

Application of Adaptive Resizing for Preserving Morphological Features in Human Chromosome Classification

Huong Pham Thi Viet¹, Trang Phan Ha Van², Vu Tran Anh^{2,*}, Huy Hoang Quang²

¹ International School, Vietnam National University, Ha Noi, Vietnam

² School of Electrical and Electronic Engineering, Hanoi University of Science and Technology, Ha Noi, Vietnam

* Corresponding author email: vu.trananh@hust.edu.vn

Abstract

Several genetic illnesses have been linked to chromosome abnormalities. The diagnosis of these abnormalities has received attention in recent years. One of the most popular and useful ways to solve this problem is based on Karyotyping. Karyotyping is a laboratory procedure that allows doctors to examine a set of chromosomes. Therefore, it plays a crucial role in genetic disorder diagnosis. Karyotyping requires considerable manual effort, domain expertise, experiences, and is very time-consuming. Clinical cytogeneticists frequently utilize karyotyping during metaphase to study human chromosomes for diagnostic purposes. This paper proposed a method to classify human chromosomes, which is an important step in detecting chromosome abnormalities. A highlight from this article is optimizing the quality of the initial dataset by concentrating on preprocessing. Besides, the categorization accuracy of some models belonging to convolutional neural networks is considered, which will be mentioned in the next part. This article's results outperformed other traditional classifications. Moreover, when comparing with different models of convolutional neural network, model EfficientNet-b3 gave the highest accuracy with the same dataset.

Keywords: Adaptive resize, chromosome classification, karyotyping, morphological features.

1. Introduction

Human typically have 46 chromosomes arranged in 23 pairs, in which the first 22 pairs are called autosomes, and the last pair is the sex chromosomes. In the 23rd pair, males usually carry one X and one Y chromosome, whereas females have two X chromosomes. These chromosomes contain the genetic information which is essential for the development of the body.

While most people possess this typical chromosomal complement, alterations can sometime occur. Such alterations, referred as chromosome abnormalities, are categorized into two types: structural and numerical. Structural abnormalities occur when a part of a chromosome is missed, duplicated, inverted, or transferred to another chromosome. In contrast, numerical abnormalities are when an entire chromosome is absent or in excess. Chromosome abnormalities can lead to various consequences, such as diseases, infertility, pregnancy loss, congenital anomalies, or neurodevelopmental disorders. For example, Trisomy 21, or having an extra copy of chromosome 21, causes Down syndrome, a common example of a numerical chromosomal abnormality [1].

Fig. 1 shows one of the typical situations that are related to chromosome abnormalities.

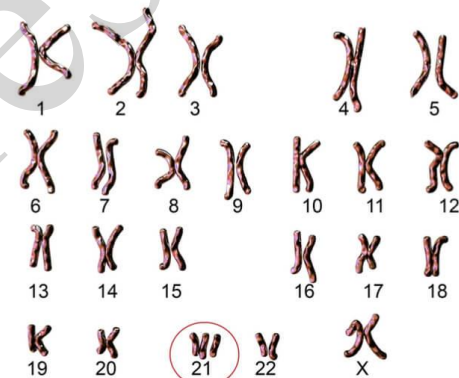


Fig. 1. Down syndrome – a type of disease related to chromosome abnormalities

Since the 1980s, many studies have concentrated on automatic chromosome classification, leading to the development of various computer-aided systems aimed at detecting chromosomal abnormalities and genetic disorders [2]. A typical automatic chromosome classification system has three main steps: image processing, feature extraction, and classification. During image processing, metaphase images are first enhanced to eliminate noise and improve clarity for subsequent analysis. Segmentation is then employed to separate chromosomes from the surrounding background. Skeletonization is carried out to facilitate feature extraction, which may rely on either geometric

properties or banding patterns. Finally, the classification step assigns each chromosome to its appropriate class. According to studies in this field, artificial neural networks (ANNs) are among the most used techniques, because of the parallel processing capabilities that enhance efficiency and reduce both computational complexity and processing time.

