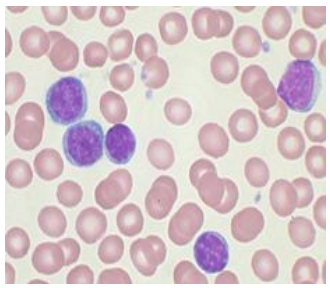


Figure 3: Chronic Lymphocytic Leukemia (Cml) [8]

- **Acute myelogenous leukemia (AML)** occurs more commonly in adults than in children, and more commonly in men than women. AML is treated with chemotherapy. The five-year survival rate is 40%, except for APL (Acute Promyelocytic Leukemia), which is over 90%.Subtypes of AML include acute promyelocytic leukemia, acute myeloblastic leukemia, and acute megakaryoblastic leukemia.

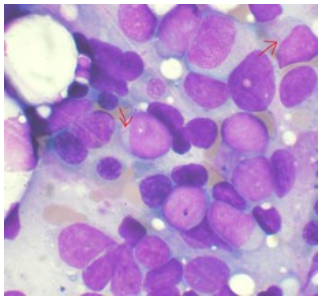


Figure 4: Acute myelogenous leukemia (AML) [8]

- **Chronic myelogenous leukemia (CML)** occurs mainly in adults; a very small number of children also develop this disease. Treatment is with imatinib (Gleevec in United States, Glivec in Europe) or other drugs. The five-year survival rate is 90%. One subtype is chronic myelomonocytic leukemia.

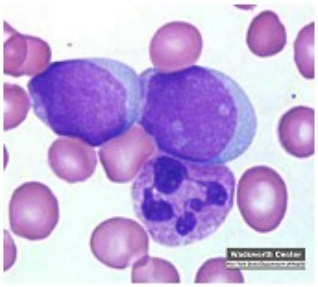


Figure 5: **Chronic myelogenous leukemia (CML) [8]**

III. Related work

A. Iterative Thresholding for segmentation of cells from noisy images [9]

Iterative Thresholding algorithm is used for segmentation purpose especially from noisy images. This algorithm overcomes the problem of cell extraction and segmentation from heavy noisy images. This algorithm works over the adjusted threshold of images iteratively providing robustness to image.

B. Segmentation of blood images using morphological operators [10]

This system detects and classifies malaria parasites in Giemsa stained blood slides images. Then after parasitaemia evaluation is done. Morphological approach to cell image segmentation is more precise than the classical watershed-based algorithm is shown in this paper. Grey scale granulometries are applied based on opening with disk-shaped elements, flat and non-flat. Non flat disk shaped structuring element enhances the roundness and the red cells compactness.

C. Analysis of Infected Blood Cell Images Using Morphological Operators [11]

These systems classify and identify malaria parasite by using microscopic images of blood cells. Morphological approach and the major necessities in developing this system is the best techniques for blood cell images segmentation.

D. An accurate segmentation method for white blood cell images [12]

A precise method of segmentation for counting white blood cells automatically is presented here. First a simple thresholding approach is applied and the algorithm is derived about blood smear images from priori information. The labels are adjusted then in order to produce meaningful results. This approach uses of knowledge of the blood cell structure. This method is more influential as compared to traditional methods which uses information of local context. It can perform accurate segmentation of white blood cells though they have unsharp boundaries.

E. The curvelet transform for image denoising [13]

The curvelet transform implements curvelet subbands and uses a ridgelet transform as a component step, and idea throughout is that transforms should be over complete, more willingly than critically sampled. In this digital transforms are applied for de-noising of some standard images rooted in white noise.

F. Automatic Morphological Analysis for Acute Leukemia Identification in Peripheral Microscope Images [14]

The usefulness of an automatic morphological method to recognize the Acute Lymphocytic Leukemia (ALL) with the help of images of peripheral blood microscope. The presented methodology individuates the leucocytes from the others blood cells, after that it selects the lymphocyte cells (the cells causes acute leukemia), morphological indexes from those cells are evaluated then after and at last classification is performed whether the presence of the leukaemia is there or not.

