What does it mean to understand the brain?

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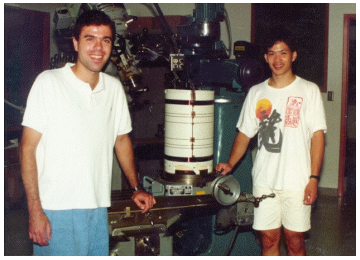
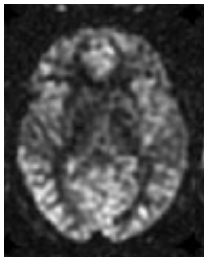
A Little Background

- I am an MRI physicist
- Worked in the early 1990s on tools for fMRI



- From 1995, worked on MRI tools for fMRI, diffusion, and fast imaging, with a primary focus on developing MRI based perfusion imaging methods using ASL.



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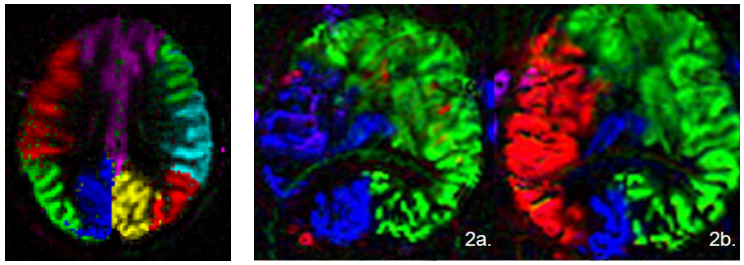
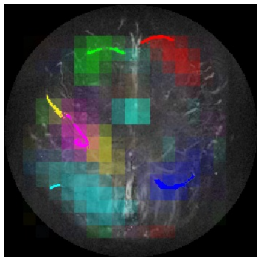


Vascular Territories

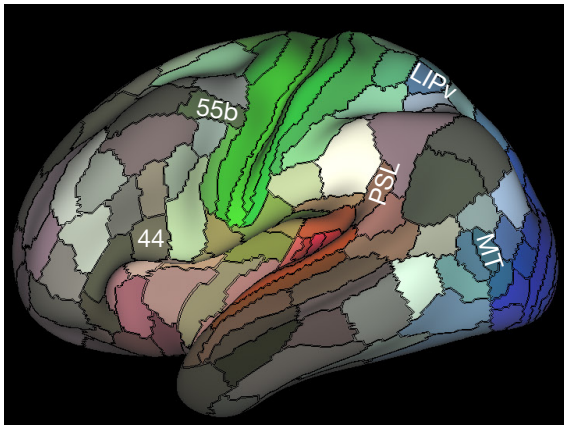


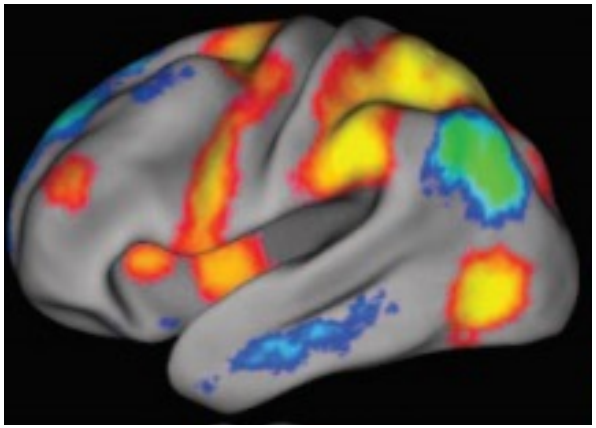
Venous Territories

Blood Oxygenation

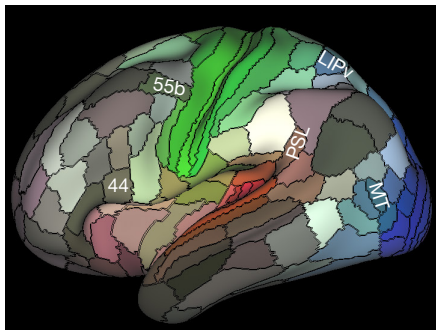
Opportunities for application of new technologies to fMRI

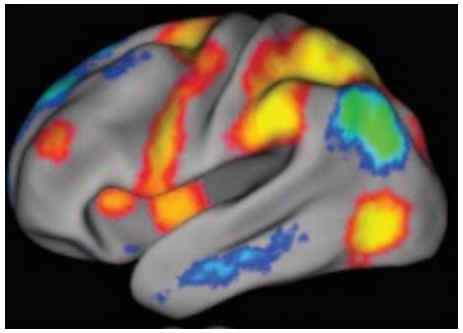
- Parallel imaging -> escape from k-space
- Constrained or model based reconstruction such as Compressed Sensing
- A lot of fMRI data is evaluated as parcels or networks
- Typical whole brain fMRI:
  - A million voxels
    - 100K gray matter voxels
    - 100-500 parcels or networks

