Biologically Inspired Anomaly Detection in Pap-Smear Images

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Abstract. Uterine Cervical Cancer is one of the most common forms of cancer in women worldwide. Papanicolau smear test is a well-known screening method of detecting abnormalities in the uterine cervix cells. In this paper we address the problem of anomaly detection in pap smear images. Our method avoids modeling the normal pap smear images which is a very complex task due to the large within class variance of the normal target appearance patterns. The problem is posed as a Visual Attention Mechanism. Indeed the human vision system actively seeks interesting regions in images to reduce the search export in tasks, such as anomaly detection. In this paper, we develop a new method for identifying salient regions in pap smear images and compare this to two previously reported approaches. We then consider how such machine-saliency methods can be used to improve human performance in a realistic anomaly detection task.

Keywords: microscopic images, anomaly detection, saliency, SVM classification.

1 Introduction

In general terms, Anomaly Detection (AD) is the process of discovering data that are different, in some sense, from the patterns defined by a observed data set. The main challenge in an AD system is how to define what an anomaly is, because, normally, we have the descriptions of the regularity of the problem. For that reason, AD is frequently defined in a negative way: the target is to determine what is not normal or what does not fill a specific rule.

In the special case of AD in medical image, a lot of works have been reported [1]. AD algorithms have been applied in the detection of tumours [2], malformations [3], abnormal cells [4], etc.

Cervical cancer, currently associated with the Human Papilloma Virus as one of the major risk factors, affects thousands of women each year. The Papanicolaou test (also known as Pap test) is used to detect pre-malignant and malignant

Fig. 1. Pap-smear cell images. (a) Dark blue parts (yellow squares) represents the nuclei. Pale blue and reddish parts (blue boxes) are the cytoplasm. Magenta parts (orange boxes) are the background. (b) Touching cells (surrounded in yellow). Isolated cells (surrounded in orange). Noise (surrounded in red).

changes in the cervix [5]. Cervical cancer can be mostly prevented by early detection of abnormal cells in smear tests.

As illustrated in Fig. 1, three classes of regions are considered: nucleus, cytoplasm, and regions that include background, noise, and other kinds of cells.

Developing automated algorithms for AD continues to pose interesting challenges. The goal of the present work is to develop an automated and computationally efficient algorithm for the detection of anomalies, associated principally with cancer, in Pap smear images.

Biological vision systems demonstrated a remarkable ability to recognize objects under adverse conditions, such as highly cluttered scenes. The use of saliency mechanisms is believed to play an important role in this robustness to clutter. They make salient locations “pop-out”, driving attention to the appropriate regions of the visual field [6]. Biological vision systems rarely need to perform an exhaustive scan of a scene in order to detect an object of interest. These saliency detectors have been widely adopted in computer vision for applications such as object tracking, recognition and event analysis [7]. In these applications, saliency is used as a preprocessing step that saves computation and facilitates the design of subsequent stages.

Generally speaking, the detection of salient regions follows two paradigms: the object-based approaches [8,9], where the saliency is determined by the distribution of objects in the image, and the spatial-based approaches [10,11], where the saliency is determined by the selectivity of spatial locations. Both, object-based and spatial-based approaches, have drawbacks that one must take into account in developing biological vision systems. For the object-based approaches, it is necessary to develop robust mechanism for the detection of the objects in the image. On the other hand, spatial-based approaches usually fail when scenes are cluttered, the objects are overlapping, or objects distribution is heterogeneous or unbalanced. Many object-based saliency estimators have been reported in the literature. In most of them [12,13,7], the saliency of a region is determined from region’s contrast, size, shape, and location.

In this work, anomaly detection based on Visual Attention Mechanism is proposed. The paper proposes a visual attention model to (i) first determine salient

Fig. 2. Framework for detection of anomalies in Pap smear images

areas defined as Region-of-Interest (ROI) where anomalies could lie, and (ii) a second a saliency measure characterizing abnormal cells for the final anomaly detection.

The reminder of the paper is organized as follows. Section 2 describes the framework for the detection of anomalies in Pap smear images. Section 3 presents and discusses the obtained results. Finally, conclusions are presented in Section 4.

2 Materials and Methods

The general framework for anomalies detection in Pap smear images is shown in Fig. 2. This process has two main steps: the selection of Region of Interest (ROI), and the salient regions detection.

