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Leaf Biometrics Based Karyotyping of G-Band Chromosomes

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ABSTRACT In the field of medical imaging,chromosome karyotyping plays the major role to diagnose the birth defect problems like Down syndrome, Turner syndrome. To detect and recognize these problems in early stage,it is necessary to analyze over the chromosome are necessary to karyotype. In previous methods, karyotyping analysis is done based on statistical measurement and feature based analysis. In the over headed chromosome images, the previous methods are insufficient to identify its pairs and when the chromosome twisted or overlapped over other chromosomes. Overlap occurs from the point of Centromere or from the endings of each arms of chromosome. In this paper, LEAF algorithm based method is used to identify the biometric points in each chromosome. In this method, identification of chromosome pairs is possible even in the chromosomes arm having tilt from the centromere. Here the primary parameter is Band gap between each chromosome band, and secondary parameters are different band lengths to endorse the pair of each chromosome.

I. INTRODUCTION

The various genetic problems which can occur in future generation can be predicted by analysing the morphological behaviour of a chromosome. There are 23 pairs of chromosomes in a human cell (Wu et al.1987).The first 22 pairs of chromosomes are called the Autosomes and the 23rd pair is the sex chromosome. Karyotyping analysis (Mehrsan Javan Roshtkhari and Seyed Kamaledin Setarehdan 2008; Xinwei Feng et al. 2012) is an important screening and diagnostic procedure for detecting several genetic diseases / chromosomal anomalies. In Fuzzy based method Vanderheydt and Dom (1981), the Fuzzification process not merely adoptable for banded chromosomes and analysis through the normal chromosomes makes the problem while identifying the band misalignment problems. In semi-custom automated method (Moradi and Kamaledin 2006; Legrand et al. 2008) overlapped chromosomes causes few of the bands to be eliminated from the process which is necessary to identify the matching. The geometric feature and density profile of each chromosome can be identified using Medial Axis Transformation (Piper and Granum 1980; Frans et al.1989; Grisan et.al 2009; Wang et al.2009). The MAT algorithm helps in obtaining the skeleton of each image as a one dimensional view for two dimensional images. MAT helps more in pattern classification applications. There are many existing methods for segmenting the foreground and background image. Few of the methods are Otsu method (Frans et al.1989), global thresholding method (Mehdi Moradi and Kamaledin Setarehdan 2006; Wang et al.2009), k means clustering (Vanderheydt and Dom 1981), watershed segmentation (Mihail Popescu and Paul Gader 1999). The above mentioned methods have their own disadvantages such as intensity problems and over segmentation. In this paper, leaf Biometrics based karyotyping method is explained. This method improves matched chromosome pair and provides the better result for overlapped chromosomes.

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II. METHODOLGY

II. 1 Proposed Method

Figure 1 shows that initially each chromosome is converted into a binary image. Here concave and convex based method is used to detect the centromere points in each chromosome. These centromere points are verified based on the histogram based centromere detection method. After identification of centromere point, our Leaf Algorithm is applied using the method is explained below.

II. 1.1 Centromere Detection

In the chromosome classification based on centromere it is necessary to identify p-arm and

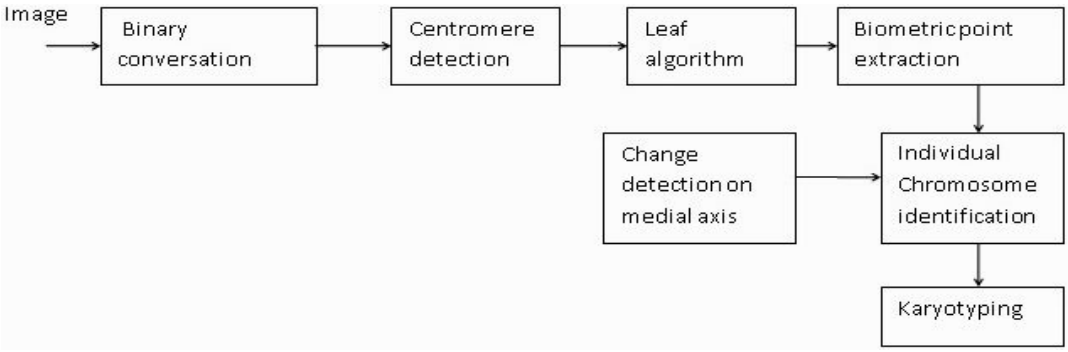

Fig. 1. LEAF biometrics method

q-arm portions of a chromosome.Initially medial axis is identified, and from the medial axis, outer non-linear intensity points are measured based on ideograms. From Chromosome boundary to middle axis, the minimum intensity point is taken as centromere point. Centromere to the larger arm is p-arm and least distance arm is q-arm.

