

# CELL IMAGE SEGMENTATION: REVIEW OF APPROACHES

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**Abstract.** Many techniques have been developed during last 10 years for cell recognition in biomedical images. Differences depend on both application field and researcher's scientific background. We consider here methods most commonly used for cell extraction in biomedical images. We briefly review a number of papers that are representative of the various approaches.

## 1. INTRODUCTION

The objective analysis of biomedical (cytological and histological) images has been the subject of research for many years. One of the most difficult fields in biomedical image analysis is automated extraction and classification of cells. This task can be divided into four sub-tasks: (1) the isolation of single cells, cell clusters and clumps as well as artifacts, (2) the segmentation of the cell image into cells, nucleus and cytoplasm, (3) the extraction of cell features such as size and density of the nucleus and cytoplasm, grey level extrema, fractal dimension, texture parameters and shape measures, and (4) the use of these features to classify the cell as normal or abnormal.

However, due to a complex nature of biomedical images, it is practically impossible to select or develop automatic segmentation methods that can be applied for any type of these images. That is why most of the papers consider particular features of cell images and methods of their segmentation. The results also depend on a cell image quality and when difference between cell or nuclear (kernel) and background is small, most of the methods do not work.

In this paper, we consider methods that are most commonly used for cell extraction in biomedical images. We briefly review a number of papers, that are representative of the various approaches. The comparison of approaches is also given.

## 2. BIOMEDICAL IMAGES

Biomedical images have usually a quite complicated structure. They can contain cells, fibers, vessels and other objects. Moreover, one object in the image may be a component of another. The majority of objects on biomedical images has low contrast and they are characterized by various geometrical and optical characteristics.

The general biomedical image is formed by the various fragments of a fabric consisting of groups of homogeneous cells or fibres. These fragments are the objects interesting for researchers, and frequently have textural character.

In biomedical images, the ratio of intensified characteristics of a background and objects is usually important. More often emptiness, very fine cells, fibres, any particles form a background. Images of the structures creating a background are so small that their gray-scale images form a smooth surface.

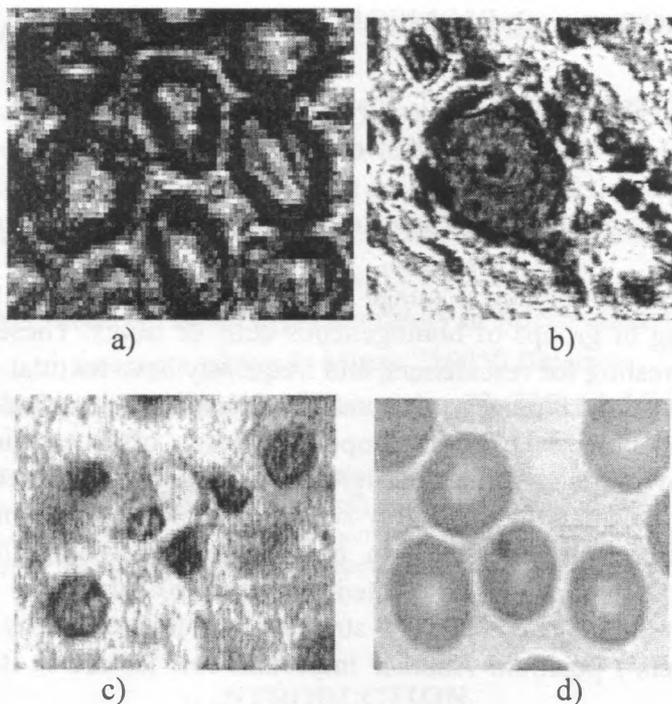
Cells, fibres and vessels can be classified by using their shape and structure. The cell shape can be treated as almost round-shaped (circular-based primitive) and not elongated. The cell structure is characterized by its nuclear and nucleolus (kernels') position. Another important cell feature is its position in a tissue.

Examples of some biomedical images are shown in Figure 1.

Methods that should be selected for segmentation of a cell in a tissue depend on image gray-scale characteristics of cells and background, and their correlation. By these characteristics, cell images can be divided into three following groups:

1. Images containing cells of one type, and cell gray values are different from background values (Fig.1d). This is the simplest case.
2. Image containing cells of one type where cell gray values are changed monotonically and can be equal to background pixels in some cases (Fig1c).
3. Image containing various cells and object types (vessels, noise) (Fig.1a,b). Pixels can have any value.

Depending on the image complexity different segmentation algorithms can be chosen.



