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PLoS COMPUTATIONAL BIOLOGY

Review

The Human Connectome: A Structural Description of the Human Brain

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Introduction

Introduction

- **Why connectome?**
  - Fundamentally important
  - How functions emerge from structural substrate
  - Brain dysfunction affected by disrupted structural substrate
  - A unified, time-invariant, and readily available neuroinformatics resource
- **BUT**
  - Lack of information about the neuronal units and their connections in the human brain
  - No information on the finer connectivity patterns
  - No single standardized data form
  - No open access

Introduction

1. Scales and Levels of Structural Description
2. Microscale: Single Neurons and Synapses
3. Macroscale: Brain Regions and Pathways
4. Mesoscale: Minicolumns and Their Connection Patterns
5. Individual Variability and Development
6. Steps Toward the Human Connectome
7. Conclusions: The Potential Impact of the Connectome

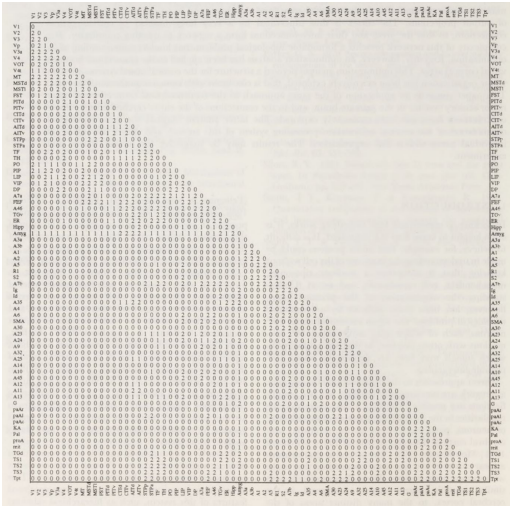
Scales and Levels of Structural Description

Neural elements & Neural connections

- Basic descriptors defining the network architecture of the connectome
- Old way: structural description that combines connection topology and biophysics
  - The binary connection matrix + connection-specific physiological data

	W10	W11	W12	W13	W14	W24	W25	W45	W46	W8A	W8B	W9
W10		E	E	E	E	E	E	A	A	E	A	E
W11	E		E	E	E	E	E		A	A	A	E
W12	E	E		E	E	E	E	A	E	E	E	E
W13	E	E	E		E	E	E	A	A	A	E	E
W14	E	E	E	E		E	E	A	A	A	A	E
W24	A	E	E	A	E		E	E	E	E	E	E
W25	E	E	E	E	E	E		A	E	A	E	E
W45	E	E	E	E	E	E	A		E	E	E	E
W46	E	E	E	A	A	E	E	E		E	E	E
W8A	E	A	E	A	A	E	A	E	E			E
W8B						E			E	E		E
W9	E	E	E	E	A	E	E	E	E	E	E	

Stephan, K. E. et al (2001)



Young, M. P. (1993)

Challenges

1) Great complexity of the human brain
2) Difficulty of defining the basic structural elements of the human brain
   - Microscale / Macroscale / Mesoscale

➜ Which level is the most appropriate for ***a first draft*** of the human connectome?

Microscale: Single Neurons and Synapses

Microscale: Single Neurons and Synapses

- Individual neurons and synapses are **inappropriate** as basic elements for an initial draft of the connectome ***(Unrealistic!)***
    - The vast number, high variability, and fast dynamics of them
    - Impossible & unnecessary

Macroscale: Brain Regions and Pathways

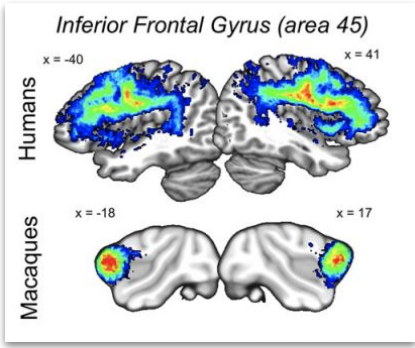
Macroscale?

