Frontiers in Computing and Intelligent Systems
ISSN: 2832-6024 | Vol. 6, No. 3, 2023

Development of Machine Learning and Artificial Intelligence in Toxic Pathology

Tianbo Song [1, *], Quan Zhang [2], Guoqing Cai [3], Meiqing Cai [4], Jili Qian [5]

[1] Computer Engineering, Arizona State University, Tempe, AZ, USA
[2] Information Studies, Trine University, Phoenix AZ, USA
[3] Information Studies, Trine University, Phoenix AZ, USA
[4] Computer Science, Independent researcher, Nanchang, Jiangxi, China
[5] Information Studies, Trine University, Phoenix AZ, USA

*** Corresponding author:** Tianbo Song (Email: sportlemon@gmail.com)

Abstract: Toxicity pathology is an important part of preclinical drug safety evaluation. With the development of computer science and full-slice digital scanning technology, artificial intelligence (AI) has been widely used in the field of drug safety evaluation, including all aspects of pathology, such as diagnostic pathology, veterinary diagnostics, pathology research, regulatory toxicology and pathology primary film review and peer review. Toxicology is one of the most valuable disciplines to promote the development of animal and human health, and the toxicity research of drug non-clinical safety evaluation. The development and application of a wide variety of algorithms for histopathology suggests that AI pathology platforms can profoundly influence the future of digital toxic pathology, precision medicine, and personalized medicine. However, as with all other revolutionary technologies, there are many challenges in the implementation and application of AI pathology platforms. This paper reviews the development of artificial intelligence and machine learning, the application of artificial intelligence in toxic pathology, the application of machine learning in digital toxic pathology, and the impact of artificial intelligence on digital toxic pathology, in order to provide some reference for the application of artificial intelligence and machine learning in toxic pathology in China

Keywords: Toxicity Pathology; Artificial Intelligence; Machine Learning; Artificial Neural Network.

1. Introduction

Artificial intelligence (AI) is based on machine algorithms to predict or simulate what a human would do in the same situation. It is the inevitable product of the development of computer science and ultra-fast computing speed, and it is also the strategic point of future scientific and technological development. Deep learning is a special machine learning method that has emerged during the development of artificial neural networks and is considered one of the most advanced techniques in image analysis applications. The most used deep learning model is the convolutional neural network, which can abstract local features and is therefore very suitable for application in the field of computer vision [1-3].

Toxopathological evaluation in non-clinical safety evaluation of drugs is an important part of general toxicity test and carcinogenic test. The histopathological results of paraffin embedding, hematoxylin and eosin-stained sections are the gold standard for toxicological evaluation. These standardized approaches are time-tested and will continue to play a key role in the non-clinical safety evaluation of drugs. Digital toxicology, artificial intelligence (AI), and machine learning (ML) can significantly improve the efficiency and quality of the work of toxicologists. In the past, the development of digital toxicology, AI, and ML has been slowed by computational costs and the inability to effectively digitize histopathological data for nearly 10 years. See the rapid development of computational pathology and convolutional neural networkCNN. The continued adoption of new technologies in medical imaging has resulted in an impressive, brain-rivaling technology. Even new applications above the human brain. AI consistently outperforms humans in performing repetitive and detailed tasks quickly and accurately [4]. Regardless of time constraints, AI's diagnosis of whole slide images (WSI) is already comparable to that of pathologists. The advantage of a pathologist is a high level of cognitive ability. The advantage of AI is fast and accurate computing power. The complementary and even synergies between diagnostic pathologists, veterinary pathologists, and toxicologists and AI could be far-reaching. It has a strong development prospect and practical value [5]. For example, diagnostic pathologists with AI-assisted diagnosis were able to identify metastatic breast cancer cells in lymph nodes more accurately (99.5% accuracy) than diagnostic pathologists without AI-assisted diagnosis were able to identify metastatic breast cancer cells with 96% accuracy and AI alone with 92% accuracy. Therefore, toxicity pathologists should be aware that with the emergence of effective AI-assisted technologies for non-clinical safety evaluation of drugs, trial design and histopathology workflows for toxicity trials may fundamentally evolve in a direction that is more favorable to the work of toxicity pathologists.

