Classification of Metaphase Chromosomes Using Deep Learning Neural Network

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***Abstract*—Karyotyping of Banded Metaphase Chromosomes is one of the preliminary steps used in cytogenetics to analyze the chromosomes for diagnostic purposes. Deep learning is a subfield of machine learning concerned with structure and function of brain. It exploits a way to automate predictive analysis. The key aspect of deep learning is that the layers of features are not designed by human engineers. They are learned from data using a general purpose learning procedure. This paper proposes a convolution based deep learning to classify the chromosomes for automated karyotyping. The developed architecture allows us to train and test images that helps in predicting the chromosome abnormality. The performance analysis is based on loss and accuracy curves and the graphical representation clearly exhibits better classification results for this architecture.**

Keywords-deep learning; chromosome; karyotyping; convolutional neural networks

I. INTRODUCTION

Karyotyping of chromosomes combines the study of chromosome morphology and genetic diseases. Though the process of karyotyping requires more manual effort, time consumption, human visual perception and domain expert, it remains as a very important task for cytogeneticists to perform this process efficently. An approach for addressing such problem is to create an automatized system to classify the chromosomes using a classifier. Recently, Deep learning tool is mainly employed to perform the various tasks by the process of automation. Karyotyping is performed based on the various features extracted from chromosomes. The important features to recognize the chromosome are centromere position, length of the chromosomes, centromere index, banding patterns. Chromosomes are visualized as a continuous sequence of light and dark bands and they become evident by staining techniques. Karyotyping allows us to determine whether there are any abnormalities or structural problems in them. Normally, Karyotyping process is carried out during the metaphase stage of cell division. Metaphase chromosome images are taken in this study as they are seen easily and have unique light and dark bands.

Generally there are 23 pairs of chromosomes in every human cell [1]. The first 22 pairs are autosomes and the 23rd pair is the sex chromosome. Chromosomal abnormalities are related to the structure and number of these 23 pairs of chromosomes. Karyotyping [2, 3] is a standard profile of chromosomes as shown in Fig. 1.

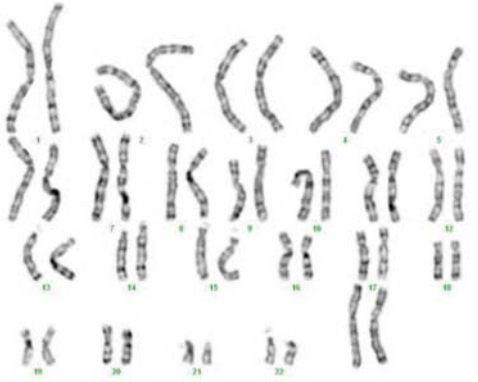

Figure 1. Karyotyped Image

All 23 pairs of chromosomes are differentiated using various staining procedures. They are G (Giemsa) banding, Q (Quinacrine) banding, R banding and C banding as in Fig. 2. Out of all, G banding is preferred because they give a distinct pattern of light and dark bands.

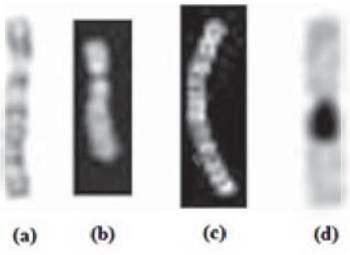

Figure 2. Stained Images (a) G band image (b) Q band Image (c) R band image (d) C band Image

Dan Cireşan et.al presented the concept of multiclass deep neural network for improving the image classification benchmarks recognition for traffic signs [1]. Swati et.al proposed a different straightening techniques that was applied to chromosome images prior to classification of chromosomes using siamese methods [2]. But it is used only for limited data. Altan et.al provided a comprehensive review of past and recent research in the area of neural networks based automatic human chromosome classification system and feature extraction [3]. Wenzhong Yan and Lei Bai proposed a classification algorithm based on deep belief networks by extracting the features based on Hilbert Huang transform [4]. Performance of classification was examined to diagnose the subjects with or without the coronary artery disease. Xingwei Wang et.al applied a higher order neural network for the classification of human chromosomes [5]. A new automated chromosome karyotyping scheme with ANN based two decision layer classifier [6] was demonstrated. This was applied only to normal chromosomes and not tested with abnormal or cancerous metaphase chromosomes. The paper [7] presented a summarization of major advanced classification methods and techniques used for improving classification accuracy. Also it discussed important issues affecting the success of image classifications.

