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Artificial Intelligence

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[AP2-E2-4-03] Basic Study of Artificial Intelligence Model with Deep Learning Algorithms for Peripheral Blood Leukocyte Classification

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Keywords: Artificial Intelligence, Deep Learning, Hematological Examination, White Blood Cell

Deep learning is one of the AI technologies that make accurate and efficient decisions. AI is able to perform multi-layered analysis with neural network and discover potential features. In this study, we examined a blood morphology analysis AI model with the deep learning method. The AI model learned with training images of mature white blood cells (WBC) that show typical morphology, and parameter tuning for optimization was performed. The AI model obtained by transfer learning calculated the classification prediction value with the test image. And it compared with visual classification by clinical laboratory technologists. Two classifications between the specific cell group and the mixed cell group showed an accuracy of 82.6 to 100%. After pre-training with background-removal images, addition-al transfer learning and fine-tuning for six classifications was performed on original images with background cells. The learning model showed 99% accuracy, and a highly accurate AI model for leukocyte classification was obtained. It is considered that incorrect classification can be detected and corrected by performing two-classification analysis on the results obtained by six-classification analysis. This AI model is useful as a leukocyte classification and screening technique in cell groups showing a typical cell image.

Basic Study of Artificial Intelligence Model with Deep Learning Algorithms for Peripheral Blood Leukocyte Classification

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Abstract

Deep learning is one of the AI technologies that make accurate and efficient decisions. AI is able to perform multi-layered analysis with neural network and discover potential features. In this study, we examined a blood morphology analysis AI model with the deep learning method. The AI model learned with training images of mature leukocyte that show typical morphology, and parameter tuning for optimization was performed. The AI model obtained by transfer learning calculated the classification prediction value and accuracy with the test image. And it compared with visual classification by clinical laboratory technologists. Two classifications between the specific cell group and the mixed cell group showed an accuracy of 82.6 to 100%. The learning model for six classification showed 99% accuracy, and a highly accurate AI model for leukocyte classification was obtained. It is considered that incorrect classification can be detected and corrected by performing two-classification analysis on the results obtained by six-classification analysis. This AI model is useful as a leukocyte classification and screening technique in cell groups showing a typical cell image.

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Introduction

The automation in clinical laboratory has been promoted by the development of robot technology, and has contributed to shortening of Turn Around Time (TAT) and reducing medical incidents. Representative of automation technologies are automatic biochemical analyzers and automatic complete blood count (CBC) analyzers, which have achieved full automation of measurement and quality control. It has been reported that these automatic analysis techniques are highly useful in clinical laboratory, and it is known the flow cytometry technology generally used in CBC can obtain high precision in normal blood cells. However, it has been reported that changes in blood cell morphology and appearance of immature cells due to chemotherapy show abnormal scattergram patterns, and the accuracy of classification calculation is poor. Therefore, microscopic observation by clinical laboratory technologists is often required, and the rate of re-testing increases in larger hospitals, and new morphological analysis technology with the thought process of clinical laboratory technologists is also required. Artificial Intelligence (AI) is rapidly developing in recent years as a technology that enables judgments that reflect thought patterns. The deep learning method is a multi-layered neural network that imitates the human cranial nerve circuit, and the computer automatically extracts the features in the data during learning. It is an AI technology that realizes accurate and efficient judgment because it can detect latent features that humans do not notice. Although AI is expected to automate blood morphology analysis including abnormal cells and immature cells by learning many cases, there are few reports on analysis techniques with deep learning methods in CBC tests. Therefore, in this study, we performed a basic verification of a blood morphology analysis method using deep learning with typical leukocyte images, and examined its usefulness in leukocyte classification.

Materials and Methods

Materials

The subjects were 40 healthy adults. A thin-layer blood smear was prepared from peripheral blood supplemented with EDTA-2Na and stained with May-Grünwald-Giemsa (MG). The MG-stained specimen was observed under a microscope using an objective 100x oil immersion lens, and a normal WBC of a typical cell images were photographed with a microscope color camera (Axiocam ERc5s, Carl Zeiss). A database of 1335 typical normal leukocyte images was created.

Dataset

Leukocyte images were classified into six categories: rod-shaped neutrophils (Band), segmental nucleus neutrophils (Segment), eosinophils (Eosino), basophils (Baso), monocytes (Mono), and lymphocytes (Lymph). The image of each cell group was trimmed at 750×750 pixels. Two types of datasets were created, one is image data set (DB-1) in which background cells such as erythrocytes and platelets were deleted and only leukocytes were trimmed, and the other is original image data set (DB-2) with leukocytes and background cells. Augmentation processing was performed to increase the number of original data, and total of 2982 images were created (500 images for Band, 500 images for Segment, 462 images for Eosino, 520 images for Baso, 500 images for Mono, and 500 images for Lymph) from original images. 80% of the randomly extracted images were used as the training data set, and the remaining 20% of the images were used as the test image data set.