- Anatomically distinct brain regions and interregional pathways
- Cerebral white matter
  - A marker of the amount of connectivity within cortical system
  - Axonal tracing methods
    - The main basis for existing mammalian large-scale connection matrices
  - Recent noninvasive imaging methods (DTI, computational tractography etc)
  - Anatomical tracing techniques with noninvasive diffusion imaging

Studying the connectome at macroscale level

- The correlated use of noninvasive structural and functional imaging methods
  - the most promising experimental route toward the human connectome
  - The patterns of connectivity can be used to identify areal boundaries
    - Individual brain regions maintain individual connection profiles
- A probabilistic map of voxel-by-voxel connectivity
  - The first draft of the human connectome
  - Provide information on the large-scale connection patterns within the corticothalamic system
  - Provide information on parcellation of human cortex into distinct areas

Kumar, V. et al (2016)



Pros and Cons

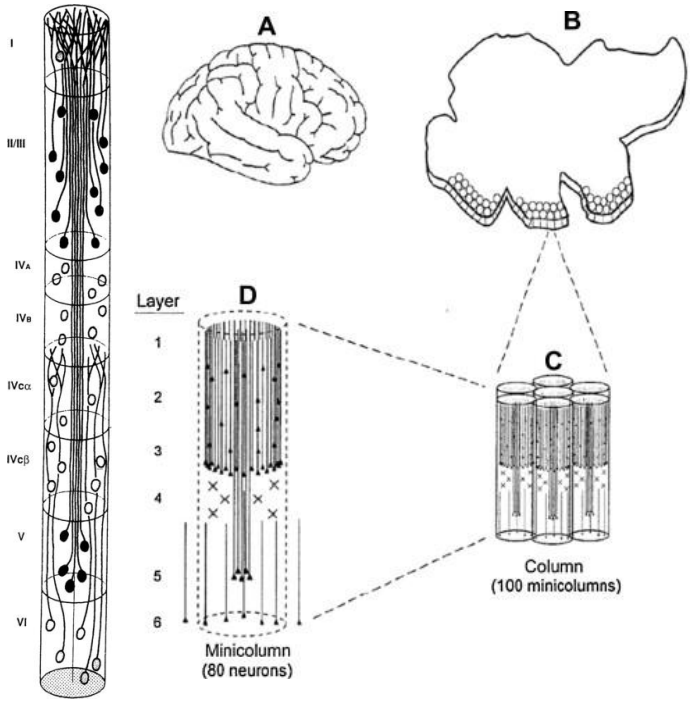
- Pros:
  - fundamental insights into ***the large-scale organization*** of human cortex
- Cons:
  - Does not incorporate information on functional subdivisions or segregated subcircuits ***within each brain region*** → insufficient basis for a complete understanding of the human brain's functional dynamics and information processing capacities

➜ Next step:
characterize connection patterns among elementary processing units (local populations of neurons such as **cortical minicolumns**)

Mesoscale: Minicolumns and Their Connection Patterns

Minicolumns

- Basic functional units of mammalian cerebral cortex
- 80-100 neurons
- Narrow chain of neurons extending vertically across the cellular layers 2-6
- All major cortical neural cell phenotypes
- Bound together by short-range horizontal connections to form cortical columns
- Stereotypic internal processing
- Generic patterns of inputs and outputs with minicolumns in other regions

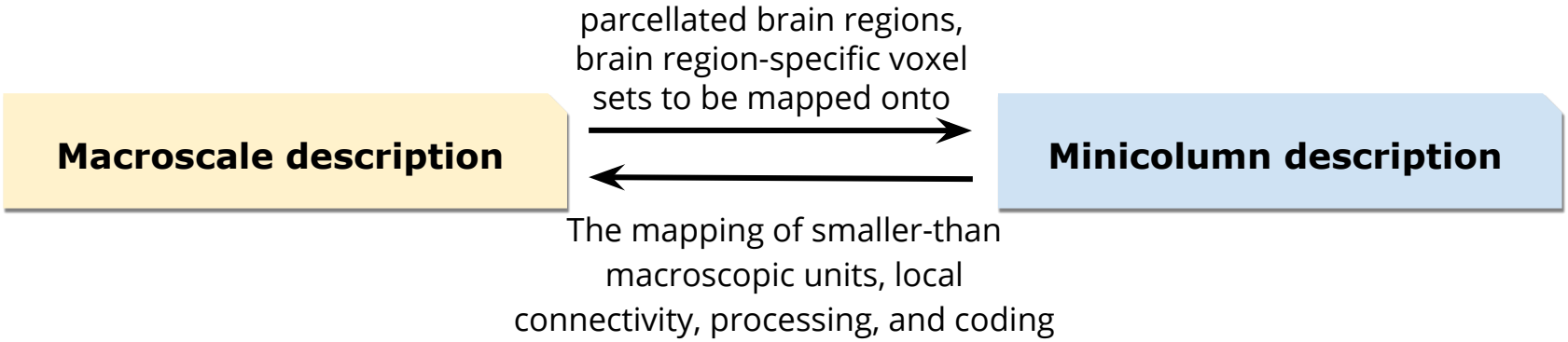


LaBerge, D., & Kasevich, R. (2013)
Mountcastle, V. B. (1997)