II. 1.2 LEAF Biometrics Method

LEAF method is a standard circular form and enfolds the chromosomes inside the circle based on a constant parameter as like length, height through the medial axis which possible to generate a circle and enclose the chromosome arms separately or together i.e., Either p-arm or q-arm or both. Chromosomes are enclosed by a circle and the geometric analysis is done in the circle which is affecting the chromosomes, points which are making changes in chromosomes are taken.

II. 1.3 Leaf Algorithm

Figure 2 shows the chromosome analysis through leaf bio metrics. This algorithm is totally different from the other methods such as neural network, genetic algorithm and M-fish. In neural network (Piper and Granum 1980) each chromosome length, perimeter, and few statistical parameters are taken to train the network.When the curved chromosome appears the neural network fails to identify the appropriate chromosome. This leads to mismatch in the karyotype process. In genetic algorithm, each chromosome pattern and its length are considered. Abnormal chromosomes having deletion in region or its band, deletion in chromosome cause the mismatched pattern and hence it is unable to identify the deletion region of chromosome. M-fish analysis (Wang et al. 2009) brings out the better result. But for highly curved chromosomes and the band distorted chromosomes it does not provide the better results. In order to overcome these disadvantages, our method provides the supportive points as centromere to band distance (Moradi et al. 2003), each band position and width, points on medial axis are used to evaluate each chromosomes.

Figure 2 provides the details of biometrics points and the extraction of data from each chromosome is explained step by step as follows,

i) Centromere point is taken as 'CP', and length of p-arm, q-arm length is D_1 and D_2.
ii) Center point is 'C' on middle axis for p-arm, i.e., $D_1/2$.
iii) Medial axis as partitioned based on the ratio of ¼, ½, and ¾ of the D_1.
iv) Each point is extended towards both sides

$$Y_n = mx + c; \quad (1)$$

v) Chromosomes boundary curvature and Maxima points are calculated in the Y_n straight lines.
vi) The curvature maximum points to the Yn, a horizontal straight line is extended from which chromosome boundary points and band gap points are taken depending upon the constant circle having origin 'C'.
vii) Origin to the each band Gap measurement and no of bands on arms are identified based on the change detection algorithm on genetic change detection.

Tangential equation is,

$$(m_1-a)\,x + (n_1-b)\,y = (m_1-a)\,x_1 + (n_1-b)\,y1 \quad (2)$$

Considering slope s = -1.

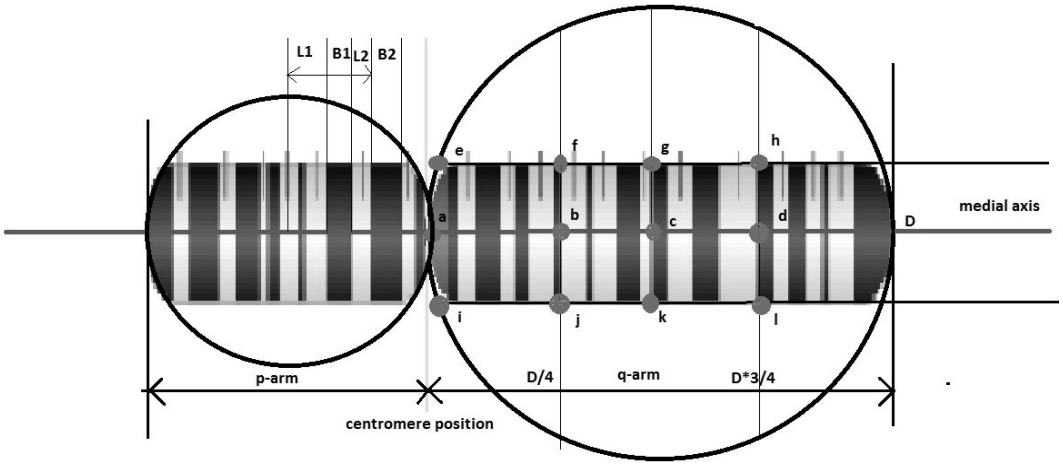

Fig. 2. LEAF points creation on a chromosome

II.1.4 Change Detection in the Medial (Medical Axis) Axis

Centre of the circle coincides with chromosome on medical axis as c (a, b)

Initialise the value of point in centromere as c (a, b) = 0.

