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Automatic Segmentation of Human Chromosomes

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Abstract— **This paper is concerned with automatic segmentation of high resolution digitized metaphases. Firstly using a thresholding technique, a binary image of the cell picture is obtained. This binary image contains the addresses of darker pixels of the gray image of the colored cell picture. Several thousand of random points are assigned from among these addresses, and then using a distance condition, typically 50 pixels, and the number of centers is reduced to near 100. These points are search centers for chromosome segmentation. Algorithm first searches eight pixels surrounding the center. Picks the coordinates of the pixels darker than the gray level 0.9, then passes to one of the pixels recently recorded as dark enough, and repeat the same procedure to the neighbors which are not visited before. If none of the new neighbors are not darker than 0.9, search reaches at the boundaries of the chromosome, and ends. Then we call the pixels of the chromosomes in the colored image from the addresses in the binary counterparts to finish segmentation.**

Keywords— Chromosome cluster, presegmentation, segmentation, thresholding, image analysis, digitized metaphases.

INTRODUCTION

To detect genetic abnormalities, and fatal diseases like leukemia, karyotyping human chromosomes is a standard tool in today's medicine (Hong, and Mark 2000, Arthur, and Bloomfield 1983). Karyotyping starts by segmentation, this consists of picking up 23 pairs of chromosomes from the cell nucleus picture in metaphase stage. Second stage is the extraction of features for classification. The most important features are obtained from the gray level profiles of chromosomes (Piper, and Granum 1989). Then segmented chromosomes are classified into 23 types. Although there are devices and computer softwares to automate the process, still it is done manually by human experts in laboratories (Neurath et. al. (1972).

This paper is concerned with automatic segmentation of high resolution digitized metaphase images. The algorithm transforms the matrix of the gray image into a list pixel coordinates whose gray levels are darker than the threshold 0.9. Then among random points are chosen from this list, the ones which are separated at a certain distance are taken as centers. From each center a search is started. Algorithm visits all eight pixels surrounding the center. The coordinates of the pixels darker than the threshold are picked. Then one of the picked points is chosen as the new search center. Search visits the neighboring points that are not visited before. Search stops when there are no more dark points to be visited. The collected coordinates are the addresses of pixels forming individual chromosomes. Calling the pixels of the colored picture that resides at these coordinates, segmentation is completed. Last check is made to for repetitions, and missed chromosomes.

MATERIALS AND METHODS

This paper is concerned with automatic segmentation of high resolution digitized metaphases. A threshold-based approach is described which at the first stage treats the cell as a whole rather than as a series of individual chromosomes or clusters. Automatic segmentation of clusters of touching and overlapping chromosomes cannot be dealt with by thresholding alone (Ji 1988, 1989), and in this work, we put them aside.

Many attempts to solve the problem of touching and overlapping chromosomes have been made, and some encouraging results have been reached (Vanderheydt et a1981, Wu et al 1989, Vossepoel 1989, Graham1989). These solutions are only used in interactive chromosome analysis systems in which the final segmentation decision still rests on the operator. For real tasks, in which hundreds or even thousands of cells per specimen may have to be scored, operator intervention with every cell is not feasible (Bishop, and Young 1977, Ji 1994).

Usually cell nuclei in metaphase stage are photographed under a light microscope as seen in Figure 1. In metaphase stage, the chromatin is condensed inside the chromosomes making their bands to be easily observed with a light microscope (Lerner et al 1995). Bands on the chromosomes are clearly distinguishable from their neighbors by their darker or brighter appearances. Each of 23 chromosomes has specific band patterns of its own (Lerner 1998).

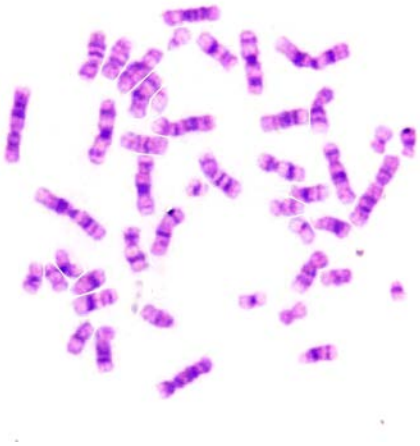

Figure 1. Cell nucleus in metaphase stage

We start by inverting the colored cell nucleus image into one with gray scales.

