Improved segmentation of abnormal cervical nuclei using a graph-search based approach

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ABSTRACT

Reliable segmentation of abnormal nuclei in cervical cytology is of paramount importance in automation-assisted screening techniques. This paper presents a general method for improving the segmentation of abnormal nuclei using a graph-search based approach. More specifically, the proposed method focuses on the improvement of coarse (initial) segmentation. The improvement relies on a transform that maps round-like border in the Cartesian coordinate system into lines in the polar coordinate system. The costs consisting of nucleus-specific edge and region information are assigned to the nodes. The globally optimal path in the constructed graph is then identified by dynamic programming. We have tested the proposed method on abnormal nuclei from two cervical cell image datasets, Herlev and H&E stained liquid-based cytology (HELBC), and the comparative experiments with recent state-of-the-art approaches demonstrate the superior performance of the proposed method.

Keywords: Image cytometry, cervical cells, abnormal nuclei, segmentation, graph-search

1. INTRODUCTION

Reliable automated detection/segmentation of abnormal nuclei in cervical cytology is of utmost importance in automation-assisted reading techniques,\textsuperscript{1} which have the potential to reduce errors and increase productivity in cervical cancer screening.\textsuperscript{2,3} Studies related to the topic of abnormal nuclei segmentation in cervical cytology usually evaluate their methods (e.g., snake-,\textsuperscript{4} watershed-,\textsuperscript{5} fuzzy C-means- (FCM)\textsuperscript{6} based), on the Herlev database\textsuperscript{7} consisting of single cell images. More practically-oriented segmentation method for detecting/segmenting abnormal nuclei within a field-of-view (FOV) had recently been reported and evaluated by our group.\textsuperscript{1,8} Our previous approach works well in most situations but may generate inaccurate boundaries when the nuclei exhibit poor staining and/or their boundary contrast is low.

In order to handle the challenges presented in abnormal nucleus segmentation, such as different size, irregular shape and non-uniform chromatin distributions of nuclei, we move away from the use of traditional cervical cell segmentation techniques,\textsuperscript{3,9} and rely on the use of graph-search based segmentation,\textsuperscript{10} specifically a 2D dynamic programming approach. Similar approaches have been successfully used in the segmentation of ellipse-like objects in other types of biomedical images.\textsuperscript{11,12} The main advantage of our graph-search based approach for nucleus segmentation is its ability to embed shape information about nuclei in the graph construction, and its flexibility to incorporate specific knowledge by designing cost function. Our method is general for improving nucleus segmentation as long as an initial segmentation is available. We show quantitative comparisons between the proposed method and state-of-the-art approaches\textsuperscript{4–6,8} on two datasets, Herlev\textsuperscript{7} and H&E stained liquid-based cytology (HELBC).\textsuperscript{8}

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2. METHODS

2.1 General Framework

Given an input image, the general framework of our improved segmentation consists of two main steps (as shown in Fig. 1): (1) A rectangle (sub-image) around each nucleus candidate is cropped according to an annotation protocol which relies on the coarsely (initially) segmented nucleus boundary; (2) a graph-search based approach is used to detect the improved nucleus boundary. In step (1), the annotation protocol is defined based on the coarse boundary of the nucleus, with which we can compute the length $L$ of the major axis and the center $x_0$ of the smallest upright bounding rectangle. Then a rectangle with sides of $Len = L + \Delta L$ centered at $x_0$ is cropped and determined to be the sub-image for graph-search based segmentation. In this application, $\Delta L$ is set as 20 pixels.

2.2 Graph-Search Based Nucleus Segmentation

The graph-search based segmentation procedure is marked by a dashed box in Fig. 1. Given a cropped image, image unfolding is performed by transforming the image coordinates from Cartesian to polar with the center of the cropped bounding box used as the unfolding center. As a result, the round-like border of the nucleus becomes a curve which starts from the first column and ends at the last column in the unfolded image. With the unfolded image, a graph with $n_g$ graph columns is constructed and searched for the optimal path, where $n_g$ equals to the number of columns of the unfolded image. In this graph, each node corresponds to a pixel in the unfolded image. The successors of a node are defined as the three nodes on the adjacent column corresponding to three possible changes of edge direction. Costs assigned to each node in the graph reflect the nucleus-specific characteristics (see Section 2.3 for details). Finally, a globally optimal path with the lowest cost is determined by dynamic programming, and the path is mapped onto the original sub-image by reversing the initial unfolding transformation.

2.3 Cost Function Design

The cost function used for the identification of nucleus boundary is of the primary importance for the success of the segmentation. In this paper, the cost assigned to the graph node contains an edge cost and a region cost, as shown in the panel “Cost Function” in Fig. 1,

$$c(i, j) = \alpha \cdot c_e(i, j) + \beta \cdot c_r(i, j),$$

(1)

where $\alpha$ and $\beta$ are the weights for the edge term and region term, respectively, satisfying $\alpha + \beta = 1$. Each of the two terms is normalized to the range [0,1].

