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Differential Count of WBC in Bone Marrow with Novel Features for Disease Diagnosis

Shri N .D.Pergad[1], Dr. S.T.Hamde[2]

Associate Professor, ETC Dept, STBCOE, Tuljapur, India[1]

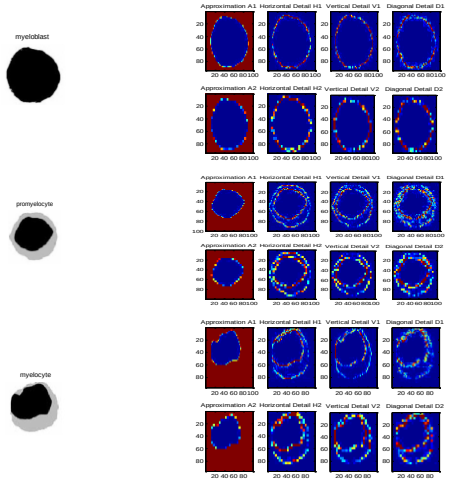
Professor, Instrumentation Dept, SGGSIE&T, Nanded,India[2]

Abstract: White Blood Cell (WBC) differential counts means the different types of cells are measured with various methods. it is necessary in the bone marrow different types of wbc counts in quantity, called differential counts, which provides invaluable information to consultants for disease diagnosis. As the differential wbc counting process is laborious work, an automatic system is preferable. In this paper, we work on investigation whether information about the nucleus alone is sufficient to classify wbcs. This is required because segmentation of nucleus is much easier than the entire cell segmentation, especially in the bone marrow where the wbc density is to much high. In the experiments, a set of manually segmented images of the nucleus are used to decouple segmentation errors. We analyze a set of wbc nucleus based features using Radon-Wavelet transform decomposition. Fivefold cross validation is used in the experiments in which artificial neural networks are applied as classifiers. The classification performances are evaluated by two evaluation measures class wise classification rates. Furthermore, we compare our results with other classifiers and previously proposed nucleus based features. The results show that the features using nucleus alone can be utilized to achieve a classification rate of 81.36% on the test sets. Moreover, the classification is applied to wbc differential count which is used for disease diagnosis.

Keywords: WBC classification,Wavelet Decomposition, wbc differential counts, disease diagnosis.

1. INTRODUCTION

Cells in bone marrow differential counts are invaluable main information source to doctors, and applied in patient's diagnosis. Diseases diagnosed such as brain tumers, AIDS, or various types of cancers by analysis the white blood cell differential counts, i.e., the cell counts of diff **W**hite Blood erent classes. The pathology expert uses a traditional method by using microscope and bone marrow slides to detect the white blood cells, with viewing an area of cell size and his expertise to classify the cells, to complete the count of the corresponding cell class, and repeat the process until all cells in the area of interest are counted. To complete all these processes manually is a very tedious job for a trained expert and, thus, an automated differential counting is necessary. Thus, an automated differential counting system which is possible after the wbc classification with their novel features related to radon-wavelet transform decomposition as shown in fig.1. The differential count of wbc in bone marrow with the myelocytic series as myeloblast, promyelocyte, myelocyte, metamyelocyte, band, and polymarohonuclear(PMN). From each count of these class is used in the various cancers diagnosis. Normally which is used for differential white cell counts for bone marrow cells. Because of , in that to its high price and complicated structure, markedly packed bone marrow and sclerotic bone marrow may yield too few cells for adequate diagnosis to various disease [1].



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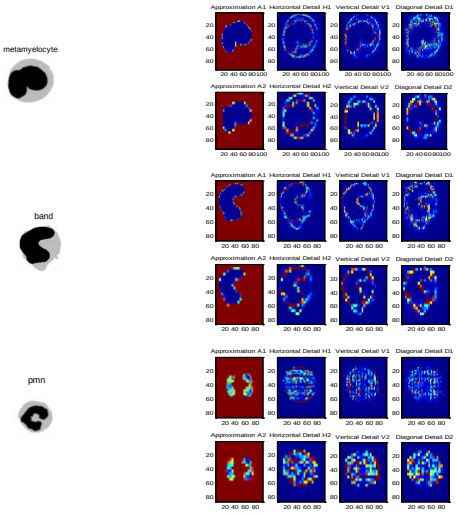

Fig1. Wbc in bone marrow Cell segmented images in the myelocytic series, with Radon-Wavelet Transform Decomposition.