The very first step is the processing of chromosome images to their best possible quality. The better the image, the more convenient the methodology. In [3], they proposed a new filter to remove the noise depending on the objects that existed in the image. Some other methods to enhance the image quality are proposed in [4], such as histogram equalization, contrast-limiting adaptive histogram equalization, gamma adjustment, and histogram equalization with 3D block matching. The method of straightening the chromosome was used in [5] to process the images. Two straightening techniques have been used, namely, straightening by the medial axis followed by human rectification and straightening using projection vectors.

Regarding the feature extraction process, many algorithms have been proposed to split touching and overlapping chromosomes. According to research [6], there were three main steps in chromosome segmentation: (1) separating the foreground and background of the chromosome to determine if the chromosome overlap or adhere to each other; (2) detecting the markers of the chromosome center point, and then, according to the maker of the center point, segmenting the pixel range of each chromosome; and (3) generating enough candidates and selecting the chromosome regions according to certain rules as the final segmentation result. The main challenge in chromosome segmentation was the separation of overlapping chromosomes [7]. In [8], the segmentation process is done by converting images into binary, and Contour algorithm is applied to identify the boundaries. Then the cut lines were drawn on the overlapped region to separate the chromosomes. A disadvantage of this research is that they do not consider the overlapped region and banding information of the overlapping chromosomes. For the same purpose, to extricate overlapping chromosome, Delaunay triangulation is used in [9] to automatically identify the number of overlaps in a cluster, followed by the detection of the appropriate cut-points. Feature extraction using the principal component was done in [10], which significantly reduced the dimension of the feature space and allowed high classification capability. A Convolution Neural Network (CNN) was also used in [6] as a feature extractor.

The last step of the classification procedure is to apply algorithms to single chromosomes to identify their correct categories. In [11], they proposed a CNN-based deep learning network to automatically classify chromosomes. The research in [12] reduced the complexity of an Artificial Neural Network (ANN) and

combined an improved multi-layer perceptron neural network for automated classification of chromosomes. Research [6] provided Faster-RCNN, an input-aware and probabilistic prediction convolutional neural network (IAPP-CNN) was also presented in [13]. a novel method named Varifocal-Net was presented in [14], which included three stages. Firstly, both global and local features were learned via the G-Net. Then, the two multi-layer perceptron classifiers were built based on the features previously acquired. Finally, a dispatch strategy was introduced to classify chromosomes.

In study focuses on optimizing the image processing stage following chromosome segmentation, which plays a critical role in the overall classification pipeline. After segmentation, chromosome images vary in size, making it necessary to standardize dimensions before putting them into a classifier. An adaptive resizing method is proposed, which combines image scaling and zero-padding to preserve morphological features while ensuring uniform input size. Then CNN is used to classify 24 types of chromosomes. The experiment results confirmed the effectiveness of the proposed method.

The paper is organized as follow: the first part introduces the dataset and the proposed method. The second part shows in detail the preprocessing procedure and classification of human chromosomes. The third part gives the results and evaluation of using the proposed method, and the final part concludes the paper and discussion.

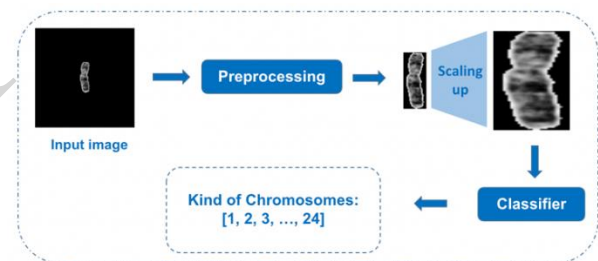


Fig. 2. The proposed pipeline

The main contributions of this study are summarized as follows:

- (1) We propose an adaptive resizing method that preserves morphological characteristics of chromosomes while standardizing input size for deep learning models.
- (2) We provide a comprehensive evaluation across multiple CNN architectures, demonstrating consistent improvements over conventional resizing techniques.

2. The Proposed Method

This section provides details on the proposed method for the task of chromosome classification. The proposed method comprises two main stages: 1) preprocessing

images; and 2) classifying 24 kinds of chromosomes. In the first stage, data augmentation was implemented to increase the training set. After segmentation, the unnecessary background was removed and then the images were resized to the original scale. In the second stage, the chromosome images were fed into several models of Convolutional Neural Network to evaluate the performance of each model. A detailed flow diagram of all the steps in the proposed method is provided in Fig. 2.

