Computerized Medical Imaging and Graphics xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Computerized Medical Imaging and Graphics

journal homepage: www.elsevier.com/locate/compmedimag

Accurate HEp-2 cell classification based on sparse bag of words coding

Shahab Ensafi[a,b,*], Shijian Lu[b], Ashraf A. Kassim[a], Chew Lim Tan[c]

[a] National University of Singapore, Department of Electrical and Computer Engineering, Singapore
[b] Agency for Science, Technology and Research, Institute for Infocomm Research, Singapore
[c] National University of Singapore, School of Computing, Singapore

ARTICLE INFO

Article history:
Received 1 December 2015
Received in revised form 4 August 2016
Accepted 5 August 2016

Keywords:
HEp-2 cell classification
Sparse coding
SIFT
SURF

ABSTRACT

Autoimmune diseases (AD) are the abnormal response of the immune system of the body to healthy tissues. ADs have generally been on the increase. Efficient computer aided diagnosis of ADs through classification of the human epithelial type 2 (HEp-2) cells become beneficial. These methods make lower diagnosis costs, faster response and better diagnosis repeatability. In this paper, we present an automated HEp-2 cell image classification technique that exploits the sparse coding of the visual features together with the Bag of Words model (SBoW). In particular, SURF (Speeded Up Robust Features) and SIFT (Scale-invariant feature transform) features are specially integrated to work in a complementary fashion. This method helps greatly improve the cell classification accuracy. Additionally, a hierarchical max-pooling method is proposed to aggregate the local sparse codes in different layers to provide final feature vector. Furthermore, various parameters of the dictionary learning including the dictionary size, the learning iteration number, and the pooling strategy is also investigated. Experiments conducted on publicly available datasets show that the proposed technique clearly outperforms state-of-the-art techniques in cell and specimen levels.

1. Introduction

Autoimmune diseases (AD) arise from abnormal immune responses of the body against normally present substances and tissues in the body where autoantibodies produced by the immune system are directed against one or more of the individual's own proteins (Cotsapas and Hafler, 2013). Early diagnosis of ADs that affect the neuromuscular system, hepatobiliary system, vasculitic syndromes, etc. plays an important role in the AD treatment. Antinuclear antibody (ANA), a type of autoantibody that binds to contents of the cell nucleus, is generally considered as a hallmark of ADs. A widely test used to detect and quantify ANAs, is the indirect immunofluorescence (IIF) test which utilizes human epithelial type-2 (HEp-2) tissue to culture cells as a substrate (Meroni and Schur, 2010). The HEp-2 tissue is used because of its large nucleus and better antigen expression, which makes the diagnosis easier and more accurate (Mariz et al., 2011).

In the IIF test, antibodies are first stained in HEp-2 tissue and then bound to a fluorescent chemical compound. In the cells which contain ANAs, the antibodies bound to the nucleus demonstrate different patterns, which can be visualized with microscopic imaging. The presence of AD can be determined through the identification of the captured visual cell patterns (González-Buitrago and González, 2006).

The imaging of the IIF test consists of five stages (Hiemann et al., 2006), starting with image acquisition with autofocus to reduce Photobleaching effects (Soda et al., 2006). The second stage involves automated cell segmentation using methods such as the similarity based watershed and adaptive edge-based segmentation (Huang et al., 2008a,b). This is followed by the mitotic cell segmentation stage which has been investigated using morphological and textural features and Local Binary Patterns (LBP) (Foggia et al., 2010). The fourth stage further classifies intensity level images into three classes, namely, *negative*, *intermediate* and *positive* intensities (Soda and Iannello, 2006). Finally, the last stage classifies the cell staining patterns into Centromere (Ce), Coarse-speckled (Cs), Cytoplasmatic (Cy), Fine-speckled (Fs), Homogeneous (H), Nucleolar (N) and Golgi (G) that correspond to different ADs.

With increasing AD occurrence, the demand for methods and procedures for fast, low-cost and repeatable diagnosis has become more and more indispensable. A number of HEp-2 cell classification techniques have been reported in recent years. The technique in Perner et al. (2002) is one of the earliest that handles the HEp-2 cell classification problems, where Otsu's global thresholding technique (Otsu, 1975) is used for cell segmentation and texture

* Corresponding author at: National University of Singapore, Department of Electrical and Computer Engineering, Singapore.
E-mail address: shahab.ensafi@u.nus.edu (S. Ensafi).

http://dx.doi.org/10.1016/j.compmedimag.2016.08.002
0895-6111/

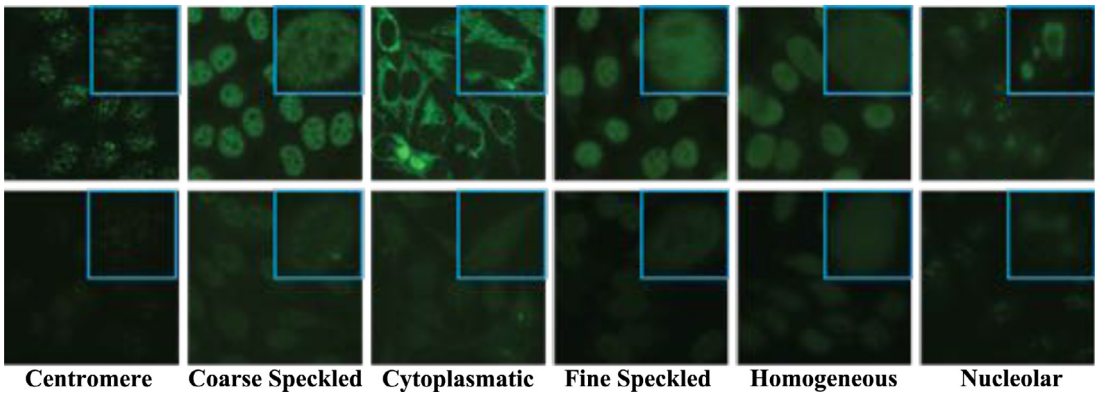

Fig. 1. The *positive* (Top) and *intermediate* (Bottom) intensity level images of ICPR2012 dataset.

