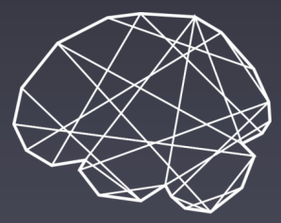


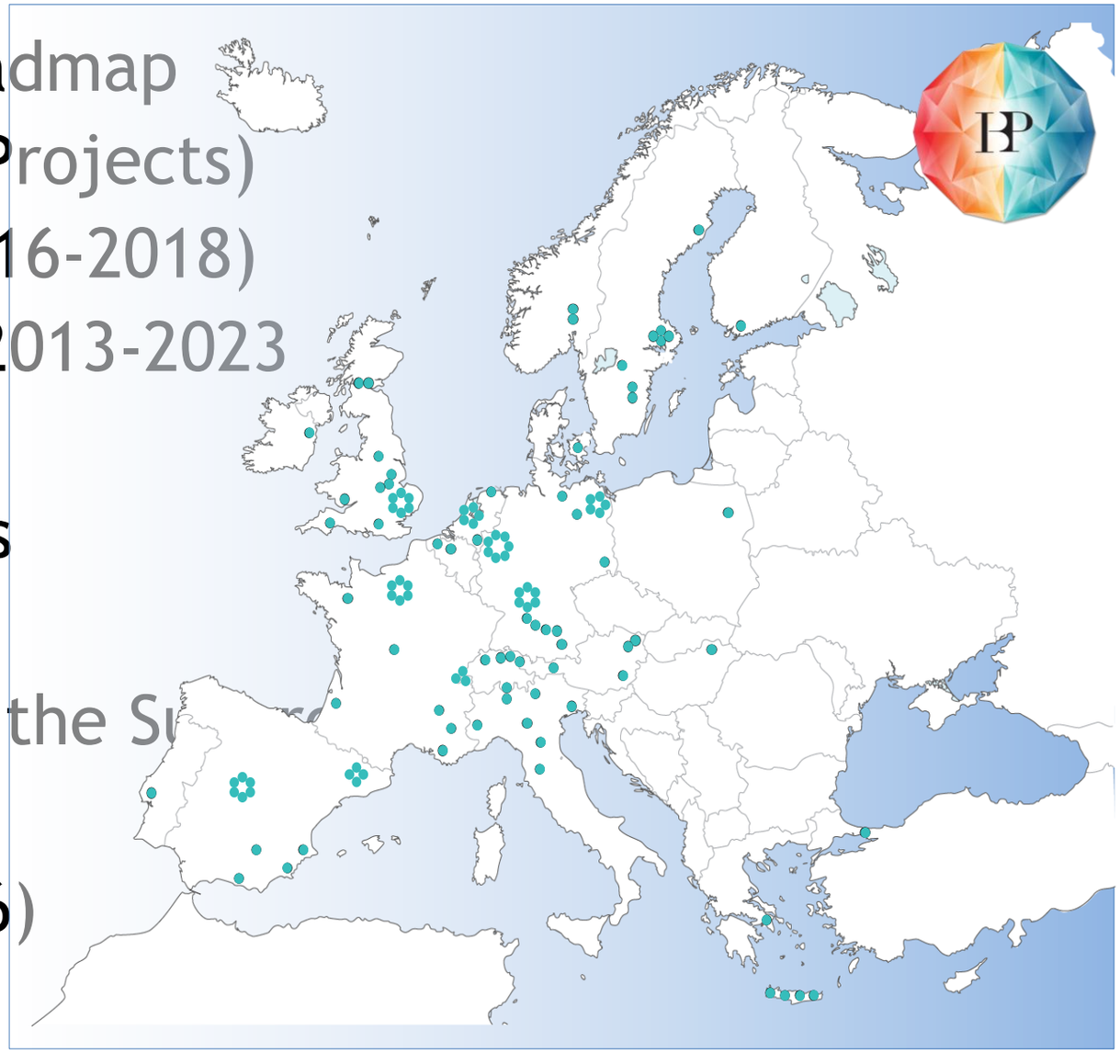
Crosstalk to the Human Brain Project
Building Bridges between Major Initiatives

Viktor Jirsa

Institut de Neurosciences des Systèmes
UMR1106 Inserm

Human Brain Project

- 10-year, EUR 1 Billion Research Roadmap
- (50% Core Project, 50% Partnering Projects)
- 89 M Euros (Core Project, SGA1, 2016-2018)
- 406 M Euros estimated EU funding 2013-2023
- 116 partners institutions
- 19 countries, 9 associated countries
- Organized in 12 Subprojects
- 6 Co-Design Projects (CDPs) linking the Su
- More than 600 researchers involved
- 6 Platforms (released in March 2016)



The Human Brain Project (HBP)

Mission

Understanding the human brain is one of the greatest challenges facing 21st century science.

If we can rise to it, we can gain profound insights into what makes us human, build revolutionary computing technologies and develop new treatments for brain disorders. Today, for the first time, modern ICT has brought these goals within reach.

April 2018 – March 2020:

Development of a European infrastructure for brain research to bridge the different scales of brain organization

Roadmap of HBP

Where are we?

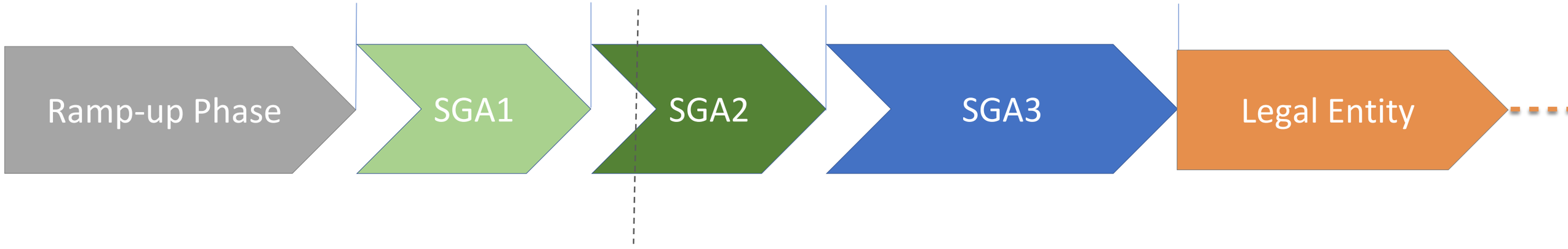
Human Brain Project

RuP End
March 2016

SGA1 End
March 2018

SGA2 End
March 2020

SGA3 End
March 2023



HBP Summit
Oct 2018

Roadmap of HBP in SGA3

High-level objectives (HO) in SGA3

HO1 Understanding the multi-level brain organization and applying this knowledge to medicine and technology

Explore the multi-level complexity of the brain in space and time.

Transfer the acquired knowledge to brain-derived applications in health, computing, and technology.

HO 2 Developing and maintaining a European HBP Integrated Platform (HIP)

Provide shared, open, computing tools, models and data through the HBP Integrated Platform as a European Research Infrastructure for enabling brain science across disciplines.

Decoding the multilevel brain organization

RESEARCH INFRASTRUCTURE

MEDICAL & NEUROINFORMATICS. SIMULATION, ATLAS, ROBOTICS

ETHICS & SOCIETY

Multiscale in space and time, multimodal

NEUROSCIENCE & BRAIN M

EXPERIMENT, THEORY, MODEL

Organization of the Human Brain Project

SP4 **Brain Theory**
Multiscale neural modeling
Learning and plasticity

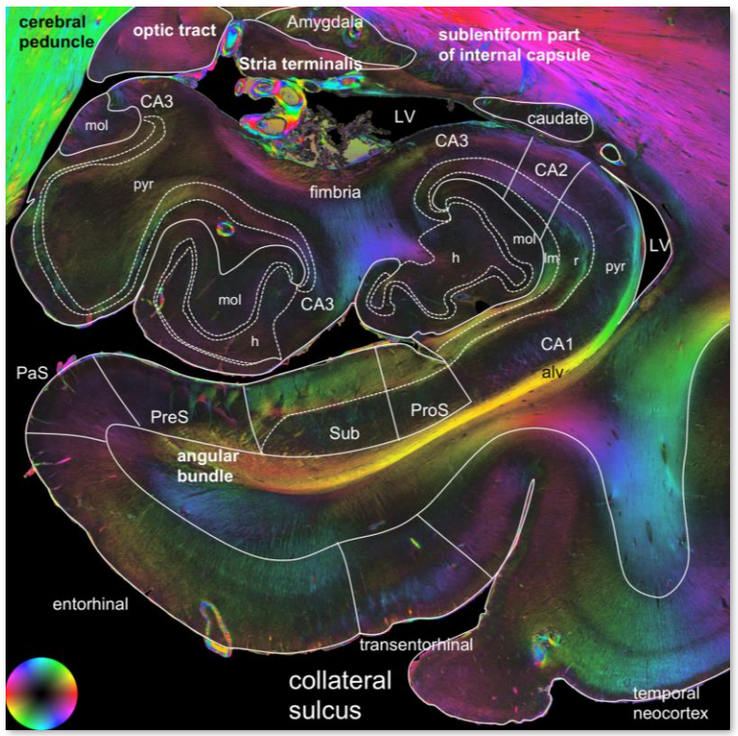
SP8 **Medical Informatics**
MIP installed in 7 hospitals
3 hospitals contributed data from 6345 patients

SP5 **Neuroinformatics**
N of files uploaded at CSCS: 181387
Reference atlas: 1.97 Mio server hits,
5278 visitors (since April 2017)

SP6 **Simulation**
N of page views -> 41050
N of collabs created by external users -> 1267

SP7 **High Performance Analytics and Computing**
400 accounts on HPC and Cloud infrastructure of the HPAC Platform

SP10 **Neurorobotics**
285 registered users at the end of SGA1 (currently >400)
37410 views of the NRP forums (280 views per thread)
775 Twitter followers

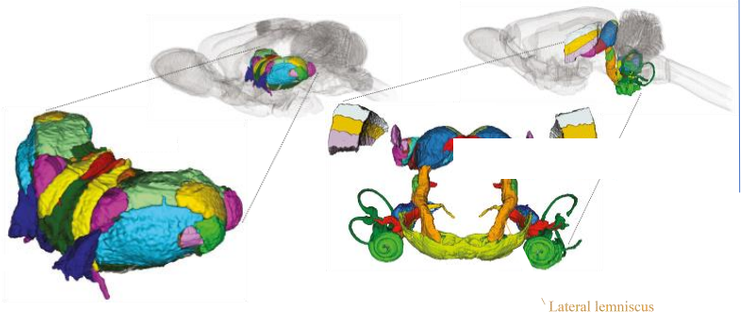


Neuroinformatics platform

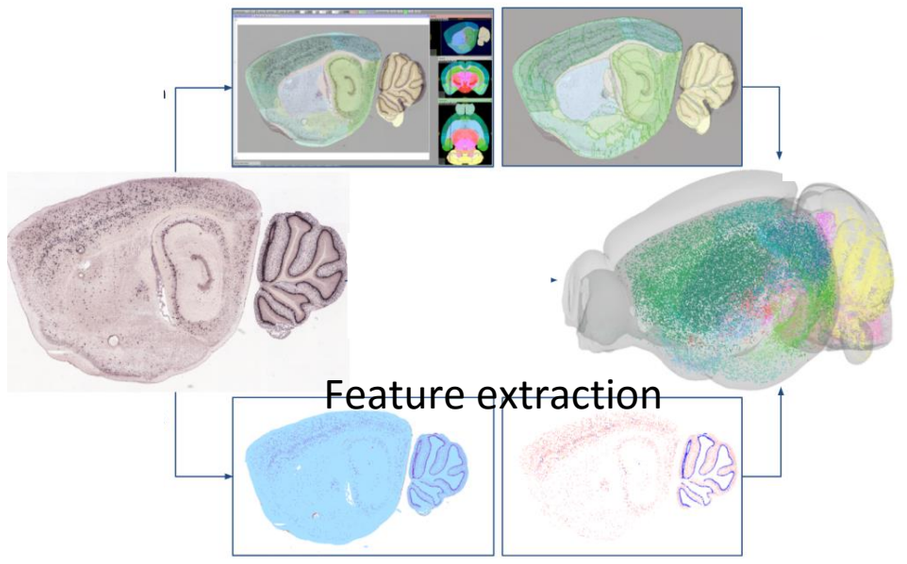
HBP Workflow for registration of images to reference atlases in routine use.

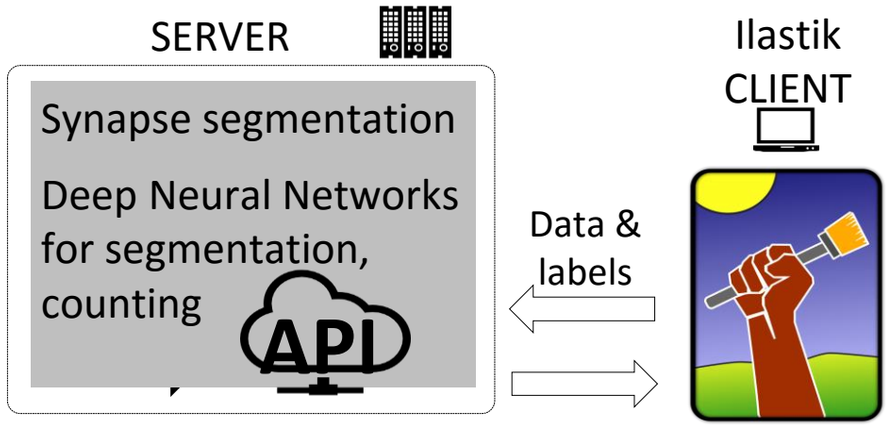
Machine-learning based feature extraction with automatic assignment of location in 3-D atlas space.

Increasing number of brain **structures delineated in Waxholm Space rat brain reference atlas**

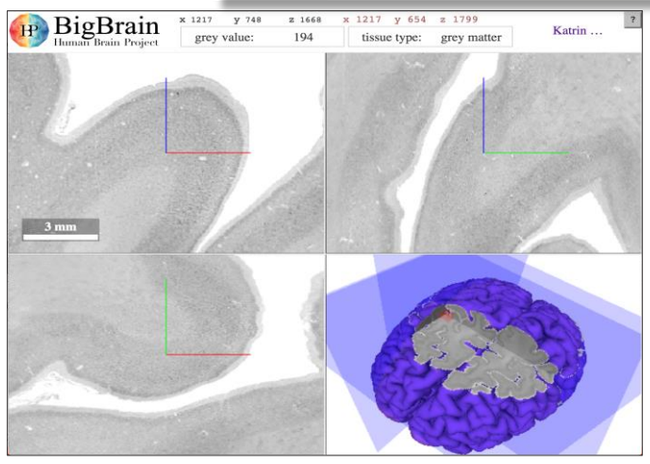


Anchoring to reference atlas





New web-based atlas **viewer for Terabyte-sizes brain volumes**, that can be extended with interactive plugins.



http://bigbrain.humanbrainproject.org/

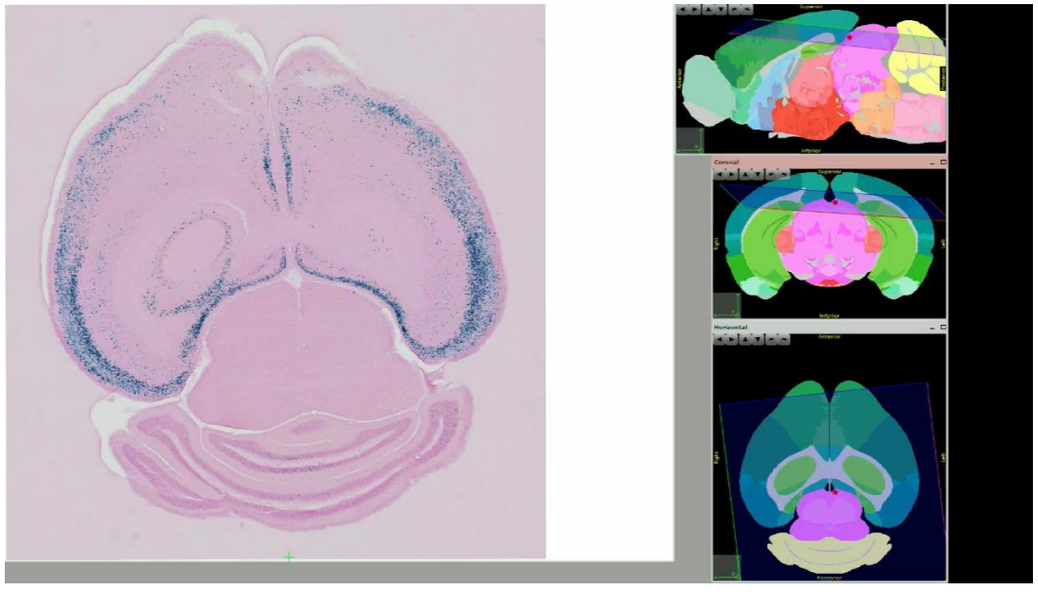
Jan Bjaalie (Univ. Oslo), Sten Grillner (Karolinska) and teams in SP5

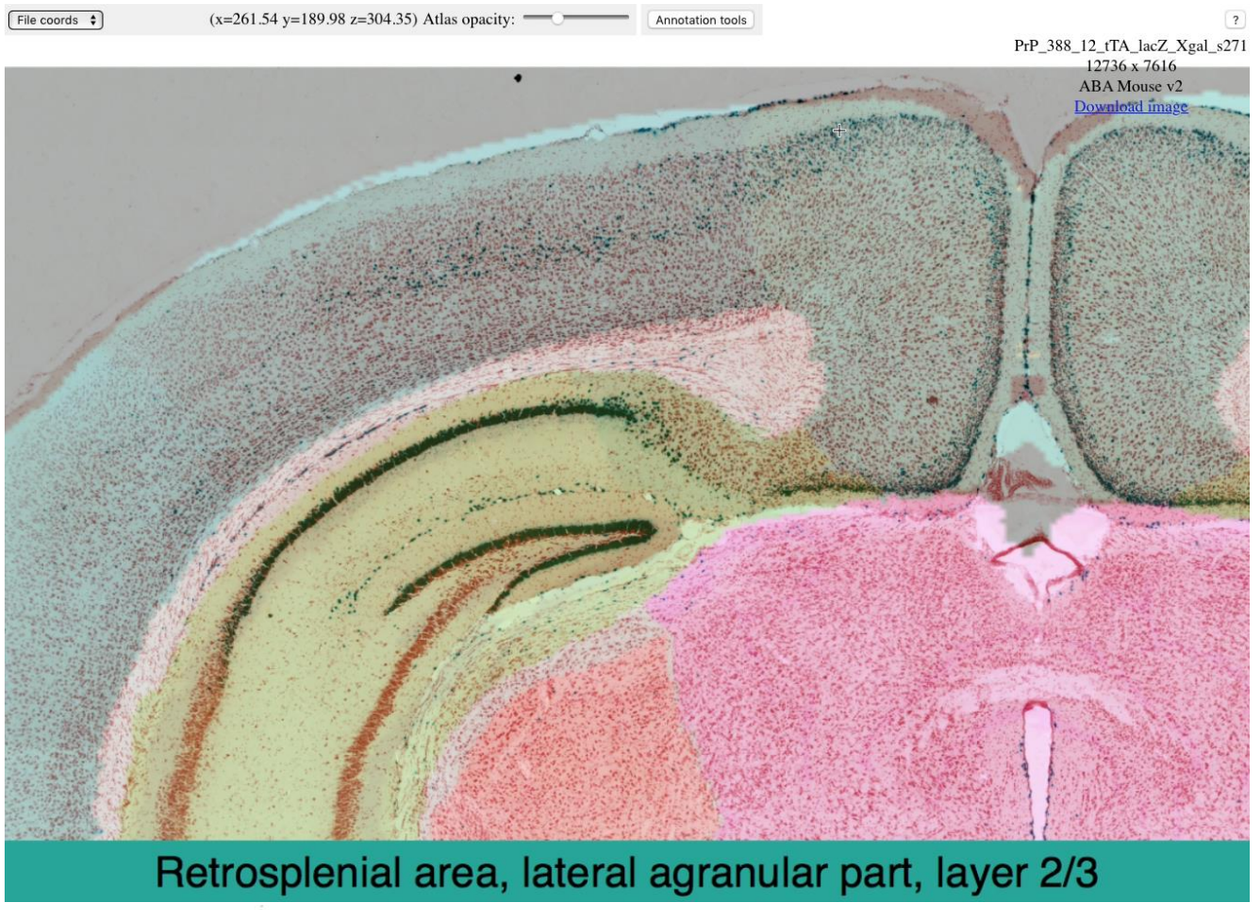
Virtual Anatomy Lab

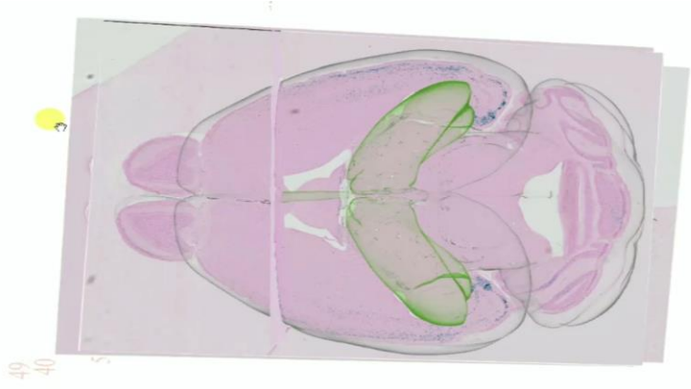
SP5

Product leader: Jan G. Bjaalie (UIO), Deputy: Trygve B. Leergaard (UIO)

VIEWING AND ANALYSIS OF DATA: Data registered to reference atlas can be viewed with overlay of atlas structures. Reference atlas coordinates available as metadata.

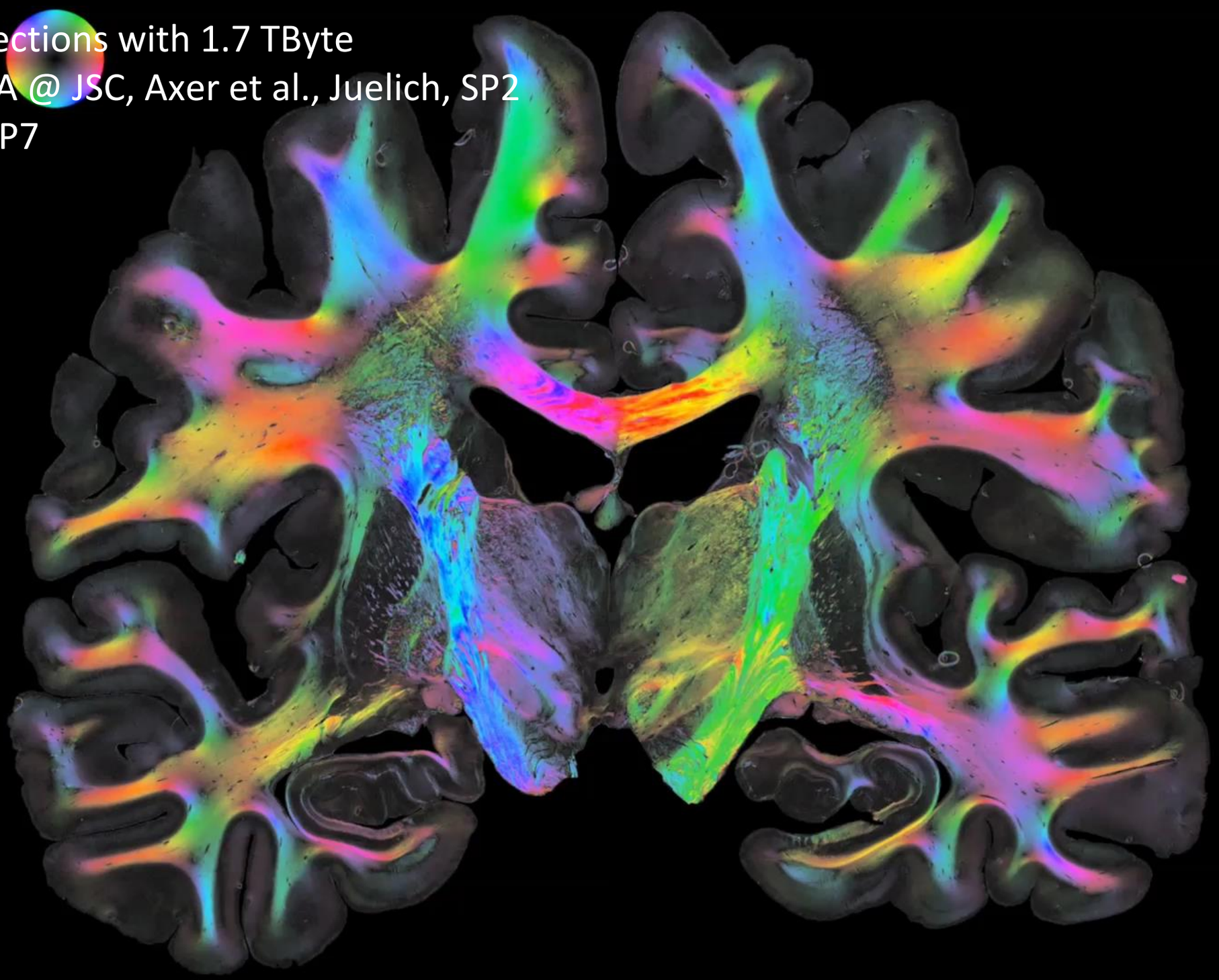






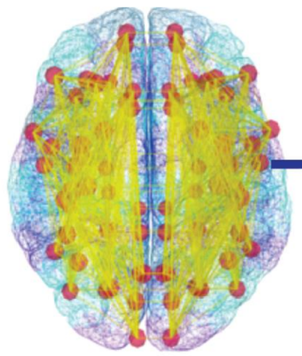
Human Brain Project

Human brain sections with 1.7 TByte
Runs on JURECA @ JSC, Axer et al., Juelich, SP2
in collab with SP7



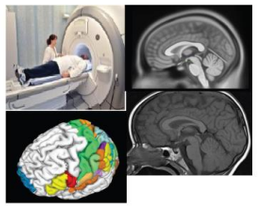
Integration of The Virtual Brain with the Big Brain