White blood cells in the myelocytic or granulocytic series can be classified into six classes, i.e., myeloblast, promyelocyte, myelocyte, metamyelocyte, band, and polymorphonuclear (PMN) in that order from the youngest to the oldest cells [2], [3]. Due to the tediousness of manual systems, several methods have been proposed for automatic or partially automatic counting systems. Most of them, however, are for the applications in peripheral blood rather than for bone marrow. It should be noted that white blood cells in bone marrow are much denser than those in peripheral blood; therefore, segmentation of white blood cells in bone marrow is a more difficult problem than segmentation in peripheral blood. Moreover, the immature cells are normally seen only in the bone marrow [3], which, thus, makes cell classification in bone marrow a more difficult and also a complex problem [4].

2. METHODOLOGY

In our research, Artificial neural networks are used as our classifiers in the six class solution. The cell features are mainly extracted from segmented bone marrow cell images with its nucleus and cytoplasm background. Here, we extract six coefficients of Radon and Wavelet transforms as the six features of the cells.

2.1 Radon and Wavelet Transform Theory:

Radon Transform forming a very important mathematical tool used in tomography is based upon works of Johann Radon born in 1887 Litom e rice. His doctoral dissertation has been defended in Vienna in 1910 and his most appreciated works were devoted to integral geometry. The Radon Transform[15] belonging to this category introduced in 1917 is defined as a collection of 1D projections around an object at angle intervals . The Radon Transform of a two-dimensional (2-D) function f (x,y) is defined as

$$R(r,\Theta)[f(x,y)] = \int_{+\infty}^{-\infty}\int_{+\infty}^{-\infty} f(x,y)\delta(r, x\cos\Theta - y\sin\Theta)dxdy$$

where r is the perpendicular distance of a line from the origin and Θ is the angle formed by the distance vector. A discrete Radon transform called Hough transform has been introduced in 1972 by R. Duda and P. Hart as a tool for image features extraction. Wavelet decomposition using Discrete Wavelet Transform (DWT)[15] provides an image analysis resulting in image decomposition into two-dimensional functions of time and scale. The main benefit of DWT is in its multi-resolution time-scale analysis ability. Wavelet functions used for image analysis are derived from the initial function W(t) forming basis for the set of Functions

$$Wm,k(t) = 1/\sqrt{a}\ W\ (1/a(t-b)) \quad \text{--- (2a)}$$

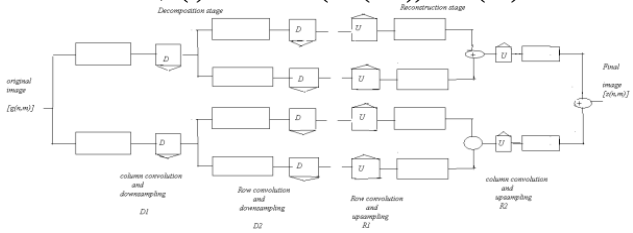

Figure 2

Wavelet transform use in image decomposition and the effect of Haar and Bio3.7 wavelet function dilation to its spectrum compression analysis. The principle of image decomposition and reconstruction for resolution enhancement is presented in Fig. 3. The decomposition stage includes the processing of the image matrix by columns at first using

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wavelet (high-pass) and scaling (low-pass) function followed by row down sampling by factor D in stage D1. To study this problem let us denote a selected column of the image matrix [g(n,m)]N,M as in image.

$$\{x(n)\}_{n=0}^{N-1} = [x(0), x(1), ..., x(N-1)]T \quad \text{.....(2b)}$$

This image can be analyzed by a half-band low-pass filter with its impulse response

$$\{s(n)\}_{n=0}^{L-1} = [s(0), s(1), \ldots, s(L-1)] \quad \text{-----(3)}$$

and complementary high-pass filter having impulse response

$$\{w(n)\}_{n=0}^{L-1} = [w(0), w(1), \ldots, w(L-1)] \quad \text{----- (4)}$$

The first stage assumes the convolution of a given image and the appropriate filter for decomposition at first by relations

$$xl(n) = \sum_{k=0}^{L-1} s(k)x(n-k) \times h(n) = \sum_{k=0}^{L-1} w(k)\, x(n-k) \quad \text{-----(5)}$$

for all values of n followed by sub sampling by factor D. In the following decomposition stage D2 the same process is applied to rows of the image matrix followed by row down sampling. The decomposition stage results in this way in four image representing all combinations of low-pass and high-pass initial image matrix processing. The reconstruction stage includes row up sampling by factor U at first and row convolution in stage R1. The corresponding images are then summed. The final step R2 assumes column up sampling a convolution with reconstruction filters followed by summation of the results again.

