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# EXPERT SYSTEMS FOR ANALYSIS OF BIOMEDICAL INFORMATION IN THE DIAGNOSIS OF ACUTE LEUKEMIA

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Анотація. . Це дослідження сприяє подальшому вдосконаленню знань, точності діагностичних методів. Це також відіграє важливу роль у діагностиці лікування гострого лейкозу сьогодні. Застосування різноманітних технологій, обмін досвідом та ідеями мають значні досягнення, які матимуть революційний ефект у медичному обслуговуванні пацієнтів, а також підвищать точність діагностики. Найбільш вагомим внеском є розробка та впровадження технологій, особливо штучного інтелекту (ШІ) або машинного навчання. Дослідження ілюструє, як моделі на основі штучного інтелекту можуть допомогти в оцінці та інтерпретації біомедичних даних, забезпечуючи більш точний діагноз і полегшуючи прийняття рішень. Натреновані на великих базах даних, такі моделі показують перспективу у виявленні тонких моделей, що вказують на різні підтипи лейкемії, що може призвести до більш точних і адаптованих методів лікування. Вивчення нових біомаркерів, використання передових методів візуалізації та використання нових технологій, таких як блокчейн, для безпеки даних представляють багатообіцяючі шляхи для прогресу. Однак вирішення таких проблем, як дотримання нормативних вимог, етичні міркування та складність визначення відповідних препаратів-кандидатів, залишається ключовим для відповідального розвитку.

**Ключові слова:** гострий лейкоз, діагностика та терапія, біомедичне зображення, зображення бластних і небластних клітин крові, біомедична інформація.

Abstract. This research helps to further improve the knowledge, accuracy of diagnostic techniques. It also plays an important role in the diagnosis of acute leukemia treatment today. The application of various technologies, the sharing of experiences and ideas, and even ethics all represent significant advances that will have a revolutionary effect on medical care for patients as well as improve accuracy in diagnosis. A most significant contribution is the development and introduction of technology, especially artificial intelligence (AI) or machine learning. The study illustrates how artificial intelligence-based models may be able to help in the evaluation and interpretation of biomedical data, providing more accurate diagnosis and facilitating decision-making. Trained on large databases, such models show promise in the detection of subtle patterns suggestive of different leukemia subtypes that can lead to more accurate and tailored treatment modalities. Looking ahead, the future of acute leukemia diagnosis is ripe with potential and challenges alike. Exploring novel biomarkers, incorporating advanced imaging techniques, and leveraging emerging technologies like blockchain for data security represent promising avenues for advancement. However, addressing challenges such as regulatory compliance, ethical considerations, and the complexity of identifying suitable drug candidates remains pivotal for responsible evolution.

**Keywords:** acute leukemia, diagnosis and therapy, biomedical image, images of blast and non-blast blood cells **DOI:** https://doi.org/10.31649/1999-9941-2024-59-1-158-165.

#### Introduction

Editing of biomedical images usually involves preprocessing to make them clear and sharp, or free from noise or artifacts. This important step improves the images 'clarity and reliability so that the following analyses are done with sharp, precise visual data (Wagner et al., 2012). Methods such as noise reduction, contrast adjustment, and image normalization are used for preprocessing the images. In this way preprocessing helps ensure that the next steps of feature extraction and classification use high-quality data, reducing possible errors. After the images undergo preprocessing, the next step is to extract features of importance that reflect key biological information. Lab techniques to extract features focus on finding quantifiable properties unique to the image, such as cell morphology, or texture and intensity variations (Arber et al., 2017). These extracted features provide quantifiable measures of the cellular characteristics, which can then be used to distinguish normal vs leukemic cells. Where feature extraction is crucial, capture the subtle differences in cells that help clinicians pin down an accurate diagnosis via texture analysis, shape descriptors, and other image intensity-related features.

