

# Effective Algorithms for Altering Human Chromosomes Shapes

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**Abstract** - Learning human cytogenetics is important for biology education and training of clinical cytogenetics technologists. To increase the resources of metaphase spreads with different chromosomes shapes for student practice, we describe effective algorithms for such purposes to enhance our cytogenetics tutorial program.

**Keywords:** human chromosome, cytogenetics, algorithms

## 1 Introduction

The function of altering human chromosome shape from curved to straight is available in the commercial karyotyping software [Cytovision, Genetix Corp., San Jose, CA] which is used by clinical genetics laboratories for chromosome analysis from patient samples. The purpose of chromosome straightening in the commercial software is to provide viewers with the appearance of neatly arranged chromosomes on the karyotype sheet. However, few cytogenetics technologists actually use this function because the straightened chromosomes do not provide more information from the G-banded chromosomes. In fact, the straightened chromosomes appear to be unnatural.

For education purposes, however, a versatile program with the capability of altering the chromosome shape can enrich the metaphase resources for student practice. A basic human chromosome modeling program has recently been introduced as a tool for cytogenetics education [1, 2]. In the early model, however, the changeable parts are limited to certain points along the chromosome. In this paper, we describe an improved method for chromosomal skeletonization which serves as a basis for programming the inter-conversion of chromosome shapes from curved to straight and *vice versa*.

The functionality of the chromosome shape alteration is to reconstruct original chromosome images into different shapes. Pixels on the original images are mapped to new positions on destination images using a transformation function. The new algorithms are capable of changing chromosome shapes at any points along the entire length of the chromosome. The new function meets the following two requirements: First, the length and width of the original chromosome image remain unchanged when the altered chromosome is created, and second, the original information

including the grayscale values and G-bands information are kept as close as possible to the newly generated model. Throughout our beta tests, there were no missing or adding G-bands on the altered chromosomes.

## 2 Chromosome Midline

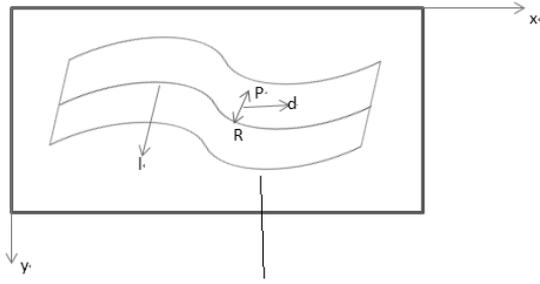
The chromosome midline is to obtain a curve to represent the approximate curvature of the chromosome. This is the pre-processing step for chromosome shape alteration. The human chromosome shape in metaphase is basically linear with the length much larger than the width; therefore, in practice, the width may be neglected so that a midline can be created to represent the chromosome curvature (Fig. 1). The midline curve is in parallel to the two sides with the same distances. The midline curve can be obtained in three steps: boundary detection, thinning, and curve fitting. Boundary detection is to acquire the boundary of chromosome image. Thinning is to convert binary shape obtained from boundary detection to a 1-pixel wide curve. Curve fitting is used to find the "best fit" line or curve for a series of data points.



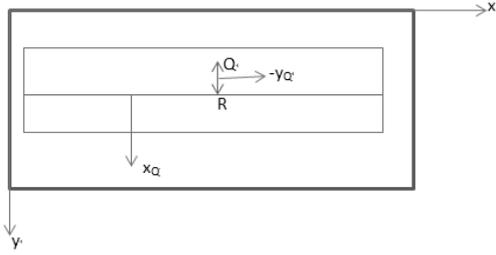
Fig. 1. Midline after curve fitting for human chromosome 2

## 3 Chromosome Straightening

Most of original chromosome images under the microscope are curved in various degrees. For beginners, it is easier to learn G-banded chromosome characteristics from straight chromosomes. Therefore, metaphase spreads with all straight chromosomes are ideal for beginning students. Fig 2.a is a schematic of an originally curved chromosome: The red line is the midline which can be calculated by chromosome midline introduced in session 2. Fig 2.b is a schematic of the same chromosome after straightening.



