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№ 6548

Investigation of the Properties of Digital Chromosome Microscopy Images for the Telemedicine Applications

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September 7, 2021

INVESTIGATION OF THE PROPERTIES OF DIGITAL CHROMOSOME MICROSCOPY IMAGES FOR THE TELEMEDICINE APPLICATIONS

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Deep cytogenetic examination of chromosomes properties is very specialized test that can be performed only in some scientific laboratories. Many problems occurred with sending the cytohistological micro preparations to laboratories of other countries because of COVID-19 pandemic. The only one way was available – to use telecommunication systems and send digital images of micro preparations to laboratories for their analysis in the limited time. Due to technical features of digital images of microslides, their informative value can vary significantly. Subjective and qualitative estimations of the parameters of microobjects are also a significant factor, which leads to decreasing the accuracy of laboratory diagnostics and complicating the repeatability of the results in scientific research. The aim of this article is to investigate the chromosome image parameters that carry the fullest informative value out of the images.

Keywords—microscopic preparation, digital microscopy system, chromosome analysis, image processing.

I. INTRODUCTION

The intensive development of computer technology and the widespread introduction of digital computer technology create new opportunities in the development of automated systems for biomedical image processing [1]. With regard to the study of microplates, such systems can automate the process of determining the number of micro-objects, as well as perform specialized calculations for scientific or clinical conclusions.

The process of examining cytohistological micro preparations traditionally consists of counting microobjects differing in certain features (brightness, colour, geometry, etc.), requires a specialist operator to pay great attention, leads to rapid visual fatigue with limited ability to obtain quantitative information about the studied microobjects. A significant factor in this case is also subjective and qualitative estimates of micro-object parameters, which lead to low accuracy of laboratory diagnostics and difficulty in ensuring repeatability of results in scientific research.

However, the tasks of automating and improving the reliability of cytological studies, which are considerably complicated by the high individual and pathological variability of biological objects, are relevant.

II. THEORY PART

A. Explanation of chromosome micriscopy analysis

For cytogenetic examination of chromosomes, short blood cultures usually are used, followed by bone marrow cells and fibroblast cultures.

Cell culture of human peripheral blood lymphocytes is performed when the cells enter the mitosis phase. It includes the steps outlined below. Lymphocyte culture staging, lymphocyte growth during 72 years (lymphocyte growth can be complicated by various factors: the presence of infectious, chronic diseases; intake of medications; diet; alcohol intake, radiation damage etc.) [2-5]. Analysis of preparations allows calculate total number of chromosomes and evaluate the structure of each chromosome. Chromosome analysis is performed for 400 to 500 objects. The process of the main stage of chromosome examination using digital microscope is shown in Figure 1.

The chromosome in the study process has long arm lengths separated by the centromere. Some chromosomes have a secondary stretch that separates a small fraction of the chromosome - a satellite. In accordance with the centromere position, chromosomes are divided into four types: metacentrics (M), submetacentrics (SM), acrocentrics (A), and telocentrics (T). Metacentrics are chromosomes where the centromere is located in the middle, and those where one arm is significantly longer than the other are called submetacentrics (Figure 2) [5]. Chromosome type may be identified accurately by the shoulder index, which is calculated by dividing the length of a long arm by a short one.

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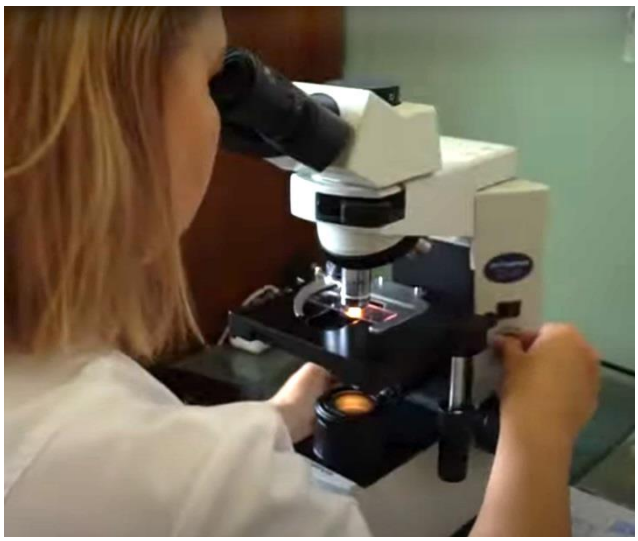


Figure 1 – Microscopy chromosome analysis

Metacenters include chromosomes with an arm index of 1-1.9, submetacenters 2-4.9, and acrocenters 5 and higher. The arm index can't be calculated for telocentric chromosomes.

