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A New Search Model for Liquid-based Cervical Cells Based on Auto-focus Microscope System

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Abstract. Liquid-based cervical cytology test which one of the most important method of detecting cervical lesions has a good effect on diagnosis and prognosis of cervical carcinomas. Speed of manual scanning is slow, furthermore large quantities of works repeated due to the presence of visual fatigue that lead to misdiagnosis. Automatic screening method for pathological cells is proposed based on auto-focus microscope system combined advanced machine vision technology and image processing technology, convenient for doctors find suspicious cells. This way can improve the efficiency of medical workers and avoid misdiagnosis. The key technology of auto-focus microscope system is that scanning automatically of liquid-based cervical cell. An efficient and accurate focus method can find a clear image quickly, which is of great significance to the detection of abnormal cells. In this paper, we proposed a new research mode for auto-focus microscope system, based on the micrograph characteristics of liquid-based cervical cytology. Results show that the approach outperforms with high accuracy and comparable performance.

1. Introduction

Liquid-based cytology test, an efficient and accurate method of cytological test which remove excess mucus and impurities cells retain exfoliated cells for detection. It’s a very important meaning, to identify early cervical lesions, as one of the effective method screening of cervical cancer[1]. Manual liquid-based cytology test need to check 300 fields in accordance with national regulations, it will be a heavy work to observe 100 slides for every day. Doctors will be fatigue with powerful effort, and the accuracy of the inspection will be reduced. However, computer can replace the human to complete the repetitive work observing cell slides and make a diagnosis with the improvement of computer performance and the development of machine vision technology.

Liquid-based cytology test based on auto-focus microscope system scan the cell samples quickly, objectively and accurately, reduce the subjective errors caused by human factors. However, it is an important prerequisite that obtaining clear and high-quality digital images by advanced machine vision technology and digital image processing and analysis technology to scan the liquid-based cells.

Auto-focus microscope system has the function of automatic scanning and focusing consists of microscope, mobile carrier platform, image collecting equipment and computer. As the center of the whole system, computer control mobile carrier platform and camera to achieve the purpose of liquid-based cervical cell screening.
It is necessary that carrier platform moving to a specific location corresponding to the focal length, then get the best picture. Carrier platform complete the operation of moving controlled by computer is auto-focusing technology. While the automatic focusing technology of the system is the key technology to acquire a high quality image with high-resolution cameras and microscopes.

Now, we can conclude from the previous literature that automatic focusing technology of liquid-based cells has direct focus and indirect focus. Technology of direct focus is assisted by other auxiliary equipment to measure the distance between the lens and the object to be observed, and then move the platform to the focal point. Indirect focus is that selecting the appropriate platform position according to the image sharpness calculated by preprocessing information of the image in the camera. It is widely used to select the appropriate location depend on the image content and collect the clear image.

In the previous literature, many focus methods are proposed on heuristics such as fast climbing search and traversing search. Modified fast climbing search is a practical real-time auto-focus algorithm improving the reliability and speed. Traversing search with a high-accurate ensures that the optimized image is found [2]-[4].

However, no proof has been provided about micrograph characteristics of liquid-based cervical cells. In this paper, first we describe a model of images focusing, then image sharpness evaluation function is provided. It is important that we study the microscopic image properties of liquid-based cervical cells. Finally, a new search mode for liquid-based cervical cell based on auto-focus microscope system is proposed. The experimental results show that the method is effective.

2. Principle of auto-focus
Principle of optical microscope image information in camera is shown in figure 1. We have shown a thin lens model for the optical system, whereas the analysis here can be easily extended to a thick lens model[5]-[7]. In this figure, let p is a point on a visible surface, and the p’ be it’s focused image. The relation between the point p and p’ is corresponding to the formula 1.

\[ \frac{1}{f} = \frac{1}{u} + \frac{1}{v} \tag{1} \]

Where u is the distance between the lens plane and the object plane and v is the distance between the lens plane and the image plane, the focal length is f. Light from the point on the visible surface is refracted through the lens, then an inverted image with the size is magnified is formed. If the focal length or image distance and object distance is not fit the formula, the point on the object will form a spot on the observation surface. The appearance of light spot on the surface will make the image unclear. Blurred image can’t be used as a basis for medical diagnosis, because the unclear image represent information inaccurately.