Maximum If x (i, j) = 0

Then i = i +1;

Minimum x (m, n) = $x_{i+1, j}$

x (i,j) ‘“ x (m,n);

$$d_p = \sqrt{(x_n - x_p)^2 + (y_n - y_i)^2} \quad (3)$$

Pixel density at ‘0’ for (x_i, y_i) = I, Where I = 0 (or) I = 1

Increment the x-axis and get the intensity values (x_{i+m}, y_i), ()

Intensity m=0, i=0

If () 0

Then

$$d_k = \sqrt{(x_{i+m} - x_i)^2} \quad (4)$$

Else

k=k+1;

m=i+1;

End

II. 1.5 Band Length Calculation

Centromere Point is ‘O’

$$BG_k = d_k - d_{k-1} \text{ for k} = 0, 1, 2, 3\ldots.n \quad (5)$$

n- No of changes in band of each chromosome

Band Gap 3 $BG_3 = d_3 - d_2$

Band Gap 2 . $BG_2 = d_2 - d_1$

Band gap 1, $BG_1 = d_1 - d_0$

Centromere to p-arm length is D_{r1}, q-arm length is r_2

Radius of the circle on p-arm, $r_1 = D_{1/2}$ (Smaller arm)

Radius of the circle on q-arm, $r_2 = D - r_1$ (Larger arm)

Center point on r_1 is (m_1, x_1)

Center point on D_1 is (m_2, x_2)

Circle on the chromosome from point ‘0’ Centromere to the end of the p - arm is

$$(x - m_1)^2 + (y - n_1)^2 = r_1^2 \quad (6)$$

Center (m_1,n_1) is $x^2 + y^2 + 2gx + 2fy + c = 0$, where, x (t) = t (cos (t)).

For n-band chromosomes,

$$\text{Leaf Band Matrix} = \begin{bmatrix} B_1 & B_{2\ldots\ldots} & B_n \\ L_1 & L_{2\ldots\ldots} & L_n \end{bmatrix} \quad (7)$$

$$\text{Leaf boundary matrix} = \begin{bmatrix} f & g & h \\ b & c & d \\ j & k & l \end{bmatrix} \quad (8)$$

II.1.6 Chromosome Classification

In the chromosome classification, different parameters are taken individually, in which the unchangeable and identical measurement is necessary for pair identification of each chromosome. The normal chromosome do not have any band distortion and the breakage of the portion.In abnormal chromosomes have these problems and previous karyotyping methods are failed to classify and match the chromosomes due to changes in the band and the length and density of the each chromosome. In such case, our proposed methods classify the chromosomes recovering the matched pair through the points

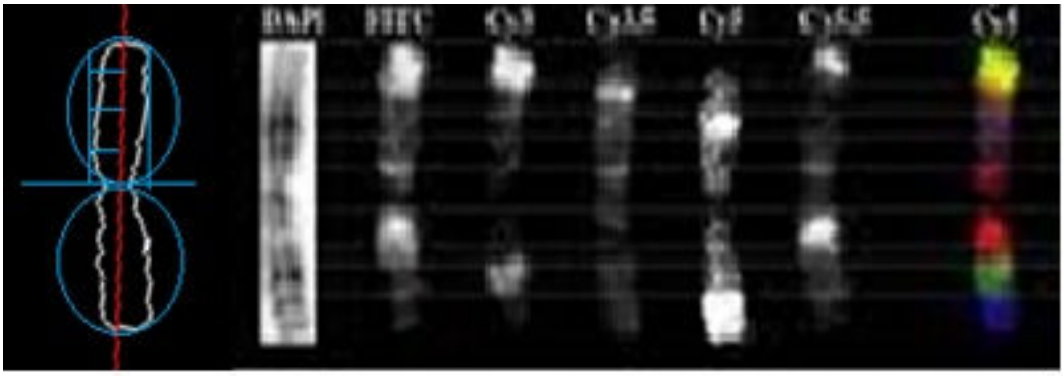

Fig. 3. Metacentric chromosome biometric extraction

which is matched from centromere to the arm portions.