2.1. Dataset

In this research, the Pki chromosome dataset from University of Passau, German is used [15]. The dataset contains 612 G-bands metaphase images and 612 corresponding karyotyped images. 2 cytogeneticists who had 3 years and 10 years of experience conducted the interpretation on the karyotyped images, and they concluded that 48 of those contain abnormalities relating to DS, ES, and KS, as shown in Fig. 3. After that, all the images from the dataset were processed to enhance contrast and brightness, resulting in improved quality images.

The dataset is split into 2 parts: 80% of those for training and validation, where validation accounts for 10%, while the remaining 20% was put aside for testing purposes, as shown in Fig. 4. There are 10404, 1156, and 2809 single chromosome images of the 24 classes for the training set, validation set, and testing set, respectively.

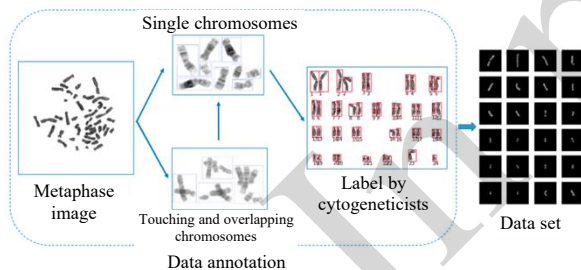


Fig. 3. Pipeline for labelling datasets

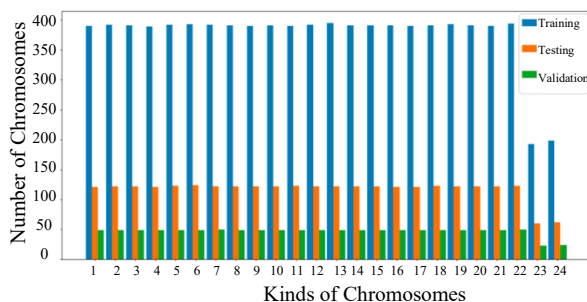


Fig. 4. Illustrate the whole dataset

2.2. Preprocessing

The original chromosome images contain overlapping and touching. The methods in [16] are utilized, which are cutting mode (when the chromosomes are touching) and smear mode (when they

are overlapping), to obtain images of only a single chromosome.

In [16], which used the same dataset, the authors applied medial axis transformation (MAT) to calculate the length of a chromosome. The obtained medial axis could determine the centromeric index and density profile, which represent the chromosome's features. The authors used such a method to compute the input features of each single chromosome image to feed SVM algorithms and used CNN models to classify the human chromosomes. The highest accuracy was 92.8%. However, the preprocessing method was quite simple, so the result might have been improved more if it had been for the optimal preprocessing technique.

Beyond the method mentioned in [16], this research applied several preprocessing techniques on the single chromosome images. These includes image cropping to eliminate black background, and adaptive resizing standardize the input dimensions of all chromosome images for processing.

2.2.1. Data-augmentation

It is widely known that data augmentation is a set of techniques to artificially increase the amount of data by generating new data points from existing data. It is useful to improve the performance and outcomes of machine learning models by forming new and different examples to train datasets. If the dataset in a machine learning model is rich and sufficient, the model performs better and more accurately. As a result, after the data preprocessing, when the training dataset was not sufficient, several data augmentation methods were applied to increase the number of training data. Each image was operated by rotation with a random angle within $\pm 45^\circ$. With some operations, such as random left-right flip, random up-down flip, and random translation, the number of training data was augmented by a factor of 30. Consequently, the number of training samples was significantly increased.

2.2.2. Cropping chromosome

It was observed that the image was still not optimal because the black background, which introduced useless information, occupied most of the image instead of the chromosome; this was not only a large and time-consuming issue but also reduced the quality of the classification step. Therefore, the black background region was removed to reduce data size and computational cost.