2. Related Work

Toxicity pathology is an important part of preclinical drug safety evaluation. Over the past few decades, pathology has established a set of standardized practices, guidelines, and/or industry standards as a key component of preclinical drug safety evaluation. However, for the pathologist, each study requires the microscopic examination of 100 to 1,000 tissue sections, which is a labor-intensive and time-consuming task, especially since most tissue organs lack changes associated with the subject matter. AI and deep learning have shown great advantages in helping to distinguish normal samples from abnormal samples, so that toxicologists can spend their time mainly evaluating the pathological characteristics of abnormal specimens under the microscope, rather than evaluating normal tissue[6-8]. This will reduce the time required for the pathology process, effectively reducing the time to drug development. In addition, AI and deep learning help reduce differences in the semi-quantitative grading of lesions between and within laboratories. With the rapid development of digital pathological section scanning technology and AI algorithm for image feature extraction, toxic pathology has also transitioned from analog method to digital method[9]. Ai-based deep learning algorithm can automatically, high-throughput and comprehensively extract feature data from images, so as to realize high-level feature learning of pathological big data, and form more abstract high-level features or attribute categories by combining low-level features, so that the feature expression is more comprehensive and objective [10-11]. With the development of algorithms and the in-depth observation of the histopathology space, AI's pathology platform is becoming one of the key factors affecting the future of precision and personalized medicine.

2.1. Digital Pathology

Digital pathology is the use of full section scanner to digitize the histopathological sections, and the use of computational methods to analyze these digitized section images. The scanner was introduced in 1999, but the development of digital pathology dates back to the 1960s. At that time, Prewitt Mendelsohn invented the ability to scan simple images from microscopic areas of ordinary blood smears and convert optical data into optical density value moments while maintaining spatial and grayscale relationships The array then identifies the presence of different cell types based on the information in the scanned images. A key component of digital pathology is the digitizing of slides into full slide scans. Scanner parts with microscope. The components are parallel, including a light source, a slide table, an objective lens, and a high-resolution digital camera. Images are typically captured as a series of line segments or image modules along the X and Y planes of the slide, which are then digitally spliced together to create the entire slide image. These pictures or lines are stored at different resolutions in several images of the same slice, and these images are coupled together as a pyramid of images, which can support the processing of very large files.

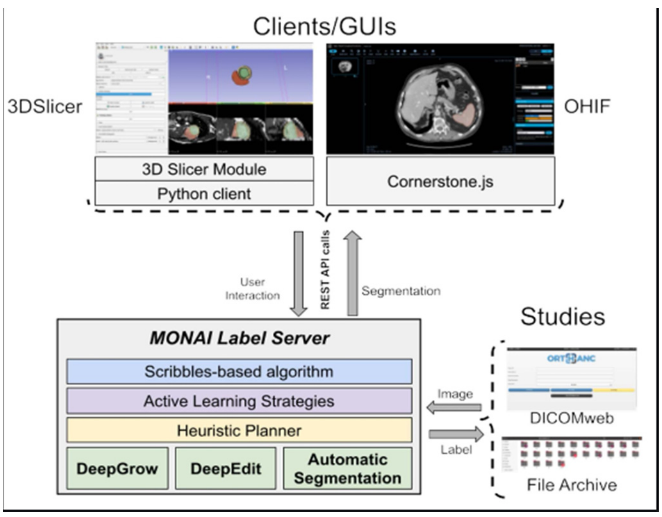

Figure 1. Digital pathology model

Partial download also avoids image lag when zooming in or out when the display views the entire slice image. One of the biggest determinants of scan quality is slide quality. The whole slide scanner

The degree of tolerance for defects in slide preparation is much lower than for human observers, and the quality of the scan can be affected by uneven sections, tissue folding, compression, tearing, over or under staining, changes in staining intensity, and batch changes.

