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

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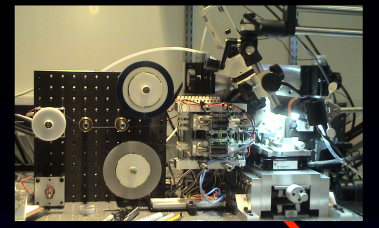
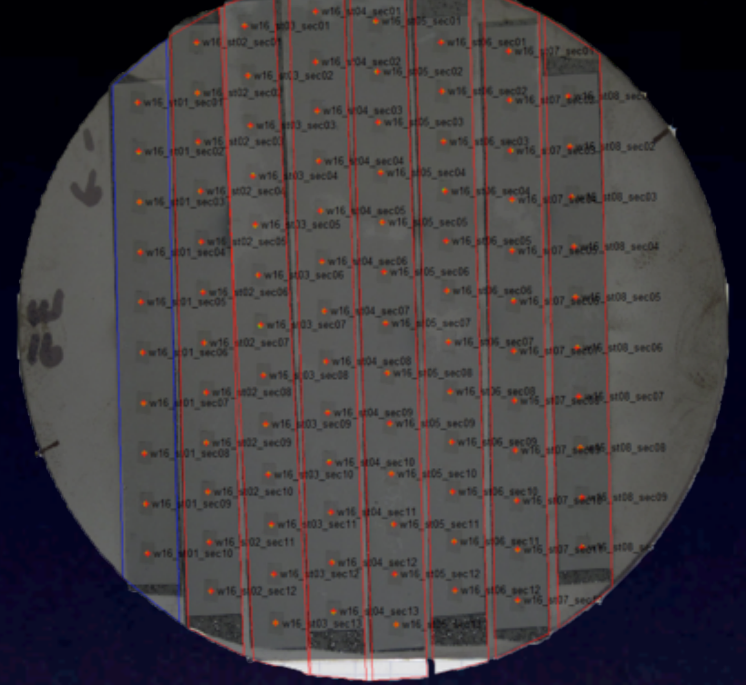
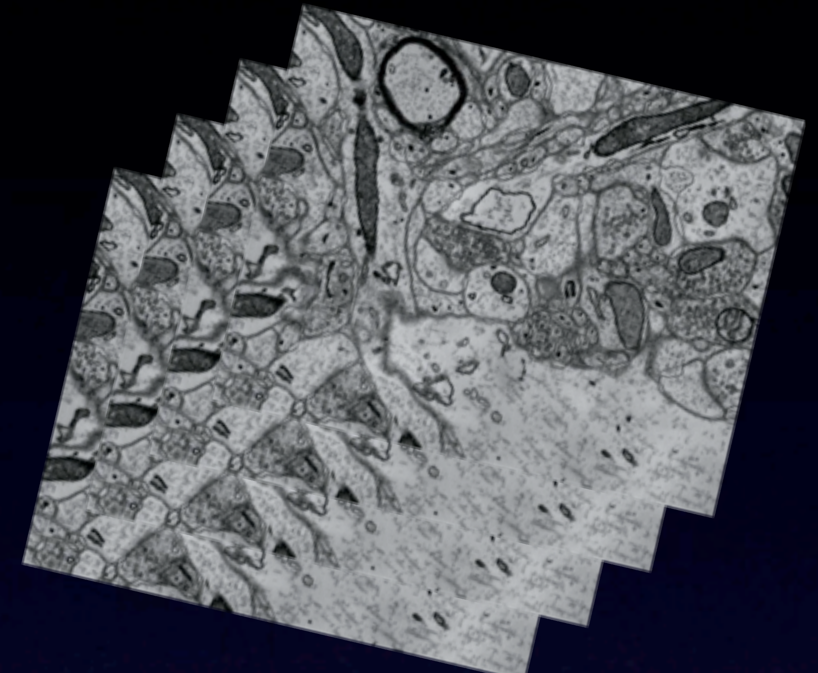
Abstract: The ability to construct a biofidelic human brain in silico has potentially unimaginable applications, including improved computational capabilities, medical diagnostics and therapeutics, and basic understanding. Previous large brain simulations were built from well studied parts, but lacked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



