AN AUTOMATIC METHOD FOR IDENTIFICATION OF CYSTINE CRYSTALS IN URINE SEDIMENT

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ABSTRACT

The analysis of urine sediments (Urinalysis) is a common procedure in diagnostic laboratories, and allows the identification of important diseases. This procedure is usually done by a professional, which performs a visual inspection of microscope slides containing urine, aiming to identify crystals, bacteria and other relevant elements, resulting in a laborious task. The automation of this task is of great value to medicine and related areas, raising the quality and reliability of diagnosis and reducing the time spent with these tasks. This paper describes a new method for automating the analysis of urine sediments in digital images that has the main goal of finding cystine crystals. Real images obtained from a microscope and from some public image databases were used to test the developed algorithm, which demonstrated satisfactory results with 73.72% and 93.08% of sensitivity and specificity, respectively.

CCS Concepts

• **Computing methodologies → Computer graphics → Image manipulation → Image processing**

• **Computing methodologies → Artificial intelligence → Computer vision problems → Object recognition**

Keywords

Urinalysis; Cystine Crystals; Computer Vision; Image Processing

1. INTRODUCTION

Urinalysis has an important role in disease diagnosis, especially those related to the urinary tract, since it helps to detect or even prevent problems, such as infections and kidney stones. Nowadays even with all the technology available in medicine, this exam is still performed by a visually trained professional in clinical laboratories. In this process, all urine samples are cataloged, centrifuged and placed on slides, to be analyzed through microscopy.

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The automation of this process, or part of it, allows the reduction of the analysis time, gives more comfort for the professional, and increases the analysis reliability. There are devices that already perform this exam independently, but it seems that they are rarely used, since none of the seven laboratories consulted in our city, during the preparation of this work, have such equipment – it is very expensive and requires skilled professionals to operate it.

The main goal of this paper is to present a method based on image processing that automates the identification of cystine crystals in digital images of urine sediment. The presence of these crystals, which have hexagonal shapes, indicates a kind of congenital metabolic error, the cystinuria, whose bearer tends to form kidney stones [1]. Besides a strong discomfort, this disease can cause infections, fever and renal insufficiency. It occurs on an average of 1 to 2% in adults and can get up to 8% in children [2]. To achieve the proposed goal we have used some known Image Processing and Computer Vision techniques, but we also developed specific algorithms for the identification of these crystals in digital images obtained from a microscope, which is the major contribution of this work.

The remaining of this paper is organized as follows: some related works that somehow contributed to the development of this work are presented in Section 2; the steps of the proposed solution are described in Section 3; the results of the experiments are presented in Section 4; and the conclusions and future works are presented in Section 5.

2. RELATED WORK

Most of the work on automatic urine analysis focuses on two approaches. The first refers to the reduction of the features analyzed in the images and the second on improving these images for future analysis or to be used as a quick decision tool (presumptive diagnosis) before submitting the sample to a longer analysis and urine culture [3].

The work from Mei-li et al. [4] uses an artificial intelligence (AI) approach for classifying and counting elements of urine sediment. It is based on Support Vector Machine (SVM) for data classification, and on the AdaBoost (Adaptive Boosting) machine learning algorithm for a pre-classification of the input set, and Harr feature [17] for object recognition. According to the authors,

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method is very effective for recognizing red and white blood cells, epithelial cells and pus cells, among others. The technique does not deal with urine crystals.

In another work that uses AI, Zhou et al. [5] proposes a method based on feature classification, using a neural network to identify 12 visual elements of the urine sediments: erythrocytes, leukocytes, cystine crystals, pus cells, small round cells from the epithelium, fungi, trichomoniasis, epithelial cells, hyaline cast, cellular cast, granular cast and waxy cast. Despite being able to identify various elements from urine sediments, the method does not distinguish between different existing types of crystals, like triple phosphate, calcium oxalate and cystine.

