Human Brain Project EBRAINS

Systematic Characterisation in The Virtual Brain

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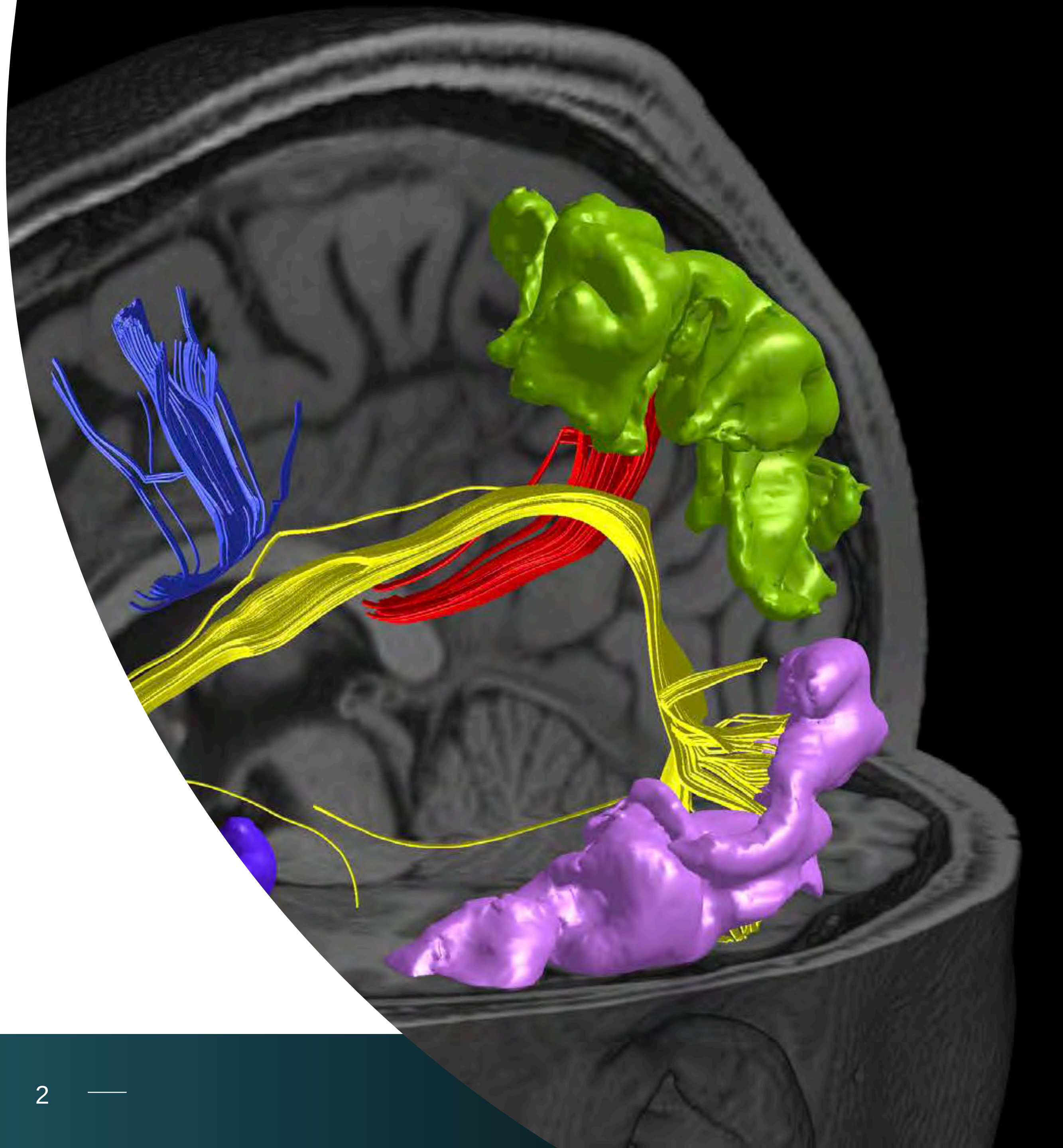
Inserm

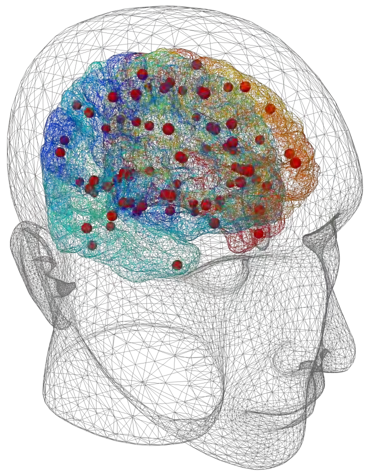
Ambition

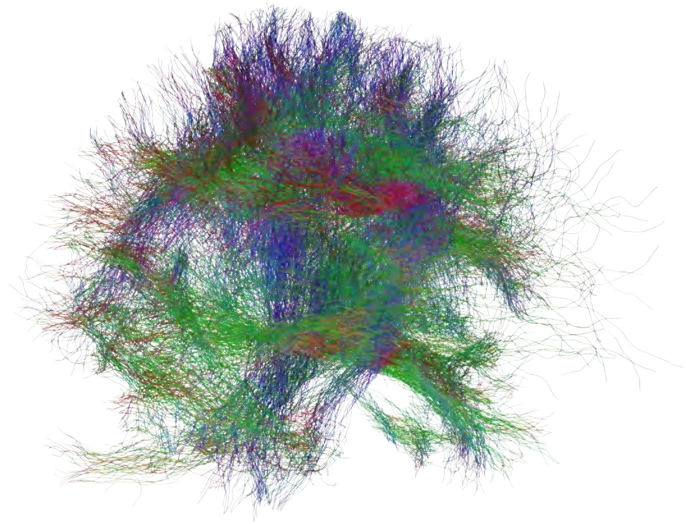
Vision: ...understanding the brain through personalized brain models and the *digital twin*.

Increase the capacity of the neuroscientific community to model multiscale neural activity of human brain networks by building a conceptual, organizational and computational framework fully embedded in EBRAINS.



Challenges





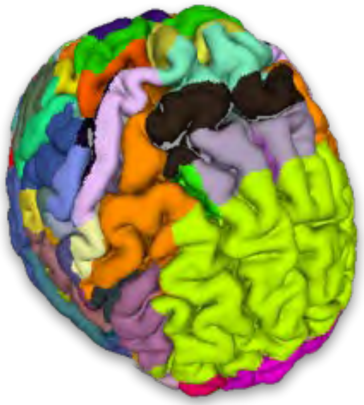
Disentangle competing mechanisms

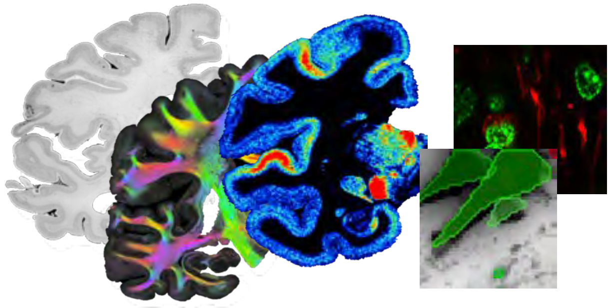
Causal inference

Multiscale organization of the brain

Neurodegeneracy and non-identifiability

Personalization (in-vivo) vs high-resolution (ex-vivo)





“*Neurodegeneracy is the key obstacle to progress in neuroscience*” (Y Frégnac, Science 2017)

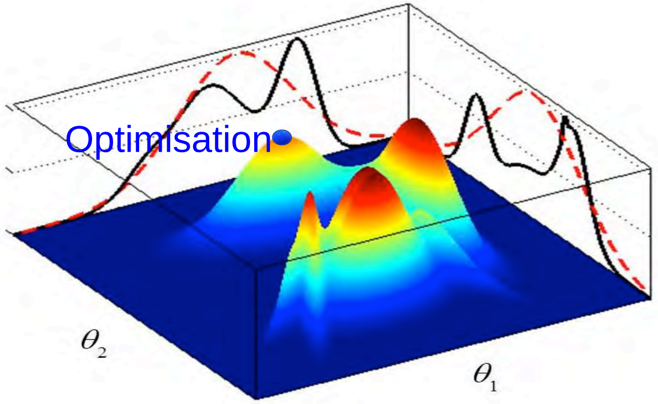
Inference

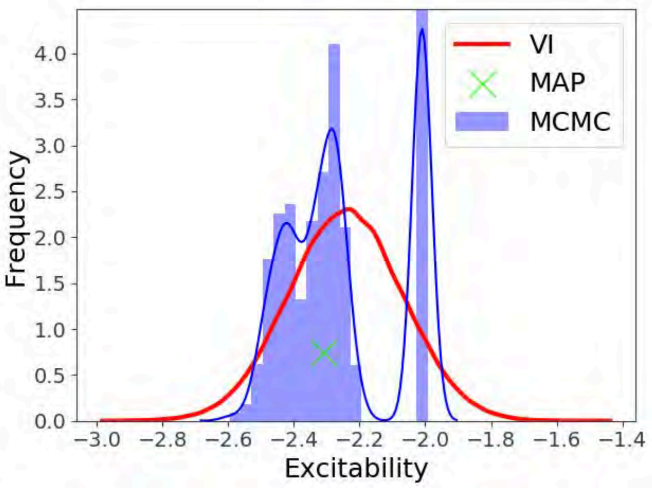
Bayesian inference

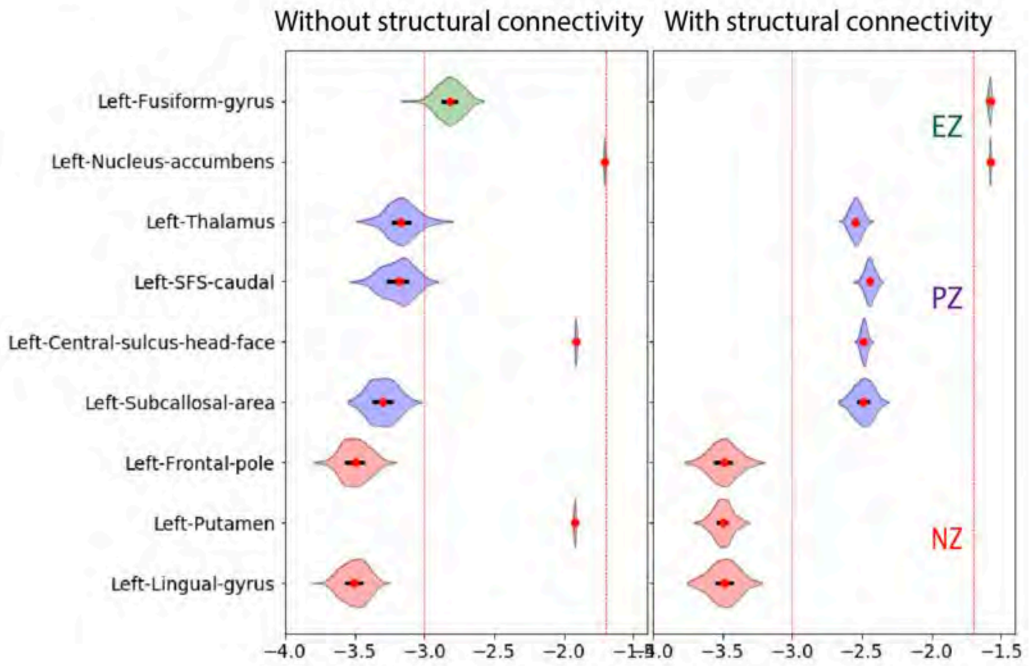
- Integration of prior knowledge
- Multimodal posterior distributions
- Diagnostics

Monte Carlo samples the true posterior distribution

No tools “fitting all needs” exist







Real world scenarios

Hashemi et al Neuroimage (2020), PLoSCB (2021); Jirsa et al The Lancet Neurology (in revision)

Personalization vs High resolution

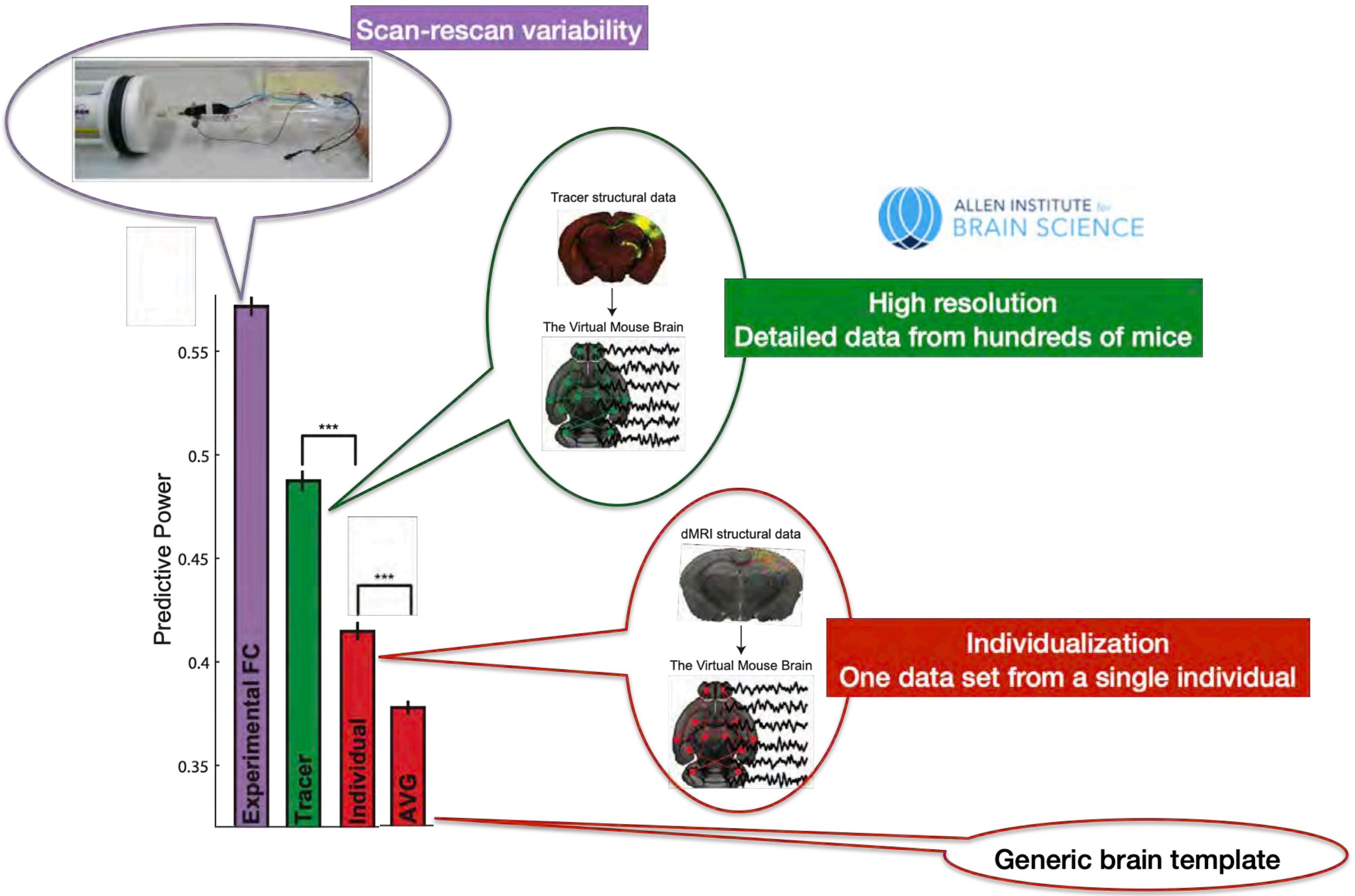
In-vivo vs ex-vivo

Demonstration of explanatory power of high-resolution connectome

The addition of high-resolution connectome substantially improves the predictive power of brain models