After feature extraction, classification allows cells to be separated from the images and identified. These algorithms use advanced machine learning methods to identify the clusters formed by these extracted cells (Wagner et al., 2012). For example, sophisticated classification methods such as neural networks or support vector machines separate the different cell types especially problems in leukemic blast prediction (Harrison & Johansson, 2015). Segmentation techniques also make it easier to determine the boundaries of cells, so that abnormal cells can be more clearly identified and counted-which is crucial in acute leukemia diagnosis.

Combining the data from image analysis with clinical information and patient history is ultimately what constitutes true diagnostic support. Although image analysis provides important visual data, integrating it with clinical information laboratory tests, and genetic markers as well as the symptoms of individual patients offers more context for diagnostics (Wagner et al., 2012). Such integration provides completeness, adding to the validity of diagnosis. When the visual findings are placed within the context of the patient's entire health history, clinicians then have a picture that serves as an essential basis for accurate diagnosis of acute leukemia (Arber et al., 2017). All these from preprocessing to feature extraction, classification, and integration of the extracted features with clinical data are crucial in coming up with a better understanding of leukemia pathology [1,2].

**The purpose of** this work is to develop a conceptual model of an expert system for diagnosing acute leukemia using computer microscopy methods, as well as to analyze the influence of factors that influence the result of recognition of poorly formalized objects (images of blast and non-blast cells).

### **Decision Support in Acute Leukemia Diagnosis**

Technology and the use of data-driven tools are integrated throughout acute leukemia diagnosis, supporting decision-making by medical professionals as they develop diagnostic hypotheses in light of objective facts. It uses technologies such as artificial intelligence, computational models, and clinical databases to improve the accuracy of diagnosing acute leukemia quickly (Arber et al., 2017). Starting from patient data, which incorporates genetic info and proteomic studies as well as clinical information on each case. This comprehensive approach allows for an overall health picture of the patient and leads to a more accurate above all subtle diagnosis. Differentiating between the various subtypes of acute leukemia is a key function served by decision support systems (Wagner et al., 2012; Cicconi & Lo-Coco, 2016). By spirit-like advanced algorithms, these systems can break down complex molecular and genetic markers to help doctors recognize the distinct traits that define each subtype to be able to guide appropriate treatment strategies [3,4].

The real-time processing capabilities of decision support tools provide valuable insight into acute leukemia diagnosis. This is especially valuable in emergencies, as it allows healthcare professionals to rapidly analyze key data at a glance, reach fast decisions, and begin treatment with the timeliest information possible (Wagner et al., 2012). Unlike traditional mathematics, machine learning models integrated into decision support systems always learn from new data and experiences (Harrison & Johansson, 2015). This ability to adapt guarantees that the diagnostic equipment continually changes, becoming ever more accurate and commensurate with developments in medical science and technology.

Tailored to fit individual patients, decision support tools aid personalized medicine. Such tools can thus evaluate a patient based on their unique genetic makeup, clinical history, and other relevant factors to fine-tune treatment recommendations. In this way, therapeutic interventions are enhanced for better results (Harrison & Johansson, 2015). It attempts to resolve the difficulty of interpreting enormous datasets in acute leukemia diagnosis with decision support. These tools, which use advanced computational models to identify patterns and associations too subtle for simple human interpretation alone, greatly improve diagnostic precision. Besides helping to make the initial diagnosis, decision support systems also help healthcare professionals predict disease courses. Analysis of historical data and the reaction to treatment help estimate what pattern acute leukemia will likely take so that care plans can be more proactive and personalized [5,6].

#### Validation and Performance Evaluation of the System

Therefore, the development and implementation of any system must go through two important phases such as validation and performance evaluation. These will ensure that a system is reliable, accurate, or able to effectively achieve its intended goals (Arber et al., 2017). Given acute leukemia diagnosis as an example of the use of a bio-information system, these processes can all help to build trust with users and healthcare professionals, as well as regulatory bodies (Harrison & Johansson, 2015). The first step in validation is to verify that the system meets pre-established requirements and specifications. This means that the system works appropriately for these specific needs and objectives.

