# Connectomics in the UK Biobank

1st AUS UKB Research Symposium — Instruction day

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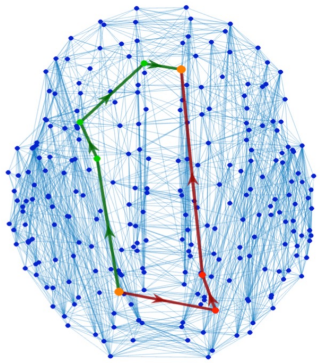
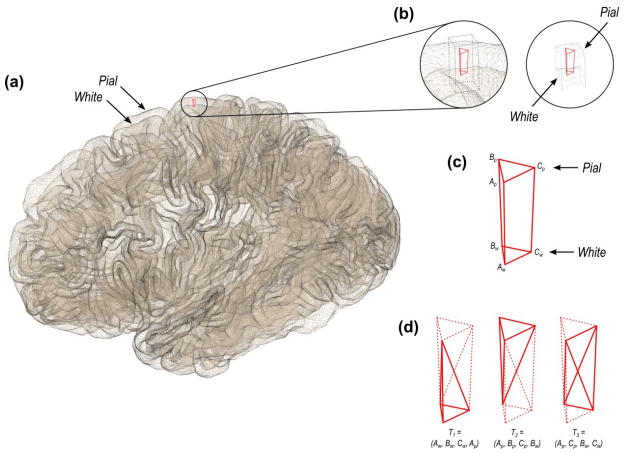
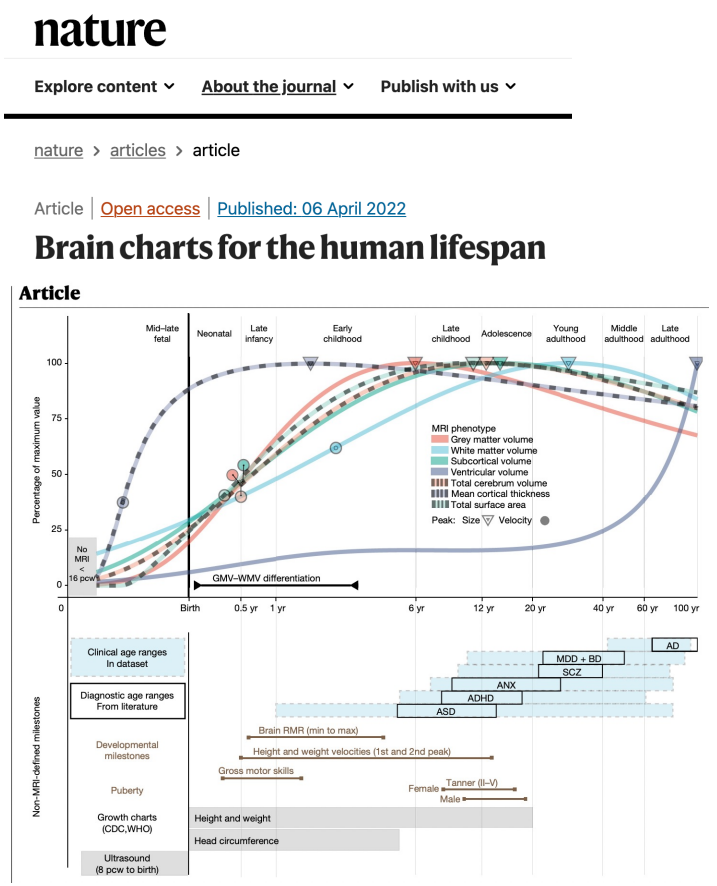


# A change in perspective: from localized function to distributed processing

- Structural MRI tells us about the **morphology** of individual brain regions
- Morphology refers to, e.g., the thickness, area and volume of the grey matter regions
- Decades of research leading to robust methods and accepted standards (e.g., FreeSurfer *recon-all*)
- Amazing progress in translational neuroimaging



