Big Questions

• What makes us think, love, talk, and ‘tick’?
• Why do each of us behave so differently?
• What goes wrong in devastating brain disorders?
  Alzheimer’s, autism, schizophrenia,…..

It’s the connections – the wiring of the brain!

  Physical wires (axons, dendrites)
  Strength of connections: “Functional connectivity”
Human Brain Parts List

Whole brain: 1500g; 86 billion neurons

Cerebral cortex:
~80% of brain mass
16 billion neurons (~20%)
150 trillion synapses
100,000 miles of axons in white matter

Cerebellum:
10% of brain mass
69 billion neurons (80%)

How do we untangle the wiring of the brain??

© 2010 Scientific American
T. Insel (April 2010)
• Focus on human brain
• Invaluable information from animal models
A view of primate cortex in 1991

- Dozens of visual cortical areas in the macaque;
- Hundreds of connections (pathways);
- Human brain circuits: very little known in 1991;
- 1992–2012: an explosion of brain imaging and analysis methods!
What’s a connectome?

A “comprehensive” map of neuronal connections

Macro-connectome
whole-brain, long-distance

Micro-connectome
(every synapse, neuron, dendrite)

Resolution: 1 – 2 mm ‘voxels’

Volume reconstructed: <<1 mm$^3$ (to date)

The Human Connectome Project:
A systematic study of the macro-connectome in 1,200 healthy adults
The “WU-Minn” HCP consortium

10 institutions:

- Washington University
- University of Minnesota
- Oxford University
- Saint Louis University
- University d’Annunzio
- Indiana University, Warwick University
- Ernst Strungmann Institute (Frankfurt)
- Radboud University (Nijmegen)
- Duke University

99 on HCP team (June, 2013)

Supported by the NIH Neuroscience Blueprint
HCP objectives (2010 – 2015)

Improve the methods of data acquisition and analysis
• 2010 - 2012 and continuing

Study brain circuits in healthy adults (2012 - 2015)
• Twins and their non-twin siblings (1,200 total)
• Relate brain circuits to behavior

Share the data with the scientific community
• Promote discoveries, accelerate progress
Structural Magnetic Resonance Imaging (MRI)

- Cerebral cortex
- Gray matter
- Subcortical white matter
- "Myelin" = insulation for faster signaling

High resolution scans (0.7 mm voxels)
Human cortical convolutions

- Surface models capture the shape of cortical convolutions
- Surface inflation ‘smoothes out the wrinkles’
- Depth maps reflect 3D shape features: “cortical brainprints”
Myelin maps in cerebral cortex

Divide and conquer: T1w/T2w ratio

Cortical myelin map individual subject

Sensory-motor strip

Auditory

MT+

Myelin content

Glasser & Van Essen (2011)
Individual variability in cortical convolutions

Two pairs of identical twins
Which are the twin pairs?

Myelin maps also vary, even in twins

Cortical folding is highly variable, but also heritable
functional MRI (fMRI)

fMRI signal reflects brain activity (over past several seconds)

Task-fMRI: compare fMRI signals during a task to a baseline (at rest, or a ‘simpler’ task)

Differences in activity reflect functional specialization
Task-fMRI activations

Move right hand

Activation in left hemisphere, central sulcus
Task-fMRI activations

‘social interaction’ vs. random movement

Random motion  “Coaxing”

A complex brain network engaged in social cognition!
Conventional fMRI

Whole Brain: several seconds to scan
“Multi-band” Brain Imaging

- Excite *multiple* slices simultaneously
- Each “coil” around the head picks up signals from nearby brain slices
- Computer algorithms decipher the original pattern

- Yields more data & better data!

Moeller et al. (2010)
The brain is very active when ‘doing nothing’

“Resting-state” fMRI reveals functional connectivity (regions that are active together are ‘wired together’)

Functional Connectivity
Anatomical substrate for fMRI visualization

Left + Right Hemisphere Surfaces
One moment in one subject’s life in the MRI scanner

Left + Right Hemisphere Surfaces

BOLD fMRI signal
Low  High

Glasser et al. (HCP unpublished)
10 seconds ‘at rest’ in scanner

- Outstanding data quality!!
- Viewing the brain at rest, but in action
Functional connectivity from resting-state fMRI

fMRI time course (locations 1, 2)

Correlate time series

Functional connectivity map (location 2)

Functional connectivity matrix (‘dense connectome’)

Functional connectivity map (location 1)
Comparing functional connectivity and myelin maps

Myelin and functional connectivity hotspots colocalize

Glasser et al. (HCP unpublished)
Structural Connectivity

Fiber bundles in white matter (brain dissection)

“Diffusion imaging” reveals fiber trajectories in white matter

7T DWI Data (CMRR)
Thompson, P. (UCLA), Lenglet C., Sapiro, G. et al. CMRR
Visualizing trajectories through white matter

“Seed” location (left hemisphere)

Trajectory through white matter

Oxford: Jbabdi, Sotiropoulos
WashU: Harwell, Coalson, Glasser
Sharing HCP Data

March, 2013: First quarterly data release (68 subjects)
June 11, 2013: Second quarterly release (another 68 subjects)
  • Unprocessed and processed data available
  • Enthusiastic response from scientific community

https://db.humanconnectome.org/
Concluding Comments

• Understanding human brain circuitry in health and disease: a grand challenge for the 21st century!

• The Human Connectome Project will elucidate brain connectivity and its variability in healthy adults.

• A ‘complete’ connectome (macro- plus micro-) is well outside our grasp

• Future studies of diseases, development, and aging will aid in diagnosis and treatment.

• Further methodological improvements are needed!
Revolutions in Cartography

**EARTH**
- Classical maps
  - 1630
- Book atlases
  - 1960
- Satellite imagery
  - Grand Canyon
  - Google Earth
- Washington University

**BRAIN**
- Classical maps
  - 1909
- Talairach atlas
  - 1988
- Satellite imagery
  - ~2005: MRI; volumes + surfaces
- Connectomics
  - 2011 and beyond

**Book atlases**
- 1960

**Talairach atlas**
- 1988