With the same concern, Cao et al. [6] presents a method for red cells detection in urine sediment images that uses just a few features to classify them. It uses an improved version of the Sobel operator to process the images and to detect cells through the Hough Transform. Thereafter, the red cells are recognized by a group of standardized characteristics, such as similar sizes, concentric circles, among others. The work was based on experiments that indicate that the radius of a red blood cell is of approximate 15 pixels. The center of the circle is obtained by the usage of three non-collinear points detected by the Hough Transform. The conclusions obtained were satisfactory, allowing the location of red blood cells in a fast and trusty manner.

The second main problem in urinalysis is to reduce the complexity of the images for further processing. Yan Liang [7], for example, removes the non-cellular objects of urine through feature analysis, in order to avoid false positives in red and white blood cells identification. On the other hand, Paranjape et al. [8] uses special images obtained from a microscope illuminated by a special polarized light source. According to the authors, uric acid and triple phosphate crystals generate images with very specific characteristics when exposed to polarized light, which can facilitate the automatic image processing.

All the works presented in this section achieved good results on the classification of elements found in urine sediments, but none of them is focused on cystine crystals. The work with the most similar approach is the one from Zhou et al [5], which addressed a category-based classification and so was able to recognize crystals in general.

3. MATERIALS AND METHODS

Our method was developed to automatically detect cystine crystals in urine sediment and was implemented using C/C++, OpenCV [9] and ImageJ [10]. The way the images used in this study were acquired, as well as the methodology, and the developed algorithms are described in the following subsections.

3.1 Image Dataset

The first step of this work was to obtain images of urine sediments containing or not cystine crystals. Initially, we consulted clinical laboratories in order to obtain real images, since images from real exams provide greater ensuring of the effectiveness of the technique. However, it was very difficult to find them in the clinical laboratories we got in touch. Then, we decided to build our dataset in two ways. First, we searched for images with cystine crystals on a public image database named UROSURF [16]; we obtained 20 images through this process. Since we only had a reduced amount of images, we "contaminated" urine samples with cystine crystals and put them in a conical tube to go through a process of centrifugation, separating the solid elements used to pick the sediment. Then, these sediments were placed on a slide, and we took pictures of them using a microscope, in the same way as in a laboratory exam. We obtained 28 images in this way, resulting in a total of 48 images to test the algorithm. Some images from our dataset can be seen on Figure 1. After obtaining all images, they were visually inspected in order to label all cystine crystals that appeared and generated a ground truth for the image dataset.

3.2 Preprocessing and the Developed Algorithm

The general idea of the cystine-detection method is to locate line segments that together form hexagonal structures. Four steps are part of the developed algorithm: image segmentation; identification of the regions with higher probability to contain a cystine; localization of the lines that potentially compose it, identifying whether these lines may in fact describe the edges of a hexagonal crystal. These steps are described below.

The image segmentation step is necessary to highlight the objects that can represent cystine crystals. For this, several methods have been applied: Isodata [11], OTSU [12] and Renyi Entropy [13]. IsoData was the segmentation algorithm that performed better for our case, therefore, it was chosen. Figure 2 shows images resulting from the segmentation with different methods, where IsoData performed better than OTSU.

On the next step, a search for contiguous areas, named BLOBs, is performed on the images, as illustrated in Figure 3a.

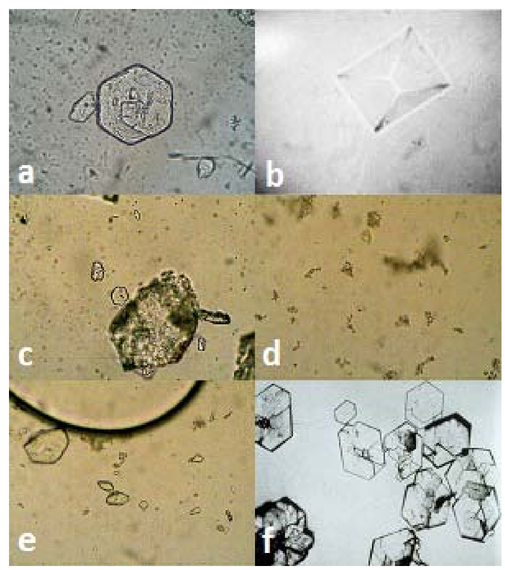

Figure 1: Image samples from the generated dataset with (a, c, e, f) and without (b, d) cystine crystals. Images b and f are from UROSURF