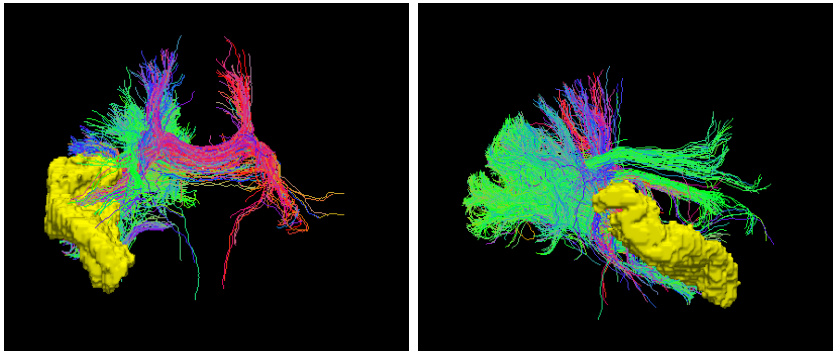

Winkler et al., 2017



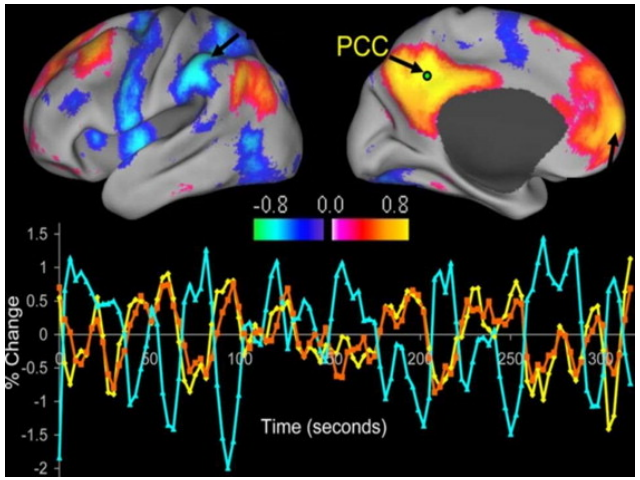

Bethlehem, Seidlitz et al., 2022

# A change in perspective: from localized function to distributed processing

- However, morphology (structural MRI) *alone* is limited to a localized view of brain function
- **Seed-based connectivity** maps the links between individual regions to the rest of the brain
- Two main categorial of brain connectivity: structural (physical links) and functional (statistical links)



- Structural connections map macroscale white matter tracts
- Diffusion weighted imaging (diffusion MRI)
- White matter tractography

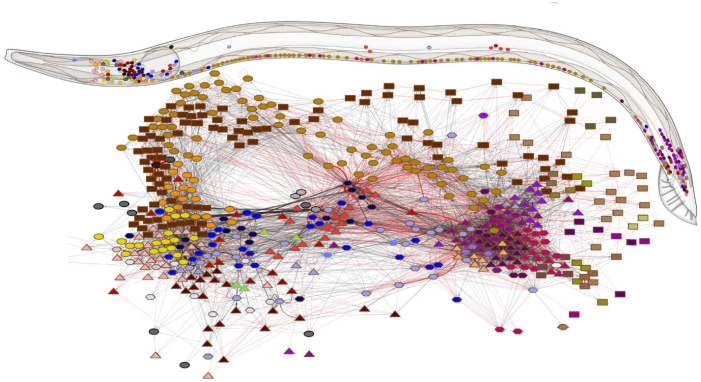



- Functional connections capture statistical dependencies in activity over time
- Functional MRI (resting-state, task)
- Statistical measures, time series analysis

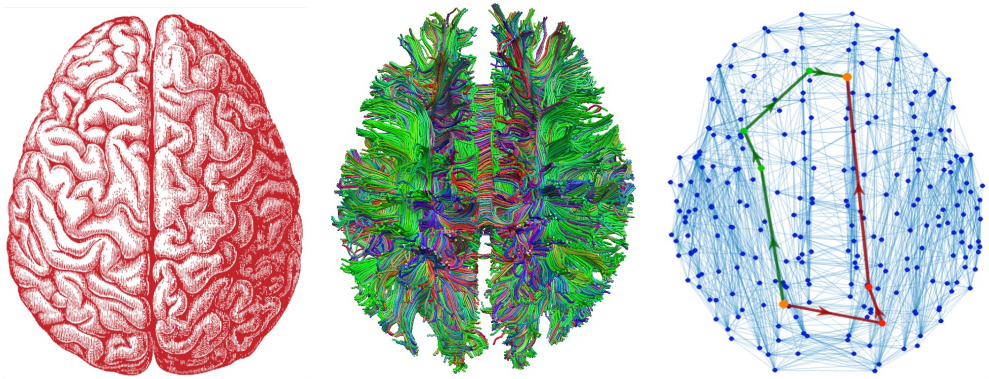
Fox et al., 2005

# A change in perspective: from localized function to distributed processing

- Seed-based connectivity changed the focus from localized towards distributed brain function
- However, this approach only tells us about interactions concerning one brain region at a time
- **Connectomics** seeks to understand inter-connectivity between all brain regions
- The **connectome** was first defined as a “comprehensive map of neural connections in the brain”
- Today, what a connectome really is depends on the spatial scale, reconstruction technique, imaging modality, etc



