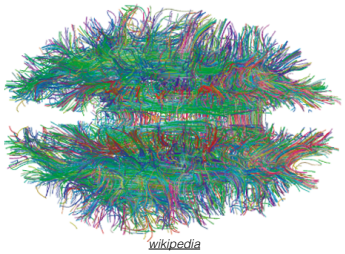
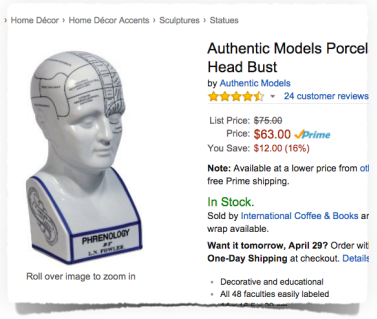
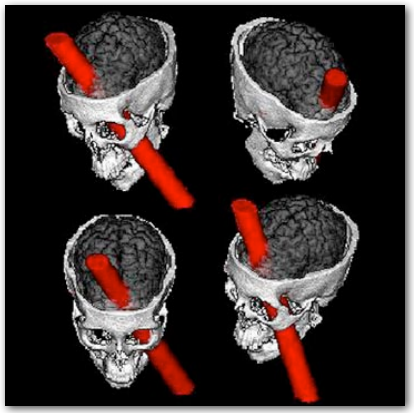
COGS 105

Final Content Week: Brains and Clinical, Part I

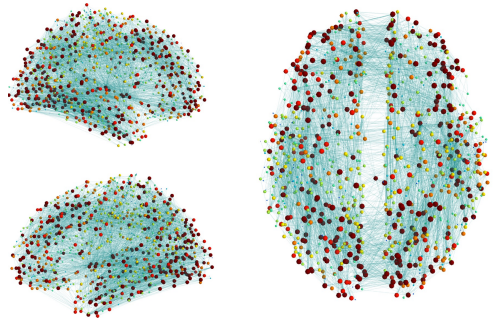


wikipedia



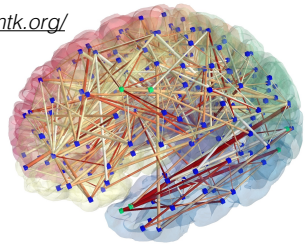


What's Next?



Gerhard et al. "The Connectome Viewer Toolkit: An open source framework to manage, analyze, and visualize connectomes"

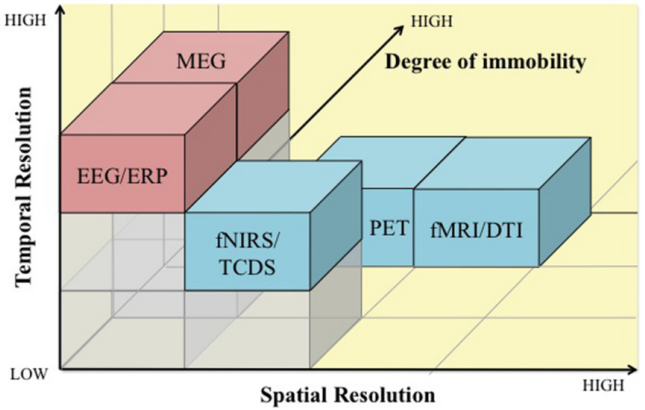
http://www.cmtk.org/



ds

Historically, most neuroimaging studies of the human brain have employed a modular view of the brain, e.g., *region* X is responsible for function Y. This modularity of mind approach, however, is insufficient for describing the vast set of cognitive and behavioral operations of which the brain is capable. A more appropriate approach considers which *network* of two or more connected and interacting regions are employed for a given function. It has not always been possible to view networks in the brain; it was not until recently that any magnetic resonance imaging (MRI) sequence was capable of discerning individual axon bundles.