G. Automatic Recognition of the Blood Cells of Myelogenous Leukaemia Using SVM [15]

The built a system to detect leukaemia cells of images of bone marrow. Using Support Vector Machine (SVM) classifier and blood cell images features that are related to geometry, texture, and statistical analysis, the system was built. The pressure is on selection and generation of features for getting out the best recognition. Textural parameters such as entropy, contrast, mean value and angular second momentum have been used .Geometrical parameters are compactness, perimeter, concavity points and symmetry radius, area and filled area. For statistical analysis parameters are mean value and for nucleus standard deviation and for gradient matrix cytoplasm, mean and standard deviation are considered. Kurtosis and Skewness for image and gradient matrix.

Training data error is 11.87%, errors of testing data is21.13%. 30 best features are selected and this produce error rate of training data up to 13.07% and errors of testing data to 18.71%.

H. Multiscale LMMSE -based image de-noising with optimal wavelet selection [16]

The uses of a wavelet-based multi-scale linear minimum mean square-error estimation (LMMSE) scheme and the way to determine the optimal wavelet basis with respect to the proposed scheme is also specified. The over complete wavelet expansion (OWE) which is better as compared to orthogonal wavelet transform (OWT) in noise reduction is also included in this methodology. To walk around the strong inter scale dependencies of OWE, the pixels at the same spatial location are combined and supposed to be a vector and LMMSE is applied to the vector.

I. Automatic Blasts Counting for Acute Leukemia Based on Blood Samples [17]

In automatic process, the segmentation technique for white blood cell (WBC) is based on HSV (Hue, Saturation and Value) color space will be used in order to eliminate the white blood cells (WBC) from the background. A simple morphological operator such as erosion is used for the overlapping cells. Results show that the proposed system has provided the highest average accuracy of 97.8% for counting both ALL and AML cases.

J. LPG-PCA Algorithm and Selective Thresholding based automated Method: ALL and AML Blast Cells Detection and Counting [18]

An automated method to detect Acute Leukemia blast cells from human microscopic blood images. It comprises four basic modules, 1] de-noising module performs two staged noise reduction by 2D PCA and LPG.2] The contrast enhancement section includes color space conversion and morphological filtering based on pixel intensities.3] In threshold selection module, threshold value is determined using two methods namely, Edge Sensitive Variational Thresholding and Otsu's Thresholding.4] Blast cells are segmented based on threshold value obtained from these two methods. Morphological operations and Connected Component Analysis are used to count the number of blast cells present in the images.

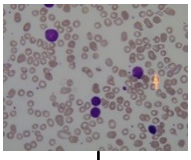
III. Proposed Methodology

A. Support Vector Machines (SVM): The support vector machine (SVM) is a classification algorithm that provides state of the art performance in a wide variety of application domains, including handwriting recognition, object recognition, speaker identification, face detection and text categorization. Two main motivations suggest the use of SVMs in computational biology. In clinical bioinformatics they have allowed construction of powerful experimental cancer diagnostic models based on gene expression data with thousands of variables and as little as few dozen samples. Moreover, several efficient and high-quality implementations of SVM algorithms facilitate application of these techniques in practice. The first generation of SVMs could only be applied to binary classification tasks.

The preliminary experimental evidence currently available suggests that some multi-category SVMs (**MCSVMs**) perform well in isolated gene expression-based cancer diagnostic experiments. In the description of methods below, k is the number of classes or distinct diagnostic categories, and n is the number of samples or patients in the training dataset.

B. **K Nearest Neighbors (KNN):** The main idea of KNN is that it treats all samples as points in the m Dimensional space (where m is the number of variables) and given an unseen sample x, the algorithm classifies it by a vote of K nearest training instances as determined by some distance metric, typically Euclidian distance.

During previous survey we found the steps for the process of automating blood recognition are as in Figure 6.



Blood slide image are obtained from digital microscope

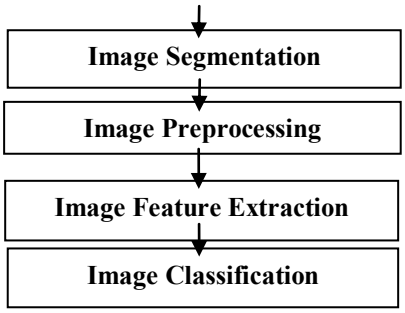


Figure 6: Automating Blood Recognition Processing Steps

Here Research methodology that will be used in this research includes:

1. Image Acquisition : Blood image from slides will be gained from nearby hospital with effective enlargement or digital microscope

2. Image Pre-processing: The main image processing tasks consists of enhancing the image's qualities and deleting overlapped blood cells in the borderline area of the image. Both tasks can be subdivided into smaller tasks.

