

Research Article

Incorporating a Local Binary Fitting Model into a Maximum Regional Difference Model for Extracting Microscopic Information under Complex Conditions

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This paper presents a novel region-based method for extracting useful information from microscopic images under complex conditions. It is especially used for blood cell segmentation and statistical analysis. The active model detects several inner and outer contours of an object from its background. The method incorporates a local binary fitting model into a maximum regional difference model. It utilizes both local and global intensity information as the driving forces of the contour model on the principle of the largest regional difference. The local and global fitting forces ensure that local dissimilarities can be captured and globally different areas can be segmented, respectively. By combining the advantages of local and global information, the motion of the contour is driven by the mixed fitting force, which is composed of the local and global fitting term in the energy function. Experiments are carried out in the laboratory, and results show that the novel model can yield good performances for microscopic image analysis.

1. Introduction

Observing and analyzing microscopic information has become one of the most important ways for exploring the microcosmic world for mankind. One typical issue is cell image analysis, which is at the forefront of clinics and bioengineering. In recent years, biological discovery and its translation into new clinical therapies have advanced rapidly. Pathologists use histopathological images of biopsy samples removed from patients and examine them

under a microscope. While examining such images, a pathologist typically assesses the deviations in the cell structures and the change in the proportion between nucleolus and enchylema across the tissue under examination [1]. It is crucial to discover an automatic method to detect the contour of the cell and its nucleolus [2]. Cell detection is critical to disease diagnosis and prevention.

Dealing with cell images, there may exist many complex conditions such as large density of many cell objects, overlapping, and complex nucleus structures. This paper proposes a hybrid contour model for segmentation of the cell nucleolus and membranes. The proposed algorithm can handle cell overlapping and calculate a number of morphological parameters as well. By adopting the affinity propagation algorithm, a classifier can be designed for cell classification. Local and global intensity information is used as the driving forces of the active contour model under the guidance of the maximum regional difference. The local and global fitting forces ensure that local dissimilarities can be captured and global different areas can be segmented, respectively. This hybrid contour can capture the image details in the nucleus area relative to the traditional contour model, which is important to study the morphological nucleus parameters.

A tremendous amount of research work has been conducted in the area of microscopic image processing [3]. There are some challenges mentioned in these studies. The noise pollution is the most frequently occurring problem. It arises from staining the biopsy samples, and uneven distribution of the stain usually causes problems in processing the stained material. Besides noise, a strong shading effect is apparent in the images so that the cell images do not appear smooth. Accurate cell segmentation often precedes other analyses such as that of the morphologic process and behavior. Active contour models have been among the most successful methods facing the challenge mentioned above [4, 5]. Techniques based on active contour models have the potential to produce better estimates of cell morphologies.

The existing active contour models can be categorized into two classes: edge-based models [5–7] and region-based models [8–10]. The edge-based model directly uses intensity gradient information to attract the contour toward the object boundaries. Therefore, this kind of model has a worse performance for weak object boundaries since the cell image is very fuzzy due to low contrast at the location of the cell membrane. The region-based model aims to identify each region of interest by using a certain region descriptor. It guides the motion of the contour and is to some extent less sensitive to the location of initial contours [11, 12]. It is therefore more suitable for cell segmentation [13].

The Chan-Vese model [14] is one of the most popular region-based active contour models. This model has been successfully used for segmenting images. However, the regions of interest in images are often not statistically smooth and, therefore, the models are not applicable to cell images. Li et al. mentioned the intensity inhomogeneity as the biggest problem in low-signal-noise-ratio images such as biopsy samples and medical images [15].

In this paper, a novel model based on the region-based active contour model is proposed, which is able to detect the local unclear boundaries and segment the main differing regions successfully according to the principle of the maximum interregional difference. An energy function with two main terms, the local fitting term and the global fitting term, is defined in this model. The local fitting term produces a strong force to attract the contours and makes them stop at the boundaries although the object boundary is not clear or even blurry. The global fitting term ensures that the curve extracts the main object regions on the principle of the maximal regional difference. In addition, a strategic weight parameter, which is defined using the image intensity gradient information, is introduced to make the

two forces work together as a hybrid model. This parametric model induces a mixed force comprising local and global information as driving force.

