Journal of Universal Computer Science, vol. 29, no. 5 (2023), 432-445
submitted: 13/10/2022, accepted: 10/1/2023, appeared: 28/5/2023

Automated Classification of Cell Level of HEp-2 Microscopic Images Using Deep Convolutional Neural Networks-Based Diameter Distance Features

Mitchell Jensen
(Electrical Engineering and Robotics School, Queensland University of Technology, Australia
mitchell.jensen@connect.qut.edu.au)

Khamael Al-Dulaimi
(Department of Computer Science, College of Science, Al-Nahrain University, Jadriya, Baghdad, Iraq
Electrical Engineering and Robotics School, Queensland University of Technology, Australia
https://orcid.org/0000-0001-7248-7522, k.aldulaimi@connect.qut.edu.au)

Khairiyah Saeed Abduljabbar
(Department of Computer Science, College of Science, Al-Nahrain University, Jadriya, Baghdad, Iraq
https://orcid.org/0000-0003-1313-0667, khairiyah.s.aldabas@nahrainuniv.edu.iq)

Jasmine Banks
(Electrical Engineering and Robotics School, Queensland University of Technology, Australia
https://orcid.org/0000-0003-1507-9682, j.banks@qut.edu.au)

Abstract: To identify autoimmune diseases in humans, analysis of HEp-2 staining patterns at cell level is the gold standard for clinical practice research communities. An automated procedure is a complicated task due to variations in cell densities, sizes, shapes and patterns, overfitting of features, large-scale data volume, stained cells and poor quality of images. Several machine learning methods that analyse and classify HEp-2 cell microscope images currently exist. However, accuracy is still not at the level required for medical applications and computer aided diagnosis due to those challenges. The purpose of this work to automate classification procedure of HEp-2 stained cells from microscopic images and improve the accuracy of computer aided diagnosis. This work proposes Deep Convolutional Neural Networks (DCNNs) technique to classify HEp-2 cell patterns at cell level into six classes based on employing the level-set method via edge detection technique to segment HEp-2 cell shape. The DCNNs are designed to identify cell-shape and fundamental distance features related with HEp-2 cell types. This paper is investigated the effectiveness of our proposed method over benchmarked dataset. The result shows that the proposed method is highly superior comparing with other methods in benchmarked dataset and state-of-the-art methods. The result demonstrates that the proposed method has an excellent adaptability across variations in cell densities, sizes, shapes and patterns, overfitting features, large-scale data volume, and stained cells under different lab environments. The accurate classification of HEp-2 staining pattern at cell level helps increasing the accuracy of computer aided diagnosis for diagnosis process in the future.

Keywords: Classification, Segmentation, Deep Convontional Neural Network, Computer Aided Diagnoses, HEp-2 cell level, Diameter distance feature
Categories: I.2, I.4, I.5, J.6
DOI: 10.3897/jucs.96293

1 Introduction

Recognition and analysis of Human Epithelial type 2 (HEp-2) at cell level in Indirect Immuno-Fluorescence (IIF) microscopy is commonly adopted for identifying the presence of autoimmune diseases in Computer-Aided Diagnosis (CAD). This process requires highly trained clinicians to accurately process and interpret the results. For example, if the occurrence of mitotic cells in the microscope image is determined by the technician to be high, the presence of autoimmune disease is possible and the cell image must be further scrutinised [Hobson u. a., 2016]. The presence of Anti-Nuclear Antibodies (ANA) indicates autoimmune disease in the subject and this presence is detectable by examining the distinct patterns that are produced by the antibodies during cell staining. Thus, practice clinical practitioners must have a deep understanding of HEp-2 staining at cell level morphology for accurate diagnosis. Currently, some techniques exists that can assist the experts in the process of cell classification; however, there is still much research to be done [Buchner u. a., 2014]. Manual classification of HEp-2 staining at cell level is a laborious process in which the final result is subject to the interpretation of pathologists. This interpretation could vary with pathologists' experience and with the visual complexity of the IIF microscope image results because the staining patterns have many types: "homogeneous, speckled, nucleolar, centromere, nuclear membrane and golgi", as shown in Figure-1, that have different shape, size and pattern. In a competitions hosted by ICPR 2014 and 2016, a study of automatic methods for HEp-2 staining patterns at cell level classification had been conducted and evaluated against manual classification by two scientists. In some cases a third scientist was needed to provide a manual opinion where the two scientists disagreed on the type of cell [Hobson u. a., 2016] due to different staining pattern,intensity level size, and shape, overlapped cell and large-scale data volume. In addition to the risk of mis-classification of the manual process, the manual procedure is time-consuming and costly [Al-Dulaimi u. a., 2020a]. Thus, it is important to be able to design a CAD system which can address these issues by giving the correct medical diagnosis, as well as decreasing the cost and time needed for testing. Achieving this can increase testing throughput and assist in training of technicians for diagnoses.

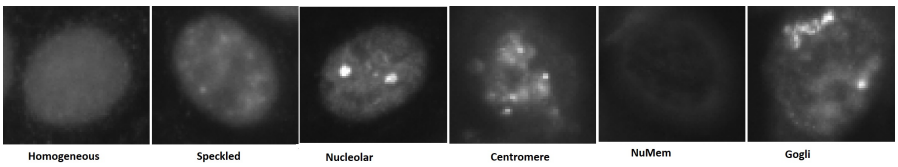

Figure 1: Types of HEp-2 staining pattern at cell levels, including nuclear membrane, nucleolar, homogeneous, centromere , golgi and speckled.