- Green Plane Extraction: The green plane is extracted from the imported blood cell image. The other planes such as red and blue are not considered because they contain less information about the image.

 Histogram equalization: This process adjusts intensity values of the image by performing histogram equalization involving intensity transformation, so that the histogram of the output image approximately matches a predefined histogram.

 Contrast and brightness adjustment: To adjust brightness of an image, and histogram of the interested image is used to determine data and display ranges of the image. The data range is the range of intensity values actually used in the image. The display range is the black-to-white mapping used to Display the image determined by the image class. Contrast adjustment is done by manipulating the Display range of the histogram while the data range of the image remains constant.

3. Image Segmentation: Many researchers have given different methods for image segmentation such as threshold-based, edge-based, region-based or clustering methods, such as,fuzzy-C mean clustering and K-mean clustering. Cseke used automatic thresholding method (1979).Threshold techniques cannot always produce meaningful results since no spatial information is used during the selection of the segmentation threshold [21]. They are often combined with mathematical morphology operations. The technique was 92% accurate. Liao presents an accurate segmentation method for white blood cells [22]. A simple thresholding approach is applied to give initial labels to pixels in the blood cell images. The algorithm is based on priori information about blood smear images. Then the labels are adjusted with a shape detection method based on large regional context information to produce meaningful results.

The proposed method for the segmentation of blood cell (leukocytes) is given below [23].

Step 1: Input the colour blood slide image to the system.
Step 2: Convert the colour image into grayscale image.
Step 3: Enhance contrast of the grayscale image by histogram equalization method (A).
Step 4: To adjust image intensity level apply linear contrast stretching to gray scale image (B).
Step 5: Obtain the image I1=B+A to brighten all other image components except cell nucleus.
Step 6: Obtain the image I2=I1-A to highlight the entire image objects along with cell nucleus.
Step 7: Obtain the image I3=I1+I2 to remove all other components of blood with minimum effect of Distortion over nucleus.
Step 8: To reduce noise, preserve edges and increase the darkness of the nuclei implement 3-by-3 minimum filter on the image I3.
Step 9: Apply a global threshold Otsu's method on image I3.
Step 10: Using the threshold value in above step convert I3 to binary image.
Step 11: To remove small pixel groups use morphological opening.
Step 12: To form objects connect the neighboring pixels.
Step 13: By applying the size test removal of all objects that are less than 50% of average RBC area is done.

It is observed that this method of segmentation yields better results than that of previous methods.

4. Feature Extraction: Classification is the task of assigning to the unknown test vector to a known class. In this step, a reinforcement learning algorithm is proposed. This approach will classify the types of leukaemia into ALL, AML, CLL and CML.

Area: The area was determined by counting the total number of none zero pixels within the image region. *Perimeter:* It was measured by calculating distance between successive boundary pixels. *Circularity:* This is a dimensionless parameter which changes with surface irregularities and is defined as,

$Circularity = 4* Pi* Area/ Perimerer^2$

5. Image Classification : Based on the features extracted in above step, classifier classifies the lymphocyte cells as blast or normal cells. Classification is the task of assigning to the unknown test vector, a label from one of the known classes [24]. The K-nearest neighbor (kNN) decision rule has been a ubiquitous classification tool with good scalability. Past experience has shown that the optimal choice of K depends upon the data, making it laborious to tune the parameter for different applications. The k-Nearest- Neighbours (kNN) is a non-parametric method of classification. It is simple but very effective in many cases. Here also kNN has been utilized to classify blast cells from normal white blood cells.

IV. Database

The ALL-IDB image datasets (Acute Lymphoblastic leukaemia Image Database) [25] is provided by Fabio Scotti to test and fairly compare algorithms for cell segmentation and classification of the ALL infection. There are two types of datasets are available. The ALL-IDB1 can be used both for testing segmentation capability of algorithms, as well as the classification systems and image pre-processing methods and ALL-IDB2 has segmented WBCs to test the classification of blast cells. The examples of ALLIDB1 dataset images are shown in figure 7.