**Fig.1. Example histological images: a) neural fibers in cross section b) Neuron of a human brain, c) human liver cells, d) cells of blood with radioisotope labels.**

### 3. CELL IMAGE SEGMENTATION APPROACHES

There are various approaches to segment biomedical images. We shall try to classify and briefly describe them. However, we can not give all references and shall give only representatives for each approach.

**Mathematical morphology.** One of the most popular approaches for cell image segmentation is based on mathematical morphology. Many morphology-based algorithms for cell segmentation have been proposed [1-3]. Thus, paper [3] proposes an iterative morphological algorithm for segmentation of textured cell images encountered in cytology. The initial image segmentation is determined by classifying the image local variation information obtained with dilation and erosion operations. A median filter is then used to smooth the initially segmented image. A modified median filter is applied subsequently to correct possible classification errors inside the cells. The modified median filter can clear small regions of misclassified pixels while avoiding significant changes to the cell profiles. An erosion operation is finally used to restore the cell regions.

**Edge detection.** Edge detection approaches for gray-scale biomedical images are probably the oldest ones. Traditionally, edge-based segmentation can be divided into two independent stages: edge detection and edge linking. The obtained edges are used to determine the cell location and contour model is further used to select the set of edges involved in this cell location. In paper [4], authors propose a new edge-based potential aimed at the elimination of local minima due to undesired edges. The new approach integrates knowledge about the features of the desired boundaries apart from gradient strength and uses a new method to eliminate local minima, which makes the segmentation less sensitive to initial contours.

**Snakes.** Classical snake models are edge-oriented and work well if the target objects have distinct gradient values. This is not always true in biomedical imagery, which makes the model very dependent on initial conditions. This approach was applied for biomedical image segmentation and has positive results but suffer from the well-known drawbacks of initialisation and minimisation. In paper [5] authors show that a Viterbi search-based dual active contour algorithm that is able to overcome many of these problems and achieve over 99% accurate segmentation on a database of 20 130 Pap stained cell images.

**Neural networks.** Neural networks started recently be used for cell segmentation. Paper [6] presents a method for automatic segmentation of sputum cells with color images based on a Hopfield neural network. The segmentation problem is formulated as a minimization of an energy function constructed with two terms, the cost-term as a sum of squared errors, and the second term a temporary noise added to the network as an excitation to escape certain local minima with the result of being closer to the global minimum. To increase the accuracy in segmenting the regions of interest, a preclassification technique is used to extract the sputum cell regions within the color image and remove those of the debris cells. The former is then given with the raw image to the input of Hopfield neural network to make a crisp segmentation by assigning each pixel to label such as background, cytoplasm, and nucleus. Paper [7] shows the algorithm for recognition of overlapping cells, and the improvement of recognizing adjoining cells by using the neural network. Initial values of the neural network are given to prevent form stacking in local minimum by the genetic algorithm.

**Fourier transform.** In spite of time-consuming computation, Fourier transform is also used for cell segmentation. In paper [8], an iterative cell image segmentation algorithm using short-time Fourier transform magnitude vectors as class features is presented. The cluster centroids of the magnitude vectors are obtained by the K-means clustering method and used as representative class features. The initial image segmentation classifies only those image pixels whose surrounding closely matches a class centroid. The subsequent procedure iteratively classifies the remaining image pixels by combining their spatial

distance from the regions already segmented and the similarities between their corresponding magnitude vectors and the cluster centroids.

**Hough transform.** The motivation in selecting the Hough transform as a means for locating nuclei is its ability to reveal any 'round' objects in an image. In paper [9], a fast method for detecting ellipses, and hence circles, is proposed. This method was applied to a number of typical cervical smear images. The inherent robustness of the Hough transform when dealing with obscured or deformed shapes resulted in few nuclei being missed, and some were detected which were not instantly obvious to the naked eye. The transform failed only in cases of severe deformation, or when nuclei had an eccentricity well outside the sought-after range. In paper [10], authors propose a multistage segmentation method for the isolation of cell nuclei in such images. In the first stage the compact Hough transform (CHT) is used to determine possible locations of the nuclei. The authors then define a likelihood function, which enables them to perform an optimization procedure based on the maximization of this function. Global gray-level histogram information is used in the algorithm to reduce the amount of computation and to reject unwanted artifacts.