From reading #2

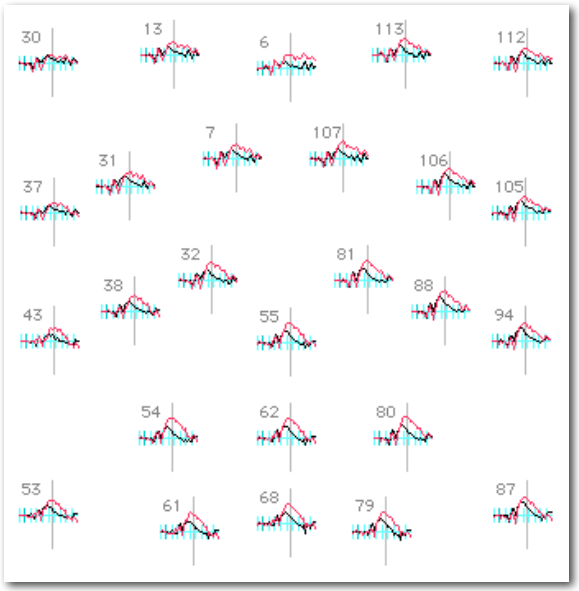


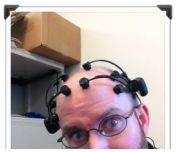
http://journal.frontiersin.org/article/10.3389/fnhum.2013.00889/full

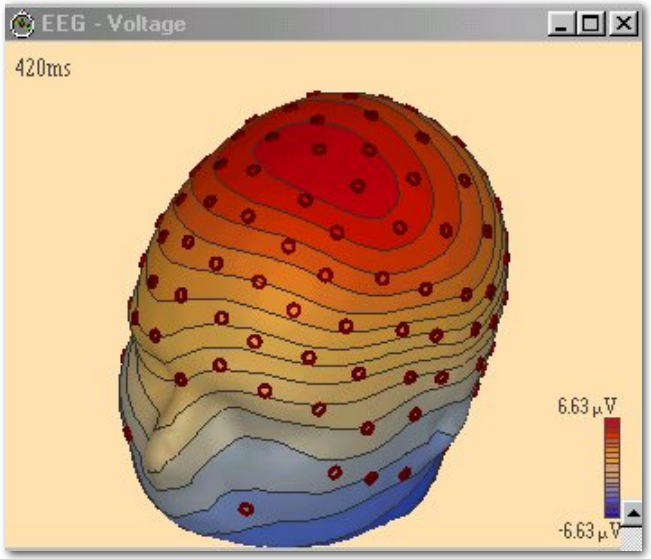
- Response to "X"
- Do not respond to "O"

O

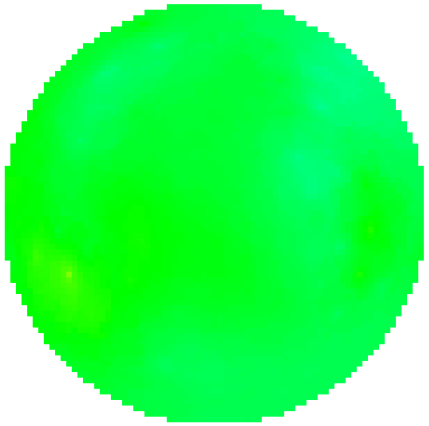
X


30
13
6
113
112
7
107
31
106
37
105
32
81
38
88
43
55
94
54
62
80
53
61
68
79
87

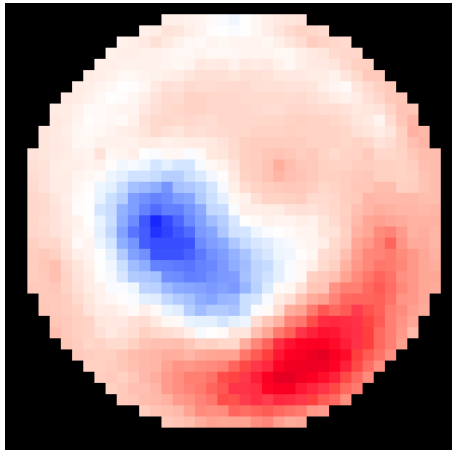



EEG - Voltage
420ms
6.63 µV
-6.63 µV

ERP Movies...