2.2. Algorithm Classification

Because deep learning methods do not rely on engineering features and can learn representations directly from raw data, they are increasingly used in the field of digital pathology. Deep learning methods typically involve learning a set of images labeled with relevant categories (such as whether a tumor is benign or malignant) and then asking for new input data for interpretation without presetting assumptions. This process involves generating images and subsequently learning image features to separate out the categories of interest. Compared with the manual extraction of image features, the method based on deep learning is widely used and its results are more accurate. As a result, many deep learning models, or algorithms for analyzing pathological images have been developed and utilized.

2.2.1. Convolutional Neural Networks (CNN)

CNN is the most widely used deep learning algorithm to date: and has been applied to a variety of pathological image analysis. A CNN is a deep feedforward network that contains multiple layers that infer outputs (usually decision categories) from inputs (such as images). The reason for the name is that there are multiple convolutional layers in the CNN, which are the building blocks of the CNN. In a CNN, filters between the input layer and the output layer learn and extract features from the image. The layers in the CNN are not fully connected, and the neurons in layer 1 only interact with the fixed region of the upper layer, rather than with all neurons.

CNNS also contain a pooling layer, whose main function is to reduce or reduce the dimension of features. CNN works by deconstructing an image in layers into low-level clues (such as edges, curves, or shapes) and then clustering these clues to form higher-order structural relationships that identify features of interest. Currently, CNN Deep Learning based methods have been used for image detection and segmentation tasks to identify and quantify cells (such as neutrophils, lymphocytes, and primitive cells), histological features (such as nuclear morphology, mitotic image morphology, stromal, and glandular structures), and areas of interest (such as tumors and peri-tumor areas).

2.2.2. Complete Convolutional Network (FCN)

Another common deep learning model is FCN, which lacks fully connected layers and consists only of a hierarchical structure of convolutional layers. Unlike CNN, which uses local information to make global predictions, FCN can learn from each pixel learning feature representation. Therefore, it is possible to detect elements or features that appear sparsely throughout the pathological image. This feature allows FCN to make pixel-level predictions, which may be an advantage for FCN compared to CNN learning from repeated features that appear throughout the image. Some researchers have used FCN to improve the efficiency of cervical exfoliation cytology screening, especially in the detection of abnormal cells.