This work aims to develop automated segmentation and classification methods to address the problems of HEp-2 cell detection from microscopic images, especially, overfitting of features, stained cell images, different sizes and shapes of cell, overlapping of cells and large-scale data volume problems. In this paper, we propose Deep Convolutional Neural Networks (DCNNs) technique for cell classification at cell level based on cell shape. The level-set method via gradient of edge detection is employed to detect cell shape. The output of DCNN is then analyzed with hyperparameters in

Deep Neural Network to identify the combination features of diameter distance and cell shape that can be discriminated between different HEp-2 cell types, which is proposed for the first time. The contributions of this paper is to design a CAD system that it: (i) produces segmentation and classification methods with improved accuracy compared with the current state-of-the-art methods to permit comparison and benchmarking;(ii) uses segmentation and classification methods that are more adaptable to variation in intensity level, overlapping cells, overfitting of features, staining pattern and cell shape than the current methods; and (iii) can recognize six classes of Hep-2 cell "(homogeneous, speckled, nucleolar, centromere, nuclear membrane, and golgi)".

The organisation of paper follows as: related work is described in Section-2; the proposed method is presented in Section-3; the experimental analysis and comparison results are discussed in Section-4; and the Conclusion is presented in Section-5.

2 Literature Review

Advanced research have used different machine learning and Deep Learning (DL) techniques for classification of medical images as have done in [Sathish und Elango, 2019; Al-Dulaimi u. a., 2018; Agaian u. a., 2018; Al-Dulaimi u. a., 2016b; Makki und Al-Dulaimi, 2022; Bollipo und KV, 2021; Al-Dulaimi u. a., 2019a; Prakash u. a., 2022], and classification of biomedical images, specifically classification of HEp-2 cell in [Li und Shen, 2019], Multi-context unsupervised domain adaption for HEp-2 cell classification in[Zhao u. a., 2022], Joint segmentation and classification of HEp-2 cell [Xie u. a., 2022], classification of HEp-2 cell using adaptive MLP Al-Dulaimi u. a. [2023] and HEp-2 Cell Classification Using an Ensemble of CNNs [Kasani u. a., 2021]. CNNs are becoming more common in HEp-2 cell classification, due to their ability to be highly adaptable to new data sets. This includes data sets of different colour-schemes, image resolution, noise/distortion and other differentiating factors. This is crucial to the implementation of a real-world cell classification system, as different labs may use different equipment and, therefore, will produce dissimilar images. [Prasath u. a., 2016] classified HEp-2 cells at both cell and specimen level using a variety of different classifiers (Support Vector Machines (SVMs), Random Forest (RF), and K-Nearest Neighbours (K-NNs)). Maximum MCA for cell-level classification was achieved using a K-NN classifier (93.16%). That study used the same dataset used in our study (the 13,596 training images from the ICPR 2014 Task 1 dataset). A split of 80% was given to the training dataset and 20% was devoted to testing. Similarly, [Li u. a., 2016] also noted that these rarer cell types were difficult to classify, as the number of cell images were significantly fewer than more common types in the data set, but that the histogram approach to CNN classification employed in their study provided a more robust approach. In [Jorgensen u. a., 2021], DCNNs was proposed for classification of HEp-2 HEp-2 specimen staining cells based on cell shape and adapted to consider overfitting using Task-2 data set. It achieved good results. " The official International Conference on Pattern Recognition (ICPR) contest in 2014", with 13 participating contestants, was documented by [Hobson u. a., 2016]. Two tasks were presented, namely, cell and specimen level classification. The methods discussed by [Codrescu, 2014] and [Gao u. a., 2016] were featured and have already been discussed in this paper. All other methods for cell-level classification in the study were presented using SVM algorithms. The greatest accuracy of 84.63% was recorded by [Qi u. a., 2016] using a linear SVM and the next best accuracy of 84.24% was achieved by [Manivannan u. a., 2014a,b], also using a linear SVM classifier. It was found that

accuracy of classification using the method by Manivannan et al. increased by 3% to 87.1% with data rotation. An observation was made that the CNN-based method by [Gao u. a., 2016] scored only 1.5% lower than the best performing method and that future research should be in the direction of deep learning. [Qi u. a., 2016] mentioned that the homogeneous and speckled types were often misclassified as each other, possibly due to similar texture and shape structures. [Nigam u. a., 2015] proposed a classification network that features two separate classification system, one for positive images and one for intermediate. Images were divided into these two sets through the use of a preliminary classifier trained to detect intermediate or positive images. This was based on the hypothesis that the information presented in positive and intermediate cell images is distinctly different within each class.

Classification accuracy can be influenced by segmentation and feature extraction process. Particular combinations of these classification and segmentation algorithms are capable of achieving high accuracy. Popular HEp-2 cell classification methods, discussed previously, include machine learning and DL algorithms, such as SVMs, RF, and K-NNs, as well as DL methods, such as (CNNs) and Artificial Neural Networks (ANN), have been used to classify HEp-2 staining cell based on different features. However, the accuracy of these methods still requires improving because none of these methods have been dealt with all HEp-2 cell classification problems at same time. This work creates a classification system for cell-level HEp-2 images using a DCNN based on the diameter distance of segmented of cell shape. This feature has been used for the first time.