Spatial anchoring of brain network models in Brain Reference Atlas



BigBrain, JuBrain
Anatomic details

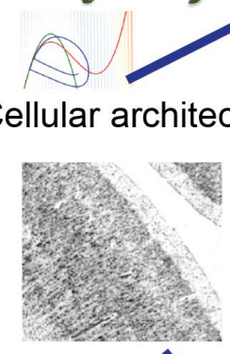
Brain imaging



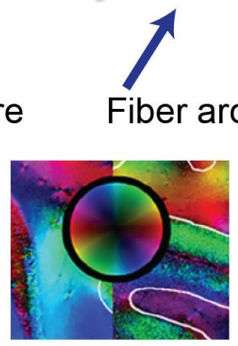
neural mass models

$$\dot{x}_i = f(a, x_i, C^l, \Sigma C^g_{ij} x_j)$$

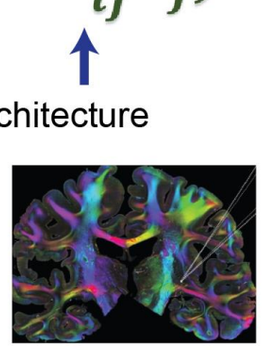
Cellular architecture



Fiber architecture



Local

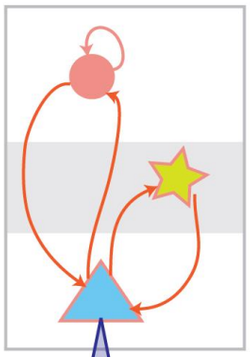


Global

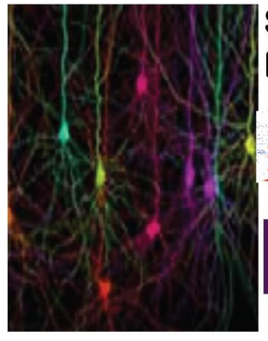
$$\dot{x}_i = f(a, x_i, \Sigma C^l_{ij} x_j)$$

signal neuron models

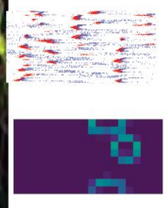
mesoscopic



microscopic

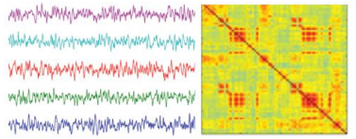


Single Neurons

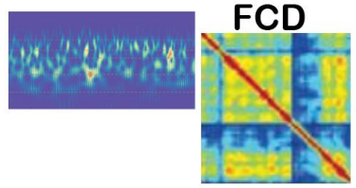


Simulation/analysis

FC

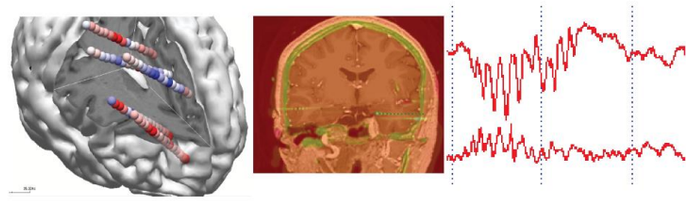


FCD

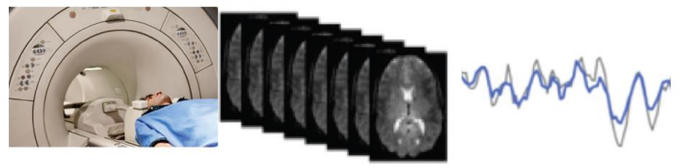


Biophysical forward models

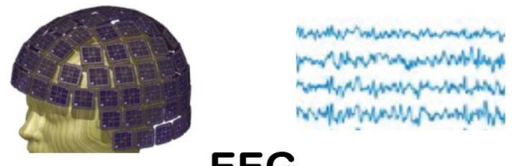
SEEG



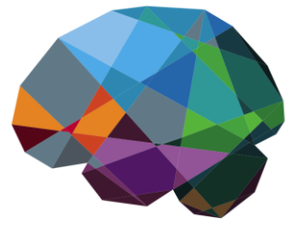
fMRI



MEG



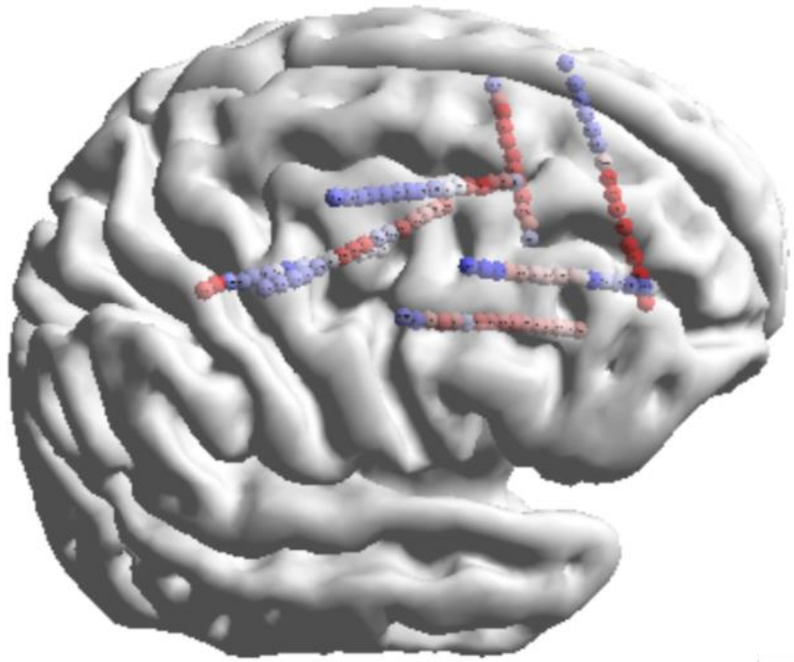
EEG



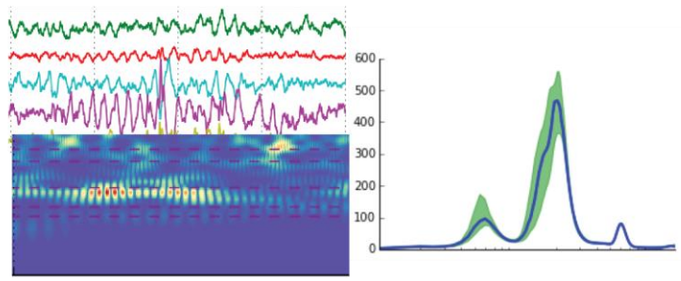
THEVIRTUALBRAIN.

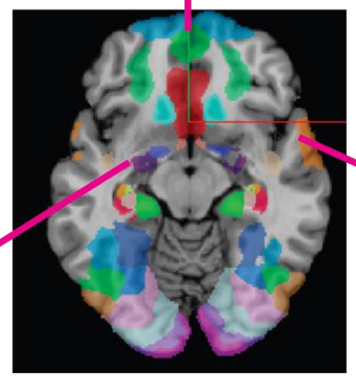
Validation of Integration using human SEEG data

On each brain region, SEEG signal patterns and frequency features

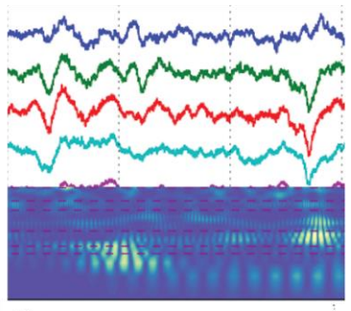


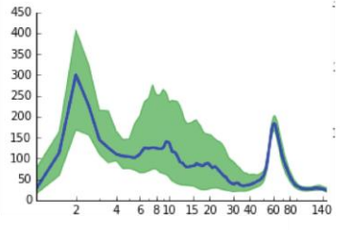
Frontal pole



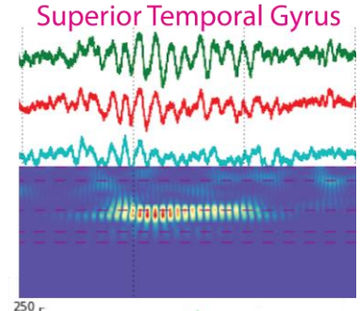


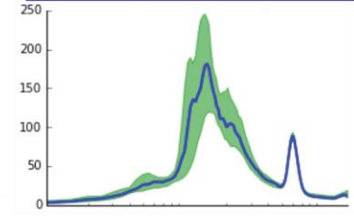
Amygdala



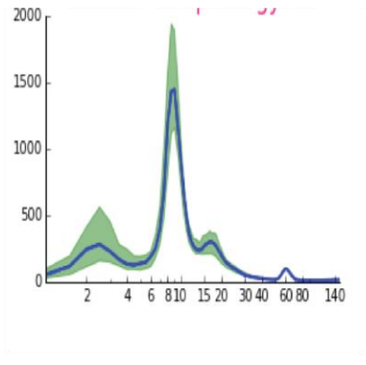


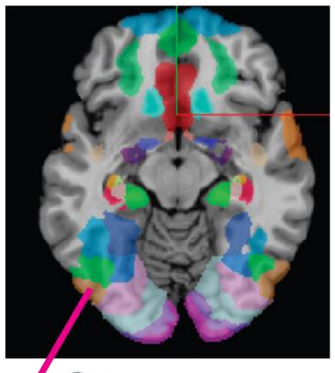
Superior Temporal Gyrus



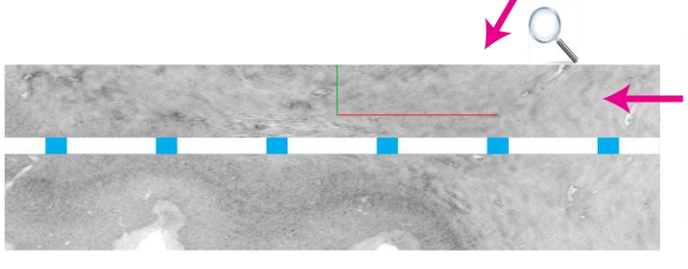


Frequency features

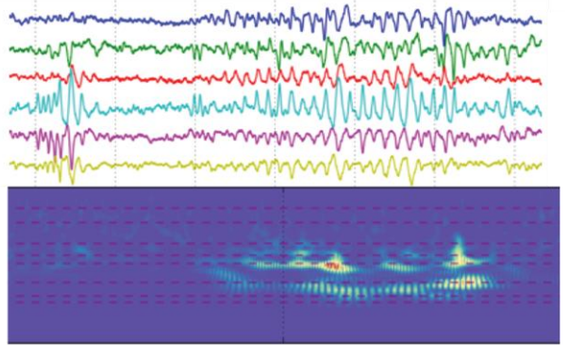


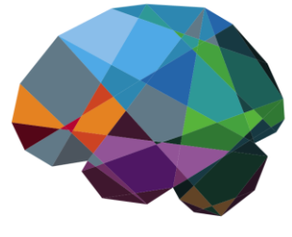


JuBrain Atlas



SEEG electrodes





THEVIRTUALBRAIN.

Base infrastructure for HBP is ready

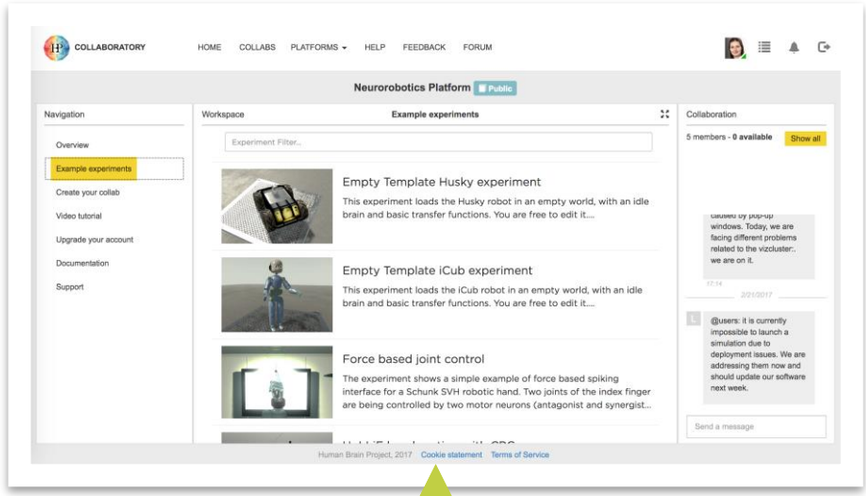
HBP Pilot Systems available as dedicated **compute resources** for HBP

Storage, HPC and other compute resources in close proximity

Fast access from other HBP infrastructure components, e.g. Collaboratory apps

Enabling of **Platform services** (e.g. SPs 5, 6, 10) on SP7 infrastructure

Collaboratory migrated to compute and storage resources hosted by SP7



openstack.

Thomas Lippert and team (Jülich) and Thomas Schulthess and team (SCSC Lugano), in SP7

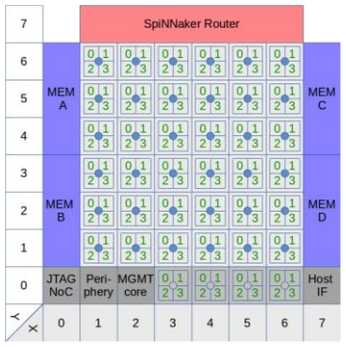
Operating the neuromorphic platform

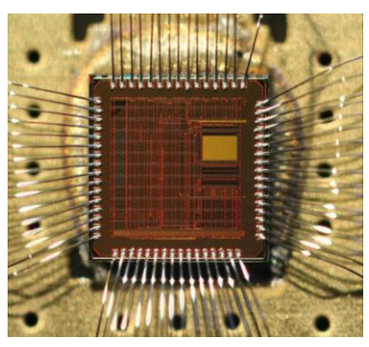
Usage highlights

SpiNNaker : Large-scale cortical models

BrainScaleS : Deep network benchmarking

Prototyping the HBP developed neuromorphic platform





Design highlights

SpiNNaker : 160 ARM cores and 80 GIPS/W per chip

BrainScaleS : Local learning, active dendrites

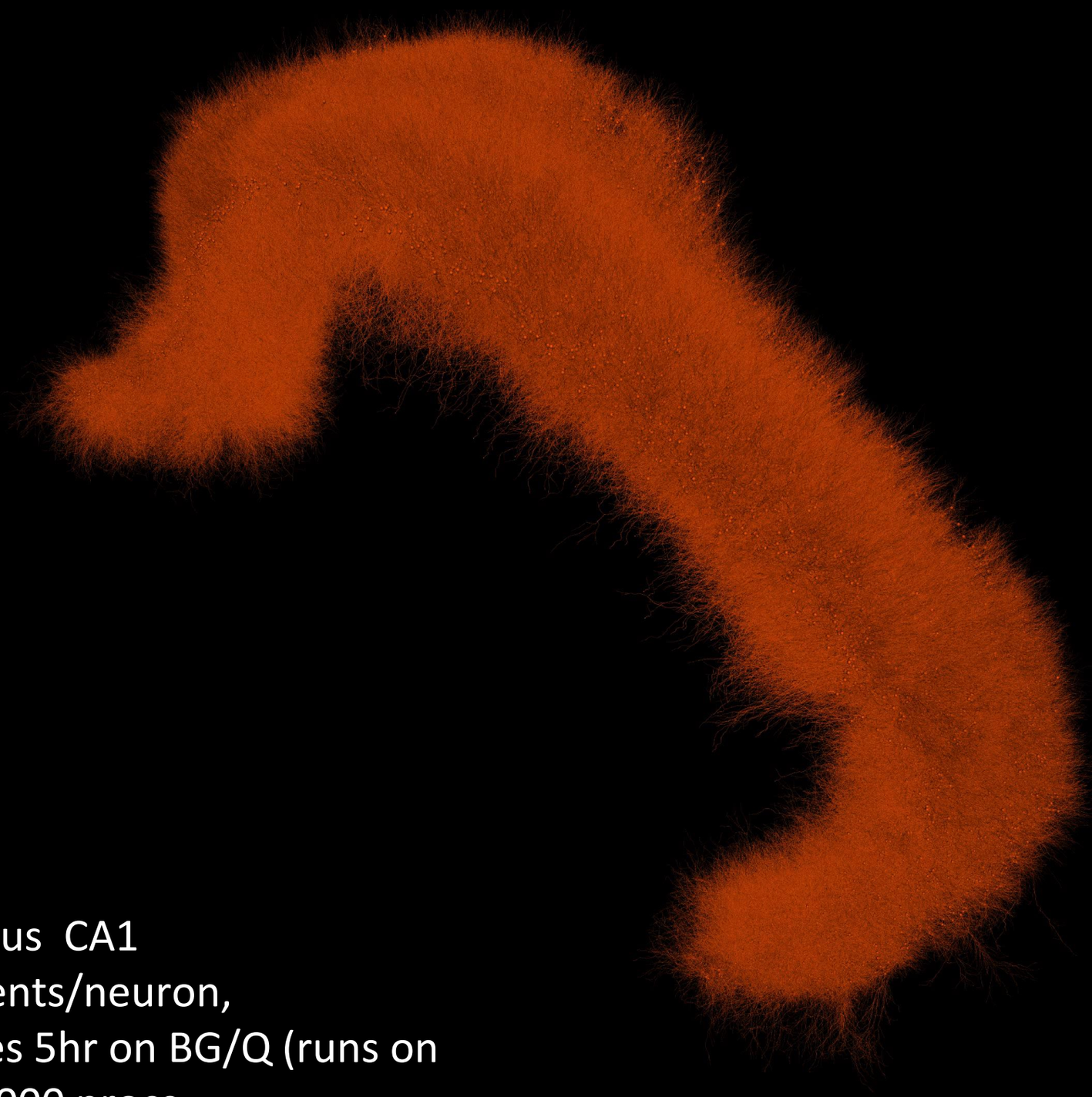
SpiNNaker-2

BrainScaleS-2

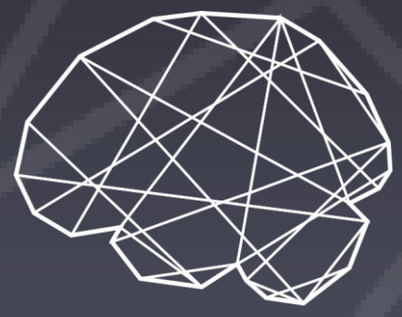
Hippocampus model

mouse, CA1 region
~1’000 compartments/neuron,
1” simulation needs 5 h on JUQUEEN
generates approx. 4TB

SP6 SP1 SP2 SP3 SP4 SP7



Mouse hippocampus CA1
~1’000 compartments/neuron,
1” of sim time takes 5hr on BG/Q (runs on JUQUEEN) with 32000 procs
produces 4TB of output data
Migliore et al., Palermo, SP6

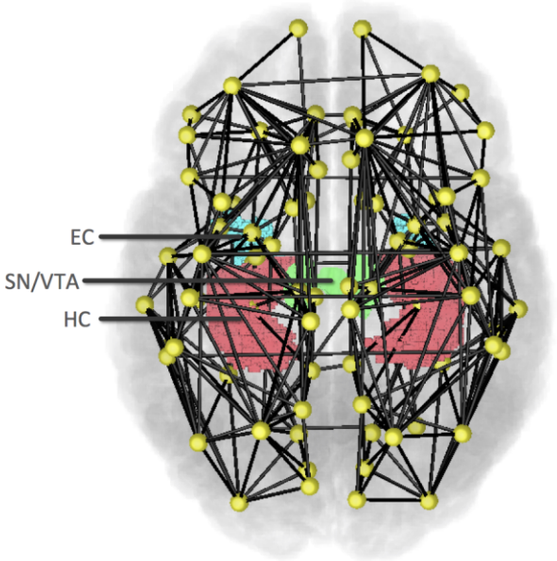


The Virtual Brain

Large-scale network concepts

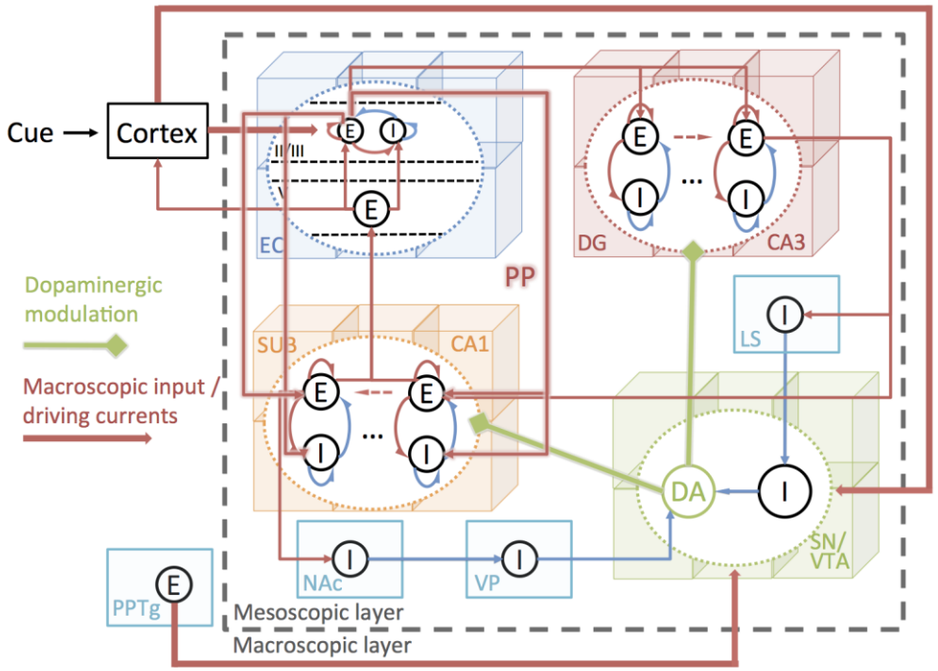
Multi-scale computational models

Macroscopic (Whole brain)

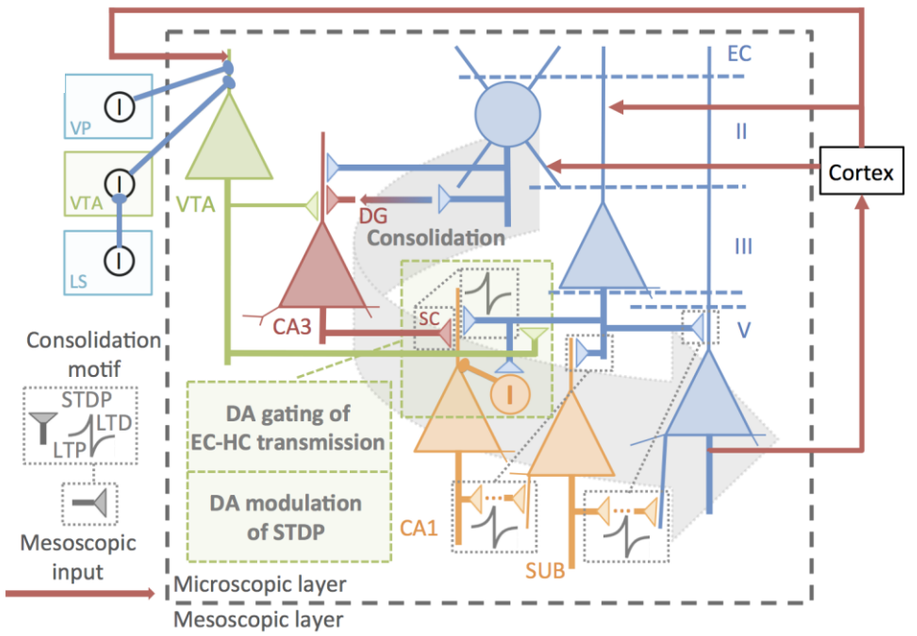


Macroscopic layer

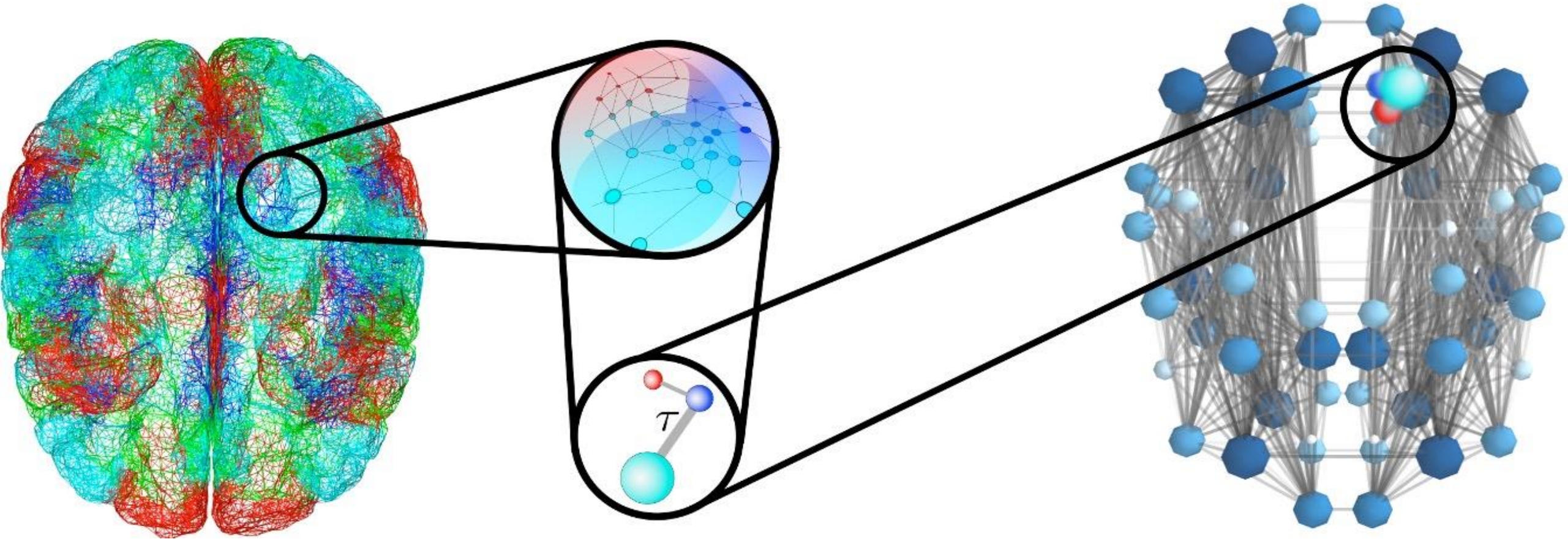
Mesoscopic (Populations)



Microscopic (Cells)



Large-scale brain networks



THEVIRTUALBRAIN.

