Reconstructing and Visualizing Models of Neuronal Dendrites

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Abstract: Neuroscientists have studied the relationship between nerve cell morphology and function for over a century. To pursue these studies, they need accurate three-dimensional models of nerve cells that facilitate detailed anatomical measurement and the identification of internal structures. Although serial transmission electron microscopy has been a source of such models since the mid 1960s, model reconstruction and analysis remain very time consuming. We have developed a new approach to reconstructing and visualizing 3D nerve cell models from serial microscopy. An interactive system exploits recent computer graphics and computer vision techniques to significantly reduce the time required to build such models. The key ingredients of the system are a digital "blink comparator" for section registration, "snakes," or active deformable contours, for semi-automated cell segmentation, and voxel-based techniques for 3D reconstruction and visualization of complex cell volumes with internal structures.

Keywords: scientific visualization, 3D reconstruction, image registration, image segmentation, contour tracking, snakes, volume rendering, dendrites, dendritic spines

1 Introduction

Neuroscientists search for links between neuronal dendritic morphology and behavior, and morphology and disease by studying the relationship between the morphology and function. Detailed morphological studies require accurate three-dimensional models of nerve cells that facilitate anatomical measurement and identification of internal structures. Neuronal dendrites and their protruding dendritic spines can be seen with a light microscope (Fig. 1), but the resolution is insufficient for detailed anatomical measurement and the internal structures are not visible. To date, the only method available for detailed measurement and study of internal cell structure is through 3D reconstructions from serial electron microscopy, or serial EM (Fig. 2) (Harris and Stevens 1988; Harris and Stevens 1989; Stevens and Trogadis 1984; Wilson *et al.* 1987).

Reconstructions from serial EM have been produced almost since the invention of the electron microscope. Initially, the reconstructions were purely manual, but over the years they have relied increasingly on computers. Even with current computer-assisted techniques, the reconstruction of a $5\mu m$ dendritic segment with all of its spines and synapses, along with the quantitative analysis of the reconstructed model, can take up to three months of work. By contrast, the tissue preparation and EM photography take only about two days! It is remarkable that so many neuronal reconstructions have been made because "... the incredible investment in time and energy

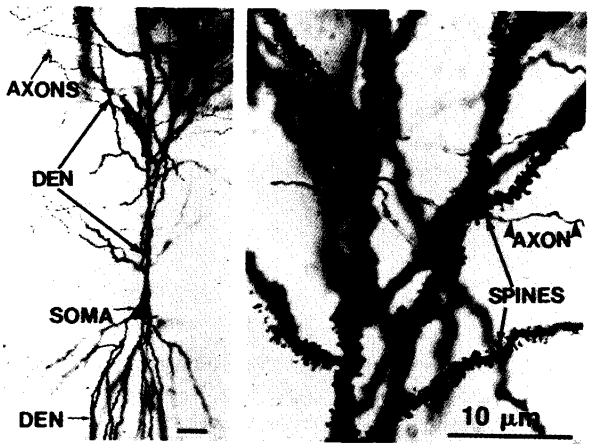

Fig. 1: A hippocampal pyramidal cell with the soma and the dendrites (den) visible. The axons are from other hippocampal cells that form synapses with these dendrites. At higher magnification the dendritic spines are seen protruding from the dendrite. Bars = $10\mu m$.
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necessary to reconstruct cells is nothing short of heroic" (Stevens and Trogadis 1984).

We present a new interactive approach to reconstructing and visualizing 3D nerve cell models from serial microscopy, and describe an interactive system which exploits recent computer graphics and computer vision techniques to reduce significantly the time required to build such models. After presenting a more detailed review of the relevant neurophysiological motivation for our work and its relationship to prior efforts, we describe the key components of our approach to reconstruction and analysis of neuronal dendrites. Our prototype system currently features a digital "blink comparator" for section registration, "snakes," or active deformable contours, for semi-automated cell segmentation, and voxel-based techniques for 3D reconstruction and visualization of the 3D morphology of dendrites along with their internal structures.

1.1 Background

A nerve cell, or neuron, has four constituent parts: the cell body (soma), the dendrites, the axon, and the presynaptic terminal of the axon (Kandel and Schwartz 1985). The soma is the metabolic center of the cell, the dendrites are the receiving units, the axon is the conducting unit, and the presynaptic terminals are the transmitting units. The areas of contact between the presynaptic axonal terminals of one cell and the dendrites of another cell are called the synapses. Most synapses are located at the end of protrusions on the dendrites, called the dendritic spines (see Fig. 1).

In humans, the dendritic spines are lost or change shape both with aging (Feldman and Dowd 1975) and with diseases that affect the nervous system, such as dementia (Catala *et al.* 1988), brain tumors (Spacek 1987), Down's syndrome (Marin-Padilla 1976), epilepsy (Scheibel *et al.* 1940), Huntington's disease (Graveland *et al.* 1985), and alcoholism (Ferrer *et al.* 1986). Detailed anatomical descriptions of the synapses and dendritic spines will provide new understanding about their function, thus improving opportunities for understanding the underlying causes and effects of these diseases.