2. Maximum Regional Difference Model

Chan and Vese [14] proposed an active contour model that segments an image into two sets of possibly disjoint regions, by minimizing a simplified Mumford-Shah function. Assume that $\Omega \subset \mathfrak{R}^2$ are the image domain and $I : \Omega \rightarrow \mathfrak{R}$ are the given image. Mumford and Shah consider segmentation as a problem of seeking an optimal contour C that divides the image domain into two approximated piecewise-constant regions with intensities u_i and u_o . Denote C as its boundary. Thus, the global data fitting term in the Chan-Vese model is defined as follows:

$$E^{CV}(c_1, c_2) = \int_{\bar{\Omega}} (I - c_1)^2 dx dy + \int_{\Omega} (I - c_2)^2 dx dy, \quad (2.1)$$

where Ω and $\bar{\Omega}$ represent the regions outside and inside the contour C , respectively, and c_1 and c_2 are two constants that fit the image intensities outside and inside C .

This model considers pixels within the same region as having the most similarity and makes up for the shortcomings of the edge detector. When the contour accurately represents the object boundary, the two fitting terms minimize the fitting energy value. In each segmented area, the clustered pixels' mean value approximately equals c_1 and c_2 , respectively. Thus the fitting terms with respect to c_1 and c_2 are the driving forces that evolve the curve motion on the principle of inner region homogeneity.

Since the regional difference is the guideline in image segmentation, the interregional differences should be considered as the model's driving force as follows:

$$E = -\frac{1}{2} \cdot (c_1 - c_2)^2. \quad (2.2)$$

This kind of region-based active contour model energy is characterized by the maximum dissimilarity between regions. To minimize the energy E in (2.2) is the same as maximizing the difference between different regions. Equation (2.2) formulates the global instructive guidance term. This paper revises the guidance term which is defined as follows:

$$E = -\frac{A}{2} \cdot (c_1 - c_2)^2, \quad (2.3)$$

where A represents the entire image area. The curve evolution of the contour C is defined as

$$E^G(c_1, c_2) = A \cdot (c_1 - c_2) \left(\frac{I - c_1}{A_{c1}} + \frac{I - c_2}{A_{c2}} \right) \cdot N, \quad (2.4)$$

where $A_{c1} = \int_{\bar{\Omega}} dx dy$ and $A_{c2} = \int_{\Omega} dx dy$, denoting the areas outside of the contour and inside of the contour, respectively, and N denotes the outward unit normal of C . In order to show a stable value of (2.4) rather than an oscillating one when the contour divides

the area with a small value, that is, to avoid the denominator in (2.4) from being zero, we approximately evolve the E^G as follows:

$$E^G(c_1, c_2) = (c_1 - c_2)(I - c_1p_2 - c_2p_1) \cdot N, \quad (2.5)$$

where p_1 represents the ratio between A_{c_1} and A and p_2 represents the ratio between A_{c_2} and A .

3. Incorporation of the Local Binary Fitting Model

Though the E^G in (2.5) regards the regional difference as the guideline of curve evolution, the region-based model has little ability to deal with the intensity inhomogeneity or shading effect caused in the imaging process. The region-based model considers the global difference as the driving force rather than local detail information, and thus it needs a term of local fitting energy to improve the performance of segmentation in the inhomogeneous area.

Li et al. proposed a local binary fitting (LBF) model, which utilizes the local intensity information [15, 16]. An important parameter called the kernel function is introduced to denote the range of the local area. Additionally, f_1 and f_2 as the two spatially varying fitting functions are used to approximate the local intensities [17, 18]. In the LBF model, the local fitting term is defined as

$$E^{\text{LBF}}(\phi, f_1, f_2) = \lambda_1 \int \left[\int K_\sigma(x-y) |I(y) - f_1(x)|^2 H(\phi(y)) dy \right] dx \\ + \lambda_2 \int \left[\int K_\sigma(x-y) |I(y) - f_2(x)|^2 (1 - H(\phi(y))) dy \right] dx, \quad (3.1)$$

where H is the Heaviside function and K_σ is a Gaussian kernel that $K_\sigma(x)$ decreases and approaches zero as $|x|$ increases. The function $f(x)$ calculates the fitting degree around point x , and x can be considered as the center point of the local area. One of the greatest advantages of this LBF model is that it discovers the object boundaries more precisely than the Chan-Vese model.