ERP Movies...



Next…

- The dominant thread in neuroscience and cognitive neuroscience for over a century has been functional localization — *region X, function Y*.
- There is a rapidly growing movement — also old in its underpinnings, but now backed with wicked new techniques — to study the *networks* of areas that underlie function.

Why?

- Two studies suggesting strict localization interpretation is problematic:
  - Thyreau, B., et al. (2012). Very large fMRI study using the IMAGEN database: Sensitivity–specificity and population effect modeling in relation to the underlying anatomy. NeuroImage, 61(1), 295-303.
  - Gonzalez-Castillo, et al. (2012). Whole-brain, time-locked activation with simple tasks revealed using massive averaging and model-free analysis. Proceedings of the National Academy of Sciences, 109(14), 5487-5492.

Whole-brain, time-locked activation with simple tasks revealed using massive averaging and model-free analysis

Javier Gonzalez-Castillo[a,1], Ziad S. Saad[b], Daniel A. Handwerker[a], Souheil J. Inati[c], Noah Brenowitz[a], and Peter A. Bandettini[a,c]

[a]Section on Functional Imaging Methods, Laboratory of Brain and Cognition, [b]Scientific and Statistical Computing Core, and [c]Functional MRI Facility, Institute of Mental Health, National Institutes of Health, Bethesda, MD 20892

Edited by Robert Desimone, Massachusetts Institute of Technology, Cambridge, MA, and approved February 21, 2012 (received for review Decembe

The brain is the body's largest energy consumer, even in the absence of demanding tasks. Electrophysiologists report on-going neuronal firing during stimulation or task in regions beyond those of primary relationship to the perturbation. Although the biological origin of consciousness remains elusive, it is argued that it emerges from complex, continuous whole-brain neuronal collaboration. Despite converging evidence suggesting the whole brain is continuously working and adapting to anticipate and actuate in response to the environment, over the last 20 y, task-based functional MRI (fMRI) have emphasized a localizationist view of brain function, with fMRI showing only a handful of activated regions in response to task/stimulation. Here, we challenge that view with evidence that under optimal noise conditions, fMRI activations extend well beyond areas of primary relationship to the task; and blood-oxygen level-dependent signal changes correlated with task-timing appear in over 95% of the brain for a simple visual stimulation plus attention control task. Moreover, we show that response shape varies substantially across regions, and that whole-brain parcellations based on those differences produce distributed clusters that are anatomically and functionally meaningful, symmetrical across hemispheres, and reproducible across subjects. These findings highlight the exquisite detail lying in fMRI signals beyond what is normally examined, and emphasize both the pervasiveness of false negatives, and how the sparseness of fMRI maps is not a result of localized brain function, but a consequence of high noise and overly strict predictive response models.

the neuronal correlates of a myriad of human be
Unfortunately, if, as the previous discussion suggests, t
ronal responses are continuously passing undetected i
our conceptualizations of brain function based on ta
fMRI research might be incomplete.

As Lieberman and Cunningham stated previously (7)
standing preoccupation with the reduction of false-pos
fMRI creates a bias toward reporting only large and
effects, neglecting what perhaps represents more subtle
cognitive and affective processes. Here, we explore this
esis in detail and evaluate whether the sparseness of ta
fMRI activation maps is real or a consequence of noise le
modeling decisions. We approach this question using l
fMRI time-series generated by combining unconventiona
amounts of data (100 runs per subject). With these data
evaluate how regional differences in BOLD response ma
how distant regions collaborate during a particular task.