SELECT PUBLICATIONS

REVIEWS AND OVERVIEWS

Deco G, Jirsa VK, McIntosh AR (2013)
Resting brains never rest: computational insights into potential cognitive architectures.
Trends in Neurosciences, Volume 36, Issue 5, 268-274

Deco G, Jirsa VK, McIntosh AR.
Emerging concepts for the dynamical organization of resting state activity in the brain.
Nature Reviews Neuroscience 12, 43-56, 2011

ORIGINAL PAPERS

EXCERPTS FROM MORE THAN 20 PEER-REVIEWED PUBLICATIONS

Sanz-Leon P, Knock SA, Woodman MM, Domide L, Mersmann J, McIntosh AR, Jirsa VK (2013)
The virtual brain: a simulator of primate brain network dynamics.
Frontiers in Neuroinformatics 7:10. doi: 10.3389/fninf.2013.00010

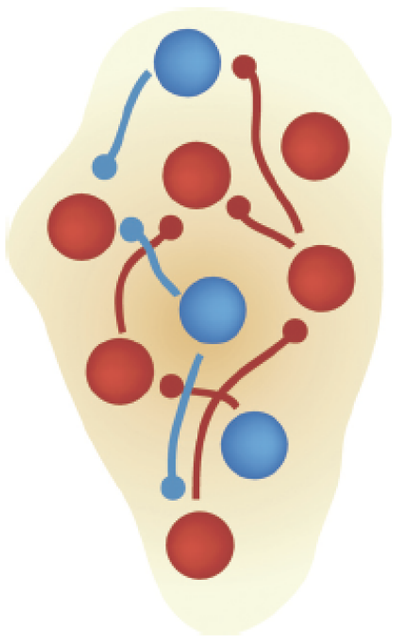
Jirsa VK, Stacey WC, Quilichini PP, Ivanov AI, Bernard C (2014)
On the nature of seizure dynamics.
Brain doi: 10.1093/brain/awul33

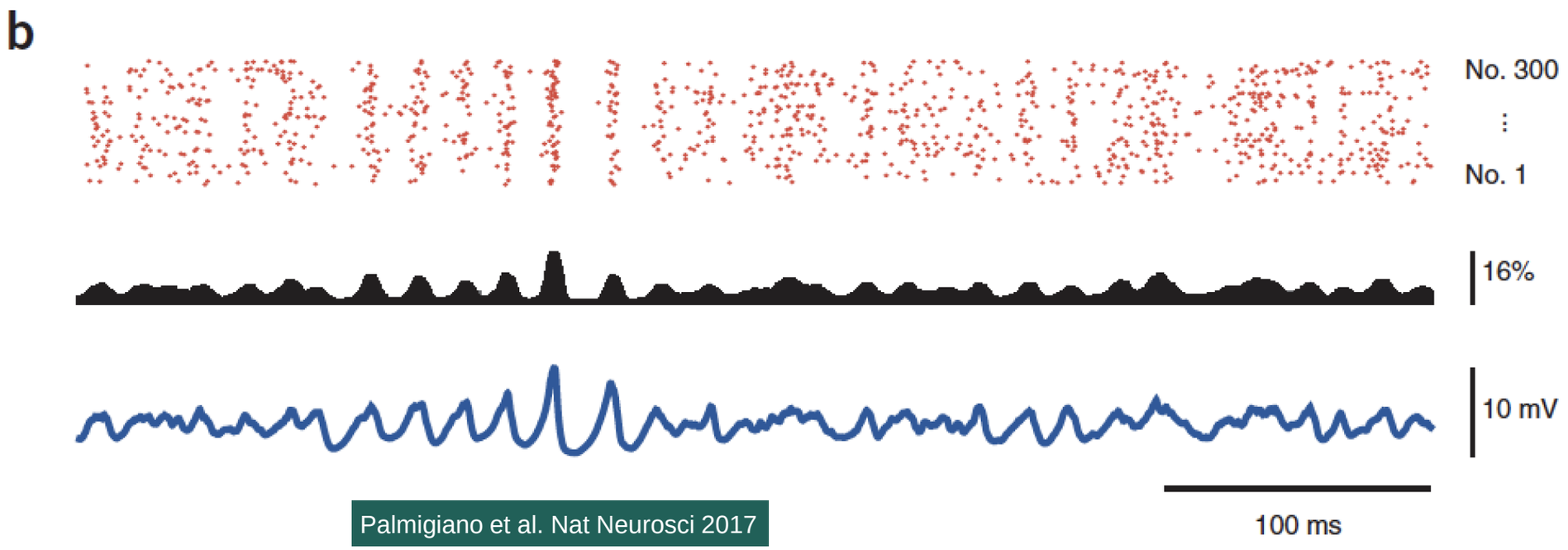
Network node:
Mean field modeling

Connectome:
connectivity & time delays

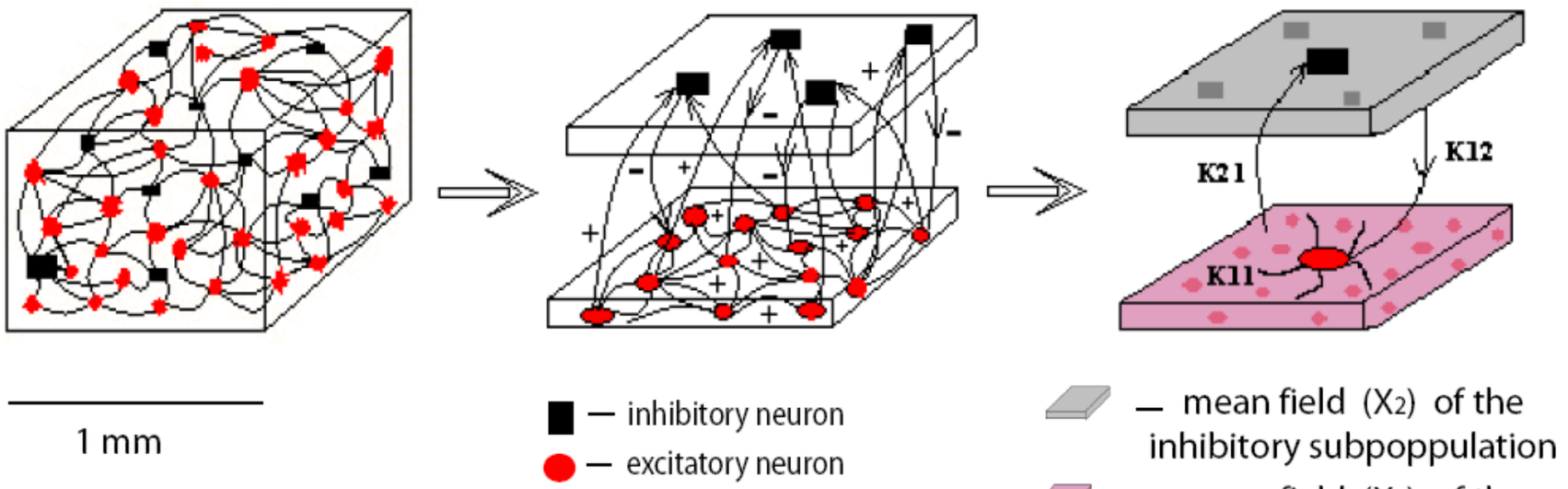
THEVIRTUALBRAIN.

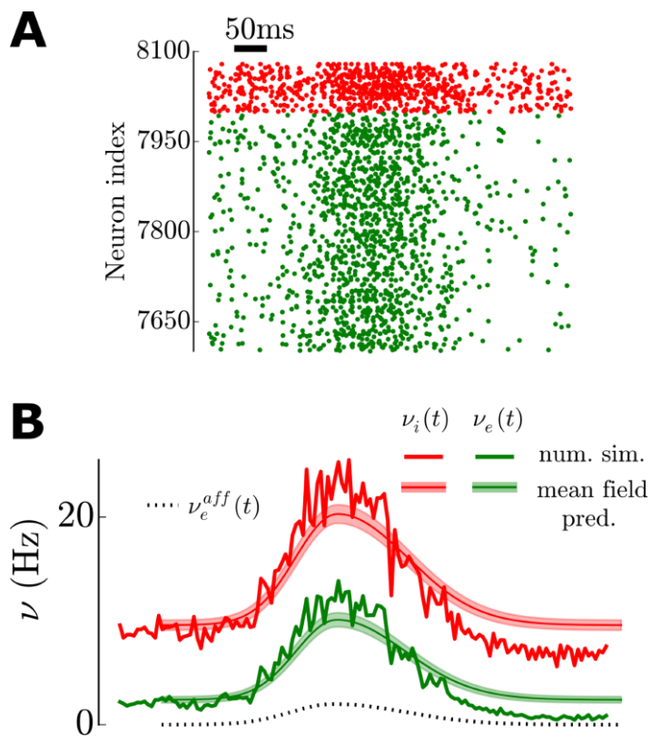
Oscillations in large-scale brain networks





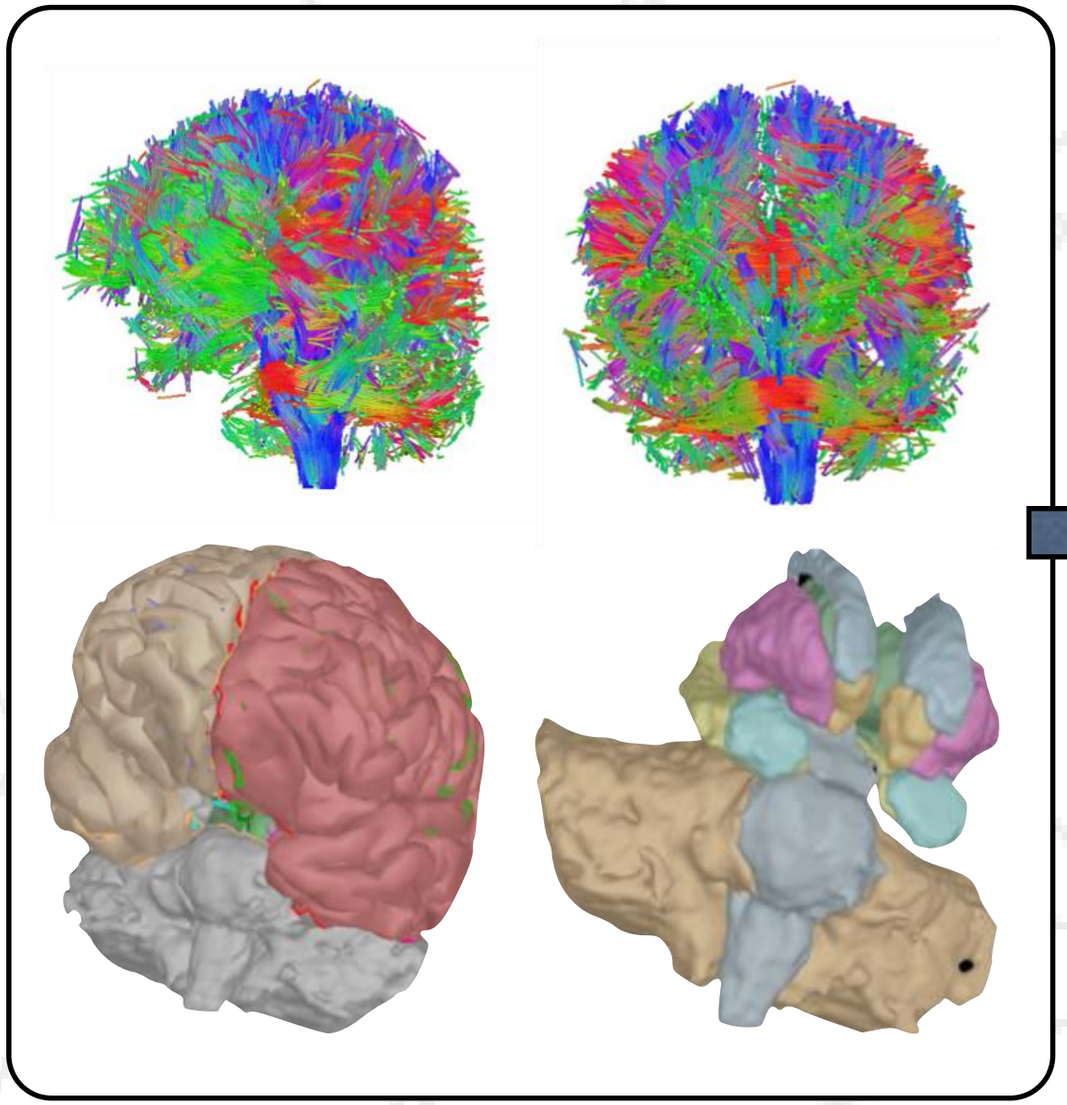
Palmigiano et al. Nat Neurosci 2017



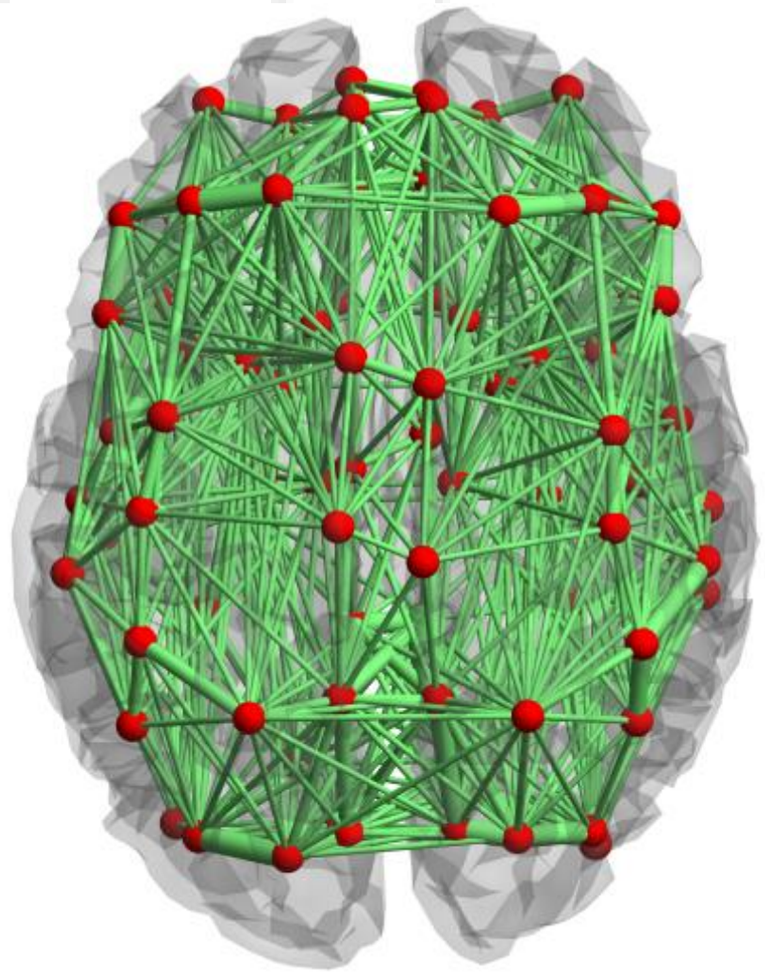


Stefanescu & Jirsa PLoS CB 2008; Bull. Math. Biol. 2010; Zerlaut, Destexhe JComp Neurosci 2017

The virtual epileptic patient: refine network pathology



Structural reconstruction of brain model



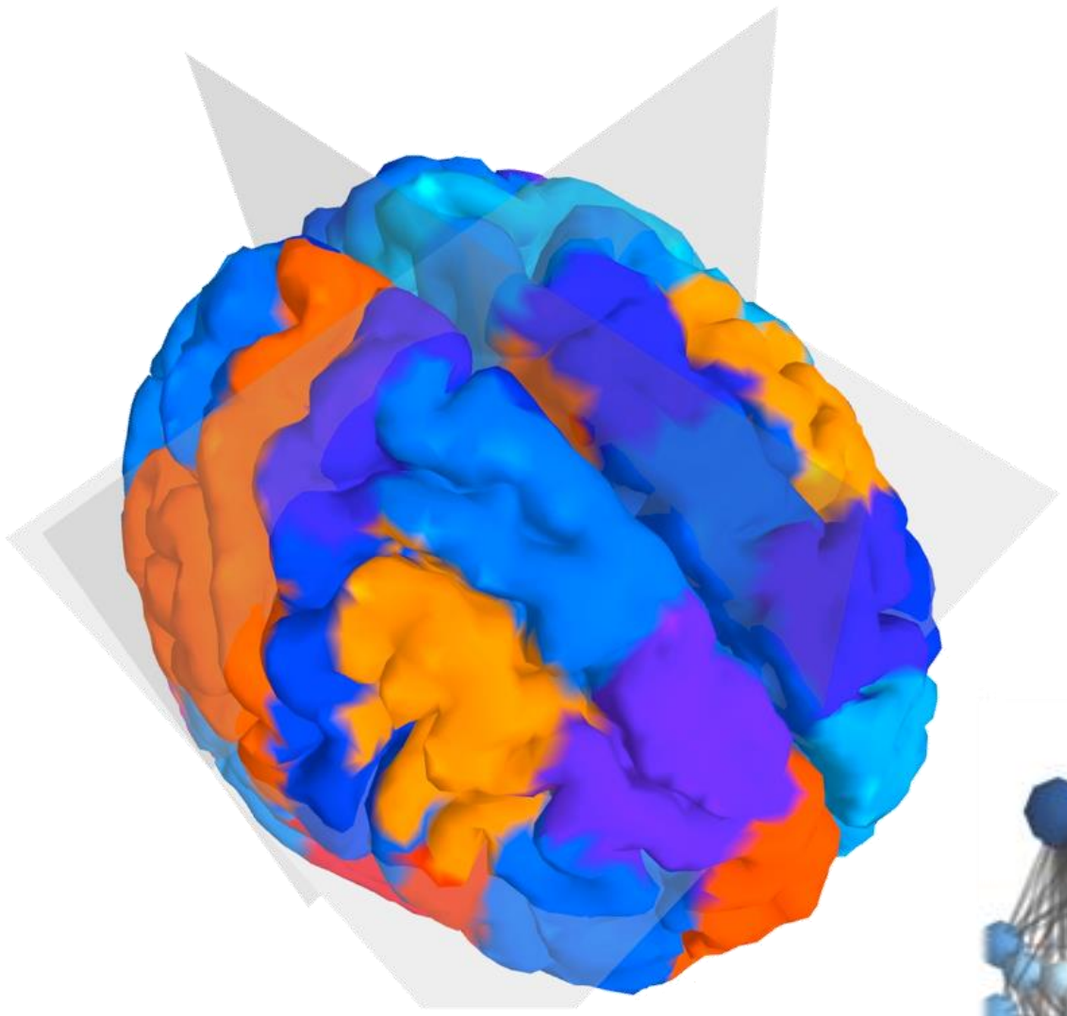
Connectivity from DTI.

Topography from MRI.

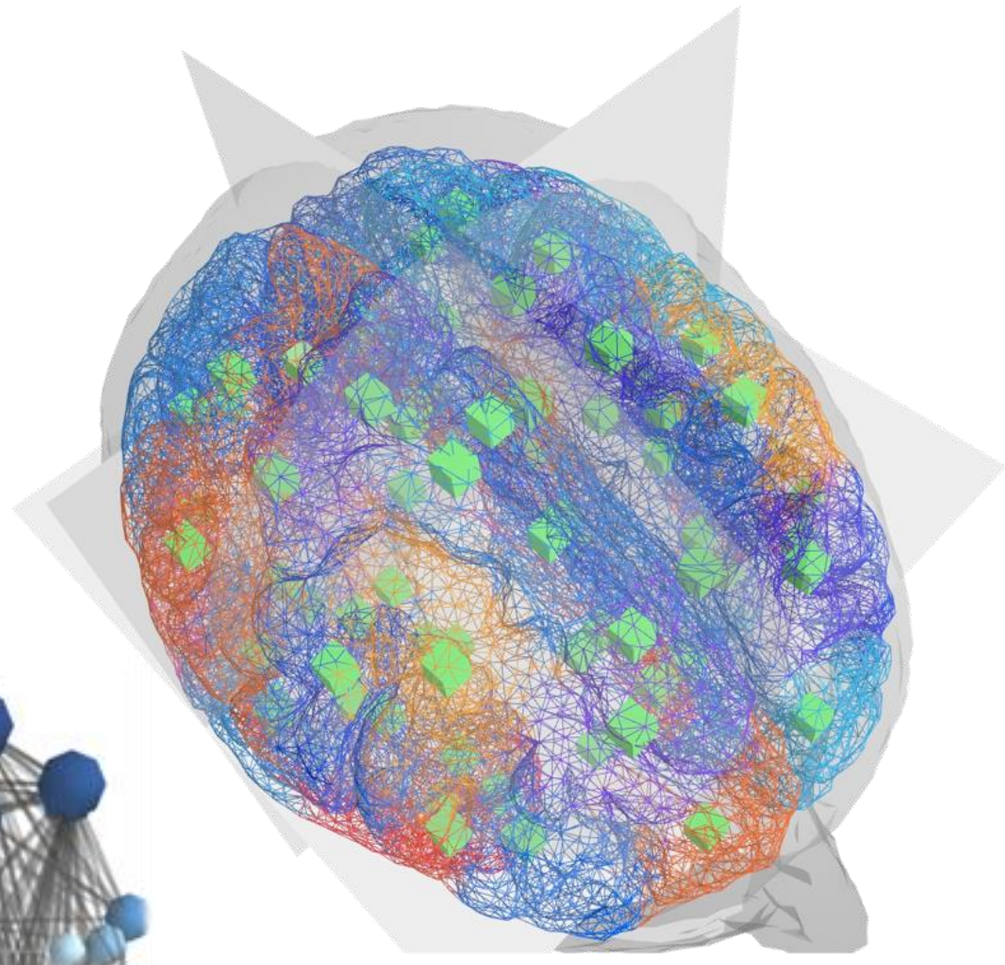
Jirsa et al. Neuroimage 2016; Proix et al. Brain 2017

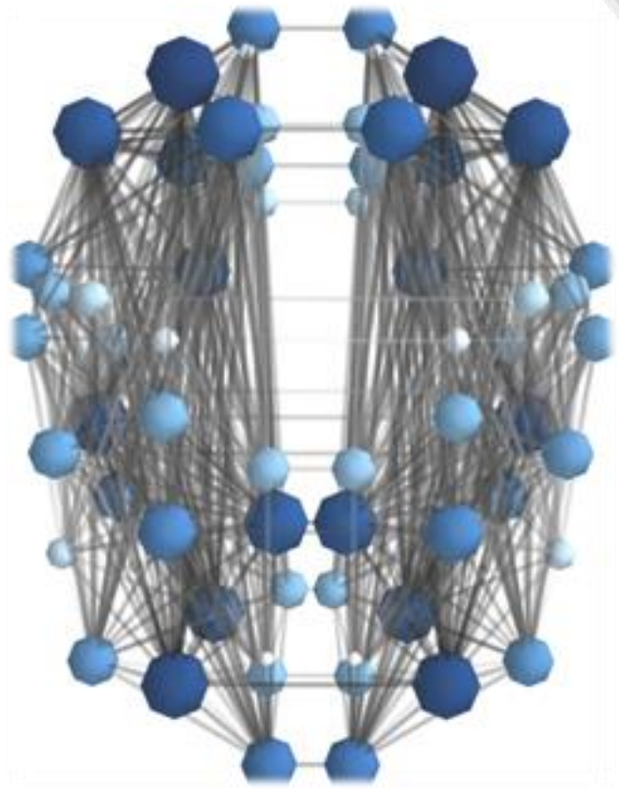
MNI brain geometry, and parcellation

region-based modeling (N=80-200)



surface-based modeling (N=5000-20000)





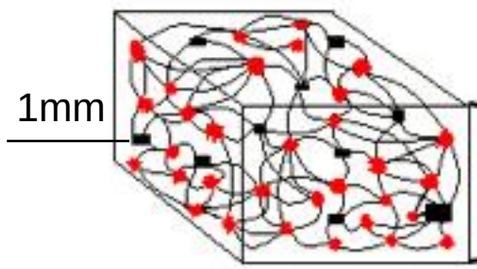
Building patient-specific large-scale brain networks

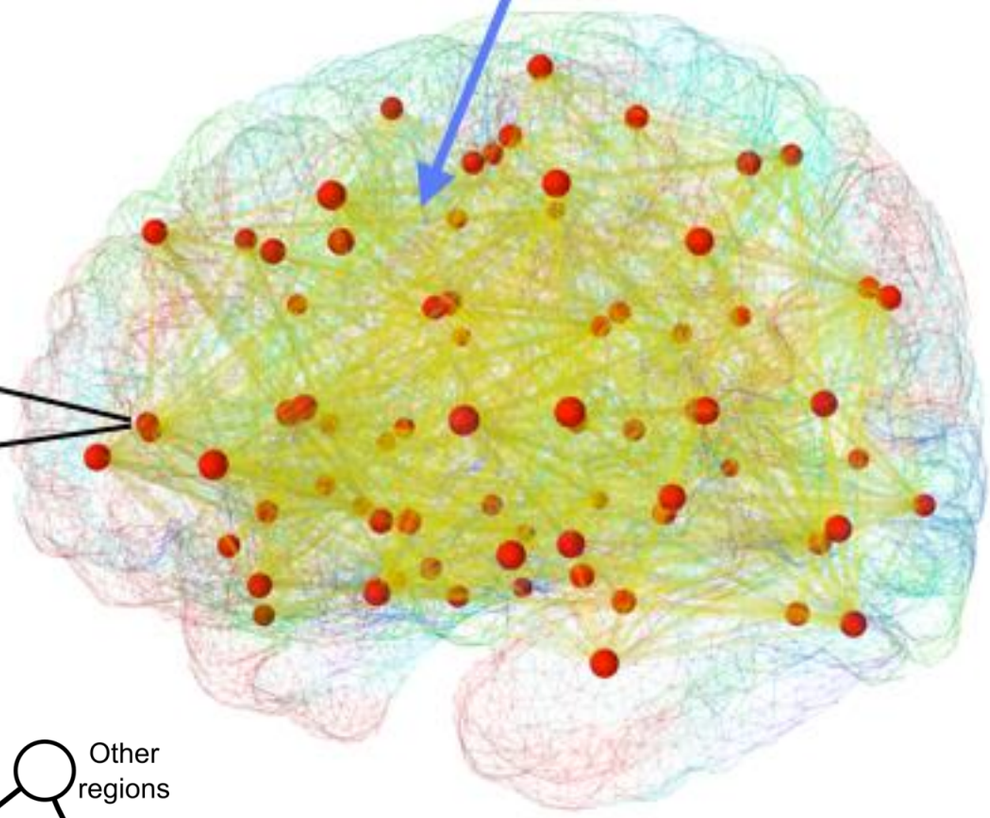
$$\psi(x,t) = N(\psi(x,t)) + \int_{local} g(x-x')S(\psi(x',t))dx' + \int_{global} G(x,x')S(\psi(x',t-\frac{|x-x'|}{v}))dx' + \text{noise}$$

Field potential

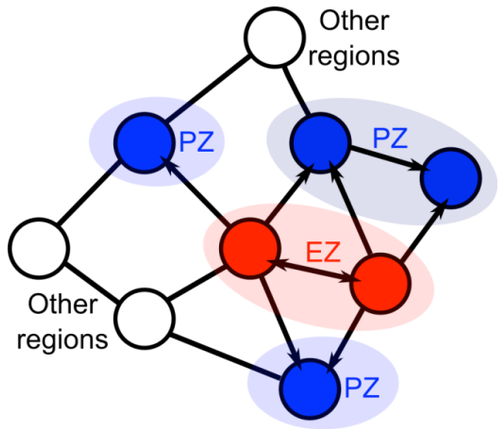
Local dynamics

Global dynamics





Challenge: identification of patient specific parameters



Jirsa et al IEEE 2002
Ghosh et al. PLoS CB 2008
Deco, Jirsa, McIntosh Nat Rev Neurosci 2011
Deco, Jirsa Journ Neurosci 2012
Deco, Jirsa, McIntosh TINS 2013
Ritter et al Brain Connectivity 2013

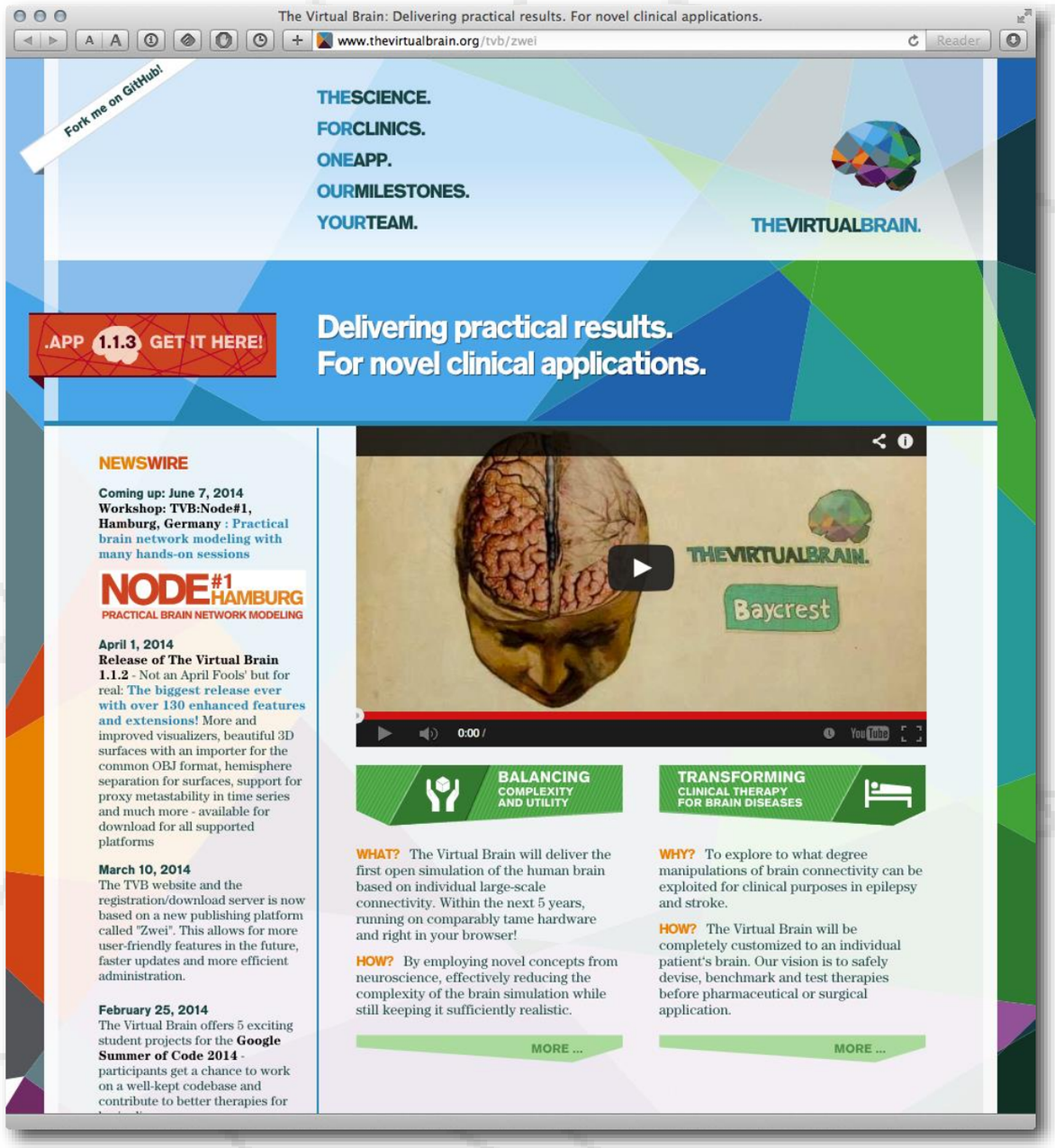
Sanz Leon et al Front NeuroInformatics 2013; Neuroimage 2015