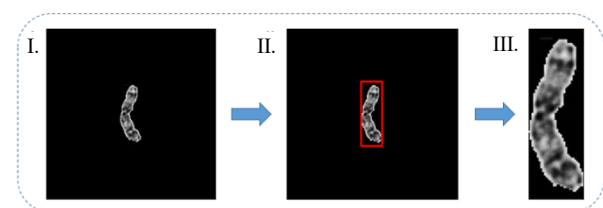


Fig. 5. Cropping chromosome pipeline

It can be seen from the pipeline that there were two steps to crop the chromosome region close to the contour of the object. In Fig. 5-I, the chromosome region accounted for only a small part, while the background constituted most of the image. Fortunately, all the background values were zero, so all indices with values greater than zero could be selected. Then, the minimum and maximum indices along the x-axis and y-axis were obtained by sorting all indices according to their respective axes. Consequently, four points based on the minimum and maximum coordinates were determined to construct the red bounding box in Fig. 5-II. Finally, an image like Fig. 5-III was obtained. In these images, most of the excess regions in the original image were removed, while the shape and values of the chromosome region of interest were preserved.

2.2.3. Resizing methods

From cropping chromosome images with diverse input sizes, the prerequisite was to resize all images to a fixed size before feeding them into the classification model. Thus, three techniques were investigated to resize image to the same size, including scaling up, zero-padding, and the adaptive resizing method, as shown in Fig. 6.

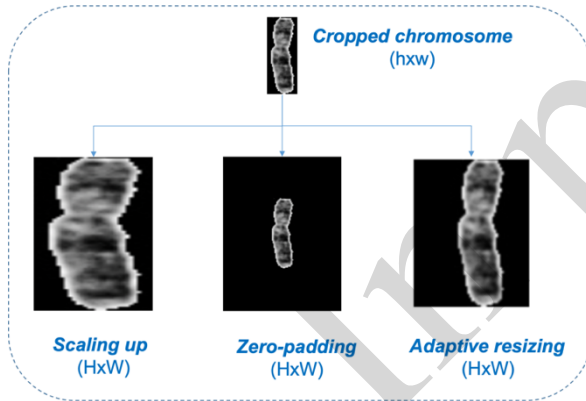


Fig. 6. Three approaches to resizing a cropped image to a fixed size

Firstly, after cropping the image, the scaling-up method was applied to enlarge all the images to the specified size. This is a wide and conventional approach used to scale all the images to the same size [17]. However, from Fig. 6, this method made chromosomes distort. In other words, the image after using this approach was quite different from the original image, which could affect the performance of the classifier.

Secondly, an experiment with a zero-padding approach was conducted to resize all the images to the same size. It was realized that while scaling carried the risk of deforming the patterns in the image, padding did not. Nevertheless, it had no effect on the classification accuracy because the neighbouring zero input units would not activate their corresponding convolutional unit in the next layer [17].

Thirdly, an adaptive resizing technique was proposed, which is considered a combination of both above methods, as described in detail in Algorithm 1. The cropped chromosome with a size of $h \times w$ was scaled to an intermediate size so that its shape was preserved with the same aspect ratio as the original image. Subsequently, a zero-valued image with a target size of $H \times W$ was created, and the scaled image was inserted into the zero-image at the starting point (x, y) . And this point was initialized randomly in a specific range during the training stage with a zero-padding augmented factor (k) , which could be considered a data augmentation technique because it enriches training data. As a result, in Fig. 7, the bigger chromosome was obtained without distortion and the minimum amount of inserted zero padding. This technique overcame the limitations of both methods of scaling up and zero-padding.

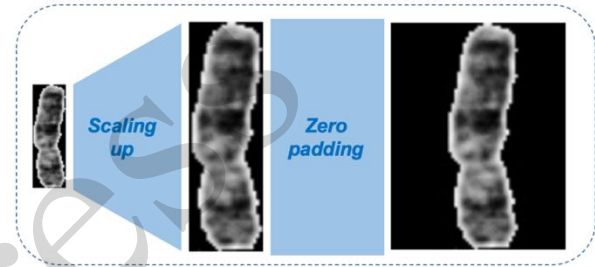


Fig. 7. Adaptive resizing method

2.3. Chromosome Classification

This section describes in detail the model for the task of classifying chromosomes. Experiments were conducted with several state-of-the-art CNN architectures for this task.