3 Proposed DCNNs classification method

The proposed DCNNs classification method of segmented HEp-2 staining patterns at cell level is shown in Figure-2 Image enhancement is used in adjusting the contrast of

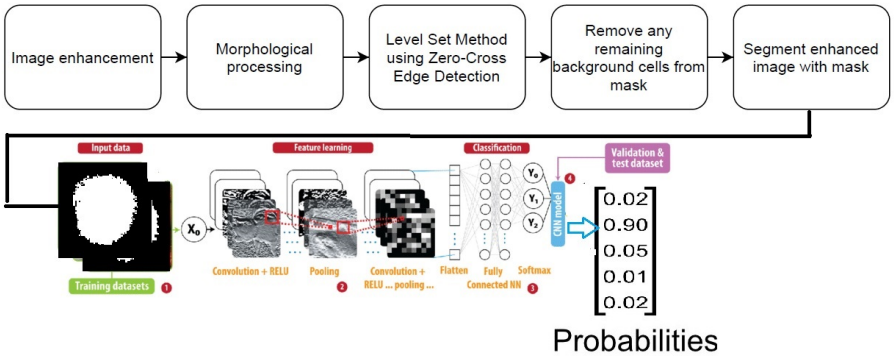

Figure 2: The proposed DCNN classification procedure of segmented HEp-2 staining patterns.

each cell staining pattern image by applying contrast stretching to the grayscale images and then morphological operators is used to initialise the shape of cell.

3.1 Segmentation of HEp-2 level cell

In this study we employed level-set force in normal direction base edge detection in previous works [Al-Dulaimi u. a., 2020b] [Al-Dulaimi u. a., 2016a] [Al-Dulaimi u. a., 2016b] to segment and separate cells. The proposed segmentation method is adapted by using Zero crossing edge detection method to address issues of overlapping cells and the variety of shapes in the database and to separate cells from cell clusters.

3.2 HEp-2 cell level Classification using DCNNs

CNNs are a class of deep learning networks that apply convolutional filtering techniques used in image processing to recognise an object in an input image. "DCNNs are commonly used to identify patterns in images and video. DCNNs considerably reduce the number of neurons required to process an image, comparing to traditional feed forward neural networks". The network can employ a "convolution" mathematical operation instead of using "matrix multiplication". The DCNN architecture can typically consist of 4 layers types: convolution, pooling, activation, and fully connected [Venkatesan und Li, 2017; Aversano u. a., 2022]. The input layer accepts cell shape as an image input, and the output layer gives a classification for the input image. The layers between the input and output are where the decisions are made regarding which features best represent the image content and classification process. A convolution—can take a set of weights and multiply them with inputs from the neural network.

The DCCNs in Figure-3 accepts an image input and applies a convolution filter by multiplying a set of of weights with inputs from the neural network. Convolutional layers have a pre-defined kernel which is used to filter the input. The kernel is a feature detector, which can be thought as 2D arrays of weights. Dot product is a mathematical process and performing during the convolution. Each filter can multiply the weight with different values of input. Then, we calculate the total inputs to provide a unique value for each filter position. Then, the procedure passes the convolution maps through a nonlinear activation layer called "Rectified Linear Unit (ReLU)", that can make negative numbers of the filtered images equal zeros [Jorgensen u. a., 2021].

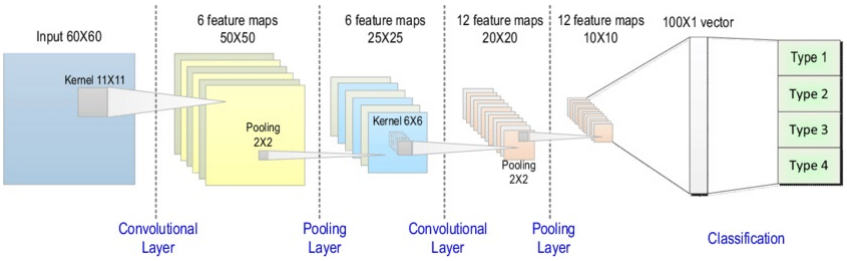

Figure 3: An example of a architecture of CNN, including a feature extraction and classification into many types [Wang u. a., 2017].

The pooling layer will reduce the size of the image. The pooling layer has a pre-defined window size, such as 2×2 and 3×3, and this layer will divide up the image into windows of this size and reduce each window into a single pixel. It does this by substituting the entire window with either the maximum value (max pooling), or the

average value (average pooling) contained within each window in the image. We reduce the number of calculations and parameters in the network by using Pooling layers to control overfitting. The Softmax function has been applied at the end for giving the probability of a type of the image to the outputs of the fully connected layers, as shown Figure-4. .

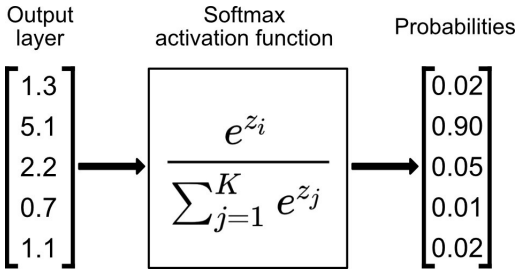

Figure 4: The Softmax function and an example of how the function transforms the weights from the output layer into probabilities that sum to 1.

The type of hyperparameters that can be selected depend on the optimisation solver being utilised by the DCNN, but three important hyperparameters are:batch size, number of epochs, and the learning rate. The latter determines how quickly the network updates its internal parameters during training. The number of epochs represents the number of times the DCNN is trained on the entire input dataset. The batch size (or mini-batch size) defines the number of training samples to be used for training within a single epoch before updating parameters.