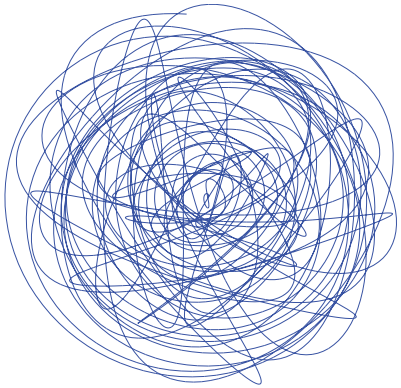




Direct Mapping of Functional Networks







Parcellation

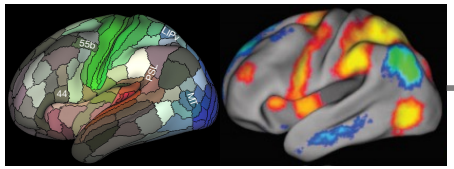
Incoherent K-space Trajectory

$$S = Ax$$

Network Coefficients

MR Signal

Encoding Matrix



$$x \approx A \setminus S$$

Current Projects

- Direct fMRI Mapping of Functional Parcels/Networks
- Functional Parcellation
- Data Driven Dynamic Whole Brain Model
- Nanodevice Mediated Functional Imaging

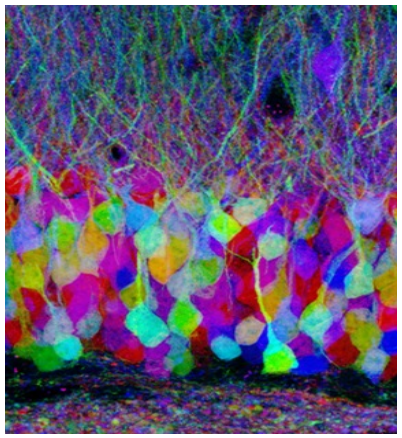
What For?

- What do people do with fMRI data?
  - Correlate tasks with local brain activity
  - Map connectivity
  - Identify networks
  - Look for changes with disease
- How does this help us understand the brain?

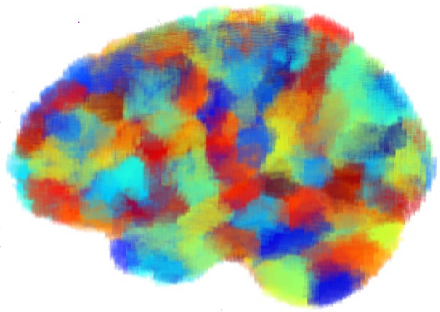
What does it mean to understand the brain?

Working definition: To understand the brain is to discover the algorithms by which it stores and processes information.

Bottom Up ⟶ ? ⟵ Top Down

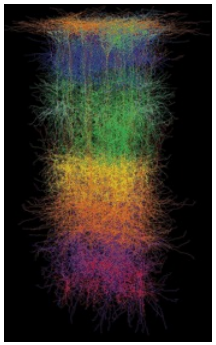
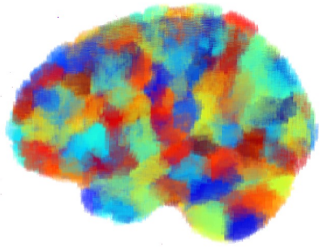


Electrophysiology
Optogenetics



fMRI
EEG/MEG

Is understanding cells and circuits and scaling up to the human brain a plausible approach?

