Measuring and Reconstructing the Brain at the Synpatic Scale: Towards a biofidelic human brain *in silico*

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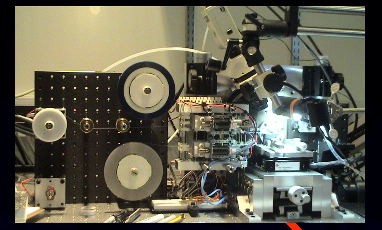
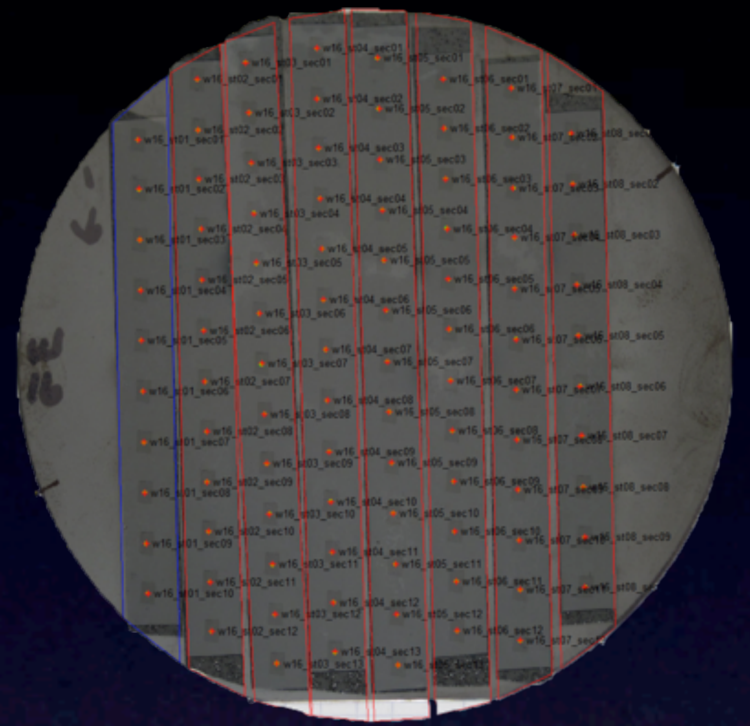
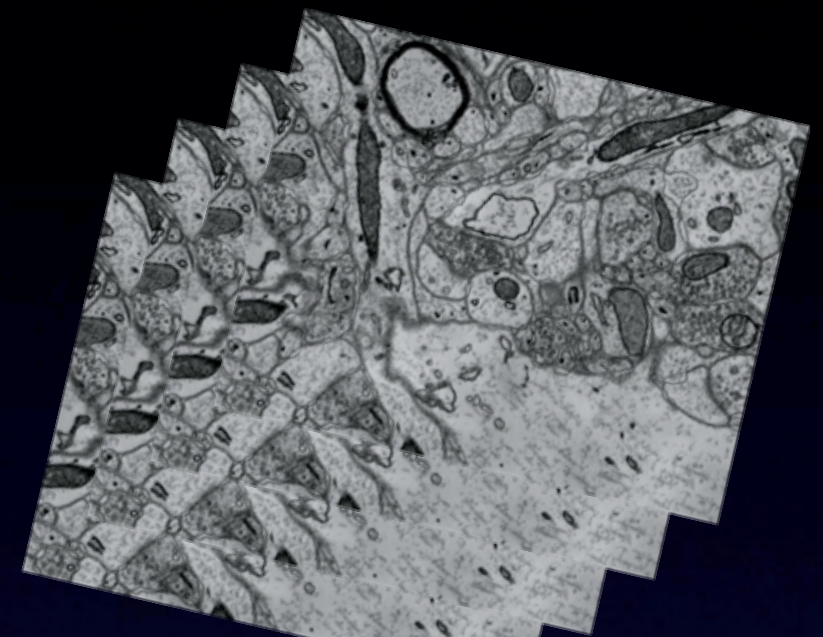
Abstract: The ability to construct a biofidelic human brain in silico has potentially unimaginable applications, including improved computational capabilities, medical diagnostics and therapeutics, and basic understanding. Previous large brain simulations were built from well studied parts, but lacked detailed knowledge of connectivity [1]. We are developing a complete pipeline to obtain the data necessary to construct the first biofidelic human brain emulation. These tools are all designed to be high-throughput, mostly automated, and robust.