The proposed method makes use of the advantages of the region-based model, as in (2.5), and the local binary fitting model by taking the local and global intensity terms into account. The entire energy model is defined as

$$E^M(\phi, c_1, c_2, f_1, f_2) = (1 - \lambda_g) \cdot E^{\text{LBF}}(\phi, f_1, f_2) + \lambda_g E^G(\phi, c_1, c_2), \quad (3.2)$$

where λ_g is the strategic weight parameter, $E^{\text{LBF}}(\phi, f_1, f_2)$ is defined in (3.1), and $E^G(\phi, c_1, c_2)$ is defined in (2.5). The strategic weight parameter λ_g is defined as

$$\lambda_g(x, y) = \frac{1}{(1 + \alpha |\nabla I(x, y)|)}, \quad (3.3)$$

where $|\nabla I(x, y)|$ represents the gradient information in image I and α is a positive constant.

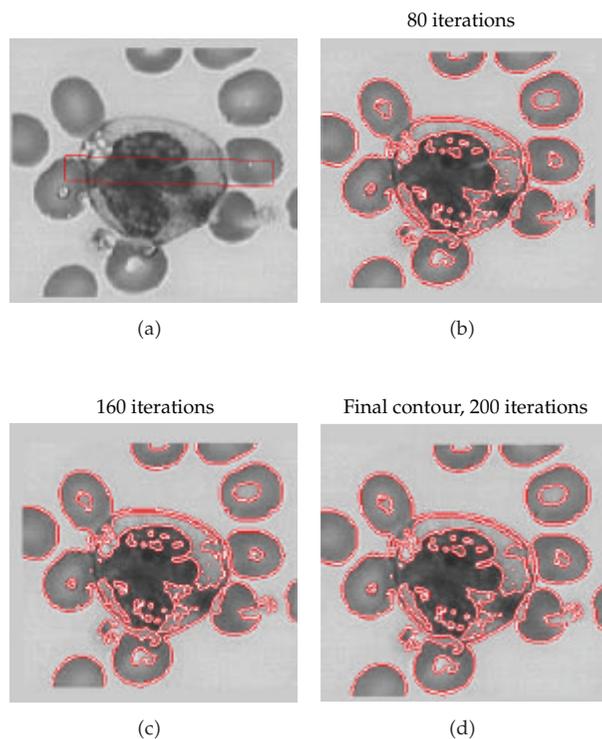


Figure 1: Neutrophil segmentation and level set function ϕ .

This strategic weight parameter realizes the trade-off into a hybrid model [19, 20]. Working with the mixed energy restriction terms, the curve's driving force appears strategically. When the local image area is flat or far away from the object boundaries, the value of $|\nabla I(x, y)|$ is relatively small therefore the right side of (3.3) has a value approximating one. The hybrid model is guided to maximize the interregional difference. $|\nabla I(x, y)|$ would gain a big value when the point (x, y) is located in the region with intensity inhomogeneity where the object boundaries exist, thus the value of $\lambda_g(x, y)$ is close to zero. The model possesses a potential force to extract local boundaries. It combines the advantages of the local fitting model and the global regional difference model by the use of intensity gradients as its strategic parameter.

