Translational Neuroscience: from network modeling to individual patient prediction

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FET Flagships – The Concept

- Large-scale, science-driven, visionary research initiatives
- Single unifying goal (“*landing on the moon*”)
- Leading to : Technological innovation
  Economic exploitation
  Benefits for society

Duration : 10 Years
Budget : up to 100 M€ per year

Federated effort of European research community and institutions, national and regional funding agencies, industry, global partners

FET FLAGSHIPS

SEVENTH FRAMEWORK PROGRAMME

HORIZON 2020

Human Brain Project

OBJECTIVES

to integrate neuroscience and clinical data from around the world into unifying computer models of the human brain

to simulate the behavior of brain models

to develop applications for medicine and future computing

Currently partner groups from 22 countries, including all major EU member states as well as Switzerland, the USA, Japan and China. When fully operational, a science and engineering workforce of approximately 550 will be in place.

Why focus on the brain ?

– Understanding the brain

- Underpins what we are,
- Data & knowledge are fragmented,
- Integration is needed,
- Large scale collaborative approach is essential.

– Understanding brain diseases

- Costs Europe over €800 Billon/year,
- Affects 1/3 people,
- Number one cause of loss of economic productivity,
- No fundamental treatments exist or are in sight
- Pharma companies pulling out of the challenge.

– Developing Future Computing Technologies

- Computing underpins modern economies,
- Traditional computing faces growing hardware, software, & energy barriers,
- Brain can be the source of energy efficient, robust, self-adapting & compact computing technologies,
- Knowledge driven process to derive these technologies is missing.

Human Brain Project

Three HBP Research Areas

A collaborative project for *ICT-based*

brain research to work towards

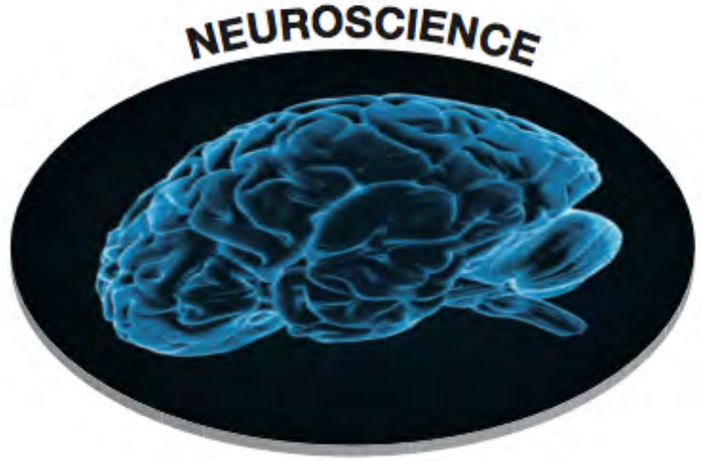
- understanding of the brain
- understanding of brain disease
- creating brain-like computing technologies

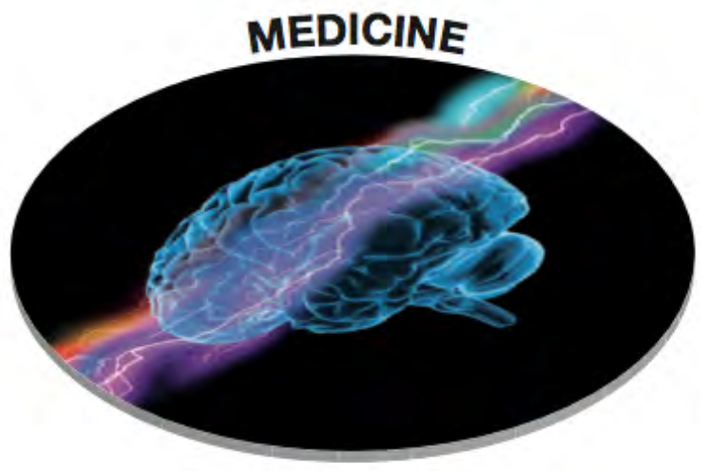
Basically:

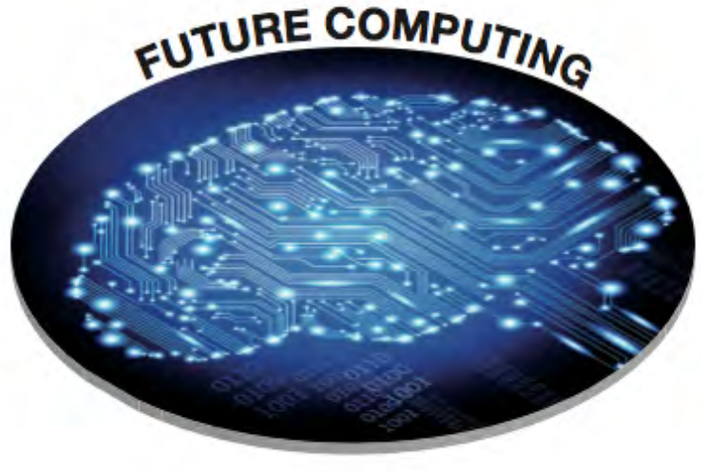
Aggregate – Synthesize – Understand

Essential:

Lasting Infrastructure - *CERN of the Brain*







The six ICT Platforms in HBP

1. Neuroinformatics Platform
   Aggregate neuroscience data, deliver brain atlases

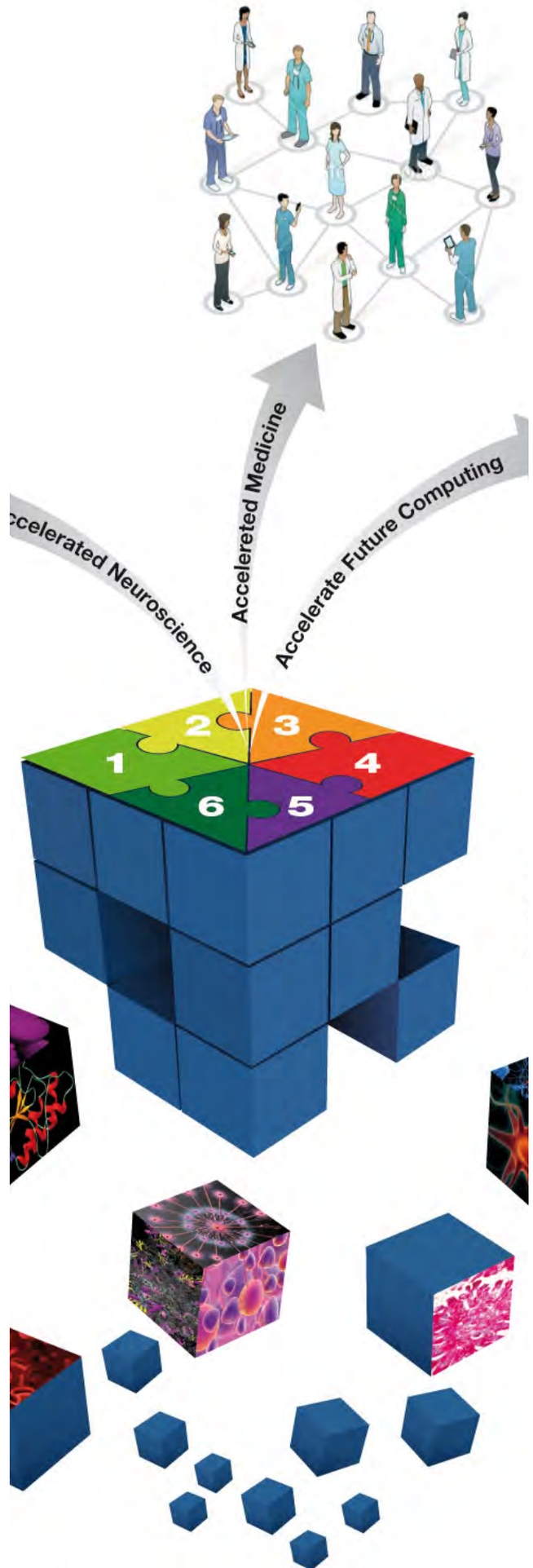
2. Medical Informatics Platform
   Aggregate clinical records, classify brain diseases

3. Brain Simulation Platform
   Develop software tools, run closed loop brain simulations

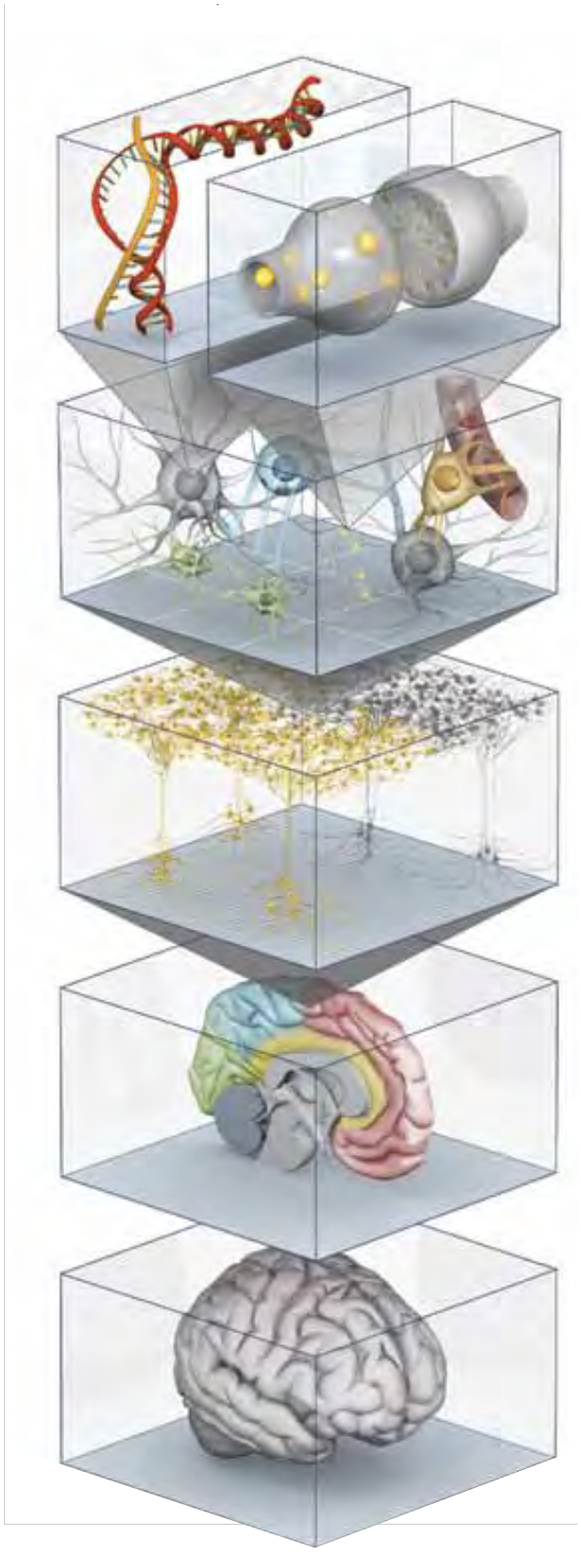
4. High Performance Computing Platform
   Develop and operate HPC systems optimized for brain simulations