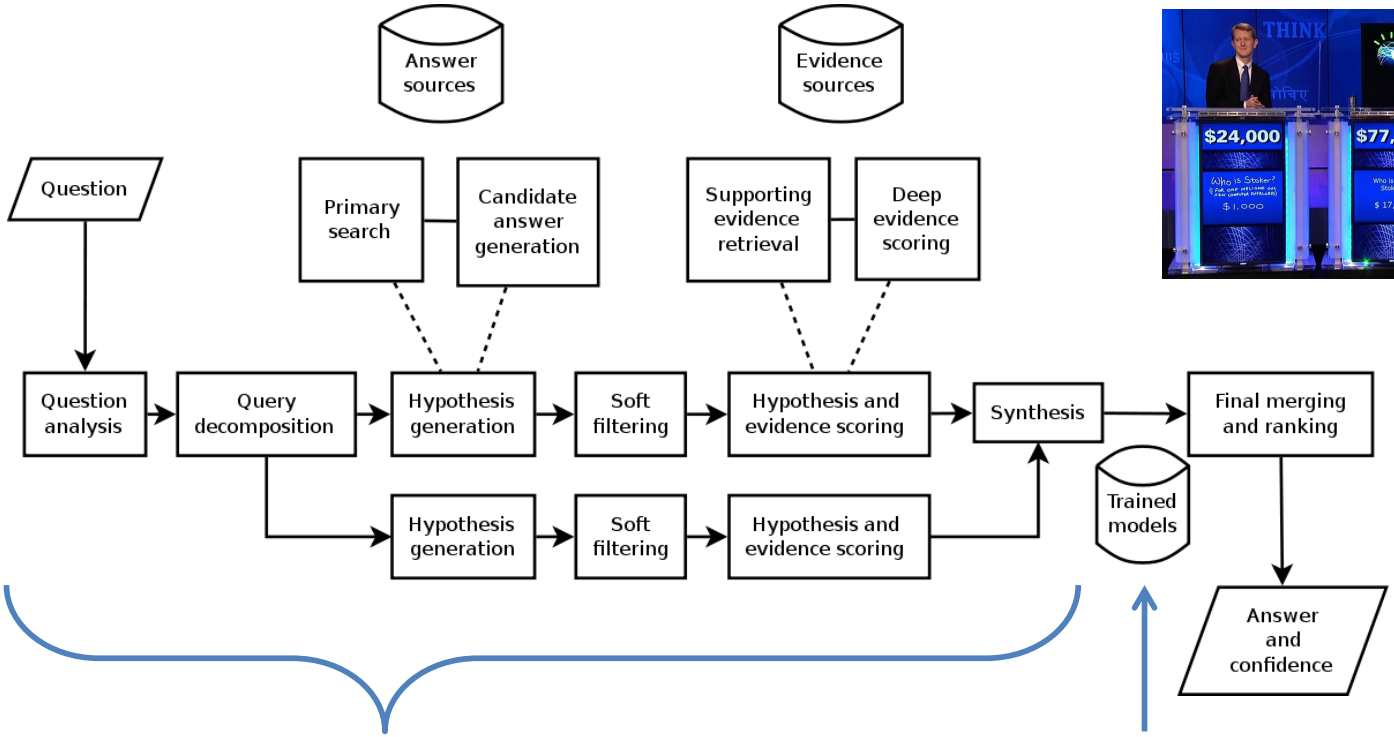




From **The Human Brain Project Framework Partnership Agreement**:

- Develop a multi-scale theory of the brain, creating a synthesis between top-down and data-driven bottom-up approaches.
- Identify bridges linking the multiple temporal and spatial scales implicated in brain activity and in the signals captured by imaging and other technologies.

Machine Learning

- We have been trying to deconstruct and reconstruct intelligence for a long time
- Watson:

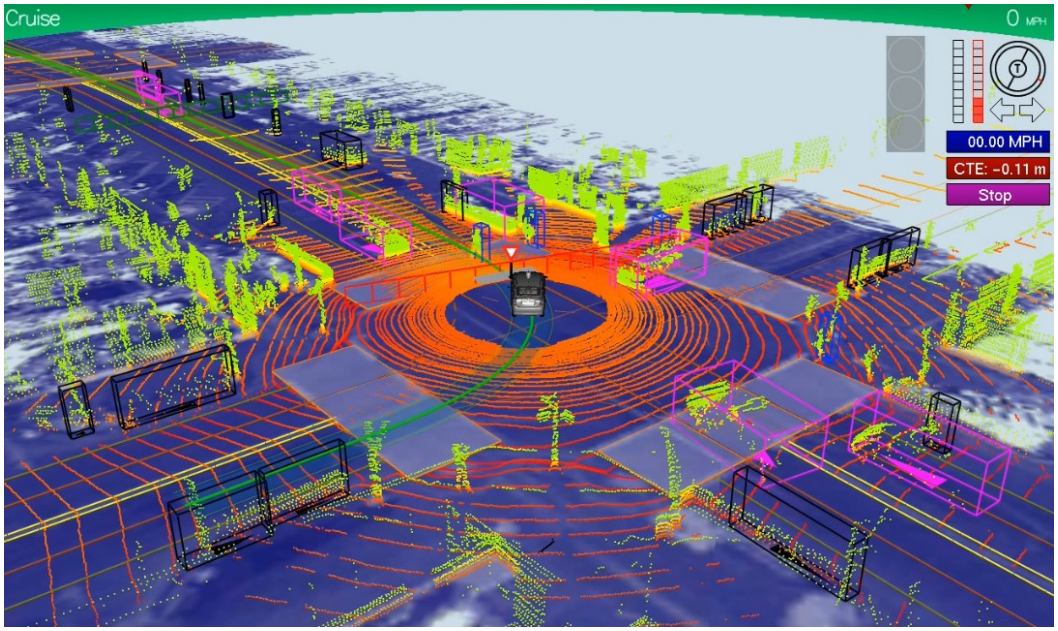


Expert System (algorithmic description)

Artificial Neural Network (???)

