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Use of Image Analysis Methods and Mathematical Statistics Methods as Tools for Assessing Toxicity of Nanoscale Materials

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***Abstract*—The results of the study of biological materials are often represented by images. The images carry a lot of information important for analysis, but at the same time, it becomes difficult to interpret this information. The problem of interpretation lies in the fact that it is influenced by the personal experience of the researcher to a large extent, therefore the search for methods of objective assessment of images is relevant in the field of biological sciences. Mathematical processing is the most rational way to increase the reliability of the evaluation of the research results in the visualization of images. The article systematizes the most common methods of image analysis in the practice of biological, environmental, and toxicological studies, which give a calculable result suitable for analysis by methods of mathematical statistics. The approaches that allow interpreting color data of images are presented in detail. There are given examples of using various approaches to schematization in the graphical information analysis with further processing by methods of descriptive, parametric and non-parametric statistics.**

Keywords—Toxicology, Ecotoxicology, Image Analysis, Microscopy, Nanoscale Materials, Statistics

I. Introduction

The problems of modern toxicology include not only studying the effects of toxic, intoxicating or medicinal substances on the human body but also assessing the risk to public health in contact with new industrial materials, including nanoscale ones [1-3]. The identification of changes in the body caused by nanoscale materials is a demanding practical task, because, firstly, it is necessary to differentiate which changes are caused precisely by nanoscale materials and which are caused by macroscale analogues [4], and secondly, the changes may appear implicitly, therefore, their registration depends on researcher's experience and is somewhat subjective in nature [5]. In order to avoid subjectivity and other errors in assessing the toxicity of nanoscale materials, it is necessary to use calculable comparison criteria, the identification of which can be automated.

The mathematical statistics method is actively used as the primary tool of evidence-based medicine when comparing the calculable values established by physical and chemical research methods [6]. However, research often involves obtaining results in the form of images, the description of which does not have unambiguous criteria. There is a problem of quantitative interpretation of data in image analysis and their subsequent statistical evaluation in determining the potential risk and toxicity of nanoscale materials.

Besides the technical problem of image analysis, there is a methodological problem, which is that specialists in toxicology are not always able to use image analysis tools and have a possibility of using mathematical statistics in relation to the results of such analysis, while specialists in mathematical statistics and modelling are often poorly informed about the specificity of risk assessment and methods in toxicology.

II. The Purpose Research

The purpose of this research is to structure information on the use of image analysis methods in conjunction with mathematical statistics in assessing the toxicity of nanoscale materials.

The study of toxic effects on biological objects is carried out by the method of setting up an experiment involving biological models, such as laboratory animals or cell cultures [7]. In particular cases, the problems of ecotoxicology include studying the effects of nanoscale particles on individual flora and fauna forms or environmental components, as well as population studies [8–9].

All images that can be obtained during such studies, regardless of the image registration tools used, can be conveniently classified into two broad categories: serial and single.

Serial images include those that are an ordered sequence relative to time scales or spatial positions relative to each other, such as sequential video frames (behaviour of laboratory animals in labyrinths of various types, mobility of micro-objects such as spermatozoa, bacteria, etc.) and layered images obtained by CT (computed tomography) or MRI (magnetic resonance imaging). Single images include cytological (individual cells on swabs and smears) and histological images (fragments of tissues and internal organs), as well as images of nanoscale materials and particles themselves, which affect the human body.

Depending on the chromaticity characteristic, images can be: monochrome (black-and-white and in shades of grey, X-ray images, images obtained by electron microscopy), primary chromatic, and secondary chromatic, and a separate group should include those images which chromaticity characteristic is not significant for analysis. The latter, as a rule, include frame-by-frame video recording images recording animal behaviour, movement cells and microorganisms in real time. The primary chromatic images include those images which chromaticity is caused by the chemical or physical properties of objects: these are cytological and histological images obtained after colouring these biological materials as a result of a chemical reaction, as well as images of native preparations (biological materials not treated with dyes). The secondary chromatic images are those in which the chromaticity characteristic is achieved at the stage of image registration, for example, images obtained by scanning electron microscopy using the colour identification method of distribution of chemical elements in a studied object.

In general terms, the classification of images, the analysis of which is of interest from the perspective of applying the methods of mathematical statistics, is presented in Fig. 1.