4 Experiment and Results

4.1 Description of Dataset

The dataset is benchmarked dataset and was collected at the Sullivan Nicolaides pathology (SNP) laboratory. The total image of this benchmarked dataset is 68,429 images. There were six patterns of cell staining in the dataset: “speckled (Sp), centromere (Cn), homogeneous (Hm), nucleolar (Nu), nuclear membrane (Nm), and Golgi (Gl)”, as shown in Figure-1. In the cell level classification of staining patterns, there are a total of 13,596 categorised cell images divided into six classes (with samples), as shown in Table-1.

4.2 Proposed Method Implementation

The proposed method is implemented using MATLAB 2021b. The steps of implementation are as follows:

1. Image enhancement and segmentation is applied to the microscopic images to assist the level-set method based edge detection to create the most accurate mask possible and to prepare the images for classification. The image enhancement is achieved

Cell name	Number of cell
homogeneous (Hm)	2.494
speckled (Sp)	2,831
nucleolar(Nu)	2,598
centromere(Cn)	2,741
Golgi(Gl)	724
nuclear membrane	2,208

Table 1: Number of each cell in the task-1 dataset

by adjusting the contrast of each cell staining pattern image and applying contrast stretching to the greyscale images. This stretched the contrast values of each image to occupy the entire 8-bit contrast spectrum. Zero-cross edge detection is then used on the morphological result to identify the initial edges in the cell images using the edge function. The algorithm for the level-set method in the normal direction, from previous work of [Al-Dulaimi u. a., 2016b], is adapted with edge detection to develop a contour to address the segmentation of HEp-2 staining patterns at cell level problems. Cell segmentation is achieved using the level-set method based edge detection. This is the first process to implement the classification algorithm. The dataset of cell images and ground truths are received to the entire dataset. The result is shown in Figure-5.

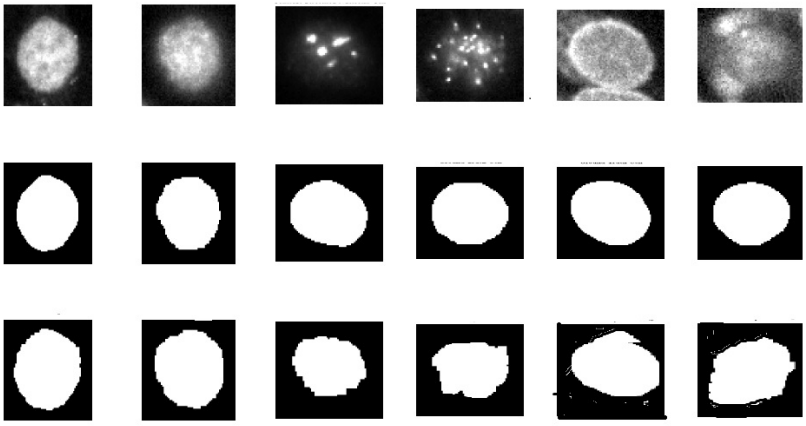

Figure 5: Contrast stretched cell images (Row-1), in addition to their ground truth images (Row-2) and the level set equivalent masks (Row-3). Each cell was randomly selected for plotting.

2. The segmented cell images are used to train and classify HEp-2 cell images using a DCNN. A model is used to rained a network and returned the trained DCNN with the

lowest validation loss at the end of training, instead of returning the trained DCNN at the last iteration . This feature is implemented in for each test. The diameter of a cell can have an identical area to identify the cell. The work of the NN model is to analyze HEp-2 cell distance and cell shape features. After separation by minimum distance, the six measures of cell shape are scaled and normalized. Then, these measures are used R statistical software, as illustrated in Figure-6 to input nodes into three net models (linear output, simple, and tuned).

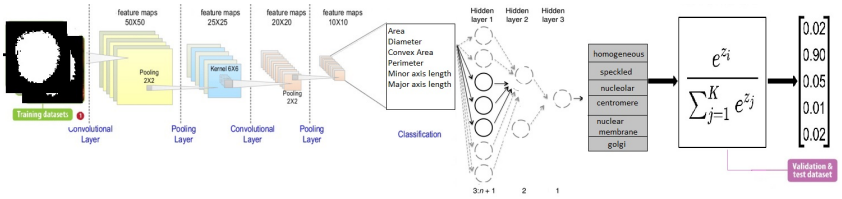

Figure 6: The proposed classification method procedure of segmented HEp-2 staining patterns.

From the DCNN output, we have obtained relative diameters distances and features of HEp-2 cell shape. Six independent measures of 2-D shape are used, that include regular perimeters, regular areas, convex area major and minor axis lengths, and diameter. R statistical software are used and analyzed these data to determine which is the best discriminated among the HEp-2 cell types. Images are organised into folders, where the folder named matched the cell label. The dataset of 13,596 images is divided into 75% for training and validation, and 25% for testing. The training and validation set is further divided into 75% for training and 25% for validation. This split is performed randomly each time a network is trained, resulting in 4077 images being used for testing, 6662 images for training and 1019 used for validation. The network comes pretrained for 1000 classes. The hidden layers of the network consists of multiple convolution, pooling, ReLU, fully connected and drop-out layers. The final 3 layers of the network are trained specific to a set of existing classes. These layers are a fully-connected layer of 1000 nodes, a Softmax layer of 1000 nodes and an output layer of 1000 nodes. These layers are removed from the network and replaced with a new fully connected layer, Softmax layer and output layer, each of 6 nodes in length.

3. Augmentations is applied to the training set. This augmentations are applied to the training set on the fly during training instead of creating physical files. The only augmentation specified was rotation between 0 and 360 degrees, and the augmenter applies rotation of a random number between these two values at each epoch. A new random number is picked at each epoch, so there is high rotation variance using this method.

