Brain Mapping @ Argonne

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1. Technological advance leads to biological insight
2. The ‘control’ is the interesting bit
3. “Anatomy is destiny” - S. Freud (1931)
Technology is (can be) the answer:

1. Cajal and Golgi (1906) - Golgi stain and compound microscope
2. Erlanger and Gasser (1944) - Oscilloscope
3. Hodgkin and Huxley (1964) - voltage clamp
5. Hubel and Wiesel (1981) - trans-synaptic tracing, single-unit recording
6. Montalcini and Cohen (1986) - explants and neuronal culture
7. Sakmann and Neher (1991) - patch clamp
8. Lauterbur and Mansfield (2003) - MRI
10. Betzig, Moerner, and Hell (2014) - super-resolution microscopy
Cajal, 1903
One hundred years of solitude

Cajal, 1903

(Llinas, Leznik, Urbano 2002)
White, et. al. 1989
Kasthuri and Lichtman

X-ray

Sample Prep

Resolution
Sample Preparation

- Perfusion with Glutaraldehyde and Paraformaldehyde

- Vibratome sectioning (100 or 200 micron slices)

- Dehydration and embedding in epoxy resin (EPON or Durcupan)

- Staining with heavy metals (Osmium, Uranium, Lead)

Species Independent
~ 450 employees; ~5,000 users per year worldwide.

More protein structures in the Protein Data Bank than any other x-ray light source in the world.

2012 Nobel Prize - Koblika and Lefkowitz - Structure of G-PCR
Serial ultra-thin slicing → EM imaging

Image alignment

2D Object Segmentation ← Image alignment

3D Object Segmentation ← 2D Object Segmentation

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EM imaging
Throughput: \(~1000\) sections/day; 30nm

- Diamond knife with water-filled boat
- Plastic embedded tissue block
- Ultrathin tissue section being collected

Automatic \(H_2O\) level maintainer

Licensed and commercialized
Tape with sections

Cut into strips and attached to 6” wafer
Visualizing the brain at the level of the connectome would consume nearly half the world’s current digital storage capacity.

Storage capacity needed to map a mouse connectome:
450,000 terabytes

Storage capacity needed to map a human connectome:
1.3 billion terabytes

Global hard drive storage, 2014:
2.6 billion terabytes

Source: Bobby Kasthuri, International Data Corporation (global hard drives)
By The New York Times
XEM

Sample preparation

X-ray

Excised volumes

Sectioned volumes

Section

EM imaging and automated segmentation

Electrons
We choose to go to the moon in this decade and do the other things, not because they are easy, but because they are hard, because that goal will serve to organize and measure the best of our energies and skills, because that challenge is one that we are willing to accept, one we are unwilling to postpone, and one which we intend to win.

But why, some say, the Moon? Why choose this as our goal? And they may well ask, why climb the highest mountain? Why, 35 years ago, fly the Atlantic? Why does Rice play Texas?
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