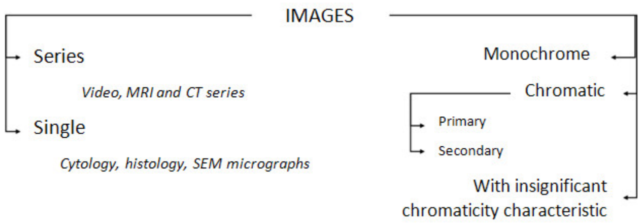

Fig. 1. General classification of image types for analysis in toxicology.

Operations from the basic category, for their part, can also be divided into two groups: chromaticity simplification and schematization.

The chromaticity simplification involves four main approaches: binarization (reducing all characteristics to black and white only); monochromatization (converting all characteristics into shades of grey); reduction of the palette (no operations with the chromaticity, but reducing the number of image colours); conversion of shades of grey into a limited colour palette (in fact, reducing all shades of grey to 3-5 colours).

The schematization involves three main approaches: contouring (separating an object's outline separately from the rest of the image), skeletonization (simplifying the image to a linear, branched scheme), diagram transformation (constructing diagrams based on the image using various methods, the Voronoi method is most often used in practice).

Fig. 2 presents the classification of image simplification methods for further analysis with separate examples.

The variety of approaches to simplifying images also determines the variety of data which can be obtained by analysis after their application. The data themselves can provide a different degree of informativeness, depending on which particular approaches of mathematical statistics will be used to process them.

When extracting data on the size and morphology of objects, there can be applied descriptive statistics methods with the separation of the mean value, standard deviation, and other indicators. In some cases, such as when describing nanoscale materials and particles [10], this may already be complete processing. This approach can also be implemented when studying serial images of CT or MRI, for example, the work of the authors [11] demonstrated how descriptive statistics were used to calculate the volume and area of the inner surface of the bronchial tree of human lungs.

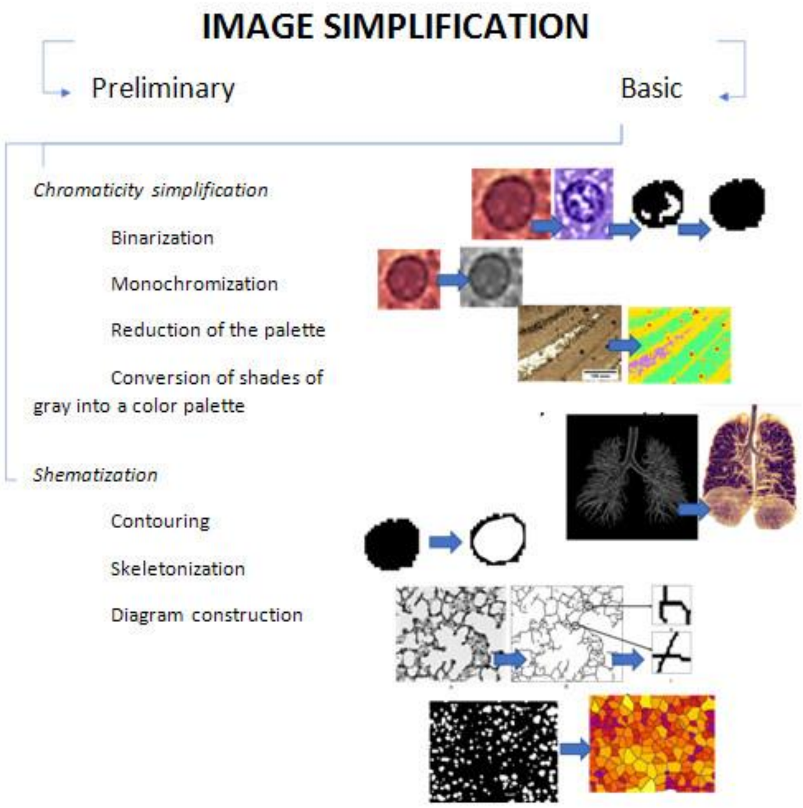

Fig. 2. Classification of methods for simplifying images when analyzing them with examples.

Descriptive statistics methods are also applicable for characterizing images processed with the construction of diagrams, as was shown in work [12]. A secondary colour characteristic of the image can be introduced as an additional tool for demonstrating data. (Fig. 2)

Correspondence of the data set to simplification methods in image analysis and recommendations for choosing a method for statistical analysis are presented in Table 1.

Table 1. Correspondence between simplification methods in image analysis, a specific data set and recommendations for choosing a method for statistical analysis.