Image analysis with deep learning algorithm

Nnabla (SONY) was used as the deep learning library, and Anaconda3.0 and Python3.5 were used as the development environment. The hardware used Intel(R) Core (TM) i7-8700 3.2GHz for CPU, NVIDIA GeForce GTX 1070 8GB for GPU, and Microsoft Windows 10 professional for OS.

1) Two-class classification for specific cell group selection

In order to verify the classification accuracy of the specific 1 group and other cell groups (5 groups) among the 6 classified cell groups, evaluation of specific cell extraction was performed by comparing specific cell group to mixed cell group. We performed transfer learning by using LeNet as a CNN model and measured and evaluated the classification accuracy and loss function.

2) White blood cell six-classification analysis

Low resolution images (3 RGB color /480 × 480 pixels and 320 × 320 pixels) as training image data set were generated from the both sets of image data. And, low resolution (3 RGB color and) images as test image data set were also generated from the both sets of image data. We performed CNN transfer learning by using ResNet-18 with each image set. Furthermore, we also performed additional learning and fine-tuning with DB2 to the pre-trained DB1 CNN model. It was compared classification accuracy and loss function in order to evaluate applicable to leukocyte classification in original microscope images.

Results

1) Two-class classification for specific cell group selection

The cost function curve, TRAINING ERROR curve, and VALIDATION ERROR curve converged at 10 to 30 Epoch in the selection of Eosino, Lymph, and Mono. Meanwhile, the Cost function curve and TRAINING ERROR curve converged at 10 to 30 Epoch in the selection of Segment and Band, but the VALIDATION ERROR curve did not converge and diverged. And the Cost function curve, TRAINING ERROR curve, and VALIDATION ERROR curve did not converge at 100 Epoch in the selection of Baso. All cell groups except Baso showed an accuracy of over 97% (Table 1)

2) White blood cell 6 classification analysis

Figure 1 shows the learning curve by additional learning and fine tuning with DB2, and Table 2 shows the evaluation results with test image data. The TRAINING ERROR curve converged at 20 epoch, and the large fluctuation of VALIDATION ERROR curve converged at 50 epoch. As a result of evaluation, Accuracy was 0.996 and Cost value was 0.109.

Conclusion

After pre-training with background cells removal images, additional transfer learning and fine-tuning was performed on original images with leukocytes and background cells. The learning model showed 99% accuracy, and a highly accurate AI model for leukocyte classification was obtained. It is considered that incorrect classification can be detected and corrected by performing two-classification analysis on the results obtained by six-classification analysis. This AI model is useful as a leukocyte classification and screening technique in cell groups showing a typical cell image. It is suggested that AI analysis contributes to accurate detection and classification of hematological morphology through additional learning of training images of immature cells and abnormal cells. We will analyze clinical cases with this AI model and technique in future studies.

Table 1- Two classifications for specific cell selection

	Specific cell group (Images)	Mixed cell group (Images)	Total (Images)	Accuracy
Eosino	475	502	977	1.000
Lymph	485	500	985	1.000
Mono	555	486	1041	1.000
Neutro (Segment)	480	499	979	0.977
Neutro (Band)	495	498	993	0.968
Baso	520	493	1013	0.826

Table 2- Six classifications with original WBC images

	Baso	Eosino	Lymph	Mono	Neutro (Band)	Neutro (Segment)
Baso	21	0	0	0	0	0
Eosino	0	45	0	0	0	0
Lymph	0	0	55	0	0	0
Mono	0	0	0	49	0	0
Neutro (Band)	0	0	0	0	45	0
Neutro (Segment)	0	0	0	0	1	51

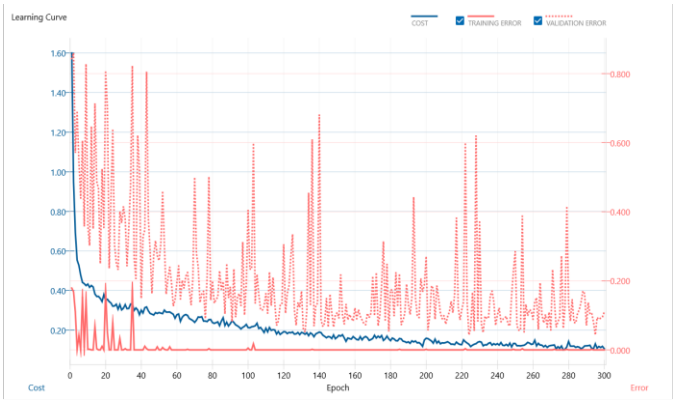

Figure 1- Learning curve with the original image set

Acknowledgments

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