## Modern Computational Neuroanatomy: Mesoscale Circuit Mapping in Mouse and Marmoset

## Partha P Mitra

Brains are distributed networks of neurons. We cannot understand how brains work, and how they fail, ie brain disorders including addiction, without understanding the architecture of these networks. Yet after a century of intense research our knowledge of brain connectivity remains quite limited, particularly for vertebrate animals including ourselves. Indirect methods such as functional brain imaging do not provide ground truth data sets on neuronal morphology and projection patterns. Research in this area has been human labor intensive, relying on the visual examination of neuronal morphology and distribution under microscopes or more recently in the form of digital images. Even quantitative analysis depends heavily on human annotation. Moreover, computable ground-truth digital data sets pertinent to circuit connectivity, particularly at the whole-brain level, have been lacking.

A decade ago, we proposed (Bohland et al, 2009) filling in this knowledge gap at the mesoscopic scale, by systematically acquiring digital microscopic data sets of whole vertebrate brains, after placing anterograde and retrograde tracer injections on a brain-wide spatial grid. This project has been carried out in the mouse, and is well underway in the marmoset, with over a peta-voxel of digital microscopic image data available on the web at <a href="http://brainarchitecture.org/">http://brainarchitecture.org/</a> This talk will briefly review this work and present the web portal containing the data, and also discuss analytical tools drawn from computational geometry and topology that are being used to analyze these data sets. Finally, comments will be made on the connection between these real neural networks and the artificial neural networks that are foundational to modern machine learning/AI.

## **References:**

Bohland, Jason W., et al. "A proposal for a coordinated effort for the determination of brainwide neuroanatomical connectivity in model organisms at a mesoscopic scale." *PLoS computational biology* 5.3 (2009): e1000334;

Helmstaedter, Moritz, and Partha P. Mitra. "Computational methods and challenges for large-scale circuit mapping." *Current opinion in neurobiology* 22.1 (2012): 162-169;

Okano, Hideyuki, and Partha Mitra. "Brain-mapping projects using the common marmoset." *Neuroscience research* 93 (2015): 3-7.;

Li, Y., Wang, D., Ascoli, G.A., Mitra, P. and Wang, Y., 2017. Metrics for comparing neuronal tree shapes based on persistent homology. *PloS one*, *12*(8), p.e0182184.

Lee, B. C., Tward, D. J., Mitra, P. P., & Miller, M. I. (2018). On variational solutions for whole brain serial-section histology using the computational anatomy random orbit model. *arXiv* preprint arXiv:1802.03453.

Funding was provided by the NIH (MH087988, MH088659, DA036400, MH 114824, MH114821, EB022899), by NSF (Eager), the Mathers Foundation, the Crick-Clay Professorship (CSHL), the H N Mahabala Chair (IIT Madras) and the Japan Brain/MINDS project.