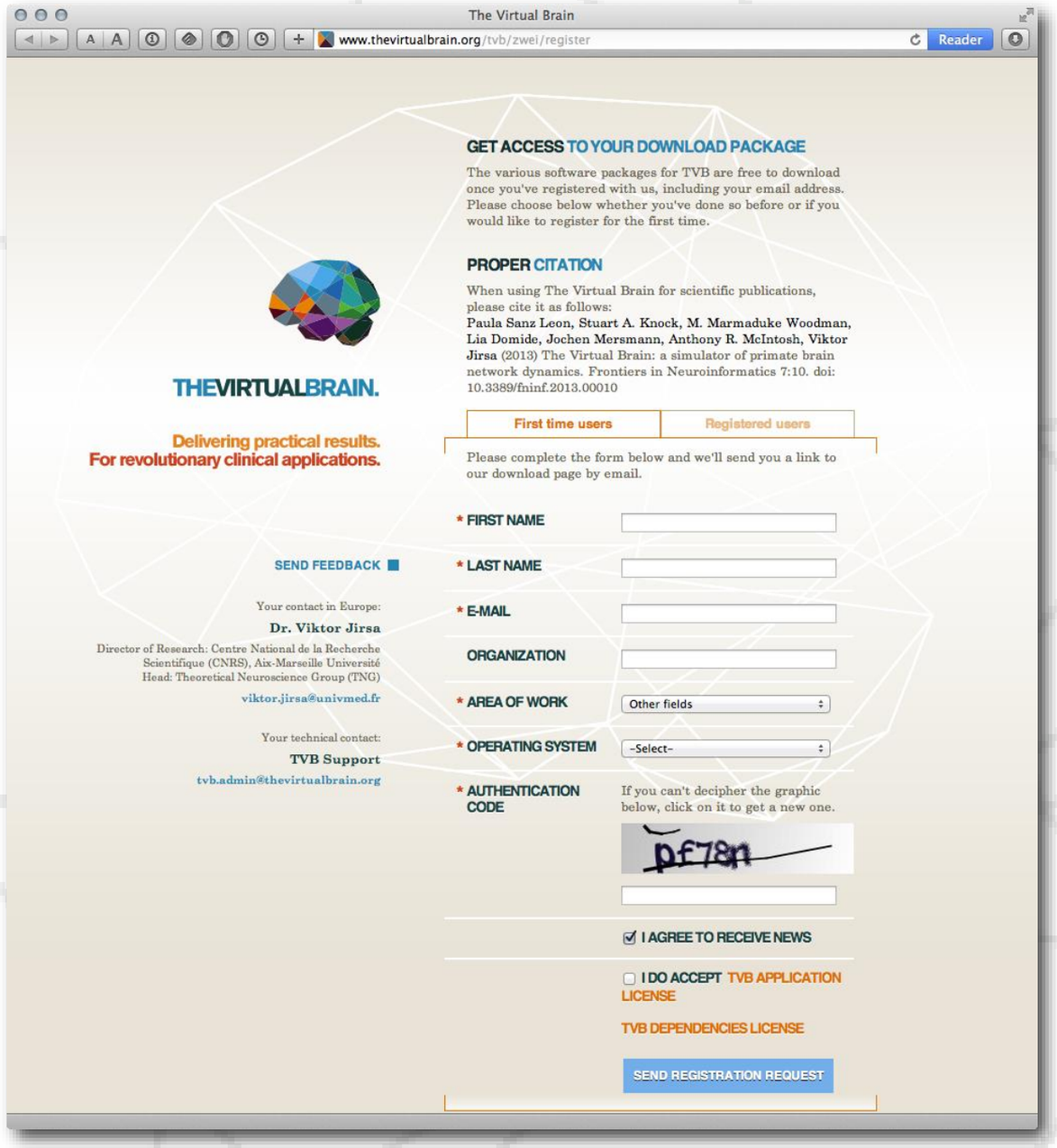
THEVIRTUALBRAIN.

TVB: The system architecture

Available under http://www.thevirtualbrain.org
or directly in the Collaboratory Human Brain Project

Download:
Windows, Mac, Linux

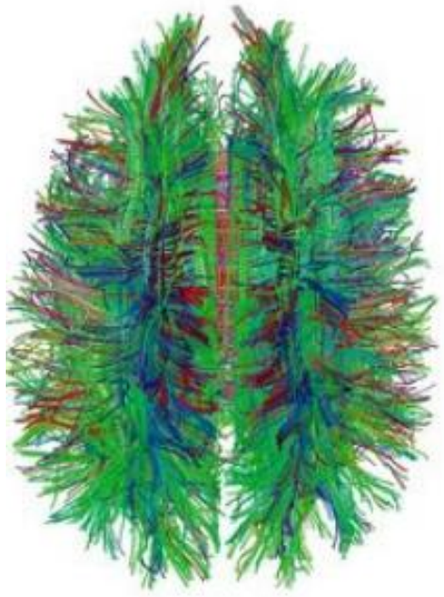


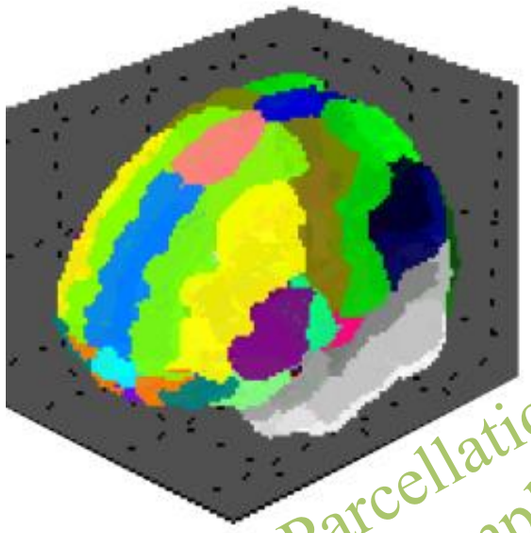


16309 registered users in October 2018
http://www.thevirtualbrain.org

The Virtual Brain (TVB) platform release in 2012

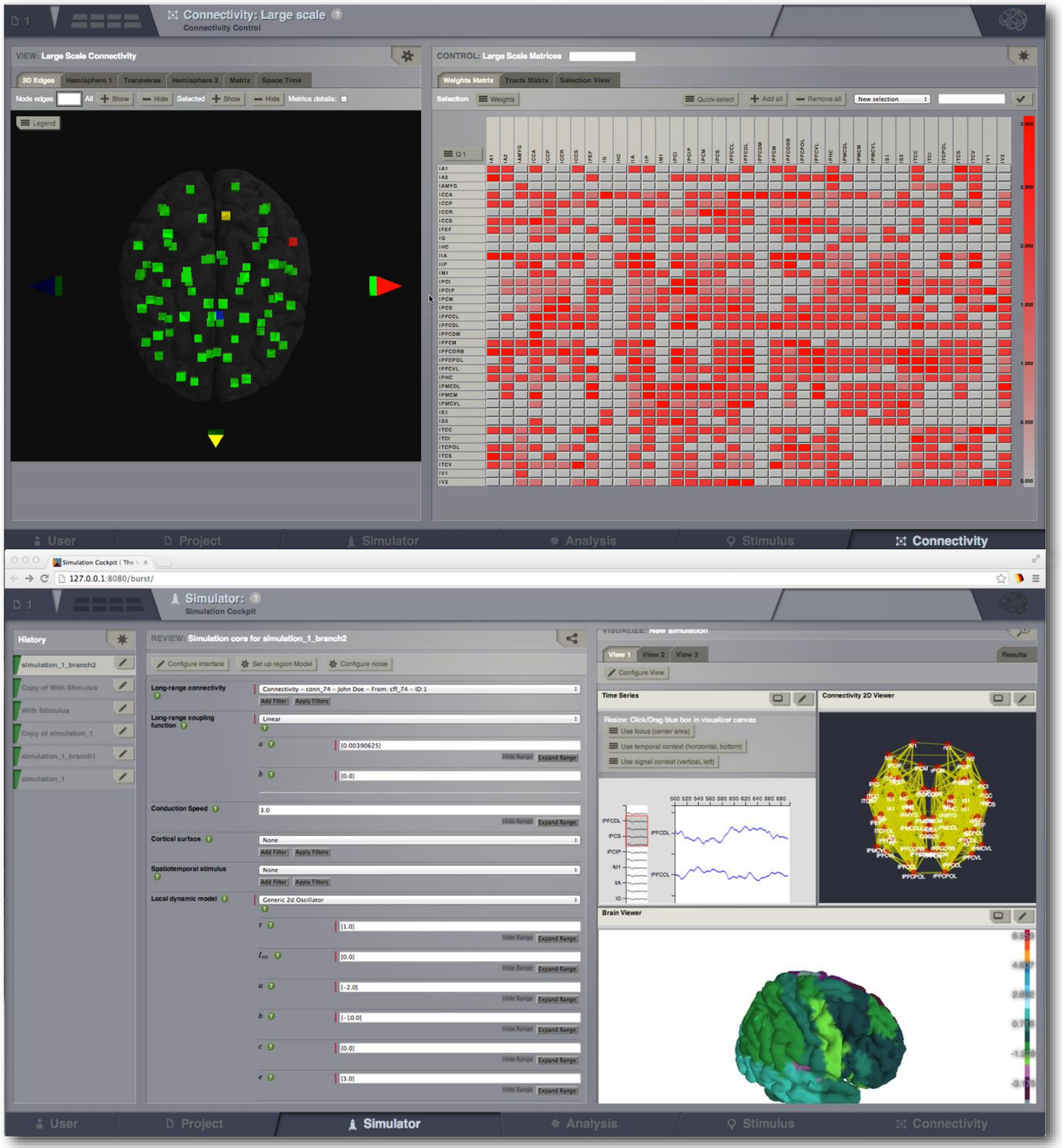
DTI/ Tractography





Parcellation Template

Jirsa et al IEEE 2002
Ghosh et al. PLoS CB 2008
Deco, Jirsa, McIntosh Nat Rev Neurosci 2011
Deco, Jirsa Journ Neurosci 2012
Deco, Jirsa, McIntosh TINS 2013
Ritter et al Brain Connectivity 2013



Sanz Leon et al Front NeuroInformatics 2013; Neuroimage 2015

THEVIRTUALBRAIN.

The Virtual Brain (TVB) platform release in 2012

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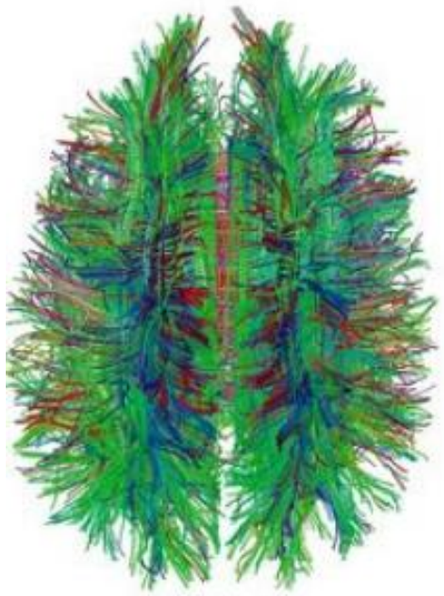
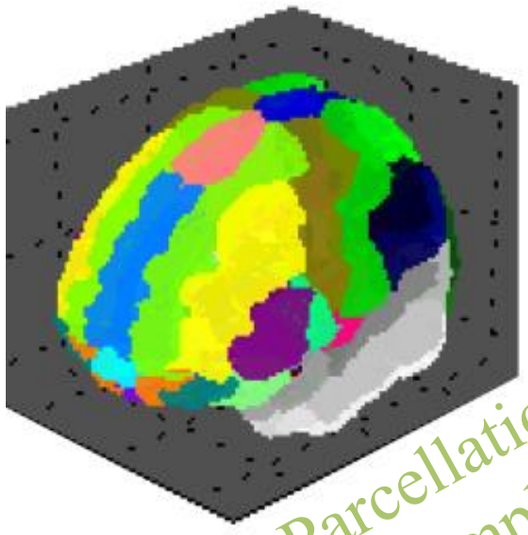
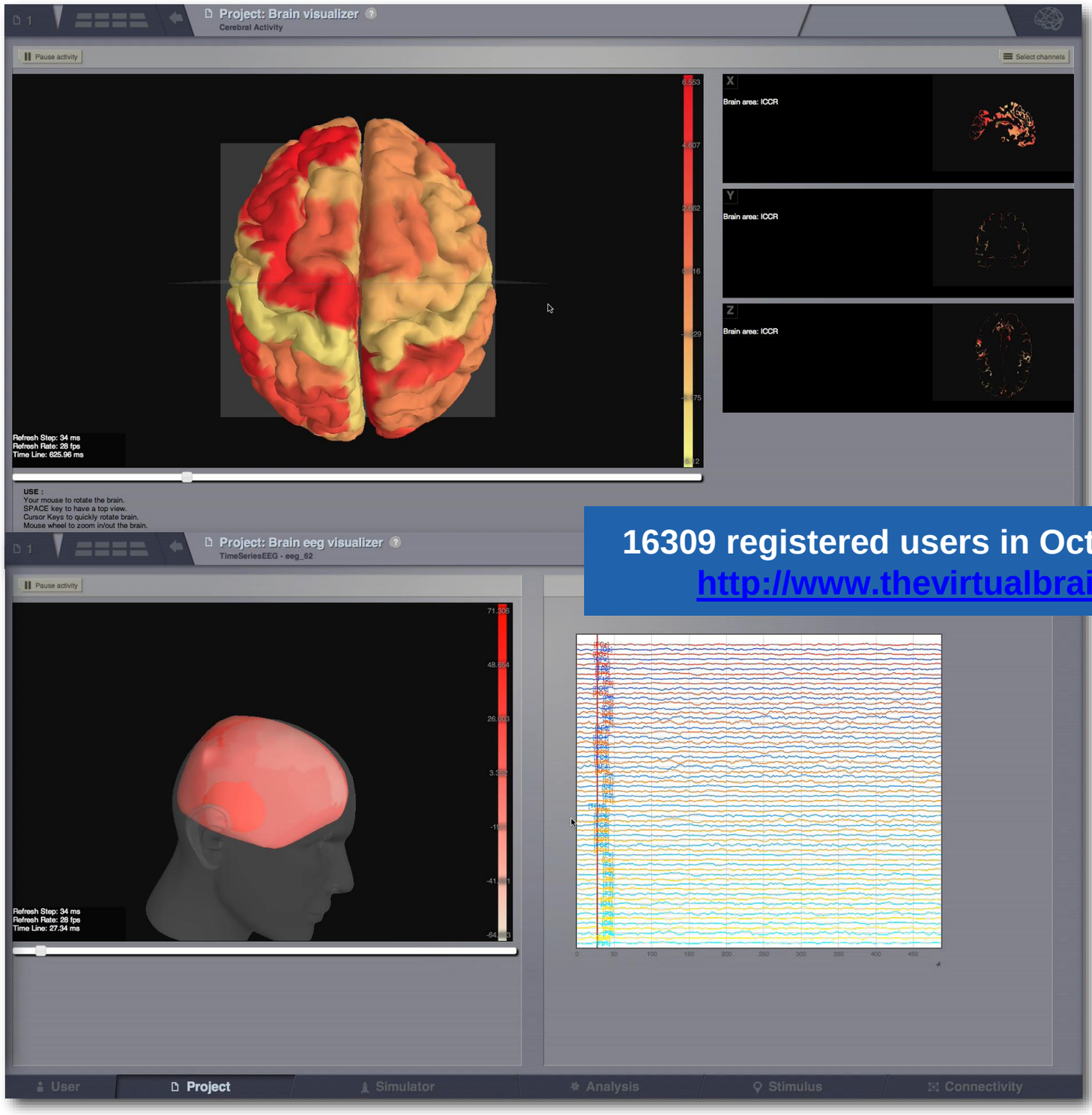




Parcellation Template



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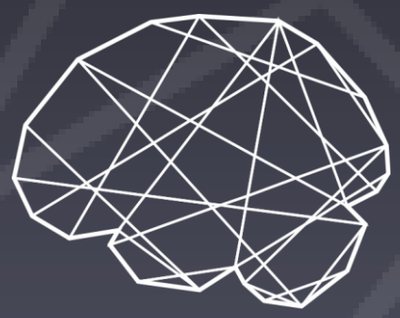
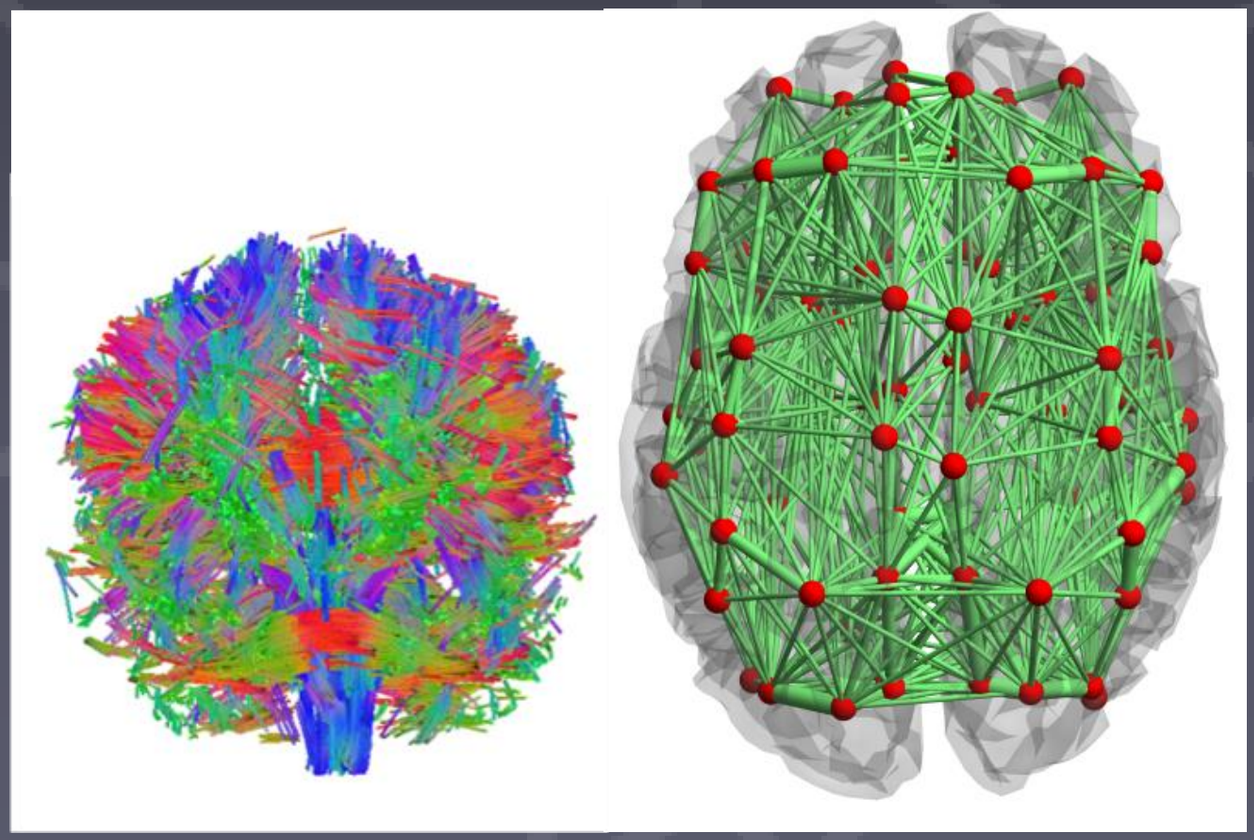
THEVIRTUALBRAIN.



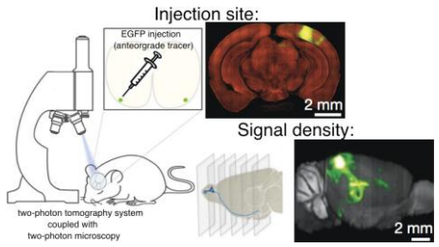
The Virtual Epileptic Patient

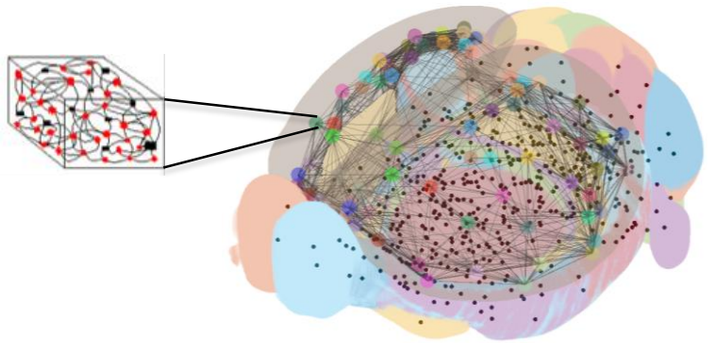
build the network from patient brains



Animal validation

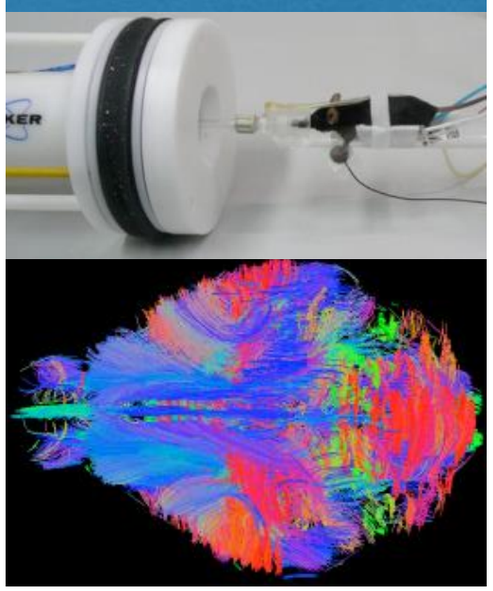
Neural Tracer

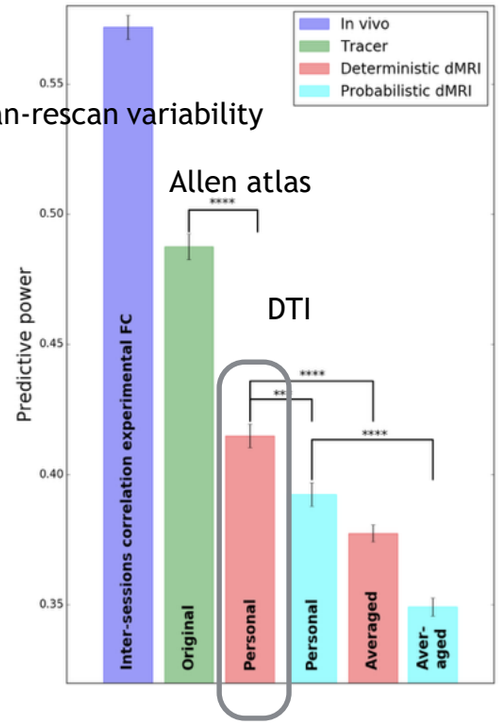




ALLEN INSTITUTE for BRAIN SCIENCE

Tractography

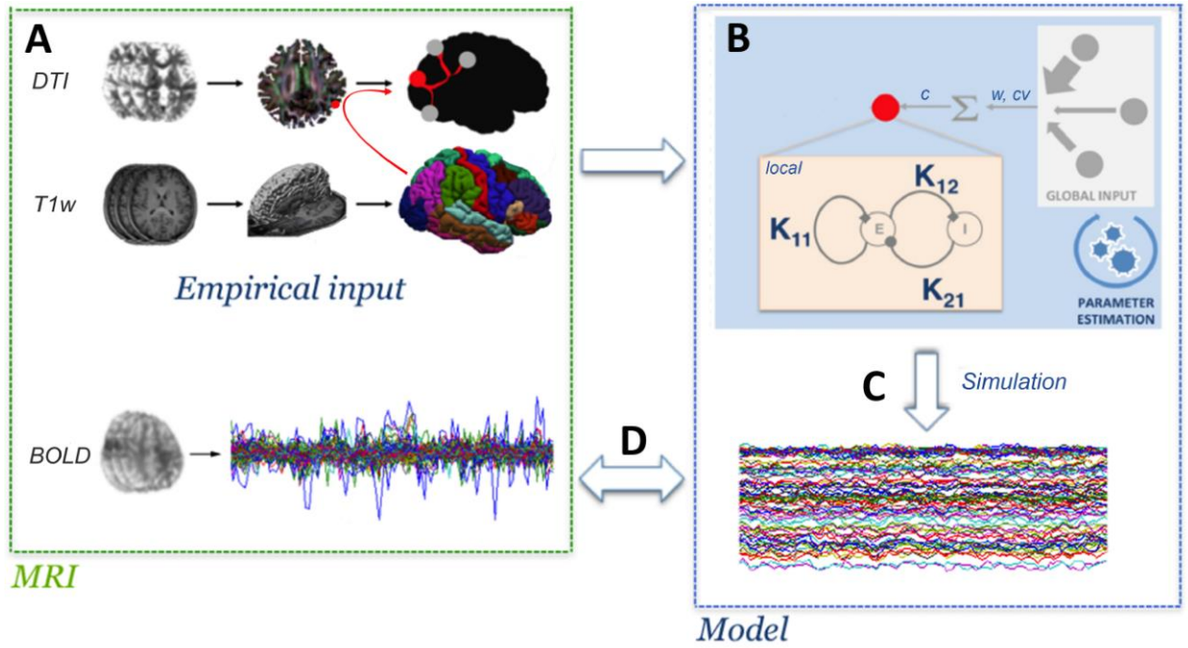


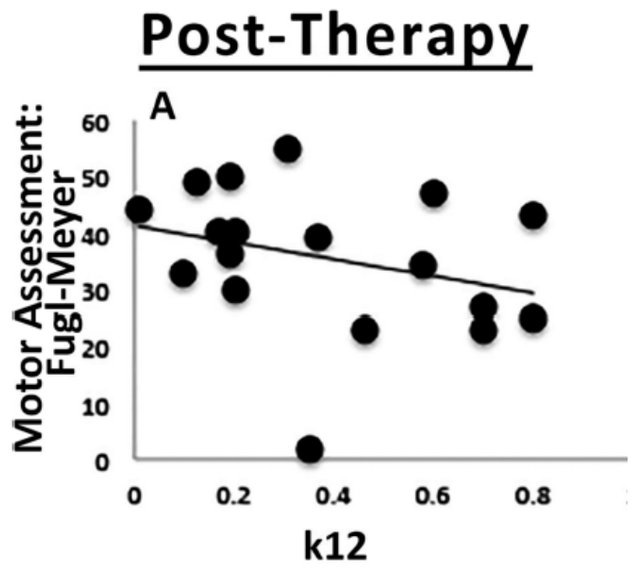


Mouse-specific brain models predict better

Melozzi et al eNeuro 2017; (in preparation)