In order to find a clear and accurate image, we should move the carrier platform to a more suitable location or change the position of camera. However, only the carrier platform can be moved in three dimensions with three stepper motors in the whole system. We can set up specific programs in the
computer, and the platform will move according to the rules. Then the auto-focus microscope system can realize the function of automatic scanning and focusing.

3. **Focus method**

As the first section says there are two ways to realize the microscope focus. First is direct focusing that the microscope platform moves to the special location automatically corresponding to the distance measured by auxiliary device[2]. Another way is indirect focusing which select the best one from a series of images collected by camera. It is more and more applied to the automatic focus of microscope with the improvement of computer processing speed and the progress of digital image processing technology. The key to this technique is how to capture images and select the best image. First we will introduce how to evaluate the image quality and how to select the appropriate acquisition strategy.

3.1. **Nature of Evaluation function**

Evaluation function is used to select the optimal image can evaluate the quality of image. An ideal sharpness evaluation function requires the following points[3].

1. Unbiasedness. Most clear image corresponds to the maximum value of the evaluation function without bias, otherwise the peak didn’t appear on other image.
2. Unimodality. Function value curve of images has only one maximum. If not, we can’t find the most clearly image.
3. Robustness. Function is stable and can be applied in situations where there are other noises.
4. Sharp. Function value curve of images change significantly around the peak, so it's easy to find the maximum value.
5. Timeliness. Algorithm runs quickly with less resources in the whole system.

Unbiased and unimodality are the most important factors for finding correctly focus images. Usual functions are frequency-domain functions, grayscale functions and informatics functions[8]. Clear image’s is obvious with more detail feature that transformed to high frequency part on frequency domain. The principle of the frequency domain function is that the clear the image is, the higher the energy in frequency domain. The function of the frequency domain is mainly refer to cosine transform and the Fourier transform function. And the informatics function evaluate the image according to the information correlation of image pixel. The grayscale function is mainly based on the gray change obviously of the clear image. There are several different ways to judge the sharpness of different images for grayscale[6][9].

3.2. **Evaluation function**

(1). Variance. Sharpness of the image corresponding to the gray variance. The clearer the image, the more obviously the grayscale change, and the bigger the variance is. (see formula 2)

\[ F_{var} = \sum_{i,j} [(g(i,j) - \bar{g})^2] \]  

(2). Sum of the absolute value of the gray difference (see formula 3). Evaluate the quality of image according to the image's grayscale characteristics. The clearer the image is, the smaller the similarity between pixels in its certain neighborhood. Then the clearer the image, the greater the difference in gray value.

\[ F_{SMD} = \sum_{i,j} [ |g(i,j) - g(i,j-1)| + |g(i,j) - g(i-1,j)| ] \]  

(3). Energy of image gradient (see formula 4). Image quality also can be evaluated according to the principle that more obviously the grayscale change, the greater the gray energy.

\[ F_{LOG} = \sum_{i,j} [ |g(i,j) - g(i,j-1)|^2 + |g(i,j) - g(i-1,j)|^2 ] \]
3.3. Image sharpness curve

Microscopic image of liquid-based cervical cells has unique characteristics. So we collect and analyze images of liquid-based cervical cells that enlarged by twenty times objective lens often used in detection of early cervical lesions. On the image sharpness function described above, the effect of Robert operator is obvious and easy to realize. Then Robert operator is used to calculate the sharpness of image under different distances between the lens plane and object plane. And the trend of the curve of the image sharpness was analyzed dynamically. Experimental steps as follows:

1. Adjust manually the microscope platform to find the clearest image.
2. Move the platform down 30 units.
3. Move the platform up 1 unit, collect image from the scene when the platform is stable, then calculate the sharpness of the image by the sharpness function of Robert operator.
4. Repeat step 3 for 60 times.

![Figure 2. Sharpness curve](image)

Sharpness curve of images with different distance will be obtained, as figure 2. Two peaks can be found in the curve. Image of bottom and images of two peaks as figure 3, figure 4 and figure 5.