After the BLOBs are detected, they are analyzed to decide whether they have cystine crystals or not. It is done by the evaluation of their foreground pixel density, which can be expressed as:

$$f(x) = \begin{cases} \text{Cistine}, & FG/_{BG} < 0{,}4 \\ \text{No Cistine}, & FG/_{BG} \geq 0{,}4 \end{cases} \quad (1)$$

where FG represents the quantity of pixels with the same color as the border of the crystal, and BG the number of the pixels in the BLOB with the same color of the background.

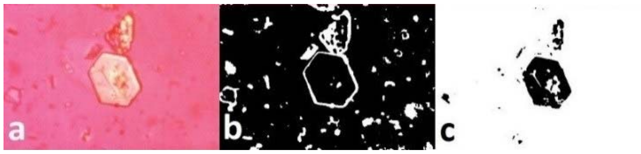

Figure 2: **Segmentation of the original image (a) with the IsoData (b) and OTSU (c) algorithms**

As cystine crystals have a transparent internal region, those BLOBs with a high density cannot represent a crystal of this type (Figure 3b). For this method, the density value was empirically determined to be 0.4, but it can be adjusted for noisy images, on which the urine contains many other suspended particles, apart from the crystals.

Other parameters like the BLOB's size cannot be used, because the crystals and the images have several sizes and resolutions, respectively.

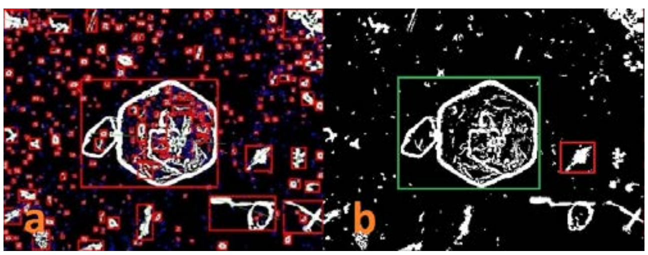

Figure 3: Blob detection: every BLOB has its own bounding box, drawn in red (a). In the green box, a BLOB that can contain cystines. In the red box, a very dense BLOB, without cystines (b).

The following step consists of determining the actual lines on the image, to verify which ones can form the borders of a crystal. For this process, the BLOBs are submitted to the Canny edge detector [14] and then lines are obtained by applying the Probabilistic Hough Transform [15]. Some examples of the resulting images of this process are shown in Figure 5.

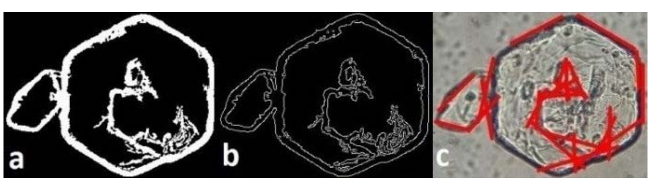

Figure 5: Blob identified (a), blob processed by the Canny algorithm (b), lines detected by the Hough transform (c)

The final step is the identification of a cystine crystal, which is done as follows: considering a line L_i, formed by two endpoints P_{i1} and P_{i2}, the algorithm arranges all the lines detected in the BLOB in a group. In order to exclude some repeated lines that the probabilistic Hough transform finds, one endpoint of a line Pi is taken as a reference and then it searches for another endpoint, from another line L_j $(P_{j1} – P_{j2})$, that is at a distance d, smaller than a D_{lim} threshold and that the L_i and L_j lines form, between them, an angle of $120^o \pm 15^o$ (Figure 6). The exclusion of the repeated lines is done through the calculation of the cross product between the edges $A(P_1,P_2)$ and $B(P_3,P_4)$ that share a vertex $(P_1 == P_3$ or $P_1 == P_4$ or $P_2 == P_3$ or $P_2 == P_4)$. The cross product is used to classify the orientation of the edges that define the polygon of the cystine. The possible classes are clockwise (CW) and counter-clockwise (CCW). As they are considered to have their Z coordinates equal to 0 ($Z_A == Z_B == 0$), the cross product between the points A and B is described as