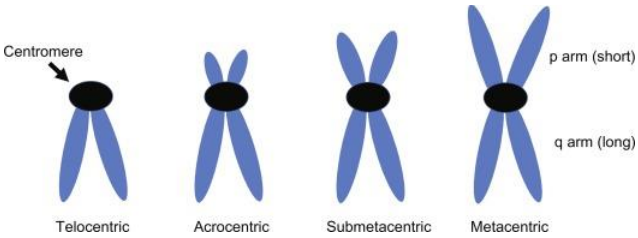


Figure 2 – Types of chromosomes by centromere position

B. Classification of chromosome aberrations

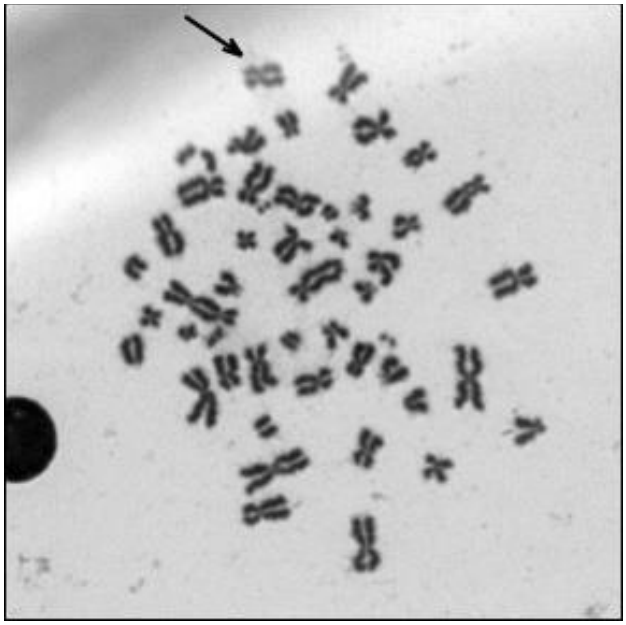
Chromosome aberrations lead to a rearrangement genetic material and change the chromosome structure within the karyotype. Either occur spontaneously or be induced by mutagenic factors that result in chromosome aberrations. Chromosome mutations, chromosome rearrangements - disruption of the structure (chromosomes (chromatids) structurally altered and accompanied by their breakage, which often results in the broken ends joining into new new combinations.

There are chromosomal and chromatid type aberrations. The former include are: intrachromosomal (eccentric rings, lamellar chromosomes, eccentric inversions, paracentric inversions) and interchromosome (reciprocal and polycentric translocations). The aberrations of the chromatid type are intrachromosomal translocations (intrachromatid, interchromatid) intrachromosomal and interchromatid (interchromosomal, chromatid-chromatid, chromatid-isochromatid).

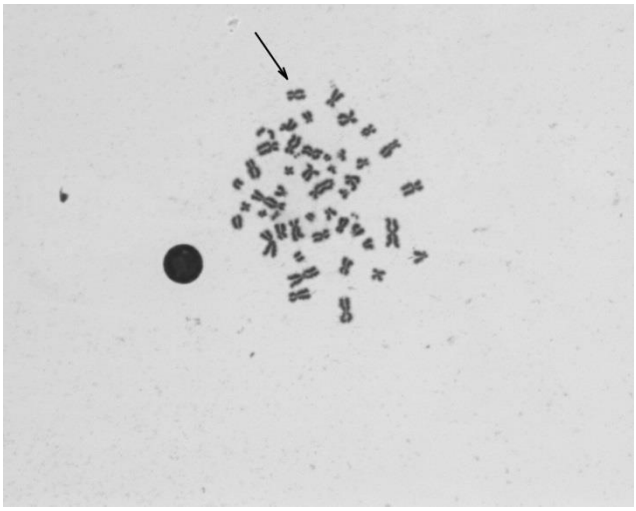
The results of visual chromosome investigations are highly depended on the properties of transmitted image files. So the problem of determining the best analysis conditions is very actual.

III. MATERIALS AND METHODS

Digital images of micropreparations obtained in the remote laboratory of radiation cytogenetics in the cultivation and staining of white blood cells are used (Figure 3). Automated image analysis of morphological properties of chromosomes images was performed using histogram and coordinate-brightness analysis.



a



b

Figure 3 – Transmitted microscopy images: a – cropped image 288×288 px; b - full frame of the same microscopy image1280×1024 px

IV. RESULTS OF THE RESEARCH

A. Telemedicine microscopy system

Modern biomedical digital microscopy systems allow taking images of medical micro preparations, transmitting them to remote computers and performing their automated processing.