The Virtual Stroke Patient



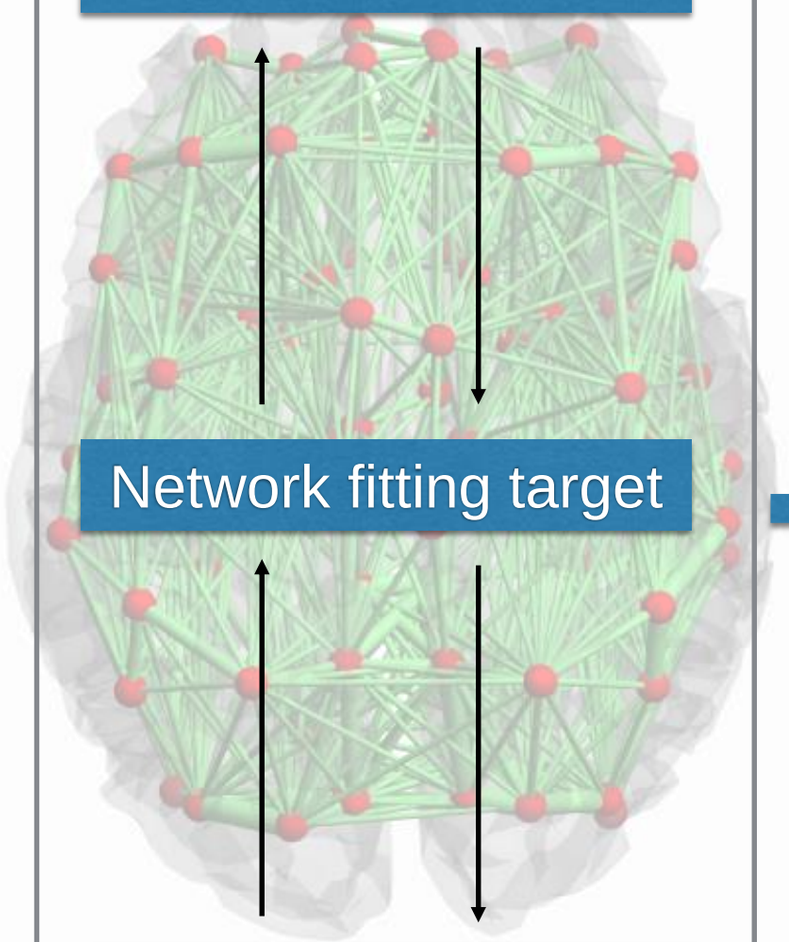


p=0.035 (post therapy); p=0.005 one year later)

Falcon et al. 2016 eNeuro

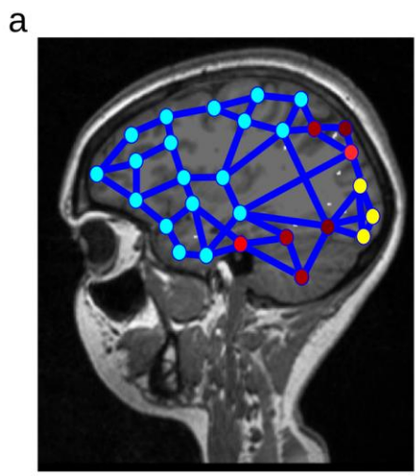
Conditions to satisfy for successful clinical translation

Network data feature

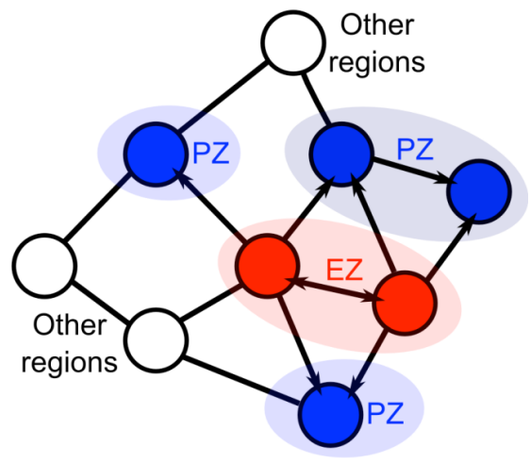


Network fitting target

Network intervention



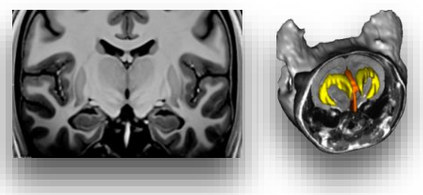
Seizure propagation



Epileptogenic Zone

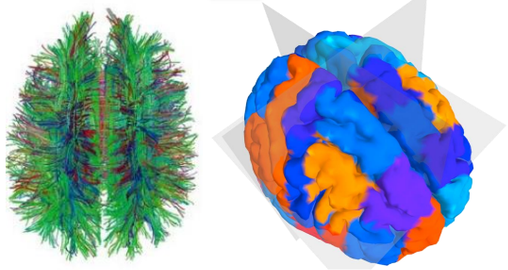
Resection of Epileptogenic Zone

The Virtual Patient Modeling process



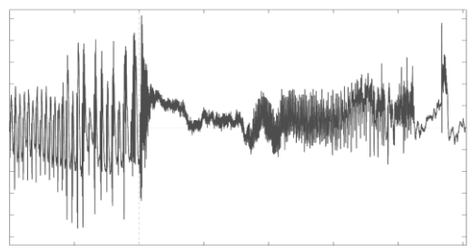
Noninvasive brain imaging

Standard pipelines:
FSL, MrTrix, FreeSurfer,…



Construction of brain avatar

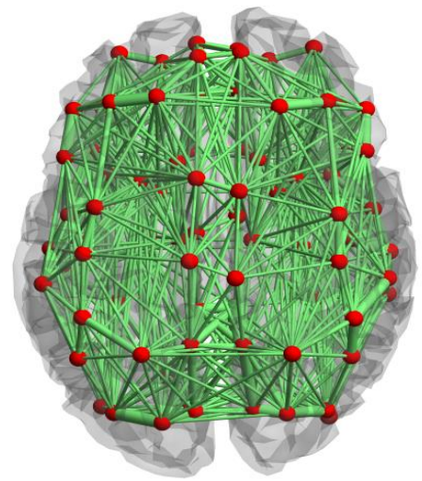
Nonlinear dynamic model
Not physiologically detailed/realistic
Dynamically detailed



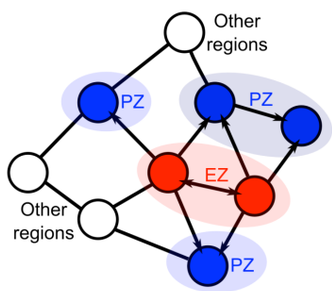
Functional region model selection

Jirsa et al Brain (2014)
Jirsa et al. Neuroimage (2016)
Proix et al Brain (2017)

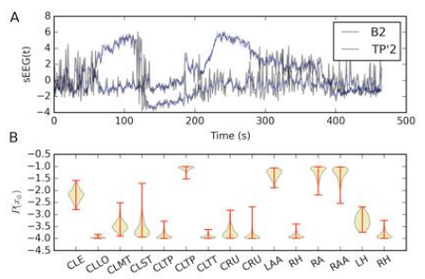
Functional Personalized Brain Network model



Refine network pathology

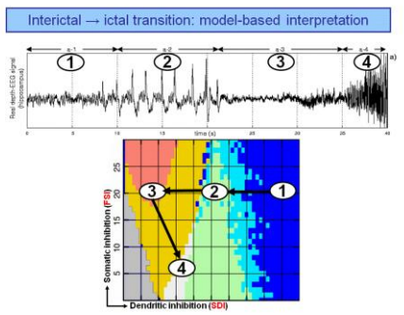


Finger printing of patient



Data fitting

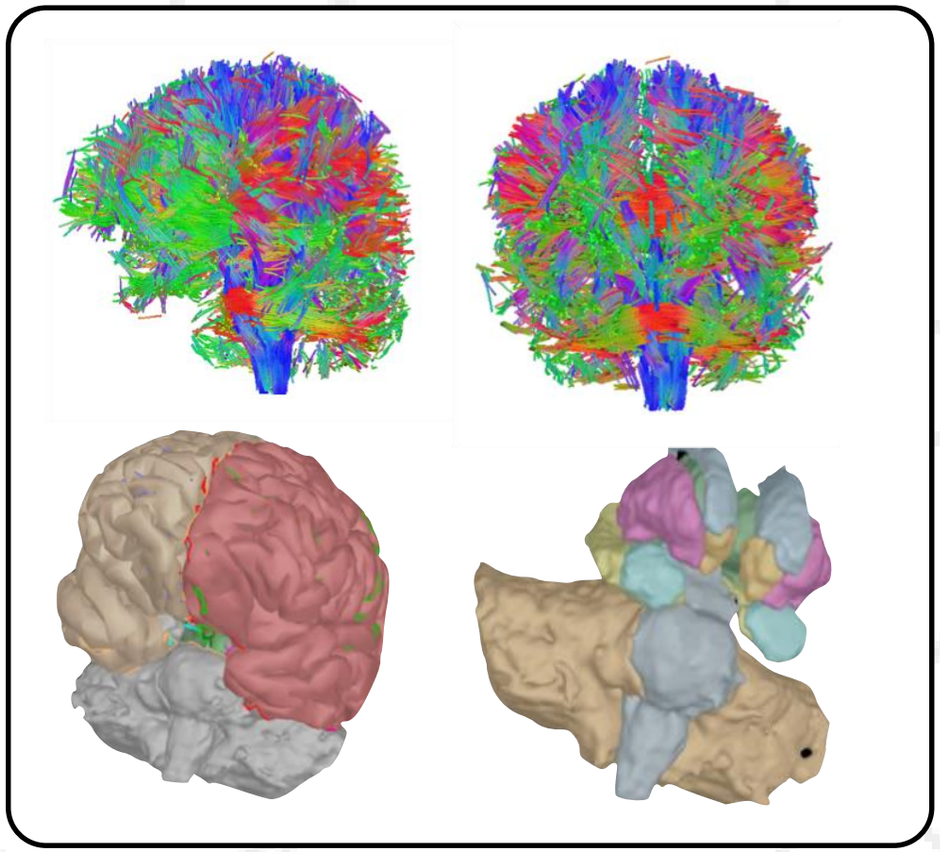
Develop patient charts

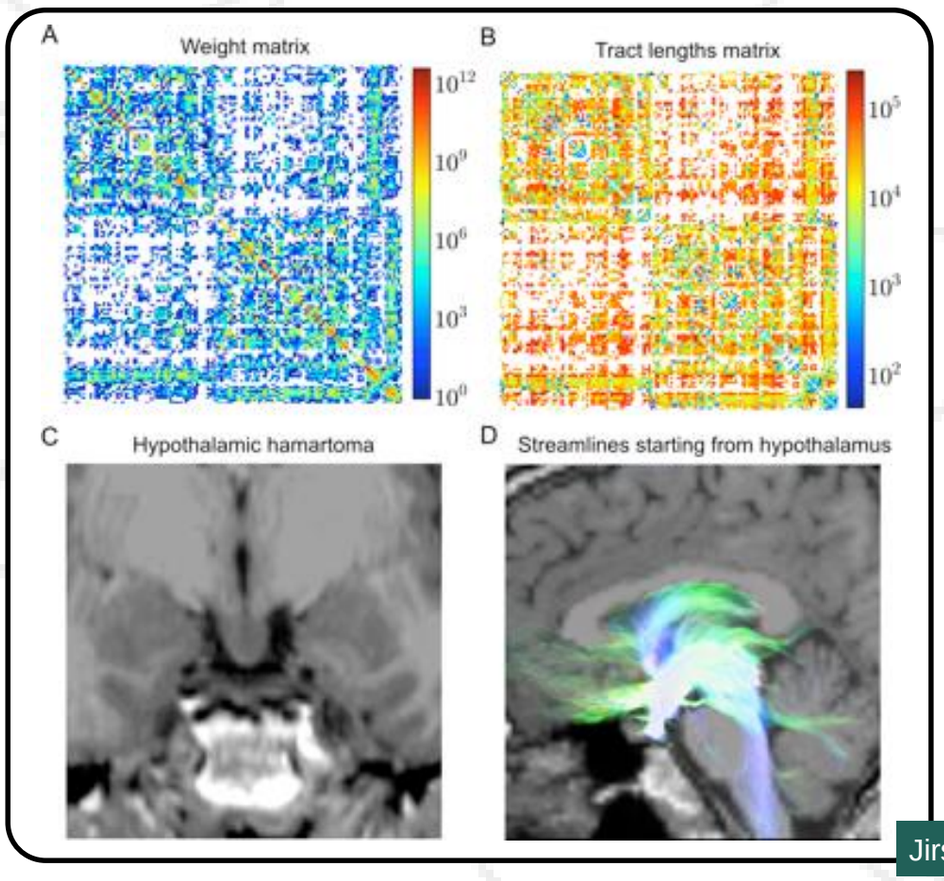


Parameter space exploration

Patient specific interventions

The virtual epileptic patient: refine network pathology



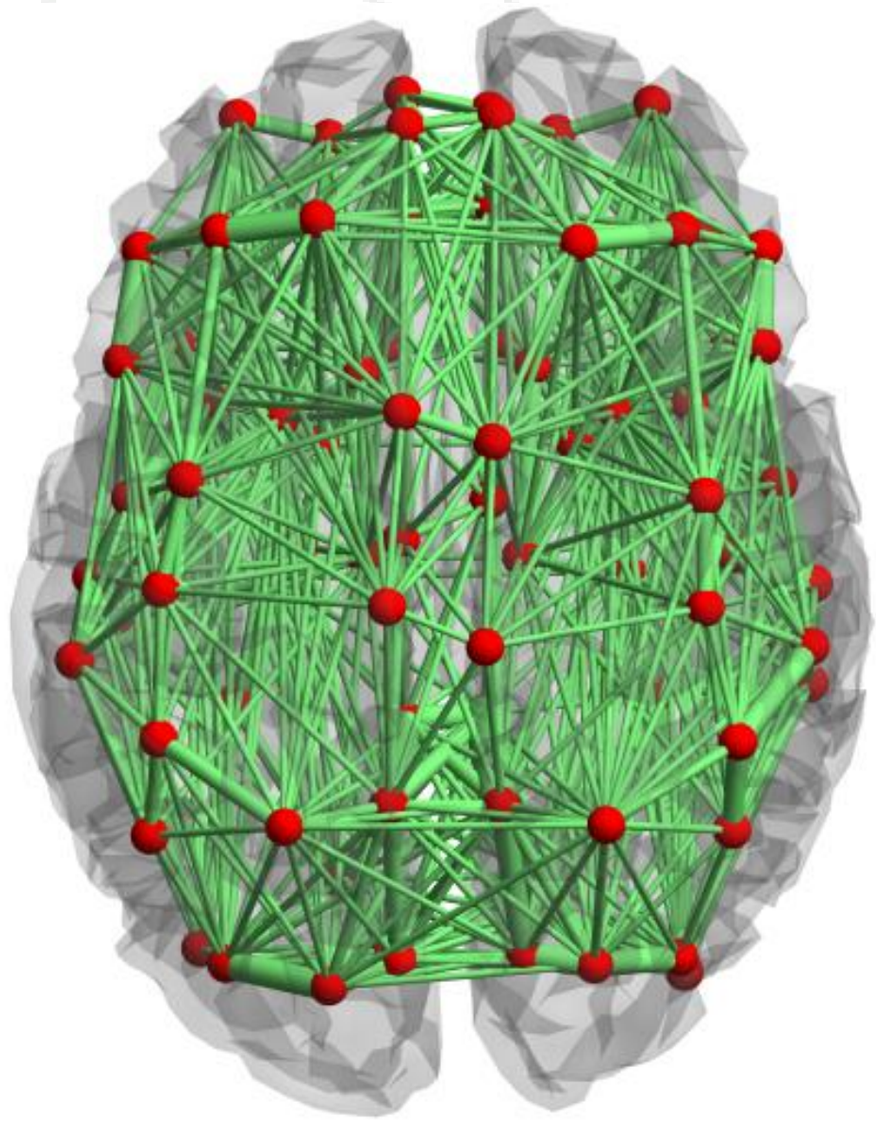


Connectivity from DTI.

Topography from MRI.

MRI positive in hypothalamus

Structural reconstruction of brain model



Jirsa et al. Neuroimage 2016; Proix et al. Brain 2017

Simulation: seizure propagation

Key entries into the virtualization

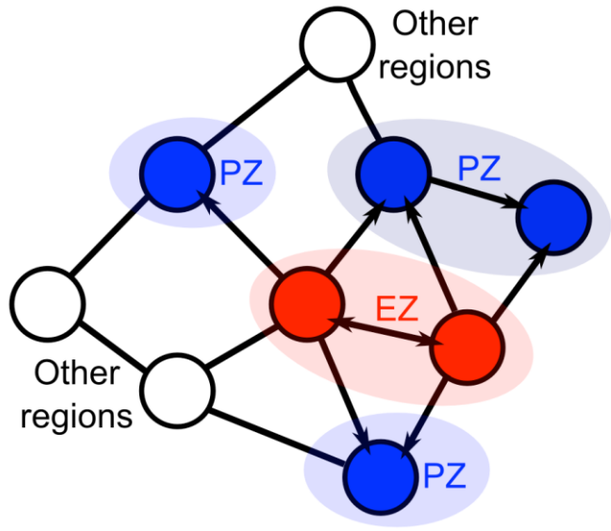
Topology: connectivity from DTI

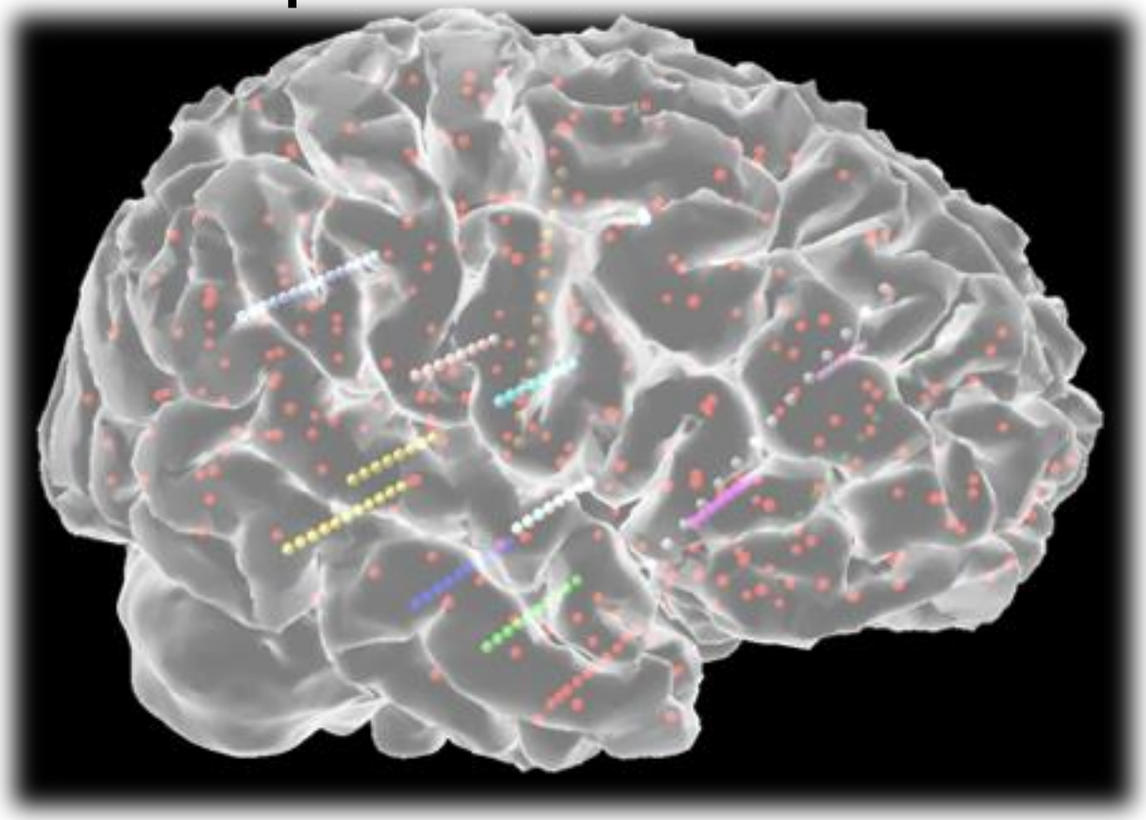
Topography: surface reconstruction from MRI

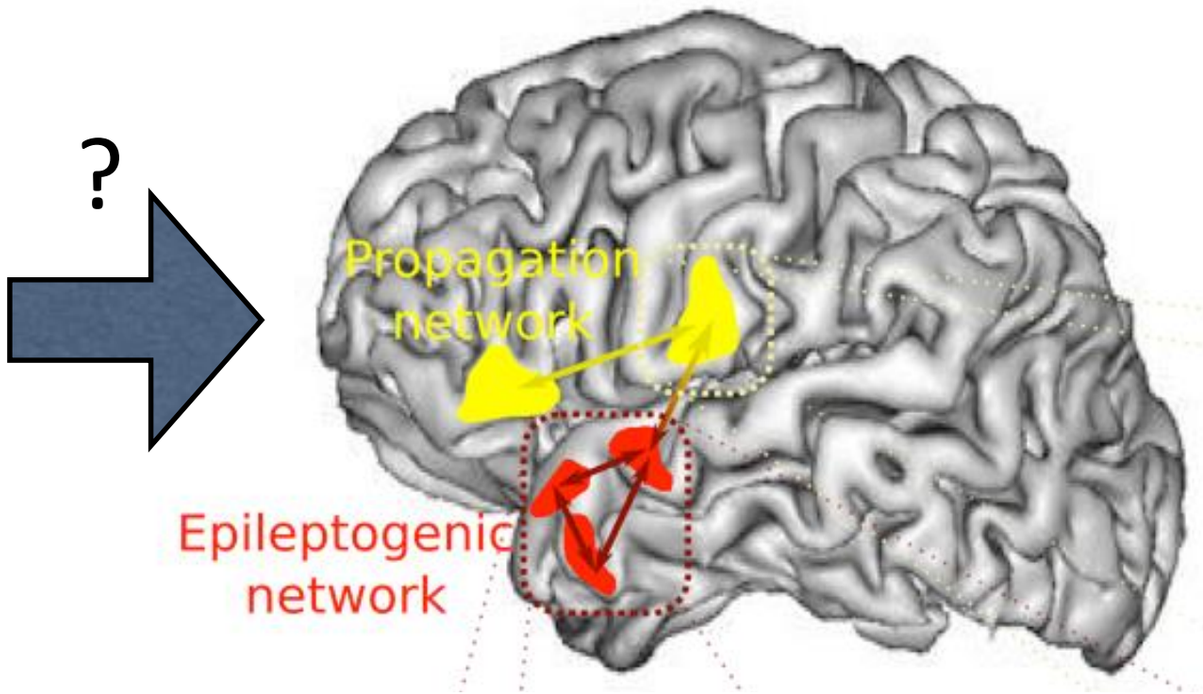
Dynamics: Network node model implementation