4. Training is used Adaptive Moment Estimation (ADAM) with a mini-batch size of 32. Training is conducted for a total of 80 epochs, with an initial learning rate of 1×10^{-4}.

5. Classification tests were conducted on a small laptop with an Intel Core i7-8565U CPU and an integrated Intel GPU. Training times were found to be unsatisfactorily

slow, so training was moved to a 64-bit Windows 10 machine with a 3.8 GHz AMD Ryzen 5 3600X CPU, an NVIDIA GeForce GTX 1660 Super GPU and 16 GB RAM. The GPU was used in both training and classification.

4.3 Results and Discussion

4.3.1 Results of Proposed Method

The confusion matrix of classification of segmented HEp-2 cell is shown in Figure-7. The confusion matrix is calculated using True positive, True negative, False negative and False positive parameters for each class [Hobson u. a., 2016; Al-Dulaimi u. a., 2019b]. The highest accuracy value is achieved on the centromere, nuclear membrane and nucleolar in the first iteration, and centromere, nuclear membrane and speckle in the second iteration. Homogeneous cells are commonly classified as speckled cells and, similarly, speckled cells are commonly misclassified as homogeneous. However, the result has shown that homogeneous cells are more often misclassified than the speckled cells, with 59 and 96 homogeneous classification as speckled, and 41 and 24 speckled classification as homogeneous. The trained network is then used to classify the test dataset, and the total overall accuracy and Mean Class Accuracy (MCA) are calculated for the testing and validation sets, and confusion matrices are produced to show the total number of classifications and misclassifications for each class of cell. The test result is based on the entire image dataset to test the accuracy of the combination of level-set segmentation and deep CNN classification systems. The average accuracy of the proposed method is 95.24%.

4.3.2 Comparison with Other Methods and Discussion

Our classification system achieves a high level of accuracy, comparable with many of the current high performing methods for HEp-2 cell classification. The confusion matrices of all methods listed in [Hobson u. a., 2016] have shown that all methods achieved high accuracy with three classes nucleolar, nuclear membrane and the centromere. The latter class results are the most accurate over all the methods in Task-1. They have also shown that a small number of golgi class in data set had a negative impact over the MCA values of some methods listed in Table-2, such as Paci [Nanni u. a., 2016], [Sarrafzadeh u. a., 2016], [Han u. a., 2016] and Roberts [Lovell u. a., 2014], where the accuracy of this pattern is lower than 50%. This is because the cells belonging to the golgi class are typically overlapped with the nucleolar and nuclear membrane classes, while the errors regarding the speckled cells are typically due to overlapped “with the centromere and homogeneous classes. We also note that homogeneous samples are often misclassified as nuclear membrane or speckled. This common behaviour is due mainly to the high similarity, both in terms of shape and texture, among such classes”. By contrast, our proposed method is achieved high accuracy over centromere, nucleolar, homogeneous and nuclear membrane classes at accuracies of 97.2%, 96.2% 94.2%, and 98.2%, respectively. Golgi class is achieved better accuracy than other methods in benchmarked dataset due to the use of proposed segmentation method which has shown the ability to split according to the shape of the class. Although deep learning methods have not been widely used over benchmarked dataset, it is worth mentioning that the methods of [Codrescu, 2014] and [Gao u. a., 2014] used CNNs. The highest accuracy has achieved by [Gao u. a., 2014] with 83.23% respectively. Other methods in this study have used linear Support Vector Machine (SVM), such as [Manivannan

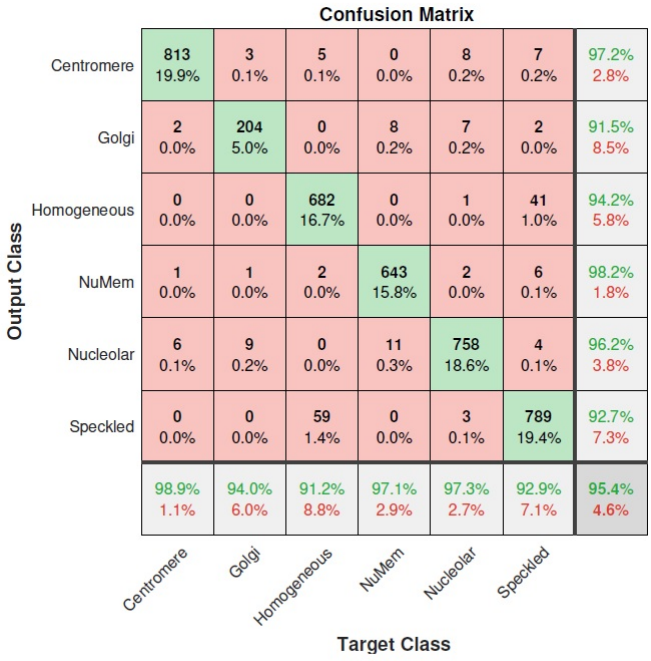

Figure 7: Confusion matrices for classification of segmented cells with contrast stretching performed.

u. a., 2014a]; [Theodorakopoulos u. a., 2014]; [Gragnaniello u. a., 2016]; and [Qi u. a., 2016] and produced MCA values between 83%-84%. In addition, classification methods described in this study were influenced by segmentation and feature extraction methods which negatively affected the MCA values of some methods [Lovell u. a., 2014];[Han u. a., 2016]; [Nanni u. a., 2016]; and [Sarrafzadeh u. a., 2016].