Individual informative priors further improve prediction

Justification for hierarchical approach using a high-resolution brain template for personalization



Melozzi et al. PNAS 117 (2019); Hashemi et al Neuroimage (2020); PLoS CB (2021)

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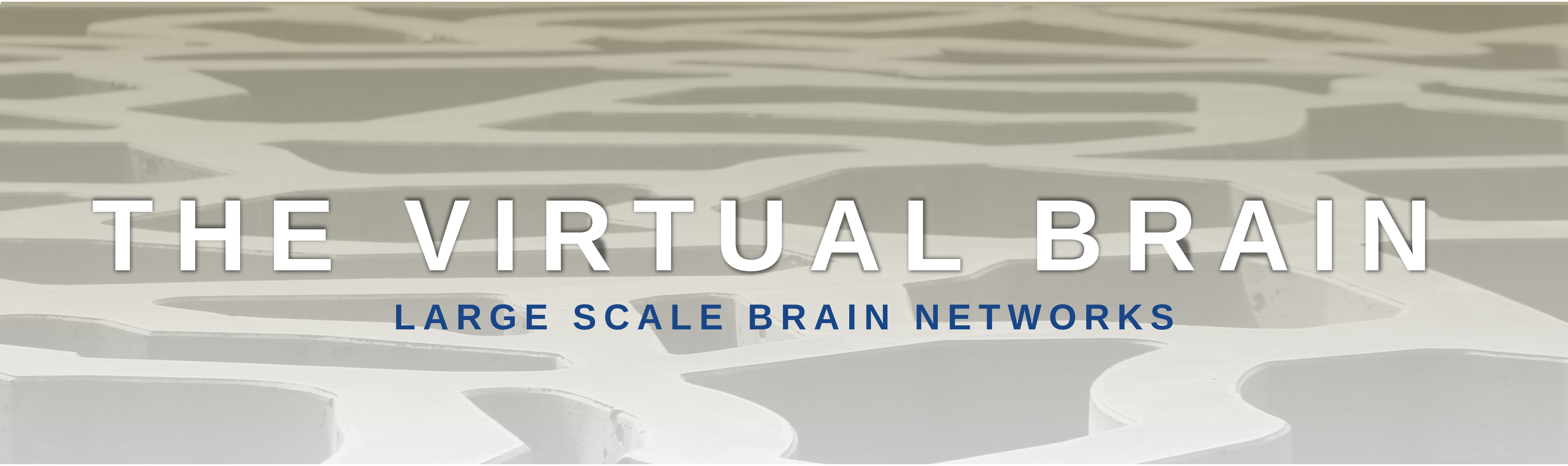


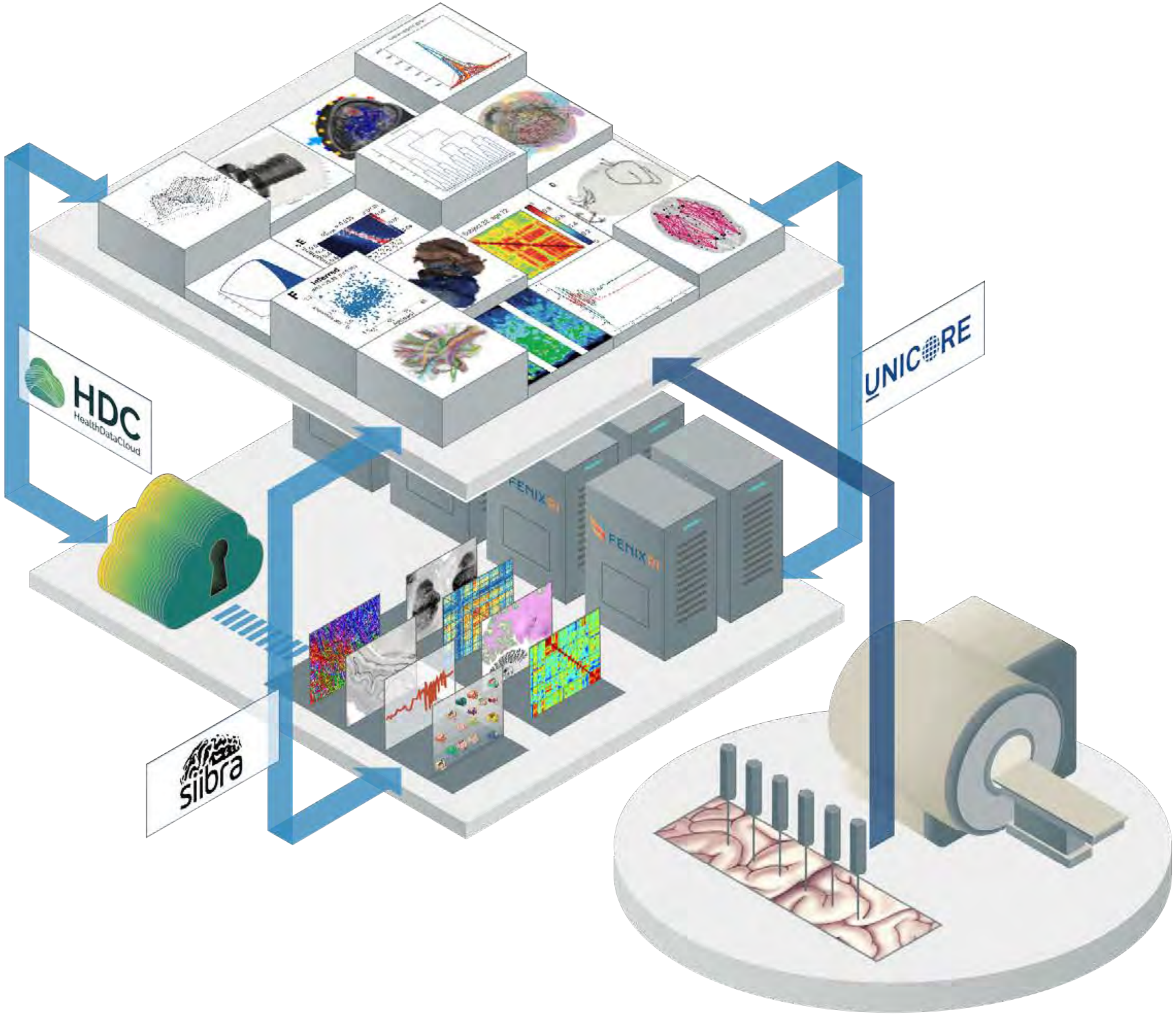
THE VIRTUAL BRAIN

LARGE SCALE BRAIN NETWORKS

Workflows

EBRAINS establishes reusable **science workflows** operating in the same eco-system, guiding the development of **technical workflows.**

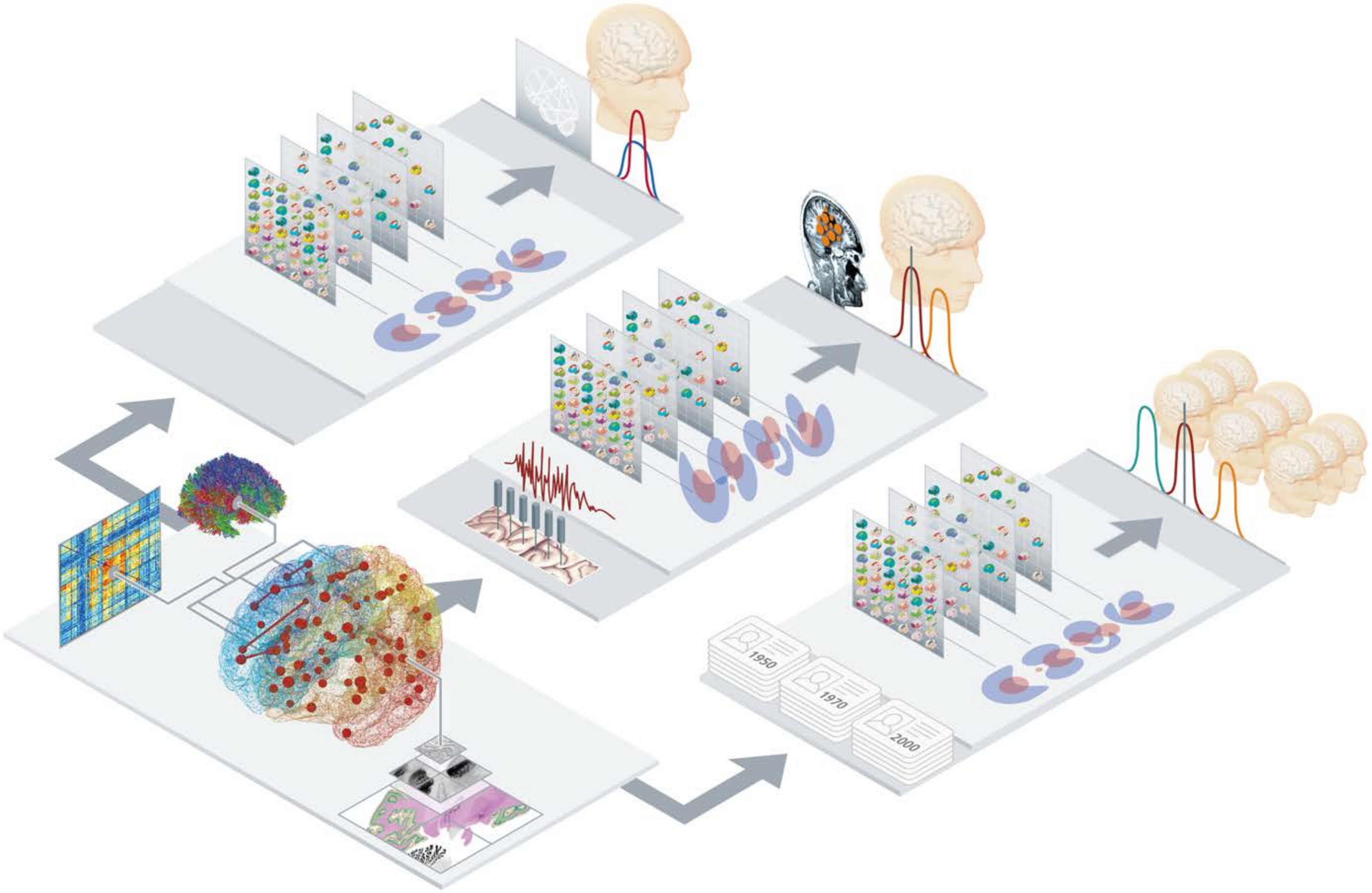
Co-design in EBRAINS.



Workflows

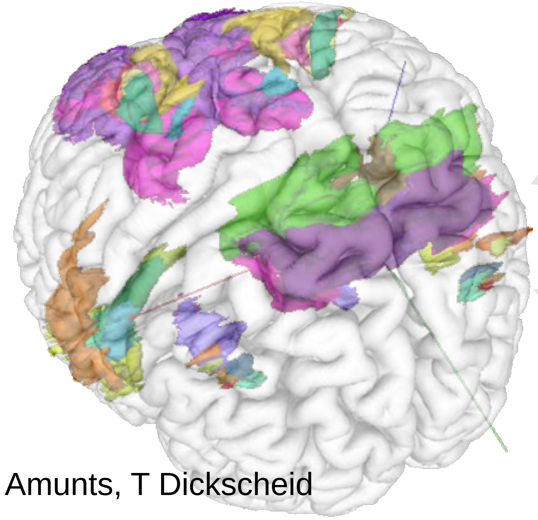
Showcases establish reusable **science workflows** operating in the EBRAINS eco-system, guiding the development of **technical workflows.**

Co-design in EBRAINS.