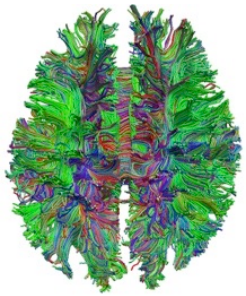
C. Elegans complete neuronal connectome
(Cook et al., 2019)



Human macroscale structural connectome

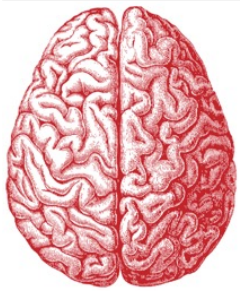
# Structural connectivity mapping (crash course)

**Data**: Diffusion MRI (*UKB DF 20250*)
**Technique**: White matter tractography
**Software**: MRtrix3



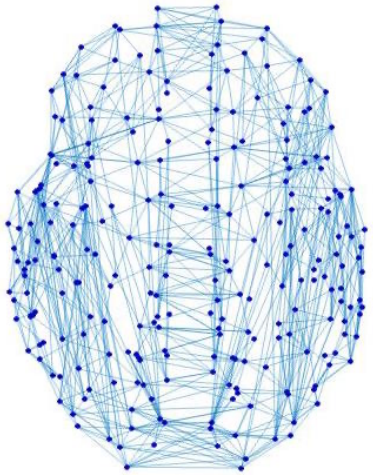
Whole-brain tractogram

Human structural connectome

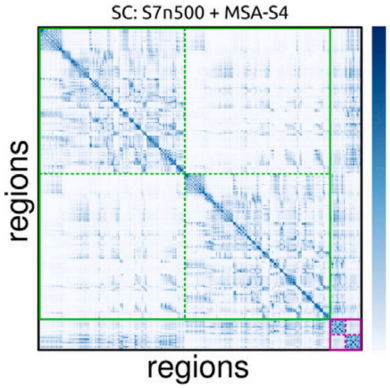


Humble brain

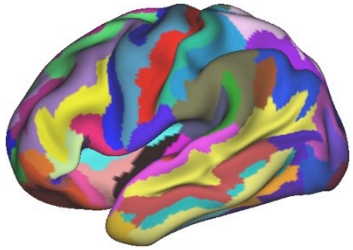
Grey matter parcellation



Network representation



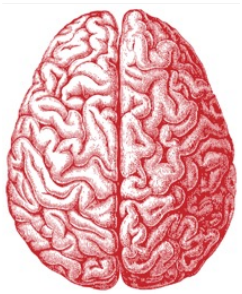

Adjacency matrix representation



**Data**: T1w structural MRI (*DF 20252*), T1w surface models (*DF 20263*)
**Technique**: Registration/segmentation/parcellation
**Software**: FreeSurfer, in-house code

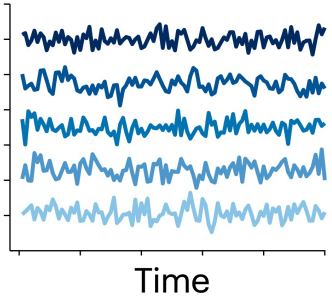
# Functional connectivity mapping (crash course)