In accordance with the tasks being solved the system usually includes a prepared specimen (enriched chromosomal preparation - cultured and enriched white blood cells) which is mounted on the microscope slide, the optical system of which allows obtaining an enlarged image of the microsample. A digital camera converts the image into a digital code, a coupling unit that transfers the data set to the computer (Figure 4). The data supplied through the Interfacing Unit and the associated Interface Module are converted into post-processing, segmentation, and image description modules [6-9].

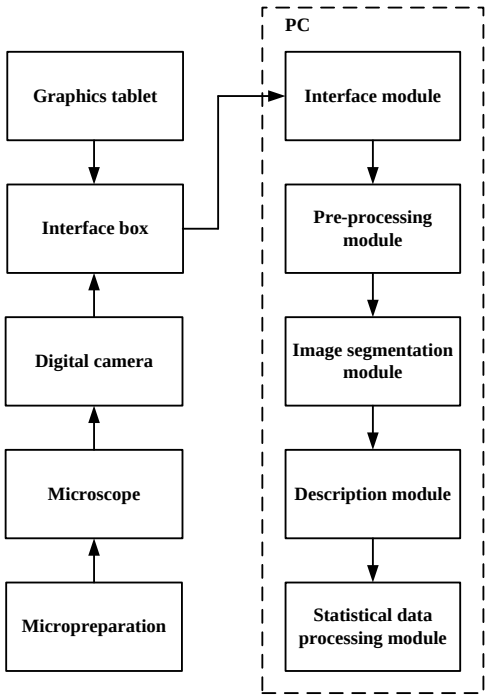


Figure 4 – Schematic diagram of a biomedical digital microscopy system

The colored image of histological image is a discrete function F (i , j) of intensity, defined on an image of size I×J elements, which accepts values in the range of magnitude from 0 to 255 (Figure 5).

Let us describe the main stages of analysis of images of microsamples. The first stage of image processing is analysis of image intensity, brightness and contrast [5-9], we will consider the most specific processing steps for histological images, one of which is the step of eliminating the non-uniform background. This effect may be caused by improper adjustment of the selected illumination or by a defect committed during preparation of the preparation.

B. Analysis of microscopy images

Information about microscopy images consists of:

- image description (geometric and optical characteristics of objects). Such characteristics are usually color and area, local contrast and so on [10] – [16].

Brightness image profile *P(x)* is selected through the point selected in the first step, a horizontal line across the object of one-pixel width is carried out. For each point of this line the brightness of the image is determined. Then a brightness graph is generated. Because we analyze the image in 8-bit greyscale, so for each point of the section, a segment of up to 255 pixels high may appear, as shown in Figure 5.

To determine the morphometric dimensions of an object on the image I×J a rectangular fragment WH of size *(q - b)* × *(k - f)* pixels is allocated. Analysis of the brightness of the pixels in the WH fragment is performed by scanning *(k - f)* lines of *(q - b)* pixels. As a result, we obtain *(k - f)* one-dimensional matrices of brightness values, from which an array of brightness values is formed in the whole fragment WH:

$$WH = \begin{bmatrix} P(x_b, y_f) & P(x_{b+1}, y_f) & .... & P(x_q, y_f) \\ P(x_b, y_{f+1}) & P(x_{b+1}, y_{f+1}) & .... & P(x_q, y_{f+1}) \\ ..... & ..... & ..... & ..... \\ P(x_b, y_k) & P(x_{b+1}, y_k) & ..... & P(x_q, y_k) \end{bmatrix}.$$