Minicolumns as mesoscale neural elements

- Minicolumns may represent **basic functional elements** that are crucial for cortical information processing
- Evidence for functionally specialized and precisely wired subnetworks of neurons (Yoshimura Y et al (2005) & Ohki K et al (2005))
    - Correspond to minicolumns, coexisting within single cortical columns
    - Promote greater intracolumnar functional independence and informational heterogeneity
- **How to study** connection patterns *between each region's constituent elements*?
    - **Axonal tracing methods** (Functional imaging at columnar resolution in the future?)
    - Minicolumn anatomy for selected brain regions
    - Fit into the appropriate positions within the macroscale connection matrix

Macroscale and Mesoscale as complementary datasets



<u>Successful cross-level integration</u>

➜ a single mesoscale connection matrix of the human brain,
with minicolumn elements directly cross-referenced to voxels in the macroscale map

Individual Variability and Development

Individual Variability and Development

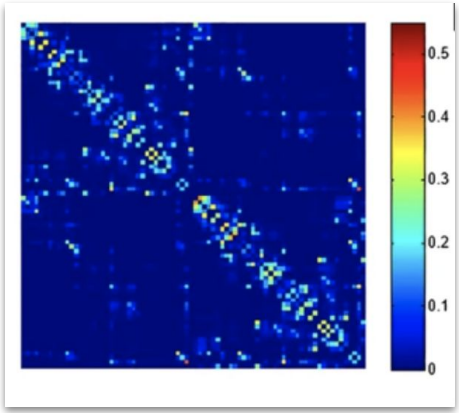
- Potential problems and limitations? → **NOT** a fundamental weakness
- Incorporating individual variations and developmental stages → *Important*
  - significant variations between individuals and development from the embryo to adolescent to adult age

- **BUT**
  - The potential insights from a first draft
  - A further step could be mapping of interindividual variability
  - Examples of Genome

Steps Toward and the Human Connectome: Its Compilation, Assembly, and Integration

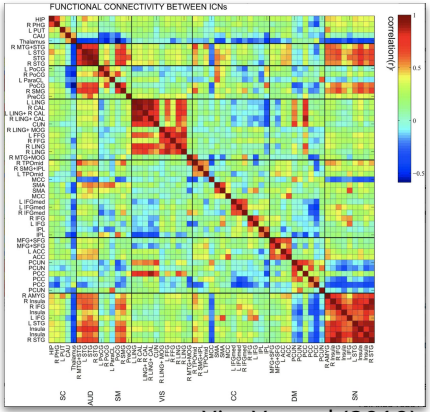
5-step strategy for a first draft of the human connectome at the macroscale

Structural connectivity matrix



Tsai, S. Y. (2018)

Functional connectivity matrix



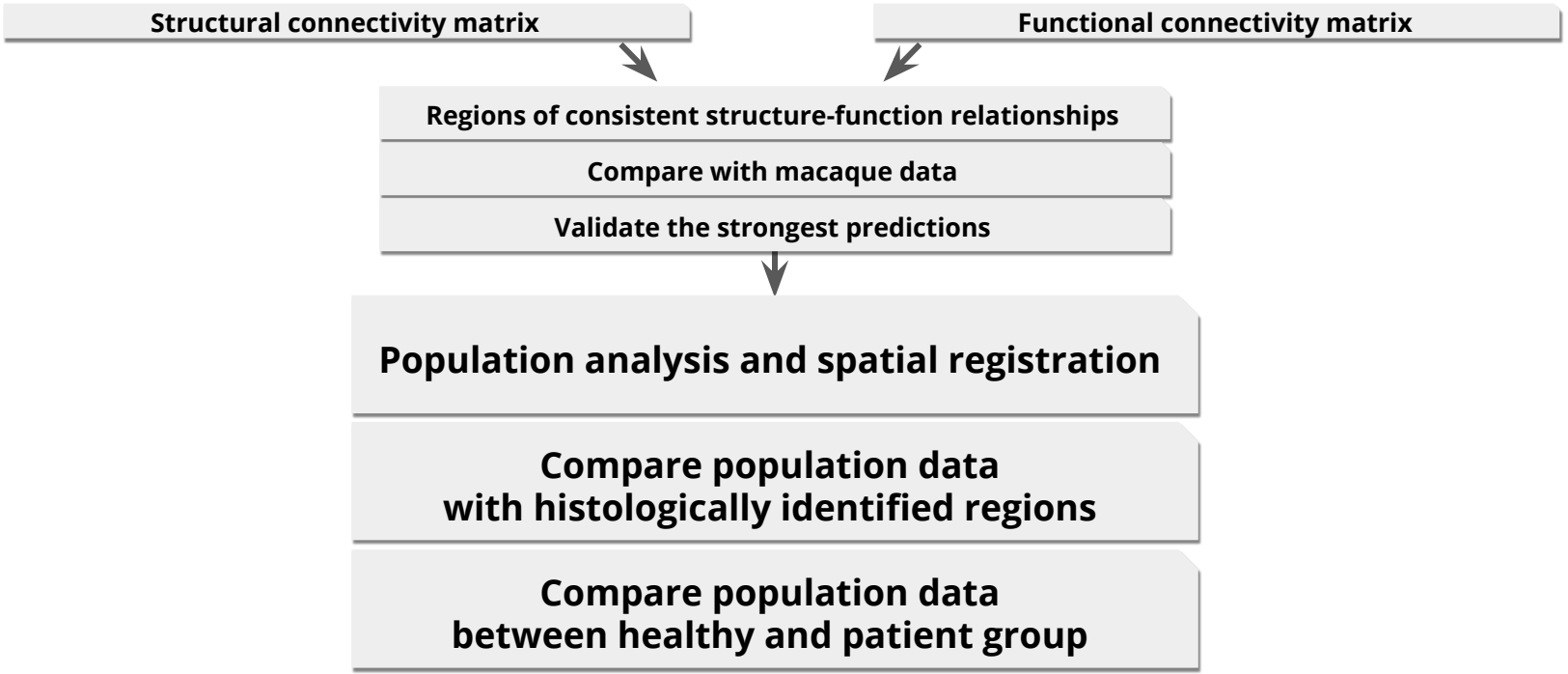
Xia, Y. et al (2019)

