Mapping the Brain: An Introduction to Connectomics
From Brain to Graph and Everything In Between

Adam Chang, Daniel Lopez, Kevin Peng

January 21, 2016

1 Abstract

Current technology has advanced to the point where generating a map of the entire brain, or connectome, is possible, as evidenced by the quickly expanding field of connectomics. However, the important structural motifs of the brain, namely the existence of cortical columns, requires the identification of each individual neuron in the brain and the connections it makes. Unfortunately, a development of a map at such a scale is incredibly costly and time consuming and there are no concrete numbers concerning the creation of an entire human connectome. Thus, we have developed an optimized method by which a human brain can be successfully mapped efficiently and cheaply with the state of the art technology at this time. Our results have provided figures by which future efforts to map the brain can be compared to, encouraging the development and use of more efficient and cost effective methods. With our plan, it will be possible to map an entire human brain in 120 years, thus allowing us to analyze the map and identify motifs that are present. Thus we would be able to determine if there truly are cortical columns in the brain and analyze whether these structures can be useful to map, potentially increasing the speed and usefulness of generating a connectome.

2 Results

Beginning with scanning, we decided on a microscopic scale based on Frank Wood's project proposal to scan the entire brain, including synaptic strength[1]. We did not pursue a macroscale as it is too large nor a mesoscale to avoid the possibility of incorrectly identifying conglomerates of neurons as minicolumns or cortical columns. The best imaging technique to do a microscale involved TEM and SEM, and Serial Block Face SEM. We choose Multi-Beam Zeiss SEM because it is currently the fastest SEM, while also only costing as much as a high-quality TEM[4]. Although TEM offers better resolution, it is more damaging and not as fast as the Multi-Beam SEM[2]. For the Serial Block Face SEM, it is unable to scan the entire brain, missing out on a key part of our goal. After deciding on the 4-6 million dollar Multi-Beam SEM, we calculated that we would need about 2000 machines in order to scan one average human brain in around 85 years. Since the number of machines is quite large, we plan on using the incentive of receiving a Multi-Beam SEM as compensation for the use of a University's facility until the completion of the scanning. Our next ordeal involved providing the computing capabilities to be implemented in processing the resulting images. We decided upon cloud computing services, which would allow for dynamic configurations that suited our needs[11]. Also, utilizing the cloud would eliminate costs of gathering the necessary hardware and the complications of storage of those machines after the computation is complete[11]. In order to ensure that the processing of the images does not take too much time, we determined that it would require 3.5 million of Amazon's extra large 10-Gigabit instance, costing nearly $76 billion[5] [10]. To convert the large amounts of images from the SEM, we concluded using the automated i2g would be the cheapest and quickest solution for it is free and state-of-the-art [5]. Compared to other manual and semi-automated reconstructions reveal that an automated one is best, and the i2g happens to incorporate the parts, such as algorithms for segmentation, they found useful from others, including a 2013 automated pipeline[5]. Finally, to store and upload the resulting data, we will have our own private facility and data servers. The estimated data size is 3 zettabytes and a storage facility for such a large amount of data would require $1.5 billion[9]. This is a fairly reasonable price compared to that of other options, most notably cloud storage, which would cost upwards of $300 billion every month if the kind of accessibility and retrieval capabilities necessary, considering the human connectome data is to be used, is to be present[10]. Once the data is stored in the facilities, it can be analyzed and mapped to determine if cortical columns truly exist and figure our the source of brain-related diseases.

3 References

[1]: http://www.robots.ox.ac.uk/f̃wood/teaching/3YP_2015/

[2]: Omwenga, Susan. "Difference between Scanning and Transmission Electron Microscope", TheyDiffer, 11 July 2015. Web. 20 Jan. 2016.

[3]: EBERLE, AL, MIKULA S, SCHALEK R, LICHTMAN J, TATE MK, ZEIDLER D . "High-Resolution, High-Throughput Imaging with a Multibeam Scanning Electron Microscope." Journal of Microscopy 259.2 (2015): 114–120. PMC. Web. 21 Jan. 2016.

[4]: G. Delleman, T. Kemen, A. Eberle, T. Garbowski, M. Malloy, B. Bunday, B. Thiel, D. Zeidler, "Advances in Mulit-Beam SEM Technology for High-Throughput Defect Inspection,"Zeiss, 2015.