Linking the microscopic to the macroscopic scale

BigBrain histological space (20 micron)

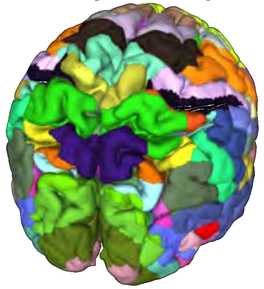


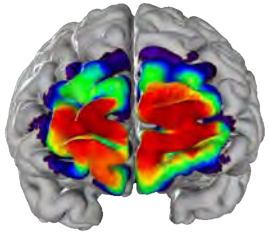
K Amunts, T Dickscheid

Corres-
ponding
regions

Coordinate
Trans-
formations

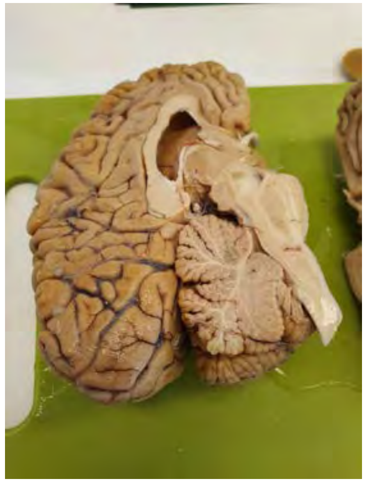
MNI space (1mm)

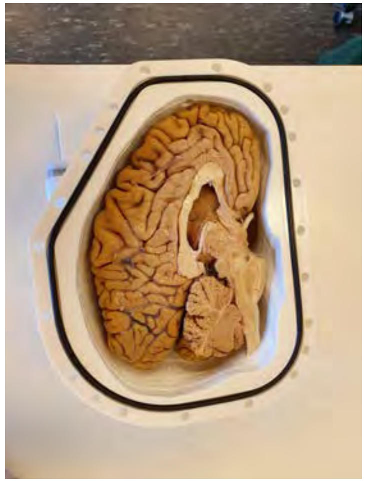


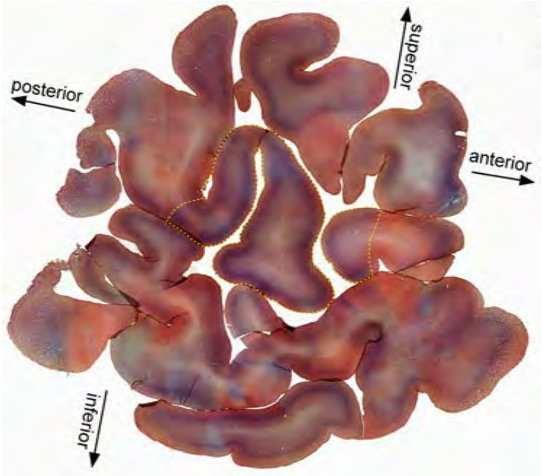


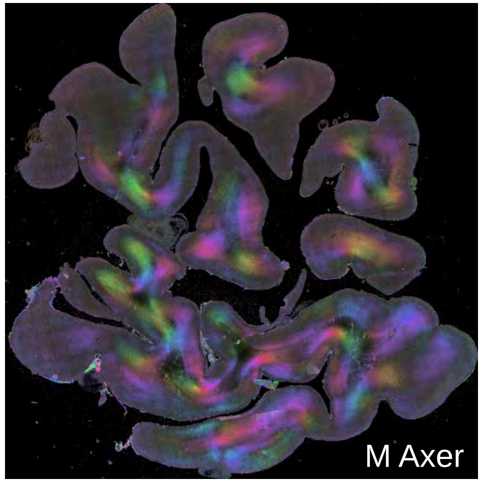
Surface space

Surface projection:
J. Mangin, & D. Rivière, Neurospin

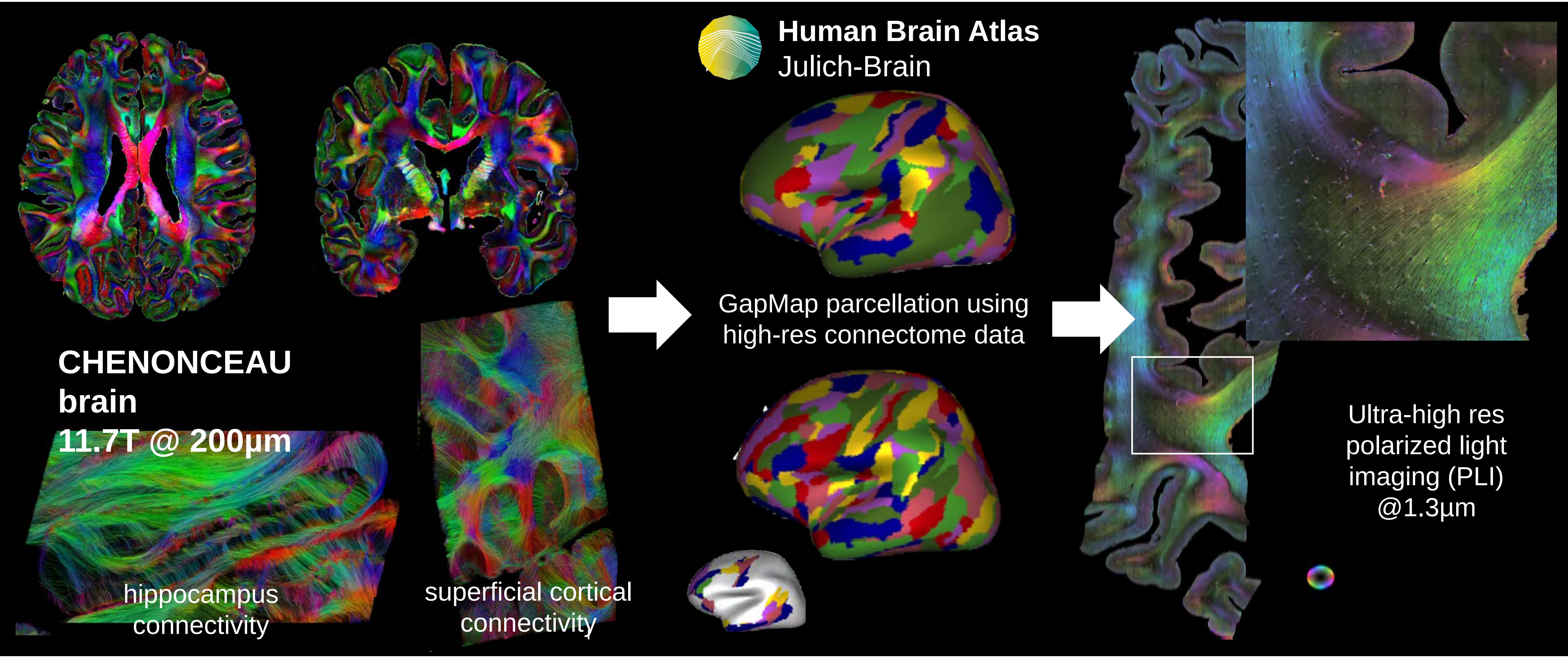








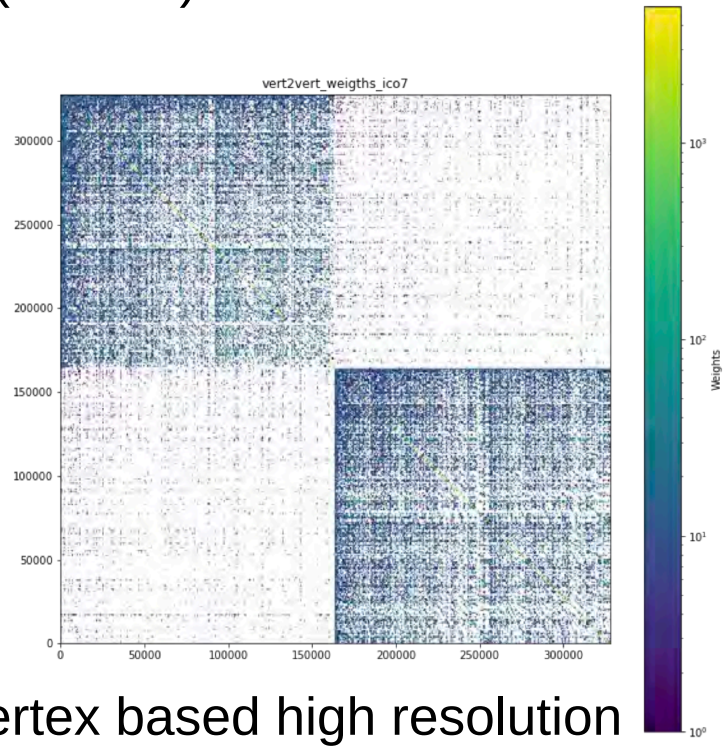
High-resolution connectome data



Linking the microscopic to the macroscopic scale

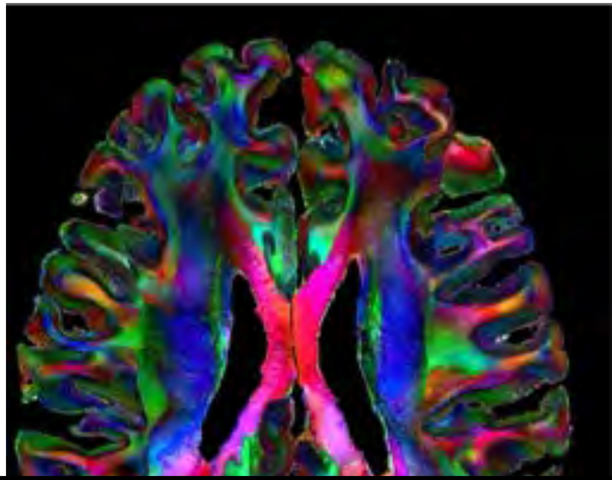
Integration of high-resolution data

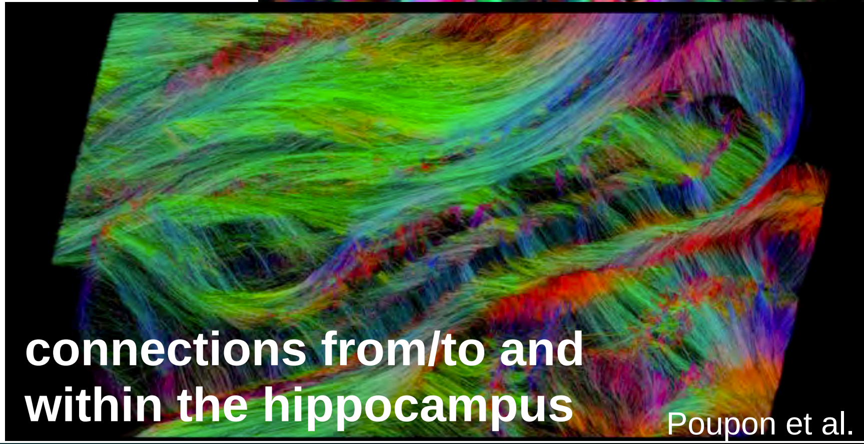
In-vivo patient specific imaging (~$1mm^2$)



Vertex based high resolution connectome is atlas independent

CHENONCEAU post-mortem high-resolution (200 µm) imaging





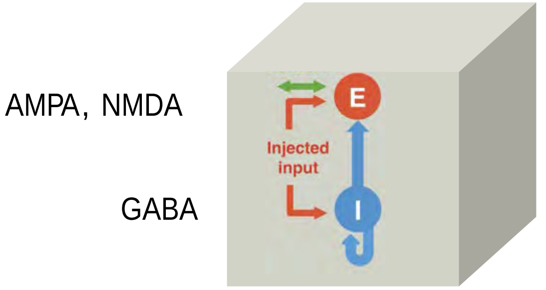
Poupon et al.

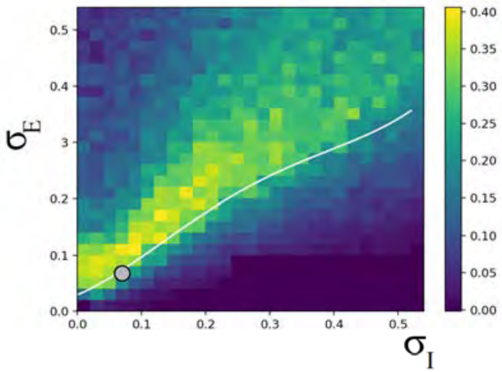
with Paul Triebkorn and Huifang Wang

Linking scales

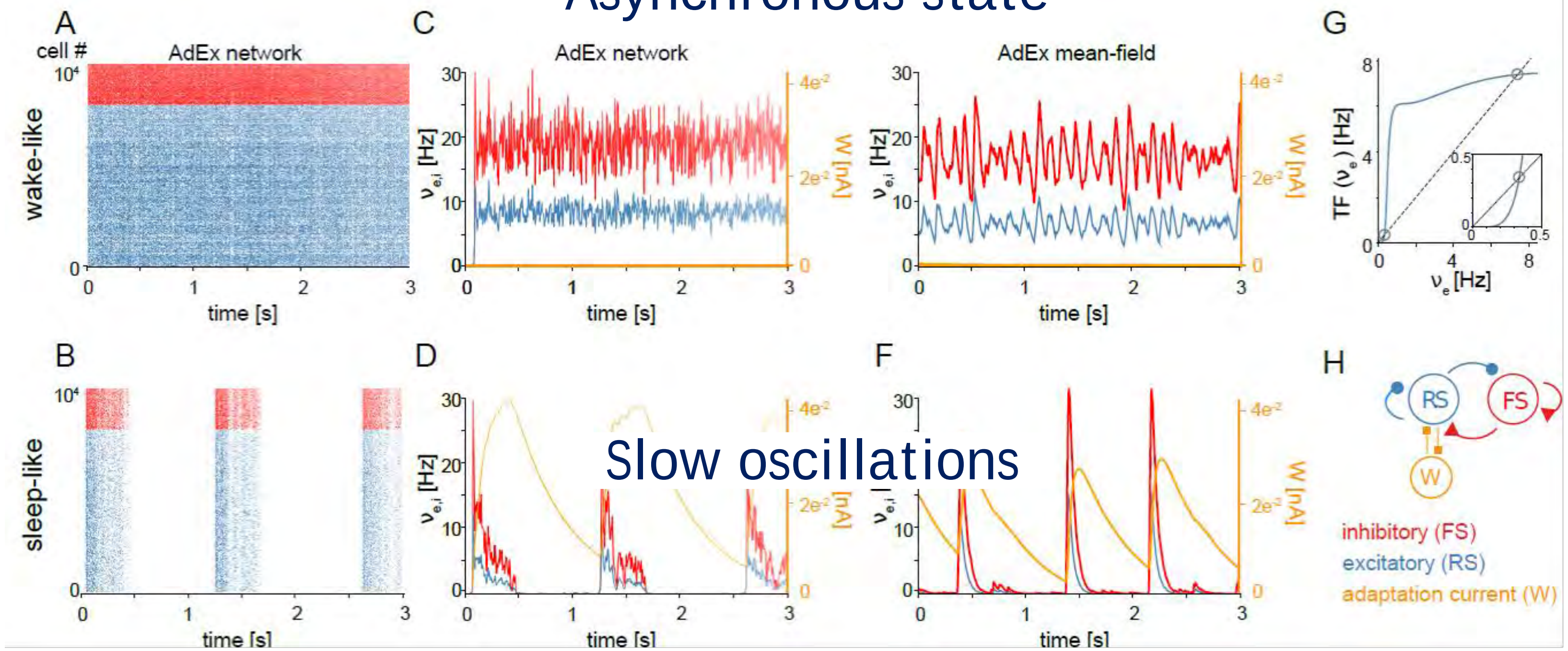
Mean-field models of neuronal populations, linking cellular to large scales

Neural Mass as network node





Asynchronous state



Slow oscillations

Mean-field models include neuronal heterogeneity at large scales

Stefanescu & Jirsa PloS CB 2008
Di Volo et al., Neural Computation 2019
Goldman et al. BioRxiv 2020, 2021
Di Volo & Destexhe, Sci Reports 2021

Linking the microscopic to the macroscopic scale

Network size:

Low-resolution mesh: 100-200 nodes

High-resolution mesh: 260,000 nodes

Connectivity:

- High-resolution intracortical
- High-resolution corticocortical
- personalized connectome from DTI