Regions of consistent structure-function relationships

Compare with macaque data

Validate the strongest predictions

3 additional steps to further test and verify



Compilation, Assembly, and Integration

- Standardization of parcellation schemes, elimination of unreliable data, and incorporation of additional structural levels for the initial draft.
- The continued innovation in data acquisition and analysis techniques → progressive revision, refinement, and extension of the connectome
- Compilation, assembly, and integration efforts
    - Large-scale collaboration
    - Coordinated data collection and dissemination
    - The establishment of new computational methods, data standards and mechanisms for controlled validation and quality assurance

Conclusions: The Potential Impact of the Connectome

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- Central hypothesis
  - The structural connectome constrains brain dynamics & shapes the operations and processes of human cognition
  - → data of the human brain activity in combination with the connectome will help to discern **causal interactions** in large-scale brain networks
- What can the connectome do?
  - Structural-function relationships are <u>not directly evident from</u> the connectional dataset itself, rather requires further intense study
  - Provides computational neuroscience with structural information
  - Understanding of brain damage and subsequent recovery

References

- Stephan, K. E., Kamper, L., Bozkurt, A., Burns, G. A., Young, M. P., & Kötter, R. (2001). Advanced database methodology for the Collation of Connectivity data on the Macaque brain (CoCoMac). *Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences*, *356*(1412), 1159-1186.
- Young, M. P. (1993). The organization of neural systems in the primate cerebral cortex. *Proceedings of the Royal Society of London. Series B: Biological Sciences*, *252*(1333), 13-18.
- LaBerge, D., & Kasevich, R. (2013). The cognitive significance of resonating neurons in the cerebral cortex. *Consciousness and cognition*, *22*(4), 1523-1550.
- Mountcastle, V. B. (1997). The columnar organization of the neocortex. *Brain: a journal of neurology*, *120*(4), 701-722.
- Yoshimura Y, Dantzker JLM, Callaway EM (2005) Excitatory cortical neurons form fine-scale functional networks. Nature 433: 868–873. 61.
- Ohki K, Chung S, Ch'ng YH, Kara P, Reid C (2005) Functional imaging with cellular resolution reveals precise microarchitecture in visual cortex. Nature 433: 597–603.
- Kumar, V., Croxson, P. L., & Simonyan, K. (2016). Structural organization of the laryngeal motor cortical network and its implication for evolution of speech production. *Journal of Neuroscience*, *36*(15), 4170-4181.
- Tsai, S. Y. (2018). Reproducibility of structural brain connectivity and network metrics using probabilistic diffusion tractography. *Scientific reports*, *8*(1), 1-12.
- Xia, Y., Chen, Q., Shi, L., Li, M., Gong, W., Chen, H., & Qiu, J. (2019). Tracking the dynamic functional connectivity structure of the human brain across the adult lifespan. *Human brain mapping*, *40*(3), 717-728.