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PERFORMANCE ANALYSIS OF ALGORITHMS FOR THE SEGMENTATION OF METAPHASE CHROMOSOMES

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Abstract: Cancer is a destructive disease that affects each patient differently. A precise and rigorous diagnosis is essential for personalized treatment . ***Nowadays*** sophisticated test procedures are being used to measure the stage and progression of the disease . Cytogenetic researches have been highly appreciated as diagnostic aids in cancer medicine .In diagnosis, study of chromosomal aberrations plays a crucial role. Karyotyping is an inevitable process which is used to identify anomalies in the structure of cells. In the present scenario, considerable effort and time is spent for the segmentation of chromosomes from the images, and classifying the ***individual*** chromosomes into one of the 24 types. The process of segmentation of individual chromosomes in metaphase images is labour intensive and time consuming. When overlapping, touching or bending chromosomes are present in the metaphase, then mannual intervention is usually required as they are not easily separable by image processing techniques . Many techniques have been proposed to automate the process of segmentation and classification of chromosomes from metaphase images with admissible accuracy. But still segmentation of complex occluded images is an open problem and is necessary to investigate further to develop methods for enhancing the accuracy. This work gives a detailed review of various research in the domain of automatic karyotyping systems.

Index Terms **- karyotyping, segmentation, metaphase, chromosome**

I. INTRODUCTION

Cytogenetics is referred to as the study on the structure of human chromosomes and the study of disorders due to structural and numerical aberrations of chromosomes. Most of the recent history of automated karyotyping research has focused on designing intelligent and fully automated karyotyping systems. Automated karyotyping of chromosomes plays a potential role to help the clinicians diagnose cancers and also many genetic abnormalities can be detected at an early stage more efficiently and precisely.

The chromosomes cannot be seen even with a microscope when the cell is not dividing. But during cell division the chromosomes get more tightly packed and become visible under a microscope. The images taken during this stage are known as metaphase images.

Several inconsistencies have been observed in terms of number and structure of chromosomes and are responsible for many incurable diseases . For instance a Trisomy 21 is the cause of Down Syndrome while Trisomy 18 and 13 are the inconsistencies observed for Edward's Syndrome and Patau's Syndrome respectively. In the case of structural aberrations there may occur some changes or rearrangement of parts of the chromosome. Some commonly observed inconsistencies are deletion, duplication, translocation, inversions etc. Diagnosis of chromosomal disorders require analysis of chromosomes. As stated above, standard cytogenetic examinations demand the analysis of chromosomes at its metaphase stage. By karyotyping it is possible to identify the inconsistencies that are existing in the whole set of chromosomes.l

The remainder of this paper is outlined as follows. Section 2 discusses commonly detected disorders due to chromosomal aberrations. Section 3 briefs the process of karyotyping. Section 4 is a brief description of the works and their contributions to the feature extraction process and Section 5 lists various segmentation procedures and various karyotyping methods in the literature and finally in Section 6 a detailed review of the survey is presented.

II. CHROMOSOMAL ABERRATIONS AND DISORDERS

Chromosomal abnormalities can be divided into two major categories: numerical and structural. Numerical abnormalities arise when there exist variations in the sets of chromosomes. Triploids (3N), tetraploids (4 N), loss of a single chromosome (monosomy) or gain of a single chromosome (trisomy) are common in numerical aberrations. Structural inconsistencies of chromosomes arise when there is a chromosomal breakage and the broken ends are conjoined to form a new one. *A*n example of the short hand system used to describe numerical and structural aberrations is 47, XY ,+8, t(11; 22)(q24;q12), in which 47 indicates the total chromosome number, XY indicates the sex constitution, and +8 indicates an extra copy, trisomy, of chromosome 8. The "t" is an abbreviation for translocation and in this example specifies an exchange of chromosomal material between the long arms of chromosomes 11 and 22 at bands q24 and q12, respectively[1].

III.KARYOTYPING

Karyotyping is a common process in cytogenetics by which pictures of human chromosomes are arranged in a specific order and are presented for diagnostic purposes. Automating the process of chromosome segmentation and classification is the initial step in designing an automatic karyotyping system.

One of the major challenges associated with automatic karyotyping techniques is the poor quality of the metaphase spreads due to the non rigid nature of the chromosomes. Due to this nature the chromosomes may appear in unpredictable shapes and sizes in various images. Another major obstacle observed is the occlusion of chromosomal images which requires human intervention to resolve the same.