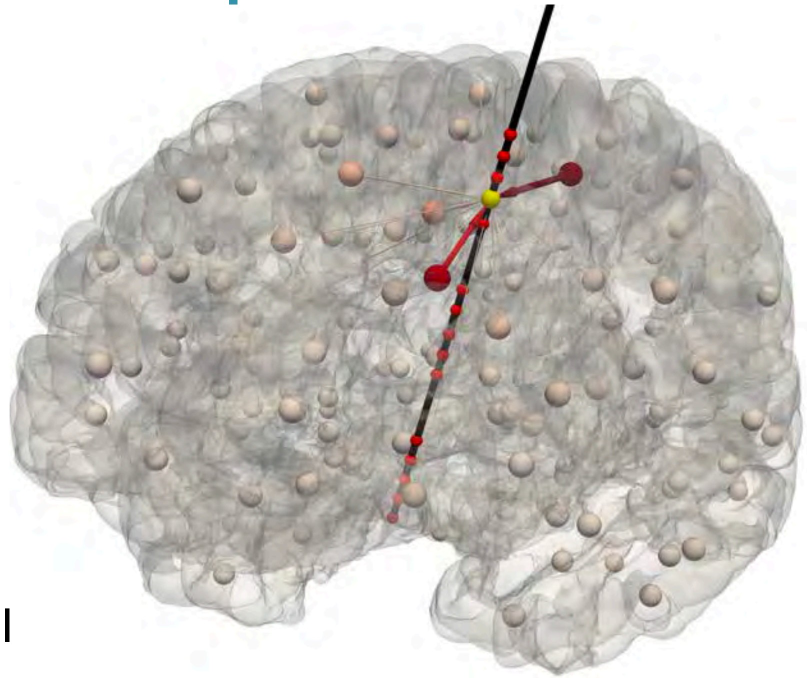
Average region size:

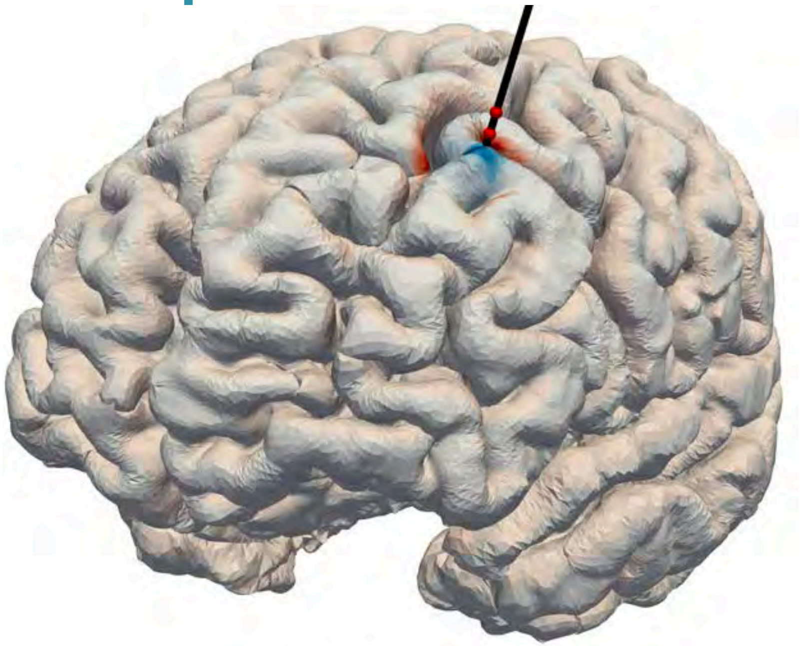
10-20 cm2 (low resolution)

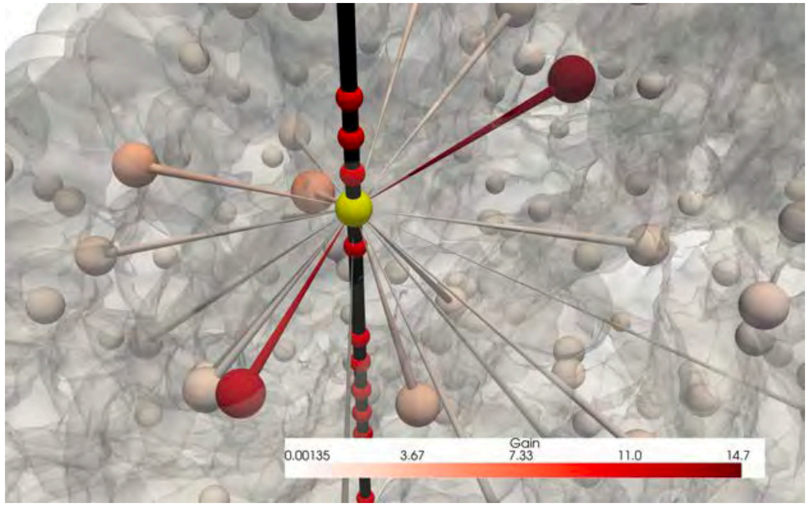
2-3 mm2 (high resolution)

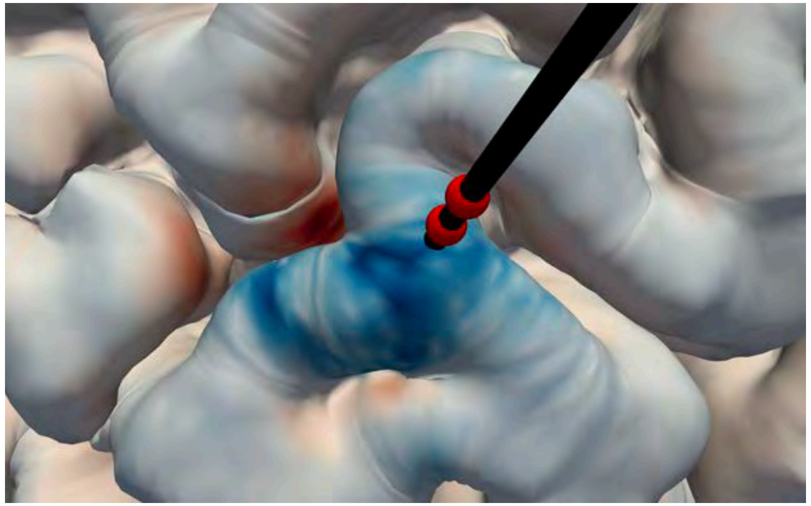
Minimal fiber lengths:

1mm









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EPILEPSY

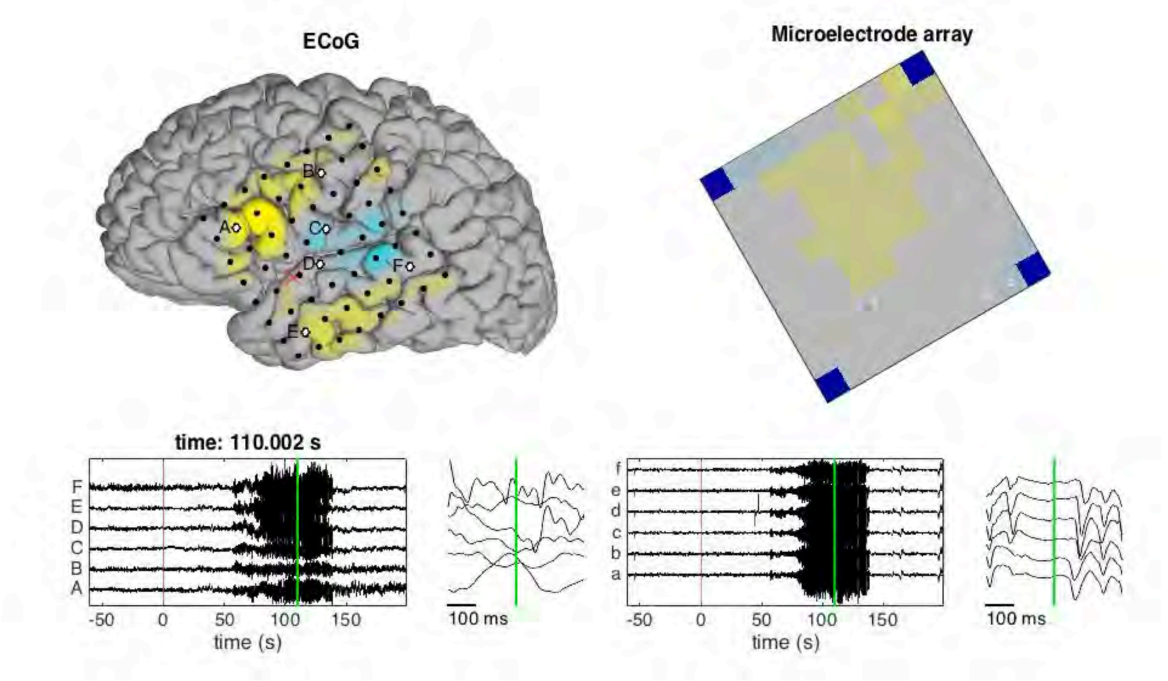
VIRTUAL EPILEPTIC PATIENT (VEP)

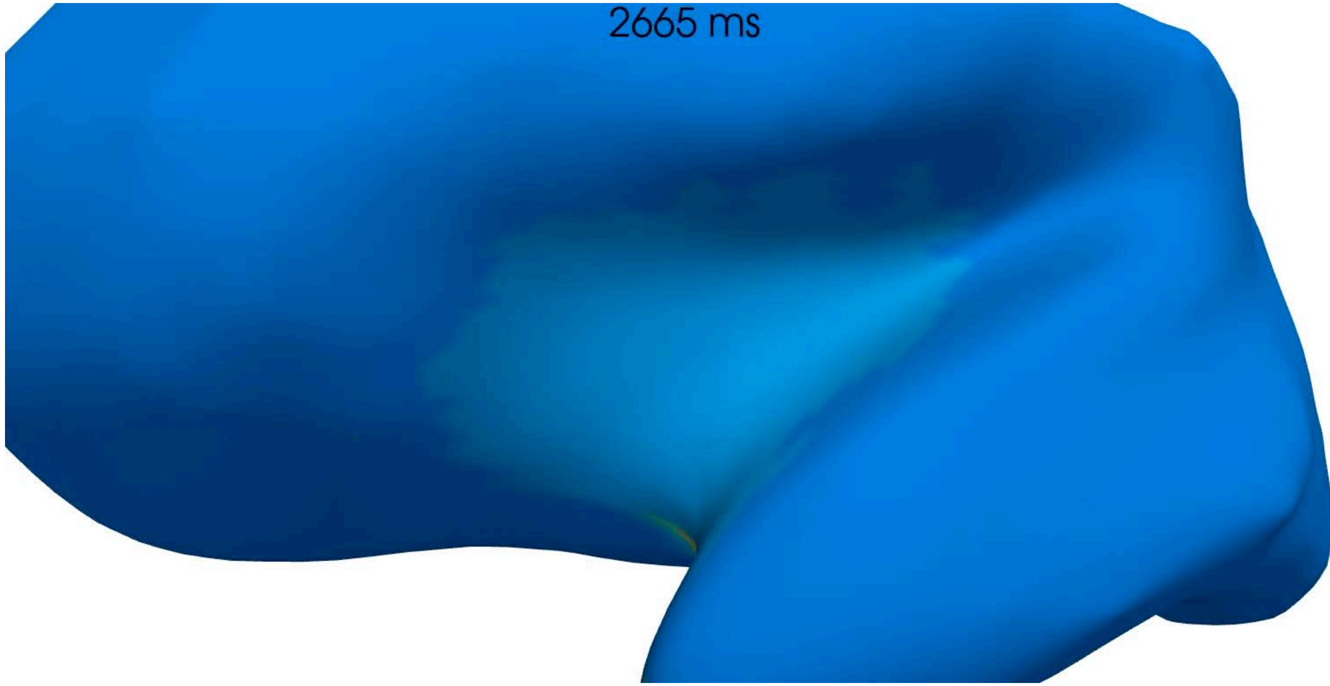
Linking the microscopic to the macroscopic scale

Improved representation of spatio-temporal seizure dynamics.