Heat map: Hypothesis on Epileptogenic zone

Lesion map: anomalies from MRI

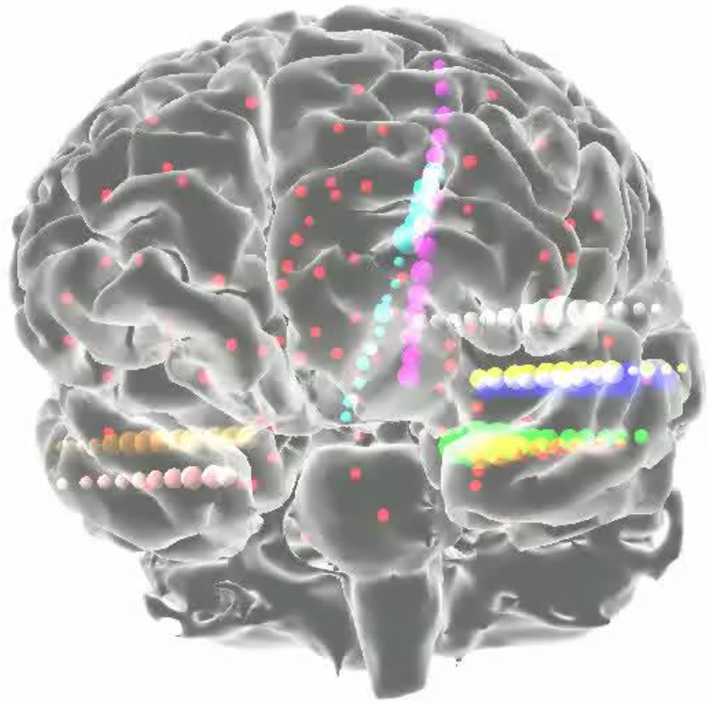


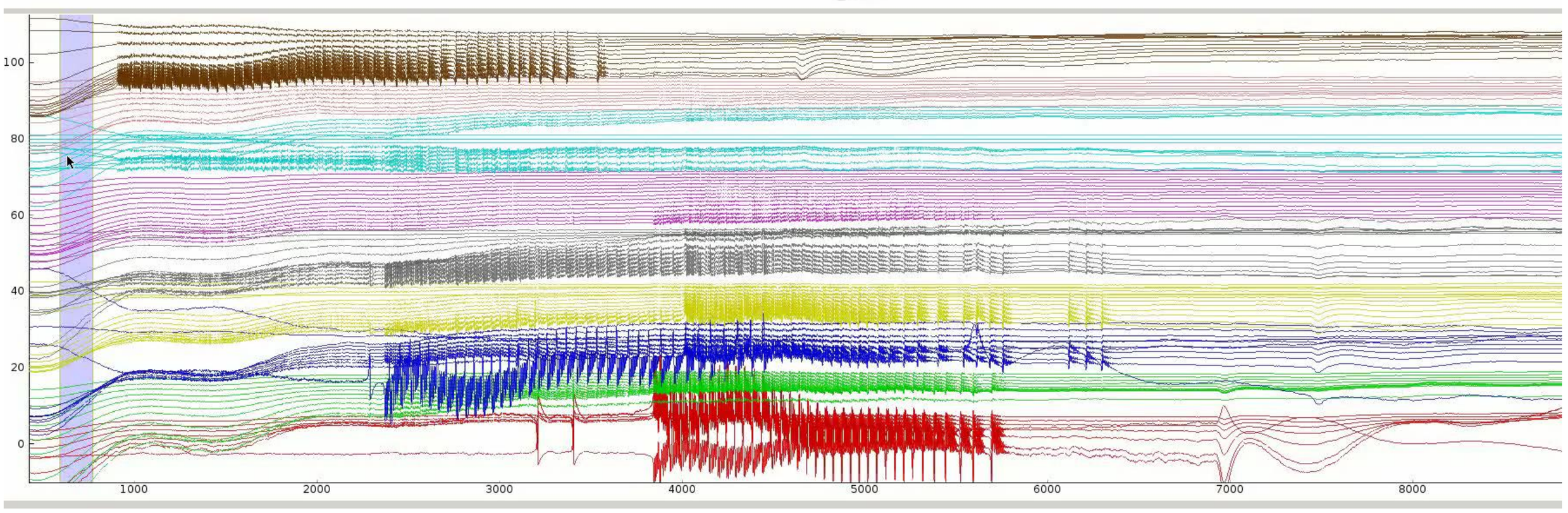




Jirsa et al. Neuroimage 2016; Proix et al. Brain 2017

Simulation: Complex seizure – see it in action





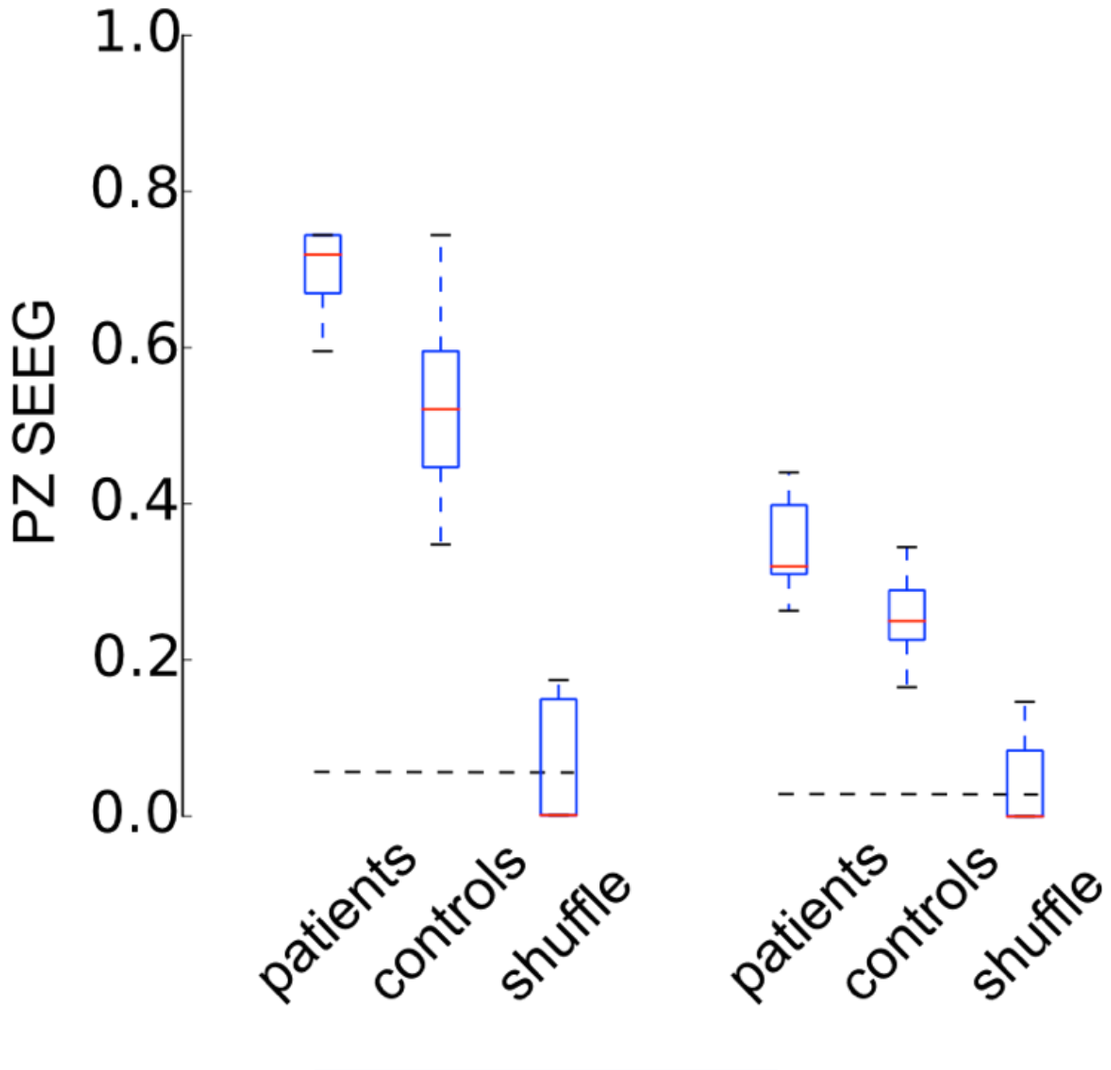
Jirsa et al. Neuroimage 2016

The virtual epileptic patient: validation for 2 cohorts

Scoring of predicted propagation zone for various connectomes

Binary Score

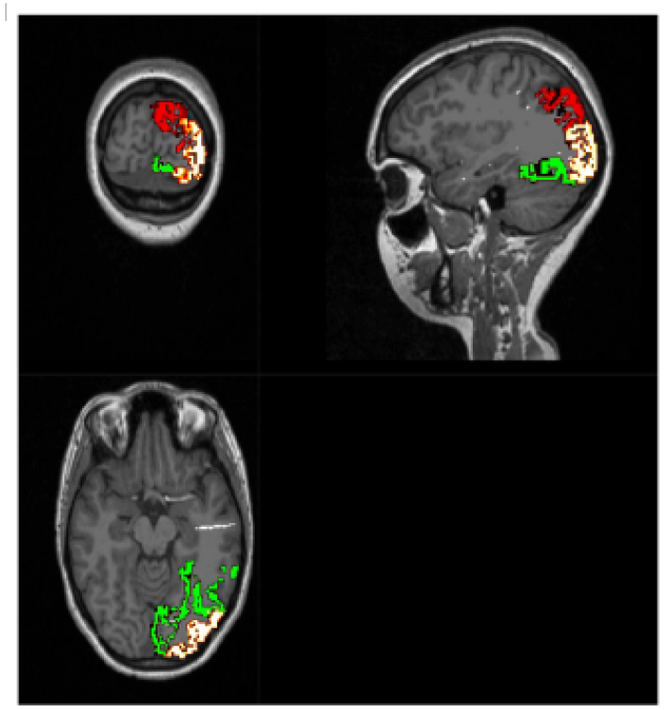
Continuous Score



Connectomes

Engel score classifying postoperative outcomes for epilepsy surgery

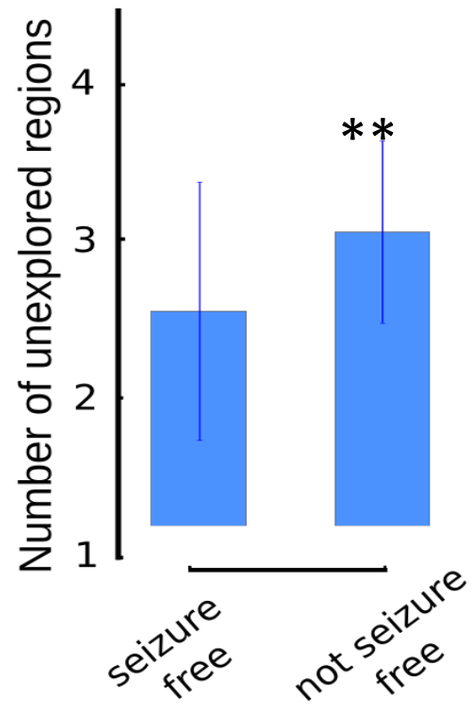
EZ prediction



Epileptogenic map

Green: discrepancy with TVB
Yellow: Epileptogenic Zone
Red: Propagation zone

Engel score



**p<0.05
Mann-Whitney U-test

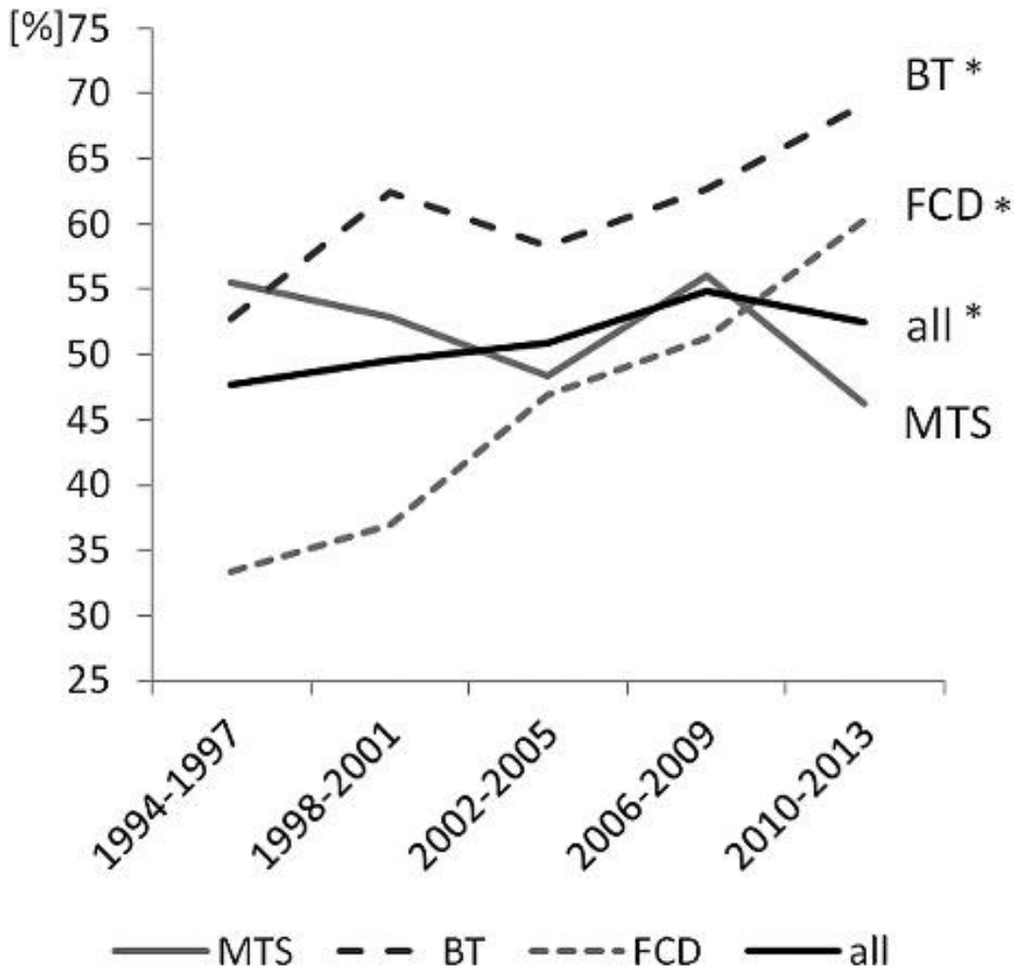
Proix et al. Brain 2017

The virtual epileptic patient: validation for 2 cohorts

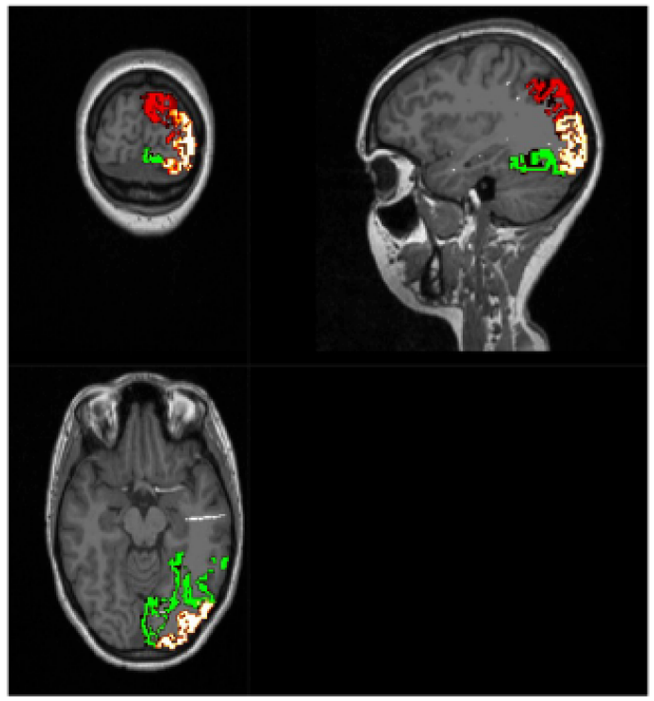
Postoperative surgery outcome over past 30 years

Engel score classifying postoperative outcomes for epilepsy surgery

Evolution of surgery success



EZ prediction



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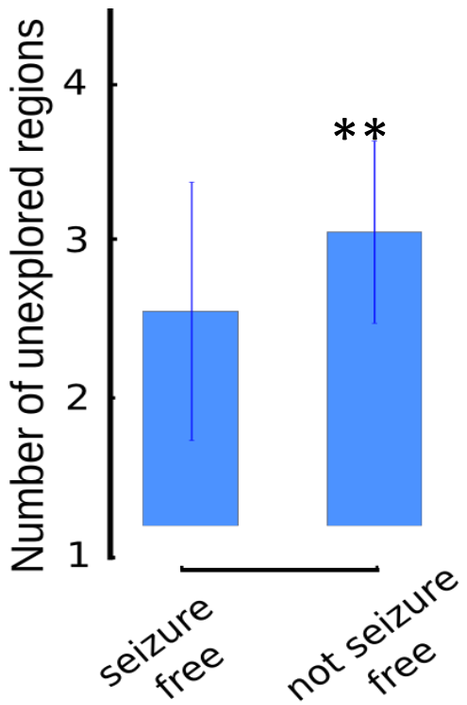


**p<0.05
Mann-Whitney U-test

Proix et al. Brain 2017

The virtual epileptic patient: validation for 2 cohorts

Engel score classifying postoperative outcomes for epilepsy surgery

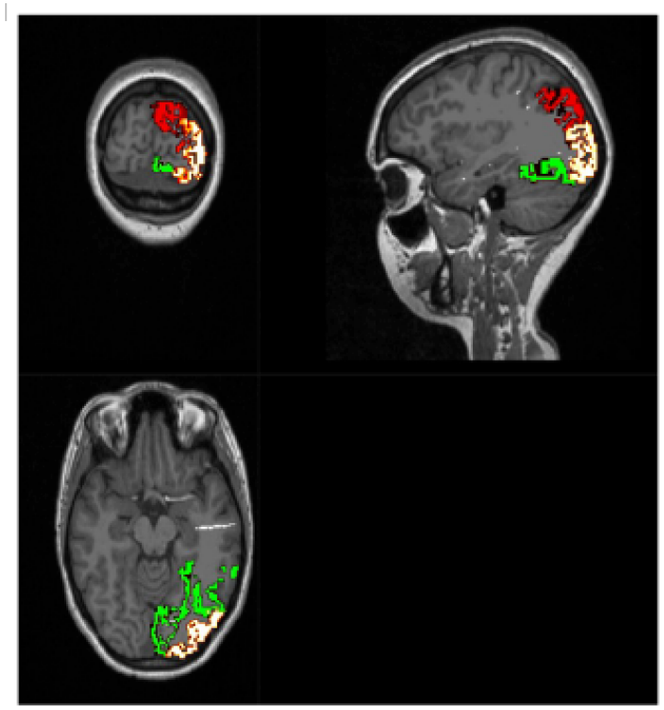
First clinical trial:

randomized parallel-group study
clinical trial (F. Bartolomei)

Objective:

evaluate the role of personalized
Virtual Epileptic Patient brain models
for surgery planning and outcome
11 French clinical centers
400 prospective patients
2018 – 2022

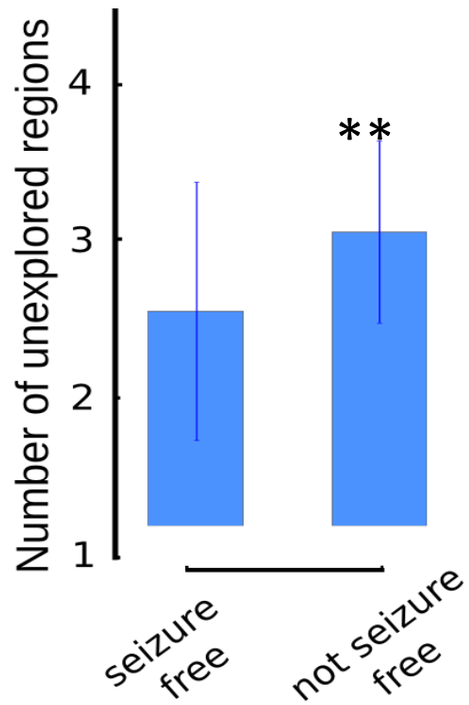
EZ prediction



Epileptogenic map

Green: discrepancy with TVB
Yellow: Epileptogenic Zone
Red: Propagation zone

Engel score

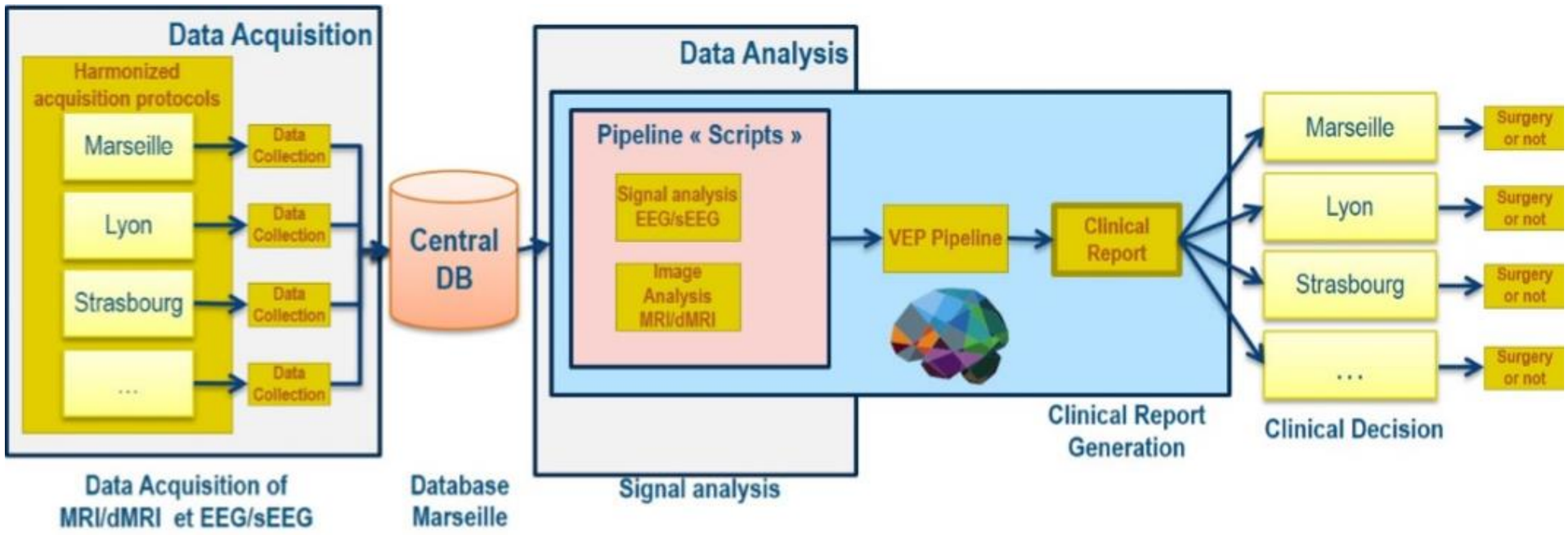


**p<0.05
Mann-Whitney U-test

epinov
UN PROJET RHU

Proix et al. Brain 2017

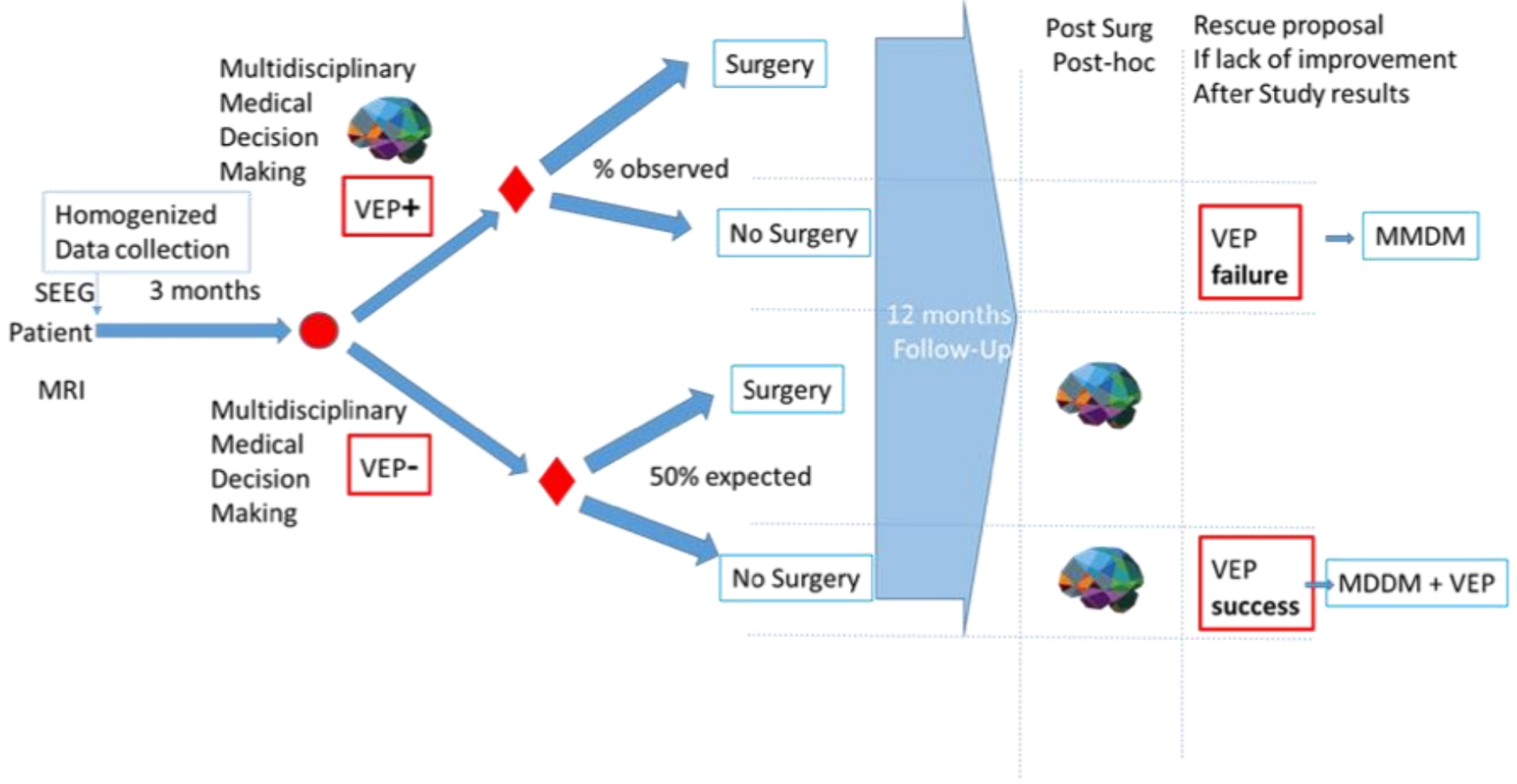
Clinical trial and TRANSLATION : 400 prospective patients undergoing epilepsy surgery (2018-2022)



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

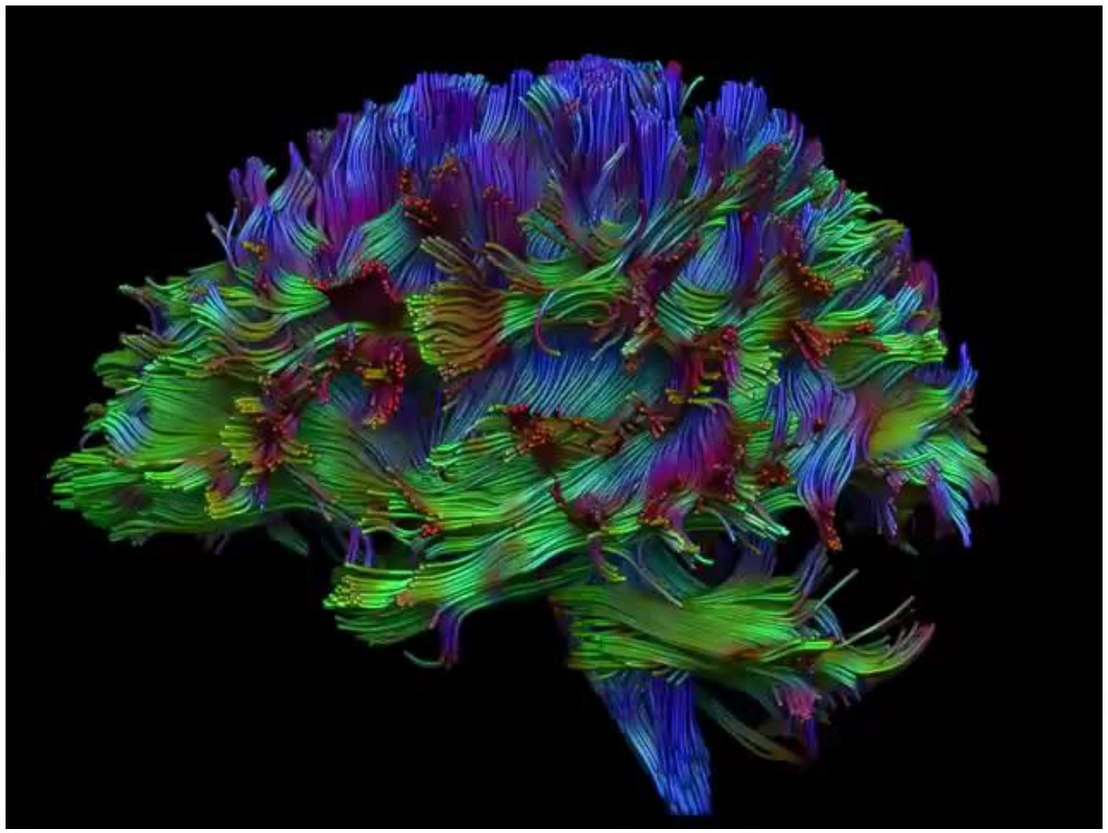
Objective:
evaluate the role of personalized **Virtual Epileptic Patient brain models** for surgery planning and outcome