5 Conclusion and Future Work

This work used DCNNs for segmentation and classification of cell level of HEp-2 staining images. The DCNNs are designed to used diameter distance feature of segmented cell shape to produce classification method with improved accuracy over current methods under various of conditions,including variations in cell sizes, shapes and patterns, overfitting of features, stained cells and poor quality of images. We produced a classification method which achieved higher mean class accuracy than the current methods in the literature, specifically ICPR-2014 and ICPR-2016. The results of the research have shown that cell shape segmentation significantly affects the accuracy of classification. A DCNNs and a level set-based segmentation algorithm have proved to be successful in achieving performance comparable to that found in the state-of-the-arts methods. However, some cells are not segmented well due to highly stained images. Future works may consider focusing on using MASK R-CNN deep learning techniques to segment and classify these

References	Classifier	Training	Testing
[Codrescu, 2014]	QR-FIRMLP	98.94	74.60
[Gao u. a., 2014]	CNN	99.95	83.23
[Manivannan u. a., 2014a]	Linear SVM & Platt rescaling	98.04	84.24
[Lovell u. a., 2014]	Multi-class boosting algorithm	100 .00	81 .55
[Lovell u. a., 2014]	Linear SVM	72.99	67 .00
[Theodorakopoulos u. a., 2014]	Linear SVM	93.82	83.33
[Ensafi u. a., 2016]	Linear SVM	98 .07	80 .82
[Gragnaniello u. a., 2016]	Linear SVM	95 .47	83 .64
[Han u. a., 2016]	Linear SVM	94 .68	64 .30
[Nanni u. a., 2016]	SVM (one-vs-all)	100.00	79.85
[Ponomarev und Kazanov, 2016]	Linear SVM	95.85	75.46
[Qi u. a., 2016]	Linear SVM	99.91	84.63
[Sarrafzadeh u. a., 2016]	Gaussian mixture model	88.59	73.33
[Cascio u. a., 2016]	SVM	90.25	80.12
[Vununu u. a., 2020]	Unsupervised Deep Learning	98.74	90.05
Proposed method	**Deep CNN**	**99.09**	**95.45**

Table 2: Comparing proposed method with state-of-the-art methods using the task-1 dataset

images employing improved feature extraction. This may further improve the accuracy of HEp-2 cell image classification.
9pt

References

[Agaian u. a. 2018] Agaian, Sos ; Madhukar, Monica ; Chronopoulos, Anthony T.: A new acute leukaemia-automated classification system. In: *Computer Methods in Biomechanics and Biomedical Engineering: Imaging & Visualization* 6 (2018), Nr. 3, S. 303–314

[Al-Dulaimi u. a. 2019a] Al-Dulaimi, Khamael ; Al-Sabaawi, Aiman ; Resen, Rajaa D. ; Stephan, Jane J. ; Zwayen, Amani: Using adapted JSEG algorithm with Fuzzy C Mean for segmentation and counting of white blood cell and nucleus images. In: *6th IEEE Asia-Pacific Conference on Computer Science and Data Engineering (CSDE 2019)* Bd. 2019 10.1109/CSDE48274.2019.9162402 (Veranst.), 2019, S. 1–7

[Al-Dulaimi u. a. 2023] Al-Dulaimi, Khamael ; Banks, Jasmine ; Al-Sabaawi, Aiman ; Nguyen, Kien ; Chandran, Vinod ; Tomeo-Reyes, Inmaculada: Classification of HEp-2 Staining Pattern Images Using Adapted Multilayer Perceptron Neural Network-Based Intra-Class Variation of Cell Shape. In: *Sensors* 23 (2023), Nr. 4, S. 2195

[Al-Dulaimi u. a. 2020a] Al-Dulaimi, Khamael ; Banks, Jasmine ; Nguyen, Kien ; Al-Sabaawi, Aiman ; Tomeo-Reyes, Inmaculada ; Chandran, Vinod: Segmentation of White Blood Cell, Nucleus and Cytoplasm in Digital Haematology Microscope Images: A Review-Challenges, Current and Future Potential Techniques. In: *IEEE Reviews in Biomedical Engineering (1937-3333)* 14 (2020), S. 290–306

[Al-Dulaimi u. a. 2016a] Al-Dulaimi, Khamael ; Banks, Jasmine ; Tomeo-Reyes, Inmaculada ; Chandran, Vinod: Automatic segmentation of HEp-2 cell Fluorescence microscope images using level set method via geometric active contours. In: *23rd International Conference on Pattern Recognition (ICPR)* IEEE (Veranst.), 2016, S. 81–83

[Al-Dulaimi u. a. 2018] Al-Dulaimi, Khamael ; Chandran, Vinod ; Banks, Jasmine ; Tomeo-Reyes, Inmaculada ; Nguyen, Kien: Classification of white blood cells using bispectral invariant features of nuclei shape. In: *International Conference on Digital Image Computing: Techniques and Applications (DICTA)*, 2018, S. 19–26

[Al-Dulaimi u. a. 2019b] Al-Dulaimi, Khamael ; Chandran, Vinod ; Nguyen, Kien ; Banks, Jasmine ; Tomeo-Reyes, Inmaculada: Benchmarking HEp-2 specimen cells classification using linear discriminant analysis on higher order spectra features of cell shape. In: *Pattern Recognition Letters* 125 (2019), S. 534–541

[Al-Dulaimi u. a. 2016b] Al-Dulaimi, Khamael ; Tomeo-Reyes, Inmaculada ; Banks, Jasmine ; Chandran, Vinod: White blood cell nuclei segmentation using level set methods and geometric active contours. In: *2016 International Conference on Digital Image Computing: Techniques and Applications (DICTA)* IEEE (Veranst.), 2016, S. 1–7

