Voronoi-Based Segmentation of Cells on Image Manifolds

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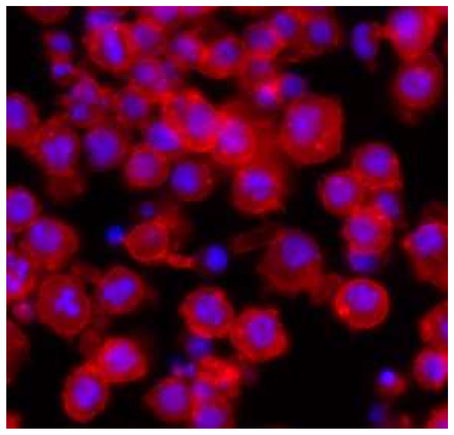
1. Background. Segmentation of Cells in Fluorescence Microscope Images

Protocol and Assumptions:

- Cells are stained with fluorescent dyes that mark nuclei and cytoskeleton.
- Nuclei are easily located through automatic methods, and well-separated in the images.
- Cells are roughly the same size, and have a homogeneous interior.
- Cells can be automatically differentiated from background.



Our algorithm is used to identify which pixels of an image belong to which cell, i.e., where the boundaries between cells should be drawn. The approach is based on finding the Voronoi regions of the nuclei in a manifold whose metric is defined by the cell image.

2. Voronoi Regions Under an Image-Based Metric

A common approach in segmenting cells is to use a fixed offset from the nuclei. When cells are close together, this is equivalent to using Voronoi regions in the plane, i.e., without reference to the cellular appearance.

Another common approach is to use a Watershed transformation to locate boundaries. However, this assumes that the boundaries between cells are substantially brigher or darker than the interiors.

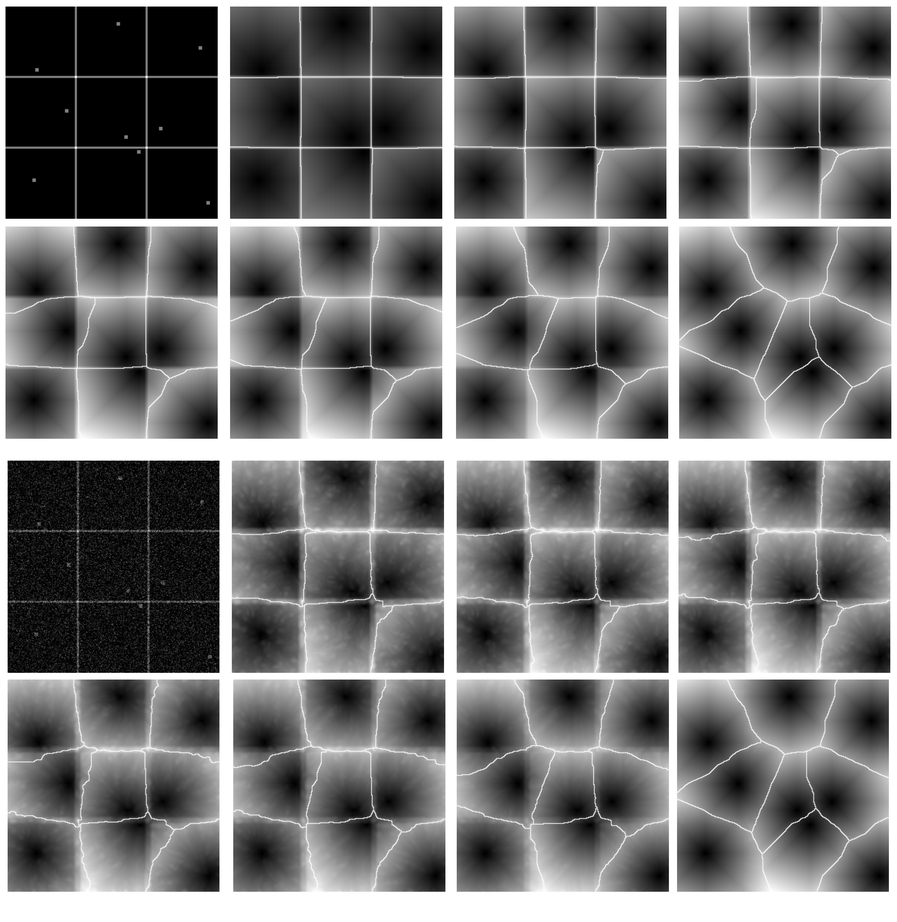
Our method is similar to the fixed-offset method, but is guided by the appearance of the cells. We define a metric:

$$\mathbf{G} = \frac{\nabla \mathbf{g}(\mathcal{I}) \nabla \mathbf{g}^T(\mathcal{I}) + \lambda \mathbf{I}}{1 + \lambda}$$

where I is the image, $\boldsymbol{g}$ is a blurring filter with a small radius, and $\mathbf{I}$ is the 2x2 identity matrix. λ is a regularization parameter, which makes the metric more Euclidean as it increases. The metric has the effect of pronouncing distances measured across edges in the image.