![Figure 3. First peak](image)
![Figure 4. Image of bottom](image)
![Figure 5. Second peak](image)

It is obvious in the three images that there are more cell membrane components in the peak place, and the image of the valley bottom rarely sees the cell membrane. In this field, we look for a special area with rich information and analyze the grayscale distribution of three images. There are three histograms which correspond to the minimum value between the peak and the two peaks. As figure 6, figure 7 and figure 8 shown.

It is concluded from the experiment that the double peak is normally. Cells are collected and the saved temporarily in cell preserve fluid. And its structure is not destroyed on the whole process, whether settlement or centrifugal production. Cell’s structure is well preserved, so there will be a certain thickness. The difference of thickness will bring different focal length.

First peak is due to the existence of the upper side cell membrane, which results in an obvious small peak value, and second peaks correspond to the cell membranes below. Nucleus will be closer to the cell membrane below because of the effect of gravity. Therefore, a larger peak will appear near that point.
4. Search mode
Nuclear information is the main basis for diagnosing diseases. Images acquired from microscope are excepted contain nuclear information as much as possible to reduce the impact of noise when analyzing images with a computer. Therefore, the image of the maximum value on the second peak is chosen to be used to analysis of cell status, and the nuclear structure can be seen clearly. It is of great significance in diagnosing diseases. By analyzing the microscopic images, we can see that the sharpness of image changes slowly and monotonously near the focal point and attenuates quickly far away from the point. So we can find firstly second peak according to the idea of simulated annealing, and then find the optimal solution.

4.1. Initial solution and acceptance criteria.
Focal length is stable in the same slide. Result of the last successful focus can be used as the initial value of simulated annealing in this search, and then find the optimal solution. Acceptance criterion is set corresponding to the characteristics of image sharpness change. It can be concluded by analyzing of changes in images that the sharpness of image should not be lower than the highest value of 0.95. If the value is lower, then search is abandoned, which is regarded as far away from the focus.

4.2. Step of search
(1). Sharpness of the image is collected and calculated in the last position where we get the best solution, which is regarded as the initial solution of this search.
    (2). Platform moves 20 units up, then collect and calculate the sharpness of the image. Select the best image of the two as the new initial solution. If the new image, within the scope of acceptance, repeat the second steps until the iteration terminates. If not, end of the iteration.
    (3). Search the optimal value near the result with ergodicity. The moving range is set to around 20 units, and moving 5 units each time.
    (4). Best image obtained from the search taken as the final image of this focusing.
4.3. Experimental summary

Clear images can be found quickly and accurately by the method described previously and conform to the diagnostic criteria collected from different scene. Effect of the captured image is as figure 9. We comparable the new search mode with the traditional traversal search, then find the difference. The step of traditional traversal search is set search three times near the last result, and the carrier platform moves fifth units each time. We can see from figure 2 that the moving step should not be too long or too short. Because we need to ensure search as much as possible in a short time[10]. Results shown as table 1. It is concluded that the new search mode has a high accuracy with an uncertain step than a traditional traversal search mode. And the total time of scanning a sample will be less than the traditional search.

Table 1. Compared with experimental results

| number | New search mode | Traditional traversal search |
|--------|-----------------|------------------------------|
|        | Search steps    | Search steps                 |
| 1      | 7               | 7                            |
| 2      | 7               | 7                            |
| 3      | 6               | 7                            |
| 4      | 8               | 7                            |
| 5      | 6               | 7                            |

|        | Final sharpness | Final sharpness |
|--------|-----------------|-----------------|
| 1      | 1. 18453        | 1. 18453        |
| 2      | 1. 17870        | 1. 17525        |
| 3      | 1. 21198        | 1. 20154        |
| 4      | 1. 13097        | 1. 12837        |
| 5      | 1. 25467        | 1. 24612        |

5. Conclusion

It’s an effective means to help doctors diagnose early cervical lesions that liquid-based cytology detection with machine vision. In this paper, the image’s characteristics of liquid-based cervical cells have been systematically studied, and the image sharpness curve has been analyzed in detail. There is a certain difficulty in cell image focusing, attributed to the thickness of cell with a complete structure. The formulated method searching focal point based on the principle of simulated annealing, which can effectively focus the clear image for doctor’s diagnosis with high accuracy. It has great research value in image sharpness evaluation function, and further optimization needs to be done to ensure the accuracy of focusing.

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