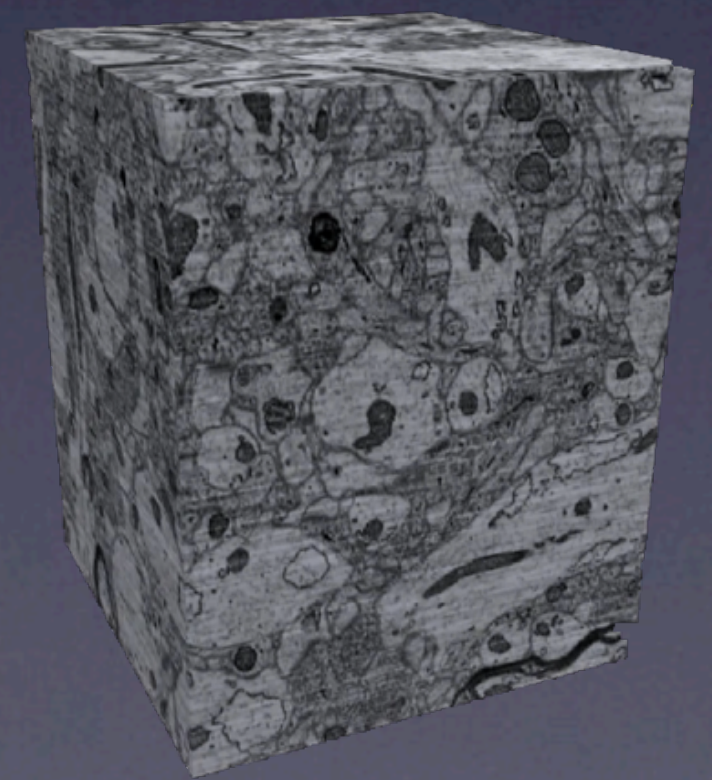
Step 1: The Automatic Tape-collecting Lathe UltraMicrotome (ATLUM) [2], efficiently and robustly converts an ex vivo brain into XX slices, each X x Y x 30 nm^3.