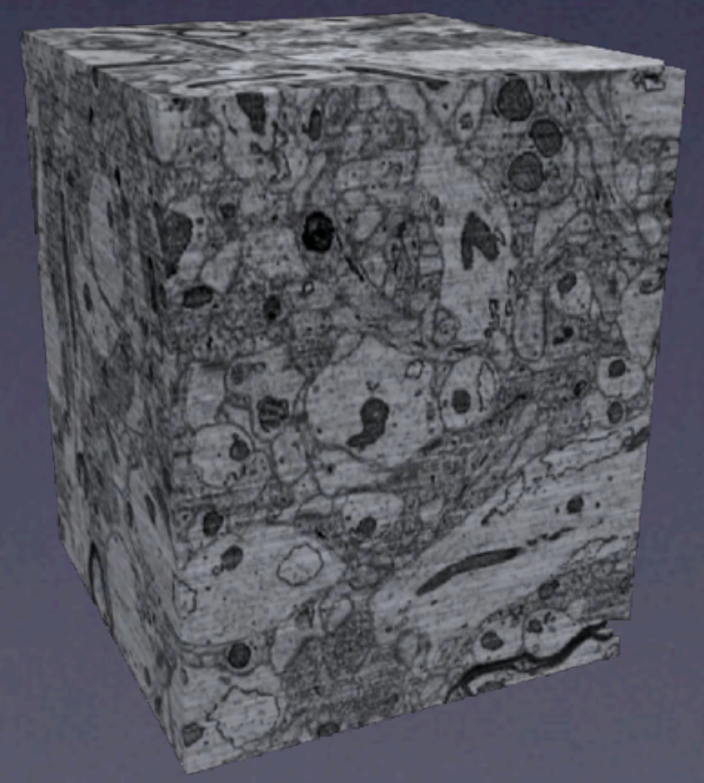
Step 1: The Automatic Tape-collecting Lathe UltraMicrotome (ATLUM) [2], efficiently and robustly converts an ex vivo brain into XX slices, each X x Y x 30 nm^3.

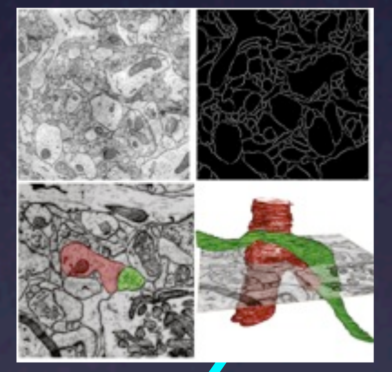


Step 2: Our Thin Section Scanning Electron Microscope (TSSEM). converts the brain slices into a collection of XX two-dimensional images, with spatial resolution of 3 x 3 x 30 nm^3. Together the raw images require 3.3 exobytes of data, and the imaging itself would require XX years [3]. A new serial electron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