5. Neuromorphic Computing Platform
   Develop and operate novel brain derived computing hardware

6. Neurorobotics Platform
   Develop virtual robotic systems for closed loop cognitive experiments



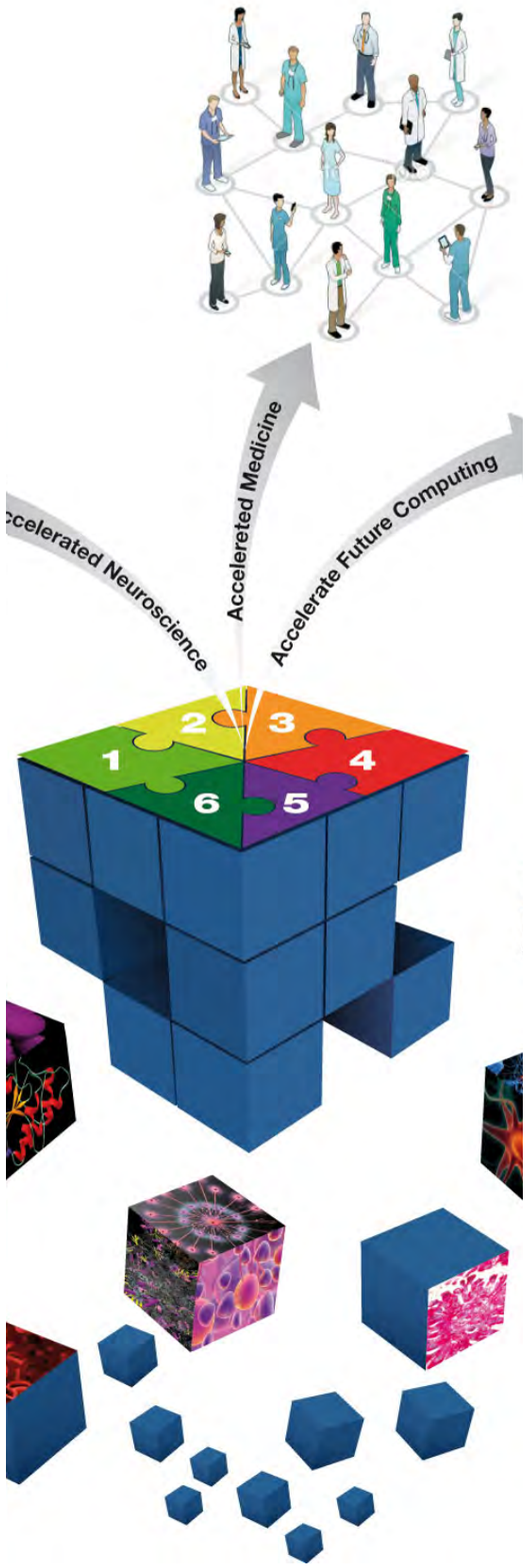
ICT based Neuroscience



Build and simulate unifying human brain models

1. Gather and organize existing fragments of data
2. Fill knowledge gaps using predictive ICT tools
3. Generate strategically selected missing data
4. Prioritize biological experiments
5. Provide publicly accessible brain atlases
6. Perform large-scale brain simulations

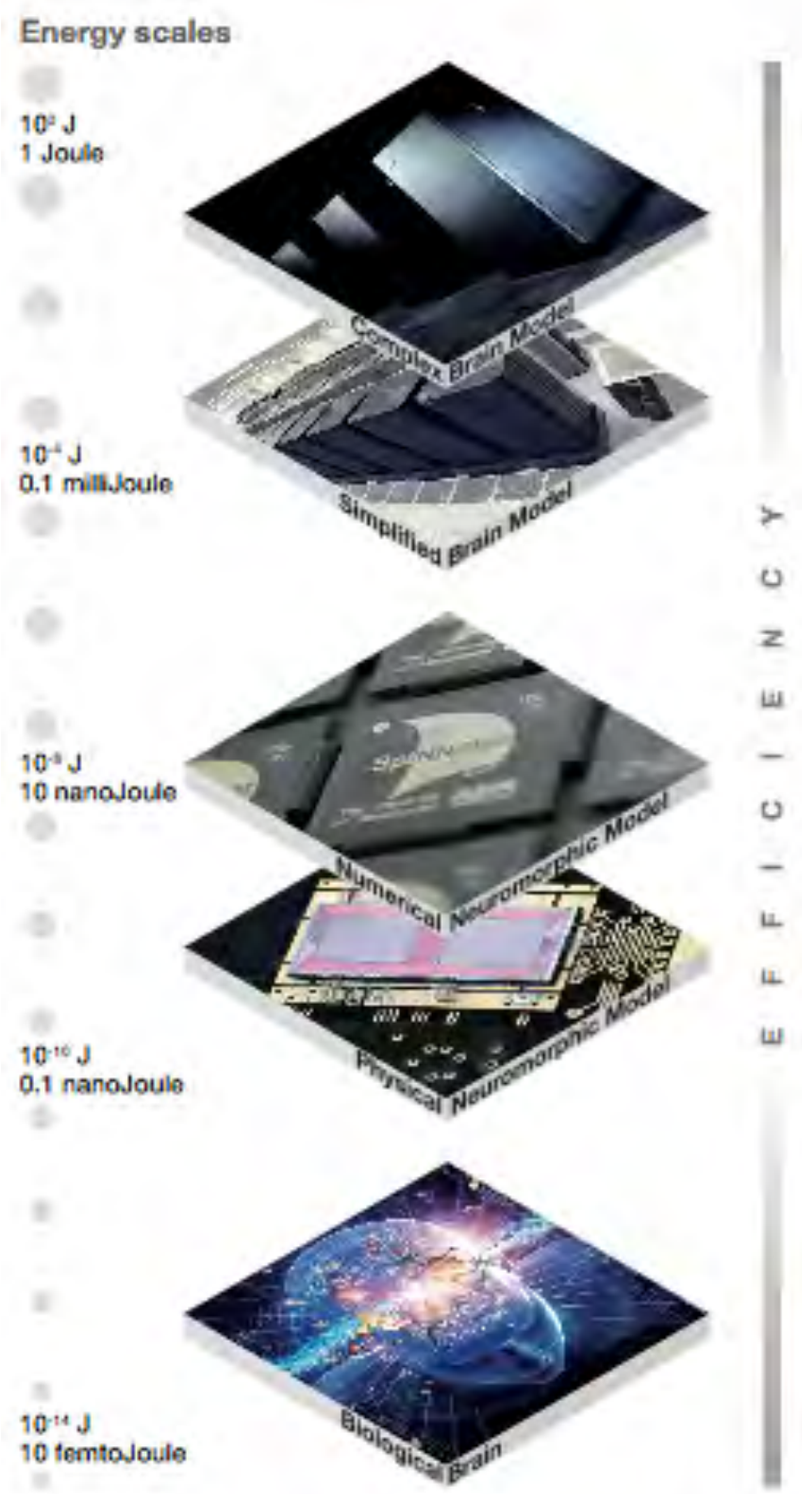
ICT based Neuromedicine



ICT-based diagnosis and treatment of brain diseases

1. Gather and organize existing fragments of data
2. Derive biologically-grounded signatures characterizing brain diseases
3. Understand the similarities and differences of brain diseases
4. Provide ICT based tools for pharmaceutical and nutrition companies to prevent, diagnose and treat brain diseases