**Data**: Resting-state fMRI (*DF 25751*)



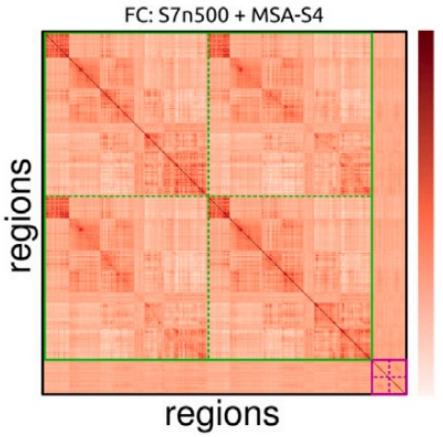
Humble brain

Voxel-level BOLD time series



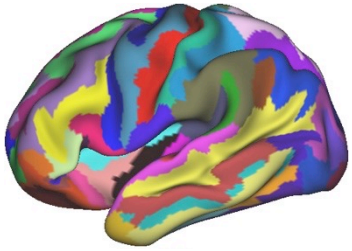

**Technique**: Regional averaging + Pearson correlation

Human functional connectome




Adjacency matrix representation

Grey matter parcellation



**Data**: T1w structural MRI (*DF 20252*), T1w surface models (*DF 20263*)
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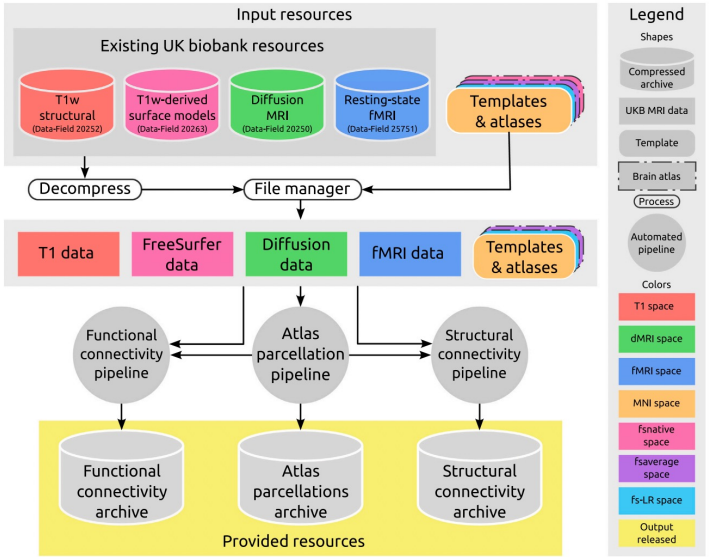
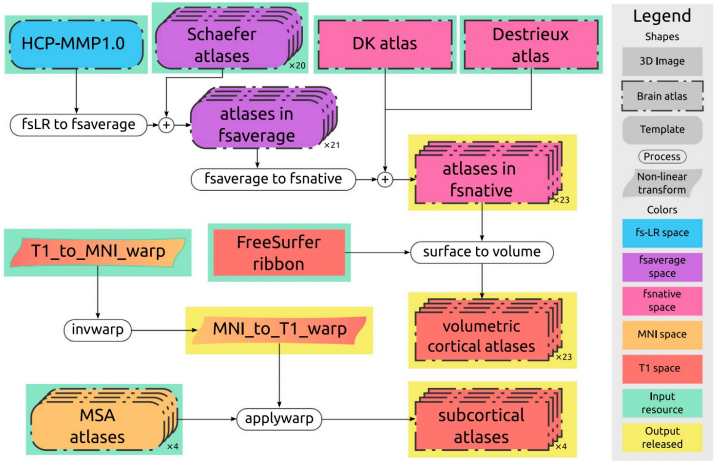
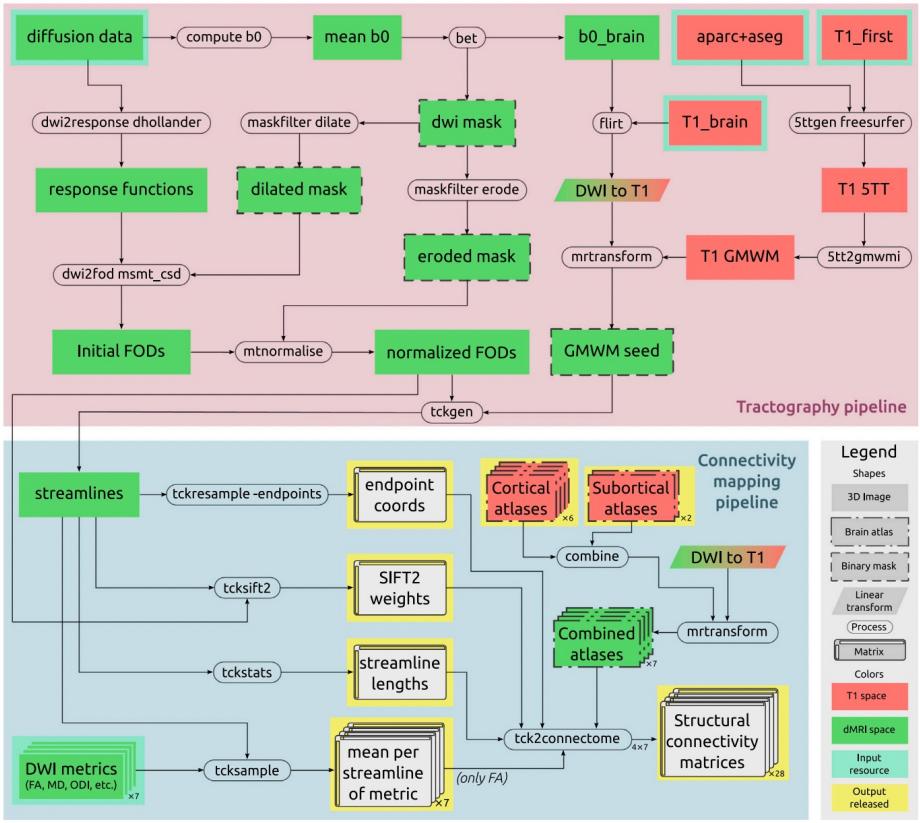
# Bad news: connectivity mapping (reality)




