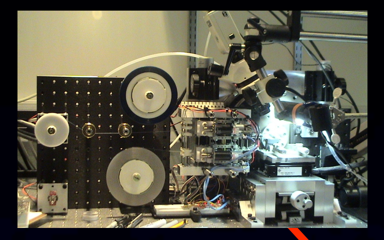
Measuring and Reconstructing the Brain at the Synaptic Scale: Towards a Biofidelic Human Brain *in silico*

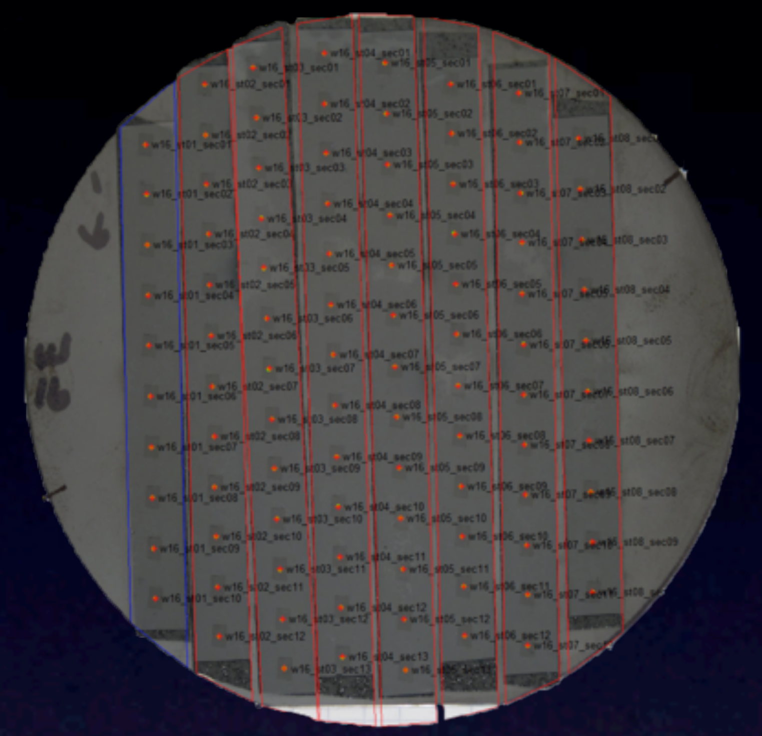
Joshua Vogelstein[1], Carey E. Priebe[1], Randal Burns[2], R. Jacob Vogelstein[3], Jeff Lichtman[4]

[1] Dept. Applied Math & Stats, Johns Hopkins University (JHU), [2] Dept. of Computer Science, JHU, [3] National Security Technology Department, JHU Applied Physics Lab, [4] Dept. of Molecular & Cellular Biology, Harvard University

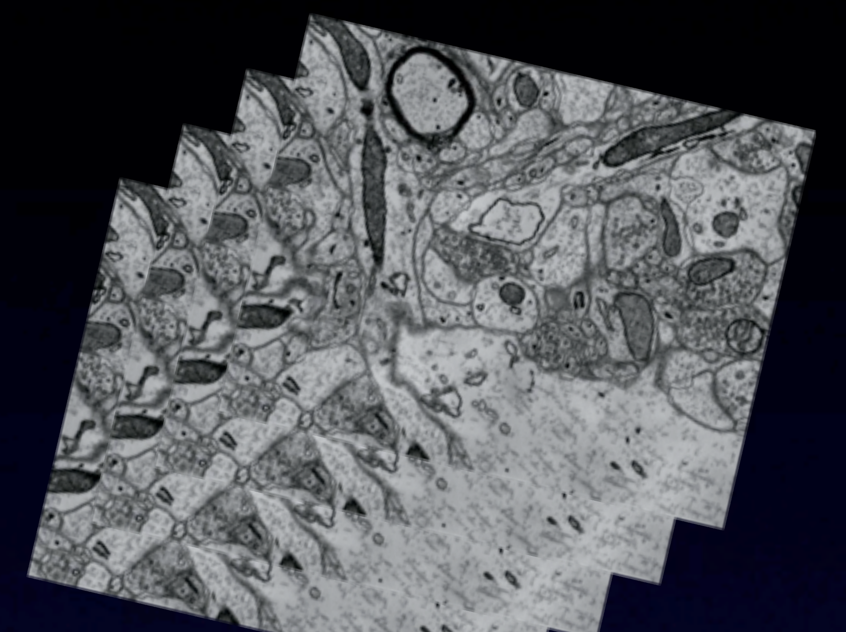
Abstract: The ability to construct a biofidelic human brain in silico has potentially transformative implications for artificial intelligence, medical diagnostics and therapeutics, and our basic understanding of the brain and the mind. Previous large-scale brain simulations were built from well studied parts, but lacked detailed knowledge of connectivity [1]. We are developing a complete pipeline to construct the first biofidelic human brain emulation. These tools are all designed to be high-throughput, mostly automated, and robust.



