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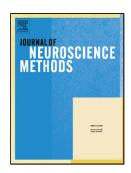
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### ACCEPTED MANUSCRIPT

# Automated dendritic spine detection using convolutional neural networks on maximum intensity projected microscopic volumes

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#### **Highlights**

- A deep learning method is used to automate dendritic spine detection in 2D.
- Detection pipeline is designed around Fully Convolutional Neural Networks (FCNs).
- FCNs achieve F scores > 0.8 with predicted coordinates  $< 0.1\mu$  away from annotations.
- Small training dataset achieves detection indistinguishable from that of experts.
- FCNs outperform NeuronStudio and Neurolucida, especially in thin spine detection.

#### Abstract

*Background*: Dendritic spines are structural correlates of excitatory synapses in the brain. Their density and structure are shaped by experience, pointing to their role in memory encoding. Dendritic spine imaging, followed by manual analysis, is a primary way to study spines. However, an approach that analyses dendritic spines images in an automated and unbiased manner is needed to fully capture how spines change with normal experience, as well as in disease.

New Method: We propose an approach based on fully convolutional neural networks (FCNs) to detect dendritic spines in two-dimensional maximum-intensity projected images from confocal fluorescent micrographs. We experiment on both fractionally strided convolution and efficient sub-pixel convolutions. Dendritic spines far from the dendritic shaft are pruned by extraction of the shaft to reduce false positives. Performance of the proposed method is evaluated by comparing predicted spine positions to those manually marked by experts.

Results: The averaged distance between predicted and manually annotated spines is  $2.81 \pm 2.63$  pixels  $(0.082 \pm 0.076 \text{ microns})$  and  $2.87 \pm 2.33$  pixels  $(0.084 \pm 0.068 \text{ microns})$  based on two different experts. FCN-based detection achieves F scores > 0.80 for both sets of expert annotations.

Comparison with Existing Methods: Our method significantly outperforms two well-known software, NeuronStudio and Neurolucida (p-value < 0.02).

Conclusions: FCN architectures used in this work allow for automated dendritic spine detection. Superior outcomes are possible even with small training data-sets. The proposed method may generalize to other datasets on larger scales.

Keywords: Dendritic spine detection, deep learning, convolutional neural networks

#### 1. Introduction

Dendritic spines are postsynaptic structures emanating from dendritic branches of most excitatory neurons in the mammalian brain. Presynaptic nerve terminals appose functional spines, and together they form excitatory synapses, units of excitatory chemical synaptic transmission in the brain. A mature dendritic spine consists of a spine head connected to the dendritic branch by a thin neck. A spine head houses postsynaptic molecular machinery needed for generating excitatory postsynaptic potentials, but also to initiate growth or retraction of the spine structure itself. With the advent of modern high-resolution imaging techniques, it has been shown that the density of dendritic spines, and thus the overall density of synaptic

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