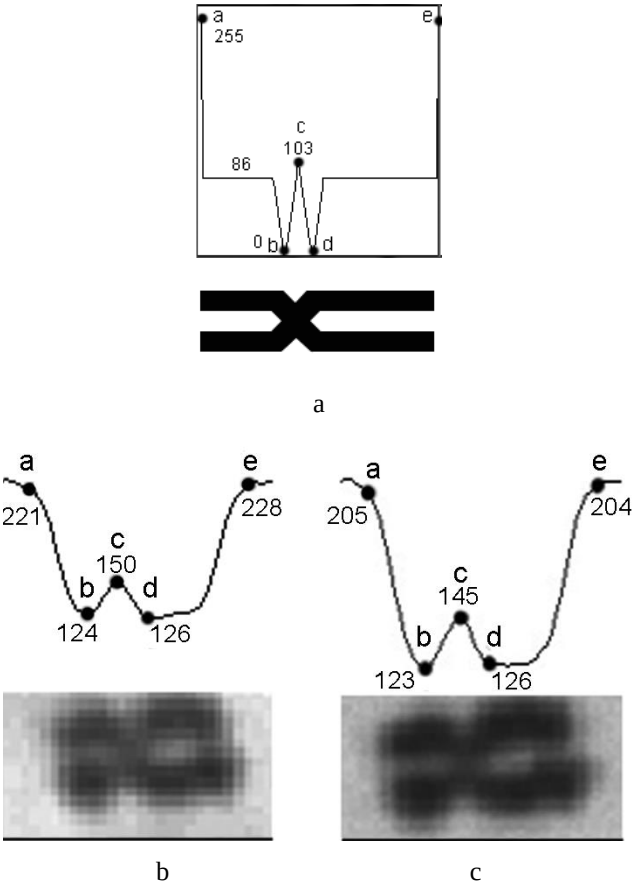


Figure 5 – The horizontal average brightness profiles of metacentric chromosome images (marked by arrow on fig.3): a – ideal metacentric chromosome image and its average brightness profile; b – chromosome profile of image fig. 3a; c – chromosome profile of image fig. 3b

Find the sum of the brightness values for the columns and the average brightness value for each column of the matrix WH as

$$\overline{P}_i(x_i) = \frac{\sum_{j=f}^{k} P(x_i; y_j)}{k - f} \quad .$$

A one-dimensional array of average brightness values is formed as

$$\overline{WH} = \left[\overline{P}_b(x_b) \quad \overline{P}_{b+1}(x_{b+1}) \quad \ldots\ldots \quad \overline{P}_q(x_q)\right].$$

This array provides an average of the brightness distribution of the pixels in the image fragment WH.

The array analyzed for maximum and minimum brightness values (Figure 5). As the argument x increases, the values of $\overline{P}(x_a)$, $\overline{P}(x_c)\,\overline{P}(x_e)$ and are determined sequentially. This method allows clearly define extreme points *a…e* due to digital brightness profile analysis.

The whole length of analyzed chromosome *ae* on Figure 5b was measured as 25 px, on Figure 5c as 50 px. So we clarified that images were saved with resolution differ by two times. That's why the results of the analysis of the first series of images were unsatisfactory.

The distance (x_c - x_a) gives a value of size of one chromosome arm, and the distance (x_e - x_c) - a value of size of the second arm. It's allow to calculate arm ratio. For ideal chromosome (Figure 5a) ratio is defined as 1.44. For image Figure 5b we have arm ratio 1.19 and for Figure 5c - 1.22 respectively. So all these objects are metacentric chromosomes. Arm ratio 1.22 of image Figure 5c is more accurate due to higher image resolution.

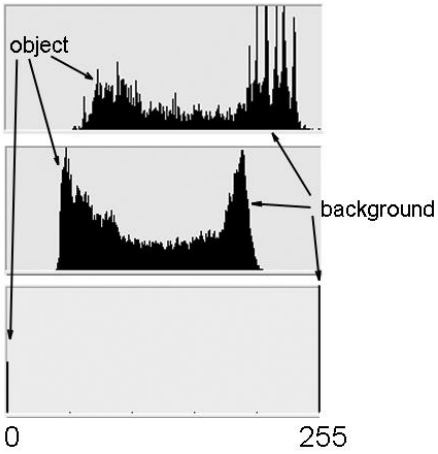


Figure 6 – The histograms of chromosome images (fig.3): a – histogram of image fig. 3a; b – histogram of image fig. 3b; c – histogram of ideal binary image (fig. 5a)

Histogram analysis (fig. 6) confirmed that low image resolution caused significant irregularity of histogram (Fig.3a), so determination the segmentation threshold for the next automatic analysis will be complicated.

V. Conclusion

The diagnostic relevance and informativeness of cytohistological methods can be improved by developing high-precision digital microscopy systems that include precision equipment and specialized software. The use of such systems greatly automates the laborious process of analyzing histological images and obtaining quantitative data. This achieves maximum efficiency of the practitioner's research. The difficulty of obtaining high quality cyto- and histological specimens significantly reduces the efficiency of computerized analysis.

The main medical and technical requirements for these systems are: ensuring the required increase in the microscope's performance and the integration of a digital video camera into the optical path of the microscope, linking and control of the camera without interface devices, implementation of algorithms of automated processing and analysis of micro-object parameters. The use of methods and algorithms of digital image processing can accelerate the process of analysis of cyto- and histological specimens and increase the accuracy of the study results [17-20].

The perspective of the work is to develop a fully automated hardware system of digital microscopy, improve data analysis algorithms and adapt them for various types of research with a high degree of automation and accuracy.

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