Mathematical model of the chromatin structure of the nuclei of blood cells

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Abstract. This paper describes the model of images of the nuclei of blood cells for research informative texture features in the diagnostics of acute leukemias on the basis of computer microscopy. The proposed model allows to simulate the structure of chromatin and factors distorting the signal in the formation of image.

1. Introduction

Currently, diagnosis of acute leukemia is based on an objective analysis of the results obtained in laboratory studies [1-3]: blood smears prepared with an general clinical analysis, bone marrow preparations, cytochemical, immunological, cytogenetic.

In practice, the use of modern diagnostic technology does not replace the study of blood smears and bone marrow preparations under the microscope for analysis of cellular composition [4-5].

Microscopic analysis of blood smears and bone marrow is difficult, tedious, time-consuming, requires mental and physical tension, according to some estimates, the error reaches 30 – 40 % depending on experience and qualifications of a physician hematologist.

The automated analysis techniques, based on pattern recognition methods, are used to reduce the complexity and difficulty of visual study of microscopic preparations. The use of medical decision support systems, based on computer microscopy would reduce the subjectivity of the diagnostic process. Unexplored region in automated image processing systems for the diagnosis of acute leukemia is the use of models of blood cell images based on texture analysis. Texture characteristics of nuclei of blood cells can be used for automatic classification of the blood cells. In this regard, the task of modeling texture images of nuclei of blood cells is relevant [6].

The aim of this work is the creation of model of images of the nuclei of blood cells for experimental studies of the information content of texture features in the diagnostics of acute leukemias on the basis of computer microscopy.

Computer graphics systems display information about the processes or objects in the form of synthesized display on the screen or other surface. For computer graphics systems, the source of the input data is not the physical processes, but their mathematical models. Such models generally represent an ordered set of data, numerical characteristics, parameters, mathematical and logical dependency mapping the structure, properties, relationships and the relationship between the elements of the object, as well as between the object and its surroundings.

Models usually are generalized, intended to describe a class of objects. Individual objects described by the input specific values of system parameters. The image that is associated with the simulated analog, known as the original.

2. Formation model

The model of formation of images of the nucleus of blood cells based on the specified distribution of the basic elements – model of chromosomes. In our model, one chromosome is a sequence of circles, whose centers are equidistant from each other and are on the same line. The length of the chromosomes, the radius of the circles and their brightness is a random variable, distributed according to the normal law of mathematical expectation. In two-dimensional space models of chromosomes "attached" to the nodes of the grid covering the entire area of the digital image.

The whole field is covered with a conventional grid, a step which is set as a parameter, and the nodes are circles of random brightness, the center of which is deviated from the node to the random variable, radius, brightness, and distance along the axes OX and OY are normally distributed, their mean value and standard deviation are specified as parameters. Areas of intersection are colored weighted sum of brightness of the circles.

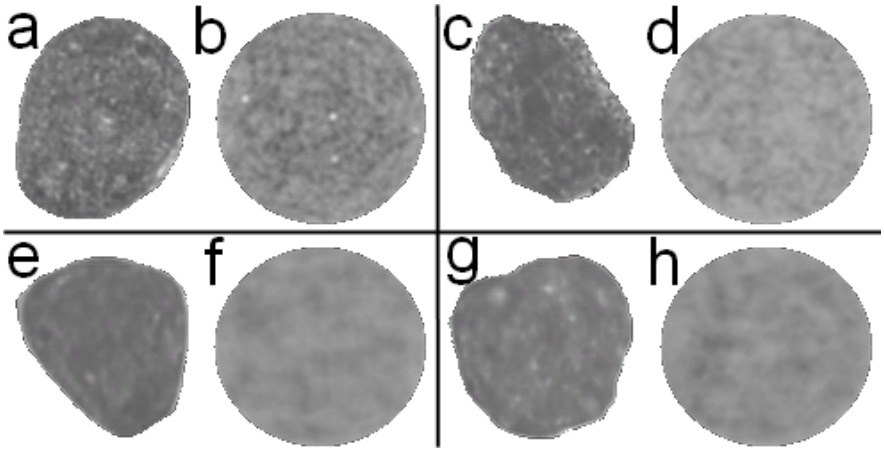

Figure 1. Image of blast cells a), myelocyte c),lymphoid cell e) and lymphocyte g) and the generated structures for each type b), d), f), h).

The advantages of this model include the ability to generate specific textures for all proposed types of blood cells, the corresponding model and the original image is set visually and meaningfully textural features.

Based on the analysis of the structure of blood cell nucleus suggests the following mathematical model of the nucleus image.