The way to simplify the image in the analysis	Specific data set	Recommendations for choosing a method for statistical analysis
Chromaticity simplification		
Binarization	Coefficients, shape description, number of objects, diameter, perimeter and area of objects	Parametric statistics
Monochromatization	The distribution of color intensity in different parts of the image, the ratio of dark and light tones	Non-parametric statistics + processing by subsequent simplification methods
Colour number reduction	Area of the number of objects with different colour characteristics and their number	Parametric and non-parametric statistics
Conversion of shades of grey into a colour palette	Area of the number of objects with different colour characteristics and their number	Parametric and non-parametric statistics
Schematization		
Contouring	Contour length, fractal contour complexity	Parametric and non-parametric statistics
Skeletonization	Fractal complexity, dendritic geometry parameters (the number of double, triple, quadruple intersections, the number of branches and their length)	Non-parametric statistics
Construction of diagrams	Number of cells, cell size, cell area, cell perimeter	Parametric statistics

In most cases, the data obtained during image analysis correspond to the normal distribution [13] and therefore can be compared with each other for presence or absence of significant differences using the appropriate methods of parametric statistical analysis, such as the calculation of Student's t-test or F-test.

However, in the practice of the authors, some approaches to the image analysis do not provide data which distribution law would be known. These data include the results of most schematization methods, as well as the calculation of fractal complexity. In this case, non-parametric statistics methods provide a reasonably stable result for a comprehensive characterization of the image analysis results, as was shown in work [14].

III. Conclusion

Mathematical statistics and image analysis can improve the efficiency of biological research. Structured information on the use of image analysis methods with recommendations on the choice of mathematical statistics methods for their analysis in assessing the toxicity of nanoscale materials is presented.

References

[1] Amini, A.A., Bookstein, F.L., Wilson, D.C.: Biomedical image analysis. Computer Vision and Image Understanding, Volume 66, Issue 2, 95-96 (1997).

[2] Robertson, T. A., Sanchez, W. Y., Robert, M. S.: Are commercially available nanoparticles safe when applied to the skin? J. Biomed Nanotechnol 6, 452-468 (2010).

[3] Berman, M.: Image analysis. Statistics and Computing, 10, 91–93 (2000).

[4] Ignatova, A. M., Zemlyanova, M. A., Stepankov, M. S., Ignatov, M. N.: Determination of the Morphometric Characteristics of the Microdispersed Aluminium Oxide System by Image Analysis Method. Software systems and computational methods 3, 70-85 (2017).

[5] Zemlyanova, M. A., Ignatova, A. M.: Investigation of Morphological Changes of Tissues of the Internal Bodies of the Laboratory Animals Under Exposure to Nanodispersed Oxides of Transient and Light Metals and Nonmetals. Bulletin of Perm University. Series: Biology 3, 320-326 (2019).

[6] Brady, S. M., Highnam, R., Irving, B., Schnabel, J.: Oncological image analysis. Medical Image Analysis. 10, 7-12 (2016).

[7] François, G. M., Ronald, R.: Brushlets: A Tool for Directional Image Analysis and Image Compression. Applied and Computational Harmonic Analysis, 4, 147-187, (1997).

[8] Bezel, V. S.: Ecological Toxicology in the Biosphere Science System. Biosphere 2, (2012).

[9] Zaitseva, N. V., Zemlyanova, M. A., Stepankov, M. S., Ignatova, A. M.: Scientific Forecasting of Toxicity and Evaluation of Hazard Potential of Aluminum Oxide Nanoparticles for Human Health. Human ecology 2, 39-44 (2019).

[10] Ignatova, A. M.: The Algorithm of Image Processing of Thin Layer Computed Tomography for Creating a Three-Dimensional Model of the Human Bronchial Tree Outer Contours. Bulletin of Physiology and Pathology of Respiration 64, 23-28 (2017).

[11] Zaitseva, N. V., Zemlyanova, M. A., Stepankov, M. S., Ignatova, A. M.: Comparative Assessment of Aluminum Bioaccumulation and Morphological Changes in the Lungs and Brain after a Single Inhalation Exposure to Nanodispersed Aluminum Oxide. Nanotechnologies in Russia 14(1-2), 63-68 (2019).

[12] Bruno, O. M., Nonato, L. G., Pazoti, M. A., Batista N. J. Topological multi-contour decomposition for image analysis and image retrieval. Pattern Recognition Letters, 8, 1675-1683, 2008.

[13] Zaitseva, N. V., Zemlyanova, M. A., Koldibekova, Y. V., Ignatova, A. M., Mashevskaya, I. V.: Morphometry of sperm head in rats treated with an antifungal medication Bulletin of Experimental Biology and Medicine 167(4), 525-528 (2019).