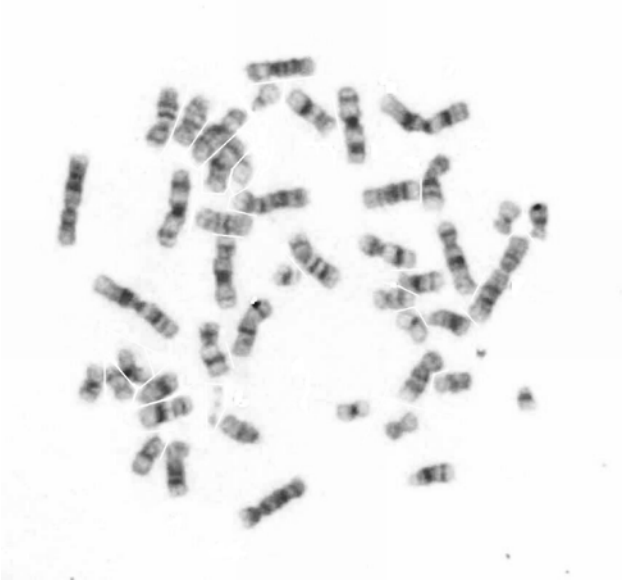

Figure 2. Grayscale version of the cell nucleus photograph

Presegmentation

Algorithm developed in this research first registers addresses of darker pixels in grayscale nucleus photograph in Figure 2. The threshold is set at the gray level 0.9 (1.0 is white, 0 is black) and search is started to find these darker pixels and their coordinates.

This algorithm transforms the matrix of gray levels into a list of coordinates of pixels darker than the threshold. The ListPlot of this list gives a black-white image of the nucleus. The aim of this presegmentation is to register the addresses of darker pixels on the gray scale image.

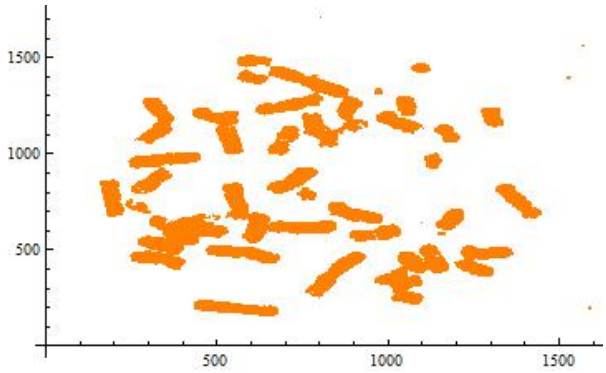

Figure 3. Binary picture for the grayscale cell nucleus photograph

Search Centers on Chromosomes

For the preparation to chromosome segmentation, first centers are found on the chromosomes in the binary pictures. To automates this selection, several thousands of random points are randomly selected among the points of the binary image. Then using a distance threshold, for example 50 pixels, the random points close to each other less than the threshold are eliminated.

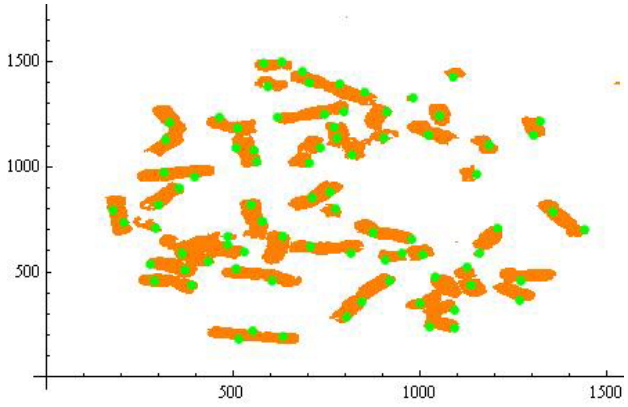

Figure 4. Search Centers on Chromosomes

Segmentation of Chromosomes Starts from search Centers

Centers are also addresses of interior points on the chromosomes of the gray image. Search is started from those interior points, called centers. Algorithm first searches eight pixels surrounding the center. Picks the coordinates of the pixels darker than the gray level 0.9, then passes to one of the pixels recently recorded as dark enough, and repeat the same procedure to the neighbors which are not visited before. If none of the new neighbors are not darker than 0.9, search reaches at the boundaries of the chromosome, and ends.

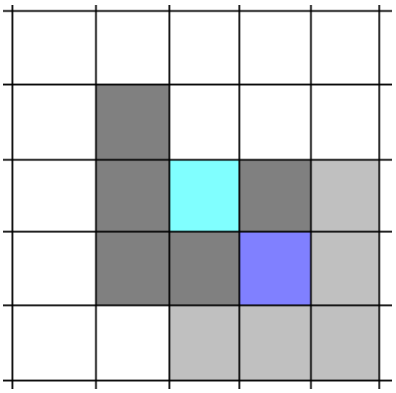

Figure 4. Coordinates of pixels darker than the gray level 0.9 are recorded.