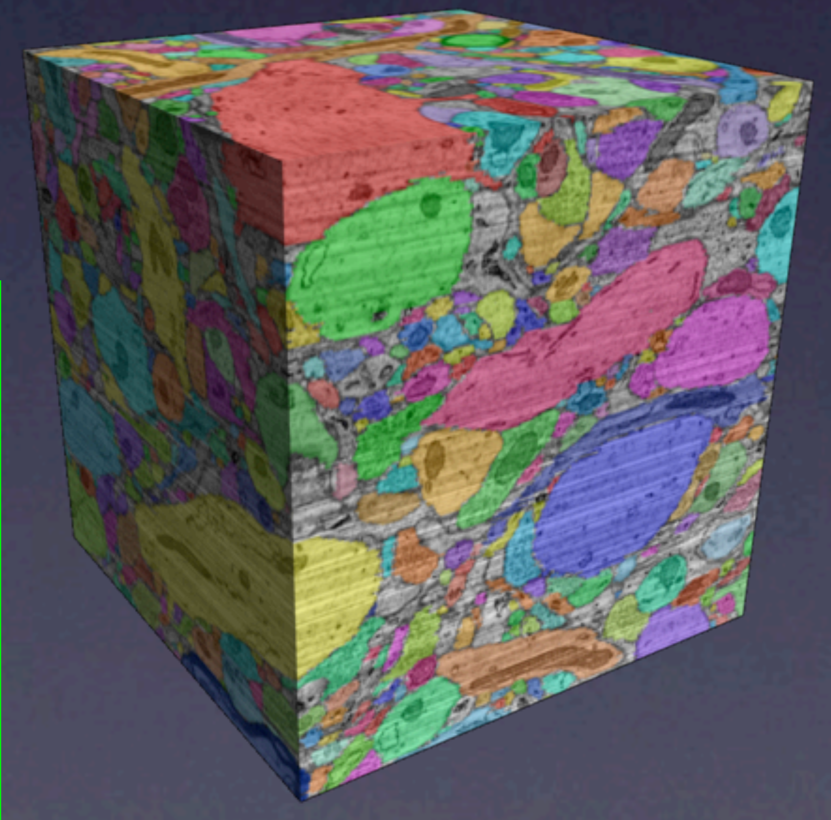


Step 3: Three-dimensional image processing tools generate a "clean" volumetric image from the collection of two-dimesional images [4]. The data is stored to facilitate efficient machine annotation, and simultaneous access by thousands of users.

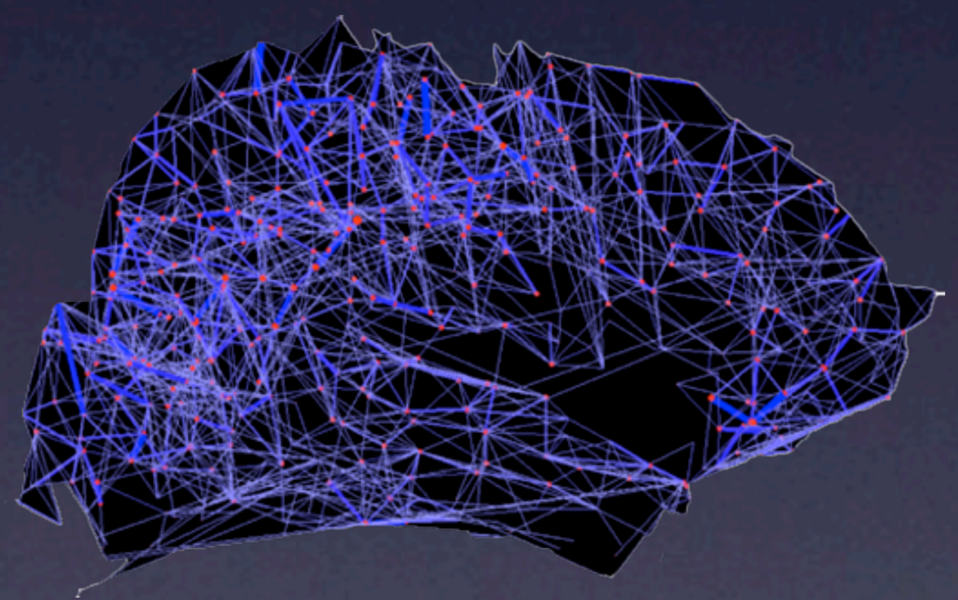




Step 4: Machine annotation algorithms can then efficiently, and in parallel, completely annotate the data, marking each pixel as either soma, axon, dendrite, synapse, etc. [5].



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 both generate biofidelic human brain simulations, and begin estimating random-graph models on these extremely large graphs [7]. These analyses will inform future experiments, including which features must be studied in greater/lesser detail to address specific neurobiological and computational questions.

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

Beyond: Detailed knowledge of a connectome (in analogy with the genome [8]),could lead to revolutionary new computing technologies, including the first ever neuromorphic biofidelic emulations of the human brain (or parts thereof).

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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] Machette et. al., in prep. [8] Lichtman & Sanes, 2008.