Real patient epilepsy

Simulated epilepsy

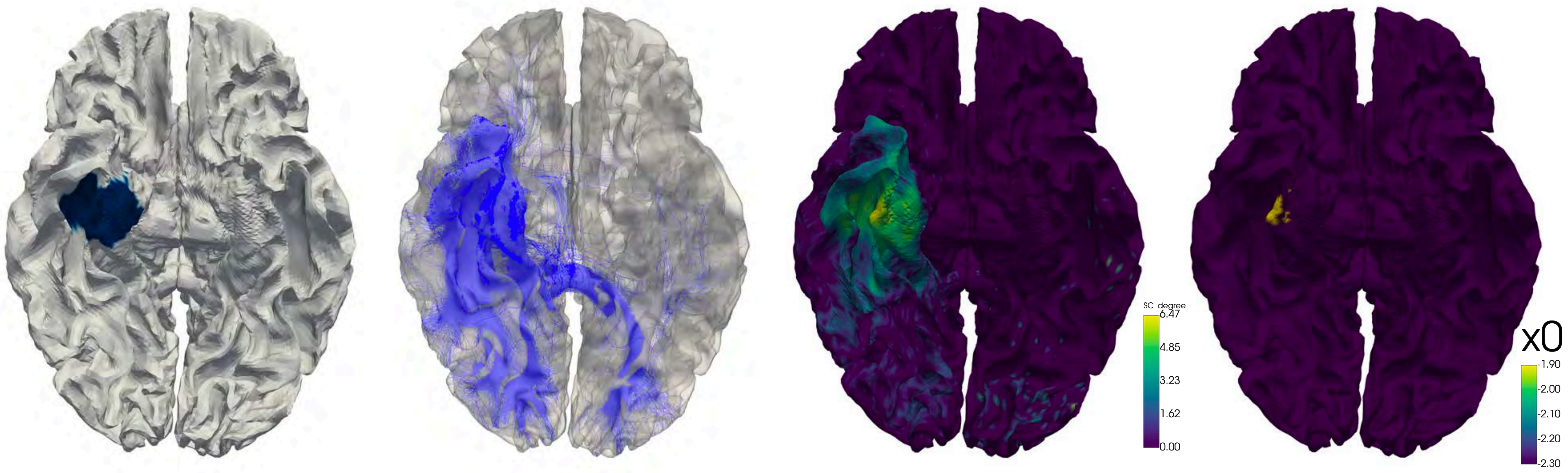


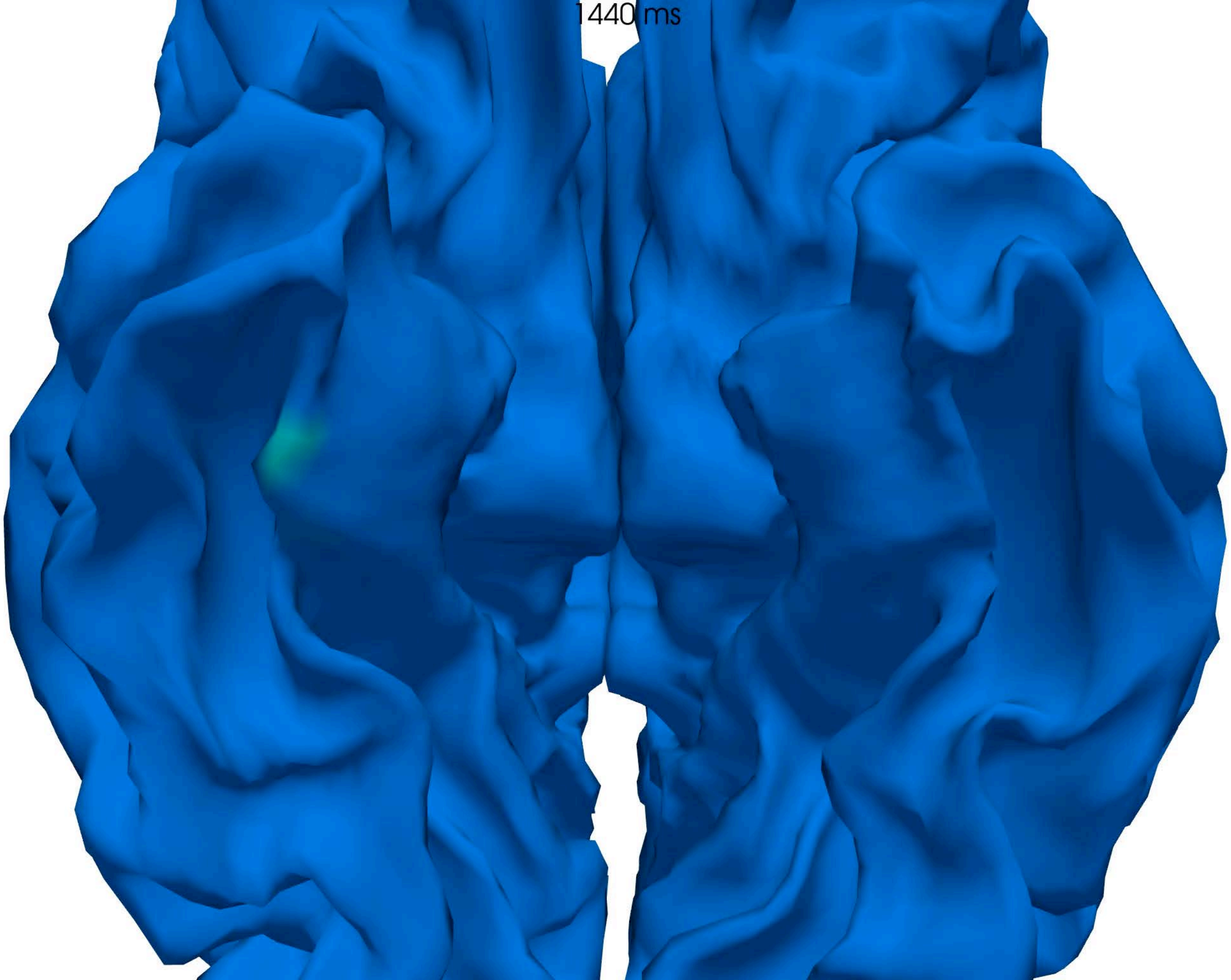


Martinet et al. 2016

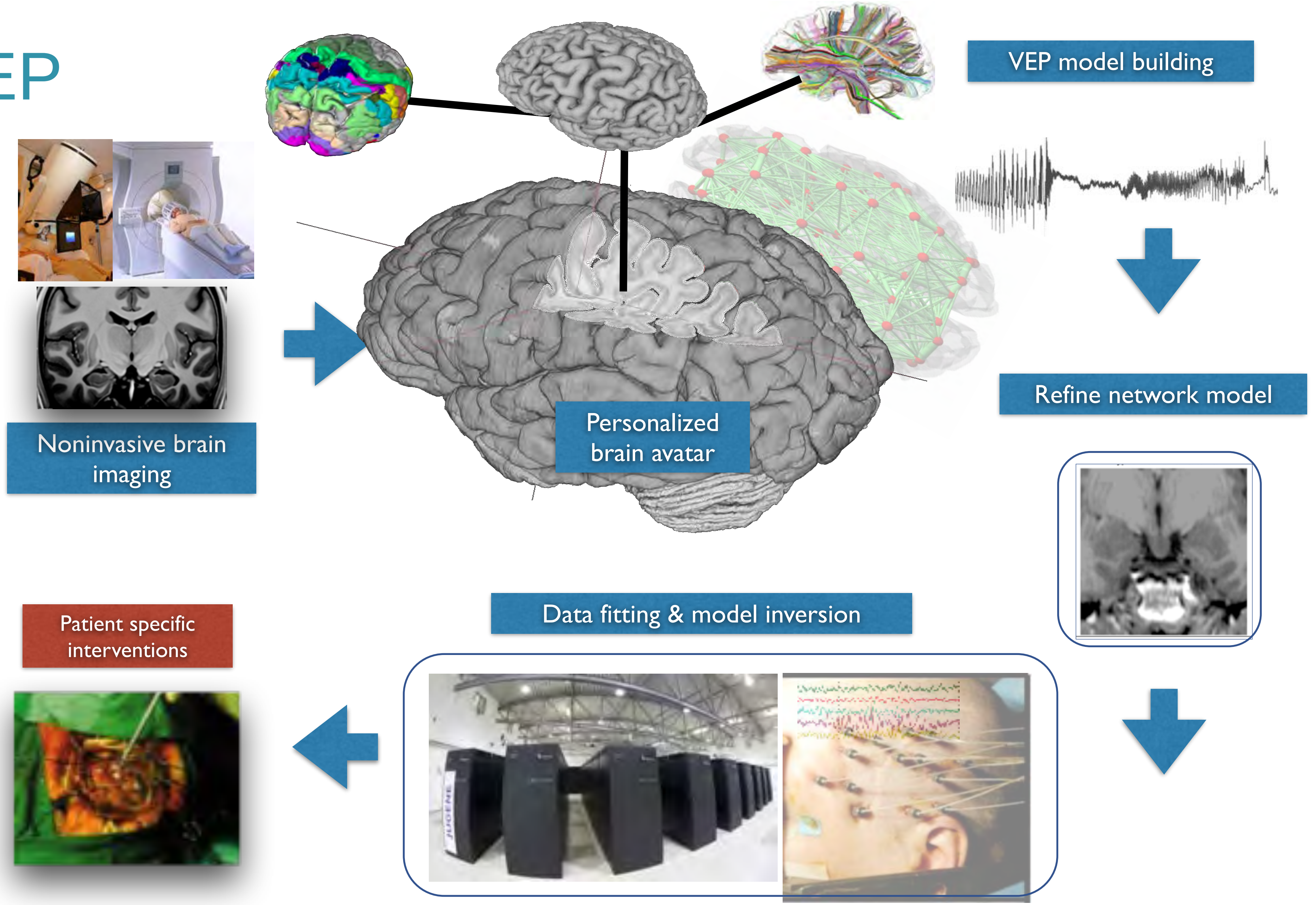
High resolution connectome

Fibres of the rhinal cortex | Vertex connectivity strength | EZ




1440 ms

Workflow VEP

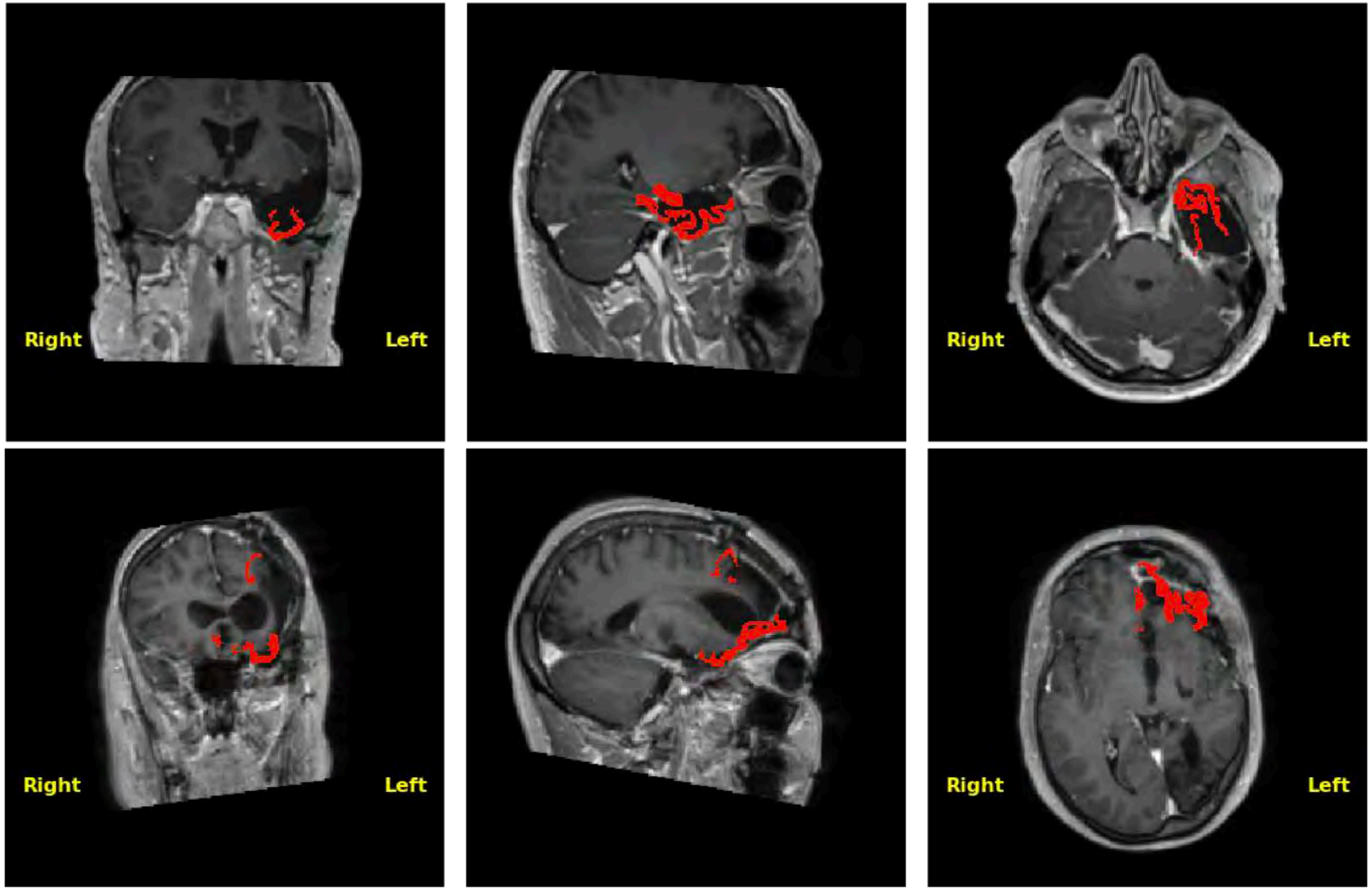


Jirsa et al Neuroimage 2016; Jirsa et al the Lancet Neurology (in revision)

Evaluation in patient cohorts

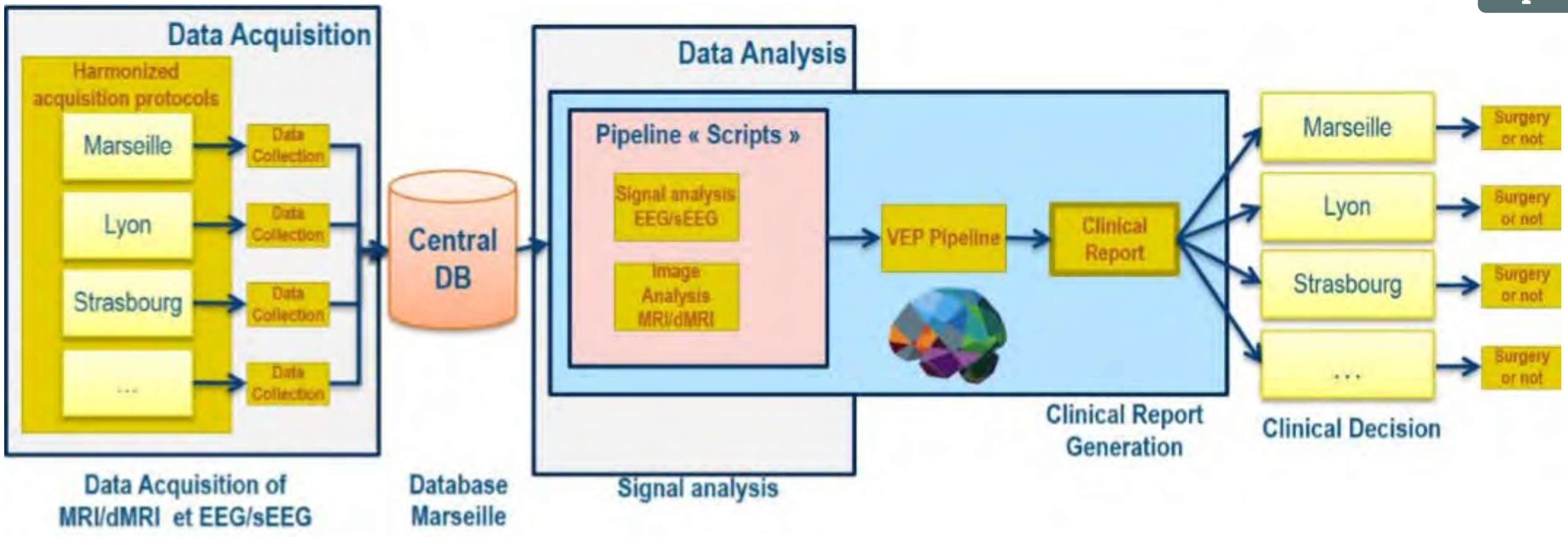
Good overlap with resection in seizure-free patients

Less overlap with resection in non-seizure-free patients



Proix et al Brain 2017, Nat Comm 2018; Jirsa et al. Neuroimage 2016

Evaluation in patient cohorts



<u>Clinical trial:</u>
randomized parallel-group study trial
(Coordinator F. Bartolomei; Scientific Director V. Jirsa)