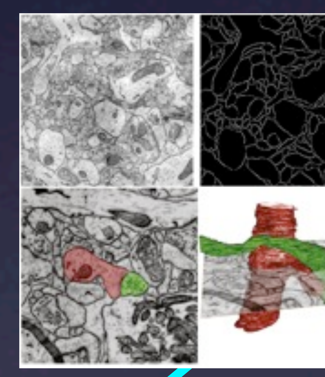




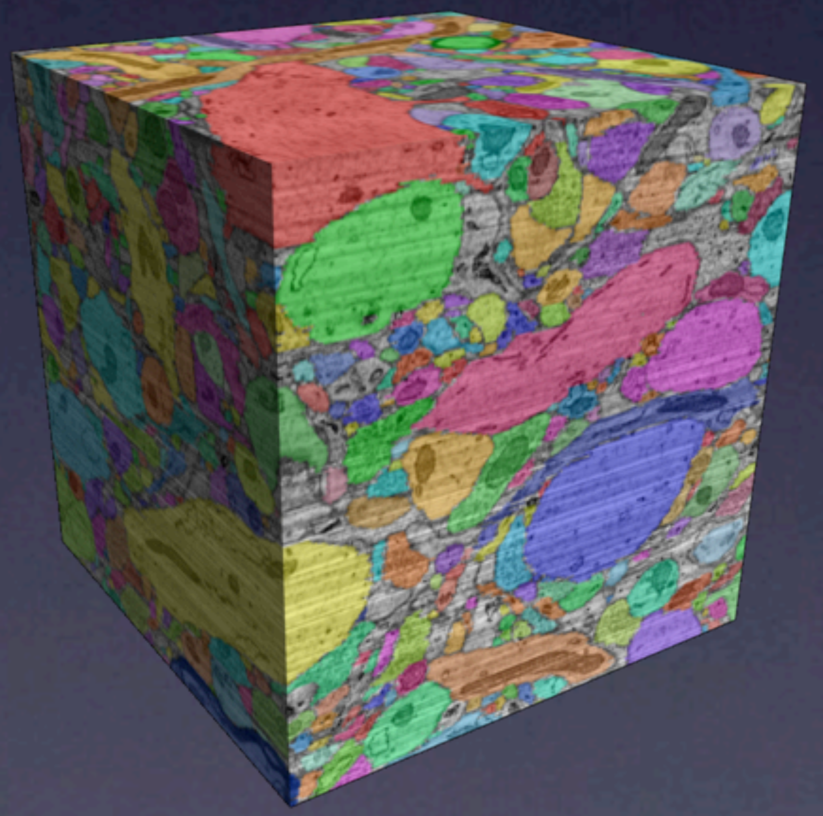
Step 2: Our Thin Section Scanning Electron Microscope (TSSEM). converts the brain slices into a collection of XX two-dimensional images, with spatial resolution of 3 x 3 x 30 nm^3. Together the raw images require 3.3 exabytes of data, and the imaging itself would require XX years [3]. A new serial electron microscope under develop would reduce that time by a factor of 200, resulting in a whole human brain in YY years.

Step 3: Three-dimensional image processing tools generate a "clean" volumetric image from the collection of two-dimensional images [4]. The data is stored to facilitate efficient machine annotation, and simultaneous access by thousands of users.

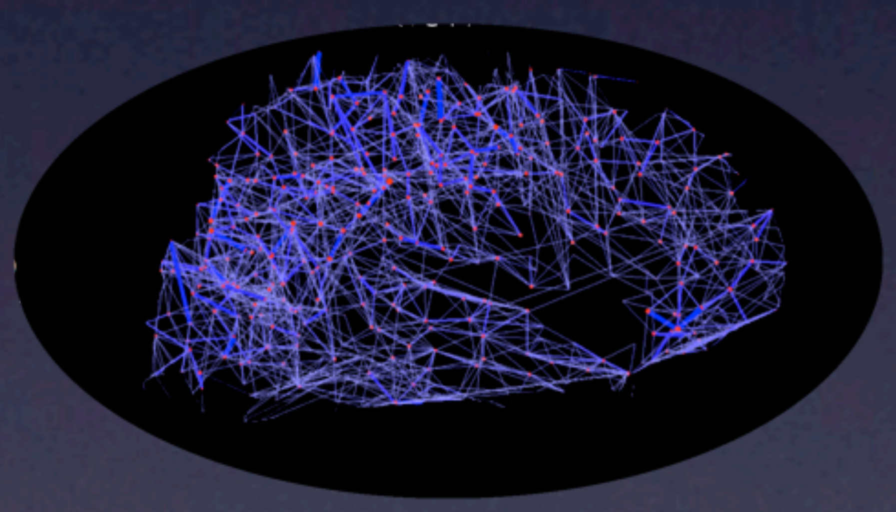




Step 4: Machine annotation algorithms can then efficiently, and in parallel, completely annotate the data, marking each pixel as either soma, axon, dendrite, synapse, etc. [5],



Step 5: The multi-exobyte 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 [6].



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 [7]. Furthermore, we can begin building random brain-graph models to explain, summarize, and design further experiments [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.

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Acknowledgements: NSF something, NIH something, etc.

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