Future Computing



Brain-inspired future computing technologies

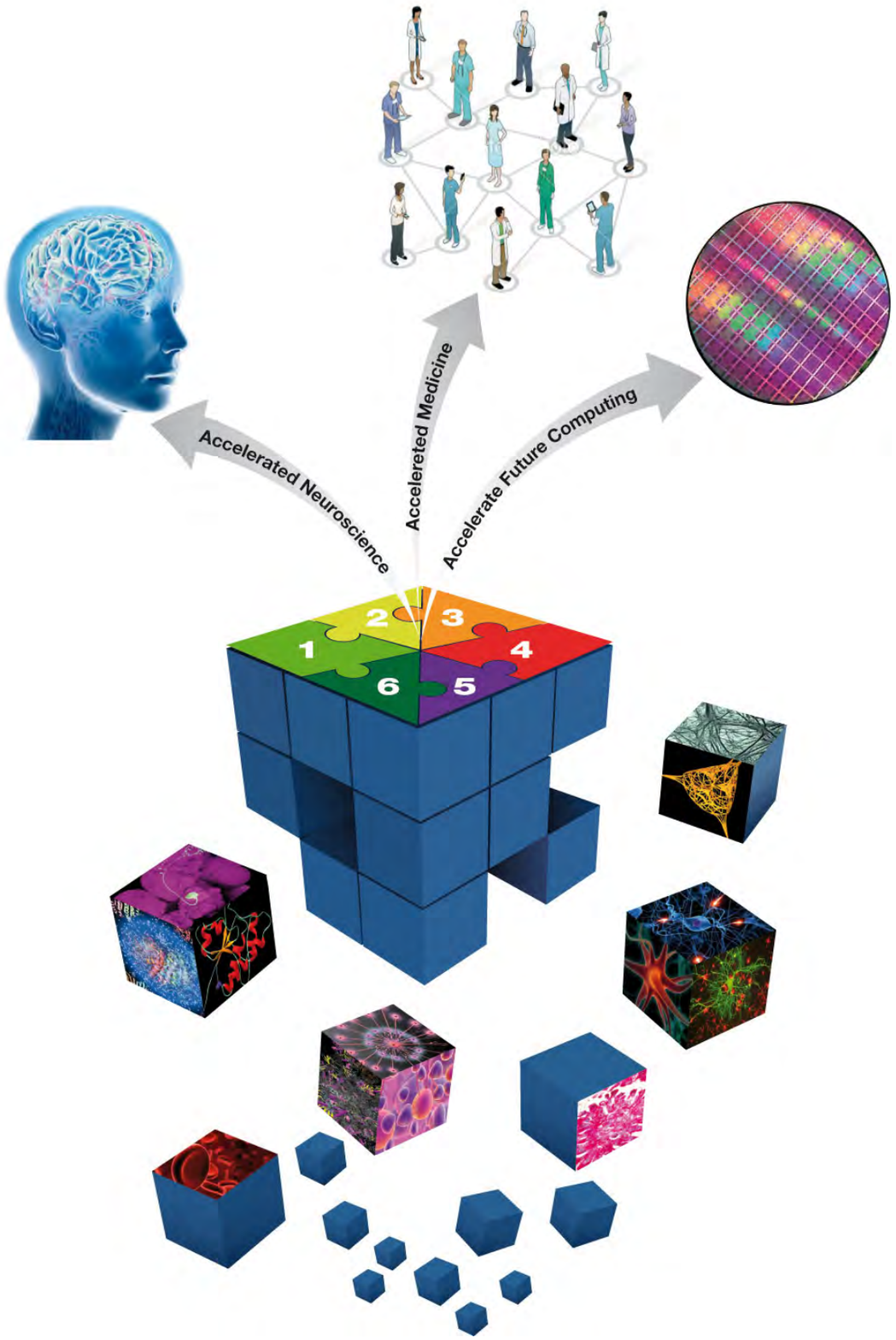
1. Build an an exascale supercomputing infrastructure optimized for brain simulation
2. Make supercomputing visually interactive
3. Systematically derive new computing architectures from insights of brain function
4. Develop low power, fault tolerant, self-adapting, generic computing and communication devices
5. Develop an experimentally and

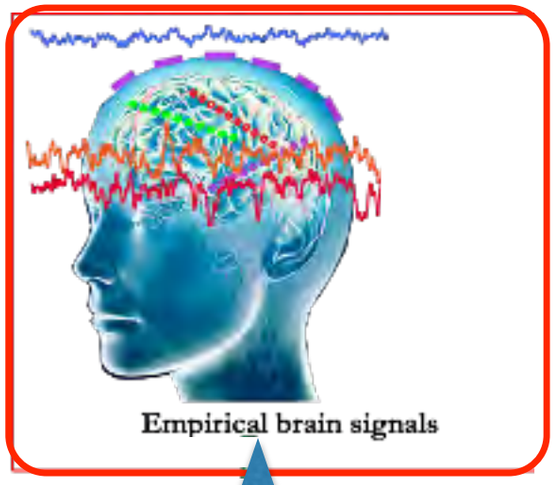
The HBP Platform Concept

• Build six ICT platforms to *accelerate* our understanding of the human brain, it's diseases and to develop future computing technologies.

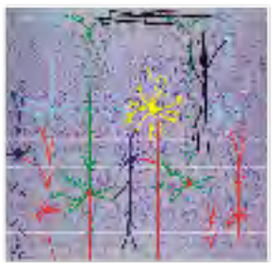
• The six ICT platforms will be developed by the HBP consortium of currently 85 partners in 22 countries across Europe and also in the US, Japan and China.

• The six ICT platforms will be open to researchers globally, facilitating collaborative science, medicine & engineering





Micro circuits



Proteomics

Genetic

Molecule

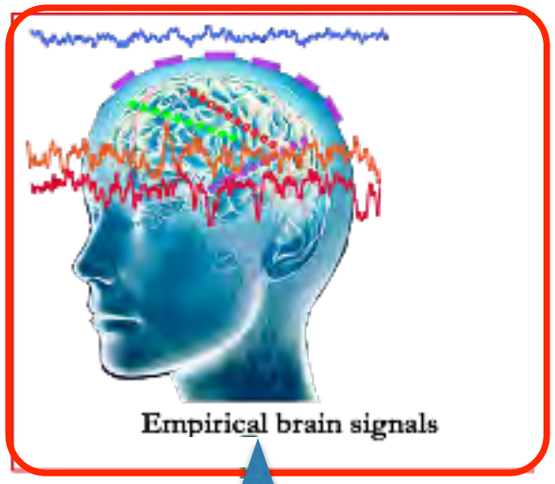
microscopic modeling

Human Brain Project

FET FLAGSHIPS

Unit of operation : neuron

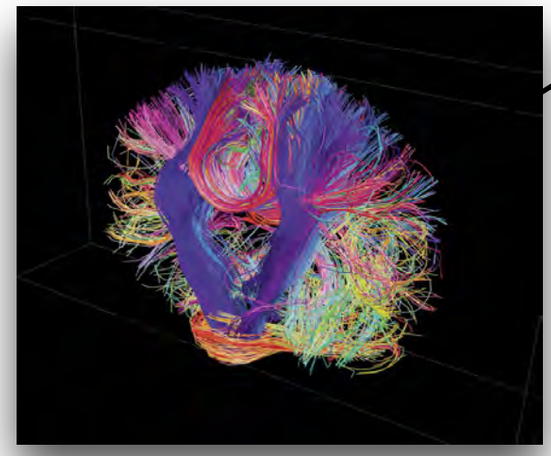
Computational neuroscience

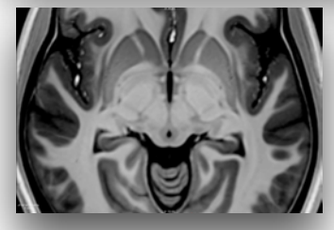


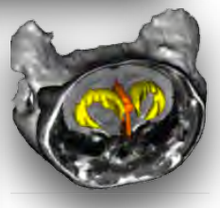
Human Brain Project

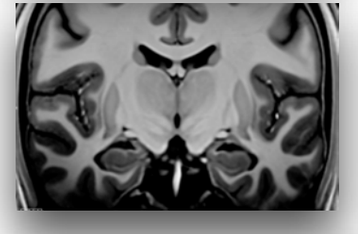
THEVIRTUALBRAIN.

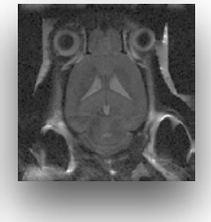
Unit of operation : neuronal population

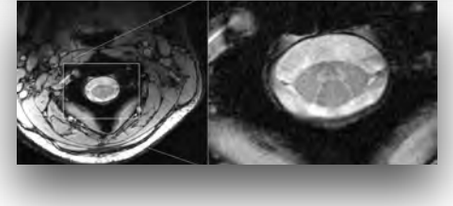












Computational neuroscience

mesoscopic
modeling

www.thevirtualbrain.org

TVB team


Viktor Jirsa


Randy McIntosh


Jochen Mersmann


Petra Ritter

N

2005 2010 2015 2020

W

JS McDonnell Foundation

RHU EPINOV

SATT

BrainScaleS (FET Open)

LIA EpiSurge

Human Brain Project (Flagship)

ANR Vibrations

ANR Connectome

A*Midex

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

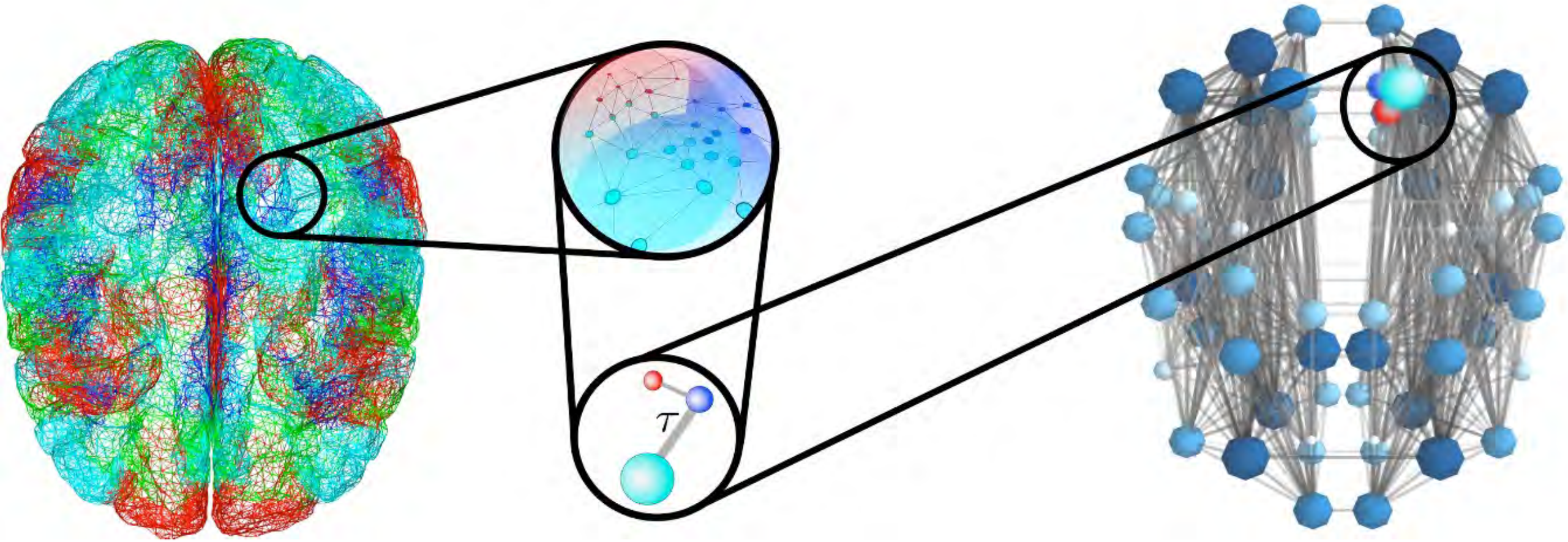
ORIGINAL PAPERS

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/awu133

Large-scale brain networks



THEVIRTUALBRAIN.