<u>Objective:</u>
evaluate the role of personalized Virtual Epileptic Patient brain models for surgery planning and outcome

13 French clinical centers
400 prospective patients during 2019 – 2022

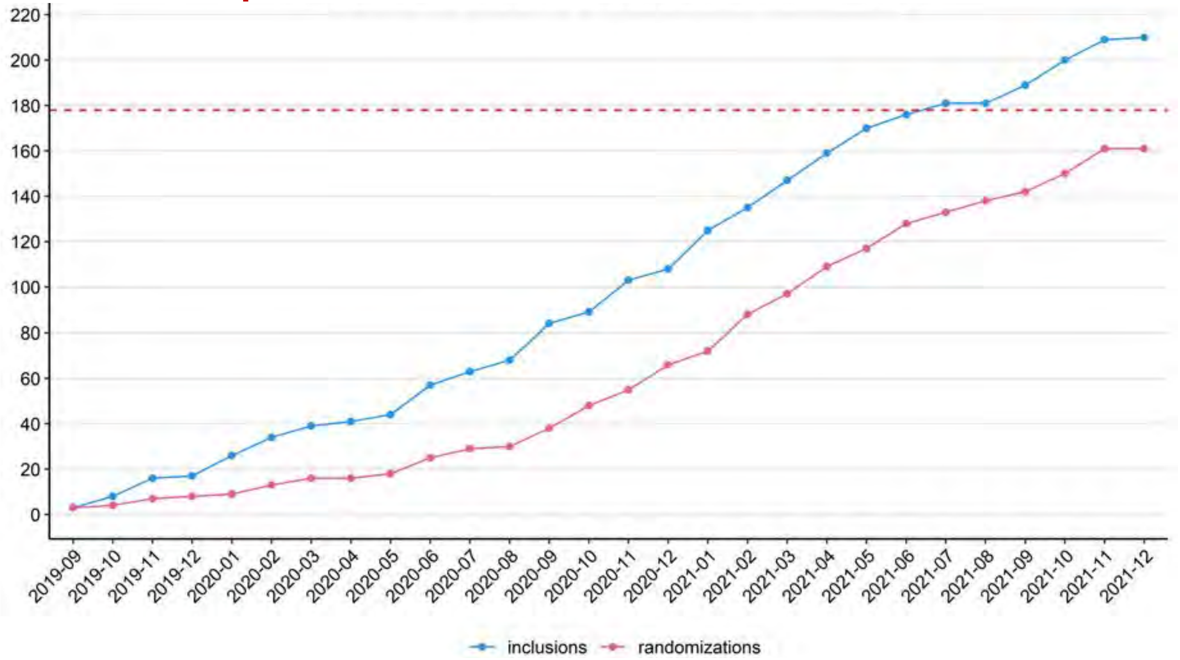
Proix et al Brain 2017, Nat Comm 2018; Jirsa et al. Neuroimage 2016

Evaluation in patient cohorts

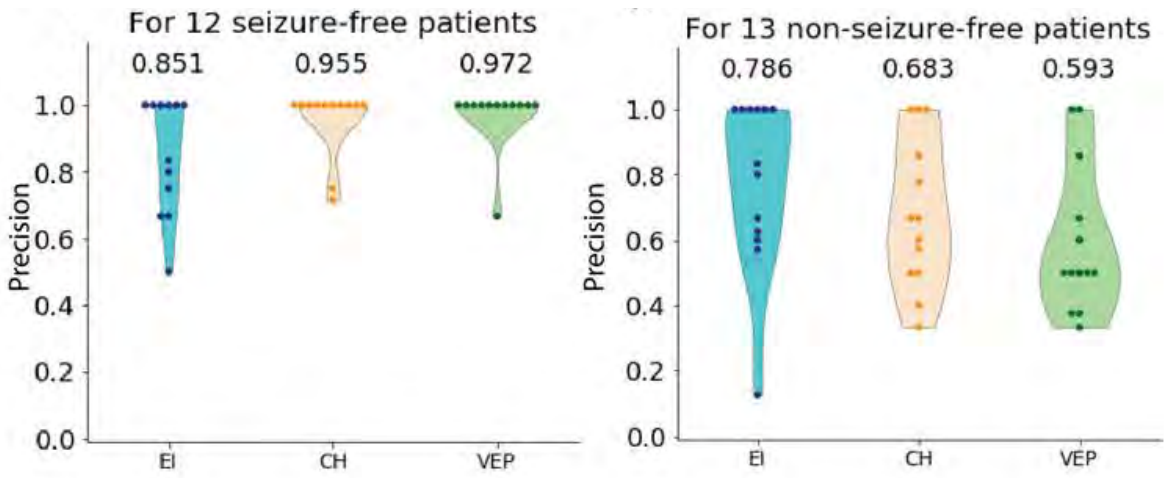
Clinical trial EPINOV ongoing in France (13 epilepsy centers, 400 prospective patients in total)

Patient inclusion

12/2021: 210 patients included, data of 161 have been randomized



State of the art applied to a cohort of epilepsy patients retrospectively.



Proix et al Brain 2017, Nat Comm 2018; Jirsa et al. Neuroimage 2016

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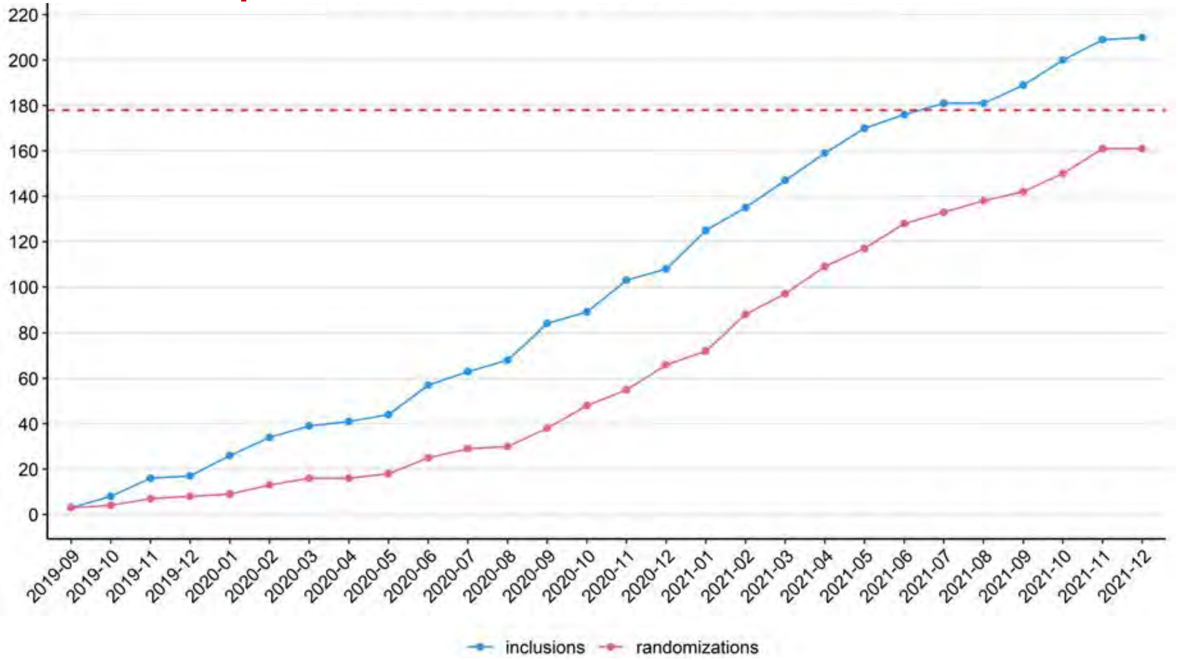

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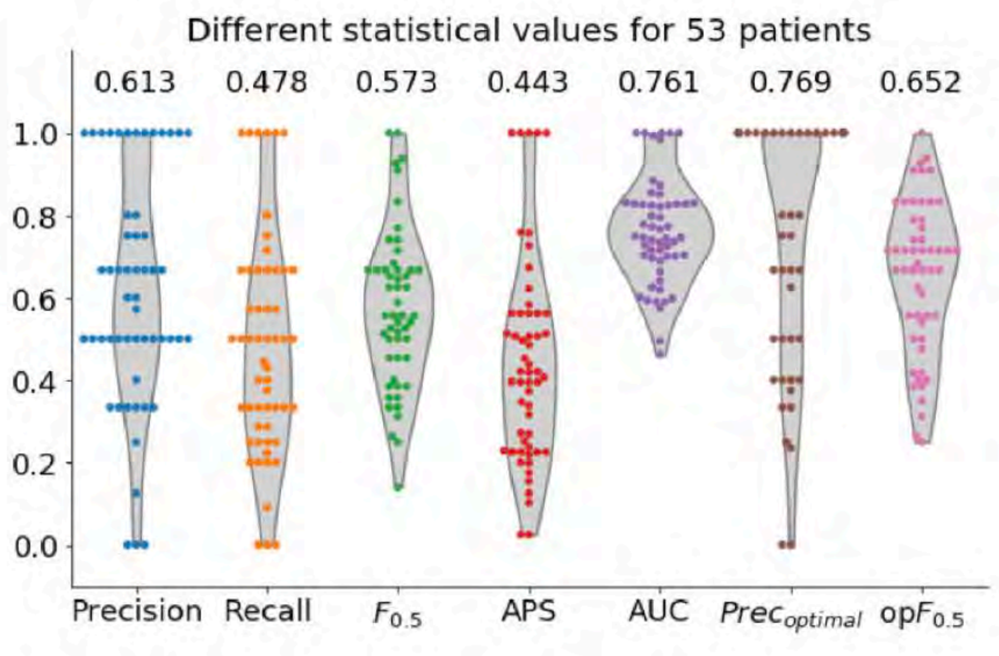

Proix et al Brain 2017, Nat Comm 2018; Jirsa et al. Neuroimage 2016

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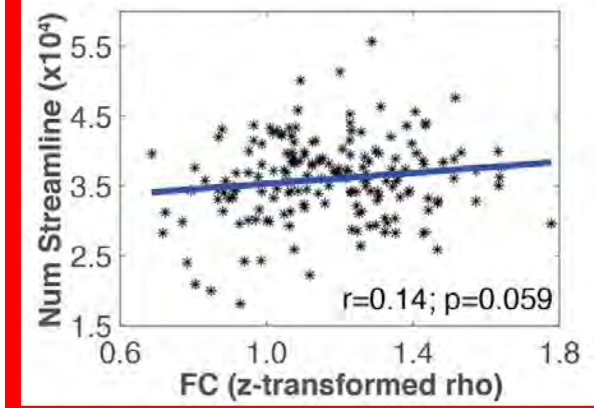
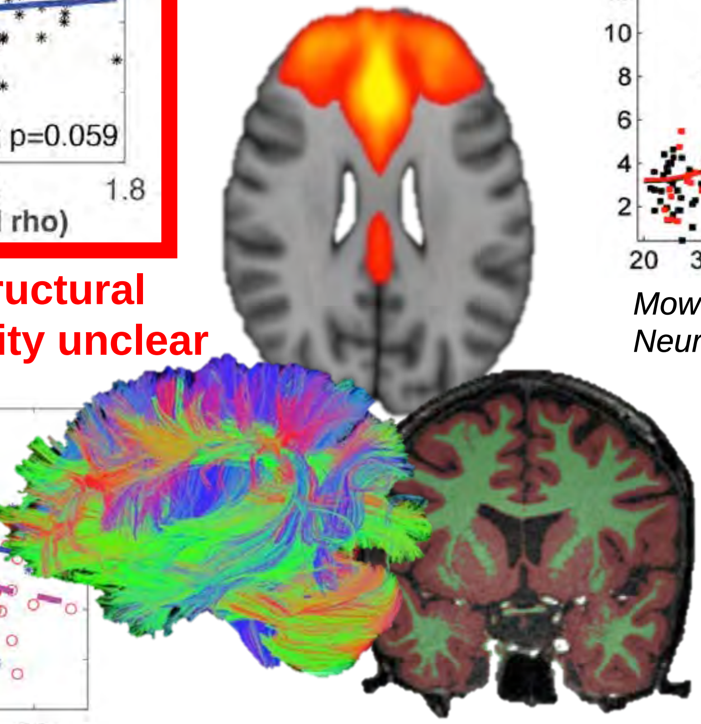
AGING

