

3D SEGMENTATION OF CELLS AND NUCLEI IN TISSUE USING DYNAMIC PROGRAMMING

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Quantitative understanding of the molecular processes underlying cell-cell interactions in tissues are lacking, in part due to the absence of an efficient and highly reliable method for segmenting every cell or nucleus in a 3D tissue image. Thus we developed an automated algorithm for this task, which incorporated two major criteria. First, it was error-free when judged against the human visual system. This was achieved by including a minimal degree of interactive guidance in the segmentation of each object. Second, it worked on very noisy images that could arise from live cell imaging. For 2D images, this requires dynamic programming (DP) for finding the globally optimal border [1]. In this study, we extended the algorithm to 3D by combining DP with combinatorial searching in order to identify the surface enclosing the object as a series of overlapping optimized ribbons. Tests performed on simulated 3D objects that mimicked the noise and spatial resolution of a confocal microscope and without any interactive correction reported an average deviation between the true and segmented surfaces of 1 to 2 voxels, demonstrated the segmentation of objects with moderately sized concavities and did not show deterioration in performance for close or touching objects. Tests on a variety of fluorescence-labeled mammalian samples demonstrated over 99% correct segmentation for whole cells and nuclei. The figures below give some examples. The method will be most useful in applications where 10s and 100s of cells per sample require segmentation with the assurance that each cell is correctly segmented based on visual judgment. Following segmentation, it is possible to quantitatively analyze both the individual properties of cells and the contextual relationships between cells in tissue, leading to a much deeper understanding of biological processes underlying development of multi-cellular organisms and solid tumorigenesis.

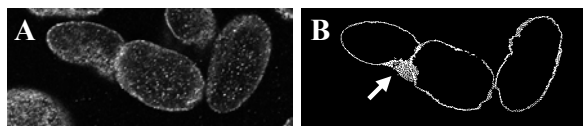


Figure 1: A: Cell nuclei labeled with a fluorescence surface marker. B: Surfaces of segmented nuclei. The contiguous area of surface marked by the arrow is where the true object border is in the xy plane of the 3D image.

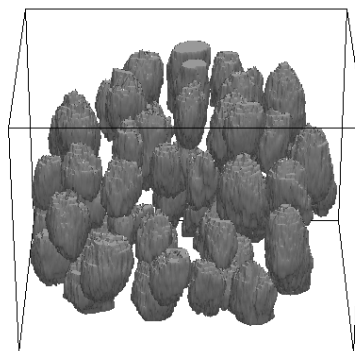


Figure 2: Surface rendering of nuclei in an acinus of MCF-10A cells following segmentation of every nucleus.

[1] D. Baggett; M. Nakaya; M. McAuliffe; T.P. Yamaguchi, and S.J. Lockett, “Whole cell segmentation in solid tissue sections” *Cytometry*, **67A**, 137-43 (2005).

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