UKB raw imaging data




Parcellation generation




Structural connectivity mapping

Goods news: We have already mapped 40,000 UKB connectomes

# Connectomes for 40,000 UK Biobank participants: A multi-modal, multi-scale brain network resource


Sina Mansour L. [a,*], Maria A. Di Biase [b,c,d], Robert E. Smith [e,f], Andrew Zalesky [a,b], Caio Seguin [b,g,*]

[a] *Department of Biomedical Engineering, The University of Melbourne, VIC, Australia*
[b] *Melbourne Neuropsychiatry Centre, Department of Psychiatry, The University of Melbourne, Parkville, Victoria, Australia*
[c] *Department of Anatomy and Physiology, School of Biomedical Sciences, The University of Melbourne, Parkville, Victoria, Australia*
[d] *Department of Psychiatry, Brigham and Women's Hospital, Harvard Medical School, MA, USA*
[e] *The Florey Institute of Neuroscience and Mental Health, Heidelberg, Victoria, Australia*
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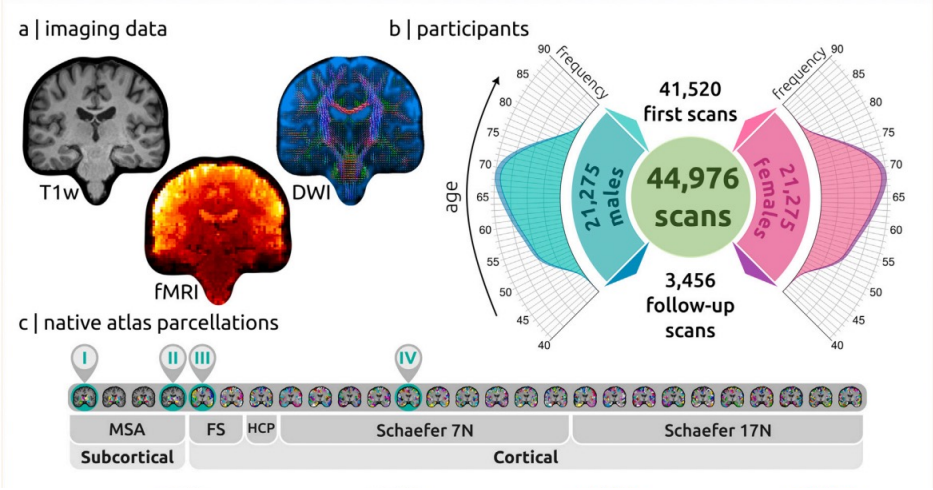
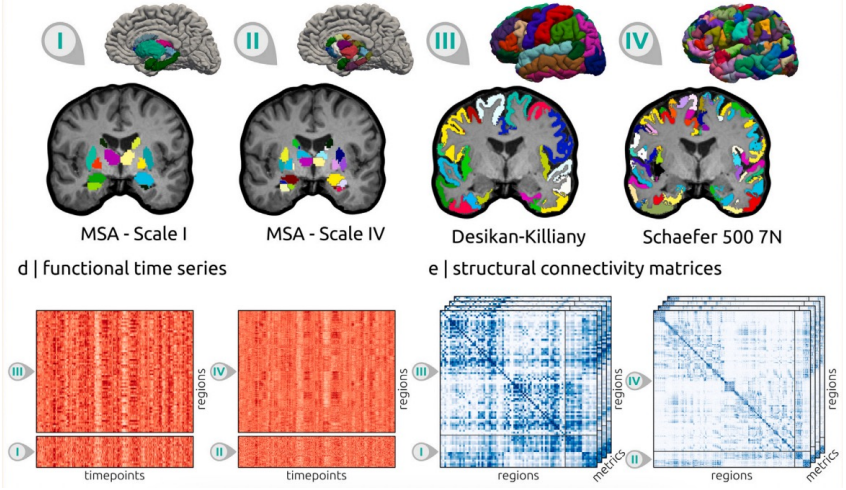
[g] *Department of Psychological and Brain Sciences, Indiana University, Bloomington, IN, USA*


Dr Sina Mansour L.

