学位論文の要旨

Abstract of Thesis

研究科 School	ヘルスシステム統合科学 Interdisciplinary Science and Engineering in Health Systems
専　攻 Division	ヘルスシステム統合科学 Interdisciplinary Science and Engineering in Health Systems
学生番号 Student No.	78501256
氏　名 Name	ASAAD MUSAED AHMED ANAAM

学位論文題目 Title of Thesis（学位論文題目が英語の場合は和訳を付記）

Advanced Deep Learning Techniques for Efficient HEp-2 Computer-Aided Diagnosis Systems
（効率的な HEp-2 細胞に対する計算機支援診断システムのための先進的深層学習手法）

学位論文の要旨 Abstract of Thesis

Autoimmune diseases are connective tissue disorders initiated by a dysfunction of the immune system affecting different body tissues and causing chronic inflammatory symptoms, such as Systemic Lupus Erythomatus, Sjorgren's syndrome, Rheumatoid Arthritis, etc. For identifying the presence of such disorders, the Anti-Nuclear Antibodies (ANAs) testing using the Indirect Immunofluorescence (IIF) method on Human Epithelial type-2 (HEp-2) cells is considered the gold-standard serological diagnosis testing for autoimmune diseases. IIF on HEp-2 cells substrate demonstrated high sensitivity and expresses a wide range of target antigens capable of revealing several types of ANAs. Unfortunately, the IIF routine protocol is time-consuming, labor-intensive, and depends heavily on the experience of the practitioners, which increases the variations across personnel/laboratories. Therefore, there has been a steady ongoing effort to develop image-based Computer-Aided Diagnosis (CAD) systems to automate the processes of the IIF HEp-2 test. Whereas, developing an efficient HEp-2 CAD system is required to support human experts in making better diagnosis responses, enhance immunology laboratories' capabilities and consistency, increase the test throughput, in addition, to provide an educational tool for medical specialists. However, due to the complex nature of the HEp-2 patterns classification problem even to human experts and the lack of sufficient annotated medical IIF HEp-2 data, still there is a need to develop an efficient HEp-2 cell images classification framework in order to construct an applicable HEp-2 CAD system with an acceptable cell classification performance.

Recently, various deep learning-based images classification methods were proposed to approach the HEp-2 cell images classification problem, demonstrating superiority over the preceding conventional methods and encouraging recent studies to further boost the performance of such tasks. However, despite its superiority, medical imaging classification using the deep learning-based approaches still have some limitations and challenges represented mainly by the lack of sufficient annotated training data and the vagueness of the feature representation that deep models learned. A large number of training data is needed to enhance the model generalization and avoid overfitting. At the same time, it is required to ensure that the model is aware of the correct association between the regions of interest (ROIs) in the

input image and the classification results. Accordingly, in this research, we suggested solutions based on advanced deep learning techniques to mitigate those limitations and proposed an efficient end-to-end training deep learning classification framework for solving the most essential and challenging tasks of the IIF HEp-2 test. Specifically, the HEp-2 cell patterns classification and the unbalancing mitotic-interphase HEp-2 cell-cycle classification task.

To remedy the training data scarcity, we proposed employing the contemporary deep learning generative adversarial networks (GANs) algorithms to synthetically generate new HEp-2 cell images for enlarging the training data. An intensive study was conducted on four different variants of GANs to assess their performance in synthesizing high-quality images and validate their applicability for data augmentation. For systematic comparison, the robust empirical quantitative metrics of Fréchet Inception Distance (FID) and 1-Nearest Neighbor classifier in two-sample tests were used to evaluate different GAN models' performance in learning the target data representations. By analyzing the statistical characteristics of the GANs-generated and the real HEp-2 cell images, these metrics provide a systematic assessment tool for comparison between different GANs models. Furthermore, we evaluated the effectiveness of employing GANs-generated HEp-2 images for augmentation using five state-of-the-art convolutional neural networks (CNNs) classifiers in the HEp-2 cell image classification literature. That is to study the effect of the training dataset regardless of the CNNs model architecture.

On the other hand, we proposed an improved self-attention deep cross residual network (Att-DCRNet) for developing an efficient HEp-2 cell image classification framework. The architecture of the baseline network was incorporated with an attention mechanism to enhance the model awareness of the class-relevant regions of interest (ROIs) among the channel and spatial dimensions of the network intermediate feature maps. The impact of this modification is to enhance the network's representation power and improve the discriminability of the classification model. We validated the effect of the proposed improvement of the Att-DCRNet through a comprehensive ablation study conducted on two tasks of HEp-2 cell datasets and supported by a gradient weight visualization method.

The results of GANs variants comparison study showed that GANs were able to generate HEp-2 cell images with high visual similarity with the real images even though their capacity to generate diverse data is within some limits. The quantitative evaluation analysis revealed that the generated data diversity limitation is caused by mode dropping and collapsing, which are inevitable deficiencies for GANs models due to the model capacity and training data limitations. Among all GANs variant understudy, the Info-WGANGP configuration achieved the best performance in terms of generated images quality. Therefore, the Info-WGANGP model was selected to synthesize new HEp-2 cell images for augmentation. The evaluation results across different variants of CNNs architectures demonstrated that combining GANs-generated data with the classic augmentation is beneficial for CNN training and can improve the classification performance.

Consequently, comprehensive experimental studies were performed to validate the effectiveness of the proposed framework of using the Att-DCRNet classifier with the Info-WGANGP augmentation against other state-of-the-art CNN models over the I3A HEp-2 public medical dataset. The proposed framework demonstrated competitive state-of-the-art results for the task of HEp-2 cell images classification with a mean class accuracy of 99.02% compared to the best previous methods' score of

Name	ASAAD MUSAED AHMED ANAAM

98.62%. Our framework attained a maximum performance of F1-score with 84.10%, Matthew's correlation coefficient (MCC) with 84.70%, and balanced class accuracy (BcA) with 99.0% for the challenging task of imbalanced mitotic-interphase cell-cycle classification surpassing the prior state-of-the-art results by 1.0% for the BcA score. The proposed framework proves to be effective for providing accurate diagnosis decision support regarding the HEp-2 cell patterns and the HEp-2 cell-cycle classification.