II.1.7 Chromosome Pair Identification

Each chromosome is segmented from the input images and individual points are generated for both p-arm and q-arm in which sorting is done on the matched points which based on the no of bands available in the arms. Undistorted chromosomes have the clear band gap until the overlapping and the curved state in which normal chromosomes are matched with those bands, based on no of band parameter. Unmatched chromosomes and its count is based on descending order sorting which is done on all chromosomes depending upon the Centromere position and the length of the arm as varied. Chromosome arrangements with different orientation with a centromere position are shown in the Figure 4. Degraded chromosomes it is unable to identify its pair and the breakage of chromosomes mislead the gene orientation and the band pattern analysis becomes complicated. In such conditions, the origin of the Centromere is fixed as static point.From that point each side of the band pattern and the biometric points are taken. In this condition, the process is to take the larger arm for consideration. Each point from Centromere is analysed based on the band gap and band distance.

Figure 6 shows few of the chromosomes affected due to the deletion and Translocate chromosomes. Change detection on the medical axis

Fig. 4. Classification of different chromosomes with its centromere position.

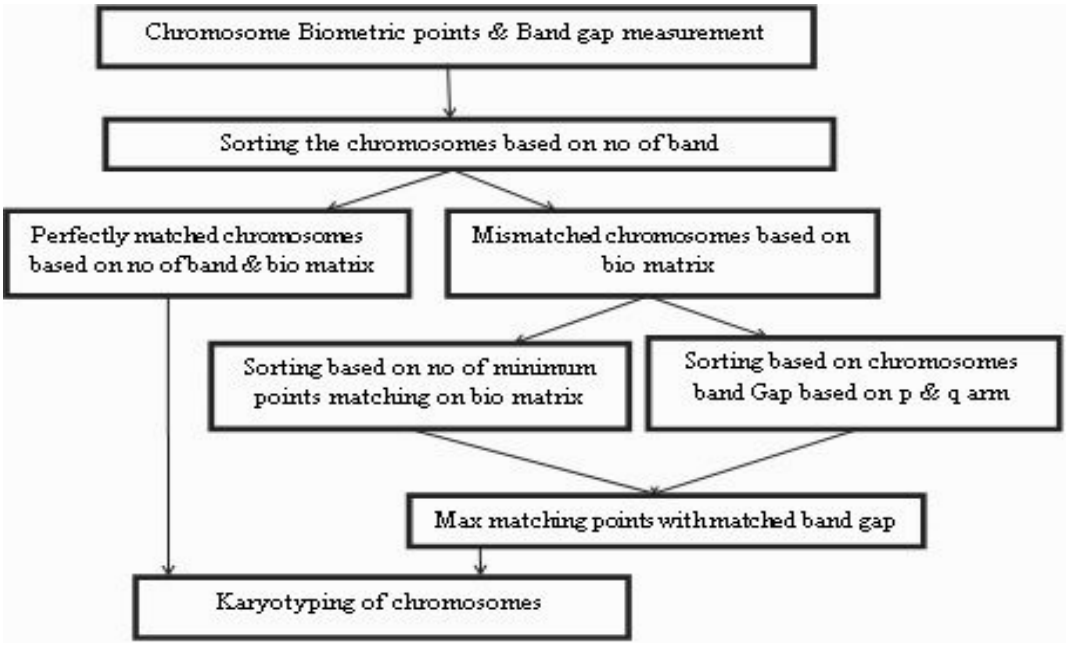

Fig. 5. Work flow of chromosome karyotype

is identified and then the no of bands is counted on each and which depend upon the no of band, bio metric a point matching is generated then it is matched with the nearest effective matched chromosomes

II.1.8 Chromosome Parameter Optimization

Leaf creation over each arm is not stationary for all the individual chromosomes with its pair, each chromosome generates different points based on our method. In such conditions the matching pattern does not generate the bio-metric. In that condition the no of the band gap, band length are taken as primary consonants , depending upon the primary factors the dimension reduction as is done with each row or column of biometrics and the maximum no of points matching as consider for the pair. In few conditions due to the deletion operation in the genetic, indifferent pair is matched by the factor of bio metrics. In such condition, the band length pattern does not coincide with that parameter. No of unpaired chromosome count will be increased in the case of miss matching such that the delimiter of the metacentric and other sex chromosomes are normally classified by its position and the band pattern matched prospect is high.