[Al-Dulaimi u. a. 2020b] Al-Dulaimi, Khamael ; Tomeo-Reyes, Inmaculada ; Banks, Jasmine ; Chandran, Vinod: Evaluation and benchmarking of level set-based three forces via geometric active contours for segmentation of white blood cell nuclei shape. In: *Computers in Biology and Medicine* 116 (2020), S. 103568

[Aversano u. a. 2022] Aversano, Lerina ; Bernardi, Mario L. ; Cimitile, Marta: Water stress classification using Convolutional Deep Neural Networks. In: *Journal Universal Computer Science* 28 (2022), Nr. 3, S. 311–328

[Bollipo und KV 2021] Bollipo, Lavanya M. ; KV, Kadambari: Fast and robust supervised machine learning approach for classification and prediction of Parkinson's disease onset. In: *Computer Methods in Biomechanics and Biomedical Engineering: Imaging & Visualization* 9 (2021), Nr. 6, S. 690–706

[Buchner u. a. 2014] Buchner, Carol ; Bryant, Cassandra ; Eslami, Anna ; Lakos, Gabriella: Anti-nuclear antibody screening using HEp-2 cells. In: *Journal of visualized experiments: JoVE* 2018 (2014), Nr. 88

[Cascio u. a. 2016] Cascio, Donato ; Taormina, Vincenzo ; Cipolla, Marco ; Bruno, Salvatore ; Fauci, Francesco ; Raso, Giuseppe: A multi-process system for HEp-2 cells classification based on SVM. In: *Pattern Recognition Letters* 82 (2016), S. 56–63

[Codrescu 2014] Codrescu, Cristinel: Quadratic recurrent finite impulse response MLP for indirect immunofluorescence image recognition. In: *2014 1st Workshop on Pattern Recognition Techniques for Indirect Immunofluorescence Images* IEEE (Veranst.), 2014, S. 49–52

[Ensafi u. a. 2016] Ensafi, Shahab ; Lu, Shijian ; Kassim, Ashraf A. ; Tan, Chew L.: Accurate HEp-2 cell classification based on sparse coding of superpixels. In: *Pattern Recognition Letters* 82 (2016), S. 64–71

[Gao u. a. 2016] Gao, Zhimin ; Wang, Lei ; Zhou, Luping ; Zhang, Jianjia: HEp-2 cell image classification with deep convolutional neural networks. In: *IEEE journal of biomedical and health informatics* 21 (2016), Nr. 2, S. 416–428

[Gao u. a. 2014] Gao, Zhimin ; Zhang, Jianjia ; Zhou, Luping ; Wang, Lei: Hep-2 cell image classification with convolutional neural networks. In: *2014 1st Workshop on Pattern Recognition Techniques for Indirect Immunofluorescence Images* IEEE (Veranst.), 2014, S. 24–28

[Gragnaniello u. a. 2016] Gragnaniello, Diego ; Sansone, Carlo ; Verdoliva, Luisa: Cell image classification by a scale and rotation invariant dense local descriptor. In: *Pattern Recognition Letters* 82 (2016), S. 72–78

[Han u. a. 2016] Han, Xian-Hua ; Chen, Yen-Wei ; Xu, Gang: Integration of spatial and orientation contexts in local ternary patterns for HEp-2 cell classification. In: *Pattern Recognition Letters* 82 (2016), S. 23–27

[Hobson u. a. 2016] Hobson, Peter ; Lovell, Brian C. ; Percannella, Gennaro ; Saggese, Alessia ; Vento, Mario ; Wiliem, Arnold: HEp-2 staining pattern recognition at cell and specimen levels: datasets, algorithms and results. In: *Pattern Recognition Letters* 82 (2016), S. 12–22

[Jorgensen u. a. 2021] Jorgensen, Brandon ; Al-Dulaimi, Khamael ; Banks, Jasmine: HEp-2 Specimen Cell Detection and Classification Using Very Deep Convolutional Neural Networks-Based Cell Shape. In: *International Conference on Digital Image Computing: Techniques and Applications (DICTA)* Bd. 2021 IEEE (Veranst.), 2021

[Kasani u. a. 2021] Kasani, Payam H. ; Kasani, Sara H. ; Kim, Han W. ; Cho, Kee H. ; Jang, Jae-Won ; Yun, Cheol-Heui: HEp-2 Cell Classification Using an Ensemble of Convolutional Neural Networks. In: *2021 International Conference on Information and Communication Technology Convergence (ICTC)* IEEE (Veranst.), 2021, S. 196–200

[Li u. a. 2016] Li, Hongwei ; Huang, Hao ; Zheng, Wei-Shi ; Xie, Xiaohua ; Zhang, Jianguo: HEp-2 specimen classification via deep CNNs and pattern histogram. In: *2016 23rd International Conference on Pattern Recognition (ICPR)* IEEE (Veranst.), 2016, S. 2145–2149

[Li und Shen 2019] Li, Yuexiang ; Shen, Linlin: HEp-Net: a smaller and better deep-learning network for HEp-2 cell classification. In: *Computer Methods in Biomechanics and Biomedical Engineering: Imaging & Visualization* 7 (2019), Nr. 3, S. 266–272

[Lovell u. a. 2014] Lovell, Brian C. ; Percannella, Gennaro ; Vento, Mario ; Wiliem, Arnold: Performance evaluation of indirect immunofluorescence image analysis systems. In: *International Conference on Pattern Recognition (ICPR)* IEEE (Veranst.), 2014