$$z = X_A * Y_B - Y_A * X_B . \qquad (2)$$

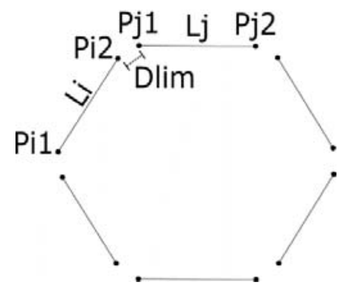

Figure 6: Description of the lines being processed

The D_{lim} threshold was empirically obtained as being 15% of the smaller side of the bounding box of the BLOB. If there is more than a pair of points matching these criteria, the nearest point is chosen. These criteria forms a set of edges that describe hexagonal structures. However, it cannot be guaranteed that there is only one cystine in this set, as can be seen in Figure 7.

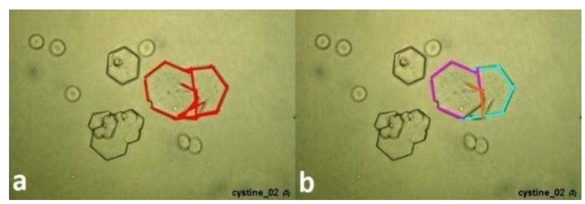

Figure 7: Example of the separation of objects in a single structure (a) into two separate cystines (b)

In order to separate multiple cystines on the same BLOB, two edges that share a vertex are chosen by the algorithm. Then, these edges are grouped as a cystine, the cross product is calculated and the orientation of the cystine is set by it. The process is repeated taking a new edge that shares a vertex with one of the edges A or B. If its orientation is the same as the other chosen vertex, the edge is removed from the initial group, and added to the new cystine. The process repeats itself until the original set is empty.

4. EXPERIMENTAL RESULTS

As previously described, the cystine crystals have a hexagonal structure. However, sometimes, as exemplified in Figure 1e, not all its sides are well formed, because of a dirty sample or a broken crystal. Thus, in order to achieve a better result, our method allows the variation of the number of edges that must be found to identify a cystine. In other words, e.g., if it finds four edges with an angle between them that indicates that they are part of a hexagon, it is assumed that a cystine was found.

Considering this possibility, for the assessment of the developed method, we have evaluated the 48 images from the dataset (section 3.1), with and without cystine crystals. For this, we computed the sensitivity and the specificity of the results, as shown in Table 1. The described method shows 73.73% of sensitivity and 93.08% of specificity. The specificity is relatively high due to large number of true-negatives.

Table 1. Evaluation of the method on real data

	Manual	Developed Method
True-positive	137	101
False-positive	-	53
False-negative	-	36
True-negative	-	713
Sensitivity	100%	73.72%
Specificity	100%	93.08%

This result was obtained considering that it is enough to find two edges of a hexagon to identify a cystine crystal. If we need to find more edges, the sensitivity decreases and the specificity reaches 100%. This occurs due to cases as exemplified in Figure 1e.

5. CONCLUSIONS AND FUTURE WORK

This paper presented a new method for automating the analysis of urine sediments in digital images, which aims to find cystine crystals. Since there were no studies specifically designed for this purpose, this method allows the reduction of the analysis time, and improves the reliability of the analysis.

As described in Section 2, several works in the literature address the classification of elements found in urine sediments, but none of them is focused on cystine crystals. For a first study with this focus, the developed method presented good results.

Besides cystine crystals, the developed approach can be extended for the detection of other elements such as crystals of triple phosphate or crystals of calcium oxalate, illustrated in Figure 1b. This can be done following the same principles of the presented solution with minor modifications of the algorithm that detects hexagonal shapes.

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