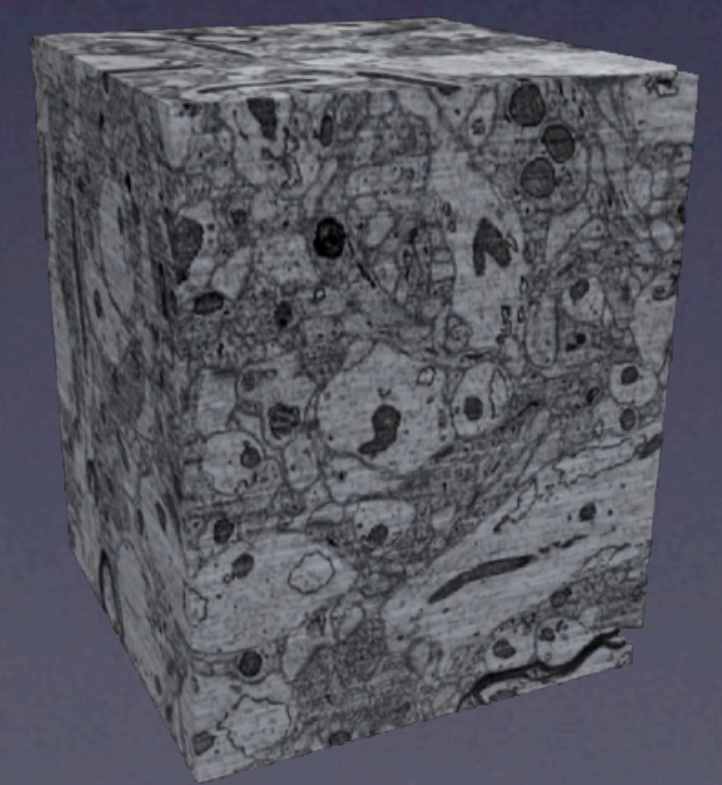
Step 1: The Automatic Tape Collecting UltraMicrotome (ATUM) cuts large areas of brain tissue (3x3 mm^2) generating thousands of 25 nm thick serial sections and cubic mms of volume with no loss [2]. The sections are collected on a firm plastic tape which is then cut into strips and placed on silicon wafers.

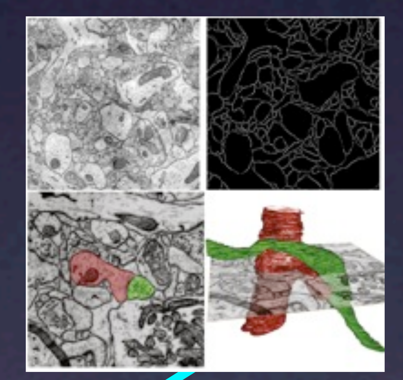


Step 2: The wafers are imaged automatically with a scanning electron microscope so that thousands of two dimensional images are generated with lateral resolutions of 3 nm [3]. New advances in imaging technology will accelerate this process from 1M pixels per second to speeds of 1-10G pixels per second over the next 5 years. At these speeds whole mammalian brains can be imaged in a few years. Depending on the resolution with which one wants to image the white matter tracks, it is for the first time possible to consider imaging entire human brains at a resolution where all the synapses are visible.

