TWO INTELLIGENT ALGORITHMS APPLIED TO AUTOMATIC CHROSOME INCISION

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ABSTRACT

The state-of-the-art in commercial chromosome image acquisition was mostly grayscale. Automated Giemsa-banded chromosome image analysis has been widely used in clinical and laboratory examination. The decomposition of touching and overlapping chromosomes is a rather difficult task during the whole analysis procedure. Two intelligent chromosome incision methods are presented in this paper: contour characteristic method and incision based on Fourier transform. The former method makes full use of the characteristic of object contours to be decomposed, while the latter method takes advantages of Fourier transform. By the combination of these two methods, most cases of conglutinated chromosomes have been solved, so they can play an important and excellent role on the automatic analysis of chromosome image, and greatly alleviate doctor's manual operation on chromosome incision.

Keywords: Karyotyping, chromosome incision, conglutination point, edge wall, contour characteristic method, incision based on Fourier transform

1. INTRODUCTION

As carrier of DNA, chromosomes are very important to people's health. If they are damaged or miscopied, many congenital diseases could be caused as a result [1]. Now there has been lots of karyotyping system [2-4] that can help doctors to analyze chromosome images in the world, and some of them play a good role. But nearly most of those chromosome analysis systems have a common fault, namely their poor automatic chromosome incision ability, and it's quite usual that with those software Chromosome Incision mainly relies on manual judgment and operation.

So in our study on computer-aided chromosome karyotyping analysis system, the emphasis of research is put on automatic chromosome incision. Two new algorithms have been presented to complete this work and the result is comparatively very good. After the automatic incision carried out by this analysis system, most chromosomes will have been separated from each other, and there is only little work left for doctors to finish manually, which will increase efficiency of chromosome analysis greatly.

Our developed system is divided into three parts: chromosome image collector, chromosome image processor and chromosome analysis result database. In this paper, the two algorithms on automatic chromosome incision will be mainly introduced, which belongs to the second parts of system, as for other parts, please refer to [8] in detail.

2. IMAGE PREPROCESSING

At first, doctors must use image collector to capture a chromosome image from the light microscope, and

Figure 1 Original Image

process it with a set of tools, so that a mended

chromosome image is gained, which contains a set of chromosomes integrally. After stretching the gray of image, system passed it (Fig. 1) to image processor.

Before chromosome incision is carried out, chromosome image must be preprocessed, so that chromosome figures can be separated from the background. We use threshold segmentation to finish the image segmentation work, because the chromosome images are usually clear enough, and background gray and foreground gray are obviously different, which means it's quite easy to recognize the foreground chromosome figures with gray information. To make threshold segmentation more accurately, we use gray histogram equalization to push the gray distribution of image to two extremes of histogram previously [5], and after segmentation, an mathematical morphological opening operation will be carried out, which will smooth the objects and remove the noise. Then, based on the preprocessed chromosome image, system will label all the objects with a set of numbers, and trace all the contours (including outside and inside contours) of objects with a set of Freeman code chains. Thus, image preprocessing has been finished.

3. CHROMOSOME INCISION

In the preprocessed chromosome image, all chromosomes have been separated from the background, but some of them are conglutinated with each other and

Figure 2 Conglutinated Chromosomes

labeled as the same objects, which means, each object in the image maybe contains two or more chromosomes (Fig. 2). So it's necessary to incise all the chromosomes from each other according to figure and contour information of objects [6-7]. In conventional analysis software, this work mainly relies on doctors' manual operation, while in our system, we provide two automatic incision methods to finish it, which makes the work more easily.

3.1 Contour Characteristic Method

The first method we use to incise chromosomes is based on the characteristic of object contours. It can be found out easily that if an object contains two or more chromosomes, its contour must be different from that of those only containing one chromosome. For example, near the conglutination points of an object, contour chain always occurs concave, two sides' asymptotes usually compose an angle, and so on. By analyzing those characteristics of contour chains, system can finish chromosome incision intelligently.

At first, system goes over all the contour chain points of current object and store all concave points, only which are possible to be real conglutination points. Among those concave points, most ones could be dropped easily because real conglutination points must be deep concave, but centromere points are difficult to be distinguished from real conglutination points, for they are much like the latter. In order to judge whether a deep concave point is centromere point or not, system will analyze the inclination of two sides' asymptotes of it and mark each point with incision level. If the inclination is beyond π (>180), the point will be marked as level 3; if the inclination is nearly a straight angle, the point will be marked as level 2; if the inclination is an acute or obtuse angle, the point will be marked as level 1. Level 2 or level 3 means this point is very like centromere point, while level 1 means this point is very like conglutination points. But it's not always that case. Sometimes, in a real conglutination point couple, one point is level 1, and the other one is level 2 or level 3. So those level 2 or level 3 points shouldn't be dropped, because they also have possibility to be real conglutination points. This system will store all the deep concave points as candidate incision points, and their other information, such as

incision level and inclination bisector direction, will also be stored simultaneously.

