

# Rapid identification of neuronal structures in electronic microscope image using novel combined multi-scale image features



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## ABSTRACT

This paper proposes an incremental scheme to identify the neurons in electronic microscope image. It first computes the probability of each pixel being cell membrane and then determines the image areas of the neurons. Our contributions also include novel combined multi-scale image features that are computationally efficient and provide strong discrimination ability for differentiating membrane pixels from other pixels. Experiment results show that the proposed system offers much higher speed than the compared state-of-the-art methods while produces comparably high accuracy.

## 1. Introduction

Identification of neuronal structures in electronic microscope (EM) image, i.e., to find the neurons and sub-cellular components, is key to 3D reconstructing neural circuits from EM image stacks [1,2], a research area drawing increasing international efforts due to its high value in assisting mankind's pursuit to understand how brains work [3,4]. One major benefit from such knowledge is the successful development of artificial neural networks.

On the road towards achieving the goal we face two challenges: (1) It is a difficult problem due to the vast variation of the shape and texture of neuron image and noise from the imaging process. Fig. 1 gives an example where vesicles, synapses and noises scatter erratically. (2) The image data is huge - a complete rat cortex of 500 mm<sup>3</sup> would produce about an exabyte (10<sup>18</sup>) of data [5]. The identification algorithm must be computationally efficient to be practically useful [6].

After many years of intense research [7,8], steady progress has enabled the state-of-the-art systems to perform the task usefully. They are however far from being very satisfactory, and continued research is highly desirable.

The main limitations of the existing approaches are: (1) The identification accuracy is not sufficiently high and the resultant mistakes [9] in the reconstructed 3D neural circuits impede a thorough understanding of how a collection of neurons work to produce cognitive abilities; (2) The computational efficiency is inadequate [10] for 3D reconstructing the neural circuits of an entire cortex within a reasonable period of time.

To overcome the limitations of the current methods, we propose a

novel two-step procedure that first uses combined multi-scale image features and random forest as classifier to obtain a probability map, and then uses improved watershed segmentation method to determine the image areas of the neurons. Our method extracts intrinsic features taking context information, intensity variation and shape cues into consideration, which significantly cuts down learning and classification time in classifying each pixel. The segmentation step obtains individual neurons to avoid mistakes in most supervised methods brought by discontinuities in imaged membranes.

The contributions of our work include:

- Proposing a novel incremental procedure, i.e., to compute a probability map first and then obtain the image areas of the neurons.
- Proposing two new features MSR and C2RB that provide strong discrimination information while being computationally inexpensive.
- Offering both high accuracy and high speed as demonstrated by experiment results.

## 2. Related work

Early in 1980s, researchers spent 10–15 years on completing the first connectome to describe the connectivity between all 302 neurons in the nematode worm *Caenorhabditis elegans* [11]. It took too long and too much manual work.

Thereafter, advances in electron microscope technology and better reconstruction algorithms change the situation and reconstruction work steps into a new stage [12].

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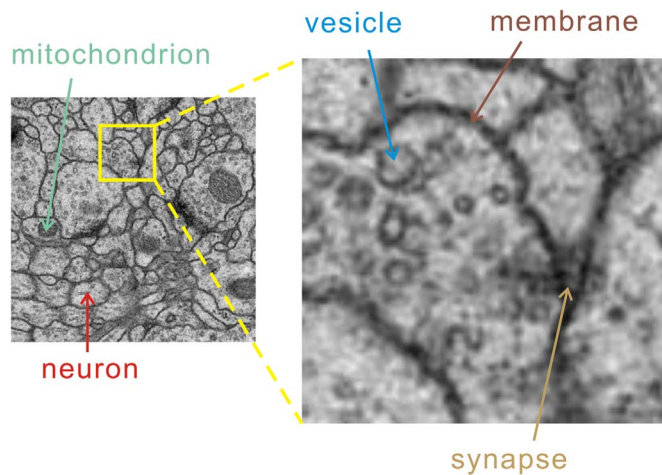


Fig. 1. An electronic microscope image of brain tissue.

Anisotropic directional filtering was applied to enhance membrane continuity [13] but lost segmentation with sufficient accuracy. Macke et al. [4] minimized an energy function for cell membranes but his active counter model failed due to mistakenly computed local minima in complex background and may find false boundaries. Nhat Vu and B.S. Manjunath [14] used graph cuts to minimize an energy defined over the image intensity and the flux of the intensity gradient field, it however required user interaction at first. All these unsupervised methods are defeated in accuracy by supervised ones since the latter train massive samples as priori knowledge.

