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# International Contest on Pattern Recognition Techniques for Indirect Immunofluorescence Images Analysis

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***Abstract*—This contest is a joint initiative organized by the University of Salerno (Italy) and the University of Queensland (Australia) with the support of the Sullivan Nicolaides Pathology (SNP), Australia. The contest primarily aims to provide a platform for scientists and practitioners for performing research to develop Computer Aided Diagnosis (CAD) systems for pathology tests utilizing indirect immunofluorescence protocol. In particular, the contest considers the Antinuclear Antibodies (ANA) test using Human Epithelial type 2 (HEp-2) cells. The competition is divided into four tasks that address specific problems: (1) HEp-2 cell classification; (2) Patient specimen classification; (3) HEp-2 mitotic cell identification and (4) Cell segmentation.**

## I. Introduction

Pattern Recognition techniques are widely used in the field of medical applications for the development of Computer-Aided Diagnosis (CAD) systems with the aim of supporting the physician with a second opinion. This helps to reduce the number of mistaken decisions during the diagnosis process, or in the mass screening campaigns by determining a pre-selection of the cases to be examined. So the physician can focus his/her attention only on the most relevant cases. The system may also be used as an aid for training and education of specialized medical personnel.

In the last few years interest has grown towards the realization of CAD systems for the analysis of Indirect Immuno-Fluorescence (IIF) images. Today IIF is the gold standard for a diagnostic methodology suitable to search for antibodies in the patient serum using the HEp-2 substrate, in order to reveal the presence of autoimmune diseases. Due to its effectiveness, we are witnessing a growing demand for diagnostic tests for systemic autoimmune diseases. Unfortunately, IIF is still a subjective method that requires manual microscopy reading, making it highly dependent on the experience and expertise of the physicians. Henceforth, there is strong demand for the complete automation of the procedure. This would result in increased test repeatability and reliability, easier and faster result reporting, and a reduction of cost for the Healthcare System.

To that end, an increasing number of research groups have provided innovative contributions to the different aspects of the analysis of IIF images: image acquisition, pre-processing, segmentation, and pattern classification. However, research in the field of IIF image analysis is still in its infancy and has great potential for further growth [1]. In fact, this research topic is gaining new enthusiasm and interest among scientists and the size of the community may now be considered significant. The large interest of the scientific community in these topics has been demonstrated by the increasing number of international benchmarking initiatives organized over the last few years hosted by the last two editions of the International Conference on Pattern Recognition (in 2012 and 2014) and by the International Conference on Image Processing (in 2013) which all attracted a very wide audience [2]–[5].

The aim of the HEP-2 CONTEST 2016 is to advance the development of algorithms and methods for HEp-2 image analysis through third party evaluation of the methods on common datasets [6], [7].

## II. Medical Background

Connective tissue diseases are autoimmune disorders caused by antinuclear autoantibodies (ANAs) and characterized by a chronic inflammatory process involving different organs. ANAs are directed against a variety of nuclear antigens and they can be detected in the serum of patients using laboratory tests. The recommended method for ANA testing is via the indirect immunofluorescence (IIF) protocol. The IIF makes use of different substrates, each one specific for the detection of certain antigens. The substrates bond with serum antibodies and form a molecular complex. Then, this complex reacts with human immunoglobulin conjugated with a fluorochrome. At the end of such reaction, the complex becomes observable at the fluorescence microscope revealing the antigen antibody reaction. In case of ANA tests, the most notable used substrate is the human larynx carcinoma (HEp-2) cells.

During the reading phase at the microscope, physicians detect and score the antigen antibody reaction according to a procedure organized in three steps: mitotic cells detection, fluorescence intensity classification and staining pattern recognition. The final goal is the recognition of the staining pattern of the cells in the specimen image, because depending on the patient clinical history, each pattern can be related to a specific disease.

## III. Contest Tasks

The contest is divided into four different tasks. Participants are free to participate in one or more than the tasks. In the following, we provide a general description of each proposed

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task, together with information regarding the adopted datasets and the indices used for evaluating performance.

### A. HEp-2 cell classification

Similar to the contest from the previous year, this task is focused on cell-level pattern classification. This task has been initially proposed at the HEp-2 Cells Classification contest hosted by ICPR 2012 and then proposed again in all the successive initiatives hosted by ICIP 2013 and ICPR 2014, using datasets of increased size and complexities of these patterns. In particular, the competitions held in years 2013 and 2014 considered the following six HEp-2 patterns: homogeneous, centromere, speckled, nucleolar, mitotic spindle and Golgi. This contest will be the continuation from the previous years to witness the advances made by the community.

The dataset has been collected between 2011 and 2013 at Sullivan Nicolaides Pathology laboratory, Australia. It utilizes 419 patient positive sera, which were prepared on the 18-well slide of HEP-2 IIF assay from Immuno Concepts N.A. Ltd. with screening dilution 1:80. The specimens were then automatically photographed using a monochrome high dynamic range cooled microscopy camera which was fitted on a microscope with a plan-Apochromat 20x/0.8 objective lens and an LED illumination source. Approximately 100-200 cell images were extracted from each patient serum. In total there were $68,429$ cell images extracted: $13,596$ images used for training, made available to the teams, and $54,833$ for testing, privately maintained by the organizers. The images were automatically segmented by using the DAPI channel and manually annotated by specialists. The labeling process involved at least two scientists who read each patient specimen under a microscope. A third expert's opinion was sought to adjudicate any discrepancy between the two opinions. We used each specimen label for the ground-truth of cells extracted from it. Furthermore, all the labels were validated by using secondary tests such as ENA and anti-ds-DNA in order to confirm the presence and/absence of specific patterns. Each cell image contained in the database is annotated with the following information:

- Cell pattern (one of the patterns defined above)
- Cell intensity
- Cell mask
- ID of the image which the cell belongs to

Performance is measured using the mean class accuracy in cell classification.