[Makki und Al-Dulaimi 2022] Makki, Teba M. ; Al-Dulaimi, Khamael: Evaluation of Blood Cell Segmentation Using Level Set-Based Force in Normal Direction via Edge Detection of Cell Shape. In: *9th IEEE Asia-Pacific Conference on Computer Science and Data Engineering (CSDE)* Bd. 2022, IEEE, 2022

[Manivannan u. a. 2014a] Manivannan, Siyamalan ; Li, Wenqi ; Akbar, Shazia ; Wang, Ruixuan ; Zhang, Jianguo ; McKenna, Stephen J.: Hep-2 cell classification using multi-resolution local patterns and ensemble svms. In: *2014 1st Workshop on Pattern Recognition Techniques for Indirect Immunofluorescence Images* IEEE (Veranst.), 2014, S. 37–40

[Manivannan u. a. 2014b] Manivannan, Siyamalan ; Li, Wenqi ; Akbar, Shazia ; Wang, Ruixuan ; Zhang, Jianguo ; McKenna, Stephen J.: Hep-2 specimen classification using multi-resolution local patterns and SVM. In: *2014 1st Workshop on Pattern Recognition Techniques for Indirect Immunofluorescence Images* IEEE (Veranst.), 2014, S. 41–44

[Nanni u. a. 2016] Nanni, Loris ; Lumini, Alessandra ; Santos, Florentino Luciano C. dos ; Paci, Michelangelo ; Hyttinen, Jari: Ensembles of dense and dense sampling descriptors for the HEp-2 cells classification problem. In: *Pattern Recognition Letters* 82 (2016), S. 28–35

[Nigam u. a. 2015] Nigam, Ishan ; Agrawal, Shreyasi ; Singh, Richa ; Vatsa, Mayank: Revisiting HEp-2 cell image classification. In: *IEEE Access* 3 (2015), S. 3102–3113

[Ponomarev und Kazanov 2016] Ponomarev, Gennady V. ; Kazanov, Marat D.: Classification of ANA HEp-2 slide images using morphological features of stained patterns. In: *Pattern Recognition Letters* 82 (2016), S. 79–84

[Prakash u. a. 2022] Prakash, R M. ; Kumari, R Shantha S. ; Valarmathi, K ; Ramalakshmi, K: Classification of brain tumours from MR images with an enhanced deep learning approach using densely connected convolutional network. In: *Computer Methods in Biomechanics and Biomedical Engineering: Imaging & Visualization* (2022), S. 1–12

[Prasath u. a. 2016] Prasath, VB S. ; Kassim, Yasmin M. ; Oraibi, Zakariya A. ; Guiriec, Jean-Baptiste ; Hafiane, Adel ; Seetharaman, Guna ; Palaniappan, Kannappan: HEp-2 cell classification and segmentation using motif texture patterns and spatial features with random forests. In: *2016 23rd International Conference on Pattern Recognition (ICPR)* IEEE (Veranst.), 2016, S. 90–95

[Qi u. a. 2016] Qi, Xianbiao ; Zhao, Guoying ; Chen, Jie ; Pietikäinen, Matti: Hep-2 cell classification: The role of gaussian scale space theory as a pre-processing approach. In: *Pattern Recognition Letters* 82 (2016), S. 36–43

[Sarrafzadeh u. a. 2016] Sarrafzadeh, Omid ; Rabbani, Hossein ; Dehnavi, Alireza M. ; Talebi, Ardeshir: Analyzing features by SWLDA for the classification of HEp-2 cell images using GMM. In: *Pattern Recognition Letters* 82 (2016), S. 44–55

[Sathish und Elango 2019] Sathish, P ; Elango, NM: Exponential cuckoo search algorithm to radial basis neural network for automatic classification in MRI images. In: *Computer Methods in Biomechanics and Biomedical Engineering: Imaging & Visualization* 7 (2019), Nr. 3, S. 273–285

[Theodorakopoulos u. a. 2014] Theodorakopoulos, Ilias ; Kastaniotis, Dimitris ; Economou, George ; Fotopoulos, Spiros: HEp-2 cells classification using morphological features and a bundle of local gradient descriptors. In: *2014 1st Workshop on Pattern Recognition Techniques for Indirect Immunofluorescence Images* IEEE (Veranst.), 2014, S. 33–36

[Venkatesan und Li 2017] Venkatesan, Ragav ; Li, Baoxin: *Convolutional neural networks in visual computing: a concise guide*. CRC Press, 2017

[Vununu u. a. 2020] Vununu, Caleb ; Lee, Suk-Hwan ; Kwon, Ki-Ryong: A Strictly Unsupervised Deep Learning Method for HEp-2 Cell Image Classification. In: *Sensors* 20 (2020), Nr. 9

[Wang u. a. 2017] Wang, Peng ; Yan, Ruqiang ; Gao, Robert X.: Virtualization and deep recognition for system fault classification. In: *Journal of Manufacturing Systems* 44 (2017), 04

[Xie u. a. 2022] Xie, Hai ; He, Yejun ; Xu, Dong ; Kuo, Jong Y. ; Lei, Haijun ; Lei, Baiying: Joint segmentation and classification task via adversarial network: Application to HEp-2 cell images. In: *Applied Soft Computing* 114 (2022), S. 108156

[Zhao u. a. 2022] Zhao, Haoran ; Ren, Tao ; Wang, Chen ; Yang, Xiaotao ; Wen, Yingyou: Multi-context unsupervised domain adaption for HEp-2 cell classification using maximum partial classifier discrepancy. In: *The Journal of Supercomputing* (2022), S. 1–19