In [8], neural networks have been applied to perform all major stages of human chromosome analysis namely feature extraction, image segmentation and classification. A comparative result analysis of SVM, DT and KNN classifier for image classification was performed [9]. The application of probabilistic neural network to the classification of normal human chromosomes [10] was described. Various methods were reported for classification of chromosomes based on banding pattern [11, 12]. The recognition rates achieved in this study are superior to those reported using either the maximum likelihood or back propagation neural network techniques.

Deep learning technology has been applied to medical diagnosis based on a large amount of accumulated X-rays, CT scans, lab data and MRIs. The proposed work exploits deep learning convolutional neural network for classification of sex chromosomes from the 23 pairs of chromosomes.

II. MATERIALS AND METHODS

A. Deep Learning Neural Network

Deep learning is a type of machine learning in which a model learns to perform classification tasks directly from images, text, or sound. Deep learning is usually implemented using neural network architecture. The term "deep" refers to the number of layers in the network—the more layers, the deeper the network. Traditional neural networks contain only 2 or 3 layers, while deep networks can have hundreds. It is necessary to develop more powerful discriminative optimization techniques to find better feature extraction models at each layer. A deep neural network combines multiple nonlinear processing layers with simple elements operating in parallel and inspired by biological nervous systems. It consists of an input layer, several hidden layers, and an output layer. The layers are interconnected via nodes, or neurons, with each hidden layer having an output and previous layer as its input. Deep-learning networks are distinguished from the more commonplace single-hidden-layer neural networks by their depth (i.e,) the number of node layers through which data passes in a multi-step process of pattern recognition.

B. Convolutional Neural Networks

The convolutional neural network (CNN, or ConvNet) is one of the most popular algorithms for deep learning with images and video. A convolutional neural network (CNN) is a type of artificial neural network used in image recognition and processing that is specifically designed to process pixel data. The layers of a CNN consist of an input layer, an output layer and a hidden layer that includes multiple convolutional layers, pooling layers, flattened layer, fully connected layers and normalization layers.

Basically, the image classification process involves two steps, namely training and testing. The number of output layers in the CNN depends on the number of classes that are to be labeled and classified. In CNN, convolution operation performs a vital role. Convolution puts the input images through a set of convolutional filters, each of which activates certain features from the images. The convolution layer and pooling layer help in the extraction of features from patches of image. The convolutional layer computes the output feature map by the following equation

$$Z^k = f(\sum_{i=1}^{q} W_k * x^k) \quad (1)$$

where x denotes input image , Z^k is the K^{th} output feature map , W_k is the weight of K^{th} feature map, * is a two dimensional convolutional operator and f(.) represents nonlinear activation function.

Pooling simplifies the output by performing nonlinear downsampling on the input data. Nonlinear downsampling is done to improve the extraction of features. It progressively reduces the spatial size of the representation, thereby reducing the feature map dimensionality and computational complexity of the network, which in turn can improve the performance.

Max pooling is performed which generalizes the results from the convolutional filter, making the detection offeature invariant to scale or orientation changes. Thus, the dimensions of the feature map reduces from (m,n) to (m/k,n/k). k needs to be chosen in consistence with the dimensions of the input feature map. In this, the input image is down sampled by a factor of 2 along each direction. This value is chosen to have minimum pixel loss and get a precise region where the features are located, thereby reducing the complexity of the model without reducing its performance.