[5] Roncal, William R. Gray, Dean M. Kleissas, Joshua T. Vogelstein, Priya Manavalan, Kunal Lillaney, Michael Pekala, Randal Burns, R. Jacob Vogelstein, Carey E. Priebe, Mark A. Chevillet, and Gregory D. Hager. "An Automated Images-to-graphs Framework for High Resolution Connectomics." (2015). Frontiers in Neuroinformatics.

[6] S.-y. Takemura et al., "A visual motion detection circuit suggested by Drosophila connectomics," Nature, vol. 500, pp. 175–181, Aug. 2013.

[7] Sporns, O., Tononi, G., and Kötter, R. (2005). The Human Connectome: A Structural Description of the Human Brain. PLoS Computational Biology, 1(4), e42.

[8] Mikula, Shawn, Jonas Binding, and Winfried Denk. "Staining and Em-

bedding the Whole Mouse Brain for Electron Microscopy."Nature.com. Nature Methods, 21 Oct. 2012. Web. 19 Jan. 2016.
[9] "NSA Utah Data Center." NSA Utah Data Center - Serving Our Nation's Intelligence Community. Domestic Surveillance Directorate, n.d. Web. 21 Jan. 2016.
[10]http://calculator.s3.amazonaws.com/index.html
[11]https://aws.amazon.com/ec2/?nc2=h_l3_c

A Figures

62.5GB for $1mm^2$, 30nm thick image at 4 x 4nm resolution

A $1mm^3$ portion would require:

$$1mm \times \frac{3\times10^5 nm}{1mm} \times \frac{30nm}{slice} \sim 33{,}333 \text{ slices}$$

The average volume of the brain is $1450cm^3$ or $1450000mm^3$, thus 1 brain would be

$$\frac{33{,}333 slices}{1mm^3} \times 1450000mm^3 \times \frac{62.5GB}{slice} \times \frac{1ZB}{1\times10^{12}GB} \sim 3ZB$$

Figure 1: Calculation of storage space needed for entire human brain

$1cm^2$, 30nm thick image at 4 x 4nm resolution in 3 hours

A 1 cm^3 portion would require:

$$1cm \times \frac{1\times10^7 nm}{1cm} \times \frac{slice}{30nm} \sim 333{,}333 slices$$

The average volume of the brain is $1450cm^3$, thus 1 brain would take a single machine

$$333{,}333 slices \times \frac{3hours}{slice} \times \frac{day}{24hours} \times \frac{year}{365days} \sim 170{,}000 years$$

However, utilizing 2000 machines would allow us to complete imaging the entire brain in

$$\frac{170{,}000years}{2000machines} \sim 86years$$

Figure 2: Calculation of machines needed to produce results in a short time frame while also maintaining reasonable costs.

60,000micron portion took 39 hours with 100 cores

A $1cm^3$ portion would require:

$$1cm^3 \times \frac{1\times10^{12}\mu m^3}{cm^3} \times \frac{\text{micron portion}}{60{,}000\mu m^3} \times \frac{39\text{hours}}{\text{micron portion}} \times \frac{\text{day}}{24\text{hours}} \times \frac{\text{year}}{365\text{days}} \sim 74{,}200\text{years}$$

Thus the entire human brain would take a 100 core computer cluster

$$\frac{74{,}200\text{years}}{1cm^3} \times 1450cm^3 \sim 108{,}000{,}000\text{years}$$

However, by increasing the number of cores, to 100,000,000, the brain images could be processed in

$$\frac{108{,}000{,}000\text{years}}{1{,}000{,}000\text{cores}} \sim 108\text{years}$$

Figure 3: Calculation of computational power necessary for efficient processing and relative low cost.

Compute: Amazon EC2 Instances:

	Description	Instances	Usage		Type	Billing Option	Monthly Cost
		3500000	100	% Utilized/N	Linux on m4.10xlarge	3 Yr All Upfront Rese	$ 0.00

Total One-Time Payment: $ 76142048675.00

Figure 4: Estimated cost of cloud computing using Amazon's AWS Simple Monthly Calculator.