$F(x,y) = A(x,y) + B(x,y) + C(x,y)$, где $F(x,y)$ – the optical density of the substance in the nucleus of blood cells at the point with coordinates (x,y), $A(x,y)$ - the optical density of a substance generated by set of chromosomes, $B(x,y)$ - the optical density of the substance generated by the nucleoli, $C(x,y)$ - the optical density of a substance generated by nucleoplasm, $A(x,y) = \sum A_i(x,y)$, where $A_i(x,y)$ – weight of i chromosome, coordinates of the chromosome anchor.

$$\begin{cases} x_1 = n * d + \Delta r * \cos\varphi_1 \\ y_1 = m * d + \Delta r * \cos\varphi_1 \end{cases}$$

where d – grid spacing, φ_1 – uniformly distributed random variable from $0°$ to $360°$, n and m – whole numbers, Δr – normally distributed quantity. The coordinates of the second end of chromosome

$$\begin{cases} x_2 = x_1 + L * \cos\varphi_2 \\ x_2 = y_1 + L * \cos\varphi_2 \end{cases}$$

where φ_2 uniformly distributed random variable from $0°$ to $360°$, L – length of rod, normally distributed quantity, $A_i(x,y) = \sum a_i(x,y)/z$, where $a_i(x,y)$ – weight of elementary circle of radius r, z - the number of intersections of elementary circles of one chromosome at the point (x,y).

$$\begin{cases} x_c = x_1 + (x_1 - x_2) * k * r / l \\ y_c = y_1 + (y_1 - y_2) * k * r / l \end{cases}$$

where (x_c, y_c) – elementary centers of circles that make up the chromosome k – non-negative integer, not exceeding L/r.

In a straight line of a given length will postpone the circles with variable brightness, brightness of each point is determined by the averaged sum of brightness of all circles containing a point with coordinates (x,y).

Formation of the image texture of the nucleus of blood cells represented by a formula: $G(x,y) = (\max - F(x,y)) * 255/\max$, where $G(x,y)$ – brightness, $\max$ – maximum value $F(x,y)$. Blur: $G_2(x,y) = \sum G_1(x+i, y+j)/(2*d+1)^2$, for all integer i and j not exceeding modulo d, where $(2*d+1)$ – size of averaging matrix, $G_2(x,y)$ – generated image, $G_1(x,y)$ – original image. Adding noise: $G_3(x,y) = G_2(x,y) + \eta(x,y)$, where $\eta(x,y)$ – additive and independent of the signal noise with Gaussian (or other) distribution density function.

Table 1. Values of the input parameters.

Parameter	1 class	2 class	3 class	4 class
Step size	10	18	25	25
Standard deviation (SD) of Rod	3	3	10	0
The radii length	200	150	200	200
SD of Rod length	100	30	50	100
Radius of the base circle	4	6	17	18
SD of Radius of the base circle	1	3	6	5
Weight of the basic of circles	3	4	7	7
SD of Weight of the basic of circles	7	3	3	2
Number of nucleoli	5	1	1	1
Radius of the nucleoli	6	2	2	2
SD of Radius of the nucleoli	2	0	0	0
Weight of the nucleoli	-120	100	350	350
SD of Weight of the nucleoli	10	0	0	0
Weight of the nucleoplasm	50	50	200	200
Degree of averaging	3	3	3	3

For the simulation of nucleoli used circles whose centers are uniformly distributed in the image area. The radii and brightness of nucleoli - random variables distributed according to the normal law of mathematical expectation, standard deviation, and number of nucleoli are set as initial data of the model. Since nucleoplasm is liquid uniformly distributed in the nucleus, to model it the brightness of the entire working area changes by an amount set as a model parameter. As analyzed images obtained in a microscopic system, the diffraction of light waves is simulated by image blur filter.

3. Experiment

To check the adequacy of the model, we conducted an experiment study during which selected parameters of the model, allowing to obtain characteristics similar to real cells (presents four classes: 1 – blast, 2 – myelocytes, 3 – lymphocyte, 4 – lymphoid cell). The selected values are presented in Table 1.

Visually, the model images like the original on the degree of graininess of the texture of chromatin, although it looks more blurry.

4. Conclusion

The developed computational model allows you to create a texture image corresponding to the nuclei of various types of blast and non-blast cells. Computing model parameters found experimentally to ensure compliance generated image with the original image. The proposed model is designed to generate a texture image characteristic of different types of leukocytes (including lymphocytes, blast cells, etc.) to study the informativeness of features in the diagnostics of acute leukemias.

References

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