**Thresholding.** Thresholding-based approaches are one of the more old, often used and simple approaches for cell image segmentation. Flexible and adaptive thresholds are required to consider variation in gray level intensities of the background and of the cell. Paper [11] evaluated three different methods of threshold determination: 1) A statistical procedure, which uses the interclass entropy maximisation of the gray level histogram. The iterative algorithm can be used for multi-threshold segmentation. The contribution of iteration step 'i' is  $2^{\sup i-1}$  / number of thresholds; 2) A numerical approach, which detects local minima in the gray level histogram. The algorithm must be tailored and optimized for specific applications like cell recognition with two different thresholds for cell nuclei and cell cytoplasm segmentation; 3) An artificial neural network, which is trained with learning sets of image histograms and the corresponding interactively determined thresholds.

**Deformable templates.** Many deformable models have been proposed in literature in which only one object is present and/or initialization is performed by hand that is not always convenient. Paper [12] presents an automatic method, based on the deformable template approach, for cell image segmentation under severe noise conditions. A cell extraction methodology is defined in three processes: 1) obtain evidence from the image about the location of the cells; 2) use this evidence to calculate an elliptical approximation of these locations; and 3) refine cell boundaries using locally deforming models.

**Color cell image segmentation.** Color became an important feature in cell image segmentation. Paper [13] proposes a set of effective algorithms to automatically detect lung cancer cells in the cytological color image of sputum

smears. To increase the stability and efficiency of the detection of the cancer cells, a hierarchical processing architecture is adopted for the segmentation and recognition. For segmentation, RGB space and Lab space are combined to segment cells. By this method, both the nucleus and cytoplasm of cancer cells can be separated from background. Then, the candidate cancer cells are selected using some morphological features of nuclei, the purpose of this step is to pick out most of the non-cancer cells and leave a few doubtful cells for further verification, therefore improving the efficiency of the whole recognition process. As the last step, for all the candidate cells, some statistic parameters in different color space are calculated, which are used as features for recognition. Paper [14] presents a new version the Constraint Satisfaction Neural Network (CSNN) algorithm that is used to segment color cell images in various details. This is accomplished by incorporating in the CSNN algorithm multiresolution scheme using pyramid structure. In paper [15], a new colour system is proposed to segment biomedical images.

#### 4. COMPARATION OF APPROACHES

Advantages and disadvantages of these techniques are summarised in Table 1.

Table 1. Summary of techniques for cell image segmentation

Technique	Advantages	Disadvantages	Types of objects to be processed	Time processing
Mathematical morphology	Fast, easy to implement	For simple enough images	Cells, nucleus of cells, vessels and fibers in longitudinal and cross section	Fast, medium.
Edge detection.	Simple and fast	For simple enough images	Cells, vessels and fibers in cross section	Fast
Snakes.	Precise cell extraction	Problem of initialization and mini-mization of energy function	Cells, nucleus of cells, vessels and fibers in cross section	Medium, long
Neural	Classification	Necessity to	Cells, nucleus	Long

networks	time is fast	have training data	of cells, vessels and fibers in longitudinal and cross section (only specific objects)	
Fourier transform.	Precise segmentation	High computational cost	Cells, nucleus of cells, vessels and fibers in longitudinal and cross section (only specific objects)	Long
Hough transform.	Good segmentation with clutter, occlusion and non-random noise	High computational cost and need of precise description of cells	Cells, vessels in cross section (only specific objects)	Long
Thresholding	Simple and fast	For simple enough images	Only contrast images	Fast
Deformable templates	Fast and robust	Initialization problem	Cells, nucleus of cells, vessels and fibers in cross section	Medium, long

From point of view of frequency with which different techniques have been used in various biomedical image interpretation system, we can say that the more often used approaches are based on thresholding, morphological operations and edge detection. Another quite a big group of algorithms is based on snakes and Hough transform. And the third group of approaches that are rare used are based on Neural networks and Fourier transform. Many new developed algorithms are based on the combination of the thresholding, edge detection, thinning, etc. We believe that a substantial part of cell image segmentation process can be built up with a suitable combination of them.

However, some peculiar techniques will always be necessary for accessing the whole informative content of cell images. Consequently, it is hard to clearly

answer the question whether general techniques for cell extraction are actually available, or the state of the art in this field is rather a collection of domain-dependent algorithms.

In spite of fast development of this area, several problems seem to be still open. How to correctly evaluate the result of segmentation? What errors can be allowed in the result of segmentation? Should errors be grouped according to their type?

Among the many algorithms that are in use for cell image segmentation, which are the best for each biomedical image type? Several of them are already well established as regards the obtainable results and could be applied in different contexts. To what extent are they transportable from one image type to another?

## CONCLUSION

The most commonly used algorithms for cell extraction in biomedical images have been briefly reviewed and several representative papers have been analysed. Cell images have been grouped into three families according to their complexity. Comparison of algorithms for cell image segmentation has been done.

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