More specifically, the edge cost $c_e$ is calculated based on the normalized image gradient magnitude and image gradient direction. We only consider the direction from dark to bright since the nucleus is always darker than the surrounding cytoplasm,

$$c_e(i, j) = \begin{cases} 0 & \text{if } g_{dir} \leq 180 \\ -g_{mag}(i, j) & \text{otherwise} \end{cases},$$

(2)
where \( g_{mag} \) and \( g_{dir} \) denote normalized gradient magnitude and gradient direction, respectively. Note that small deviations from this pattern are not critical because of the smoothness constraints of graph connections.

The region cost \( c_r \) is calculated based on the Mumford-Shah functional as proposed by Chan and Vese.\(^\text{14}\)

For our constructed graph, this cost is assigned as the sum of the inside and outside variances computed in the graph column as follows:

\[
c_r(i, j) = \sum_{j'=0}^{j \leq j} (I(i, j') - a_1)^2 + \sum_{j'=j+1}^{j'<J} (I(i, j') - a_2)^2 ,
\]

where the two constants \( a_1 \) and \( a_2 \) are the mean intensities of pixels below \((0 \leq j' \leq j)\) and above \((j < j' < J)\) the boundary, respectively. This term allows segmentation without the presence of gradients.

### 3. EXPERIMENTAL RESULTS

#### 3.1 Data

The experiments were carried out on two types of abnormal cervical cell images, which were acquired by different slide preparation and different staining methods: 1) Herlev\(^\text{7}\) — Pap-smear with Papanicolaou (Pap) stained cervical cell images and 2) HELBC\(^\text{8}\) — liquid-based cytology with H&E stained cervical cell images. In the Herlev dataset, there are four types of abnormal cells: mild dysplasia, moderate dysplasia, severe dysplasia, and carcinoma, with cell counts of 182, 146, 192, and 150, respectively. The Herlev dataset also provides manual segmentation for all nuclei. In the HELBC dataset, there are 64 abnormal cells from 15 cervical cell images. A pathologist manually traced boundaries of all abnormal nuclei twice, the expert segmentations served as the ground truth and were used to conduct inter-observer variability analysis.

#### 3.2 Nucleus Segmentation on Herlev Data

Extracting nucleus candidates is the first analysis step and is mainly followed by Li et al.’s\(^\text{4}\) preprocessing approach. Briefly, the \( L^* \) channel in CIELAB color space is extracted, and the spatial K-means clustering algorithm is used to divide the image pixels into three classes including cytoplasm, nuclei and background. Then, geometric information is used to select the most likely nucleus candidates. After that, different from Li et al.’s\(^\text{4}\) method, we simply select the segmented component with the closest distance to image centroid as the nucleus candidate, on which our annotation protocol is applied to crop sub-image for graph-search based segmentation.

The evaluation of the proposed segmentation method was based on comparison with three state-of-the-art methods including snake-\(^\text{4}\), watershed-\(^\text{5}\), and FCM-based\(^\text{6}\) approaches using pixel-based criterion including precision and recall as in Ref.\(^\text{4–6}\)

The precision and recall indicate the fraction of the amount of nucleus correctly identified in the segmented object, and in the reference ground truth, respectively. The parameters in this experiment are set as \( n_g = 180 \), \( \alpha = 1 \) and \( \beta = 1 \).

Fig. 2 shows some examples of our segmentation results on the Herlev dataset. It can be seen that our method generates accurate nucleus boundaries across a variety of challenges (different size, irregular shape and non-uniform chromatin distributions) presented in abnormal nuclei. Table 1 shows the quantitative comparison of different methods in terms of average precision and recall of segmentation for all types of abnormal nuclei from Herlev dataset. It can be seen that our new graph-search based method outperforms the state-of-the-art approaches\(^\text{4–6}\) on most sub-datasets. Note that Ref.\(^\text{3}\)’s results in this table are from the reproducing in Ref.\(^\text{5}\). The proposed graph-search based method was implemented using Matlab and tested on an HP Z400 workstation with 3.33 GHz Xeon W3680 CPU, 24 GB of RAM, running Windows 7 SP1 Enterprise. The mean execution time of graph-search is 0.05 s per sub-image.
Figure 2. Examples of graph-search based segmentations on abnormal cervical nuclei from Herlev dataset. In each sub-figure ((a)–(d)), from the first to the third rows are original image, ground truth (green boundaries), and our segmentation results (black boundaries), respectively.
Table 1. Comparison of average nucleus segmentation performances of snake-, \(^4\) watershed-, \(^5\) FCM-, \(^6\) and our graph-search based methods on the abnormal cervical cells from Herlev data. \(^7\) Bold values indicate the highest performance for each column.

