

Optical result of seed  
detection affects the  
accuracy



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Optical microscopy is widely used to quantify single cell characteristics such as cell size or intracellular density. Accurate quantification is highly dependent on the cell segmentation results in the microscope image. The cell segmentation algorithms do not converge to a single solution with good performance and is developed with various algorithms depending on the characteristics of the target cell.

The imaging hardware and analysis software platforms have developed rapidly, but such cell segmentation studies have been relatively lagging behind. Cell segmentation is challenging due to the following three reasons. First, various experimental configurations, such as cell types or imaging protocols, produce images with different shapes or brightness characteristics. Second, since cells generally have dynamically changing shapes over time, we cannot mathematically define the cell shape. Third, the boundaries of some cells that are in contact with each other during cleavage or migration may be unclear, and experts may have different opinions whether one cell or more cells are connected. In order to overcome the various brightness problem of cells appeared by the image condition, representative image binarization methods such as Otsu method [2-4] or Watershed transformation [5] were improved to brightness-invariant localization or adaptive binarization. These methods are simple to use without any additional parameters, but it is difficult to expect good performance in complicated backgrounds or splitting overlapping or adjacent objects. Energy-minimization based image segmentation techniques show better results than the intensity-based techniques in the above-mentioned difficult environmental conditions. ACM (Active Contour Model) [6-9] is a representative energy-minimization technique

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that generates appropriate results on noise images based on initial points defined by a user. GC (graph cut) [10-14], another segmentation method based on energy minimization, finds a globally optimal solution for a given initial value.

Machine learning-based methods typically show more than a certain level of segmentation performance in various datasets [15-19]. Especially, unsupervised-learning based cell segmentation method using blob detector produces boundaries similar to those perceived by humans [2021]. Conventional cell segmentation studies usually consist of seed detection to find the approximate location of a cell and cell split to divide the region. In the conventional studies, due to the structure in which the result of seed detection affects the accuracy of cell division, precise seed detection must be preceded.

Furthermore, since these techniques require a large number of parameters and the parameters should be appropriately selected depending on the type of the target cell and the imaging condition, the segmentation results are sensitive to the parameter configuration. In this paper, we propose a cell segmentation method using a cell region discriminator  $R$  that detects a cell region and a multi-cell discriminator  $M$  that determines whether a cell region is divided by an Expectation-maximization algorithm (see Fig. 1).  $R$  identifies regions of interest for cells using linear regression analysis and features of statistical cell imaging and distribution characteristics for image brightness. The region of interest (ROI) is divided into two cells using expectation-maximization to the coordinates of the detected ROI and their local maximum point coordinate feature.

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In the process of dividing the region, M determines whether to re-segment the region by finding a hyperplane for the surface error in the cell area and the area of the segment boundary. The research has the following two contributions. The proposed method does not require seed detection because it divides the cell independently of the seed detection. Using various learning techniques trained from each image data, ROI detection and cell division show high accuracy without changing parameters according to data.