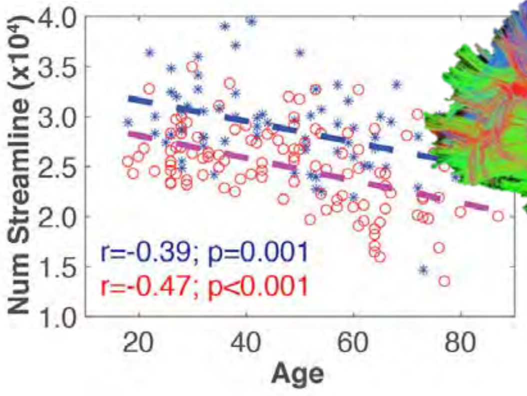
HIGH RESOLUTION AND MULTISCALE

Interindividual & regional variability of brain phenotypes

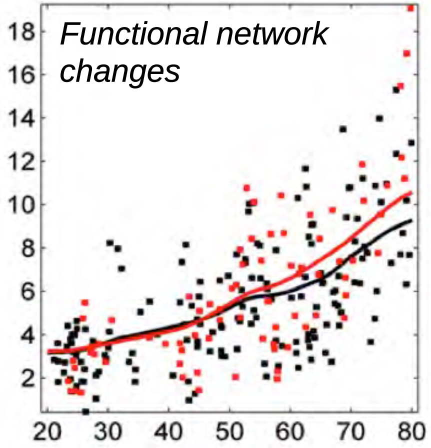


relation between structural & functional connectivity unclear

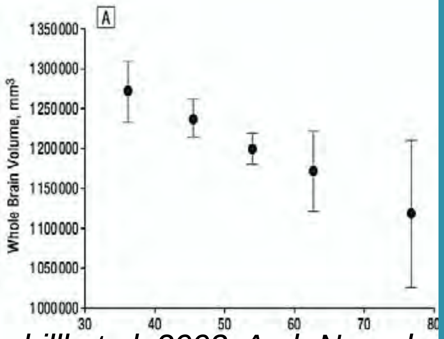




Tsang et al. 2017, Front Aging Neurosci

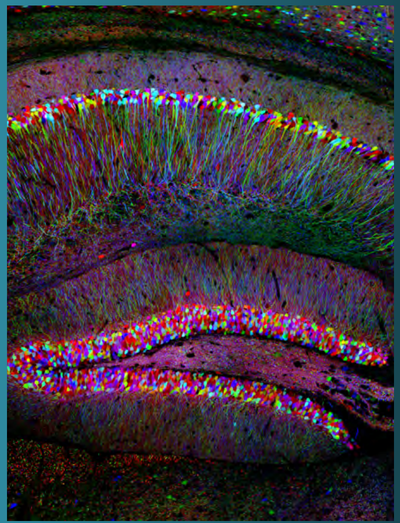


Mowinckel et al. 2012, NeuroImage

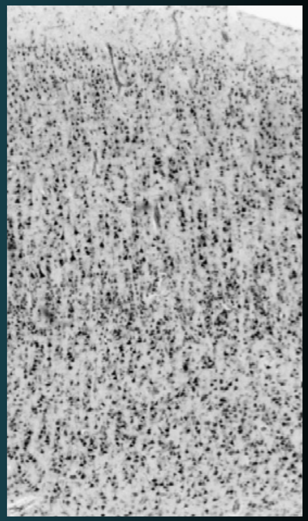


Scahilll et al. 2003, Arch Neurol

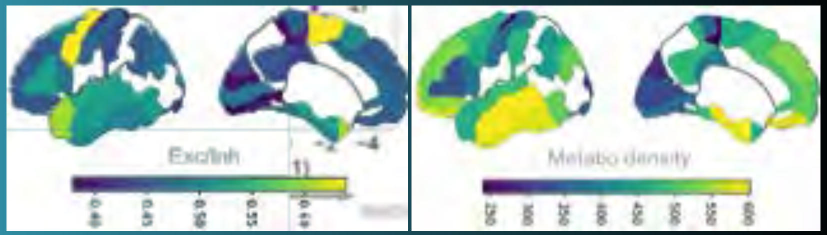
Neuron types



Cytoarchitecture



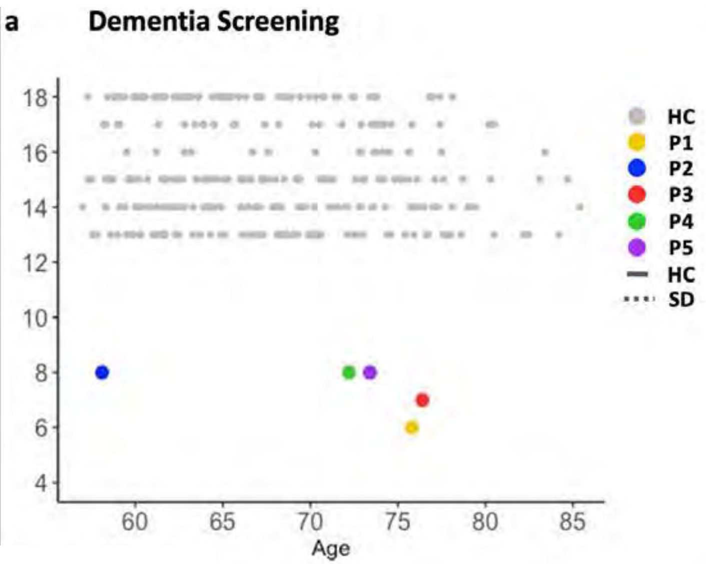
Receptor distributions

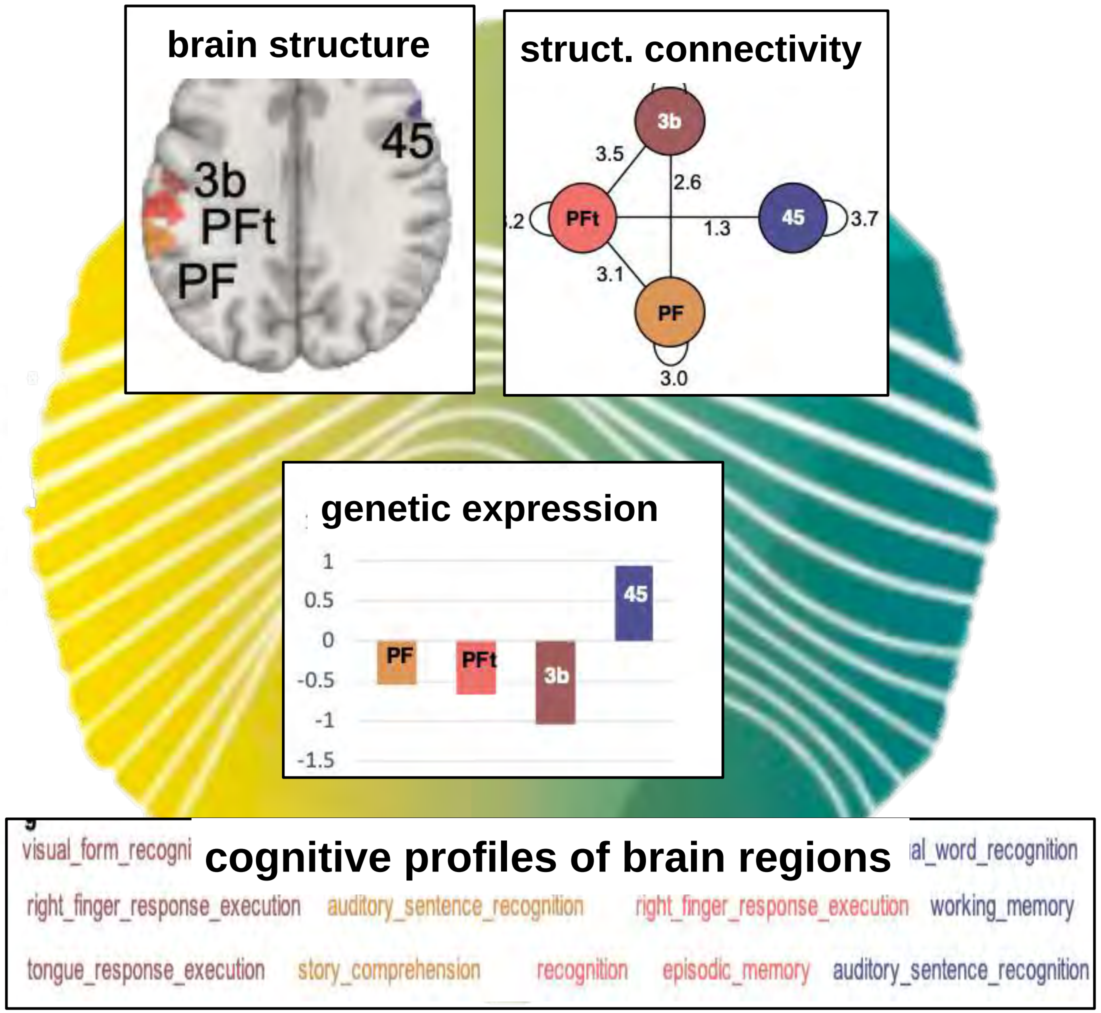


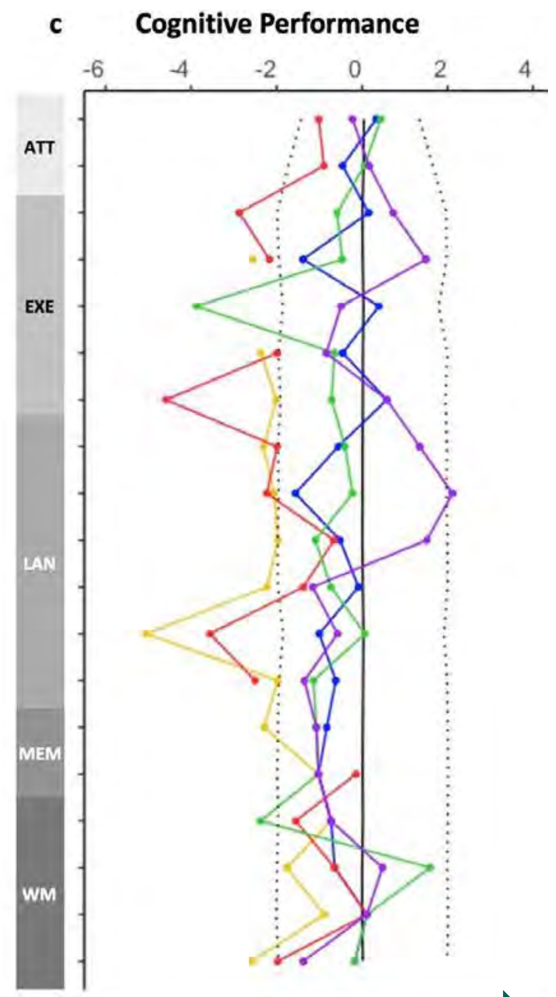
Goulas et al, PNAS (2021)

Relevant multilevel brain features

cognitive profiles of subjects







Jockwitz et al. 2021
Curr Opin Behav Sci

conspicuous finding

deep characterization (via EBRAINS)

personalizing interpretations

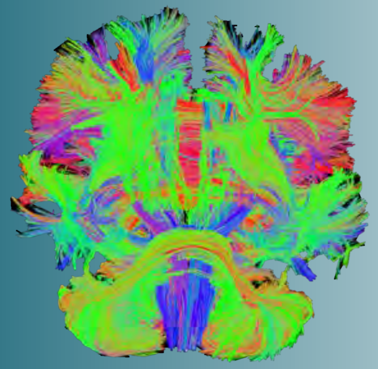
Model building – the virtual cohorts

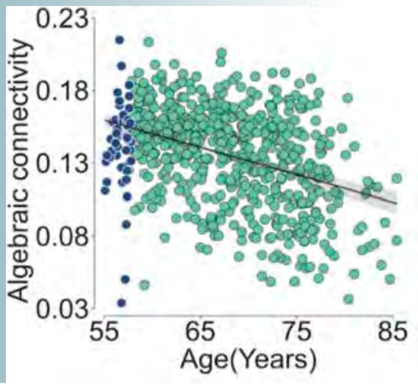
Modelling framework

Modelling output

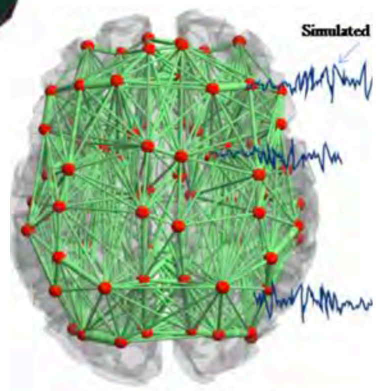
Human Brain Atlas

Interhemispheric SC decreases
(as a proxy for age-related decline)

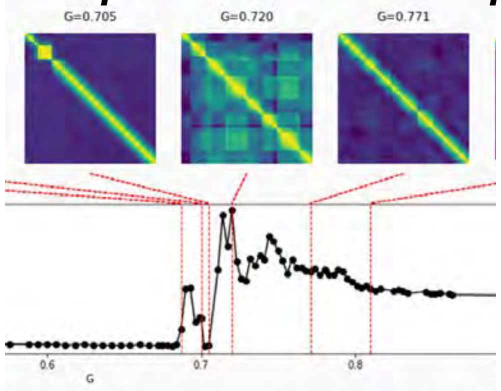


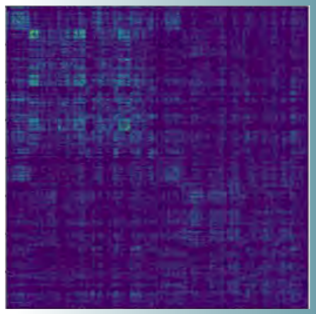


THEVIRTUALBRAIN.



point of optimal network coupling

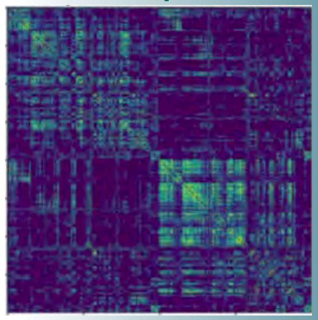




simulated

FC dynamics
(age-related)