Rectified linear unit (ReLU) allows for faster and more effective training by mapping negative values to zero and maintaining positive values. These operations are repeated over tens or hundreds of layers, with each layer learning to detect different features. The convolution layer is parameterized by the number of filters, size of each filter and the activation function used. In the proposed architecture, 3 convolutional layer, 3 subsampling layer and 2 fully connected layer is used. The number of filters used is 32, the

size of each filter being 3*3, and the activation function is the rectifier function, which is used at fully connected layer to determine probabilistic confidence value of output.

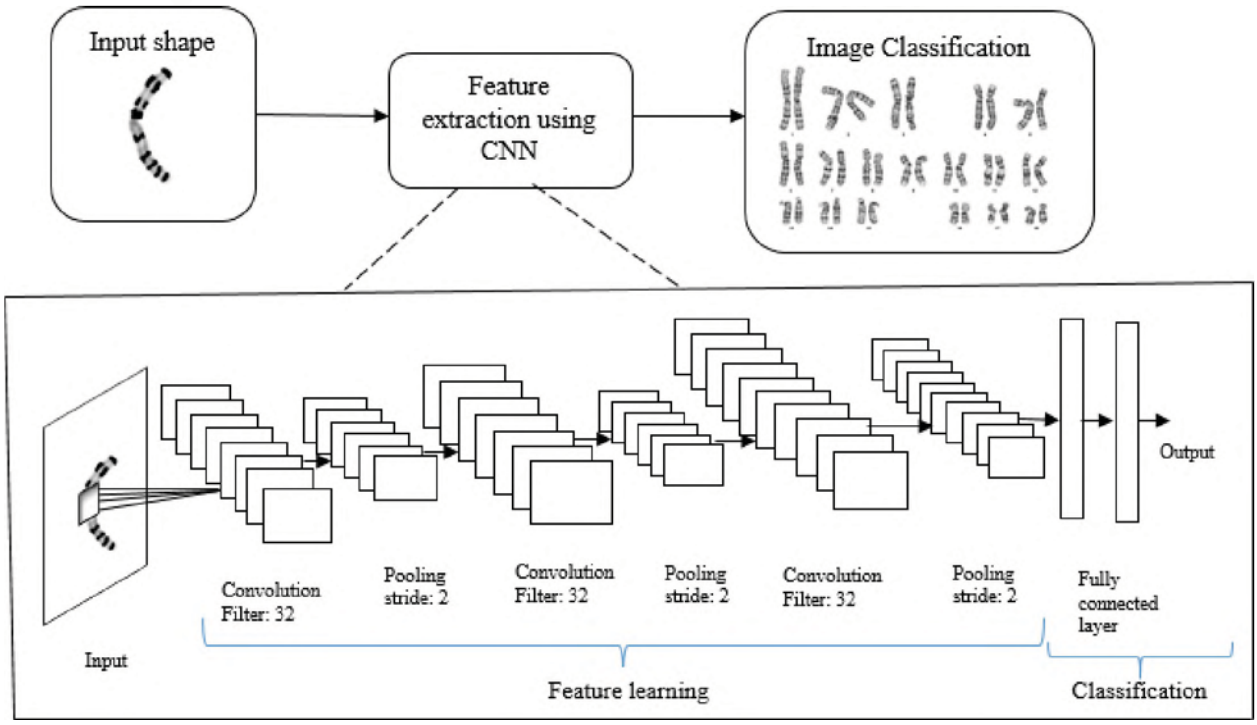

Figure 3. Block diagram of proposed work

The last stage of a convolutional neural network is a classifier, called as dense layer. It needs individual features i.e., it needs a feature vector to perform classification. In order to convert the output of convolutional part of the CNN into a 1D feature vector, flattening operation is done. It gets the output of pooled image pixels (2D array), flattens all its structure to create a one dimensional single feature vector to be used by the dense layer for the final classification. A fully connected layer connects the set of nodes got after the flattening step. Fully connected layer performs non-linear transformations of the extracted features and classifies the inputs. This process completes the building up of the convolution neural network model. Image classification with CNN works quite well when enough training data is provided.