Deep Blue and AlphaGo have similar architectures

Google Car



Expert System

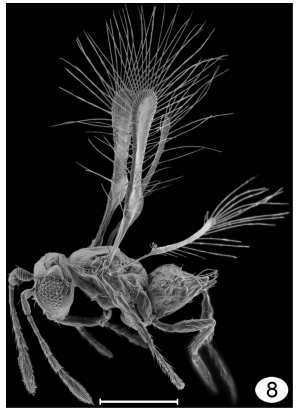
+

Artificial Neural Network

What is our capacity for describing things algorithmically?

100μm (!)

Unfortunate Conclusions



- An expert system contains about as much brain power as a fly
- The human brain has many orders of magnitude more complexity than it is capable of understanding in a compact algorithmic way.

Unfortunate Conclusions (cont'd)

- If we had signals from our billions of neurons and trillions of synapses, we could simulate a brain but still could not understand it.
- **The concept of 'scaling up' from neurons to brains, for the purpose of understanding our brains algorithmically, contains an inherent barrier, and that barrier lies at only thousands of neurons.**

This is consistent with:

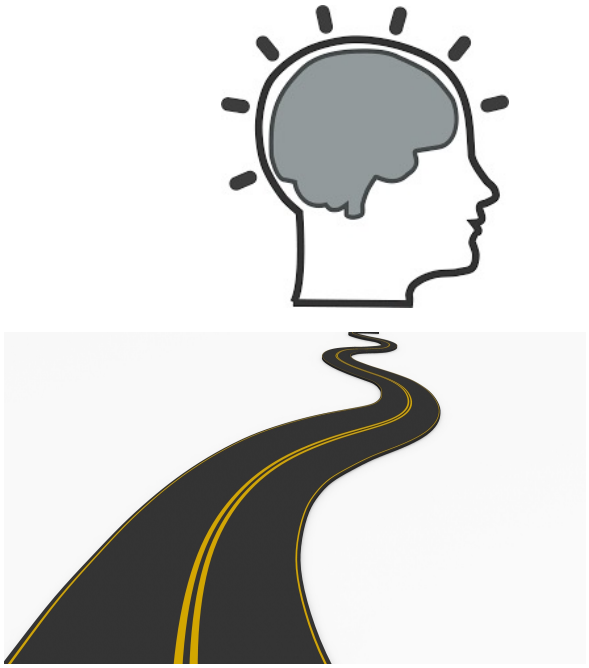
- The fact that highly expert humans in Chess/Go/Jeopardy do not understand what their computer counterparts are doing with only a few thousand simulated neurons, even though we know all the weights and responses.
- The fact that most activities that we become expert at involve 1% formal specific instruction and 99% practice.

I'm wrong if:

- Somebody figures out how to effectively transform trillions of weights into a dramatically smaller dimensional space to make them humanly understandable.
- The brain is modular and can be broken down into units that can be separately understood, and integrated.
- The analogy to artificial neural networks is a bad one.

Re-examine ‘Understanding’

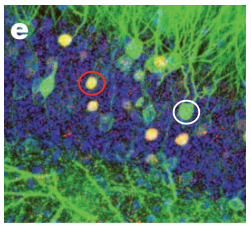
Complete algorithmic understanding

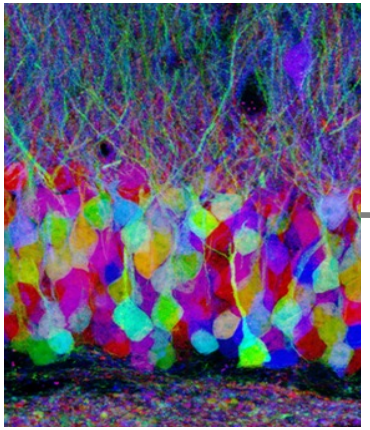


Mechanistic or phenomenological understanding

Intuitive understanding

Grand Challenges: Play to our Strengths

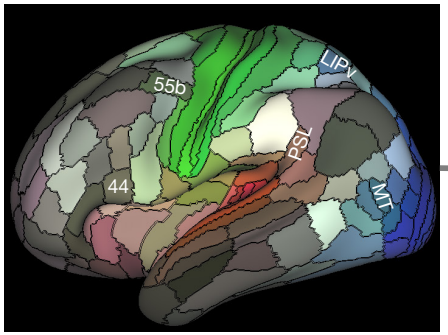




Memory
Learning

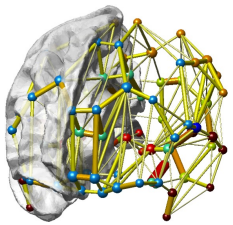
Pharmaceutical
Genetic
interventions

PBS



Functional
Organization

Network-
opathies



Summary

- Spanning spatial scales may not be a useful core concept in the quest to understand the brain
- Proposed Grand Challenges:
  - Microscale: Memory and Learning
  - Macroscale: Functional Organization