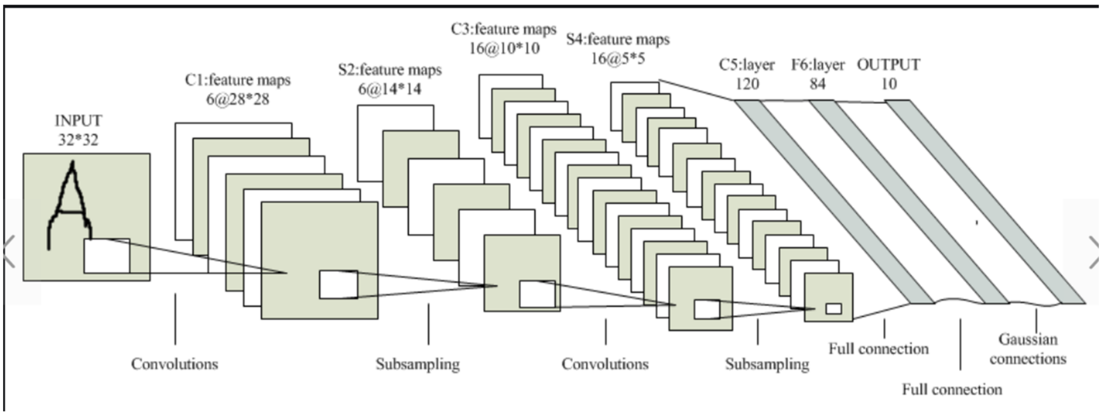

Figure 2. Digital CNN structure

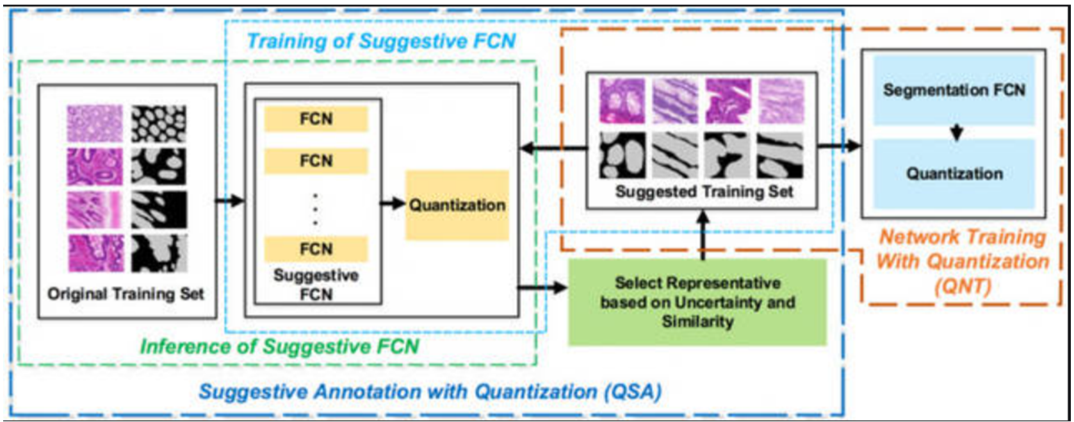

Figure 3. Digital FCN structure

2.2.3. Recurrent Neural Network (RNN)

Unlike CNNS and FCN, RNNS are not limited to analyzing data at a single time, but can store inputs at different time intervals or points in time and process these inputs sequentially, that is, learning from discrete earlier steps. RNNS take into account input states at different points in time and therefore exhibit dynamic behavior. Long short-term memory network (LSTM) is a type of RNN that is enhanced by the existence of loop gates, that is, CNNS can complete learning tasks by recalling extended errors [23]. The advantage of using the LSTM network is that the model is able to learn from each patch, and all of these learning patterns are aggregated to generate patient-level predictions.

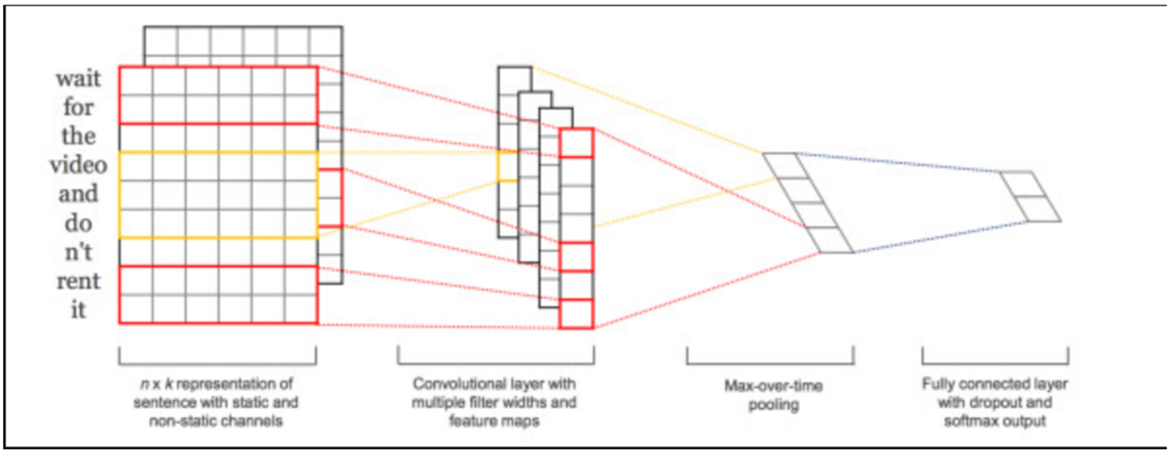

Figure 4. Digital RNN structure

Studies have shown that the average area under the curve (AUC) value of LSTM network predictive performance is 0.69, which is higher than the predictive performance of histology grade, whose average AUC value is 0.57, and the average AUC value of visual risk score predicted by 3 pathologists is 0.58[24]. The potential use of the RNN method is to analyze tissue images obtained at different time points to assess patient prognosis or disease outcome.