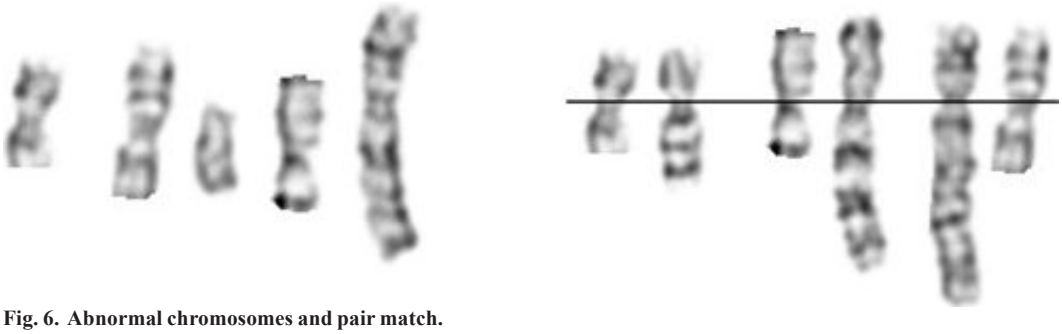

Fig. 6. Abnormal chromosomes and pair match.

II.1.9 Abnormal Chromosome Identification

Abnormalities in chromosomes are the measure of band inclusion, deletion and distortion, breakage in the chromosome. The abnormality leads to changes in the medial axis, no of the band, and distance between bands. When a band's inclusion as done on a candidate, factors of no of the band will change then the identification and matching is more difficult through it. In such condition the bio-metric points as taken as the primary factor. Minimized biometric points matching as done on each, in that condition stage one normal matched pair will be removed from the group. When reducing the size of biometrics, the second degraded chromosomes are identified. This has to be extended up to single point biometric its Centromere position. Each stage excluded chromosome is taken into consideration and the matching as done on it.

III. RESULTS AND DISCUSSION

All karyotyping has its own limitation depend upon its flexibility and adoption of the method in which the limitation is when the degradation or breakage has an abnormal chromosome then matching the pair becomes more complicated because biometric points are reduced up to single point biometric which depend upon the Centromere position of chromosomes. When the chromosomes overlap with 180 degree angle, then the band separation becomes highly complicated in such condition the classification of chromosomes are affected and it is too grim to analyse. Figure 3 shows the feature extraction based on proposed method. In that, each band pattern is considered and the extraction is based on the each p-arm, q-arm leafs. Figure 4 shows the centromere point based matching with different chromosomes. Figure 6 shows the abnormal chromosome matching performed based on the proposed method, the deletion of bands are not affected in matching. Our proposed method provide the better results compared to other methods which is shown in the Table 1.

(a) Spread chromosome, (b) Proposed biometric based karyotype (c) Neural network based Karyotype, (d) TS-fuzzy based karyotype.

in which deviations occur in the result between actual karyotyping to the processed results is shown in Figure 7 different methods. This is classified by means of the normal to abnormal chromosomes which is present in the group, in a pair anyone is an effect of the genetic problems can be identified by making another one as origin and the increased sampling will result in the actual abnormality identification, when both the individual chromosomes are affected then the pair matching is very difficult through the other methods of karyotyping. Single point method, it provide the solution for this problem until dilution or breakage occurs in the Centromere in such a way that, pre training is not required for this method, instantly it will generate those points and compare it with the previous generated chromosome pattern and identify the pair and abnormality.

IV. CONCLUSION

The proposed method provides a new approach in chromosome karyotyping using biometrics. Our method had a minimum deviation from actual karyotyping compared to other methods. This gives better results for curved chromosomes and eliminates the process step of straightening in the chromosomes. Few of the uncertainty make this method unstable in few conditions like highly degraded chromosomes, perfectly overlapped chromosomes. Beyond those factors this improves the accuracy

Table 1. Karyotype analysis based on various methods

Method of karyotype	*Possible p-arm to q-arm angle*	*No. of matched pair chromosome (23 Pair) %*		*No. of unmatched pair %*		*Deviation from actual karyotype (%)*
		Normal	*Abnormal*	*Normal*	*Abnormal*	
Neural network[6]	$180< \theta < 90$	78.3	43.4	21.7	56.6	72.5
Genetic algorithm[4]	$180< \theta < 45$	86.95	69.56	13.05	30.44	81.4
Fuzzy based[2]	$180< \theta < 90$	73.9	46.4	26.01	53.6	76.5
M-fish [5]	$180< \theta < 60$	90.4	70.3	9.6	29.7	85.5
Proposed method	**$180< \theta < 30$**	**95.65**	**73.91**	**4.35**	**26.09**	**93.6**