Two major categories of image classification techniques include unsupervised (calculated by software) and supervised (human-guided) classification. Training images are labeled in a supervised way by an analyst, but the feature learning and classification are automatically done by software in an unsupervised way. While human visual image interpretation techniques rely on shape, size, pattern, tone, texture, shadows, and association, digital image interpretation relies mainly on color, i.e. on comparisons of digital numbers found in different bands in different parts of an image. In deep-learning networks, each layer of nodes trains on a distinct set of features based on the previous layer's output. The further advancement into the neural net, the more complex the features the nodes can recognize, since they aggregate and recombine features from the previous layer.

III. Results and Discussions

Diagnosis by deep learning are typically more objective and accurate. To test the architecture, chromosome images are collected and total number of chromosome images are randomly divided into groups for training, validation and test sets respectively. The training set consists of 175 images and the testing set consists of 83 images. Each chromosome image is assigned a label from the 24 categories. For all the experiments, the resolution of the image is set to 64*64.

Data augmentation is done to increase the number of data in the dataset. The network is tested on various datasets which in turn is tested for different number of epochs (iterations). Higher the learning rate, lesser number of epochs is required. Learning rate determines how quickly or slowly the update of weights have to takes place. For smaller values of learning rate, too many iterations are needed to converge to the best values. Typically, learning rates are assigned at random based on the user. All models were trained using convolutional neural networks. To regularize the network training, a sufficiently large number of epochs are provided while training each model. Models are trained for different values of epochs. By observing the validation results (i.e) loss and accuracy at each epoch, epoch can be varied to obtain the highest validation accuracy. This is implemented using keras with tensorflow as backend.

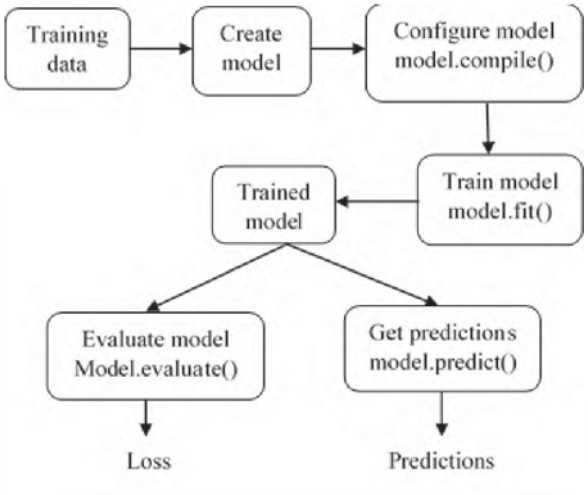

Figure 4. Workflow of the proposed work

After the model is created, compile it using an optimization algorithm. Additionally loss type is specified depending on the number of classes to be classified. In this proposed work, number of classes is 2, (x and y chromosome) and loss type is considered as binary. Accuracy is the metric used for analyzing while training the model.

The model is trained using fit () function by storing the results of the function. It can be used to plot the accuracy and loss function plots between training and validation to analyze the performance of the model. The model is evaluated and graph is plotted for loss and accuracy between training data and validation data. Probability value is obtained which determines the type of chromosome. In this case, if the probability score is less than 0.5, the predicted result is X else Y will be displayed.