A set of state-of-the-art deep CNN models had been investigated and evaluated on the testing set, including Inception-ResNet-v2 [18], EfficientNet-B0 [19], EfficientNet-B1 [19], EfficientNet-B3 [19], DenseNet121 [20], DenseNet161 [20], DenseNet169 [20], and DenseNet201 [20]. These CNN architectures are high performing for image classification tasks. In addition, the power of the pre-trained CNN models was exploited in a large image dataset to fine-tune for the research problem.

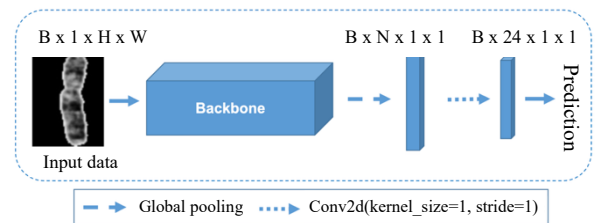


Fig. 8. Model architecture

In Fig. 8, after preprocessing, input data was resized to a shape of $B \times 1 \times H \times W$ (B : batch size) and then fed into the model. The CNN network considered

the pre-trained backbone as a feature extractor; after that, output would be applied to a global pool, and then a tensor with the shape $B \times N \times 1 \times 1$ (N : the number of channel features) is obtained. And finally, after coming through a 2D convolution layer, a softmax function was used to calculate the probability of each output. To determine what kind of chromosome it is, we would get the index of greatest probability.

In the training stage, all pre-processed images with the adaptive resizing method were fed into the network with the same size of ($H \times W$). The number of training epochs was set at 200, and the early-stopping technique was applied to avoid overfitting the training dataset [21]. This allowed us to stop training once the model performance stopped improving on a hold-out validation dataset. During the training process, Adam Optimizer was used [22] with an initial learning rate of 10-3. In the end, the cross-entropy loss function between the groundtruth labels and the predicted labels was minimized by the model over all training samples.

3. Experiment and Results

3.1. Evaluation Metrics

To evaluate the performance of the classifier, several metrics are used, including accuracy, macro-average precision, macro-average recall and macro-average F1-score. These metrics are particularly suitable for multi-class classification problems with class imbalance, as they treat all classes equally regardless of their frequency. These metrics can be calculated using the following formulas:

$$Accuracy = \frac{TP+TN}{TP+FP+TN+FN} \quad (1)$$

$$Precision = \frac{TP}{TP+FP} \quad (2)$$

$$Recall = \frac{TP}{TP+FN} \quad (3)$$

$$F1 - score = 2 \times \frac{Precision \times Recall}{Precision + Recall} \quad (4)$$

Where TP, TN, FP, and FN are the numbers of True Positive, True Negative, False Positive, and False Negative samples, respectively.

3.2. Model Performance on Test Set

First, the effectiveness of the preprocessing stage in improving classification performance was demonstrated. The model was evaluated with and without the preprocessing step under the same architecture and dataset conditions. As presented in

Table 1, the model performance increased by approximately 2% across all evaluation metrics.

Table 1. The effect of the preprocessing stage on the performance of the model

Pre-processing stage	F1-score	Precision	Recall	Accuracy
Cropping	0.9655	0.9659	0.9655	0.9712
Non-cropping	0.9433	0.9437	0.9433	0.9516

Table 2. Experiment results between CNN models when trained with input images of size 256 x 256

Network architecture	F1-score	Precision	Recall	Accuracy
Inception-ResNet-v2	0.9404	0.9362	0.9446	0.9475
DenseNet-121	0.9563	0.9568	0.9567	0.9626
DenseNet-161	0.9511	0.9513	0.9518	0.9590
DenseNet-169	0.9519	0.9524	0.9526	0.9587
DenseNet-201	0.9532	0.9530	0.9542	0.9601
EfficientNet-b0	0.9591	0.9587	0.9598	0.9658
EfficientNet-b1	0.9634	0.9638	0.9634	0.9687
EfficientNet-b3	0.9655	0.9659	0.9655	0.9712

Table 2 compares the quantitative performance results for some classification models with different CNN backbones on the test set. EfficientNet-b3 is the best model, with a macro-averaged F1-score of 96.55%, a macro-averaged precision of 96.59%, a macro-averaged recall of 96.55%, and an accuracy of 97.12%. and then, this network architecture was used to conduct the next experiments.