2.3. AI Pathological Diagnosis

The application of AI in pathology is still in its infancy, so the current regulation of AI in pathology remains a very challenging work. The regulatory guidelines for the use of AI and deep learning software in Good Laboratory Practice (GLP) evaluation are based on general Validation principles of GLP regulations, such as the methods for validating analytical procedures outlined by the International Coordinating

Council for Human Pharmaceutical Technology Requirements (ICH) [40] or the standard evidence methods for creating biomarkers and diagnostics identified by the American Committee on Pharmaceutical Research and Manufacturers. In general, these include defining parameters, analytical accuracy and precision, linear ranges of detection and limits of quantification, and robustness. The test must be credible, relevant to pharmacological effects or mechanisms, or relevant to disease and toxic effect results in addition to meeting the basic principles of analytical validation. Regulation should also consider the principles for evaluating the clinical use of software as a medical device set out in the International Forum of Medical Device Regulators and the Medical Device Working Group Guidelines, as well as following the Medical Digital Imaging and Communication (DICOM) standard for processing image data.

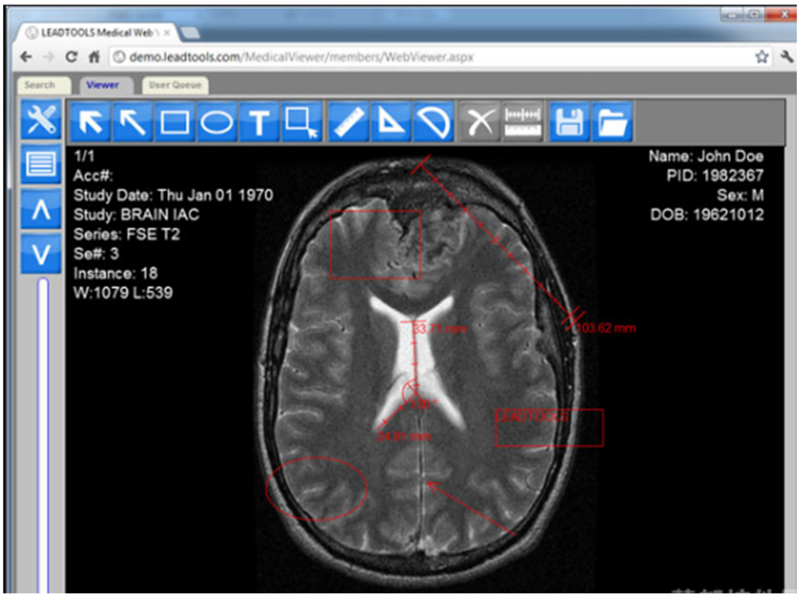

Figure 5. DICOM diagnostic image

International DICOM standard is an international standard for medical image information transmission, storage, retrieval, printing, processing and display. The DICOM Basic Standards Committee meets regularly to review the task outputs of the 31 DICOM working groups and to identify trends and projected changes that may affect the integrity of medical image imaging information. The basic goal of the organization is to develop standards for the digital exchange of information between medical imaging devices and other information technology systems. It is worth noting that pathological diagnostic medical imaging also falls under this DICOM standard. Following DICOM standards, digital pathology can facilitate interdisciplinary collaboration, and scientists and medical professionals using different systems can easily access the same information and data without having to reformat it for system compatibility, thus avoiding data loss. This is critical to the success of AI and deep learning. As a result, veterinarians and toxicologists, when making widespread use of digital image acquisition related to AI and deep learning applications, need to ensure that full-slice scanners generate DICOM-compliant images and that Personal Access Communication System (PACS) users can import and view files. In short, with the continuous development of AI technology and its applications, but also promote the standardization of medical imaging data information exchange, DICOM's importance and influence is growing.

