Complexity Constrained 3D Skeletonization Algorithms for Automated Extraction of Dendrites and Spines from Fluorescence Confocal Images

by

Xiaosong Yuan

An Abstract of a Dissertation Submitted to the Graduate

Faculty of Rensselaer Polytechnic Institute

in Partial Fulfillment of the

Requirements for the degree of

DOCTOR OF PHILOSOPHY

Major Subject: Electrical, Computer and Systems Engineering

The original of the complete thesis is on file
In the Rensselaer Polytechnic Institute Library

Approved by the
Examining Committee:

Badrinath Roysam, Thesis Adviser

Wm. Randolph Franklin, Member

Richard J. Radke, Member

Barbara Cutler, Member

Rensselaer Polytechnic Institute
Troy, New York

May, 2009

Abstract

The structure of neuronal dendrites and dendritic spines are linked to many important aspects of brain cognitive functions. Current techniques are not adequately developed in accuracy, efficiency and automation for detection of dendritic morphology and spine geometry. It remains a difficult task for algorithms to reduce the false positive and classify the clusters into spines and other protrusions. One challenge is the smallness of these structures compared to the achievable resolution of optical microscopes; A second challenge relates to achievable signal quality with fluorescence imaging. The signal to noise ratio and contrast can be poor especially when live neurons are being imaged, or when the slices are thick; A third challenge relates to the structural complexity of spiny dendrites, especially when they are inter-twined in a complex manner; Finally, the high degree of variability exhibited by neuroanatomic structures (morphological and appearance variability compounded by imaging system variability) make it difficult to robustly model spines, and cause the detection to be ambiguous.

We present a minimum description length (MDL) based algorithm to analyze the morphologic variation of dendritic branching and spine density/distribution on 3D confocal microscopy images. The algorithm can take into consideration spine prior knowledge and spine spatial correlation and translate them into model description length. The algorithm estimates the model complexity and model parameters altogether in an optimization problem. The dendrite and spine extraction is derived when the optimal model with proper complexity and coverage makes its MDL criterion to reach minimum.

Instead of realizing segmentation before the central line extraction, we can work directly on the intensity images without discarding original image intensities that are informative to the skeletonization. An algorithm utilizing the gradient vector field to locate the skeletons of the tubular objects is applied after an anisotropic diffusion process. In order to explore the dendritic structure from the 3D skeleton, a minimum spanning tree algorithm based on intensity weighted edges (IW-MST) is employed. Graph morphology methods are used to further adjust the skeleton structure and remove spurs and non-spine-related branches.

The complexity constrained models are developed and optimized for the dendritic backbones (neuron main dendrite structure) and tree branches in neuronal structure. The dendritic backbones are extracted as the primary structure of neuron. Its representation in MDL model is based on B-spline functions with smooth curves of low degree, and with optimal intervals and knots. The secondary neuronal structures, dendritic spines, are derived as attachments to the dendrite backbones. The spine models comprise both conciseness and coverage in the MDL criterion and take prior knowledge into the model consideration.

The dendrite and spine morphological structure can be further analyzed with level set methods. By creating the surface models for the dendrites and spines separately from both the intensity 3D images and the skeleton points, we can perform various measurement of dendrites and spines, such as size, radius, volume, etc.

Experimental results on multiple datasets show the efficiency of our algorithms on different sources (from UCLA, Caltech, MBF Inc.) of real 3D fluorescence images and time series. These include 30 datasets in 8 different groups or time series. On confocal microscopy images of various scales, contrasts, noise levels, we have achieved the detection of spines with false negative less than 10% in most datasets (the average is 7.1% on all 30 datasets), and at the same time low false positive rate of about 11.8% on average.