Then, based on these candidate incision points, system creates a set of incision point couples that contains two candidate incision points each. In all possible incision point couples, most can be dropped easily, because the distance between the two points of a real couple will never be very large (Width of any chromosome cannot be very high.), and at least one point of a real couple must be marked as level 1 (Otherwise this couple is probably centromere point couple.). And if the inclination bisector directions of the two points of a couple are not nearly reverse or the direction of line connecting the two points is quite different from inclination bisector directions of the two points, this couple should also be dropped. Thus only a few incision point couples are left, which are very like real conglutination point couples. And it's still probable that some candidate incision point belongs to two or more couples simultaneously. But it's obvious that one candidate incision point can only be incised no more that one time. So according to each candidate incision point, a procedure must be carried out to find the real couple that contains it, during which distance between couple points is the key parameter, because the two points of real couple are always nearer than those of wrong couples. After a real couple is found and incised, the two points of it must be marked with incised points, so that they won't be considered and incised any more. By this means, all real incision point couples will be detected and incised, and most chromosomes will be separated. And if some overlapping chromosomes are found, which are difficult to be simply incised as others, this system will use a so-called two-tier template technique to process them [8], which maps different chromosomes to different layers.

3.2 Incision Based on Fourier Transform

With the method above, most conglutinated chromosomes could be incised. But there are still some conglutinated chromosomes left in the image, which cannot be dealt with accurately. So another method is presented to process them, which is called incision method based on Fourier transform. It takes advantage of Fourier low-pass filter to process the chromosome image and create a new image, in which gray of objects are distributed with the gradient. When we use threshold segmentation based on a low gray to deal with it, kernels of all chromosomes will be outlined (Fig. 3).

Then let's redefine threshold segmentation as a band-pass filter rather than a low-pass one, that is, replacing the gray in a certain range with foreground gray, while other gray with background gray. When we use this kind of threshold segmentation based on the gray near the edge of objects to deal with the image, edges of all chromosomes will be outlined (Fig. 4). At the beginning, kernels of different chromosomes are separated by edge walls; when we increase the threshold gray and push edge wall outward, kernels will expand and sometime meet with each other, which can be judged by kernel dilation detection and means those chromosomes are conglutinated. After all conglutinated kernels have been found, all conglutinated chromosomes have also been detected, and then automatic chromosome incision can be carried out easily.

Figure 3 Outlined Kernels

Figure 4 Edge Wall

This method is comparatively more accurate, especially when faced with profound conglutinations, but its calculation cost is also much more than that of contour characteristic method. And when a long chromosome has two focuses after being Fourier transformed, it may be divided into two parts with this method. So finally we recommend contour characteristic method as the primary method to incise chromosomes, incision based on Fourier transform as the secondary one, and the result is proved to be very excellent. During the whole chromosome incision, only when the two automatic

methods are invalid simultaneously or make some mistakes, manual judgment and intervention of doctors is needed.

4.CHROMOSOME CLASSIFICATION

After all chromosomes are incised and separated, the next work is to classify them, list them in order according to classification result (Fig. 5), and create karyotyping analysis report. There are much detailed work and many corresponding algorithms on them, which have been introduced in [8], and won't be dealt with any more here.

5. EXPERIMENT & CONCLUSION

About 40 cases of clinical samples provided by the affiliated hospitals of Zhejiang University have been used for evaluating the function of these two algorithms, more than 92% conglutinated chromosomes can be decomposed successfully by using these methods, which

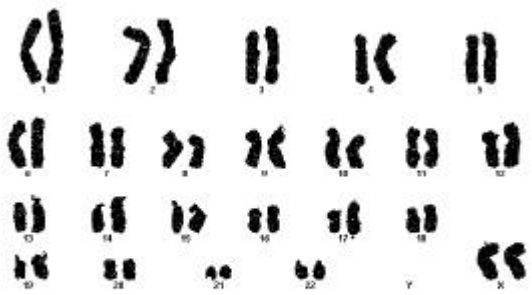

Figure 5 Karyotyping Image

is greater than other methods reported in reference [2-4]. In conclusion, two algorithms on automatic chromosome incision have been introduced. With them, the automatic incision ability of chromosome analysis system could be greatly improved, efficiency greatly increased, and manual operation greatly alleviated. All of these two algorithms have been involved in our system and large amount of experiments based on clinical cases have demonstrated their effectiveness and efficiency.

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