By minimizing the energy function in (3.2), we face solving a partially differential equation. The gradient descent algorithm is chosen to give a numerical solution with respect to the PDE. In addition, we introduce a fitting term mentioned in [5] to regularize the level set function for accurate computation by penalizing the deviation of the level set function ϕ from a signed distance function. It is defined as

$$P(\phi) = \int \frac{1}{2} (|\nabla \phi(x)| - 1)^2 dx. \quad (3.4)$$

Besides, we introduce a length restriction term that has been used in the Chan-Vese model to

smooth the zero level set contour,

$$L(\phi) = \int |\nabla H(\phi(x))| dx. \quad (3.5)$$

Now, the entire model proposed in this paper is defined as

$$\begin{aligned} E^E(\phi, c_1, c_2, f_1, f_2) \\ = E^M(\phi, c_1, c_2, f_1, f_2) + P(\phi) + L(\phi). \end{aligned} \quad (3.6)$$

The fitting functions f_1 and f_2 are given by

$$\begin{aligned} f_1(x) &= \frac{K_\sigma^*(H(\phi) \cdot I)}{K_\sigma^*H(\phi)}, \\ f_2(x) &= \frac{K_\sigma^*[(1 - H(\phi)) \cdot I]}{K_\sigma^*[1 - H(\phi)]}. \end{aligned} \quad (3.7)$$

c_1 and c_2 are constants defined as in [14].

4. Experiments and Results

4.1. Implementation Issues

To minimize the energy function with respect to ϕ defined in (3.6), we give the solution using a gradient descent algorithm which is defined as

$$\begin{aligned} \frac{\partial \phi}{\partial t} &= \lambda_g \cdot \delta(\phi) \cdot (c_1 - c_2)(I - c_1 p_2 - c_2 p_1) + (1 - \lambda_g) \cdot \delta(\phi) \cdot [\lambda_1 e_1 - \lambda_2 e_2] \\ &+ v \cdot \delta(\phi) \operatorname{div} \left(\frac{\nabla \phi}{|\nabla \phi|} \right) + \mu \left(\nabla^2 \phi - \operatorname{div} \left(\frac{\nabla \phi}{|\nabla \phi|} \right) \right), \end{aligned} \quad (4.1)$$

where λ_1, λ_2, v , and μ are constants and $\delta(\cdot)$ is the Dirac delta function. e_1 and e_2 are given by

$$e_i(x) = \int K_\sigma(y - x) |I(x) - f_i(y)|^2 dy, \quad i = 1, 2. \quad (4.2)$$

The iteration scheme is used by discretizing the PDE (4.1). The level set function ϕ ultimately sets the image object boundaries at $\phi = 0$. Furthermore, we set the parameters $\lambda_1 = \lambda_2 = 1$, $\mu = 1$, and $v = 60$. α equals three in the expression of $\lambda_g(x, y) \cdot \sigma$ in the Gaussian kernel K_σ equals two.

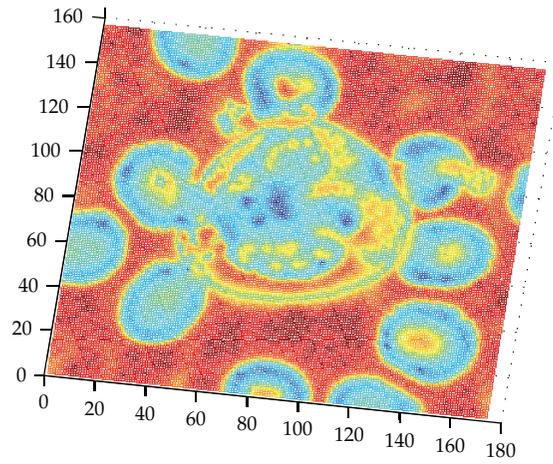


Figure 2: Level set function ϕ after 200 iterations.