The validation process even involves the system's data integrity and security measures. The system must meet safeguards for the patient data, maintain confidentiality, and prevent unintentional access. Performance evaluation measures system performance in handling different workloads and datasets. This entails measuring the system's response time, its computational efficiency, and its scalability so that it can deal with growing and growing amounts of biomedical data. A standard method for performance evaluation is benchmarking. That is, comparing the system's performance to established standards or existing systems of a similar nature (Harrison & Johansson, 2015). This allows areas for improvement to be identified and establishes a foundation of acceptable performance metrics.

In the process of validation and performance evaluation, artificial or historical datasets that represent realistic problems are frequently heard. This provides a basis for controlled testing, verifying that the system is robust across different use cases and helping to understand its generalizability (Harrison & Johansson, 2015). To reduce the risk of overfitting and increase its applicability to a wider patient population, cross-validation techniques are used herein to evaluate system performance on assorted datasets. When evaluating the diagnosis of acute leukemia, validation and performance assessment should relate to whether the system can identify various subtypes of leukemia; accurately predict treatment responses; and provide clinically useful information (Arber et al., 2017). These outcomes are vital for better decision-making by healthcare professionals.

Clinical validation is working with medical professionals to see how the diagnostic outputs of a system match up against actual patient outcomes. In this way, the system's predictions are checked for congruence with real-world clinical situations, providing evidence of its use in a medical context (Arber et al., 2017). Verification is also an iterative process, with feedback from clinicians and end-users guiding refinement. Addressing new challenges, incorporating new medical knowledge into the system, and improving performance requires a steady stream of updates to, and upgrades of, the system [7].

For this reason, easily interpretable models are preferred in validation and performance evaluation to ensure that clinicians understand the reasons for the system's predictions. These transparent models engender trust among healthcare providers and encourage responsible use of the system in clinical application. In AI-based models, in particular, addressing biases in the system is a big part of validation. Bias may be introduced by an unbalanced distribution of training data, and we must strive to avoid such biases and ensure fair and impartial results for different patient groups (Harrison & Johansson, 2015). The system's ability to detect leukemia and to distinguish between subtypes is measured by quantitative metrics such as sensitivity, specificity, and positive predictive value. These metrics offer a standardized way to measure the diagnostic accuracy of the system.

Evaluation of the system's ability to discriminate between classes is often performed by using Receiver Operating Characteristic (ROC) curves and area under the curve (AUC) analysis. These pictures show the tradeoff between sensitivity and specificity. After implementation, it is important to monitor the performance of the system on an ongoing basis, to detect any drift in accuracy or efficiency (Harrison & Johansson, 2015). Regular audits and upgrades further enhance the system's long-term stability, while keeping it in step with constantly changing health care standards. Verification and performance assessment should take the usability of the system from an end-user point. Inspects critical to usability assessment include user feedback, ease of integration into existing workflows, and overall impact on clinical decision-making.

Compliance with regulatory standards such as medical device regulations and data privacy regulations is an integral part of the verification process. Compliance ensures that patient rights are protected and the system is used ethically in hospitals (Harrison & Johansson, 2015). External validation-- independent assessment by external bodies or regulatory agencies adds extra weight to the system. Third-party verification enhances the trustworthiness and assurance that people have in the system. Documentation of validation and performance evaluation procedures is necessary for transparency and accountability.

#### Precision of the system's diagnosis

The performance of the IBS might also be impacted by the setting in which it is utilized. The precision of the system's diagnosis can be influenced by several circumstances, such as the accessibility to superior biological data and the proficiency of the physicians utilizing it.