After that, an experiment was conducted to compare three approaches to resizing images to a fixed size on the performance of the selected model (EfficientNet-b3), including scaling-up, zero-padding, and the adaptive method with a default k-factor of 1. Besides, the impact of image input sizes after preprocessing was also investigated. In this experiment, the performance was evaluated on some different fixed image sizes (256×256), (175×135), and (256×200). The reason why the sizes of (175×135) and (256×200) were chosen is that size statistic of all chromosomes after cropping were performed, and the largest size was obtained with a length of 175, a width of 135, and an overall size of

256×200 , which has the same aspect ratio as 175×135 .

Table 3. Performance of EfficientNet-b3 with 3 resize methods using image size (256×256)

Resize method	F1-score	Precision	Recall	Accuracy
zero-padding	0.9445	0.9447	0.9447	0.9505
adaptive ($k=1$)	0.9655	0.9659	0.9655	0.9712
scaling-up	0.9617	0.9614	0.9621	0.9669

As a result, in Table 3, resizing the input images by the adaptive method with a k -factor of 1 for training gave the best result. The scaling-up method could change the shape of the original image, while the zero-padding method had no effect on the performance of the classifier, as mentioned in Section 2.2.3. And then the effects of input size after using the adaptive resizing method was evaluated.

Table 4. Performance of EfficientNet-b3 using adaptive resizing ($k = 1$) with different input image sizes

Image size	F1-score	Precision	Recall	Accuracy
175 x 135	0.9604	0.9601	0.9615	0.9665
256 x 200	0.9619	0.9626	0.9623	0.9690
256 x 256	0.9655	0.9659	0.9655	0.9712

From Table 4, the input size of (256×256) achieved the best performance in this experiment.

One of the contributions of this paper is that a new resizing method was proposed to both preserve aspect ratios and enrich the data with k -factors. Indeed, as a result in Table 5, the performance of the classifier increased slightly with k -factors of 3 and 5 compared to 1. Although it was not a sharp rise (about 0.5% in the F1-score), this could be considered a promising approach for other tasks because it combined the resize method and augmentation in an algorithm.

Table 5. The effect of the augmented factor on the adaptive resizing method

k-factor	F1-score	Precision	Recall	Accuracy
1	0.9655	0.9659	0.9655	0.9712
3	0.9662	0.9663	0.9665	0.9712
5	0.9695	0.9700	0.9692	0.9736