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Brain doi: 10.1093/brain/awul33

Network node:
Mean field modeling

Connectome:
connectivity & time delays

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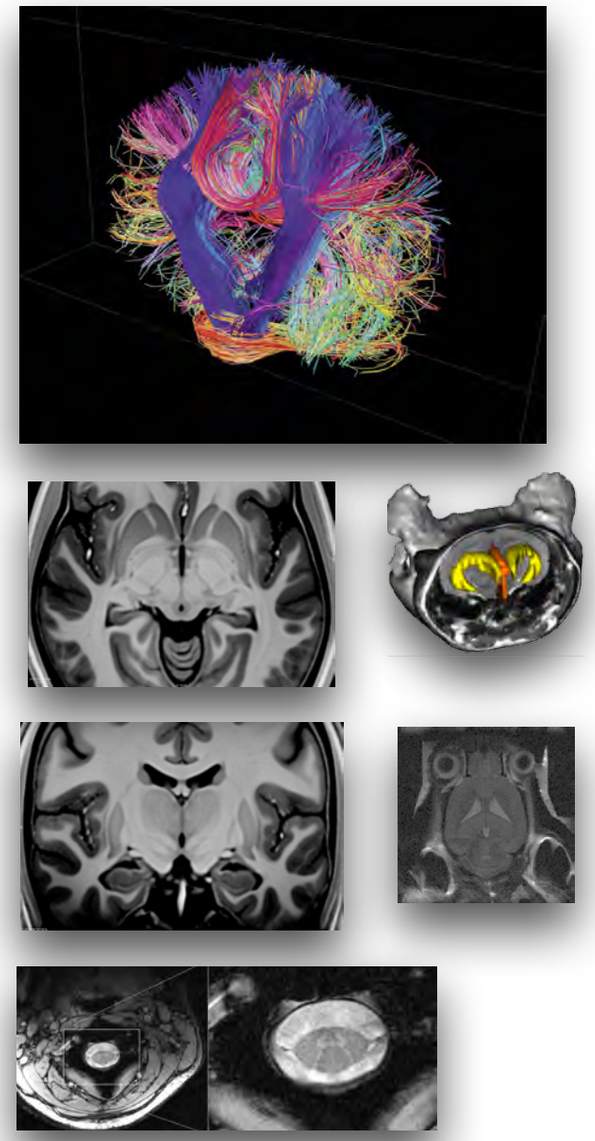
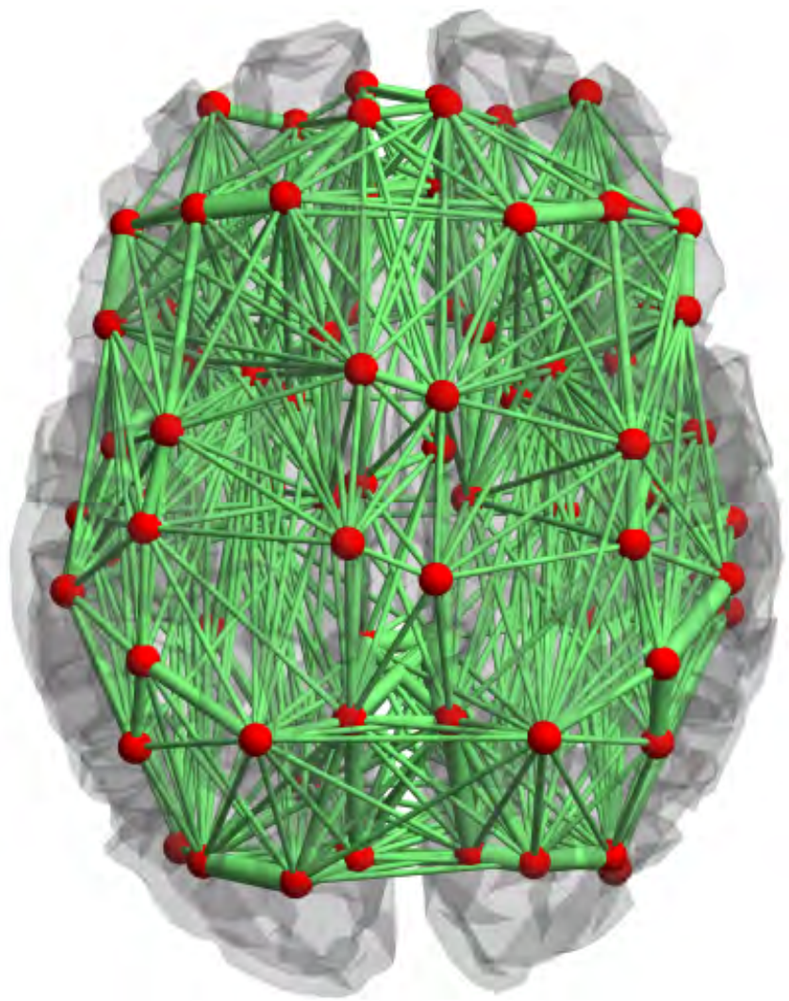
Personalized Medicine via virtual brain modeling

Working philosophy:

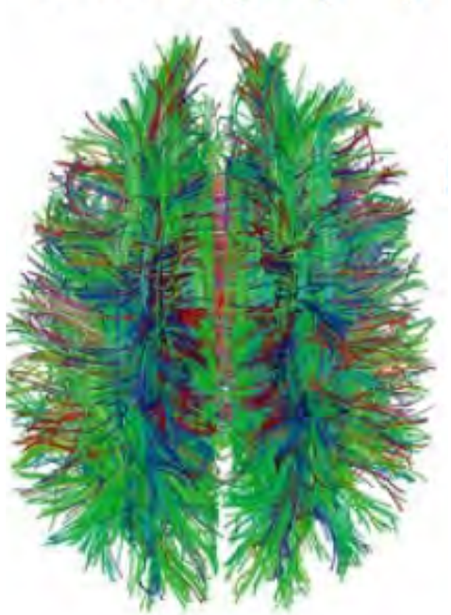
Patient-specific individual structural differences constrain the possible behaviors of personalized brain network models

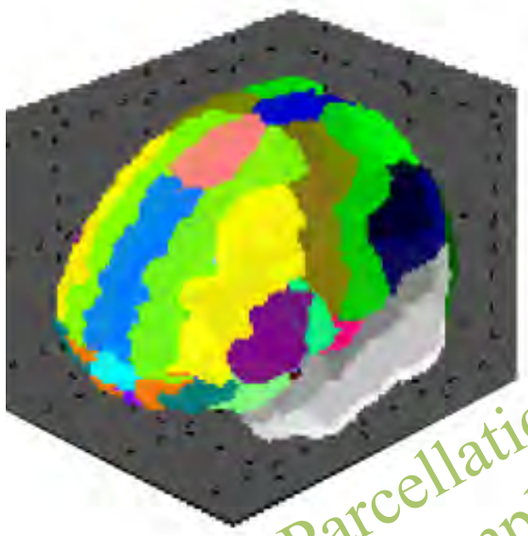




The Virtual Brain (TVB) platform release in 2012

DTI/ Tractography





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

5707 registered users in April 2017
http://www.thevirtualbrain.org

Sanz Leon et al Front NeuroInformatics 2013; Neuroimage 2015

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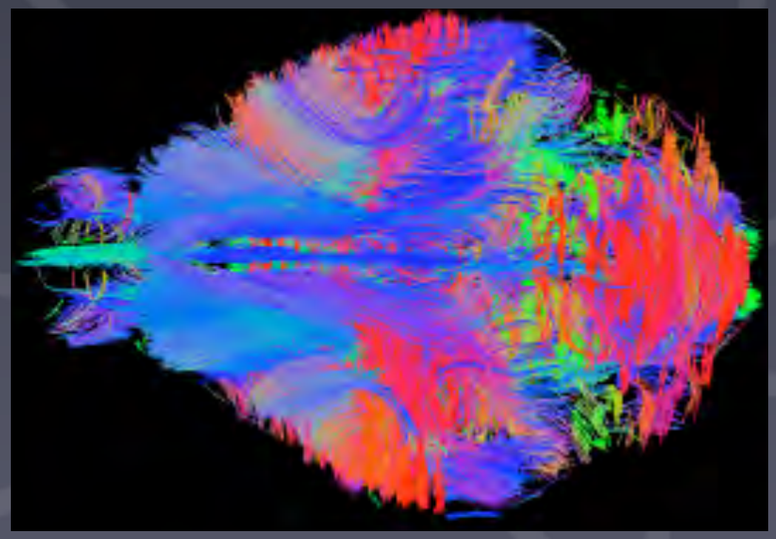
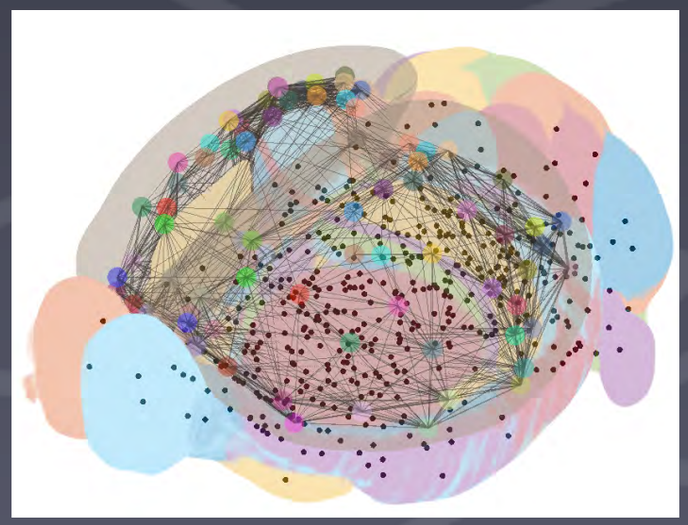
The personalized virtual brain