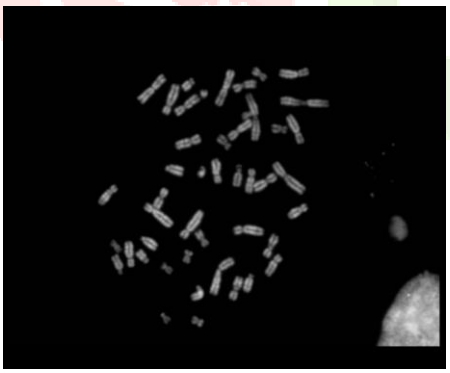

Figure 3.1 (Metaphase Image)

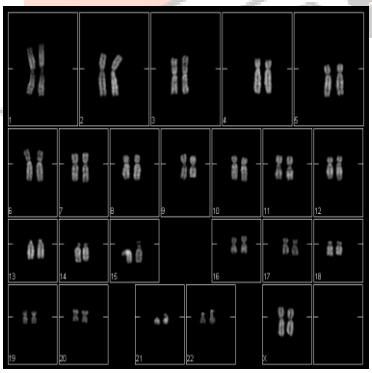

Figure 3.2 (Karyotype)

IV. FEATURE EXTRACTION METHODS

Different works in the literature attempt to extract the location of the chromosomal centromere by detecting the constriction point along the centerline. Piper et al[2] tackled this by considering the second moment along the centerline. The authors proposed some new features that can be used to describe chromosomal banding patterns and also a set of features that extract some global aspects of chromosomal shape, like the centromere location, appear to be largely invariant to metaphase contraction and chromosome bending. The notion of banding patterns is very crucial in this process. Width, intensity and relative position of the band are important factors when the banding patterns are considered[3].

Medial Axis Transformation (MAT) [3,4] is also widely used in many different works for classification. The drawback observed in MAT based algorithms is the cost of computation. The method also doesn't support when the image boundaries are not regular in shape .

Analysis of chromosomal images is not fully automatic due to various reasons that require human intervention [5]. Great efforts are reported in the literature to resolve the problem of occlusion. But the issues of occlusions in chromosomal images is yet to be effectively addressed. A dedicated procedure is thus required to resolve the problem for the classification of chromosomes.

V. STUDY OF VARIOUS ALGORITHMS

Gallus G et al [6] proposes that chromosomal banding pattern measurements can be used for the identification of human chromosomes. Severely bent chromosomes are not considered in this work. If the banding pattern of the cells could be described well by the Fourier coefficients, then the percentage of correct classification of the chromosomes ranged from 82% to 94%.Priya Chaku et al [7] proposes combination of various digital image processing techniques which are utilized for analyzing and processing chromosomal images. Here human intervention is necessary for the identification and classification of chromosomes. It is to be noted that performance of the proposed method completely relies on the quality of the input and resolution of the images.

D.Somasundaram et al [8] presents an active contour based algorithm for the segmentation of non overlapping and no touching chromosomal images and hypothesis based curvature based method of segmentation is used for overlapping chromosomes.The accuracy of the algorithm is about 96%. It is not mentioned in the work whether they have used real dataset or not. Wenbo Zhang et al[9] presents a convolutional neural network based deep learning network for classification. The proposed method was trained and tested on a dataset containing 10304 chromosome images, and was further tested on a dataset containing 4830 chromosomes. This method achieved an accuracy of 92.5%. Chromosomal images which have different orientations were not considered in the work. Prachi Vidhate et al [10] presents ANN method to identify chromosomes and various features of chromosomes like perimeter area, and centromeric index have been taken into account. The disentangling of overlapping chromosomes was out of scope for this work.

Pre processing of chromosomal images is crucial in the segmentation and classification process. Sivaramakrishnan Rajaraman et al [11] in their work make use of Connected Component Labelling and Extraction Algorithm for pre-processing.The dirt and interphase cells are also removed from the metaphase images .

Wacharapong et al [12] develops a technique to separate overlying chromosomes using computational geometry methods. Here all possible cut points are identified from the contour line of overlying chromosomes. Voronoi diagrams and Delaunay triangulations are used to select the four target cut points and overlying chromosomes are separated into two chromosomes.

Yongqiang Zhao et al [13] describes that geometric and spectral information can be extracted and is used to partition the cluster of chromosomes into regions. It has been claimed by the authors that the method is better than the conventional grayscale and multispectral segmentation methods. However, one problem identified is that the geometric information is not reliable in many cases of touching and overlapping chromosomes.

Choi et.al [14] presented a classification method for M-FISH images that does not require training of a classifier (unsupervised) nor does it require class parameter estimation (nonparametric). The classifications were performed with no preprocessing, background correction, and EM normalization. Both unsupervised-nonparametric (the minimum-distance classifier) and supervised-parametric (the maximum-likelihood classifier) methods were used as classification methods.

