

Studies and diagnoses diseases by analysis of microscopic images of cells have been a goal of human cytopathology since the middle of the 19th century. Early work in this area consisted of simple manual measurements of cell and nuclear size. In recent years we have witnessed a rapid development of medical imaging techniques. Recent advances in this field have revolutionized cytopathology by the introduction of digital microscopy. This means that glass slides are scanned and results are saved as virtual slides using special file formats for large images. Then, pathologists can visually assess the biological material on a computer screen instead under microscope. It eliminates the need for physical storage and transportation of glass slides. Pathologist can select and annotate the interesting regions of the slide, consult a sample with other doctors using the Internet or compare the viewed image with archival slides. Moreover, along with the development of vision systems and computer science, quantitative cytopathology has become a useful method for the detection of many disorders. Various methods from areas such as image processing, statistics, machine learning, data mining and artificial intelligence contribute to computer-aided cytopathology. Computer systems can support the pathologist's work by the automation of cell population count, computing statistics of morphological features or cell classification. To accomplish these tasks we need accurate algorithm for cell or nucleus segmentation. Unfortunately cell or nucleus segmentation is rather a challenging task. If we look at cytological specimen under a microscope we will see a lot of clumps of cells without clear boundaries and moreover cells tend to overlap what make the segmentation task even more challenging. A number of scientific centers and commercial companies conduct an intensive research to develop efficient and versatile algorithms for cell or nuclei segmentation. But even the rough analysis of the research achievements in this field shows that there is still a room for the improvement.

The main objective of our project is to develop a new approach for nuclei segmentation based on stochastic geometry methods and compare the effectiveness of the proposed method with the latest approaches proposed in the world scientific literature. In the first step we plan to develop software able to process very large images which size can reach over a dozen gigabytes. Next our algorithm will extract nuclei region from the rest of the image. This part of the system we plan to realize using image thresholding, data clustering and active contours. The knowledge about different regions in the cytological image will serve to build models for nuclei region and background (we assume that gray-scale values of pixels belonging to discovered regions follow a normal distribution, so parameters of probability density function can be easily estimated for each region/model). Based on the knowledge from the previous step we plan to build for each image a marked point process to extract each single nucleus from the nuclei clumps. A point process is a random configuration of points on the plane. By assigning to each point some attributes (marks) we obtain marked point process. It can be used to model random configuration of circles, ellipses or even more complicated objects. Marked point models have proved their effectiveness in such areas as analysis of microstructures, astronomy, remote sensing, stereology, cellular networks. Cytological images are random in their nature, so they can also be considered point process realization. Primary objective of the basic research in this field is to develop the stochastic model that can take advantage of prior information about preferred geometrical patterns (nuclei distribution, nuclei overlapping ratio) and information about the adequacy of object distribution respect to the analyzed image. Finally, when the stochastic model will be defined it becomes necessary to develop method to adjust its parameters. We plan to use for this purpose global optimization algorithms like simulated annealing or swarm intelligence.

A crucial part of our research is to verify the effectiveness of the proposed nuclei segmentation method and compare it to other approaches presented in the world scientific literature. The material for this study will come from the Department of Pathology of the Regional Hospital in Zielona Góra, Poland. We plan to use three different bases of virtual slides. First database is devoted to the lung cancer. Our team is going to develop a system for lung cancer classification based on nuclei morphometry. Predictive accuracy of such a system will be evaluated in relation to diagnosis results based on immunocytochemistry and molecular analysis.

Second database is devoted to radiation-induced reactions for patients with neck or head cancer. The strength and type of radiation-induced reaction will be evaluated by the radiologist. For the same patients, cytological samples will be obtained from oral mucosa. Our team will develop an automated system for classification of radiation-induced reactions using marked point process and machine learning algorithms. Its results will be compared with clinical examinations.

Third database consist of 250 virtual slides of cytological material collected for breast cancer and then processed by immunocytochemistry. The set was prepared for the group of 50 patients. In this case, the effectiveness of nuclei segmentation methods will be verified in the task of the nuclei population count. The automated nuclei population count will be compared with reference data prepared by the pathologist.

Taking into account the medical context of carried out researches we will verify the hypothesis that analysis of nuclei morphometry can be equivalent to immunochemical and molecular studies (based on the material obtained through biopsy of lung cancer). Demonstration of such concordance would significantly reduce diagnostics costs and speed up the treatment process.

Moreover, we are going to prove experimentally a possibility of early diagnosis of radiation-induced reactions based on cytological examination and show that computerized procedure of nuclei population count can help diagnose precisely the type of breast cancer in the case of immunochemical examination.