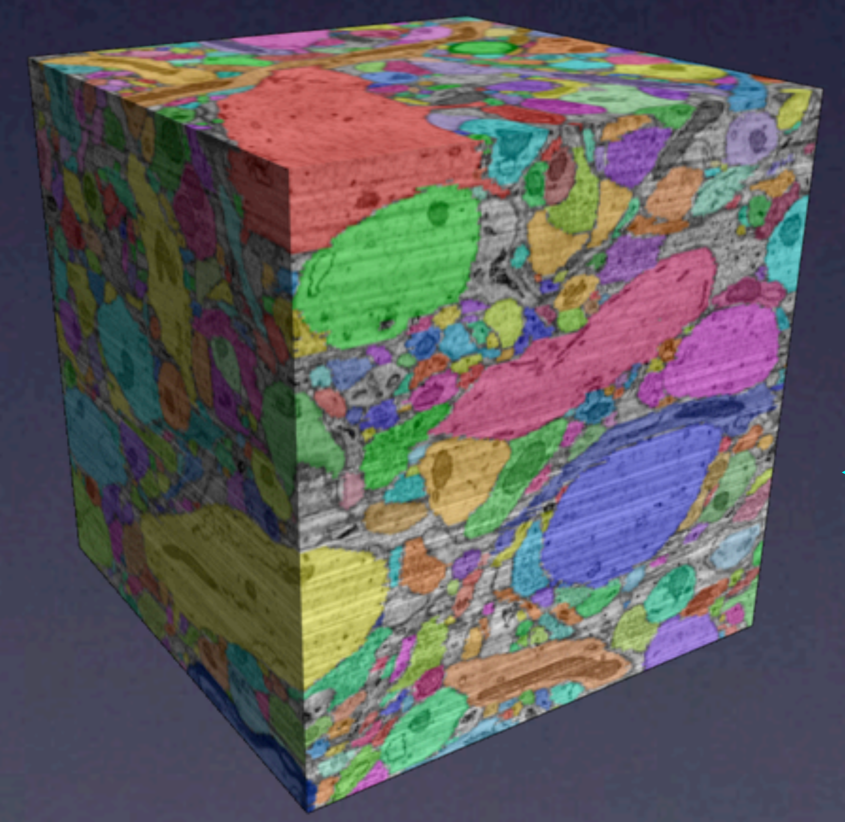


Step 3: Three-dimensional image processing tools generate a "clean" volumetric image from the collection of two-dimensional images. The data is stored to facilitate efficient machine annotation, and simultaneous access by thousands of users.

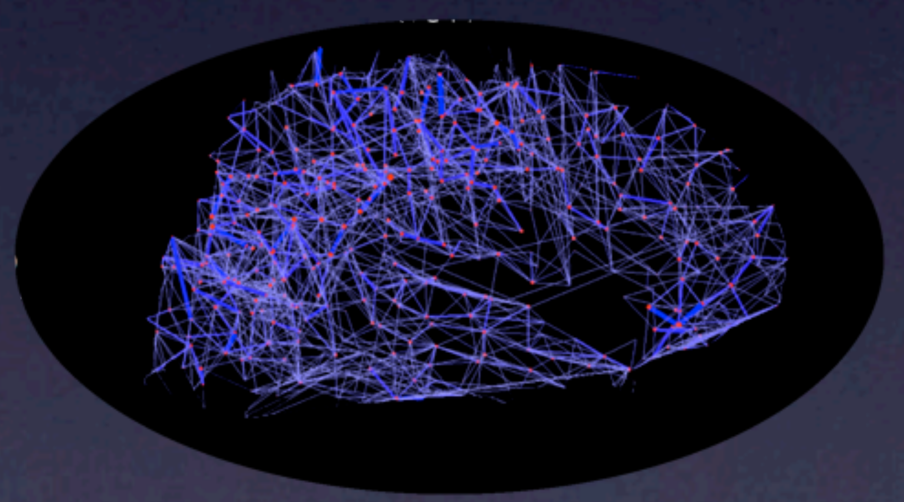




Step 4: Machine annotation algorithms can then efficiently, and in parallel, completely annotate the data, marking each pixel as either soma, axon, dendrite, synapse, etc. [4].



Step 5: The multi-exabyte annotated volumetric image is then converted into an attributed brain-graph, with billions of vertices and trillions of edges. The database on which it is stored is designed for efficient non-local querying [5].



Hagmann et al., 2008

Step 6: With the attributed brain-graph data in hand, we can generate the first ever biofidelic human brain emulations, either in software, or on dedicated massively parallel hardware [6], with potentially transformative implications for artificial intelligence and neuromimetic computing. In addition, we can begin building statistical brain-graph models to explain and summarize the data, and to design further experiments [7,8].

http://www.mitre.org/news/envision/spring_09/minnery.html

Beyond: Detailed knowledge of a connectome (in analogy with the genome [9]) could lead to revolutionary new computing technologies, medical capabilities, and more.

?

Acknowledgements: Gatsby Charitable Foundation, NIH, Harvard Center for Brain Science.

References: [1] de Garis, et al., 2010. [2] Hayworth et al., 2006. [3] Helmstaedter et al., 2008. [4] Jain et al., 2010. [5] Stanton & Burns, in prep. [6] Vogelstein et al., 2006. [7] Marchette et al., in prep. [8] Vogelstein, et al., 2010. [9] Lichtman & Sanes, 2008.