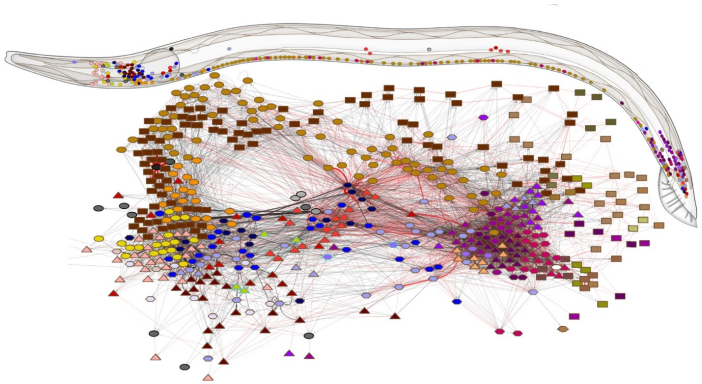


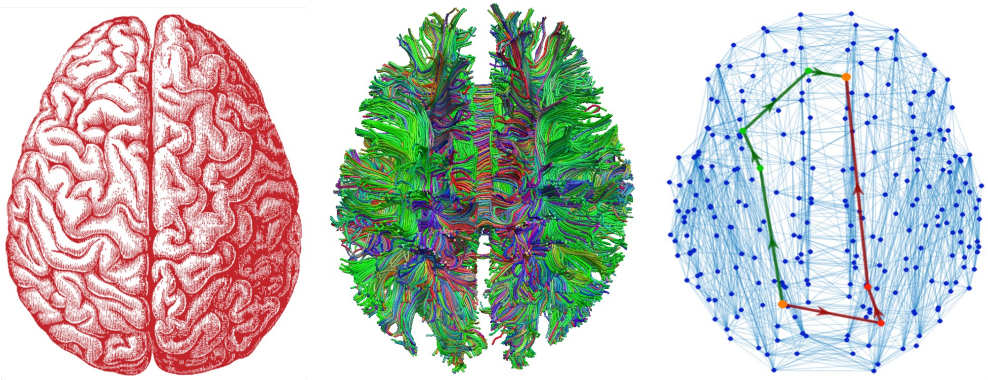

- 28 out-of-the-box connectome versions per subject
- Capability to generate +1000 connectome versions
- Open-source code
- Available as UKB bulk files
- More on day two of the symposium!

# But why study connectomes?

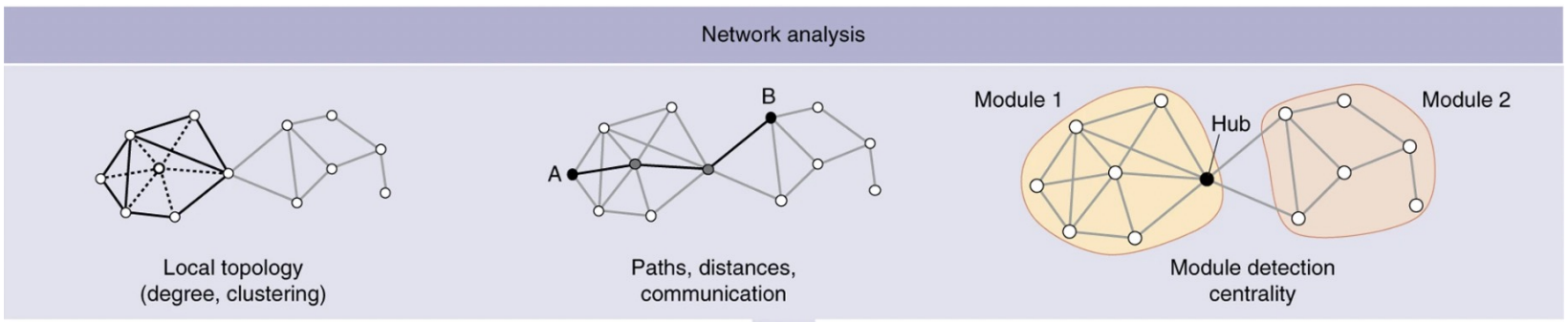
- From a basic science perspective, connectomics can illuminate fundamental principles of neural organization