### B. Patient specimen classification

The aim of the task is to classify the patient specimen. Each patient specimen (refer to Fig. 4) has multiple HEp-2 cells. This task will equip the participants with the segmented HEp-2 cells although the mitotic cells are not indicated. The participants have the liberty to either work directly on the specimen images (i.e., without using the segmentation map), or utilize the provided segmentation map. This task has been firstly proposed at the ICPR 2014 competition and, similarly to the cell-level pattern classification task, the task will be the continuation from the previous year to witness the advances made by the community.

The dataset was acquired in 2013 at Sullivan Nicolaides Pathology Laboratory, Australia. It was collected from 1001 patient sera with positive ANA test. Each patient serum was diluted to 1:80 and the specimen was photographed using a monochrome camera fitted on a microscope. Each specimen was photographed at four different locations rendering each specimen into four images. The dataset has seven pattern classes: homogeneous, speckled, nucleolar, centromere, nuclear membrane, golgi and mitotic spindle. The first four classes represent common ANA patterns whilst the remaining three classes are less common. The dataset is divided into training and test set as follows: approximately $1/4$ of the sera were in the training set and the remainder in the test set. All images are in monochromatic uncompressed format with resolution $1388\times1040$ pixels together with their corresponding cell mask which was obtained automatically. The labelling process has involved at least two scientists who read each patient specimen under a microscope. A third expert's opinion has been sought to adjudicate any discrepancy between the two opinions. Each slide image is also provided with the corresponding class (one among the patterns defined above). Furthermore, all the labels were validated by using secondary tests such as ENA and anti-ds-DNA in order to confirm the presence and/absence of specific patterns. Each specimen image contained in the database is annotated with the following information:

- Staining pattern of the specimen
- Intensity of the specimen
- Mask of the specimen

Performance are measured using the mean class accuracy in specimen classification.

### C. HEp-2 mitotic cell recognition

Cells undergoing mitotic phase will express different amount of antibodies which would be a useful sign for narrowing down the possible patient pattern. Before determining the mitotic cells, the cells are first detected. As mentioned, the scientists need to ensure that there are at least one or two mitotic cells on each patients specimen. Due to their much lower number of occurrences, we name the second task as the mitotic cell detection. In this setting, we treat the interphase cells (i.e., the non-mitotic cells) as the background cells. Recently it was found that mitotic cell detection can be addressed using the secondary counterstain. Again, the introduction of the secondary counterstain may not be economical. Thus, in this work we only target the problem of mitotic cell detection using the primary counterstain.

The images were acquired between 2014-2015 at the Sullivan Nicolaides Pathology Laboratory, Australia. It was collected from 253 anonymized patient's. Each patient serum was prepared as per industry protocol with 1:80 titer dilution and the specimen was photographed using a monochromatic camera fitted on a microscope. From 253 patient specimens, approximately $23,000$ interphase cells and $1,000$ mitotic cells

were extracted. Each image is accompanied also by the ground truth label: mitotic (+1) and interphase (-1).

Due to the low frequency of mitotic cells compared to the whole cell distribution, the mitotic cell recognition can be considered as a detection problem. Here, the interphase cells are considered as the background and the mitotic cells are considered as the cells of interest. More specifically, we define the evaluation metric using the standard object recognition/detection problem. The evaluation utilizes the detection confidence score of each image provided by the submission. The confidence score indicates the confidence that a cell image belongs to the mitotic cell. The evaluation is determined using two means: (1) the precision-recall curve and (2) the Average Precision (AP) which is calculated based on the precision-recall curve.

### D. Cell segmentation

Cell segmentation is the first step on the whole analysis. Despite its high difficulties, the segmentation problem can be solved by the secondary channel using DAPI. Nevertheless, the introduction of DAPI may complicate the laboratory work flow; thus, it may not even practical in some pathology laboratories. This means that cell segmentation on the primary channel is still not solved yet. The aim for this task is using only the primary channel, generate the segmentation map that is equivalent to the map generated from the secondary channel.

As the segmentation map from the DAPI channel can be considered as the gold standard, we opt to use the images acquired for the second task (patient specimen classification). This mean the dataset consists of 1,001 specimen images. For each image we provide both the original image and the segmentation mask obtained from the DAPI channel; the segmentation mask will be used as the ground truth with respect the performance will be evaluated.

The assessment of the segmentation quality has been carried out according to the procedure described in [8] in order to report the performance at the cell level. The metric adopted for reporting performance of each method is the $f - index$ calculated as:

$$f - index = \frac{2 \cdot Precision \cdot Recall}{Precision + Recall} \tag{1}$$

where

$$Precision = \frac{TP}{TP + FP} \tag{2}$$

$$Recall = \frac{TP}{TP + FN} \tag{3}$$

with

$$TP = \sum_{g \in G} \sum_{d \in D} \frac{|g \cap d|}{|g \cup d|} \tag{4}$$

$$FP = \sum_{d \in D} \frac{|d| - max_{g \in G}|d \cap g|}{|d|} \tag{5}$$

$$FN = \sum_{g \in G} \frac{|g| - max_{d \in D}|d \cap g|}{|g|} \tag{6}$$

where $D$ and $G$ are the sets of the detected cells and of the ground-truth cells, respectively, while $|\cdot|$ denotes the cardinality of a set.

## IV. Participations

In total the contest received 15 submissions focusing on one or more tasks.


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