2.2 PROPOSED METHOD

In this section, the rotation-invariant texture-analysis technique using Radon and wavelet transforms is introduced.This technique is depicted in Fig. 3.

Figure 3: Block diagram of the proposed technique

The illustration shows the procedure of proposed method in block diagram. At first we identify all image components using distance and Hough transform. Then we obtain the Radon transform of the image segments and then use a translation-invariant wavelet transform to calculate the frequency components and extract the corresponding features. Rotation of the input image corresponds to the translation of the Radon transform along Fig.3 shows how the Radon transform changes as the simulated image rotates. The figure presents rotation of the simulated image, whose whole the image components are same, corresponds to a circular shift along. Therefore, using a translation-invariant wavelet transform along, we can produce rotation-invariant features.

3 FEATURE EXTRACTION

The main goal of this paper is to show, how is the features are changing by use different transforms by image rotation. Our wish is to have the same image features independently of image rotation. Fig. **4** presents, how passes the features analysis of simulated image, which rotates by angle from 0◦ to 180◦ with step 2◦. Characteristic image features, shown in Table. 1 are computed of the diagonal DWT transform coefficients in the first and the second decomposition levels rotated image by angle $\Theta = 2^\circ$ and they are shown in figure as a colored dots. The dots in the figure, presenting features, are evaluated **b**y the DWT applied to the Radon transform(RT) of rotated image Below comparison of image features evaluated by methods mentioned in Fig.4.

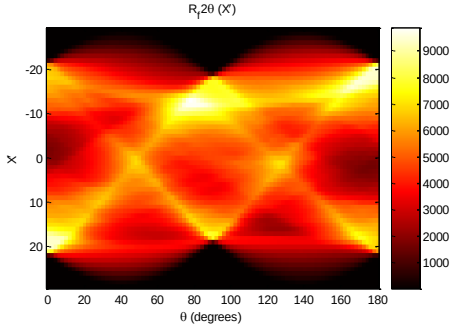

Figure 4: DWT applied to Radon transform by angle increase step 2 degree.

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Table1:Comparison of features evaluated for simulated image presenting column F1 as a diagonal DWT coefficients in the first decomposition level and column F2 as a coeffs. in the second decomposition. level, for 3 different techniques (i) HWT, (ii) BOWT and (iii) RHW

Table1:Features of Simulated Image

Angle	HWT		BOWT		RHWT	
	F1	F2	F1	F2	F1	F2
0	3.750	11.187	0.187	11.343	4.015	13.50
2	3.750	11.187	0.672	9.044	4.015	13.50
4	0.750	11.187	0.507	12.751	1.629	13.50
6	0.750	11.187	0.380	0.220	1.629	13.50
8	1.500	1.250	0.612	5.213	1.935	5.177
10	1.500	1.250	0.293	2.224	1.935	5.177
12	0.750	1.250	0.215	0.517	0.233	5.177
14	0.750	1.250	0.976	3.014	0.233	5.177
16	2.750	0.500	1.246	2.643	0.654	8.063

These features are for single cell(myeloblast),similarly other remaining are extracted as shown in fig.1. There are 720 wbc cells which features are extracted.

4.A) NURAL NETWORK RESULTS

These features are normalised and applied to ANN classification LM algorithm[16-18] for pattern recognition of bone marrow wbc cells into six types with their differential counts as shown in the confusion matrix for each training set(252cells) , test set(59), and validation test(59cells). Which are further used for disease diagnosis. The results of classification and cell counts are shown in following tables.

Table1:Training confusion matrix

O\T	Blast	Pro	Mye	Met	**Band**	pmn
Blast	25	0	0	0	0	0
Pro	1	4	3	0	0	0
Mye	1	2	163	4	0	0
Met	0	0	2	14	2	0
Bnd	0	0	0	4	30	11
pmn	0	0	0	2	13	215
Classification rate (Train) = 90.99%						

Table2:Test confusion matrix

O\T	Blast	Pro	Mye	Met	**Band**	pmn
Blast	5	1	0	0	0	0
Pro	0	1	1	0	0	0
Mye	0	2	47	3	0	0
Met	0	0	2	2	0	0
Bnd	0	0	0	0	4	3
pmn	0	0	0	2	8	56
Classification rate (Test) = 81.36 %						