C. Elegans complete neuronal connectome
(Cook et al., 2019)



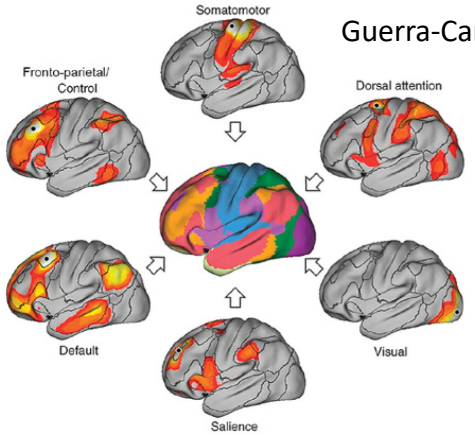
Human macroscale structural connectome



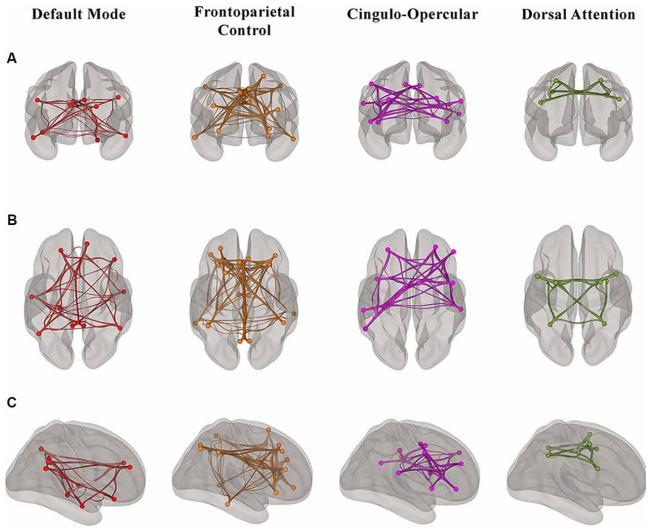

Bassett & Sporns, 2017

# But why study connectomes?

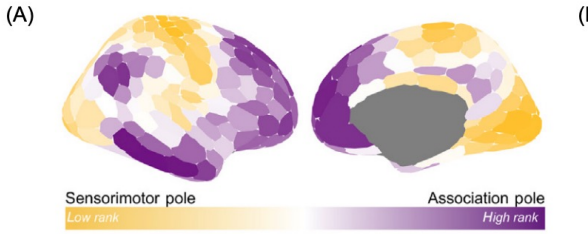
- Higher-order function is increasingly thought to arise from distributed networks rather than localized regions
- Interactions between these distributed networks are conjectured to underpin varied cognitive processes

