From Multiscale Edges to 3D-Graph Representations of Nerve Cells from Confocal Microscope Scans

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Confocal microscopy is a scanning laser technique which allows the recording of 3D images of small structures usually stained with a fluorescent dye. To analyze the neuronal structures, the scans have to be segmented accurately. This is in most of the laboratories done semi-automatically using computer assistance tools like Eutectic or Neurolucida which facilitate the manual tracing of the structures. For complicated objects like neurons, which may have 1000 or more branches, this may take several man-weeks, severely limiting the applicability of the methods in comparative neuroanatomic studies [2]. Objective morphological cell comparisons or the study of related electrical properties require a geometrically labeled graph description of the neuronal branches [6]. Designing tools for the automated analysis of confocal microscope images, in particular stained neurons is however a difficult task [5]. Problematic are: (i) large variations in object size, from several tens of microns (thick dendrites), down to the resolution limit (small processes and spines), (ii) large variations in image contrast, (iii) unequal staining of processes leading to large fluctuations of gray-values along the neuronal branches, and (iv) noise of various sources (autofluorescence, photon shot noise, detector noise) with various spatial and temporal properties.

In the current work we describe new methods for the post-processing of 3D confocal microscope images taken from stained neurons which - finally - lead to the construction of a graph describing the neuron. The performed processing stages are: I. Edge detection using a multiscale wavelet transform [3], which uses local gray-value variations for edge detection. II. A separation of object boundaries from noise using a new consistency measure which assigns high values for edges present on two or more neighboring scales, such that a threshold can be used to distinguish between boundary edges and noise. III. The foreground voxels (i.e. which belong to the object) are determined by following the gradients associated to the boundary edges. IV. The skeleton points, the estimate of the local axial direction of the neuronal processes, and the variance of this estimate are calculated using the boundary points and their associated gradients. V. The graph representation of the neuron (see Fig.) is finally constructed by connecting skeleton points in axial direction.

We show that our method: allows the detection of objects over a wide range of contrasts (I.); removes almost all noise, obtaining thus cleaner and more complete object boundaries than other methods [1] (II.); leads to a reliable seg-
mentation, which does not lose very thin and low contrasted, but biologically important structures like spines and terminals [I.] enables us to extract biological relevant information, such as branching points, varicosities, and abrupt bends of the neuron from regions of high axial variance [IV.]; uniquely traces thick as well as thin branches, preserves topology, and adapts automatically to the local noise level and smoothness of the data [V.]. All methods are computed efficiently ($O(n \log n)$, where $n$ is the number of voxels in the image) and lead to an accurate graph, despite the fact that structures come in widely different sizes and contrast levels, that noise is strong and that the staining is not homogeneous. A surface reconstruction of the neuron basing on this graph may be performed subsequently [4].

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References