Given the metric above, we assign each foreground pixel to the nearest nucleus within the manifold defined by the metic. Boundaries between cells are where adjacent pixels are assigned to different nuclei.

3. Synthetic Examples



4. Comparison to Manual Segmentation

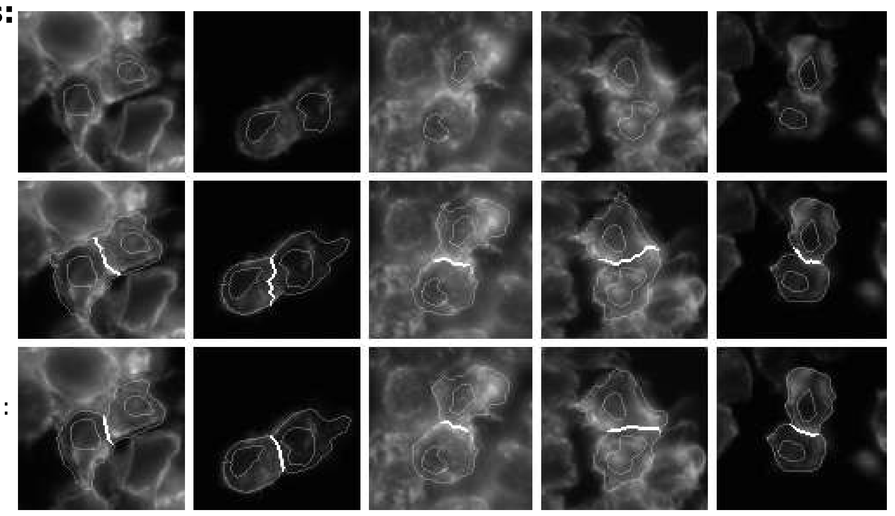
Sixteen pairs of nucleus and cell images were hand-segmented by an expert. We used these images to evlauate the performance of our algorithm.

Typical results:

Input:

Our algorithm:

Manual segmentation:

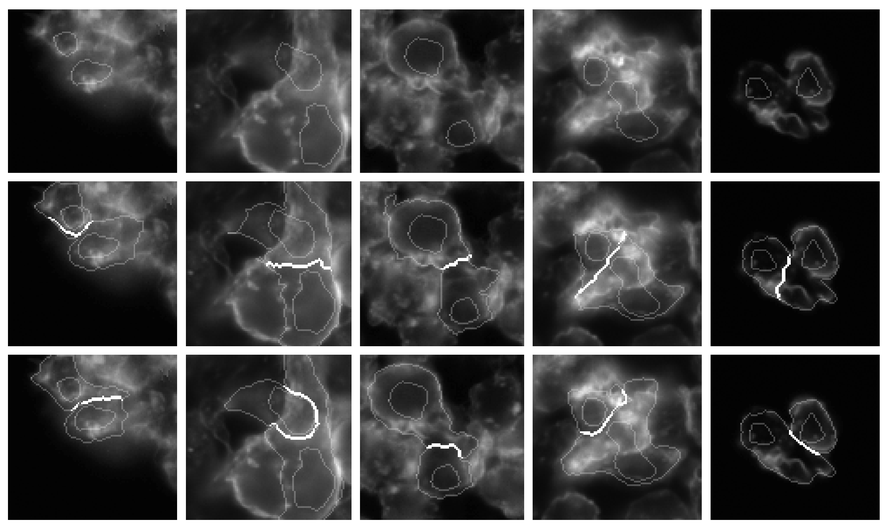


Worst results:

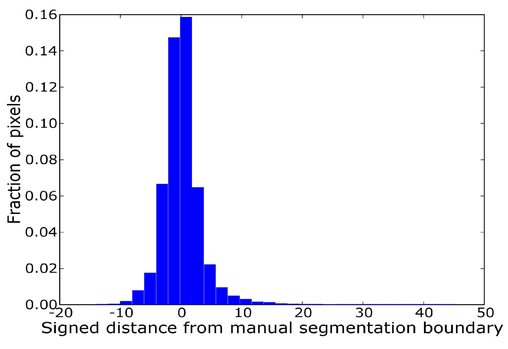
Input:

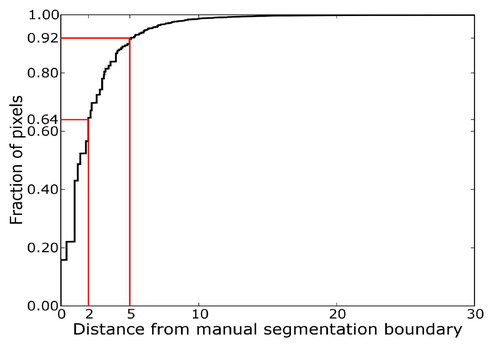
Our algorithm:

Manual segmentation:



Quantitiative comparison





5. Discussion

Using nuclei as seed regions and a metric based on cell image appearance yields a robust and simple method for segmentation of individual cells. This method compares favorably to manual segmentations by an expert.

We are interested in exploring how our metric might be used in the separation of foreground and background in the cell images. We would also like to explore the connection between our metric and metrics used in other methods, such as Geodesic Active Contours.

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