Validation in rodent brains





The Virtual Mouse Brain (TVMB) modeling - validation

Local dynamics

Global dynamics

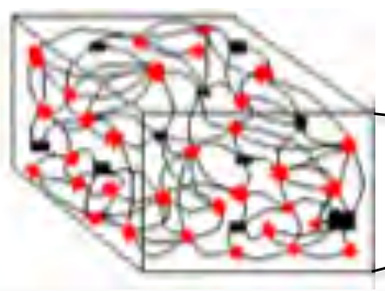
$$\psi(x,t) = N(\psi(x,t)) + \int_{local} g(x-x')S(\psi(x',t))dx' + \int_{global} G(x,x')S(\psi(x',t-\frac{|x-x'|}{v}))dx' + \text{noise}$$

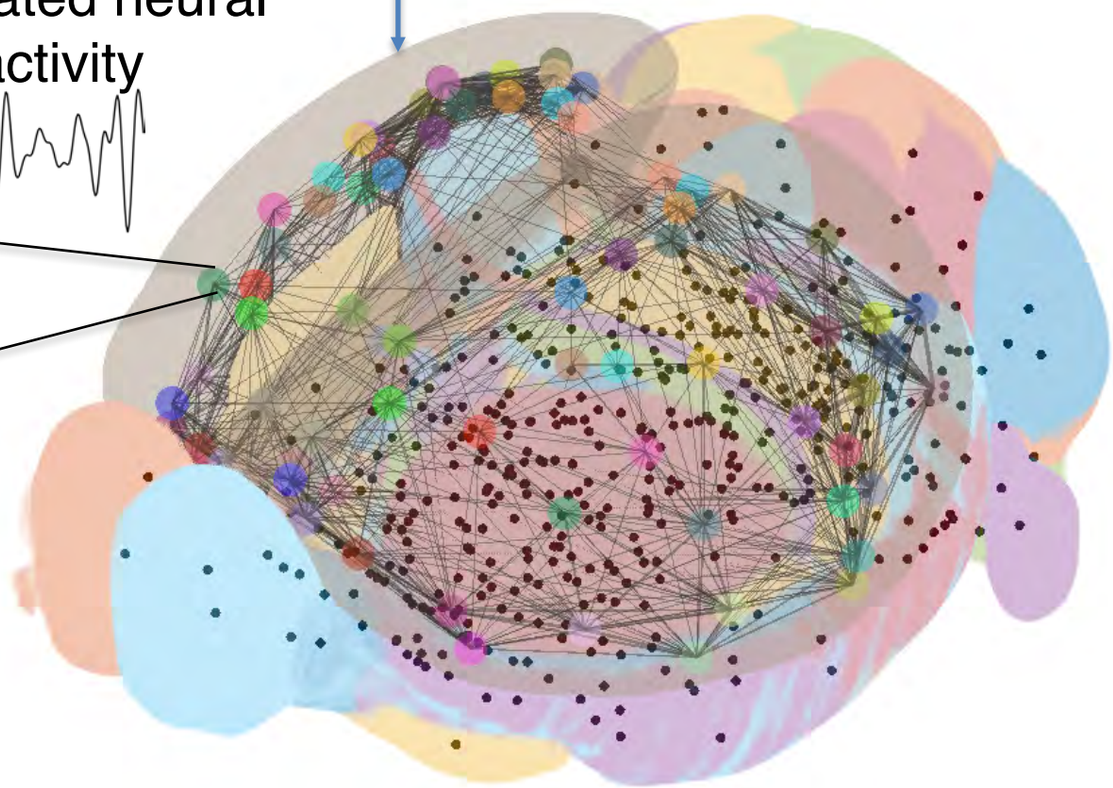
Field potential

Intrinsic activity

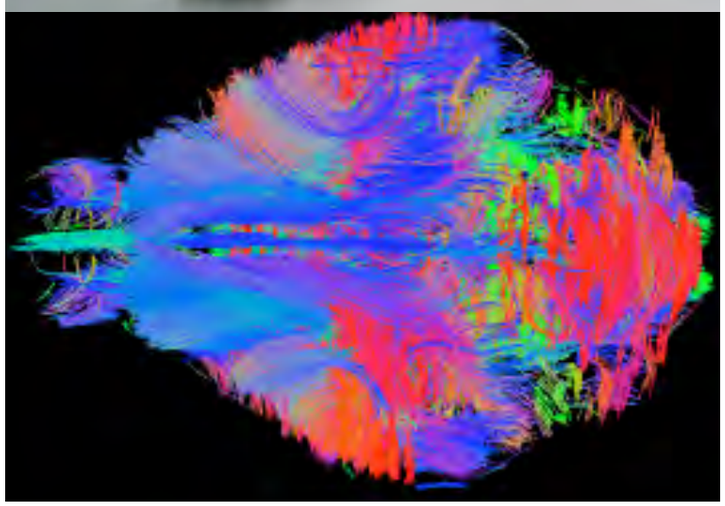
0.1-1mm

Simulated neural activity





Tractography

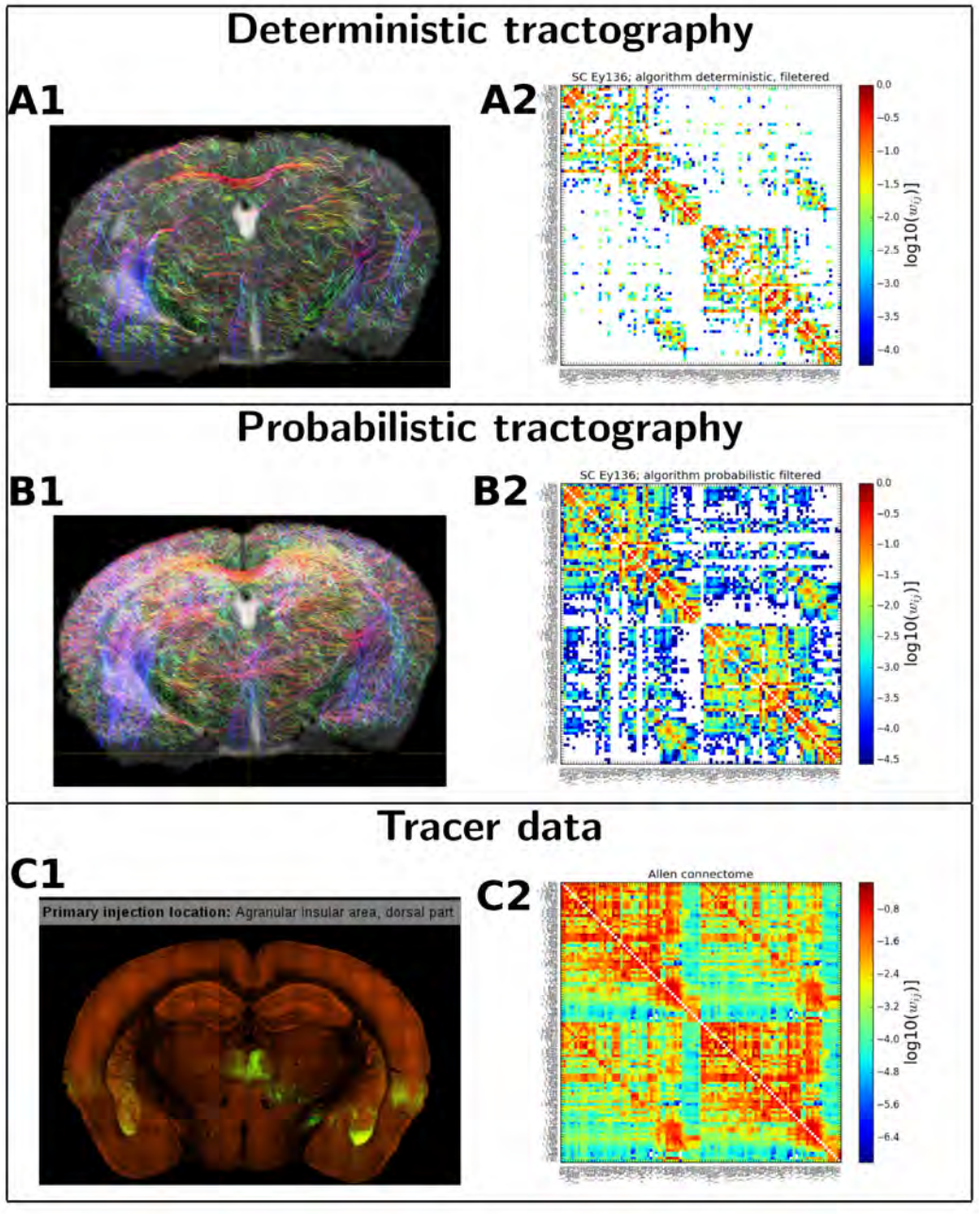


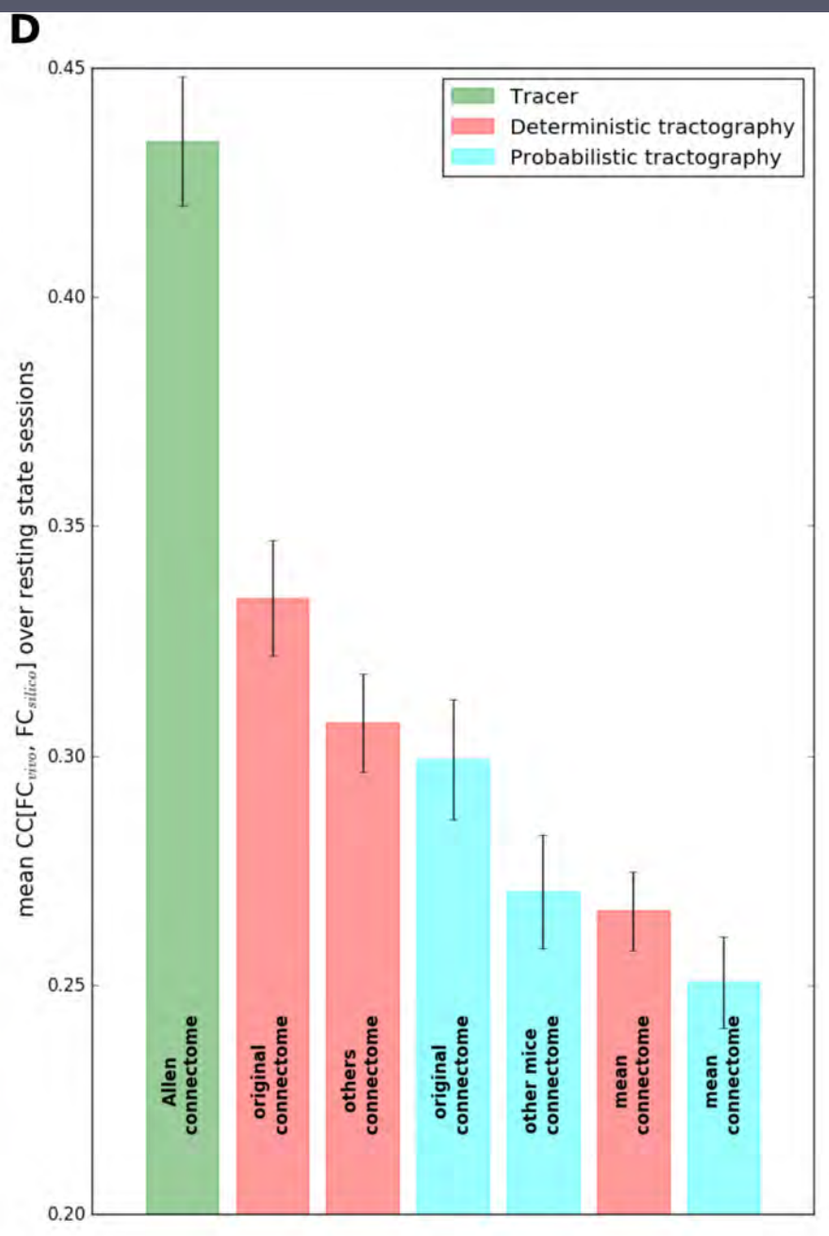
Neuronal population

Melozzi et al. (in preparation)

Human Brain Project

The Virtual Mouse Brain (TVMB) modeling - validation





	Neural tracer	Tractography
Spatial resolution	0.1 mm	1mm
Long range connections	detected	poor detection
Directionality	yes	no