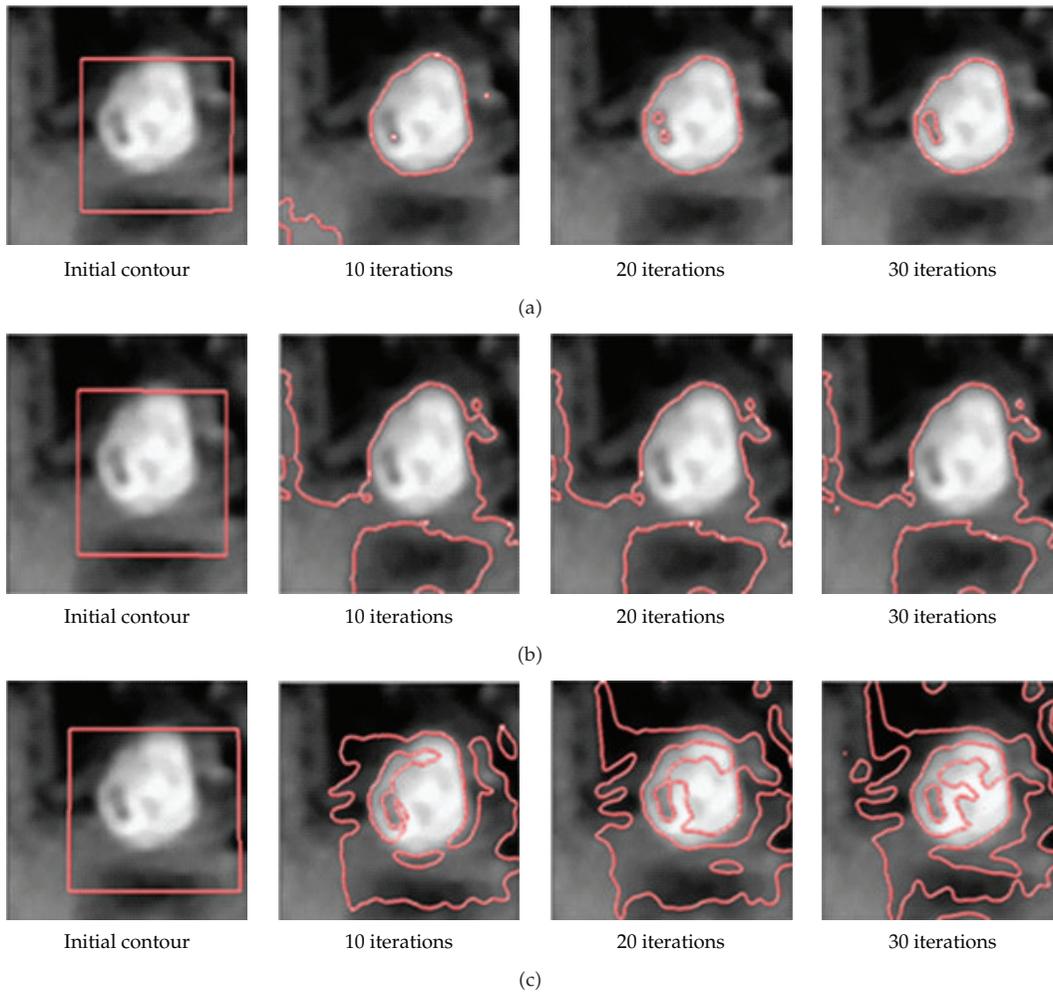


Figure 3: Comparison of different models.