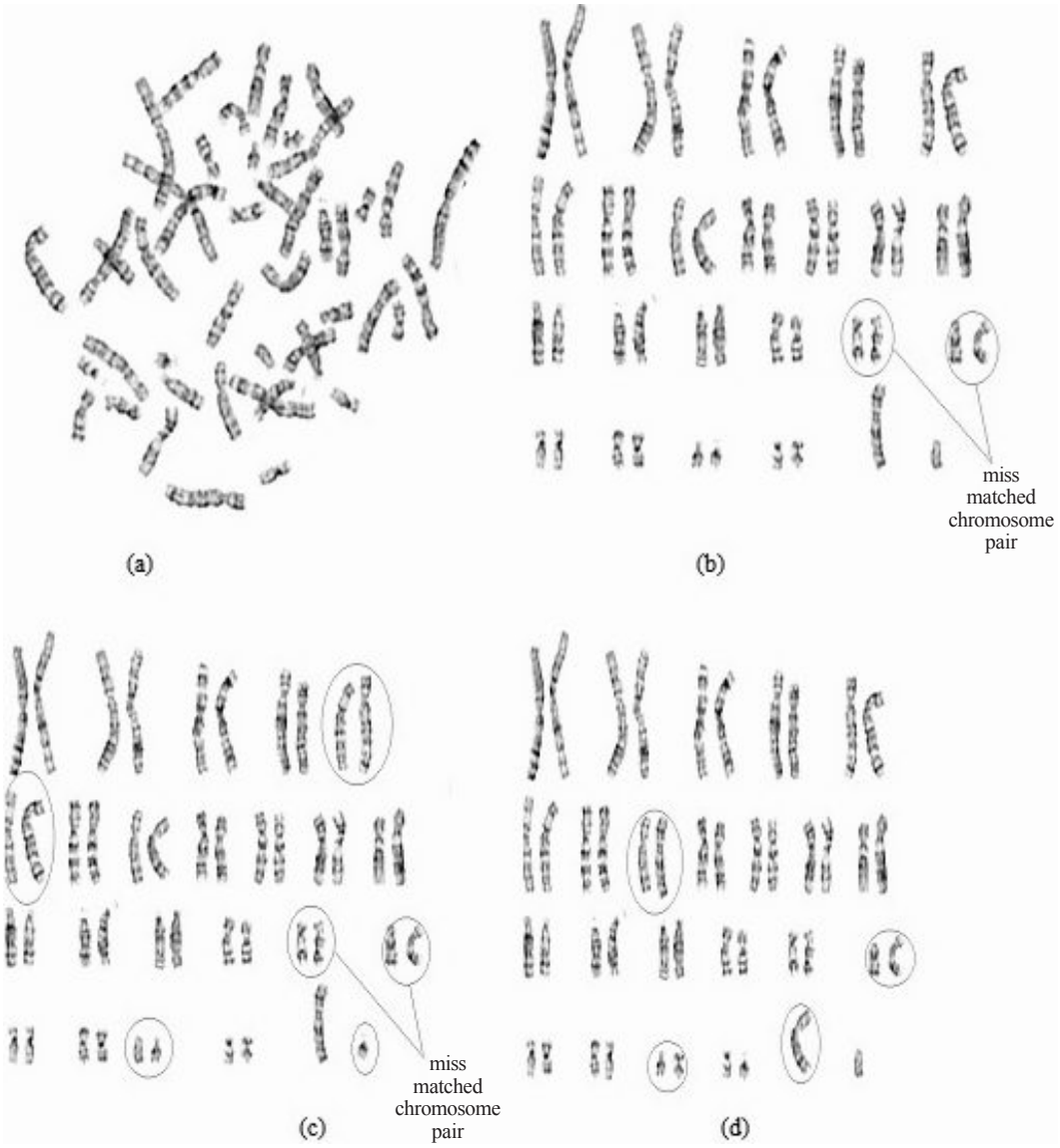

Fig. 7. (a) Spread chromosome, (b) Proposed biometric based karyotype, (c) Neural network based Karyotype; (d) TS-fuzzy based karyotype

to 94 % in the karyotyping and adaptable for normal and abnormal chromosomes. Leaf method is an adaptive method for extracting points depending upon the chromosome and minimize the points depending upon the abnormality occurring in the chromosome. This will furnish further to adopt the changes in Centromere position to minimize the error in order to get perfect karyotyping.

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