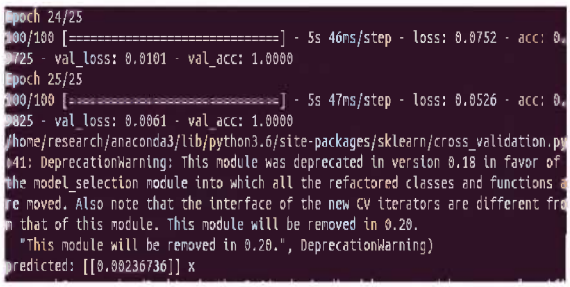

Figure 5. (a) output for X chromosome

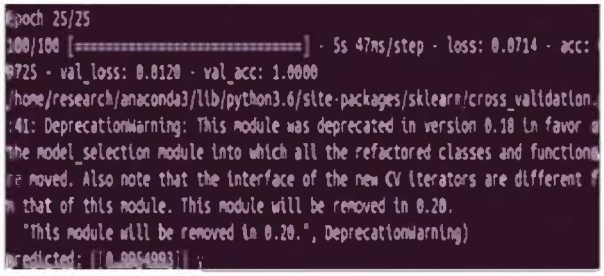

Figure 5. (b) output for Y chromosome

Fig. 5 gives the classification output for the test chromosome based on the probability score. From the Fig. 6 (b), it can be seen that the validation accuracy became slightly stable after 4-5 epochs and rarely increases at certain epochs. In the beginning, validation accuracy linearly increases with loss, then it does not increase much. The training accuracy is high and training loss is quite low. But the validation loss and accuracy are not better compared to training loss and accuracy, implying that the model is over fitting.

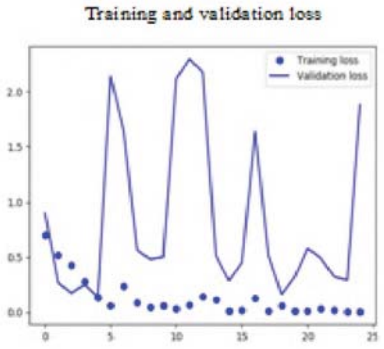

Figure 6(a). Plot between epoch and loss

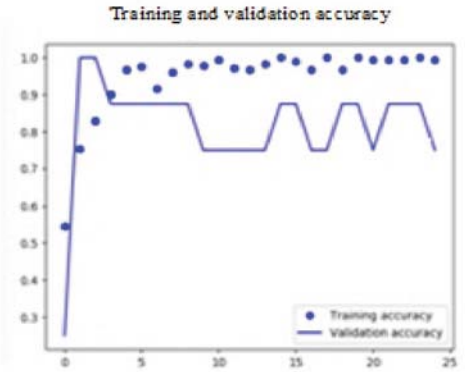

Figure 6(b). Plot between epoch and accuracy

To overcome this problem, dropout layer, a regularizing parameter is added to make the model perform better while keeping all the other layers unchanged. By adding the dropout layer in this architecture, the loss and accuracy are fairly consistent which is shown in Fig. 7(a) and 7(b).

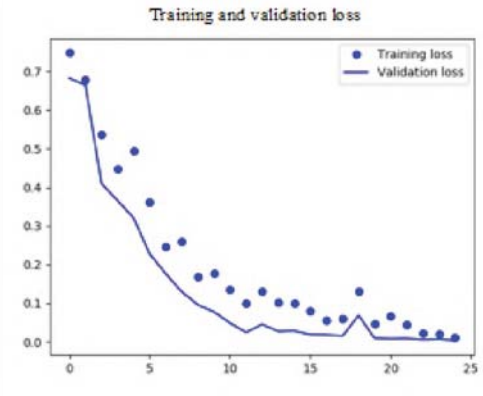

Figure 7(a). Plot between epoch and loss

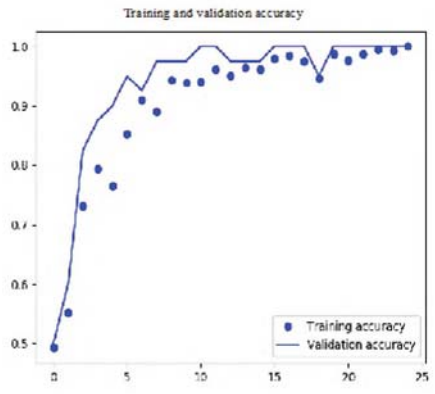

Figure 7(b). Plot between epoch and accuracy

Mostly, many classification algorithms work well when small amount of data are available. Accuracy of classifiers goes down when large dataset is taken for classification. But deep learning performs better even it comes for image classification with large amount of data. In the proposed work, the chromosome prediction gives favorable results for sex chromosomes. Few preprocessing steps like image straightening is adopted to improve the performance. In future work, deep learning convolutional neural network can be employed to classify all 22 pairs of chromosomes.