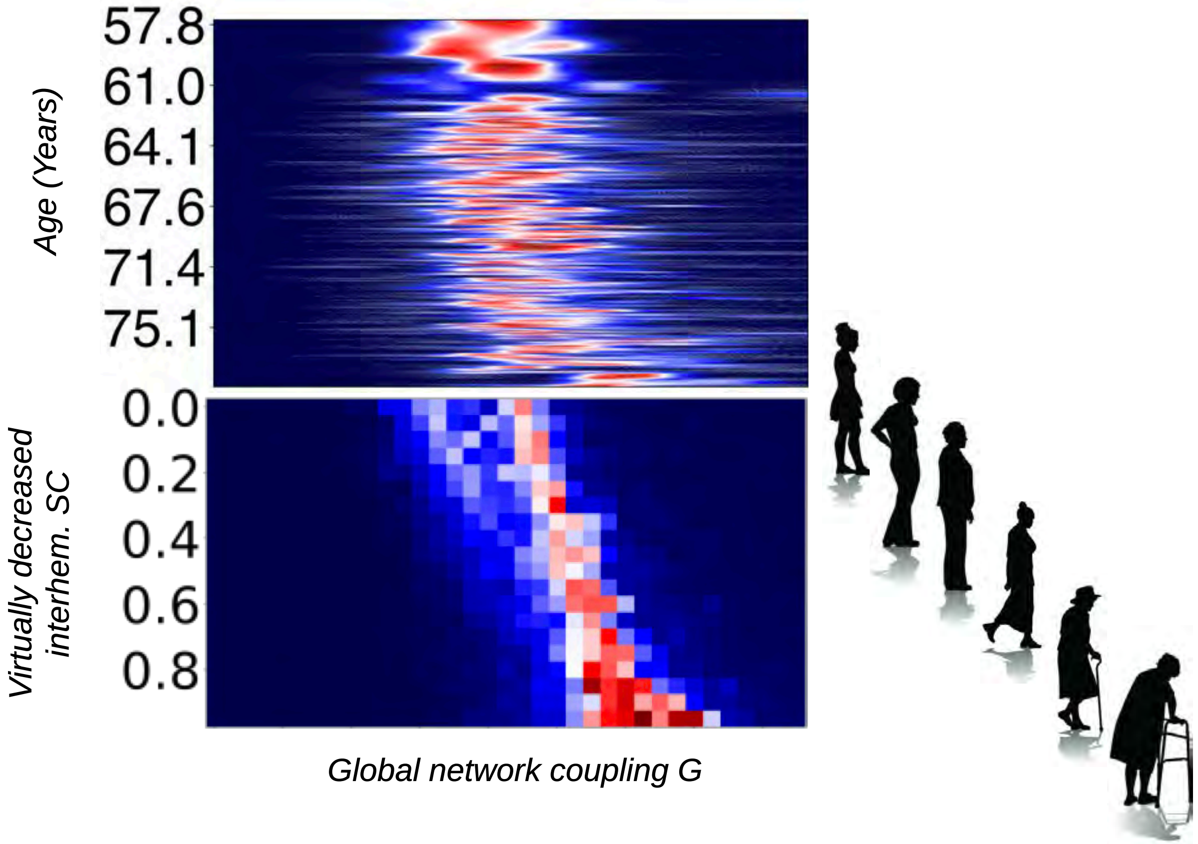
empirical



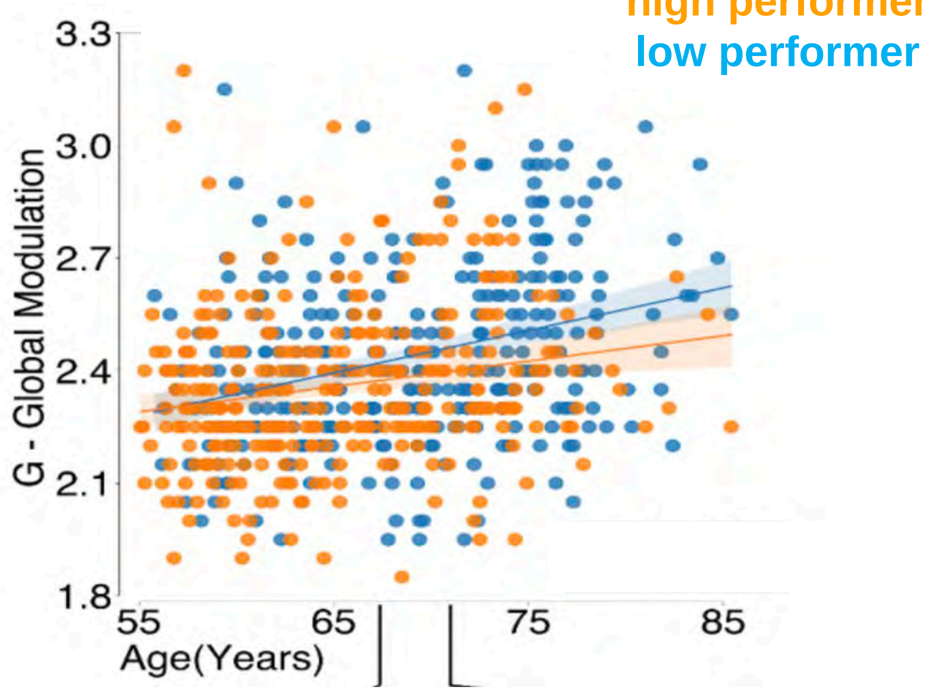
Lavanga et al bioRxiv 2022

Model based evidence for aging theory of dedifferentiation

Increased coupling by manipulation of structural connectivity



Effects on cognition



Lavanga et al bioRxiv 2022

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DIGITAL TWINS

SCIENTIFIC VISION FOR DIGITAL NEUROSCIENCE

Digital Twin technology

Origins in industry and manufacturing (Grieves, 2002)

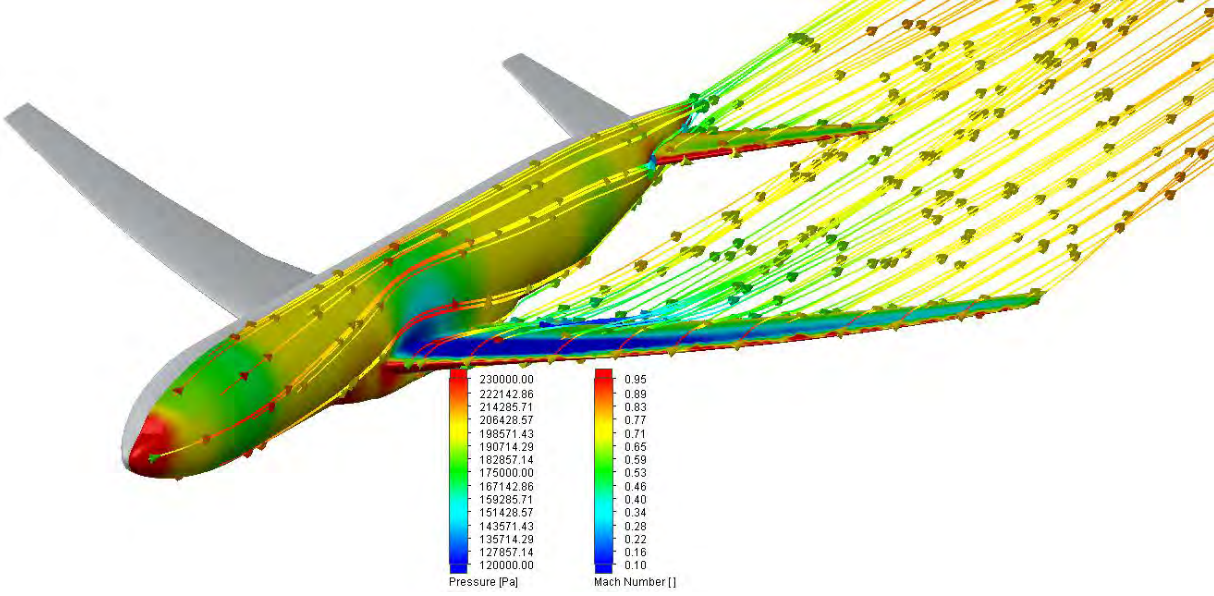
Early applications in air and space travel (Vickers, NASA Roadmap Report in 2010)

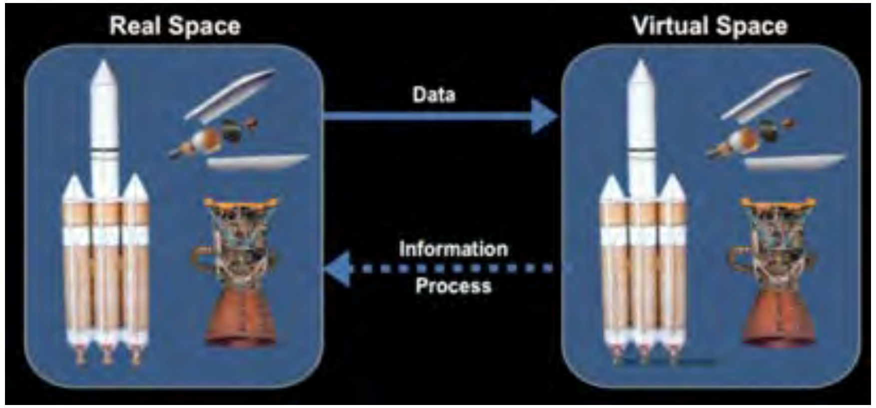
Digital Twin concept consists of three distinct parts:

- Physical object
- Virtual/digital object
- Data flows back and forth between objects

Comprehension of functional process is critical to link sensor data to inner functioning

Digital Twin is driver for
- Product development
- Planning and testing
- Optimisation of processes, maintenance, interventions



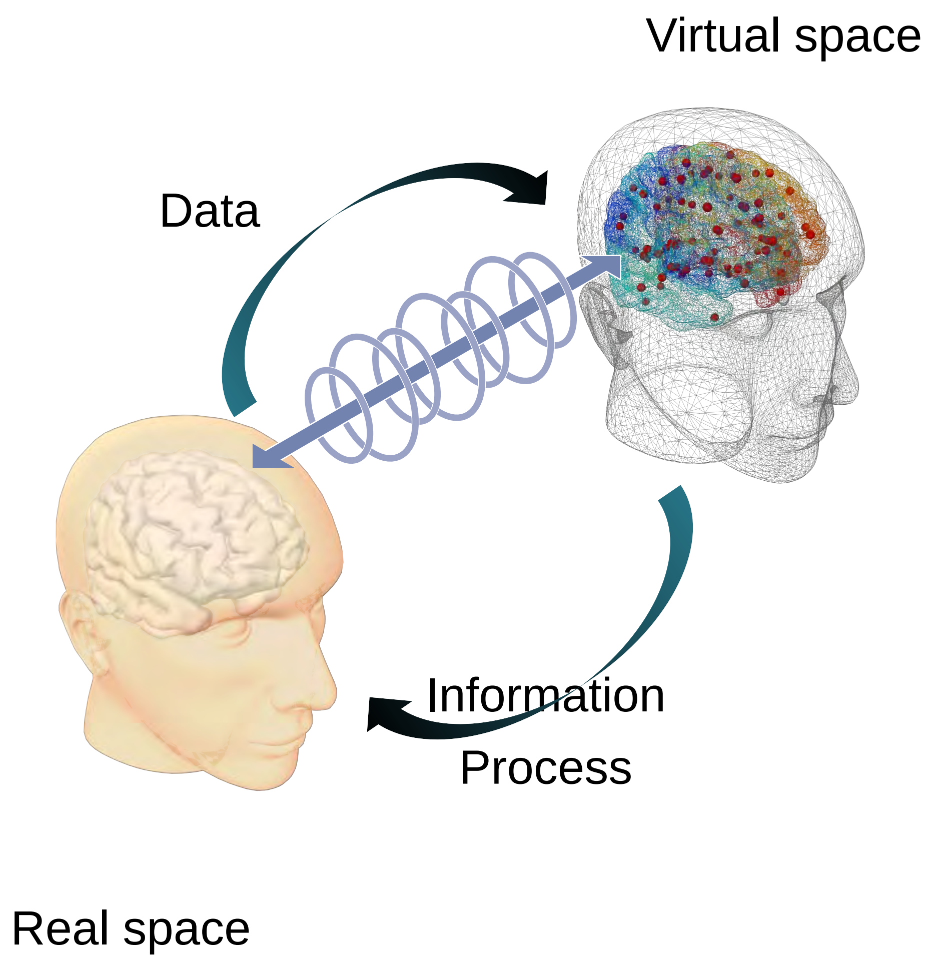


Towards Digital Twin technology in HBP

“The **digital twin** as discussed here should be understood as a virtual model designed to adequately represent an object or process that **is constrained by data** from its physical counterpart, and that **provides simulation data to guide choices and anticipate their consequences**.”

“The **digital twin is thus a copy in the practical sense**, usually associated to a model of a function or process, the *raison d’être* of which stems from its usefulness in dealing with relevant problems faced by its physical counterpart without the need (and certainly not the claim) to capture every single detail thereof.”

HBP Scientific vision paper, zenodo.org 2022



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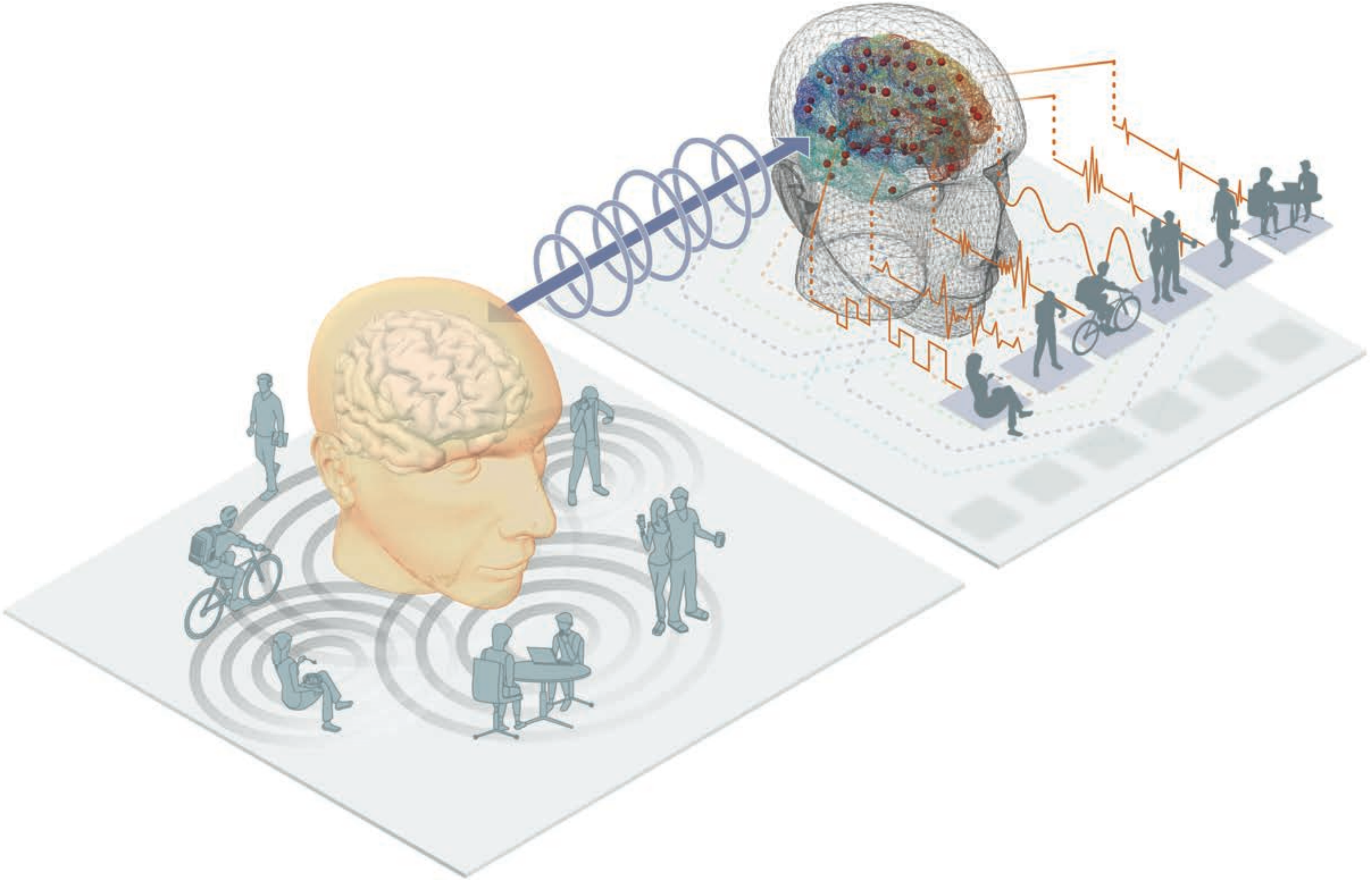

Human Brain Project

EBRAINS

Thank you

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Thank you

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