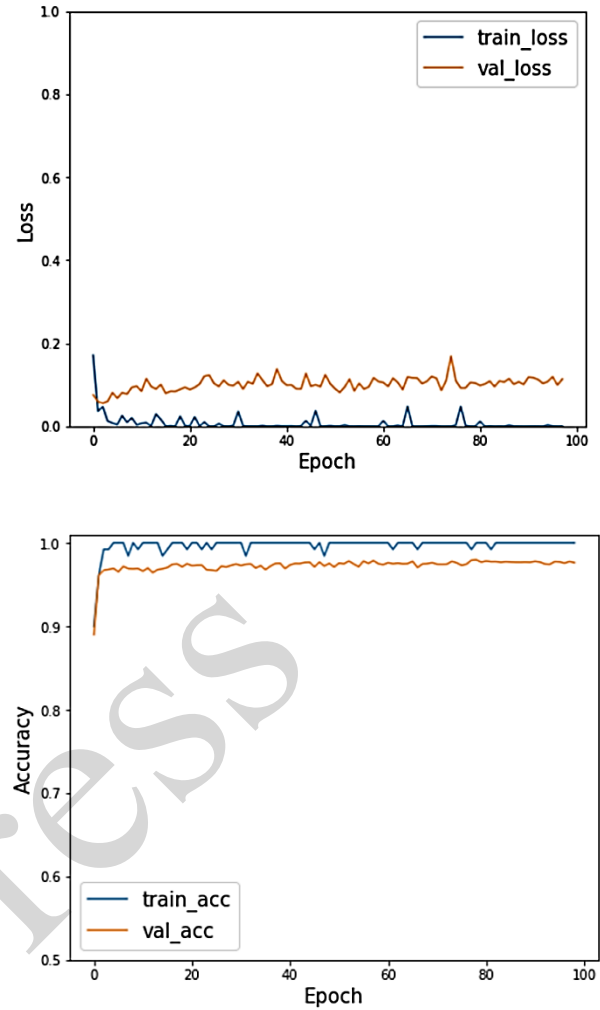


Fig. 9. Comparison of Loss curves and Accuracy curves for the training and validation stages

Additionally, the loss curves and accuracy curves of the proposed model for the training and validation stages are shown in Fig. 9. The accuracy scores get high value right from some first epochs and quickly converge and stabilize after about 30-40 epochs. The use of pre-trained models as initialization weights instead of random initialization is one of the reasons for achieving such good results.

3.3. Comparison to other Approaches

In Table 6, a comparison between the results obtained from this study and several previous approaches related to research topic was conducted. The achieved results were better than those reported in most of the referenced studies. In comparison with Wu *et al.* [23], the accuracy achieved (97.12%) was significantly higher than their reported result (63.5%). Similarly, the accuracy reported by Zhang *et al.* [11] was also lower than that achieved in this study.

Table 6. Comparison to other approaches

Article	Data	Method	Accuracy
Wu <i>et al.</i> [23] (2018)	Private data	MD-GAN& CNN	63.50%
Zhang <i>et al.</i> [11] (2018)	Private data	CNN (Lenet)	92.55%
Qin <i>et al.</i> [14] (2019)	Xiangya	MLP	99.20%
Thinh <i>et al.</i> [16] (2020)	Passau	CNN (Inception-ResNet)	92.80%
This study	Passau	CNN (EfficientNet-b3)	97.12%

With the same dataset, the accuracy of the proposed approach is higher than that of the method from Thinh *et al.* (92.8%) [16]. The reason is that there are more steps of preprocessing were carried out, thus improving the quality of the dataset by cropping the background of the image. Although the accuracy reported by Qin *et al.* (99.2%) is higher than that achieved in this study, direct comparison may not be entirely fair due to differences in dataset scale, data distribution, and experimental settings. Their study utilized a significantly larger dataset and a more complex model (Varifocal-Net), which is specifically designed to capture both global and local chromosome features.

In contrast, the focus of this study is not to achieve the highest absolute accuracy, but to demonstrate that preserving morphological feature during preprocessing can significantly improve classification performance, particularly under limited data conditions.

4. Discussion and Conclusion

In this paper, the deep learning technology represented by the convolutional neural network was applied to the task of chromosome detection and classification, and a better result was achieved with the model EfficientNet-b3. According to this research, the proposed model achieved better precision in some single-category classifications. The results of image enhancement and classification can provide a quantitative basis for the following doctor's diagnosis. The preprocessing model also helps segment and enhance band characteristics and then uses many models of CNN to classify and detect single chromosome to achieve chromosome matching.

Nevertheless, this study still contains some limitations that can be improved in the future. First, the experiments were conducted using only the Pki chromosome dataset, which consists of relatively clean and standardized G-bands chromosome images. In real clinical environments, chromosome images often exhibit significant variations in staining quality, illumination,

noise levels, and acquisition devices, which could affect the robustness and generalizability of the proposed method.

Second, the current framework assumes that chromosome have already been segmented into individual instances. In practice, overlapping and touching chromosomes remains a major challenge and are among the primary causes of failure in automated karyotyping systems. Although various approaches, such as countour-based methods, medial axis transformation, and U-Net-based segmentation, have been proposed to address this issue, they were not incorporated into the present pipeline.

It is worth noting that the main contribution of this study lies in the preprocessing strategy, specifically the adaptive resizing method. Evaluating the method on a controlled dataset allows isolating its impact on classification performance without onfounding factors.

Future work will focus on improving generalizability by validating the method on multi-source clinical datasets, as well as integrating segmentation techniques to handle overlapping chromosomes, with the goal of developing an automated chromosome classification pipeline.

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