3. Conclusion

With the development of microscope image digitization technology, the application of digital pathology has extended to all fields of pathology, including human clinical diagnosis and non-clinical safety studies. Full-section digitization has facilitated the development of automated image analysis techniques that help pathologists perform visual quantification tasks. In conclusion, pathology benefits from real-time advances in computer vision and analytical algorithms. High quality and consistent annotation of pathological data is essential for the development of algorithms and models. If this is achieved, AI can help the pathologist to free himself from tedious film reading tasks and can increase the consistency of the pathology rating system, adding a quantitative dimension to the previous semi-quantitative assessment. And support diagnostic decisions by highlighting specific areas of the image to prompt further review by the pathologist. With the rapid progress of AI, it has been confirmed that AI-based tissue evaluation can be equal to or better than the evaluation of pathologists. Especially, AI deep learning has great advantages in terms of driving efficiency and reproducibility of toxicological pathology work. However, there are still many challenges in the application of deep learning to digital pathology, such as classification tasks. The text or images needed for a computer to accurately identify a particular class are limited by a single magnification training. Second, some classes with microscopic changes (such as lung hyperplasia and adenoma) differ less than others, or there is heterogeneity among individuals of the same class of tumor, which may lead to annotation uncertainty at classification time. In addition, there will be rare cases of toxic pathology that are difficult to obtain in sufficient numbers, resulting in insufficient data for deep learning training sets.

At present, Chinese toxicologists are committed to promoting the application of AI technology in the industry, and the author believes that the development of technology should be promoted from the following aspects: First, the annotation of standardized accurate pathological image data is the cornerstone of the development of AI technology. Based on the vigorous development of domestic drug research and development, the establishment of a publicly shared database of toxic pathological images will become a necessary prerequisite for the development of AI algorithms for pathological diagnosis in the future. Secondly, the development and extension of AI algorithm technology, especially improving the generalization ability of deep learning algorithm models, may be an important way to accelerate the application of AI technology in toxicology. Finally, the feature extraction algorithm of the deep learning model mainly relies on computer experts, while the annotation of pathological pictures relies on medical experts. People with different knowledge backgrounds may have understanding biases in communication, resulting in obstacles in the development process. In particular, the current research and development of AI pathological diagnosis system mainly relies on computer experts for the purpose of improving the accuracy of the algorithm, while pathologists in most cases only annotate the data and do not really understand the process of deep learning to extract image features, which makes the new model developed by the algorithm team unable to truly solve key medical problems. Therefore, only the intersection and integration of different disciplines and expertise can achieve the integration of knowledge in different fields, stimulate innovative thinking, and promote the practical application of AI technology in toxic pathology.

In conclusion, although there are some challenges in the application of AI in the field of toxicity pathology at this stage, the complete replacement of the professional assessment of pathologists by computers will require deeper and more extensive research in model building and algorithm development. As the development of computer science becomes more and more closely related to the medical and health professions, it is possible to eventually change the existing pathology workflow, contribute to the quantitative, analytical and predictive toxicity pathology data, and bring new opportunities for the development of toxicity pathology.

Acknowledgments

Deep Learning for Precise Robot Position Prediction in Logistics.

http://8.218.247.20/index.php/jtpes/article/view/315.

Comment:

This article describes the extensive experimental progress of machine learning and deep learning-related techniques in real-world use. It has certain influence and practical effect, and the report of its first demonstration is worthy of publication in a journal. The author does a good job of directing the reader to an area where there is a great deal of work to investigate.

References

[1] Colom R, Karama S, Jung R E, et al. Human intelligenceand brain networks [J]. Dialogues Clin Neurosci, 2010, 12(4): 489-501.

[2] Janowczyk A, Madabhushi A. Deep learning for digitalpathology image analysis: A comprehensive tutorial withselected use cases [J]Pathol Inform, 2016, doi:10 4103/ 2153-3539.186902.

[3] Smith G F Artificial intelligence in drug safety andmetabolism [J]. Methods Mol Biol, 2022, doi: 10.1007.978-1-0716-1787-8 22.