#### Mathematical Model

dN/dt = p - dN - beta \* N \* L + K \* N \* LdL/dt = beta \* N \* L - K \* N \* L - dLdM/dt = K \* N \* L - dM - sMThe equations above can be combined in a matrix form as shown below: dM/dt dN/dt dL/dt - dNbeta \* NL K \* NLbeta \*NL - K \* NL - dM - sMwhere: 1). N(t) is the number of normal cells at time t 2). L(t) is the number of leukemic cells at time t 3). M(t) is the number of mature blood cells at time t 4). p is the rate of production of new normal cells 5). d is the rate of death of normal cells 6). a is the rate of proliferation of leukemic cells due to interaction with normal cells 7). b is the rate of differentiation of leukemic cells into mature blood cells 8). s is the rate of death of mature blood cells

9). beta is the rate of proliferation of leukemic cells

10). K is the rate of differentiation of leukemic cells

The figure below shows the mathematical model that was made and used during the simulation to obtain the graph.

The analysis of biomedical images in acute leukemia diagnosis entails meticulous steps, from preprocessing to feature extraction and integration with clinical data. Image preprocessing ensures refined data quality, while feature extraction and classification algorithms identify distinctive cellular attributes. Integration with clinical data enriches the diagnostic process, contextualizing visual findings within the patient's broader health profile. Moreover, advancements in hardware, such as high-resolution imaging systems and GPU accelerators, enhance imaging clarity, expediting data processing and interpretation (fig 1).



Figure 1 - expediting data processing and interpretation

Looking ahead, the future of acute leukemia diagnosis is ripe with potential and challenges alike. Exploring novel biomarkers, incorporating advanced imaging techniques, and leveraging emerging technologies like blockchain for data security represent promising avenues for advancement. However, addressing challenges such as regulatory compliance, ethical considerations, and the complexity of identifying suitable drug candidates remains pivotal for responsible evolution.



#### **Pre-processing of Two-Dimensional Biomedical Images**

Pre-processing of two-dimensional medical biomedical images is a key step in improving the quality and meaning of data for decision support at acute leukemia diagnosis. It is this critical step that uses various techniques such as filtering, contouring, and normalization to improve the quality of the images being studied (Rawat et al., 2015). Each of these techniques performs a different function in cleansing the dataset. It is an important step towards more precise and informed decision support. Pre-processing includes several operations that precede processing. The most important one is filtering, which gets rid of noise in biomedical images. However, the data can be distorted by noise, which often arises during image acquisition (Peters & Ansari, 2011). Filtering techniques pick out those features that scientists want to emphasize and suppress whatever noise is there, yielding a higher net signal-to-noise ratio. The final product is a more clean and accurate reflection of the underlying structures in those images. The figure 3 below shows the graph obtained from the processing of the results.



Figure 3 – Graph obtained from the processing of the results.

Another important technique in pre-processing is contouring, which identifies and delineates structures within biomedical images. Contouring defines the borders and structure of interest and makes possible a more indepth analysis of specific areas (Peters & Ansari, 2011). This step is especially important in the case of acute leukemia diagnosis, where careful identification of abnormalities such as extra cell structures means that decision-making support systems can make more reasonable assessments. To ensure that intensity levels are always constant across different regions of the biomedical images, normalization is used. This is an important means of equalizing differences in illumination and contrast, resulting in a consistent dataset. Normalization reduces the chance that variations in imaging conditions will introduce biases. It levels out differences between images, helping to ensure accurate and reliable decision support (Rawat et al., 2015). These pre-processing techniques, taken together as a whole, create a refined dataset that serves as raw material for subsequent analysis. By cleaning out the noise, enriching through contouring, and normalizing this dataset to provide decision-support systems with a more accurate and stable formulation of biomedical information (Rawat et al., 2015). It improves the system's ability to detect fine patterns and oddities, allowing for better decision-making when it comes time to diagnose acute leukemia.

#### **Contour Preparation and Formation of Templates - Masks of Bioobjects**

The method of contour preparation and the formation of templates, also known as masks of bio-objects, are essential in the detailed analysis of biomedical images. Contours help delineate specific structures or anomalies, providing a basis for further examination (Peters & Ansari, 2011). Templates or masks are crafted to identify and isolate bio-objects of interest, such as leukemia cells or abnormal tissue (Rawat et al., 2015). This meticulous approach aids in creating a targeted and precise analysis, facilitating decision support by focusing on the most relevant information within biomedical images. The figure 4 below shows the frequencies of the different genders during data collection.