Schematic of originally curved chromosome



Schematic of the chromosome after straightening

Fig. 2. Conversion of curved to straight chromosome

After the midline is calculated, the next step is to map the pixels. There are two mapping algorithms: forward mapping and inverse mapping [3]. The forward mapping is to map the source pixel  $(x, y)$  to an appropriate destination place  $(u, v)$ . However, since the image source pixel is represented as an integer, when applying the translation function on the source pixel, the value of destination pixel may be represented by a decimal number, which must be rounded up to an integer. It may result in one target pixel having multiple source pixels or some missing destination pixels which lead to Mosaic effects. The inverse mapping is that, with the given location of the target pixel  $(u, v)$  in the destination image, we can calculate an appropriate location of the source pixel  $(x, y)$  in the original image based on the transformation function. Thus, all the destination image pixels are mapped to pixels in the source image. Therefore, the inverse mapping method was chosen for our modeling. Below is the detailed inverse mapping calculation:

In Fig 2.a, pixel P  $(x_P, y_P)$  is the source image, and line PR is perpendicular to the midline on pixel R  $(x_R, y_R)$ . In Fig 2.b, Q  $(x_Q, y_Q)$  is the destination pixel of P. In the inverse mapping, the position of Q is given, and the position of P must be calculated for mapping from P to Q. In Fig 2.a,  $d$  is the perpendicular distance from P to midline, and  $l$  is the length from the beginning of the midline to R; therefore:  
 $-y_Q = d$  and  $x_Q = l$

Assume the equation of midline is  $y = f(x)$ , then

$$l = \int_1^{x_R} \sqrt{1 + f(x)^2} dx \quad (1)$$

$$d = \frac{\sqrt{(x_R - x_P)^2 + (y_R - y_P)^2}}{\sqrt{(x_R - x_P)^2 + (F(x_R) - y_P)^2}} \quad (2)$$

Because  $PR \perp$ midline, then

$$\frac{y_R - y_P}{x_R - x_P} \times F'(x_R) = -1 \quad (3)$$

Because R is in the midline, then

$$f(x_R) = y_R \quad (4)$$

Through solving the above functions, P  $(x_P, y_P)$  can be calculated. However, the values of x-axis and y-axis must be integers. An interpolation technique is applied here to obtain the pixel value of P. The bicubic interpolation [4] was used to determine a more accurate pixel value of P and make the destination image smoother. P can be written as P  $(i+u, j+v)$ . The pixel value of P  $f(i+u, j+v)$  is calculated from its 16 neighbors according to the bicubic interpolation. Fig. 3 shows the original image of human chromosome 2 on the left side and the straightened model on the right side.

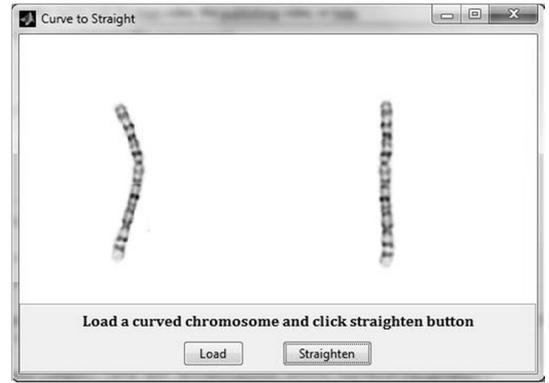


Fig. 3. Result of chromosome 2 straightening

## 4 Chromosome Curving

The algorithm for converting a straight to a curved chromosome is similar to that described in the precious section 3, but the midline of the destination chromosome is now a curved line. The shape of the curve can be set manually. Theoretically this algorithm is capable of changing a straight chromosome to any shape. A painting program (Fig 4) is provided to allow users to draw a curve as the midline of the altered chromosome. Through the curve fitting algorithm using interpolation method, an equation of the curve drawn by users can be calculated. Based on the equation, the originally straight chromosome can be converted to the designated shape. In Fig. 5, the originally straight human chromosome 2 is on the left, and the curved chromosome on the right is created according the curve drawn in Fig 4.