Table3:Validation confusion matrix

O\T	Blast	Pro	Mye	Met	**Band**	pmn
Blast	5	1	0	0	0	0
Pro	0	1	1	0	0	0
Mye	0	3	39	3	0	0
Met	0	0	2	1	0	0
Bnd	0	0	0	0	6	2
pmn	0	0	0	2	8	44
Classification rate (Validation) = 81.36%						

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As mentioned in section 3, the data set we have divided into training , test, and validation sets. However, we need to have training , test, and validation sets to train , test, and valid neural network to evaluate its generalization. Cross validation is a standard method to solve this problem. We will briefly describe the cross validation here. The experiments are performed using the 5-fold cross validation. That means we divide data points into 70% for training(502 cells),15% (59c ells each)for each of test and validation tests respectively. We train, test, and validate a neural network using these three sets and evaluate the network's performance. That is the end of the first fold. We keep doing this until we finish all sets. We choose a neural network with one hidden layer consisting ten hidden neurons. The number of neurons of ten is large enough to be used to approximate a function of six inputs and six outputs. It is also not too large so that we will not lose the generalization. The desired output is set to 0.9 for the output neuron corresponding to a given class, and 0.1 for the other output neurons. The training would stop when the maximum epochs reaches 100 or the mean square error is less than 10^{-6}.We present the results as confusion matrices of total classified outputs of all inputs , i.e., the sum of all five confusion matrices in training and the sum of all five confusion matrices in testing. Due to the space limitation, the confusion matrix of each fold is not shown here. The total confusion matrices on the training ,test, and validation are shown in Tables 1 ,2, and 3 respectively.

The confusion matrices in Tables 1 and 2 show aproblem of neural networks, i.e., there are biases to the classes those have larger number of samples (myelocyte and PMN, in this case.) Classifiers' decisions are more likely to be these classes than the others. But this is not required because we would like to minimize the mean square error in our transformation features. To increase the chance of correct classification, the network would give more probability to classes those have more input samples.

B)DISEASE DIAGNOSIS RESULTS

Table3. Mean parameters of white blood cells of patients with breast cancer.

Parameters	System Count	Normal Values
Abs. neutrophil (x103/µl)	As	1.9-8
Diff. neutrophil (%)	per	
Abs. lymphocyte (x103/µl)	the	40-74
Diff. lymphocyte (%)	patients actual	
Diff. monocyte (%)	record	0.9-5.2
Diff.eosinophil (%)	as	
	per	19-48
	the	
	diseases	3.4-9
		0-7

5. CONCLUSION

We demonstrate that features based on the Radon and wavelet transform coefficients with two decomposition levels .the pair coefficients are selected from each transform having six features for each angle step up to 18^0 rotation, these features are normalized with maximum value of coefficients. the maximum value of a each level is to be used for normalization. these values are useful in the automatic white blood cell classification. The classification rate of about 81.36 % on test and validation sets is similar to those achieved in [5] with different features and different data set. The detail information about ANN algorithm like performance characteristics, training plots, and receiver operating characteristics are discussed in next paper.We proposed a method to unbias the classifiers. The bias to the desired output using different features information of the number of samples in each class is applied and computed. This computation increases the classification rate on the test sets which we can claim that it increase the generalization of the classifier. The features we use in the computations heavily rely on the hand-segmented images. The future work is to incorporate the automatic cell segmentation to our system.

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BIOGRAPHIES

Namdev D.Pergad received the B.E. (EC.) degree from Marathwada University, Aurangabad, Maharashtra,I ndia, in1989, The M.E.(EC). degree from the Shivaji University,Kolhapur,Maharashtra, in 2006 and the Ph.D is persuing from Dr.B.A.M.U.Aurangabad. he is working as a Faculty Member in the Department of Electronics and Telecommunication Engineering,STB College of Engg.,Tuljapur-413601.He has published few novel papers in international journals and paper presentations in three international conferences. His current research interests include mathematical morphology, neural networks, medical imaging, and signal and image processing in numerous fields of applications.

Dr.S.T.Hamde received the Ph.D.degree in Instrumentation Engineering from the Shri SRT University,Nanded, in 1982. Currently he is a Full-Ranked Professor in the Department of Instrumentation Engineering, SGGS COE&T,Nanded. His current research interests include probability theory, module theory, topology, and functional analysis.