Jurrus et al. [15] presented a framework to detect neuron membranes that integrates information from the original image together with contextual information by learning a series of artificial neural networks. Nevertheless this approach ignored geometric information of membranes and too many layers of classifiers make it far from a high speed. Seyedhosseini et al. [9] proposed to apply Radon-like features in

his serial classifiers as geometric features specifically designed for connectome images apart from contextual information [10,16] etc used. However, result showed that Radon-like features only achieve modest accuracy levels. Ciresan et al. [10] applied deep neural networks for membrane detection and achieved excellent results, but it learned the filters for classification directly from data, and the multiple convolutions throughout the layers of the network accounted for an increasing filter support region. Above all, it consumed too much time. Other approaches such as [17,18] merely modified the probability map produced through their approaches but failed to solve problems at their source. Zhu F et.al [19] put forward an interesting reinforcement learning-based boundary amendment method after a multi-scale fused structure boundary detection algorithm, which achieved fairly good performance.

The supervised methods neglect intrinsic features possessed by membranes and are dependant on their classifiers which consume long time and demand a great deal of training examples. Meanwhile, membrane detection results outputted from these classifiers are discontinuous frequently. To overcome these limitations, we employ a correlation to rotational bar descriptor as our shape cues and compute intensity variation to implement contextual information to obtain suitable features. With the help of the proposed features classifiers are released from heavy computation for less processing time and finally we identify individual neurons surrounded by consecutive membranes using a segmentation strategy.

### 3. Proposed method

We adopt the 2D to 3D approach instead of directly reconstructing in 3D space due to the consideration of anisotropic nature of EM image stack, and the huge memory demand by the direct 3D reconstruction approach.

The proposed method consists of three stages as illustrated in Fig. 2:

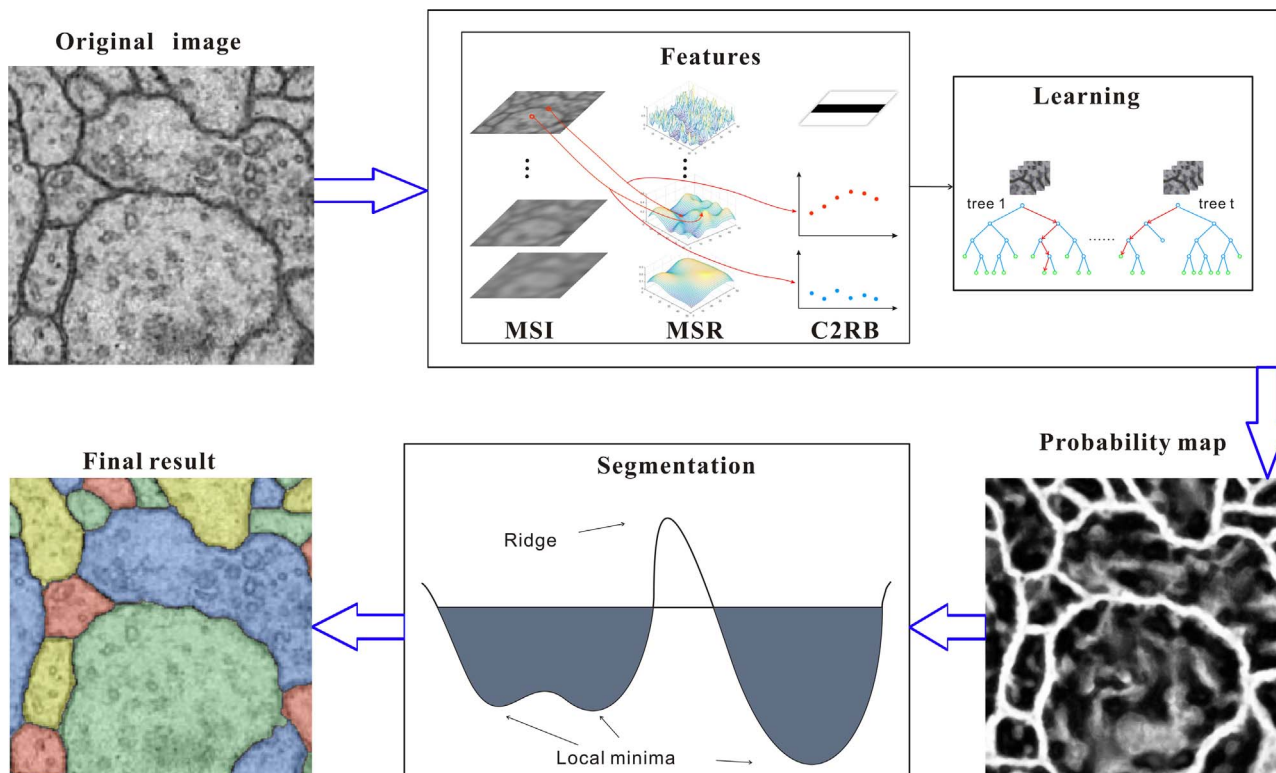


Fig. 2. Flow chart of the proposed method.

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