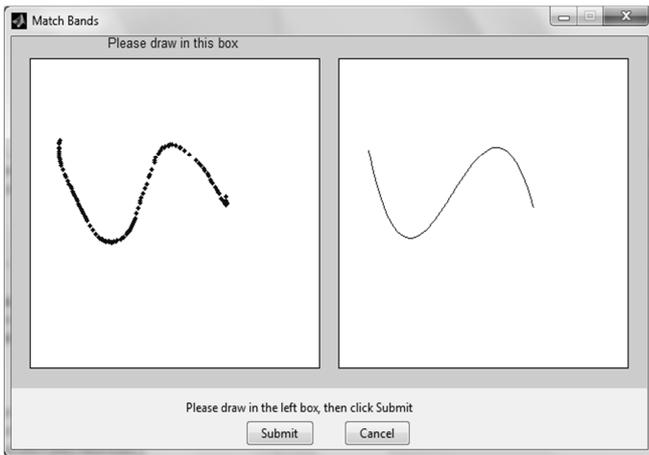


Fig. 4. Painter program accepts input such as a curve from users.

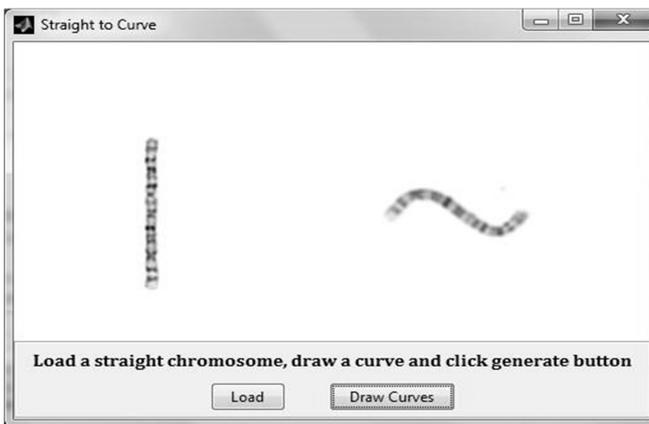


Fig. 5. Conversion of straight to curved chromosome 2

## 5 Results and Conclusions

Using the algorithms described above, metaphase spreads with all or mostly straightened chromosomes (Fig. 6) and with all or mostly curved chromosomes (Fig. 7) can be created from the original metaphase spread (Fig. 8). Likewise, karyotypes with all or mostly straightened chromosomes (Fig. 9) and with all or mostly curved chromosomes (Fig. 10) can be generated from the original karyotype (Fig. 11).

This paper describes effective algorithms for alteration shapes of human chromosome images, including straightening and curving at any points along the entire chromosome. With these algorithms, we are able to model and generate a wide range of human chromosome images with different shapes, thus increasing the teaching resources for learning human cytogenetics. The new program can be used in conjunction with our computer based cytogenetics learning programs [1, 2] as a new teaching tool.