Seed region	Stereotaxic coordinates	Anatomy
Personalized	no	yes

Human Brain Project

Melozzi et al. (in preparation)

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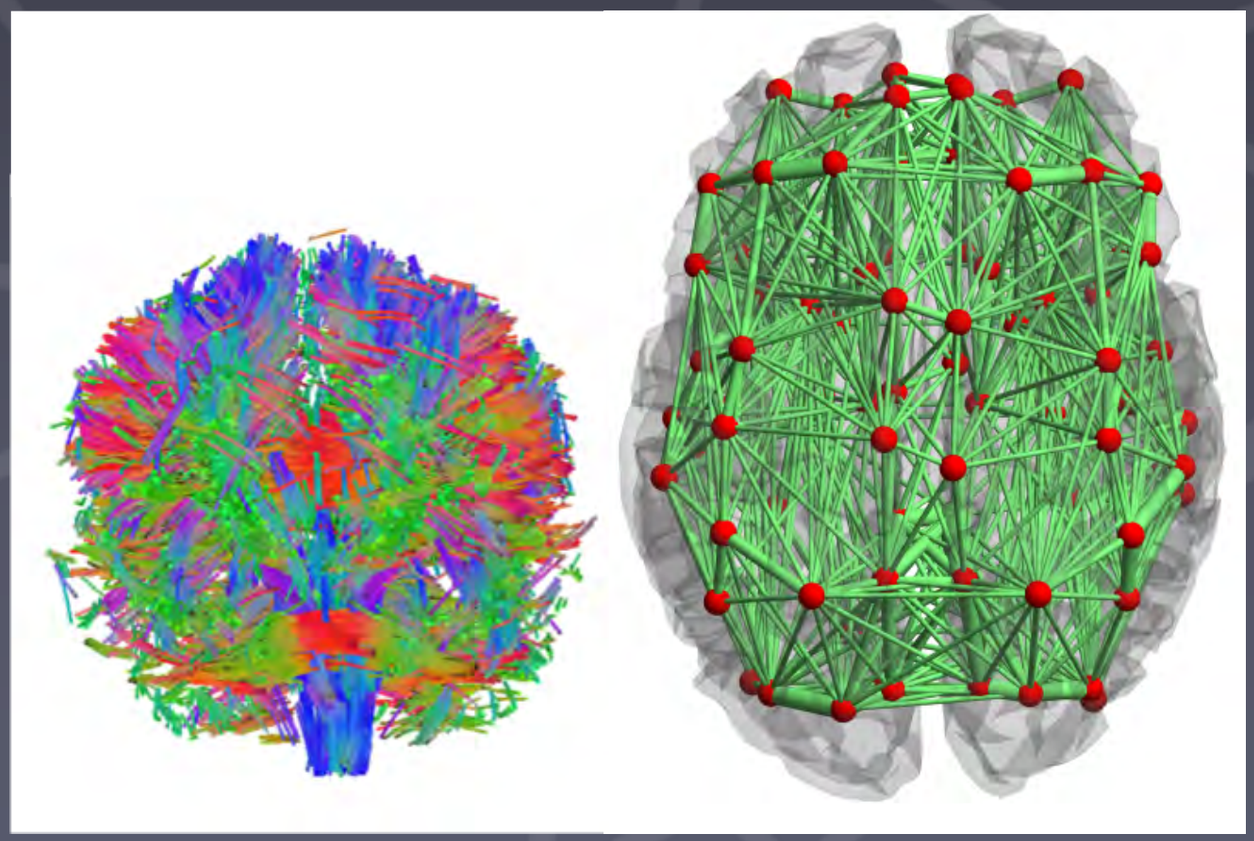
The Virtual Epileptic Patient

build the network from patient brains

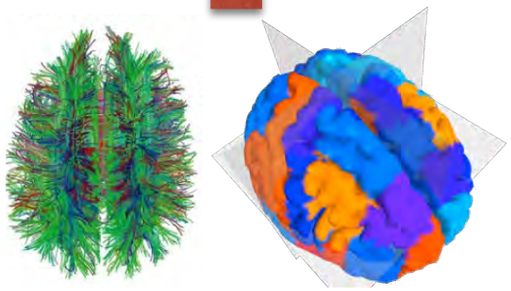


The Virtual Patient Modeling process

Jirsa et al. Neuroimage (2016)

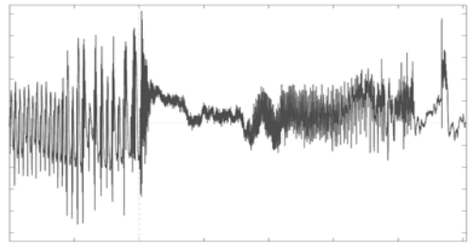
Noninvasive brain imaging

Standard pipelines:
FSL, MrTrix, FreeSurfer,…



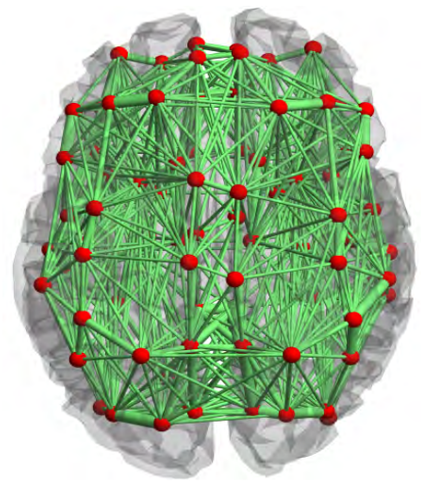
Construction of brain avatar

Nonlinear dynamic model
Not physiologically detailed/realistic
Dynamically detailed

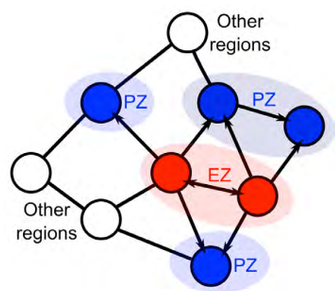


Functional region model selection

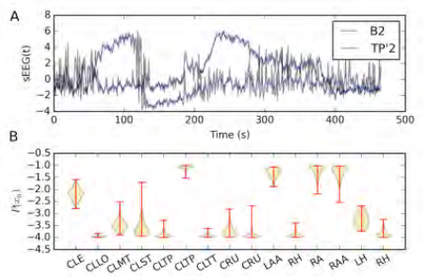
Functional Personalized Brain Network model