IV. CONCLUSION

In this proposed work, classification of chromosomes is done using convolutional neural networks. The input considered for CNN is the individual metaphase chromosomes. Rectified linear unit (ReLU) is the activation function used for extracting the features in CNN. The extracted feature helps in the classification of chromosomes. The proposed work gives an accuracy of 100% for sex chromosmes but not as favourable for autosomes as the chromosomes do not have a proper size and structure. In the future work, a better deep learning algorithm can be employed to extract better features and the network will be trained and tested with large number of datasets for improved performance and accuracy.

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REFERENCES

[1] Dan Cireşan, Ueli Meier, Jürgen Schmidhuber, Multi-column Deep Neural Networks for Image Classification, CVPR '12 Proceedings of the 2012 IEEE Conference on Computer Vision and Pattern Recognition (CVPR), 3642-3649, 2012

[2] Swati, Gaurav Gupta, Mohit Yadav, Monika Sharma, Lovekesh Vig, Siamese Networks For Chromosome Classification, 2017 IEEE conference on Computer Vision Workshops (ICCVW), 2017

[3] Altan, Novruz Allahverdi, Yakup Kutlu Diagnosis of Coronary Artery Disease Using Deep Belief Networks, European journal of engineering and natural sciences, Volume 2, Issue 1, pp. 29-36, 2017

[4] Wenzhong Yan, Lei Bai, Algorithms for Chromosome Classification ,*Engineering*, **5**, 400-403, 2013

[5] Xingwei Wang, Bin Zheng, Shibo Li, John J. Mulvihill, Marc C. Wood, and Hong Liu, Automated Classification of Metaphase Chromosomes: Optimization of an Adaptive Computerized Scheme, Biomed Inform. 42(1): 22–31, 2009.

[6] D. Lu & Q. Weng ,A survey of image classification methods and techniques for improving classification performance, International Journal of Remote Sensing, 28, 5, 823-870, 2007

[7] Boaz Lerner, Toward A Completely Automatic Neural Network Based Human Chromosome Analysis, IEEE Trans Syst 28(4):544–552, 1998

[8] M. Zardoshti-Kermani and A. Afshordi, Classification of Chromosomes Using Higher-Orde Neural Networks, Proceedings of ICNN'95- International Conference on Neural Networks, IEEE, 1995.

[9] Sandeep Kumar, Zeeshan Khan, Anurag Jain, A Review of Content Based Image Classification using Machine Learning Approach, International Journal of Advanced Computer Research, Volume-2 Number-3 Issue-5, 2012

[10] Walter P. Sweeney Jr., Mohamad T. Musavi,' and John N. Guidi, Classification of Chromosomes Using a Probabilistic Neural Network, Journal of the international society for advancement of cytometry, Volume 16, issue1,Pages 17–24,1994

[11] Maximo E. Drets, Margery W. Shaw, "Specific banding patterns of human chromosomes (heterochromatin/ Giemsa stain/ chromosome bands)", 1971, Proc. Nat. Acad. Sci. USA, Vol. 68, No. 9, pp. 2073-2077

[12] J.H. Tjio, A. Levan, The chromosome number in man, Hereditas 42 (1956) 1–6.

[13] William James Kenneth Cummino, Noi MaCumming Nevin, A system for automated chromosome analysis, Humangenetik 7 (1969) 349–350.

[14] J. Graham, J. Piper, Automatic karyotype analysis, Humana, Totowa, NJ, 1994.

[15] S. B. Kotsiantis, Supervised Machine Learning: A Review of Classification Techniques, Informatica 31 (2007) 249-268

[16] Chrysa Daiou, Alexandros Lambropoulos, Christoforos Markou, Christos Maramis, Anastasios Delopoulos, Automatic Chromosome Classification using Support Vector Machines

[17] T Arora, R Dhir, A review of metaphase chromosome image selection techniques for automatic karyotype generation Medical & biological engineering & computing, Springer, 2016

[18] F Abid, L Hamami, A survey of neural networks based automated systems for human chromosome classification, Artificial Intelligence Review, Springer, 2018.