Both steps use a segmentation of the image obtained using the Mean-Shift segmentation algorithm [14]. Mean-shift is a popular method to segment images and videos. It has been widely used in cell images segmentation with good results [15,16,17].

2.1 Selection of the ROI

The goal of Region-of-interest (ROI) extraction is to separate the part of the image that contains the objects of interest (i.e. cells, tissues, parts of cells, cancerous cells, anomalies) from the parts that contain unusable information (i.e. background, small noise areas, dirt particles).

In our approach, ROI detection is based on Visual Attention Mechanism, using the Selective attention algorithm proposed in [18]. The saliency map is calculated using a frequency-tuned approach based on low level features of colour and luminance. For the objects, region saliency value is calculated by averaging the pixel-based saliency map over the pixels of a region. This method separates the background and very large cytoplasms from the rest of the segments in the image (see Fig. 3). This method, by itself, is not able to detect cells with abnormal changes.

2.2 Salient Regions Detection

Our method for anomaly detection is based, principally, on the method used by pathologists to determine some kinds of anomalies. The main characteristic of an abnormal cell in Pap test are [19]:

Fig. 3. Extraction of the ROI

- Nuclei are too big with an irregular texture without a clear pattern.
- Cytoplasms are too small.
- Cells are frequently crowded.

Formally, the saliency of a region r_i at the segmentation $R = \{r_1, r_2, \dots, r_n\}$ is given by:

$$S(r_i) = \zeta(r_i) \cdot \frac{1}{\phi(\Pr(r_i \in \text{Anomalies}))} \cdot \frac{\text{AreaFactor}(r_i) \cdot \text{RelativeAreaFactor}(r_i)}{\text{Compactness}(r_i)} . \quad (1)$$

ROI Belonging: Function $\zeta(r_i)$ controls the belonging to the ROI.

$$\zeta(r_i) = \begin{cases} 0 & \text{if } r_i \notin \text{ROI} \\ 1 & \text{if } r_i \in \text{ROI} \end{cases} . \quad (2)$$

Area Factor: The term $\text{AreaFactor}(r_i)$ is calculated as:

$$\text{AreaFactor}(r_i) = \frac{\text{Area}(r_i)}{\text{Area}(\hat{r}_i)} \quad (3)$$

where $\hat{r}_i$ is the region in the ROI that contains r_i .

Relative Area Factor: The relative area factor of a region is the ratio of the area of the region and the area formed by the region and its neighbours. Formally, the relative area factor of a region is given by:

$$\text{RelativeAreaFactor}(r_i) = \frac{\text{Area}(r_i)}{\text{Area}(r_i) + \sum_{r_j \in \xi(r_i)} \text{Area}(r_j)} \quad (4)$$

where $\xi(r_i)$ is the set of neighbours of the region r_i .

Compactness: Compactness function takes its values up to 1 and it measures the compactness degree of a region where a perfect circle is the most compact region with compactness equal to 1.

$$\text{Compactness}(r_i) = \frac{\text{Perimeter}^2(r_i)}{4 \cdot \pi \cdot \text{Area}(r_i)} . \quad (5)$$

Potential of Being an Abnormal Cell: Similar to [20], the parameter $\phi(\Pr(r_i \in \text{Anomalies}))$, represents the potential of being an abnormal cell, is here defined as follows:

$$\phi(\Pr(r_i \in \text{Anomalies})) = \frac{1}{1 + \Pr(r_i \in \text{Anomalies})} \quad (6)$$

where $\Pr(r_i \in \text{Anomalies})$ is the probability of r_i to be an abnormal cell, given the feature vector $\mathbf{f}(r_i)$.

In our approach, $\Pr(r_i \in \text{Anomalies})$ is calculated by using the method of Platt [21], from the output of a two-class (normal or abnormal) SVM [22] trained by using as feature vector $\mathbf{f}(r_i)$, the mean of the L , a , and b channels and the standard deviation of the L channel of the region in the Lab colour space. SVM training was carried out using a training set of images.