11 French clinical centers
400 prospective patients during 2018 – 2022



The Virtual Patient

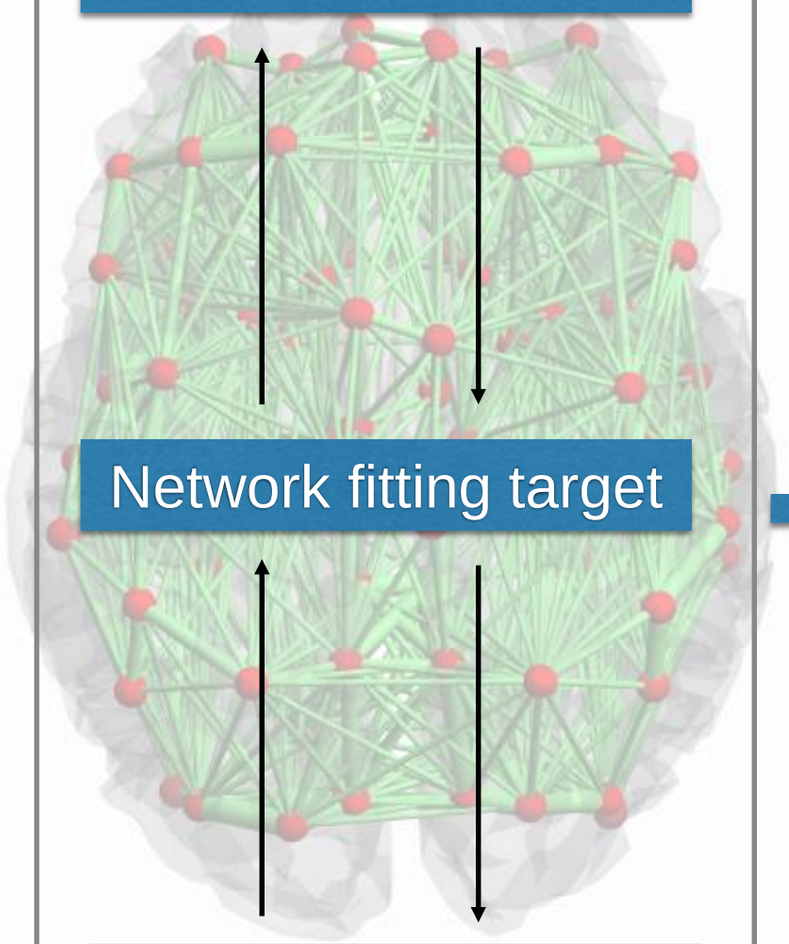
build personalized
neurodegenerative networks
from patient brains



Translation of Virtual Brain Network Modeling

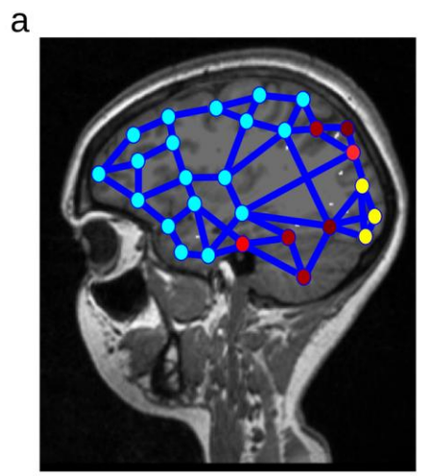
Conditions to satisfy for successful clinical translation

Network data feature

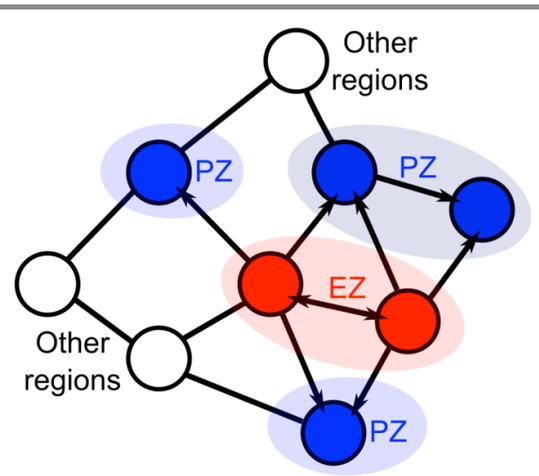


Network fitting target

Network intervention



Seizure propagation

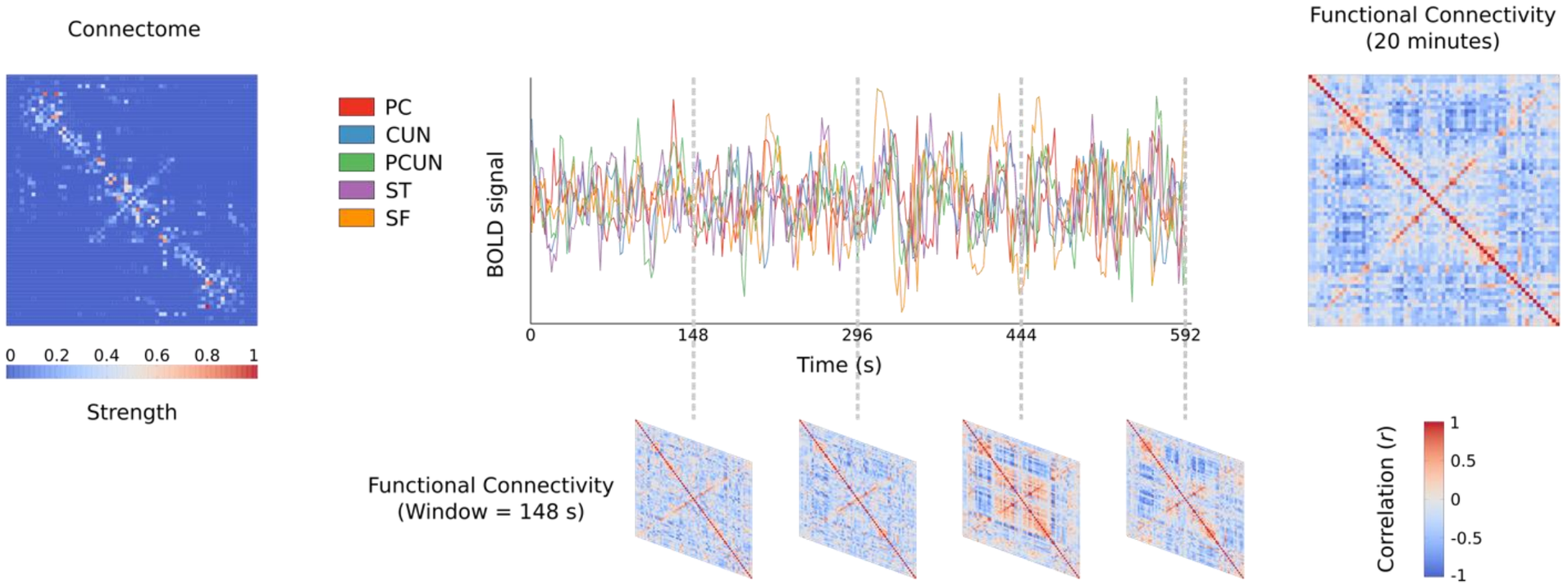


Epileptogenic Zone

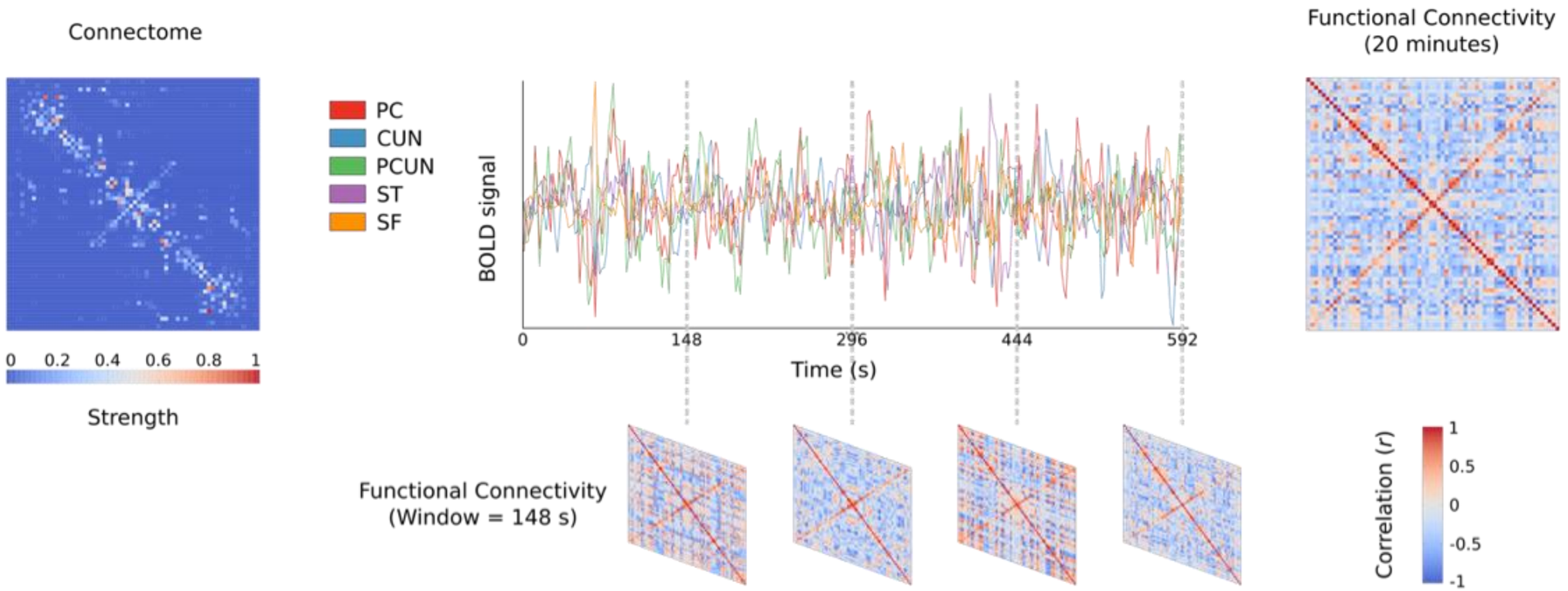
Resection of Epileptogenic Zone

Non-stationarity in empirical data

Subject 1

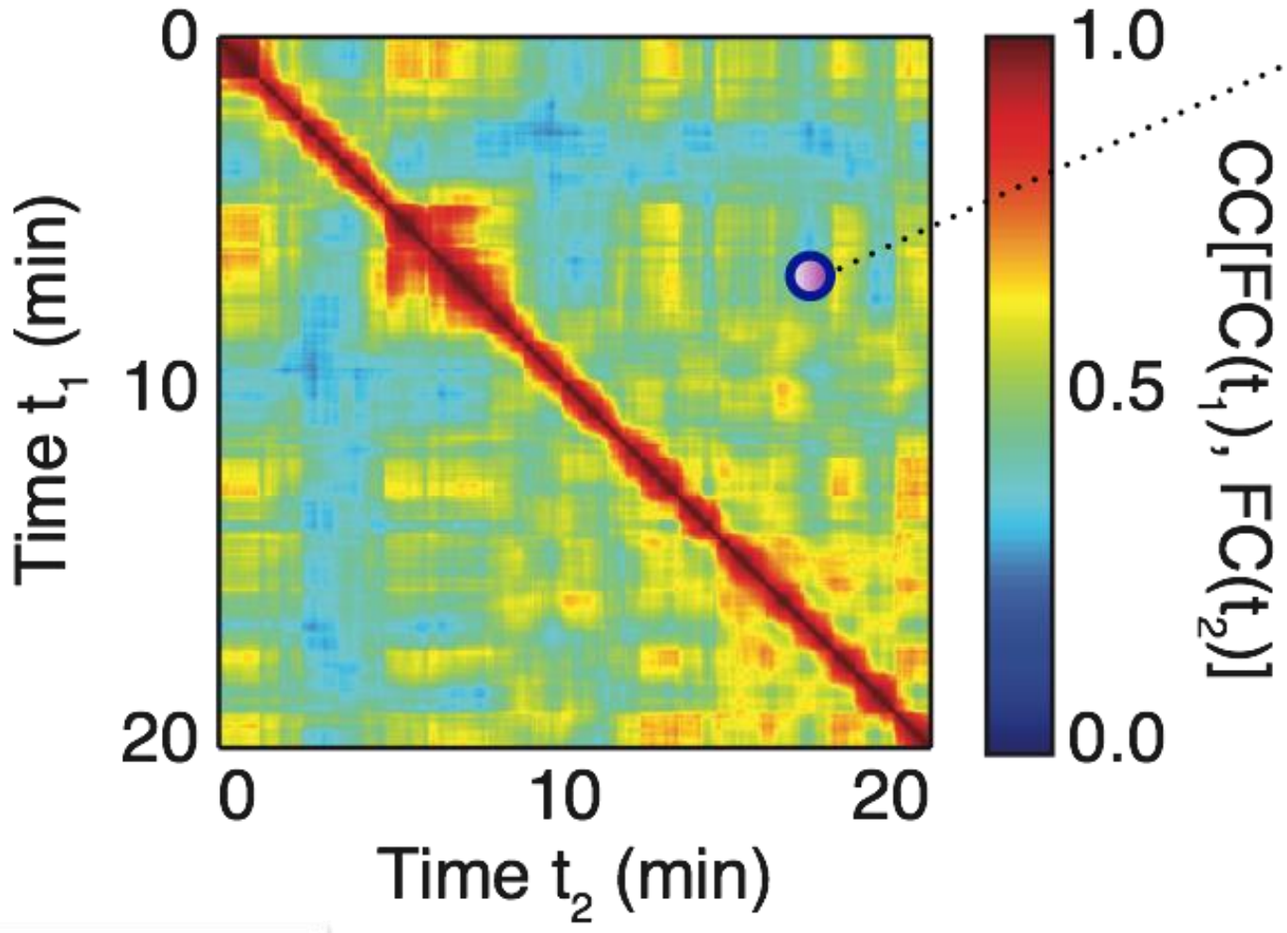


Subject 2



Allen et al Cereb Cortex 2012; Hansen et al Neuroimage (2014)

Transiently stable FC states?



FCD matrix

CC(,)

"Checker-board" correlations between FC networks at different times

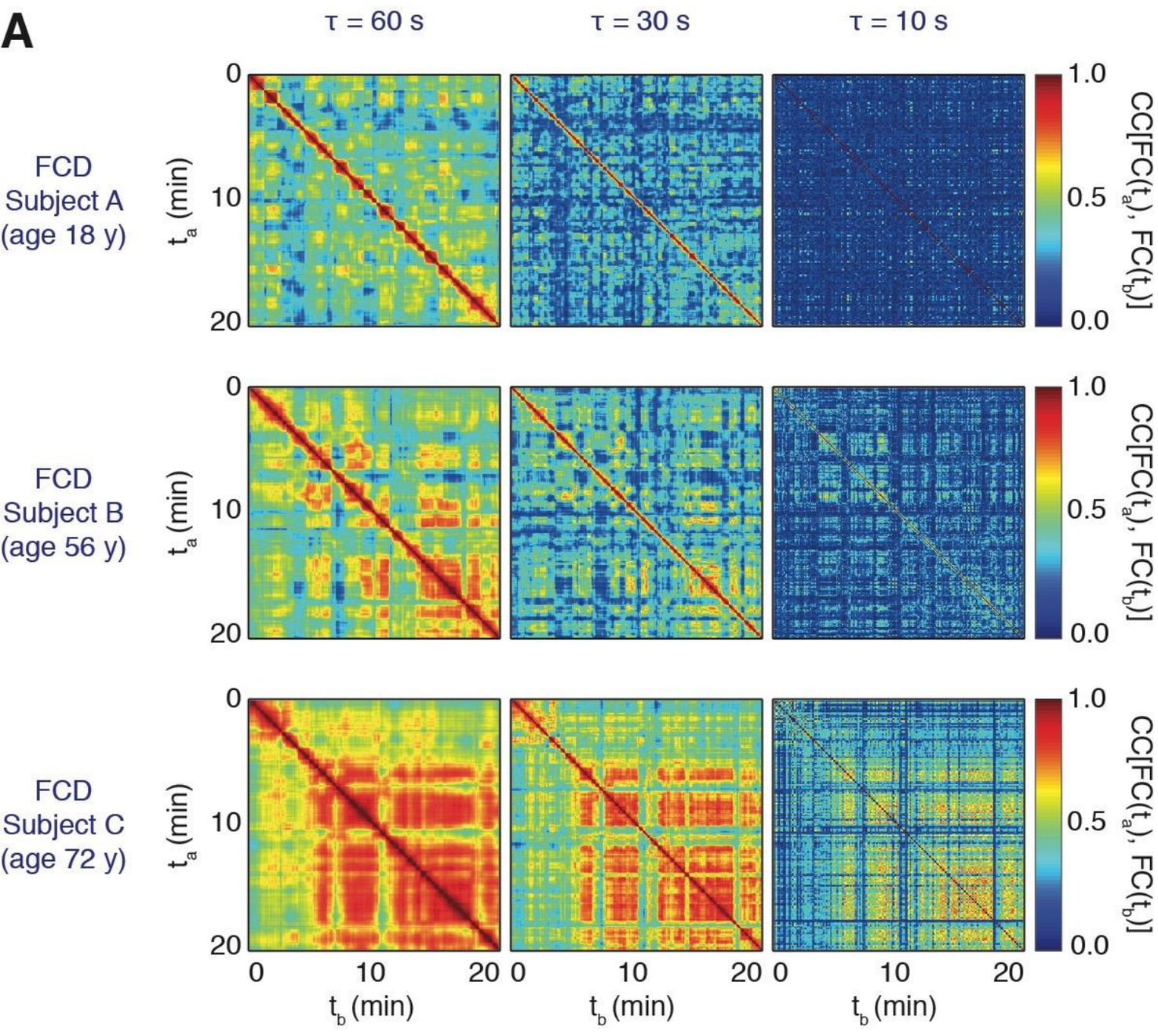
"Clusters" of FC matrices

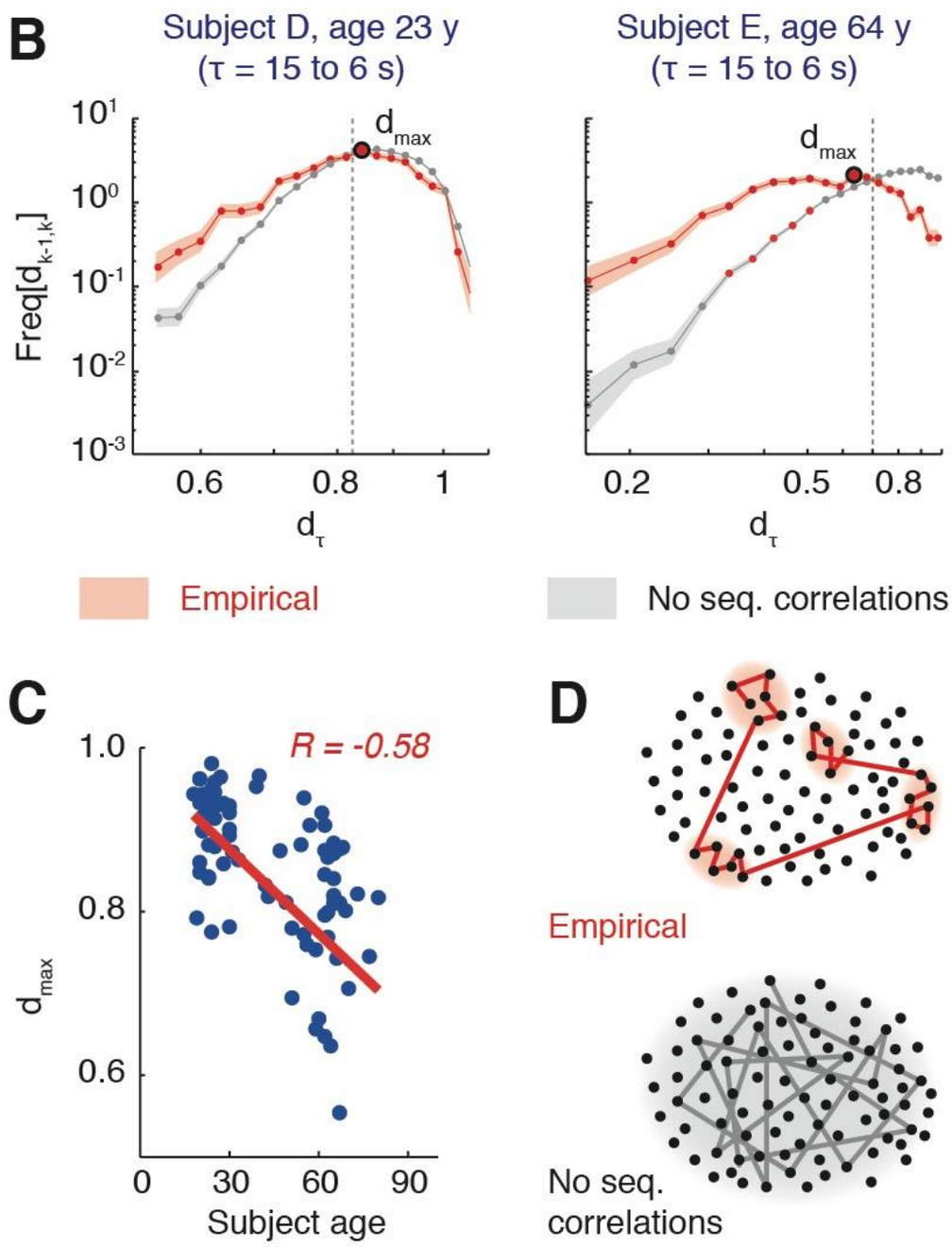
Allen et al. 2012
Hutchison et al. 2013
Hansen et al. 2015

rsfMRI data from Petra Ritter
66 regions parcelation

Hansen et al. Neuroimage 2015

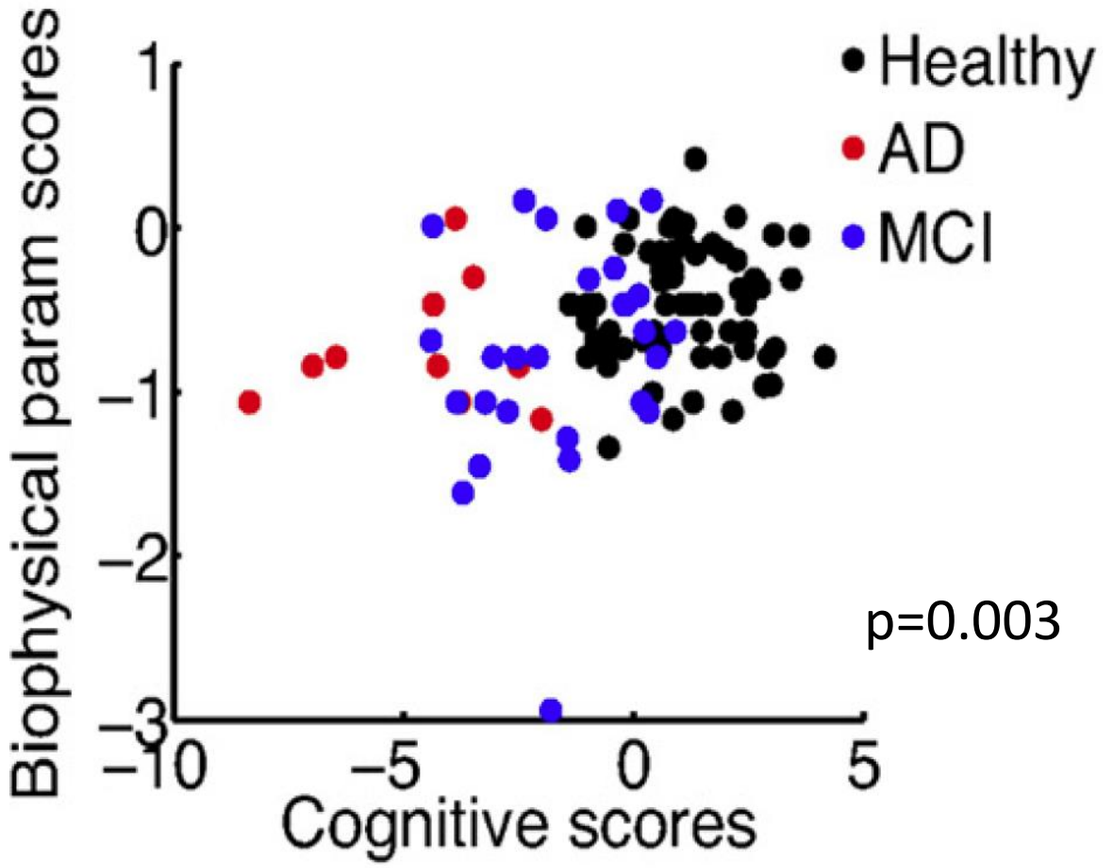
FCD tracks individual functional repertoire : ageing





Battaglia et al. (under review)

The Virtual Alzheimer's Patient



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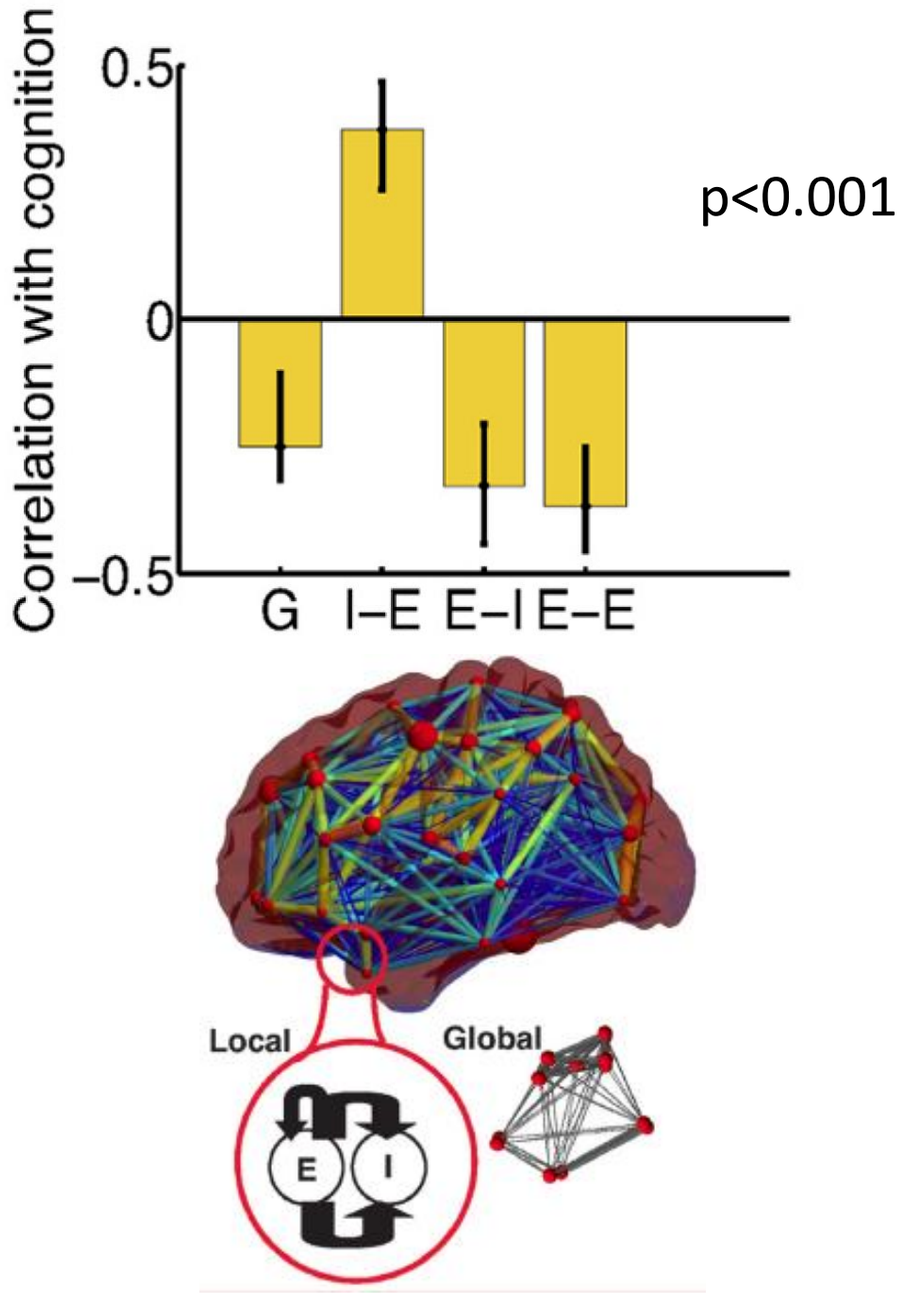
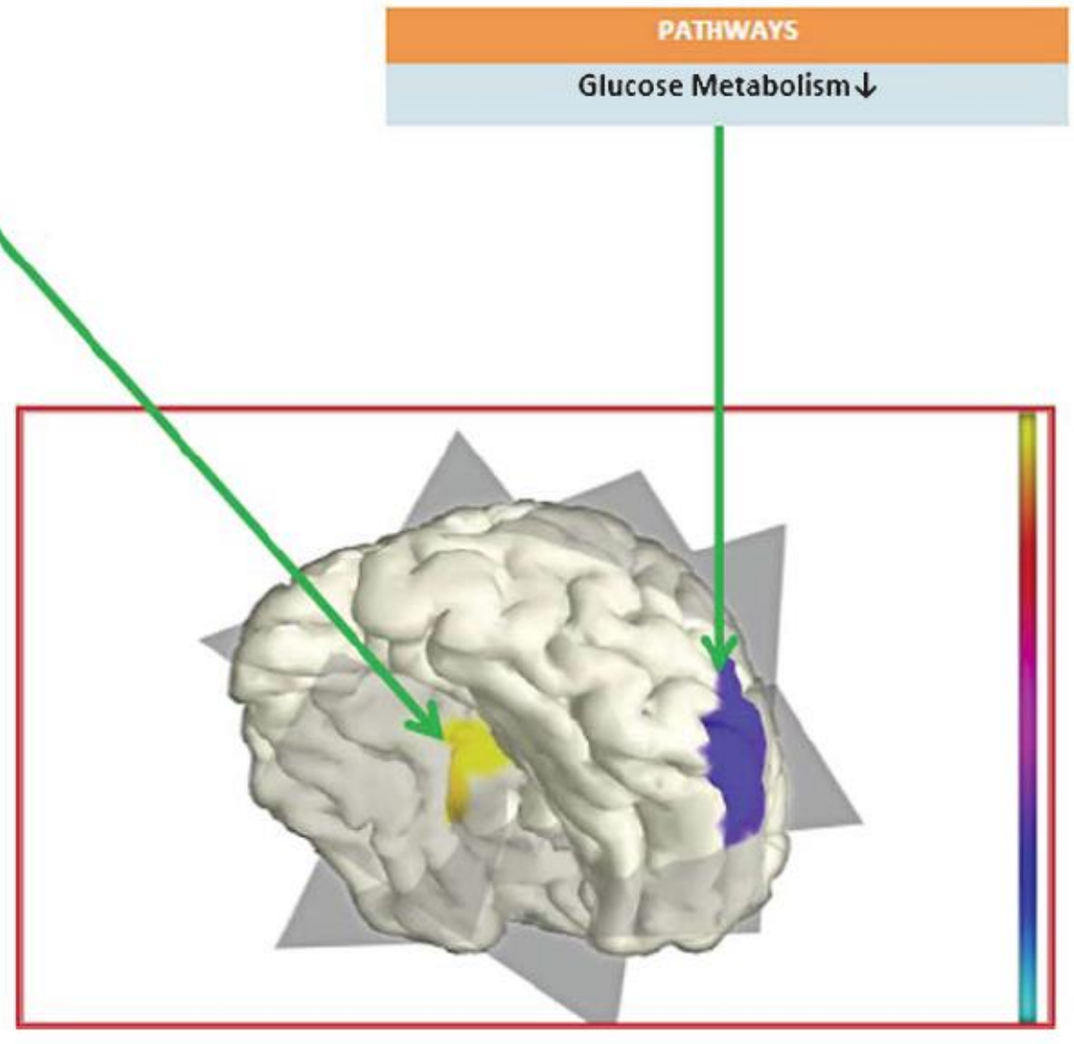


p<0.001

Differentiation of Alzheimer's disease based on local and global parameters in personalised Virtual Brain models. Zimmermann et al. 2018 Neuroimage Clinical

