Neuron Tree Construction and Model Building Pipeline for Investigation of Neuronal Integration

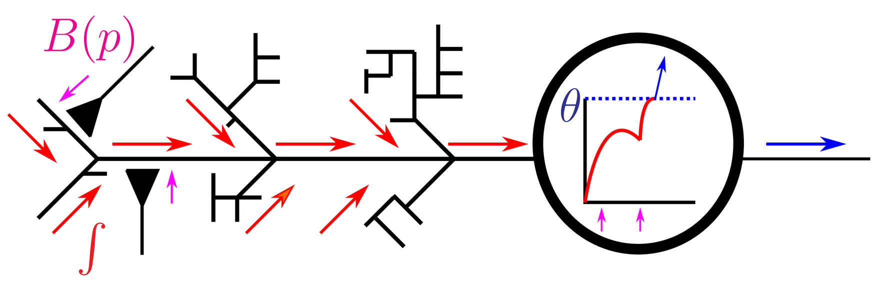
JAMES WILSENACH[1], CHARLOTTE DEANE[1] AND GESINE REINERT[1]
[1]Department of Statistics, University of Oxford

UNIVERSITY OF OXFORD

INTRODUCTION

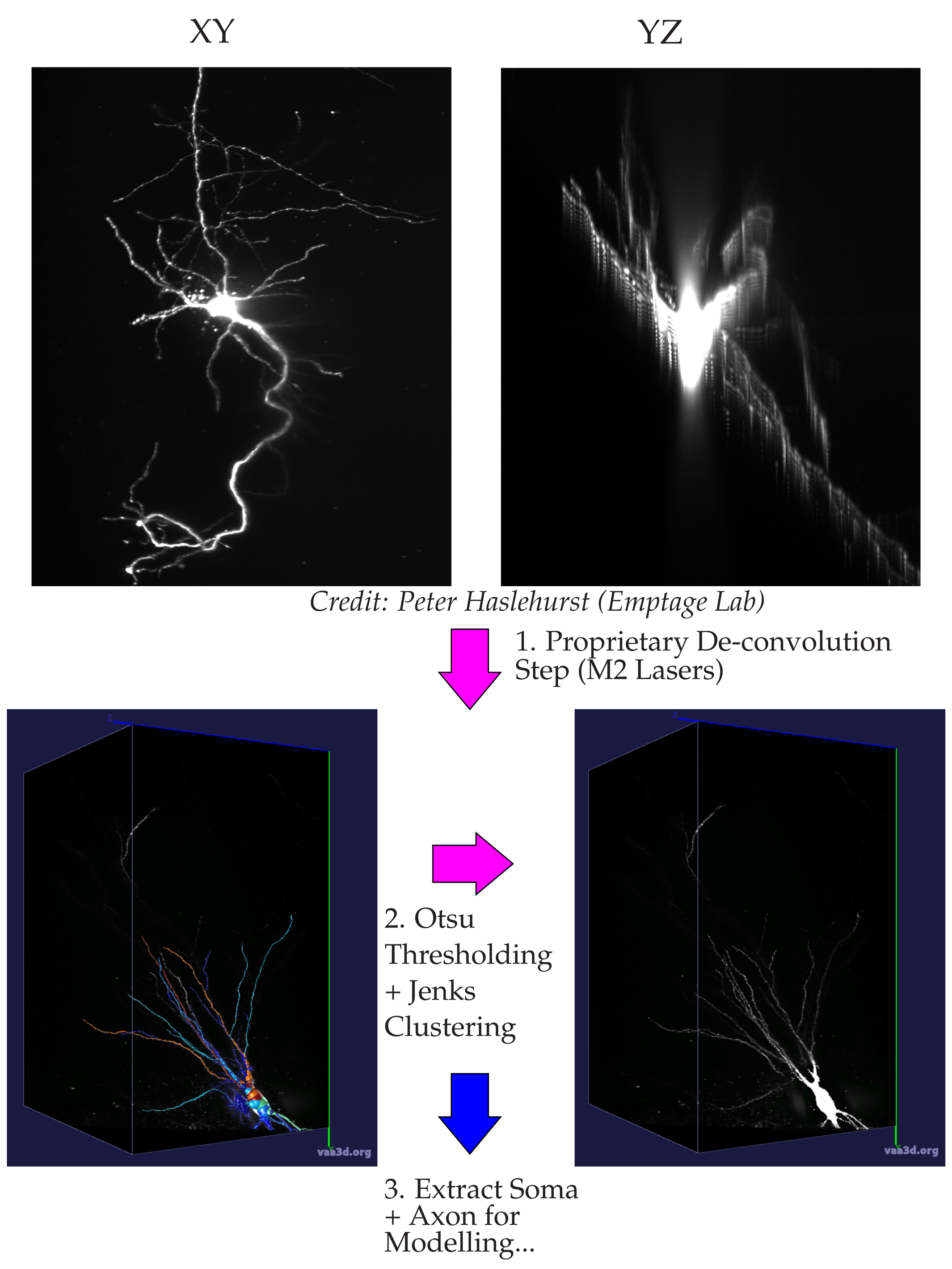
Hippocampal pyramidal neurons integrate incoming signals through an interaction between:

- input location - stochastic synapse ($B(p)$)
- input timing - dynamic, rate encoded
- cell shape - tree-like, shapes integration ($\int$)
- spike generation - thresholded output (θ)

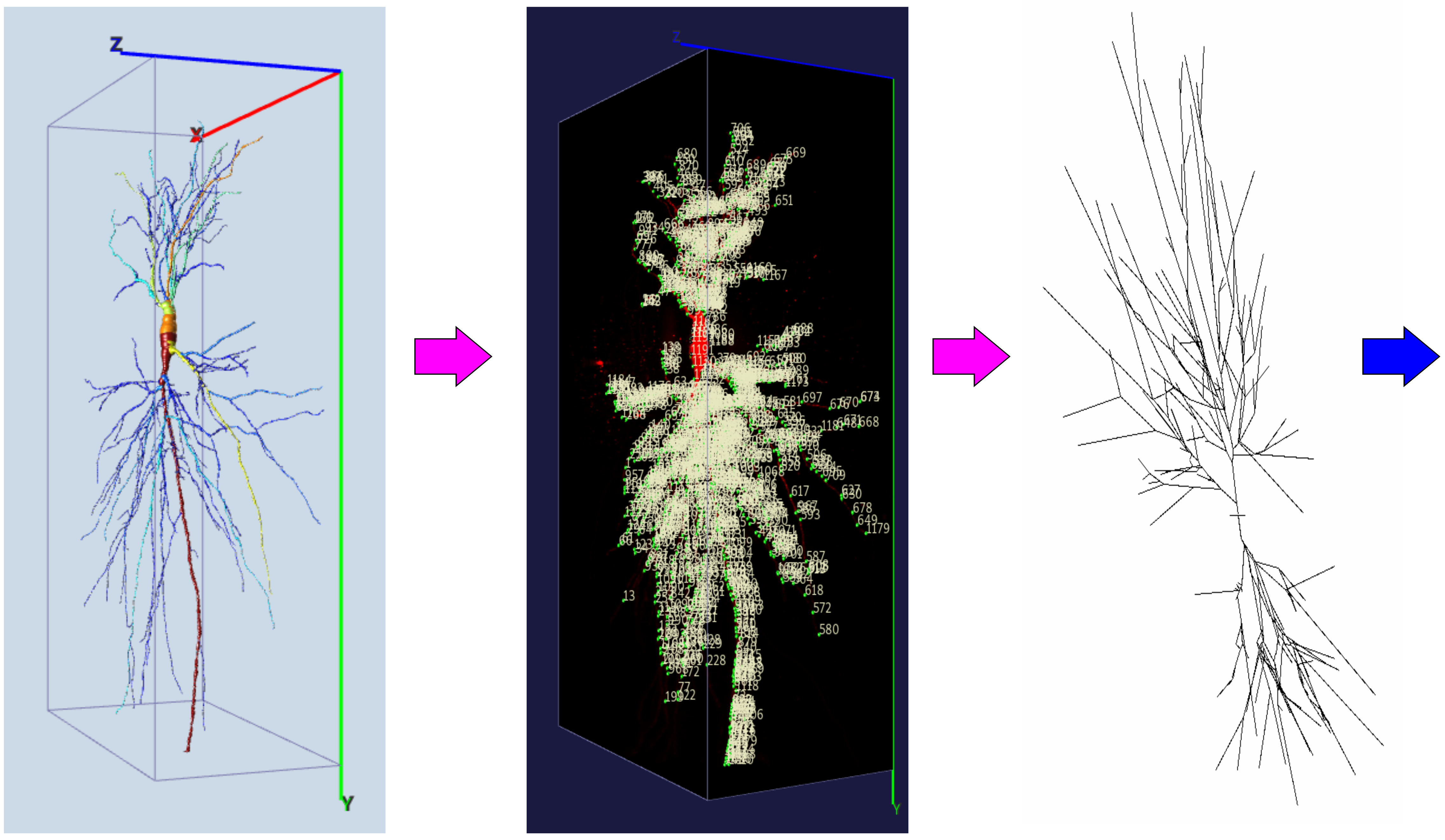


Through Light Sheet Microscopy (LSM), collaborators in the Emptage Lab (OU, Dept. of Pharmacology) are producing 3D images of neuronal structure (used for simulation) and later 4D images of intracellular Ca^{2+} dynamics. These large image datasets will be used to understand this input-output relationship.