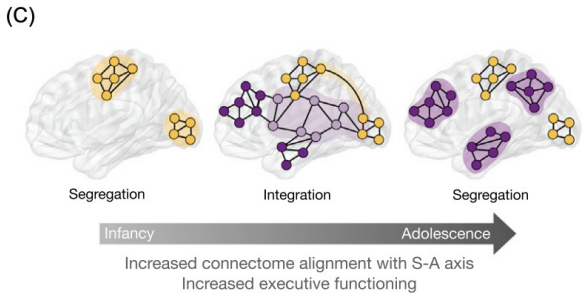


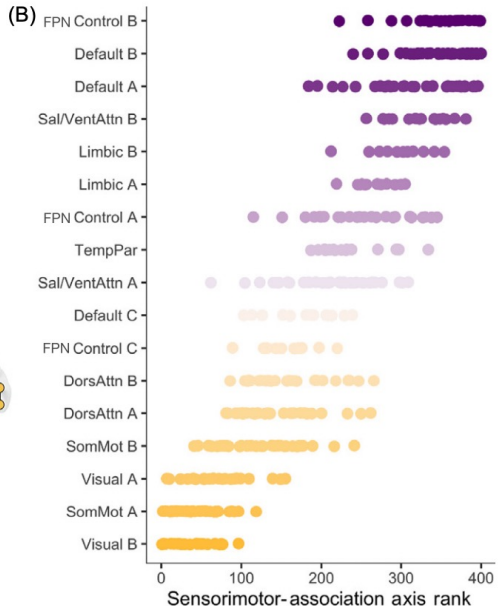

Guerra-Carrillo et al., 2014




Hausman et al., 2020



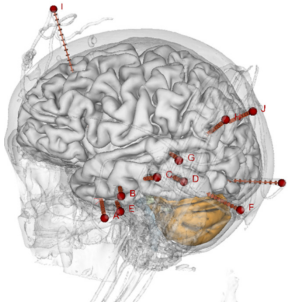



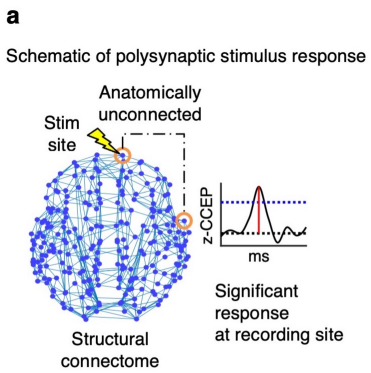

Keller et al., 2020

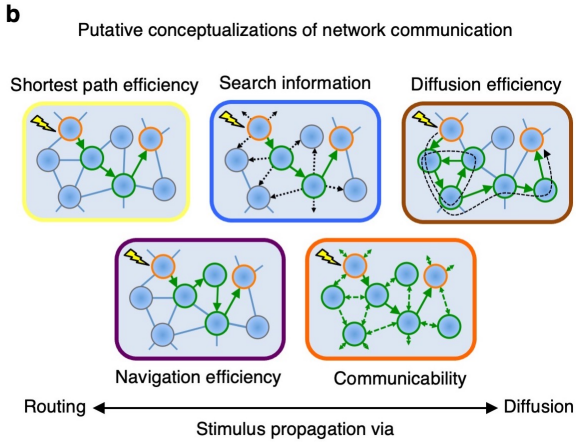
# But why study connectomes?

- Connectomes facilitate the unfolding of varied neural communication processes
- Modelling the propagation of focal brain stimulation
- Predicting the spread of neurodegeneration

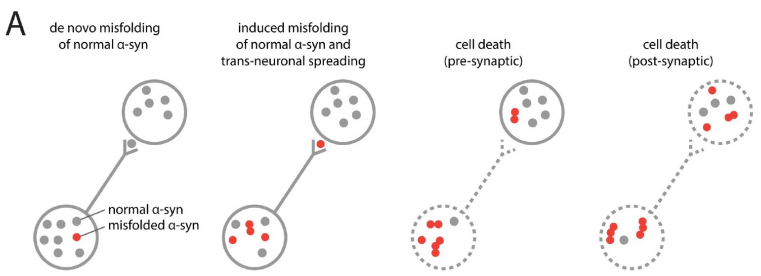


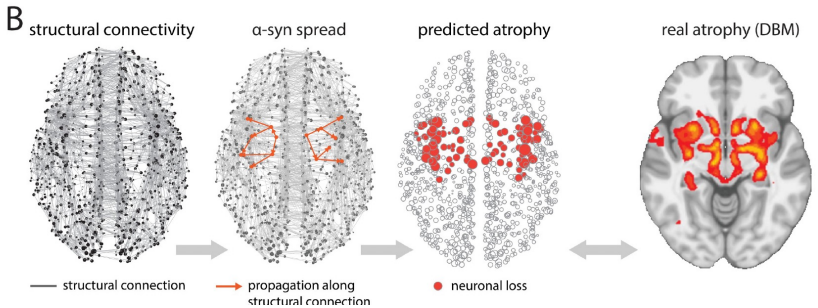
Intracranial EEG electrodes
in an epilepsy patient
(sourced from www.parcdesalutmar.ca)




Seguin et al., 2023




Zheng et al., 2019

# Closing remarks

- Connectomics provides a framework to investigate brain function from systems-level, integrative perspective
- This allows research into brain-wide processes that are not reducible to the activity of individual regions
- Structural and functional human connectomes can be mapped from MRI
- Connectomes mapped for 40,000 participants of the UK Biobank are available
- More on the day 2 of the Research Symposium!

## Connectomes for 40,000 UK Biobank participants: A multi-modal, multi-scale brain network resource

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Thanks for the attention! Questions?

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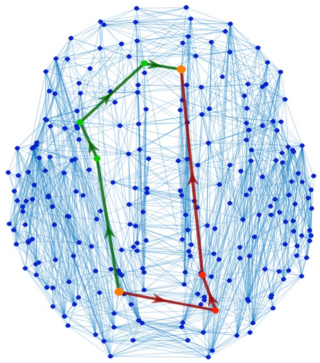

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