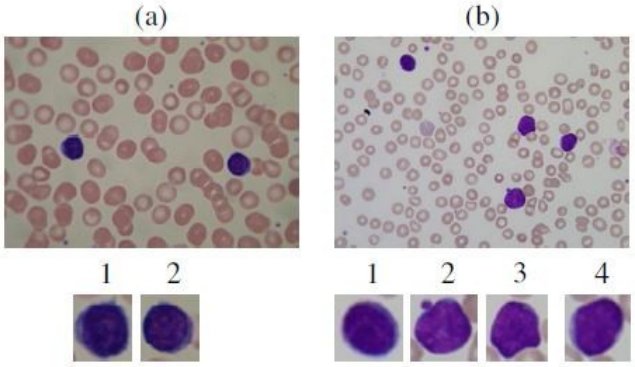


Figure 7:
Healthy blood images examples (a), blood with ALL blasts (b). (a1-2) and (b1-4) are zoomed subplots of the (a) and (b) images centered on lymphocytes and lymphoblast respectively.[26]

V. Experimental Result

The proposed technique has been applied on 121 peripheral blood smear images obtained from the public dataset as mentioned earlier. A microscopic blood image of size 2592 × 1944 is considered for evaluation [3]. As mentioned in section 4, algorithm applied to input image. The resulting images of segmentation are shown in figure 3, 4, 5 and 6.

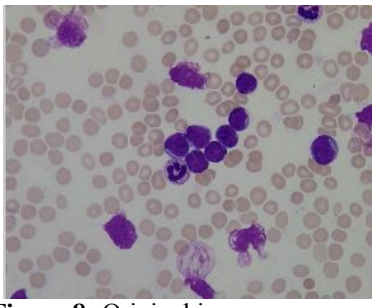


Figure 8: Original image

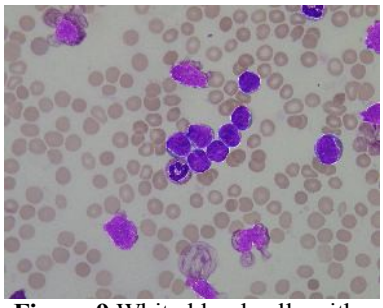


Figure 9 White blood cells with white imagespots over nucleus

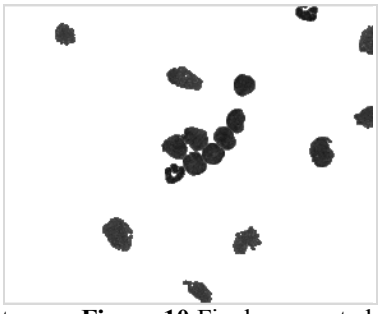


Figure 10 Final segmented

In the result, numbers of WBCs are also counted. For a given figure 8, numbers of WBCs present are fig 11. WBCs are separated from other blood components by white spots over nuclei. In the final segmented image only WBCs are kept with darker nucleus by removing all noisy components by minimum filter. After this segmentation lymphocyte cells are detected from all WBCs by blast segmentation and features of lymphocyte

are calculated. Depending on those morphological features it is decided whether it is leukemic slide image or not. Final lymphocyte blast segmented image is shown in figure 11.

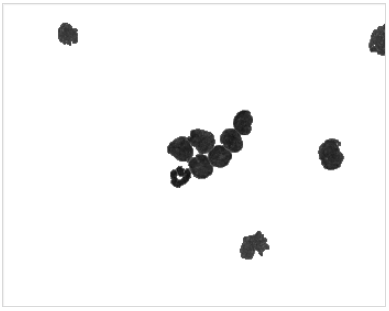


Figure 11 Lymphocyte blast segmented image This method is applied on all 121 images. The accuracy of 93% is obtained using this method.

VI. Conclusion

In this paper involves detecting the types of WBCs and RBCs using microscopic blood sample images. The system will be built by using features in microscopic images by examining changes on texture, geometry, colors and statistical analysis as a classifier input. The system should be efficient, reliable, less processing time, smaller error, high accuracy, cheaper cost and must be robust towards varieties that exist in individual, sample collection protocols, time and etc.

The SVM algorithm can handle this case by using trade off (cost) parameter and penalty parameters (slack variables). The real power of Support Vector Machines is to map the data (implicitly) to a higher dimensional space via a kernel function and then identify the maximum-margin hyper plane that separates training instances. Leukemia detection with proposed features were classified using kNN classifier giving overall accuracy of 93%. Furthermore the system should be robust to excessive staining and touching cells. Results obtained encourage future works which includes classification of lymphoblast into various subtypes. Alternate techniques can be investigated for stain independent blood smear image segmentation and leukemia type classification.

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