3D IMAGE PROCESSING



NEURONAL TREE MODEL BUILDING & SYNAPSE DISCOVERY

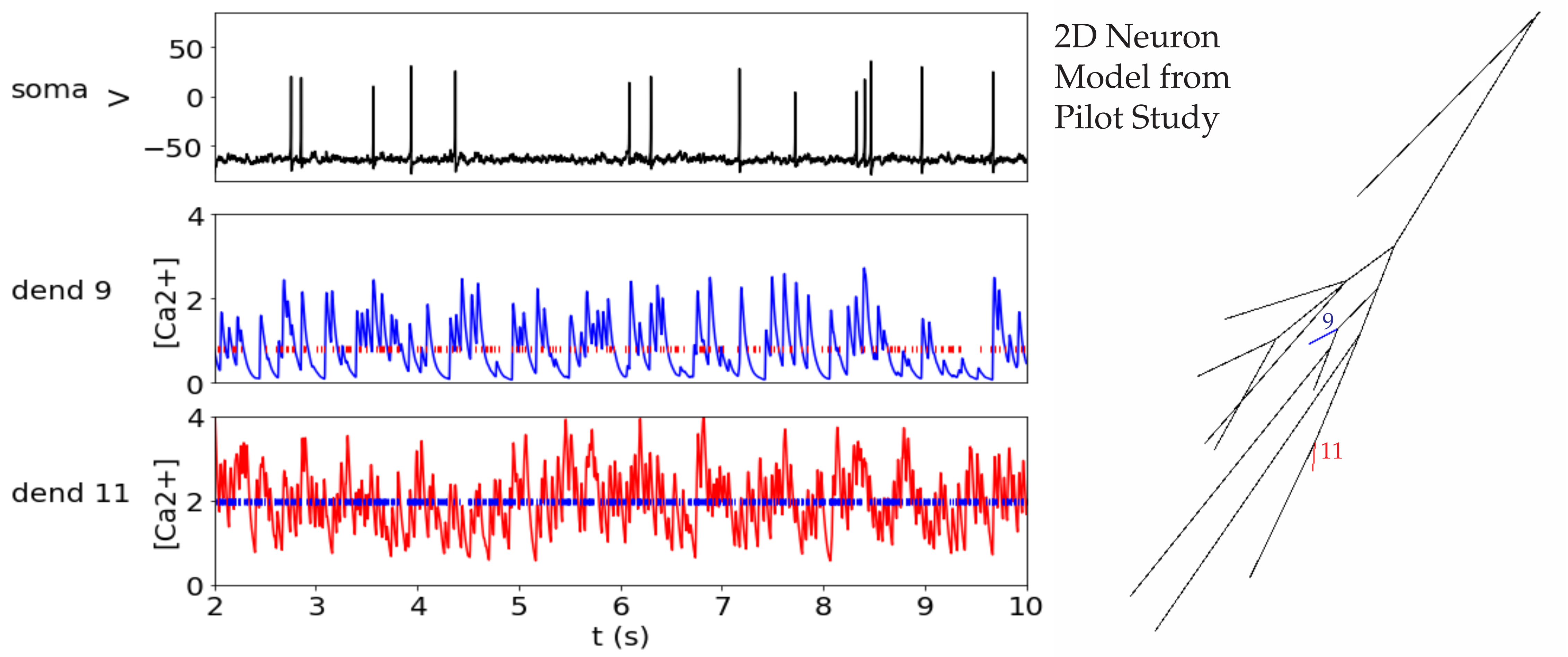


1. Construct neuronal tree using APP2 fastmarching method (Xiao, 2013)

2. Detect putative dendritic spines (Li, 2017)

3. Produce compartmental 'cable' model of neuron for simulation (biophysical properties based on Smith, 2014) for modelling...

FUTURE WORK: SIMULATION & RANDOM TREE EXPERIMENTS



1. Use model building pipeline to determine expected topology and location/number of detectable synapses.
2. Analyse topological features of synapses associated with spike generation using dynamical simulations in NEURON.
3. Repeat experiment for randomly generated trees with features based on expected topology from 1.

REFERENCES

[1] Nicholas T Carnevale and Michael L Hines. *The NEURON book*. Cambridge University Press, 2006.

[2] Peter Haslehurst, Zhengyi Yang, Kishan Dholakia, and Nigel Emptage. Fast volume-scanning light sheet microscopy reveals transient neuronal events. *Biomedical optics express*, 9(5):2154–2167, 2018.

[3] Spencer L Smith, Ikuko T Smith, Tiago Branco, and Michael Häusser. Dendritic spikes enhance stimulus selectivity in cortical neurons in vivo. *Nature*, 503(7474):115, 2013.

[4] Hang Xiao and Hanchuan Peng. APP2: automatic tracing of 3d neuron morphology based on hierarchical pruning of a gray-weighted image distance-tree. *Bioinformatics*, 29(11):1448–1454, 2013.

ACKNOWLEDGEMENTS

This research is funded by the Commonwealth Scholarship and The Oxford University Oppenheimer Fund with special thanks to The Oxford Protein Informatics Group and collaborators Nigel Emptage and Peter Haslehurst of the Synaptic Pharmacology division (Emptage Lab) at the Oxford University Department of Pharmacology.

COMMONWEALTH SCHOLARSHIPS

opig