What Is the True Extent of BOLD Activations? Previous rese
shown that if fMRI noise is reduced by time-series av
activation area significantly increases with number of a
runs (8, 9). Fast increases in activation area during init
aging stages were followed by a progressive decrease in
of area growth with averaging. Still, no asymptotic beha
reported. Moreover, voxels with subtle hemodynamic r
not strong enough to attain significance with fewer trials
no significant differences in hemodynamic delay from vo
were significantly active with fewer trials (8). This finding

> Taken together, these two sets of results reveal that conventional fMRI is a bit of a blunt instrument.
>
> As an analogy, suppose that all you knew about your neighbours was from the noises that you heard through the wall. The shouts and screams would be loud enough to reach your ears; the normal conversations and whispers wouldn't. If you concluded that all your neighbours did was shout, not talk, you'd get a misleading picture of their relationship.
>
> That's the bad news. On the other hand, fMRI is clearly more powerful than most neuroscientists have realized, and this holds out hope for cracking some of the trickiest questions facing the field in the future, with larger studies and more sensitive techniques.

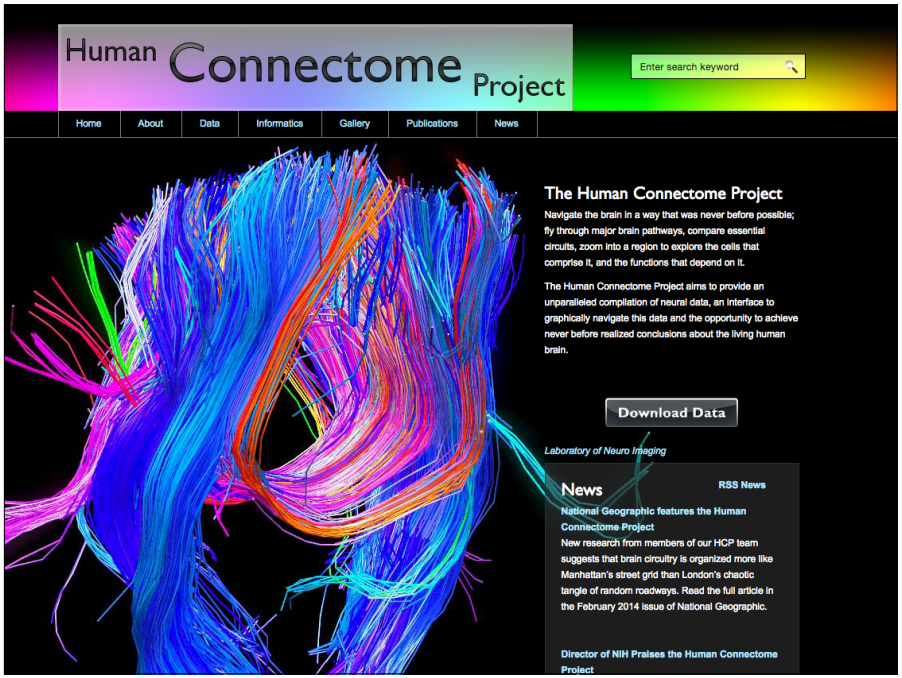
http://blogs.discovermagazine.com/crux/2012/04/25/does-brain-scanning-show-just-the-tip-of-the-iceberg/

Neuroskeptic

> Researchers are now developing statistical methods to pull meaningful information out of a single scan. In one study[16] published in 2010, a team trained a computer to pick out patterns in brain-scan data collected when participants were resting. They did this for nearly 240 people aged 7–30 years to build up maps of brain connectivity at different ages. They then showed that they could take a single brain scan from a different person and, by comparing it with their reference set, work out the owner's brain maturity. Such techniques might eventually be used to diagnose a developmental delay or psychiatric disorder, and there are hints that they can identify teenagers genetically at risk for depression[17].