<table>
<thead>
<tr>
<th>Methods</th>
<th>Mild dysplasia</th>
<th>Moderate dysplasia</th>
<th>Severe dysplasia</th>
<th>Carcinoma insitu</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Precision</td>
<td>Recall</td>
<td>Precision</td>
<td>Recall</td>
</tr>
<tr>
<td>Ref.(^4)</td>
<td>0.92±0.13</td>
<td>0.90±0.16</td>
<td>0.89±0.15</td>
<td>0.87±0.17</td>
</tr>
<tr>
<td>Ref.(^5)</td>
<td>0.88±0.17</td>
<td>0.86±0.16</td>
<td>0.91±0.17</td>
<td>0.86±0.14</td>
</tr>
<tr>
<td>Ref.(^6)</td>
<td>0.80±0.31</td>
<td>0.86±0.26</td>
<td>0.81±0.25</td>
<td>0.88±0.19</td>
</tr>
<tr>
<td>Our</td>
<td>0.87±0.17</td>
<td>0.96±0.11</td>
<td>0.88±0.14</td>
<td>0.97±0.06</td>
</tr>
</tbody>
</table>

### 3.3 Nucleus Segmentation on HELBC Data

Extracting nuclear candidates is an extension of our previous approaches,\(^8,\(^15\)\) a multi-way graph cut is used to segment the cytoplasm, and an adaptive thresholding is used to coarsely locate nucleus candidates for further refinement. For more details, please refer to the work of Zhang et al.\(^8,\(^15\)\) On the cropped sub-image, the pixel values of background region (obtained from cytoplasm segmentation stage) are replaced by zeros. Then mean-shift filtering\(^16\) is applied to eliminate noise and smoothen the texture distribution of chromatin, and the V channel in HSV color space is extracted for graph-search based segmentation.

The evaluation of the proposed segmentation method was based on comparison with our previous approach\(^8\) using pixel-based criterion including precision, recall, and F-measure as in our previous evaluation.\(^8\) The F-measure measures the harmonic mean of precision and recall. Furthermore, linear regression analysis, which used nuclear area as a quantitative measure, was used to evaluate the relationship between the manual and automatic segmentation. The parameters in this experiment are chosen as \(n_g = 72\), \(\alpha = 1\) and \(\beta = 0.2\).

Fig. 3 shows some examples of our segmentation results on the HELBC dataset. Table 2 provides the comparison of our new method, previous method, and intra-observer variability in terms of average precision, recall, and F-measure of segmentation for all analyzed abnormal nuclei. As can be seen, our new graph-search based method outperformed the previous approach.\(^8\) Fig. 4 shows results of linear regression analysis. Compared with our previous approach, which achieved \(r = 0.938\), the new method showed substantially improved correlation with manual segmentation (\(r = 0.981\)), which was virtually identical to inter-observer variability of expert pathologists (\(r = 0.984\)). The mean execution time of graph-search is 0.02 s per sub-image.

Table 2. Comparison of average nucleus segmentation performance of graph cut-\(^8\) and our graph-search based methods on abnormal cervical cells from HELBC dataset.\(^8\)

<table>
<thead>
<tr>
<th>Methods</th>
<th>Precision</th>
<th>Recall</th>
<th>F-measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ref.(^8)</td>
<td>0.88±0.14</td>
<td>0.91±0.07</td>
<td>0.884±0.08</td>
</tr>
<tr>
<td>Our new method</td>
<td>0.91±0.04</td>
<td>0.95±0.04</td>
<td>0.930±0.03</td>
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<tr>
<td>Intra-observer</td>
<td>0.94±0.04</td>
<td>0.96±0.03</td>
<td>0.953±0.02</td>
</tr>
</tbody>
</table>

### 4. CONCLUSIONS

A general graph-search based method for improving the segmentation of abnormal cervical nuclei was reported. The nuclear shape constraint was embedded in the construction of the segmentation graph. Globally optimal segmentation is guaranteed according to the cost function based on nucleus-specific edge- and region-information. The method was tested on abnormal nuclei from two cervical cell datasets. The experimental results demonstrated the superior performance of the proposed method when comparing with state-of-the-art methods in terms of abnormal nucleus segmentation accuracy, indicating its potential to improve the sensitivity of automation-assisted cervical cancer screening techniques.

### ACKNOWLEDGMENTS

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Figure 3. Examples of achieved graph-search based segmentation on abnormal cervical nuclei from the HELBC dataset. In each sub-figure, from the first to the third rows are original image, ground truth (green boundaries), and our segmentation results (yellow boundaries), respectively.

Figure 4. Statistical correlation analysis between automated method and manual segmentation on abnormal cervical nuclei from HELBC dataset.

![Statistical correlation graphs](image-url)
REFERENCES