Refine network pathology

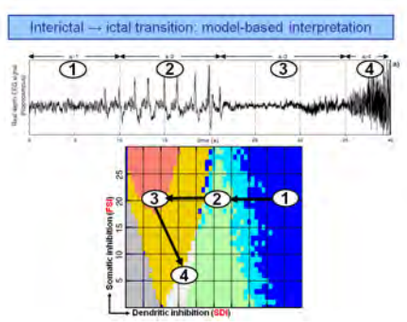


Finger printing of patient



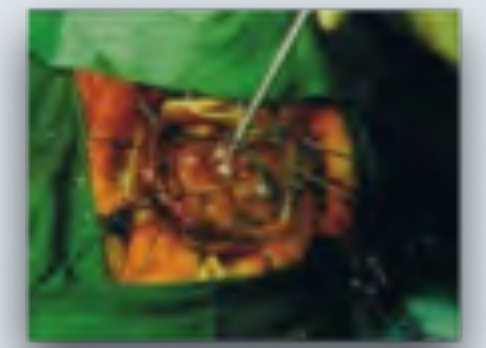
Data fitting

Develop patient charts

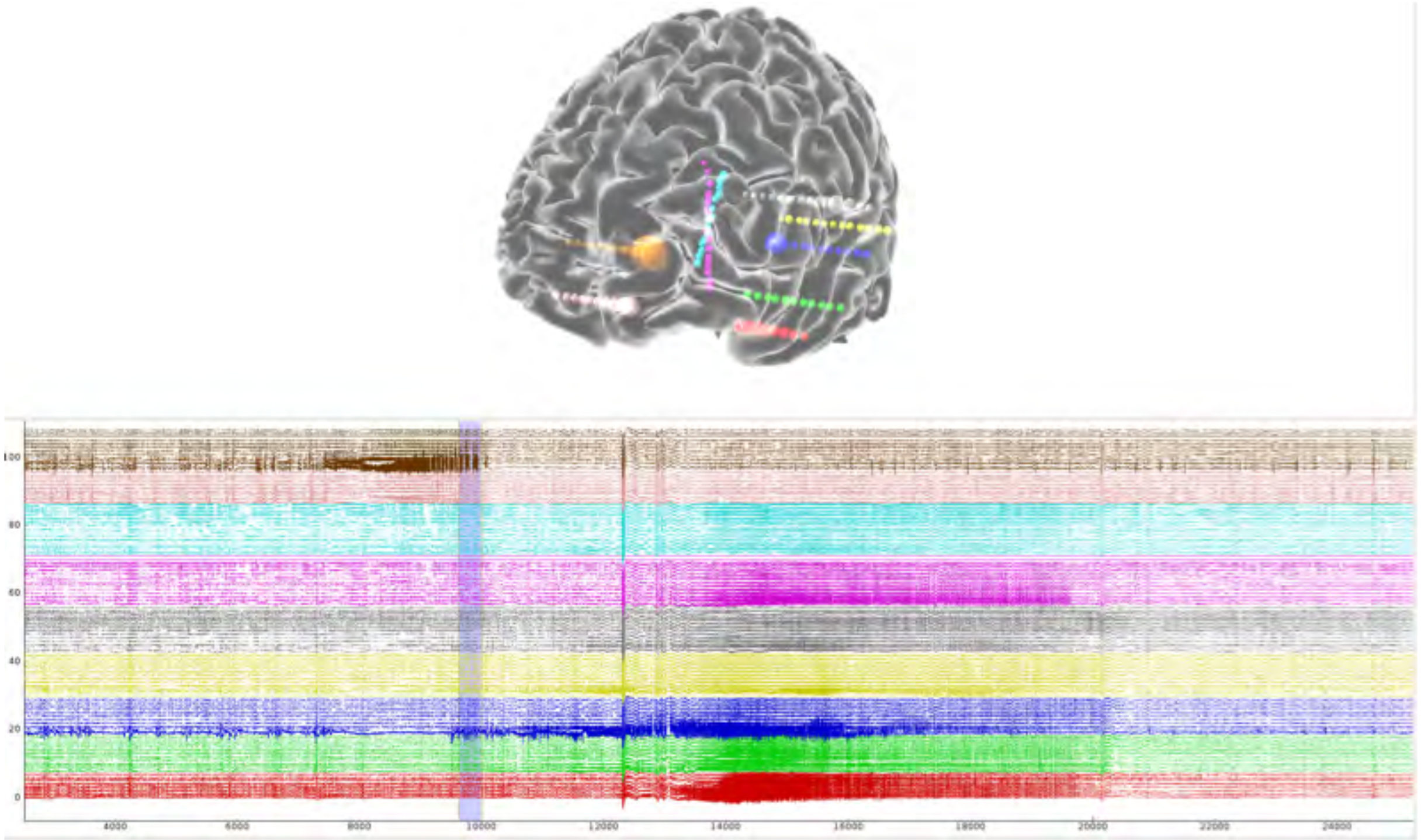


Parameter space exploration

Patient specific interventions

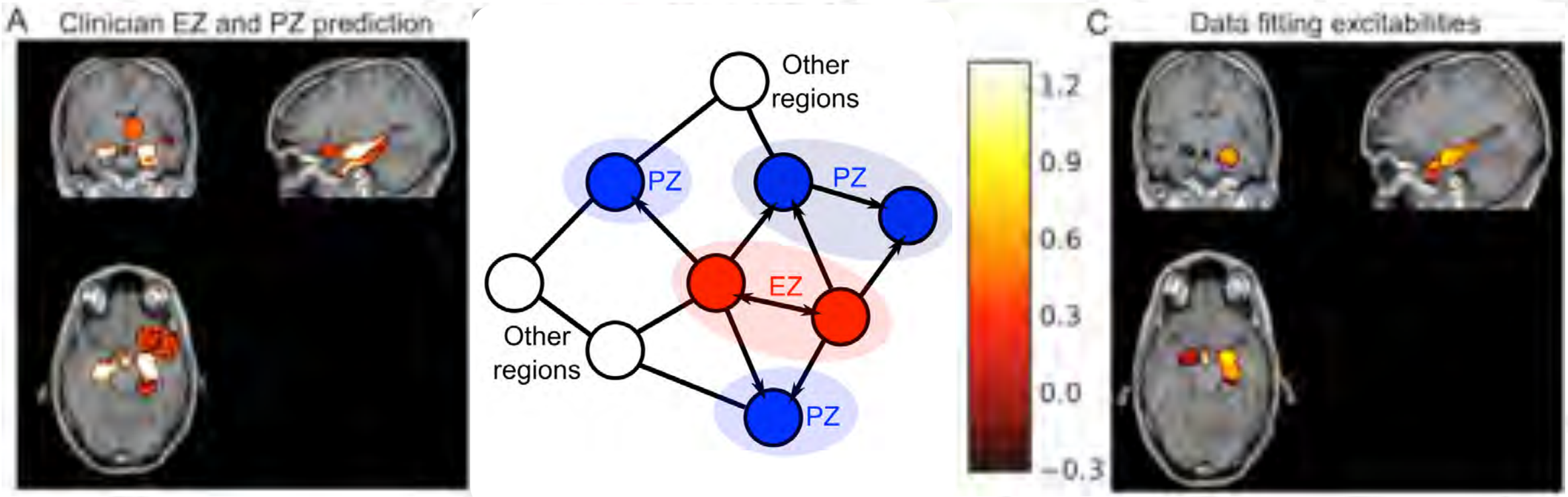


The patient: Complex partial seizure



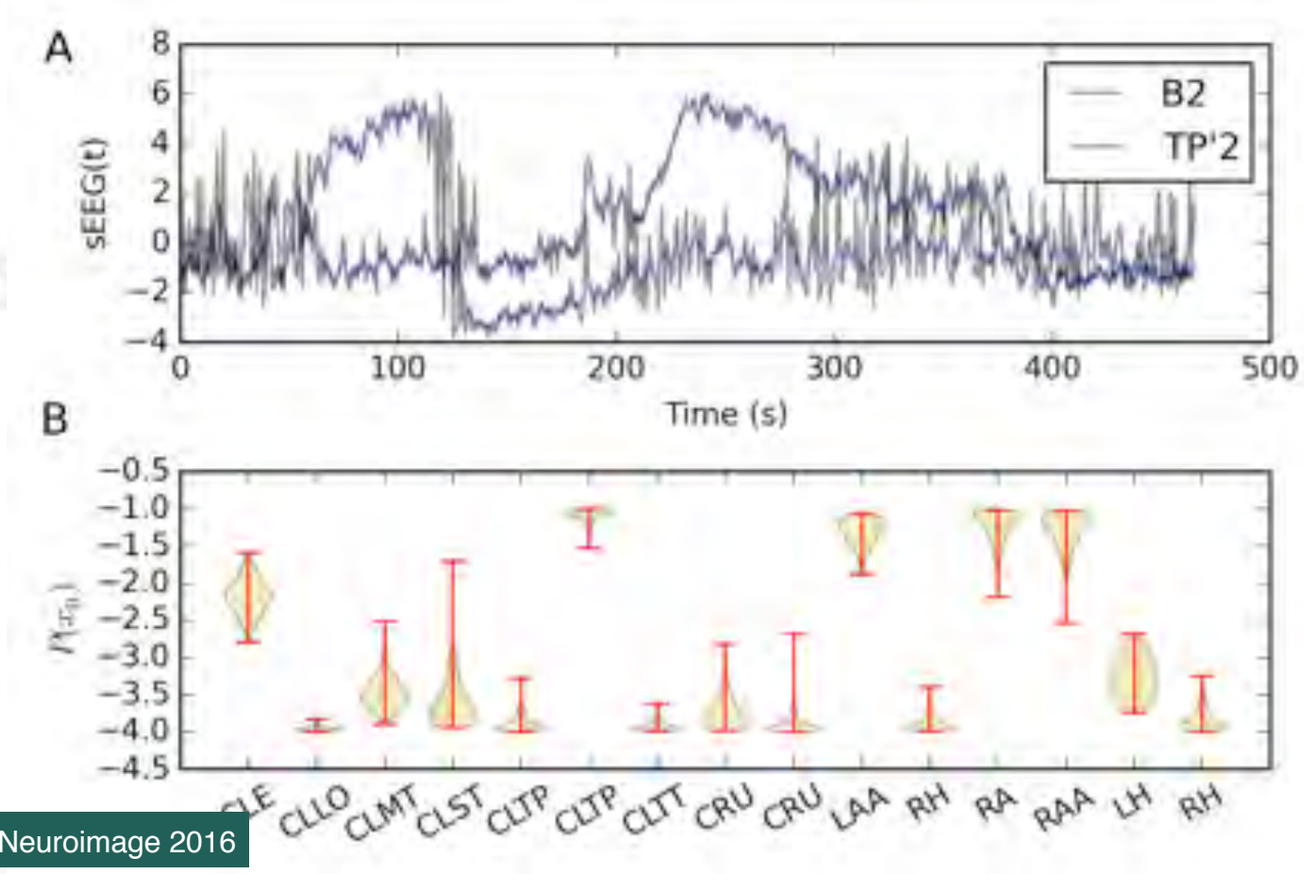
Jirsa et al. Neuroimage 2016

Finger printing: model inversion



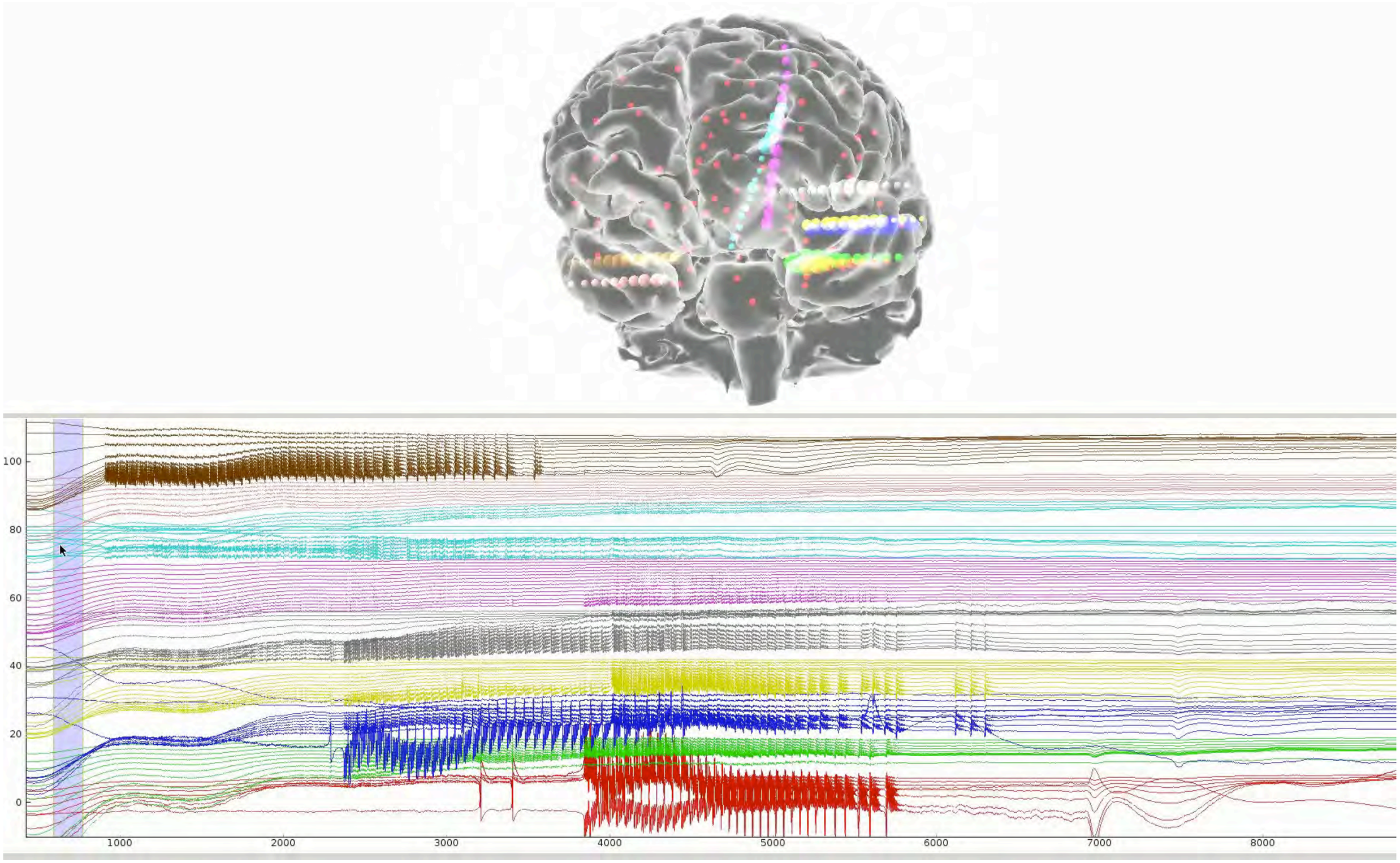
Model inversion using Bayesian inference framework

Hoffman & Gelman (2001)
Friston et al. (2003)



Jirsa et al. Neuroimage 2016

Simulation: Complex seizure – see it in action