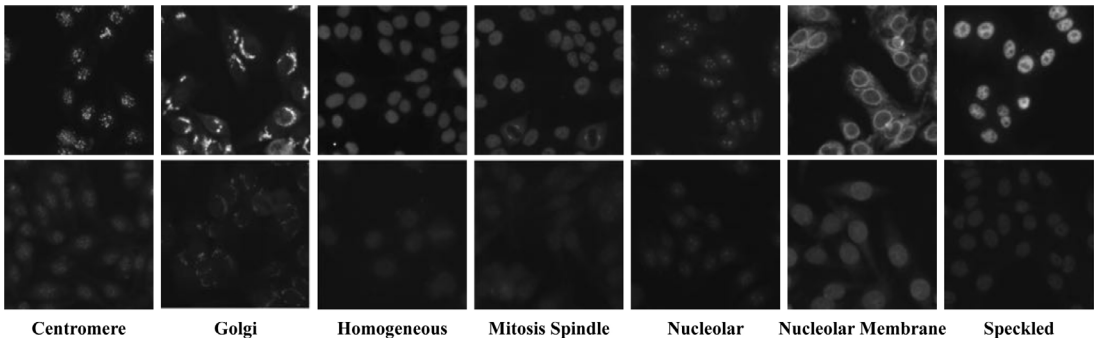

Fig. 2. The *Specimen Level* images of ICIP2013 dataset in seven classes. Top row is the *positive* and 2nd row is the *intermediate* intensity level images.

features are exploited for cell classification. Huang et al. (2012) also utilized the texture and statistical features and classified the cells with the Self-Organizing Maps. Soda and Iannello (2009) aggregated the binary classifiers on spectral textural features and introduced the reliability measure for the classification procedure. Techniques on intensity level and staining pattern classifications have also been reported in Hiemann et al. (2007), Soda et al. (2009), Sack et al. (2003).

Most works described above use their own datasets, which makes a fair comparison of different methods a nearly impossible task. The need for effective benchmarking led to the first publicly available dataset "MIVIA HEp-2 images dataset" (Foggia et al., 2013) referred to ICPR2012 dataset as it was released for the HEp-2 Cells Classification Contest at the 2012 International Conference on Pattern Recognition. At the 2013 International Conference on Image Processing, an expanded dataset which is referred to as the ICPR2012 dataset[1] (see Section 3.1) was introduced.

The dataset organizers (Foggia et al., 2013) had suggested two tasks for the ICPR2012 and ICIP2013 benchmarking datasets. The first is *Cell Level*, which classifies each cell independently without 'looking' to the neighboring cells in the specimen images. The second is *Specimen Level*, which classifies the whole specimen image by considering all the cells within the specimen image due to the assumption that most of the cells in one specimen image belong to one class (Foggia et al., 2013). The sample specimen images of two datasets are shown in Figs. 1 and 2.

Nosaka and Fukui (2014), the winner of ICPR2012 contest, made use of an extension of Local Binary Patterns (LBP) for feature selection and linear support vector machines (SVM) for cell classification. Morphological features (Sriram et al., 2014; Di Cataldo et al., 2014; Ponomarev et al., 2014) and different types of histograms (textones (Kong et al., 2014), gradients (Shen et al., 2014), regional (Wiliem et al., 2014), etc.) are also exploited to help improve classification results. Theodorakopoulos et al. (2014) combined the scale-invariant feature transform (SIFT), LBP features and a discriminative sparse representation for HEp-2 cell classification. Faraki et al. (2014) exploited the fisher tensors on the Riemannian manifold, which produces the same sized covariance matrix for all the regions in the image and learned a Bag of Words (BoW) dictionary using the *k*-means algorithm with the SVM used for classification.

One of the challenges with the ICPR2012 dataset is the classification of two classes of *fine* and *coarse speckled*, whose patterns are so close to each other as can be seen in Fig. 1 (Sriram et al., 2014). Additionally, the performance on *Specimen Level* classification is not reliable because of the small number of specimen images (28 images). In the ICIP2013 dataset, the number of specimen images is high enough to have a validated performance (Foggia et al., 2014). On the other hand, the provided cell masks of the images are tangled with noise. Additionally, several cell masks are connected to each other, which makes problem for classification stage.

Overall, most methods are based on artificial features such as SIFT, LBP and histograms in different patches of the images. These features have some parameters (size and number of patches, number of histogram bins, smoothing parameters, etc.) to be chosen manually, which can affect the final classification performance more or less. Additionally, the parameter tuning becomes troublesome when the number of training images increases as in the ICIP2013 dataset. Moreover, the prior knowledge of the intensity levels (*positive* and *intermediate*) and color data (RGB) of the input images are very useful for the cell classification performance but largely ignored by previous methods. An automatic and robust method is needed to classify the cell images with as little human intervention as possible.

We have investigated the idea of using Sparse BoW (SBoW) for HEp-2 cell classification with max-pooling operator. Ensafi et al.

[1] http://i3a2014.unisa.it/?page_id=126.

Please cite this article in press as: Ensafi, S., et al., Accurate HEp-2 cell classification based on sparse bag of words coding. Comput Med Imaging Graph (2016), http://dx.doi.org/10.1016/j.compmedimag.2016.08.002