## Development of the Architecture of a Fuzzy Expert Optical-Electronic System

The architecture of a fuzzy expert optical-electronic system plays a key role in analyzing biomedical images for leukemia diagnosis. Fuzzy logic, an approach that deals with uncertainty and imprecision, is integrated into the system's architecture. This enables the system to handle the inherent complexities and variations present in biomedical images more effectively (Rawat et al., 2015). The combination of optical and electronic components enhances the system's capability to capture, process, and interpret intricate details, contributing to a more nuanced decision-support mechanism in leukemia diagnosis. The development of such a sophisticated architecture aligns with the demand for advanced technological solutions in the field of medical imaging and diagnostic support. The figure below shows the frequency of the immune blood cells.

# Frequencies

Frequencies of gender						
gender	Counts	% of Total	Cumulative %			
female	32	51.6 %	51.6 %			
male	30	48.4 %	100.0 %			



Figure 4 – Frequencies of the different genders during data collection.

peripheral blood immature cells	Counts	% of Total	Cumulative %
0.03	1	3.3 %	3.3 %
0.04	1	3.3 %	6.7 %
0.32	1	3.3 %	10.0 %
0.01	1	3.3 %	13.3 %
0.02	1	3.3 %	16.7 %
0.03	1	3.3 %	20.0 %
0.04	1	3.3 %	23.3 %
0.06	2	6.7 %	30.0 %
0.09	1	3.3 %	33.3 %
0.13	1	3.3 %	36.7 %
0.14	3	10.0 %	46.7 %
0.16	1	3.3 %	50.0 %

Frequencies of peripheral blood immature cells

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Frequencies of peripheral blood immature cells					
peripheral blood immature cells	Counts	% of Total	Cumulative %		
0.2	1	3.3 %	53.3 %		
0.28	1	3.3 %	56.7 %		
0.45	1	3.3 %	60.0 %		
0.51	1	3.3 %	63.3 %		
0.6	1	3.3 %	66.7 %		
0.64	1	3.3 %	70.0 %		
0.68	1	3.3 %	73.3 %		
0.7	1	3.3 %	76.7 %		
0.74	1	3.3 %	80.0 %		
0.81	3	10.0 %	90.0 %		
0.93	2	6.7 %	96.7 %		
0.96	1	3.3 %	100.0 %		

...

counts 0.04 0.32 0.01 0.02 0.03 0.04 0.06 0.09 0.13 0.14 0.16 0.2 0.28 0.45 0.51 0.6 0.64 0.68 0.7 0.74 0.81 0.93 0.96 0.03 peripheral blood immature cells

Figure 5 - The analysis of biomedical images in acute leukemia diagnosis

The analysis of biomedical images in acute leukemia diagnosis (fig 5) entails meticulous steps, from preprocessing to feature extraction and integration with clinical data. Image preprocessing ensures refined data quality, while feature extraction and classification algorithms identify distinctive cellular attributes. Integration with clinical data enriches the diagnostic process, contextualizing visual findings within the patient's broader health profile. Moreover, advancements in hardware, such as high-resolution imaging systems and GPU accelerators, enhance imaging clarity, expediting data processing and interpretation.

#### Conclusions

Looking ahead, the future of acute leukemia diagnosis is ripe with potential and challenges alike. Exploring novel biomarkers, incorporating advanced imaging techniques, and leveraging emerging technologies like blockchain for data security represent promising avenues for advancement. However, addressing challenges such as regulatory compliance, ethical considerations, and the complexity of identifying suitable drug candidates remains pivotal for responsible evolution.