[4] Aeffner F, Sing T, Turner O C. Special issue on digitalpathology, tissue image analysis, artificial intelligence. and machine learning: Approximation of the effect ofnovel technologies on toxicologic pathology [J]. Toxicol Patho1. 2021.49(4): 705-708.

[5] Pantanowitz L. Valenstein P N. Evans A J. et al. Reviewof the current state of whole slide imaging in pathologI. J Pathol Inform,2011, doi:10.4103/2153-3539.83746.

[6] Chang Che, Bo Liu, Shulin Li, Jiaxin Huang, and Hao Hu. Deep learning for precise robot position prediction in logistics. Journal of Theory and Practice of Engineering Science, 3(10):36–41, 2023.

[7] Hao Hu, Shulin Li, Jiaxin Huang, Bo Liu, and Change Che. Casting product image data for quality inspection with xception and data augmentation. Journal of Theory and Practice of Engineering Science, 3(10):42–46, 2023. https://doi.org/ 10.53469/jtpes.2023.03(10).06.

[8] Turner O C. Knight B. Zuraw A et al. Mini review: Thelast mile-opportunities and challenges for machinelearning in digital toxicologic pathology [J]. ToxicolPathol,2021,49(4): 714-719.

[9] Yao, J., Zou, Y., Du, S., Wu, H., & Yuan, B. Progress in the Application of Artificial Intelligence in Ultrasound Diagnosis of Breast Cancer.

[10] Ching T, Himmelstein D S Beaulieu-Jones B K, et alOpportunities and obstacles for deep learning in biologyand medicine [J], R Soc Interface. 2018. doi: 10.1098rsif. 2017. 0387.

[11] Tianbo, Song, Hu Weijun, Cai Jiangfeng, Liu Weijia, Yuan Quan, and He Kun. "Bio-inspired Swarm Intelligence: a Flocking Project With Group Object Recognition." In 2023 3rd International Conference on Consumer Electronics and Computer Engineering (ICCECE), pp. 834-837. IEEE, 2023. DOI: 10.1109/mce.2022.3206678.

[12] Yang, D., Mashima, D., Lin, W., & Zhou, J. (2020). DecIED: Scalable k-Anonymous Deception for IEC61850-Compliant Smart Grid Systems. Proceedings of the 6th ACM on Cyber-Physical System Security Workshop.

[13] Turner O C, Aeffner F, Bangari D S, et al. Society of4)toxicologic pathology digital pathology and imageanalysis special interest group article: Opinion on theapplication of artificial intelligence and machine learningto digital toxicologic pathology [J]. Toxicol Pathol, 2020.48(2): 277-294.

[14] Lin, Q., Che, C., Hu, H., Zhao, X., & Li, S. (2023). A Comprehensive Study on Early Alzheimer's Disease Detection through Advanced Machine Learning Techniques on MRI Data. Academic Journal of Science and Technology, 8(1), 281–285. DOI: 10.1111/jgs.18617.

[15] Chang Che, Bo Liu, Shulin Li, Jiaxin Huang, and Hao Hu. Deep learning for precise robot position prediction in logistics. Journal of Theory and Practice of Engineering Science, 3(10):36–41, 2023.DOI: 10.1021/acs.jctc.3c00031.

[16] Chang Che, Qunwei Lin, Xinyu Zhao, Jiaxin Huang, Liqiang Yu Authors Info & Claims,Enhancing Multimodal Understanding with CLIP-Basedlmage-to-Text Transformation, 2023 Pages 414-418.https:// doi.org/ 10. 1145/ 3627377. 3627442.

[17] Xu, J., Pan, L., Zeng, Q., Sun, W., & Wan, W. Based on TPUGRAPHS Predicting Model Runtimes Using Graph Neural Networks.

[18] Che, C., Hu, H., Zhao, X., Li, S., & Lin, Q. (2023). Advancing Cancer Document Classification with R andom Forest. Academic Journal of Science and Technology, 8(1), 278–280. https:// doi.org/10.54097/ajst.v8i1.14333.