The record of coordinates of pixels of a chromosome darker than the gray level 0.9 is a list of points. The plot of this list gives the binary image profile of the chromosome.

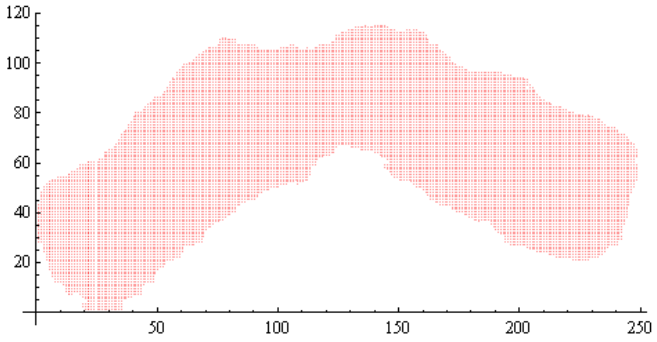

Figure 5. The plot of the points of the binary image that corresponds to the pixels of the gray image of the chromosome those are darker than the threshold 0.9.

The set of binary images are checked for the repeated chromosomes, the duplicates are removed. Then segmented chromosomes are plotted on the binary picture to check weather some chromosomes are missed.

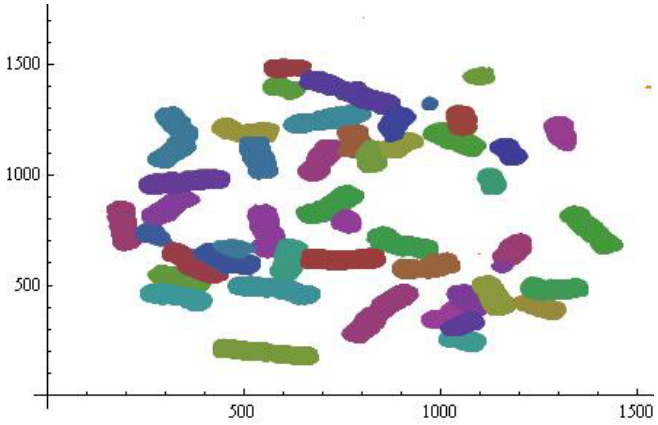

Figure 5. Segmented chromosomes are plotted on the binary picture to check weather some chromosomes are missed.

When we are sure that all chromosomes are segmented, we call the pixels of the chromosomes in the colored image from the addresses in the binary counterparts.

Figure 6. Pixels of the chromosomes in the colored image are called from the addresses in the binary counterparts

The Last Stage of karyotyping is the Classification

After classification, the set of chromosomes are put in an albume.

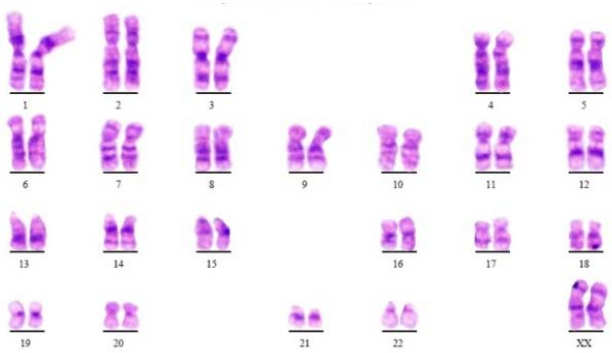

Figure 7. The result of the karyotyping process (Source INGAB Sarajevo)

CONCLUSION

The main contribution of this paper is to present an algorithm which transforms the gray image matrix into the list of points which are addresses of pixels on the chromosomes darker than a threshold. We are sure that coordinates of these points are addresses of points on chromosomes. From this list, addresses of centers on chromosomes are randomly chosen. Initially on each chromosome there may be more than one center. After segmentation we eliminate duplicates. To have at least one center on each chromosome, we choose several thousands of initial points. Once these centers are settled on chromosomes, algorithm first searches eight pixels surrounding the center. Picks the coordinates of the pixels darker than the gray level 0.9, then passes to one of the pixels recently recorded as dark enough, and repeat the same procedure to the neighbors which are not visited before. If none of the new neighbors are not darker than 0.9, search reaches at the boundaries of the chromosome, and ends after collecting the addresses all points on this chromosome. When we are sure that addresses for all chromosomes are collected, we call the pixels of the chromosomes in the colored image from these addresses in binary counterparts.

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