The parameters of the SVM classifier have been selected as follows. A linear kernel SVM and Gaussian kernel SVMs (with different values for σ) were trained by using a 10-fold cross-validation. A grid search method was used to select the best parameters of the SVM. The penalty parameter of the error C was tested in $C = \{2^i : i = -1..14, \infty\}$, as well as the parameter of the Gaussian kernel σ in $\sigma = \{2^i : i = -3..4\}$. The best performance was obtained for $C = 1024$ and a Gaussian kernel SVM with $\sigma = 1$. Finally,

$$\Pr(r_i \in \text{Anomalies}) = \frac{1}{1 + \exp(A \cdot f + B)} \quad (7)$$

where f is the output of the SVM, and the parameters A and B are fitted by using maximum likelihood estimation [21].

Finally, the detection of anomalies in Pap smear images will be done by the comparison with a threshold T . Regions with saliency greater than T will be considered the foci of attention and classified as anomalies. Selection of T was done empirically and it was fixed as $T = \max(0.01, p_{0.9})$, where $p_{0.9}$ is the 90% percentile of the saliencies of all the regions.

3 Results and Discussion

The proposed approach was applied to 40 images taken in the Gynaecological-Obstetrical Hospital of Santa Clara, Cuba. Pap smears were prepared by qualified technicians. The images were taken at 650x using a 319CU digital microscopy Camera. Regions that correspond with malignant or pre-malignant formations (abnormal growing of the nucleus) were manually segmented by experts as illustrated in Fig. 4(a) and (b).

The performance of the proposed anomaly detector, denoted as BIAD, has been evaluated via three classifier quality measures: precision, recall and F-measure [23]. True positive cases refer to the abnormal cells detected over the whole image. Abnormal cells that do not belong to the ROI are considered as false negatives.

In our evaluation, a detected anomaly region is considered as true anomaly if it intersects a ground truth anomaly region. Fig. 4 shows the anomalies detected using the proposed method in a typical pathological image.

Fig. 4. Example of anomaly detection. (a) Original image. (b) Ground truth. (c) Detected anomalies using the proposed method over the original image. (d) Detected anomalies using the proposed method over the mean-shift smoothed image.

Table 1 shows the obtained results in terms of recall, precision, and F-measure, along with comparison to existing general purposes region-based focus of attention schemes, denoted as M1 [12], M2 [13], and M3 [7], respectively. The first three columns refer to the results using the original images, and the last three columns refer to the results using smoothed images. The Mean-Shift filter [14] has been used for image smoothing.

As it can be seen, the best results were obtained using the proposed method. Indeed, compared to the general purpose state-of-the-art methods, the introduced criteria used in the estimation of the saliency (area factor, relative area factor, and compactness) well-emulate some of the criteria used by pathologists. Moreover, the incorporation of a powerful machine learning technique, a SVM, contributes to the reduction of false negatives.

On the other hand, the results for the filtered images are worse than for the original images. Abnormal cells frequently lose important characteristics useful when you want to make an evaluation. This makes difficult to detect abnormal cell in these images. After this stage, these characteristics are smoothed. The key point is the delineation of the cytoplasm (Fig. 4). Our method tries to calculate the ratio between the area of the nucleus and the area of the cytoplasm. If cytoplasm is not well-segmented or, in the worst case, it is lost, then the evaluation of the saliency using our method does not provide good results. Indeed, if the segmentation method used to determine the regions is prone to oversegmentation, undersegmentation, or poor delineation of the regions the measure of the saliency will be widely biased.

Table 1. Results obtained with the proposed method and the comparison with another methods

	No Filtering			Mean-Shift Filtering		
	Recall	Precision	F-measure	Recall	Precision	F-measure
BIAD	93.36%	63.48%	75.57%	86.53%	61.53%	71.92%
M1	50.52%	21.38%	30.05%	35.71%	18.60%	24.46%
M2	61.87%	37.58%	46.76%	50.38%	32.35%	39.40%
M3	48.62%	20.97%	29.31%	33.94%	16.17%	21.90%

4 Conclusions

In this work, we introduced a visual attention mechanism for the detection of anomalies in images of the Papanicolaou test. First, a ROI extraction is performed in order to focus the analysis in suspected areas of the image, avoiding wasting computational resource in small regions, noise, dirt, etc. In the second step, we estimate the saliency of every region in the ROI by using a region-based saliency estimator. We use a supervised approach, via SVM, to estimate the probability of being an anomaly, in combination with cytological information of the abnormal cells. Finally, most salient regions (with a saliency greater than a predefined threshold) are considered as anomalies. As future work, we planned an extensive evaluation with pathologists.

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