The Virtual Neurodegenerative Patient

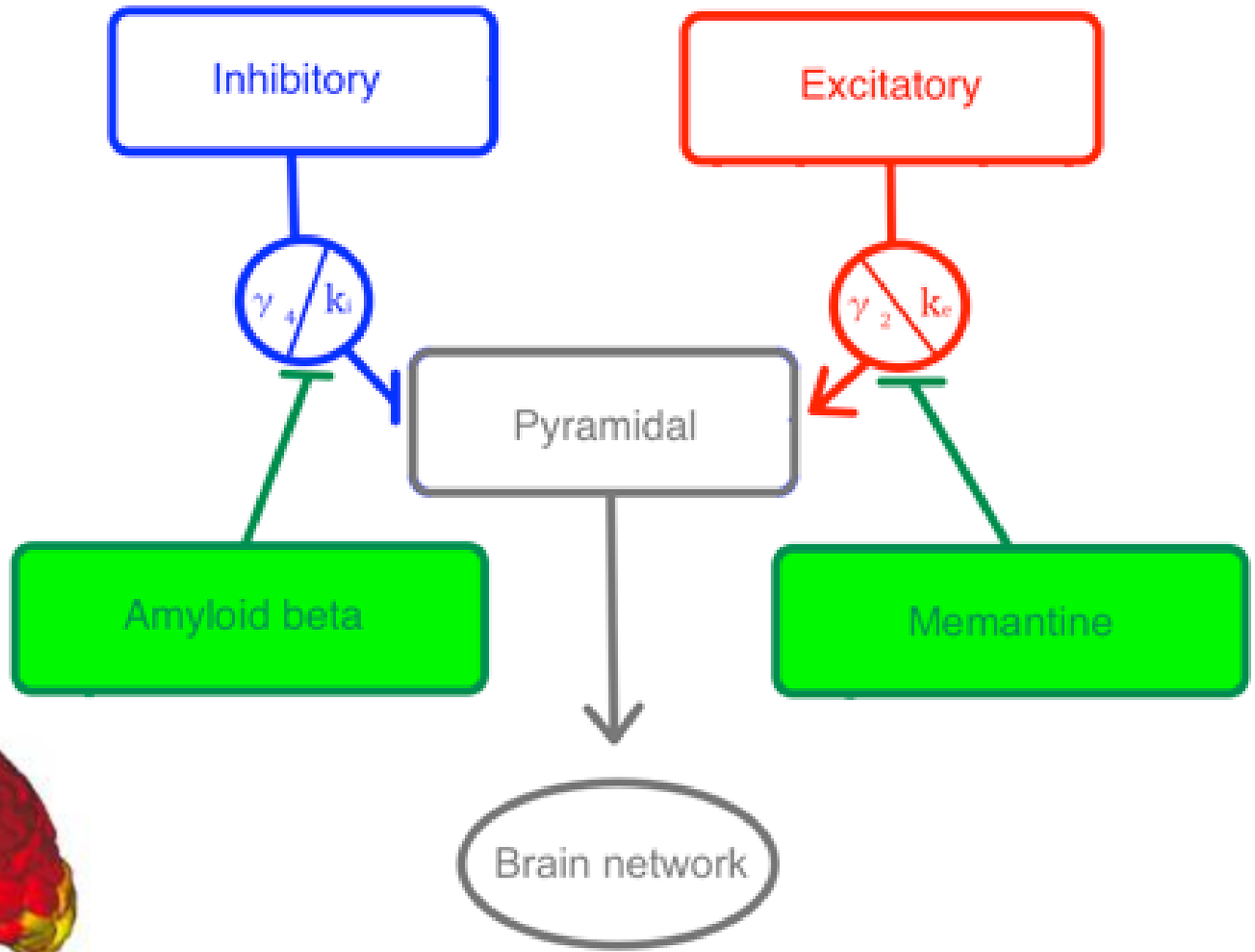
PATHWAYS
Mitochondrial Biogenesis Pathway ↓
Energy Metabolism ↓
Nogo-A to Nogo-66 receptor (NgR)Pathway ↑
Leptin Signaling ↓
Glucose Metabolism ↓
PI3K/Mtor Pathway ↓
JAK/STAT Pathway ↓
ERK Pathway ↓
p38 MAPK Pathway ↑
APP Processing ↑ - Increased neuritic "branching"
Tau Phosphorylation - Tau aggregation
Oxidative stress pathway ↑
Endocytosis pathway - Downregulation of flotillin-2
Glucose Metabolism ↓
Glutaminergic pathway ↑

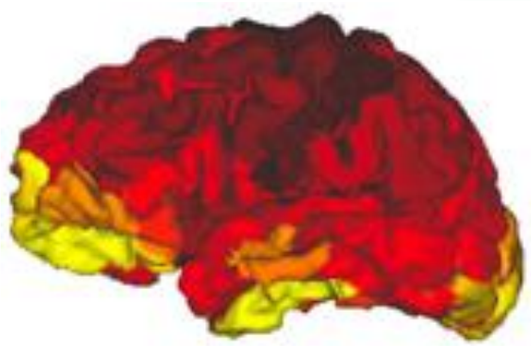


AETIONOMY

Towards a Pathway Inventory of the Human Brain for Modeling Disease Mechanisms Underlying Neurodegeneration
Iyappan et al. 2016 J Alzheimer's Disease.

Cause-effect mapping of Amyloid beta





Stefanovski et al. (in prep)

Virtual Dementia Cohort for Data Base Completion

SC	FC
12	12
76	✕
✕	156

PET IMAGE

CLINICAL

GENETIC

BIOSPECIMEN

MRI IMAGE

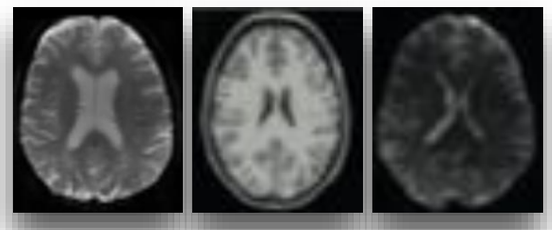
T2 ASL fMRI

DTI T2*

MRI FLAIR T1

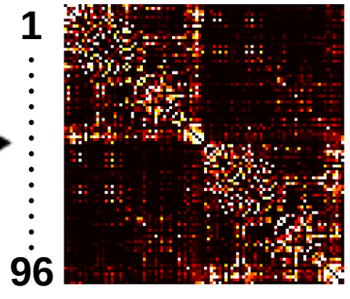
THEVIRTUALBRAIN.

ADNI
ALZHEIMER'S DISEASE NEUROIMAGING INITIATIVE

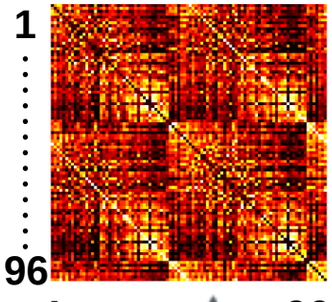


FreeSurfer
MRtrix3
FSL
SPM

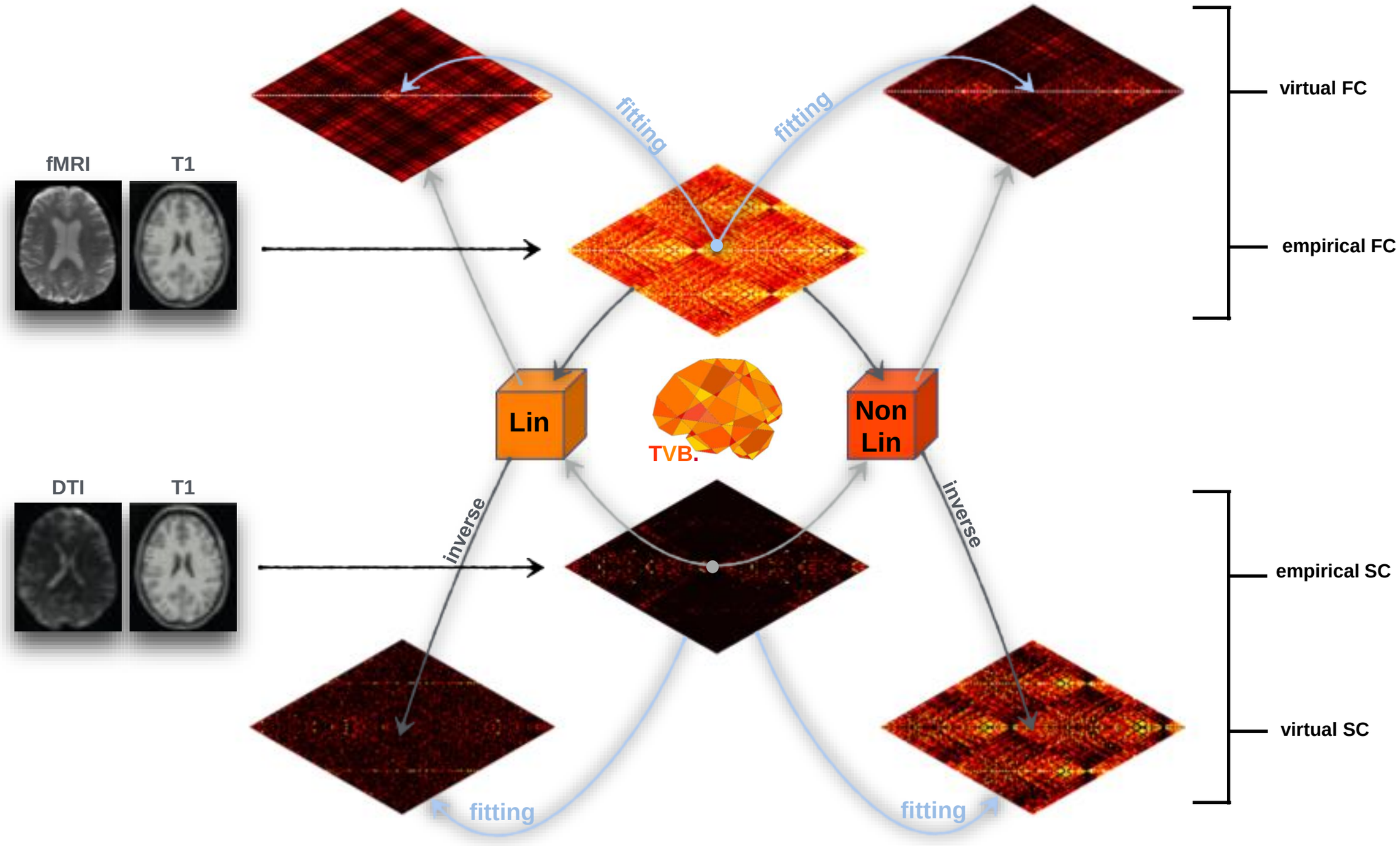
Structural Connectivity (SC)



Functional Connectivity (FC)

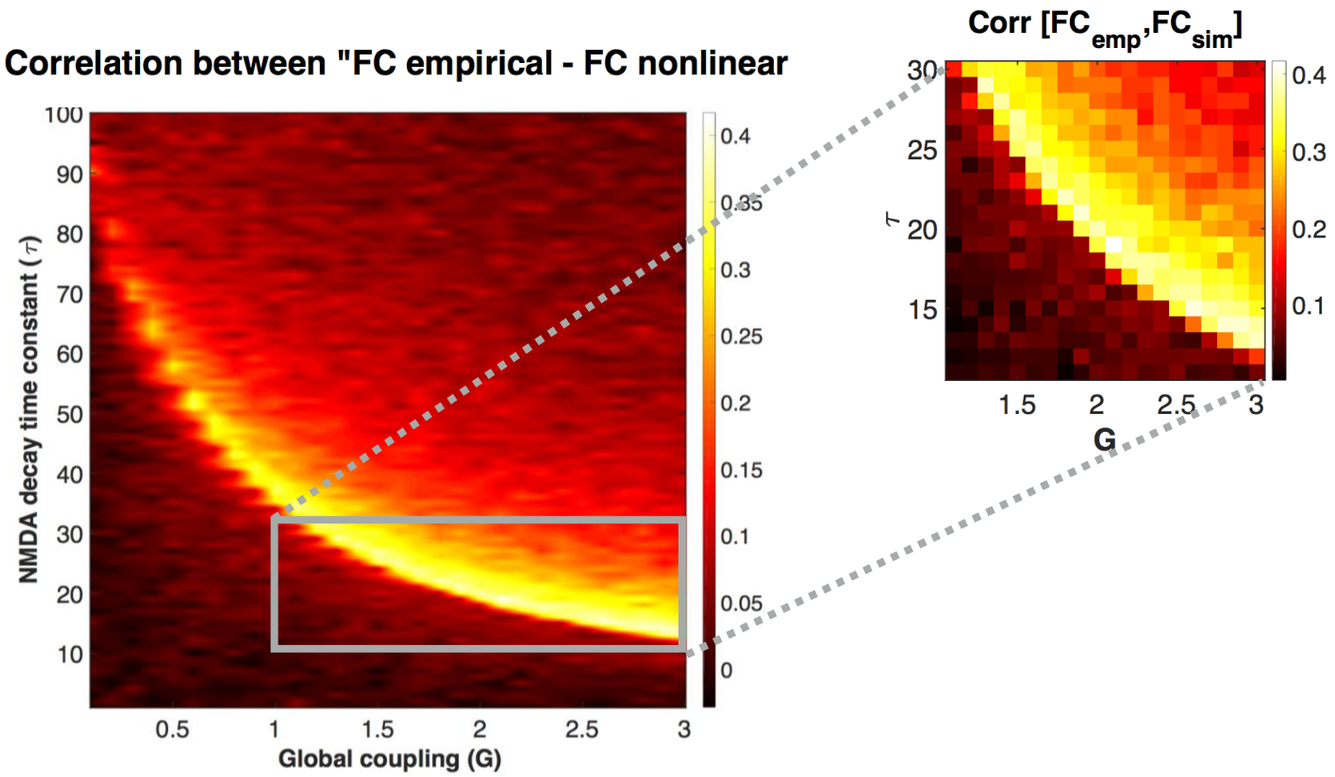


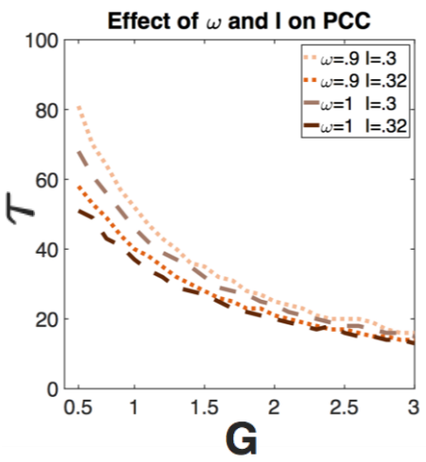
Virtual Dementia Cohort for Data Base Completion

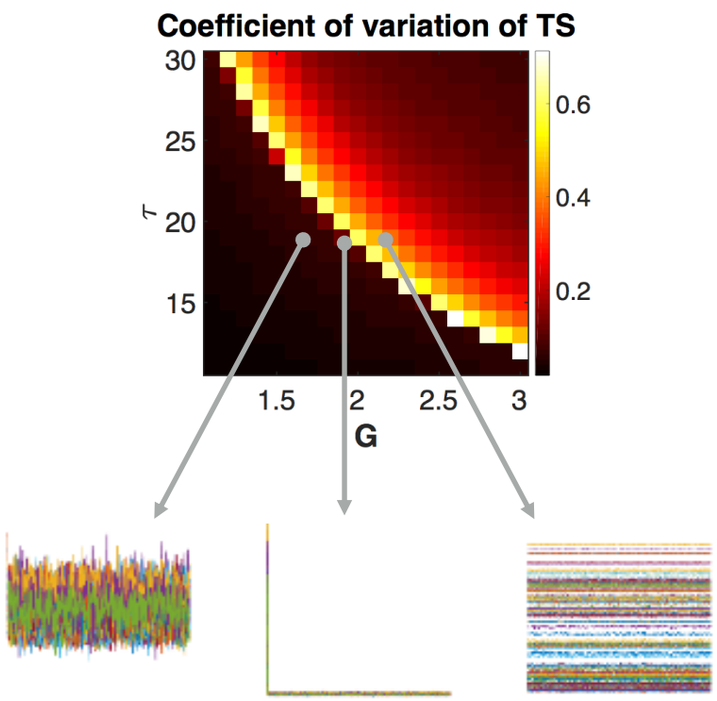


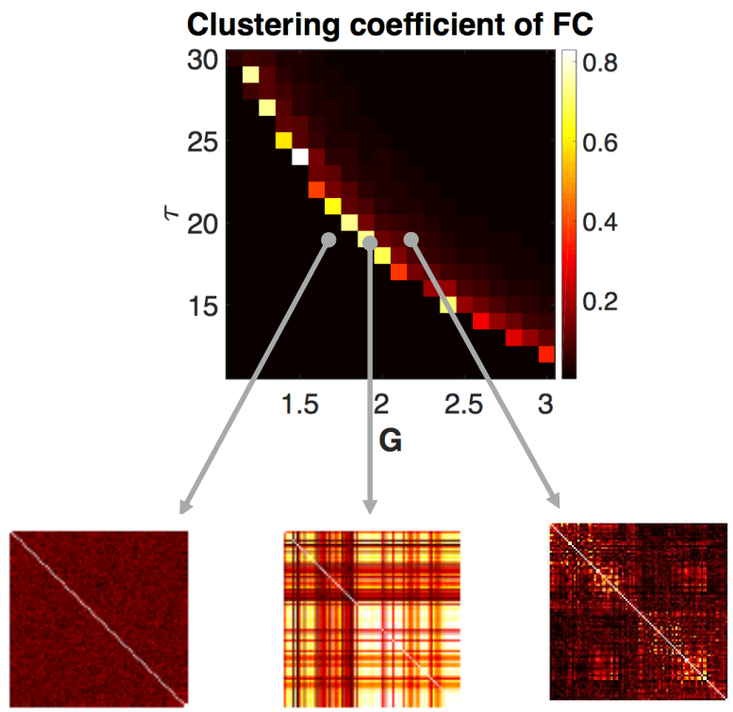
Arbabyazd et al. (in preparation)

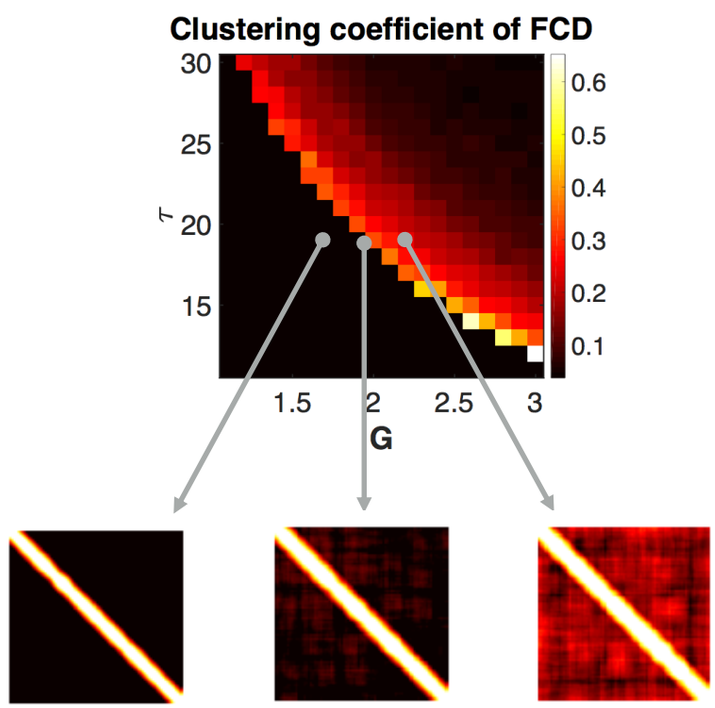
Virtual Dementia Cohort for Data Base Completion











Arbabyazd et al. (in preparation)

Virtual Dementia Cohort for Data Base Completion

MRI

ADNI
ALZHEIMER'S DISEASE
NEUROIMAGING INITIATIVE

Virtual Dementia Cohort

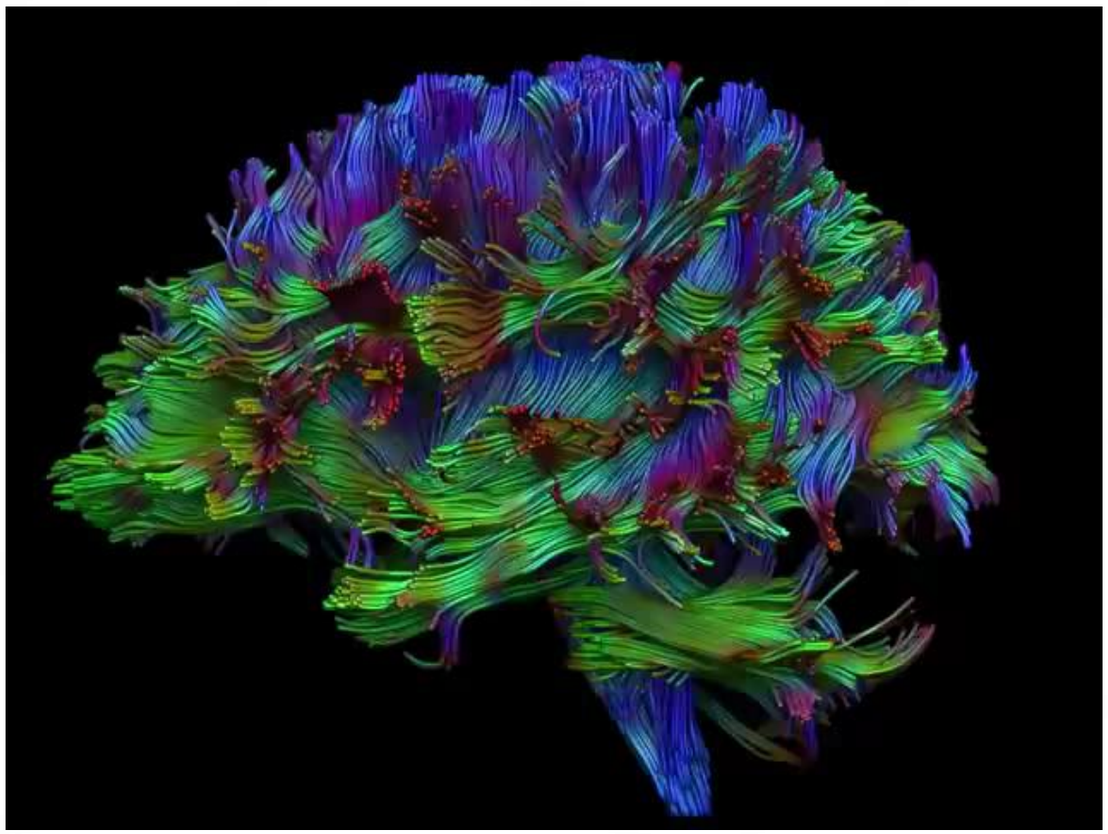
SC	FC
12	12
76	✕
✕	156

→

SC	FC	FCD,…
12	12	**12**
76	10000 0000	**76**
10000 0000	156	**156**

Arbabyazd et al. (in preparation)

In conclusion…



Final thoughts in today's context

- **Human Brain Project** advances a multi-scale modeling and simulation approach

- focus to gain a **mechanistic understanding** of mechanisms underlying brain function and dysfunction

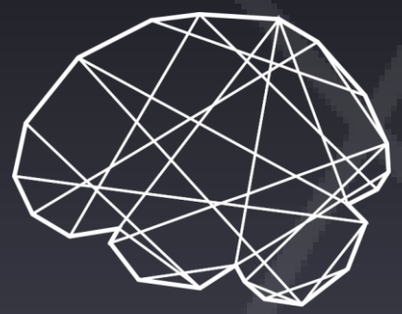
- capacity to **personalize brain network** models

- link to **brain imaging** signals

- Integration and concentration on **epilepsy, stroke** and **neurodegenerative** diseases for years 2019 - 2022

Human Brain Project

Thank you!



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