Fig. 6. Metaphase spread with all or mostly straightened chromosomes



Fig. 7. Metaphase spread with all or mostly curved chromosomes



Fig. 8. Original metaphase spread

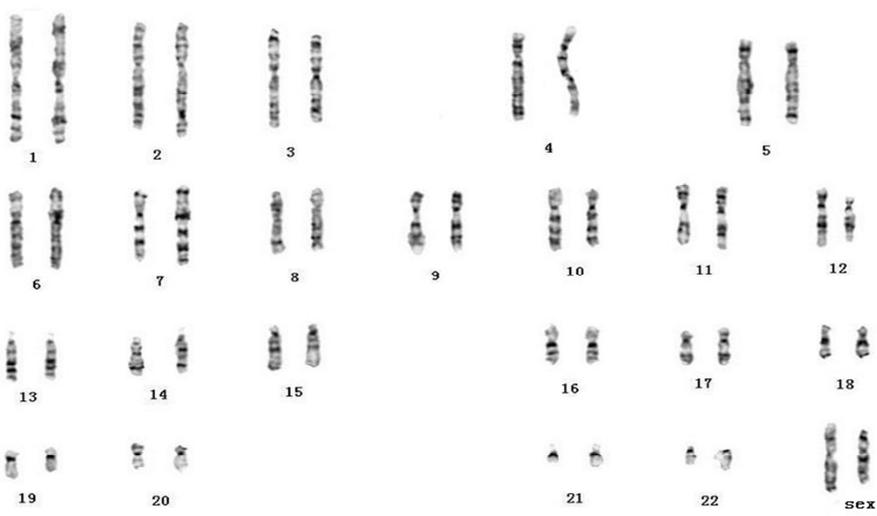


Fig. 9. Karyotype with all or mostly straightened chromosomes

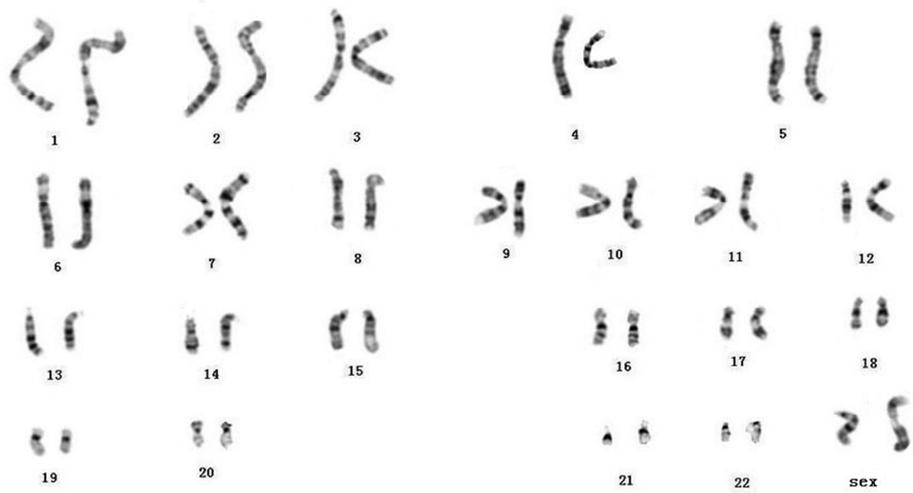


Fig. 10. Karyotype with all or mostly curved chromosomes

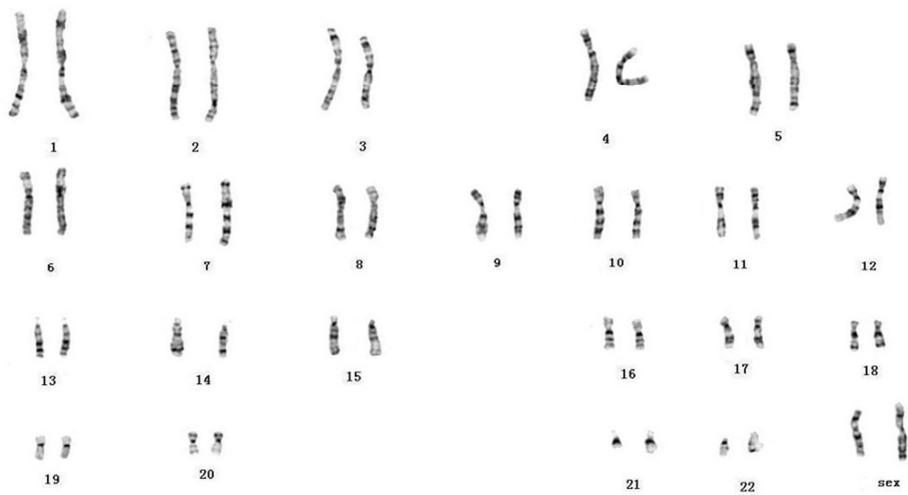


Fig. 11. Original karyotype

## 6 References

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