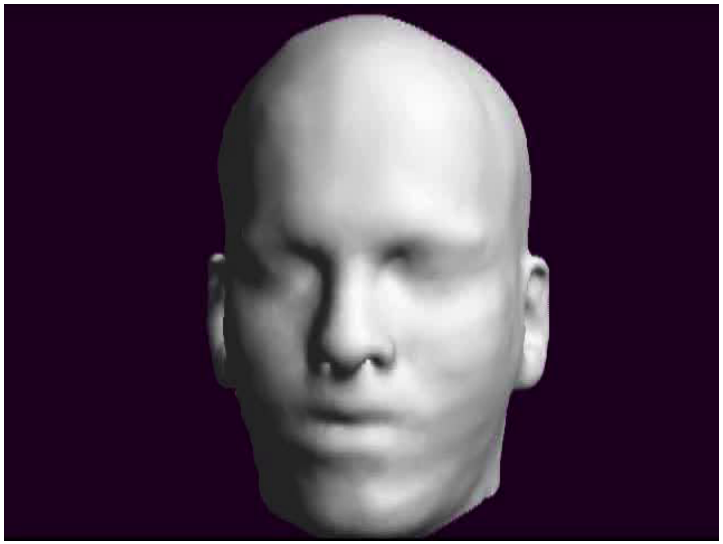
> With new ways both to examine the data and to boost the technology, many neuroscientists see a future filled with multicoloured blobs — albeit sharper and better-understood ones. "People will be very busy easily for the next 20 years," says Bandettini. "I would say that fMRI in many aspects hasn't really even begun."

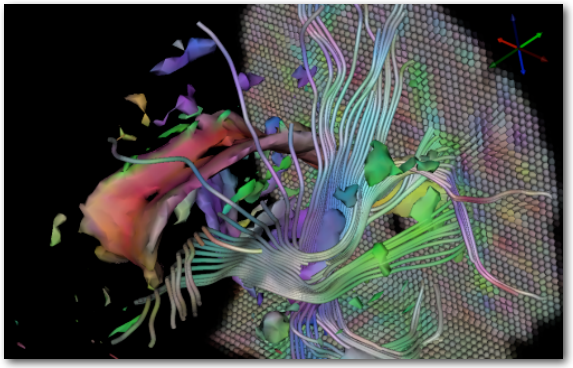
http://www.nature.com/news/brain-imaging-fmri-2-0-1.10365



Diffusion MRI

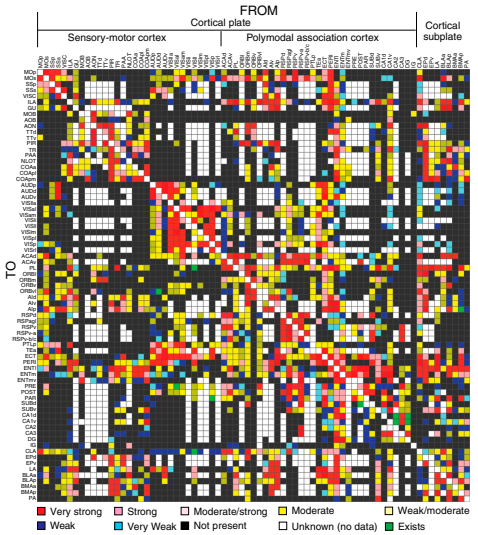
- “Diffusion tensor imaging.”
- Until recently mostly “structural” technique.
- Can detect subtle magnetic effects of axonal water diffusion
  - Direction of axons can give us a picture of “information flow.”





The connectome may be defined as the complete, point-to-point spatial connectivity of neural pathways in the brain.[4] This detailed, multiscaled, and multivariate matrix is defined computationally and statistically using sophisticated *in vivo* neuroimaging data, electrical recordings, and postmortem tissue samples to provide a detailed framework to understand the anatomically based interactions of functional regions of the brain. The connectome gives rise to population-level atlases of distributed connectivity and makes it possible to assess disruptions of connectivity in clinical samples. Demographic, genomic, and cognitive/ behavioral data can be superimposed on the connectome to permit inferences concerning

reading #2



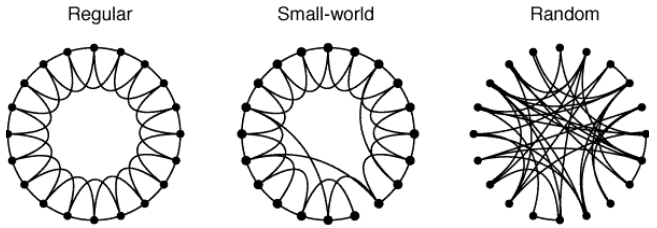
Bota et al., "Architecture of the cerebral cortical association connectome underlying cognition"