Tanvi Arora et. al. [15] proposes a region based active contours method for the segmentation of human chromosome images. The problem of touching chromosomes was addressed in the work and the method was able to resolve the issue to a great extent, as compared to previous methods. However the domain of overlapping chromosomes could not achieve much performance improvement. The main contribution of this work is that it is able to handle the meta spread images having non homogeneous background.

R. S. Remya et al [16] in their work, preprocessing of G-banded metaphase images is done for the process of karyotyping. A decision tree classifier is used for separating analyzable and unanalyzable images by making use of the features extracted from region labelled images. A four class classification of segmented parts as single straight, bended, touching or overlapped chromosome is proposed, in which top 10 Chi square selected features are used for classification. It is found that the four class classification is having 91.7% accuracy and specific post processing methods and classification techniques can be applied for these classes,for karyotyping.

Edge detection and extraction is essential to retrieve information on the shape, structure, and other vital characteristics of the image. The conventional methods for edge detection is usually performed using algorithms such as Sobel, Prewitt, Laplacian, Gaussian and other edge detection operators. Sivaramakrishnan Rajaraman et al [17] presents a Modified Bacterial Foraging Algorithm (MBFA) based on a probabilistic derivative methodology for the identification of edges in chromosomes. A swarm of bacteria searches for the nutrients in the search space in such a manner that they maximize their energy in unit time spent in foraging that drives all the bacteria to traverse through the edge pixels.

Gehad Ismail Sayed et al[18] presents an approach based on hybrid particle swarm optimization and K-Means algorithm. 40 chromosomal images from albino rat bone marrow are used in this experiment and claims 95 % accuracy for extraction.

Balaji V et al [19] proposes Maximum-Likelihood segmentation algorithms to segment the overlapping and touching human chromosome images. The algorithm worked better only for touching chromosomes images but failed to work for overlapping images.

R. Sivaramakrishnan et al [20] employs stochastic search algorithms including the Firefly algorithm (FA), Genetic algorithm (GA) and Particle swarm Optimization (PSO) in resolving occlusion.The algorithm starts with a random population of solutions from the image of occluded chromosomes. Operations borrowed from evolutionary methods are recursively done on the population.The technique yields satisfactory results even when 80% of the chromosome is occluded by the other. In this work the performance of the stochastic search algorithms in resolving occlusions in chromosome images is evaluated and finds that Firefly Algorithm gives superior results in identifying the occluded chromosomes.

Phil A. Errington et al [21] presents an approach to the automatic classification of metaphase chromosomes using a multilayer perceptron neural network.The inputs to the network are the size of the chromosome and centromeric index and a quantized representation of the chromosome banding profile.

Petros Karvelis et al [22] proposes a method for the segmentation of touching and overlapping groups of chromosomes in M-FISH images. To validate the method a benchmark database of 183 M-FISH images has been used. The proposed algorithm resulted in a 90.6% success rate for touching chromosomes and 80.4% for overlapping groups of chromosomes.

Mousami V. Munot et al [23] presents an approach for separating the touching chromosomes by using computational geometry . The technique initially uses the modified snake algorithm to disentangle the cluster of touching chromosomes from the metaphase images. Then a greedy approach based on combinatorial computational geometry of the pixels on the boundary of the cluster is used to identify and resolve the set of touching chromosomes.

Balaji.V et a [24] proposes a method for finding the intersecting (concave and convex) points in the chromosome images to separate the overlapped and touching chromosomes. This method of segmentation is applicable for large number of bents present in the chromosome structures and more number of clusters by

optimized the location of each separation point. This yields the minimal possible distance between the smoothed approximation and the original curve.

VI. CONCLUSION

In this work we tried to summarize the progress of various methods used for the process of karyotyping, preprocessing and feature extraction. Several contributions and techniques developed in the literature are studied that still represent an open problem. A great deal of research was made to improve automated karyotyping throughout the past 45 years. As part of these contributions different methods for preprocessing and feature extraction of chromosomal images were also proposed by various studies during the last few decades. Even though there exists various classification methods in the literature, still the process of karyotyping is a challenging problem and is performed by the automated karyotyping systems with the help of human intervention in the clinical laboratories. Therefore, new methods are to be developed for designing fully automated karyotyping systems. When feature extraction methods are considered, the MAT technique is widely used as it preserves the chromosomal shape. More contributions are required for the accurate extraction of features, especially centromeres of the image, which is an important attribute in chromosome classification.

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