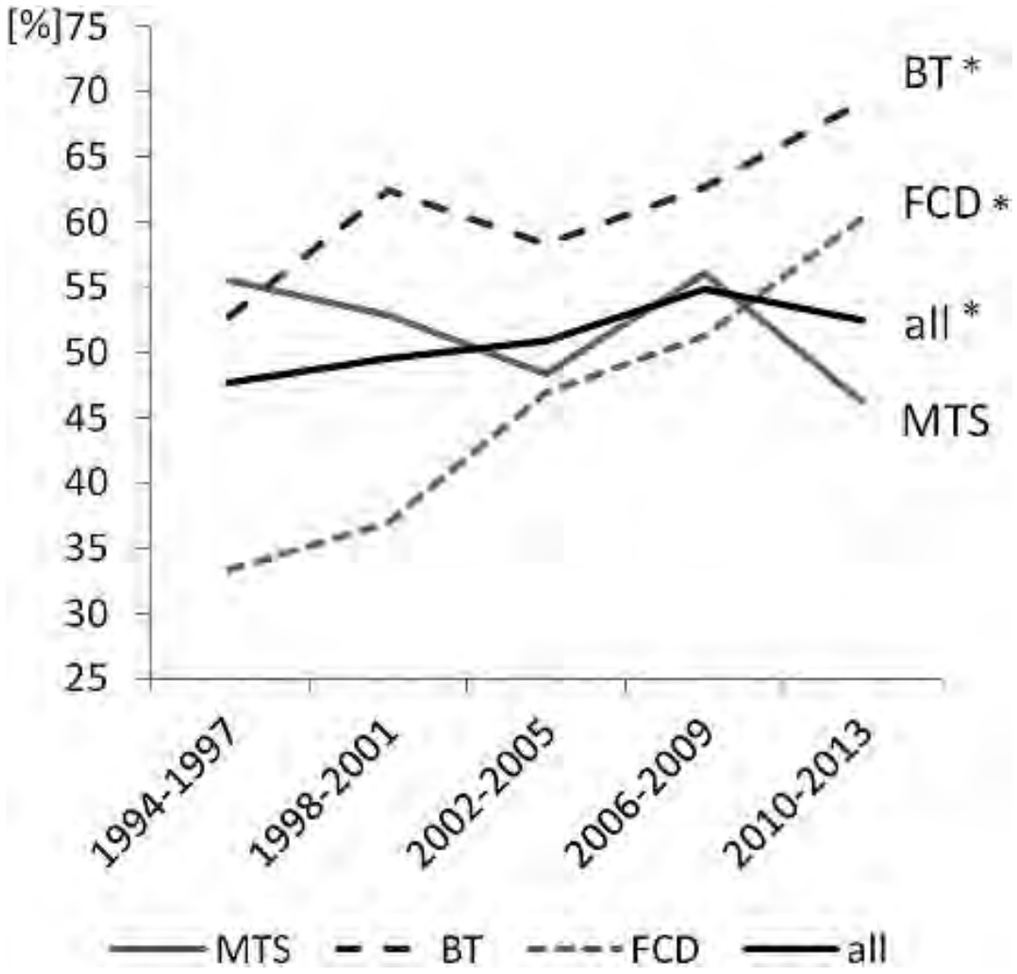
Jirsa et al. Neuroimage 2016

The virtual epileptic patient: validation for 15 patients

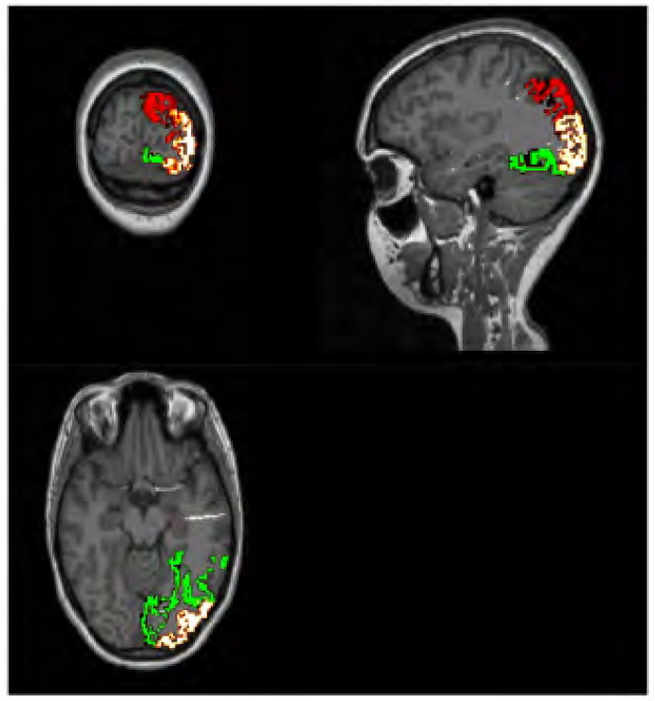
Postoperative surgery outcome over past 30 years

Engel score classifying postoperative outcomes for epilepsy surgery

Evolution of surgery success



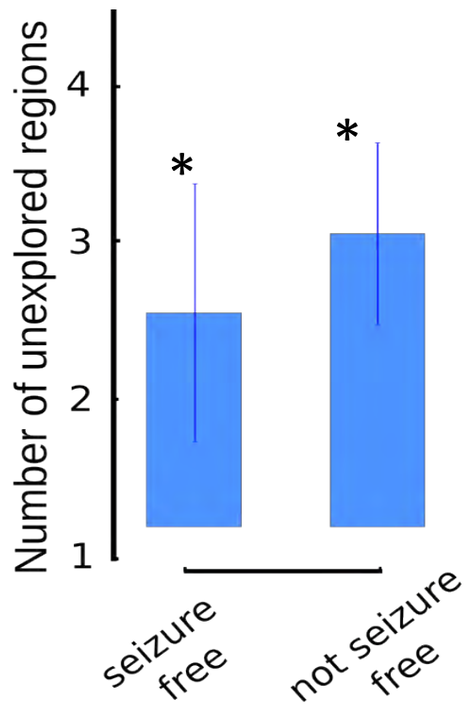
EZ prediction



Epileptogenic map

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

Engel score



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Thank you!

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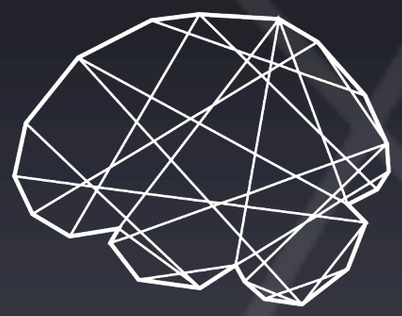

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