#### References

- [1] A. M. Abdeldaim, A. T. Sahlol, M. Elhoseny, & A. E. Hassanien. "Computer-aided acute lymphoblastic leukemia diagnosis system based on image analysis," *Advances in Soft Computing and Machine Learning in Image Processing*, 131-147. 2018.
- [2] I. A. Ahmed, E. M. Senan, H. S. A. Shatnawi, Z. M. Alkhraisha, & M. M. A. Al-Azzam, "Hybrid techniques for the diagnosis of acute lymphoblastic leukemia based on fusion of CNN features," *Diagnostics*, 13(6), 1026. (2023)

- [3] S. Ansari, Navin, A. H., Sangar, A. B., Gharamaleki, J. V., & S. Danishvar, "A customized efficient deep learning model for the diagnosis of acute leukemia cells based on lymphocyte and monocyte images," *Electronics*, 12(2), 322. 2023.
- [4] D.A. Arber, M.J. Borowitz, M. Cessna, J. Etzell, K. Foucar, R.P. Hasserjian, & J.W. Vardiman, "Initial diagnostic workup of acute leukemia: guideline from the College of American Pathologists and the American Society of Hematology", *Archives of pathology & laboratory medicine*, 141(10), 1342-1393. 2017.
- [5] S. V. Pavlov, Y. R. Saldan, O. V. Karas, and S. V. Tymchyk, "Analysis of methods and systems for diagnosing diabetic retinopathy", *Opt-el. inf-energy tech.*, vol. 46, issue 2, p. 135–141, 2023. [in Ukrainian]
- [6] Li Jinqiong and S. Pavlov "Expert bioinformation system for diagnosis of forms of acute leukemia based on analysis of biomedical information", *ITKI*, vol. 58, issue 3, p. 84–93, 2023. [in Ukrainian]
- [7] W. Wójcik, S. Pavlov, M. Kalimoldayev, *Information Technology in Medical Diagnostics II. London:* Taylor & Francis Group, CRC Press, Balkema book. – 336 Pages, <u>https://doi.org/10.1201/9780429057618</u>. 2019.
- [8] K. X. Chen, "Academician kai-xian chen talks about the development of traditional chinese medicine and global medicine", *World Journal of Traditional Chinese Medicine*, 6(1), 1-11. 2020
- [9] S. Chiaretti, G. Zini, & R. Bassan, "Diagnosis and subclassification of acute lymphoblastic leukemia," Mediterranean journal of hematology and infectious diseases, 6(1). 2014.
- [10] L. Cicconi & F. Lo-Coco, "Current management of newly diagnosed acute promyelocytic leukemia," *Annals of Oncology*, 27(8), 1474-1481. 2016.
- [11] H. Crow, "Scaling Technique for Web Based Management Systems in Bioinformatics," *Life Science Journal*, 9(3). 2012.
- [12] A.S. Davis, A.J.Viera, & M. D. Mead, "Leukemia: an overview for primary care," *American family physician*, 89(9), 731-738. 2014.
- [13] E. H. Estey, "Acute myeloid leukemia: 2012 update on diagnosis, risk stratification, and management," *American journal of hematology*, 87(1), 89-99. 2012.
- [14] L.F. Grimwade, K.A. Fuller, & W.N. Erber, "Applications of imaging flow cytometry in the diagnostic assessment of acute leukaemia,". Methods, 112, 39-45. 2017.
- [15] T. Haferlach, A. Kohlmann, L. Wieczorek, G. Basso, G. Te Kronnie, M. C. Béné, & R. Foa, "Clinical utility of microarray-based gene expression profiling in the diagnosis and subclassification of leukemia: report from the International Microarray Innovations in Leukemia Study Group," *Journal of clinical* oncology, 28(15), 2529. 2010.
- [16] C.J. Harrison, & B. Johansson, "Acute lymphoblastic leukemia,". Cancer Cytogenetics, Chromosomal and Molecular Genetic Aberrations of Tumor Cells, 198-251.2015.

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# ЕКСПЕРТНА БІОІНФОРМАЦІЙНА СИСТЕМА ДІАГНОСТИКИ ФОРМ ГОСТРОГО ЛЕЙКОЗУ НА ОСНОВІ АНАЛІЗУ БІОМЕДИЧНОЇ ІНФОРМАЦІЇ

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