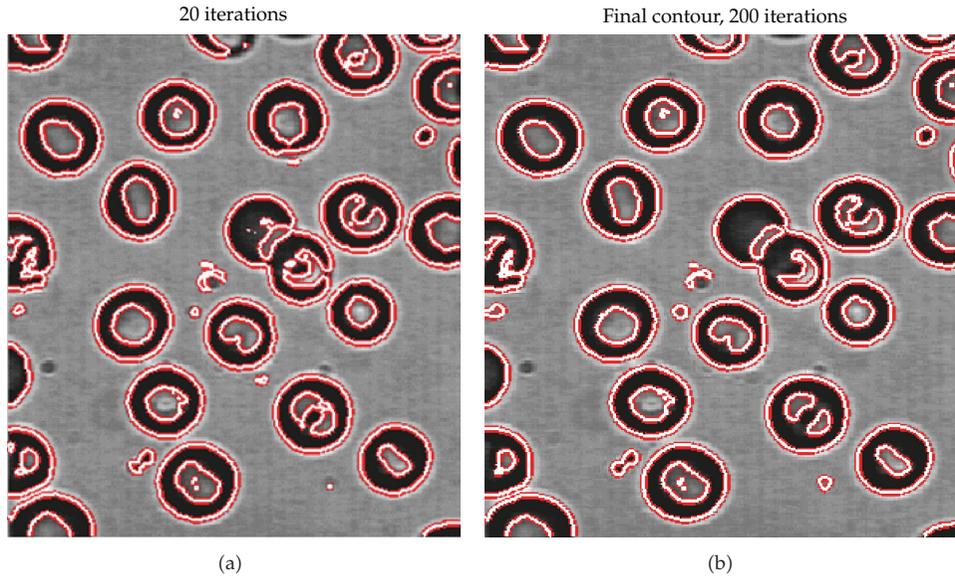


Figure 4: Another example for cell segmentation using the proposed model.

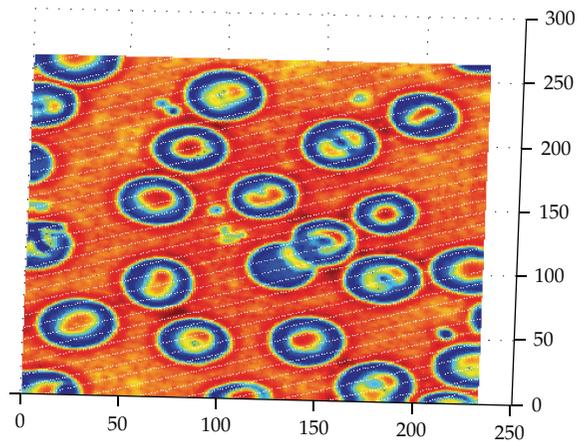


Figure 5: Corresponding function ϕ after 200 iterations.

4.2. Experimental Results

In this section, we use some cell images to demonstrate the mixed driving force in the proposed method for verifying its performance in detecting the contours of cell nucleolus and membrane. Figure 1 shows the process for segmenting neutrophil images. In Figure 1(a), the upper left picture depicts the initial contour and the Figures 1(b), 1(c), and 1(d) show how the curve evolves. It can easily establish the main cell nucleolus boundary and the weak object boundary of the cell membrane. The images resulting after 200 iterations of ϕ are shown in Figure 2. Due to its strong ability to capture local difference, the model can detect the weak boundary of the neutrophil membrane while it accurately distinguishes the nucleolus from the cytoplasm. The global driving force ensures that the model to segment the object has the

maximum regional difference and that failure cases are avoided. Moreover, a comparison has also been carried out in our experiments with the Chan-Vese model and the LBF model, using a tumor lymphocyte cell image as test images. The results are shown in Figure 3. Figure 3(a) is the result by our proposed model. Figures 3(b) and 3(c) show the results of the Chan-Vese and LBF model, respectively. The tumor cell in an intensity inhomogeneous condition is detected by the zero level set function. The model successfully extracts the nucleolus, whose size relative to the area of the cell is a significant parameter in biology.

Figure 4 illustrates another example for cell segmentation using the proposed model, where the parameters are $\alpha = 3$, $\nu = 0$, $\lambda_1 = 1$, $\lambda_2 = 2$, and $\sigma = 3$. Figure 5 shows the corresponding function ϕ after 200 iterations.

5. Conclusion

The model proposed in this paper yields a relatively more desirable performance than the traditional models, although the results still feature over segmentation in the nucleolus area. However, this over segmentation problem can be overcome by a postmorphological process. For example, we find the locations where function $\phi < 0$ and $\phi > 0$ ($\phi = 0$ denotes the contour of the object) and substitute them with a binary value of zero and one, respectively. Then, we give a postprocess by setting a threshold value of the area size in the region of the neutrophil nucleolus area to eliminate the oversegmentation.

From the experimental results, it follows that the proposed hybrid model can well capture the weak edge boundary by using the local fitting terms, while it observes the rule of regional difference and uses it as guideline to form the fitting terms that drive the contour to accurately capture the boundaries. The experiments demonstrate that it performs well in segmenting the nucleolus and cell membrane.

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