Network Methods

- *Different from (but can be related to) neural networks*. Sometimes referred to as "graph theory."
  - Neural networks are a tradition in computational modeling of cognition.
  - Graph theory is a mathematical method for studying the structure of networks.
- Each brain area is a "node" and each connection is called an "edge." We can analyze the structure of the network and its functional implications.

Example

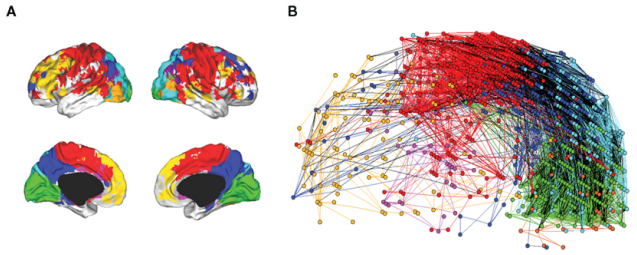
- What is a "small world."



clustering (C):
"two friends of yours are also friends of each other"

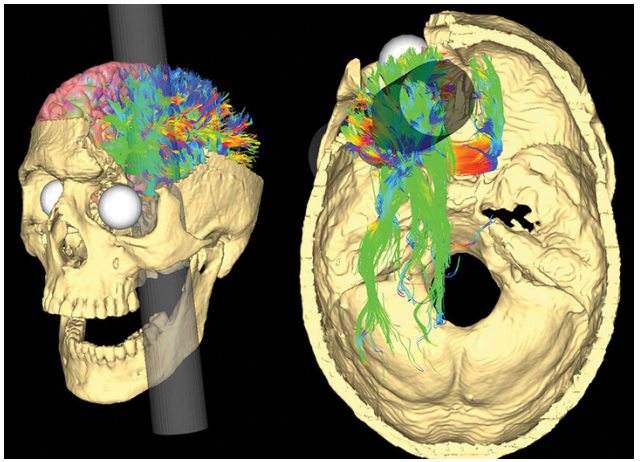
path length (λ):
getting from person A to person B in how many steps?

From Watts & Strogatz



Meunier et al., "Modular and hierarchically modular organization of brain networks"

network, i.e., those having a "shorter" λ.[31,43] These methods have also been applied to large populations of subjects to demonstrate that the overall efficiency of the brain decreases with age[44] and changes during development.[45] Additionally, graph theory constructs have been used to reveal changes in the neuroanatomical networks of subjects blind from an early age[46] and changes in the functional networks of attention-deficit hyperactivity disorder (ADHD) subjects.[47] Indeed, the mapping of the properties, organization, and structure of brain networks will require that new network theoretical metrics be developed as we extract still finer-grained elements worthy of characterization for healthy as well as diseased or damaged networks.



S. Kean, "Phineas Gage, Neuroscience's Most Famous Patient"

OPEN CONNECTOME PROJECT

COLLECTIVELY REVERSE-ENGINEERING THE BRAIN ONE SYNAPSE AT A TIME.

http://www.openconnectomeproject.org/

http://www.humanconnectomeproject.org/data/

Human Connectome Project

http://www.cmtk.org/

The Connectome Mapping Toolkit

A Python-based open source toolkit for magnetic resonance connectome mapping, data man

Final Paper Notes

- Conventional structure: **Introduction**, **Methods**, **Results**, **Conclusion** — that's fine.
- Philosophy final papers: Essay style narrative weaving from thesis to argument to conclusion (*with background review).*
- Neurosynth project may be **Introduction**, **Analyses**, **Conclusion**.