NODE #7 WORKSHOP

AUGUST 7-8, 2018 I MONTREAL, CANADA

A Generative Model of the Brain: Describing the building blocks of a brain network model

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THEVIRTUALBRAIN.

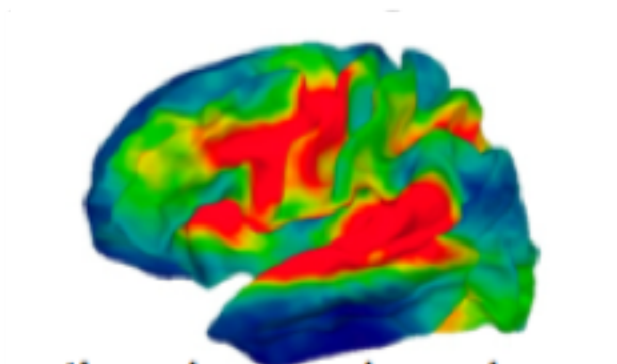
Outline

- Motivation for The Virtual Brain
- The Virtual Brain Platform
  - Architecture and access
  - Dynamics
  - Geometry & Connectivity
  - Simulations & Data Generation
- Examples

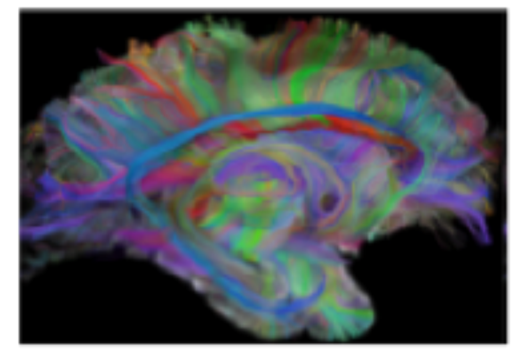
Brain Connectivity

Structure, dynamics and function

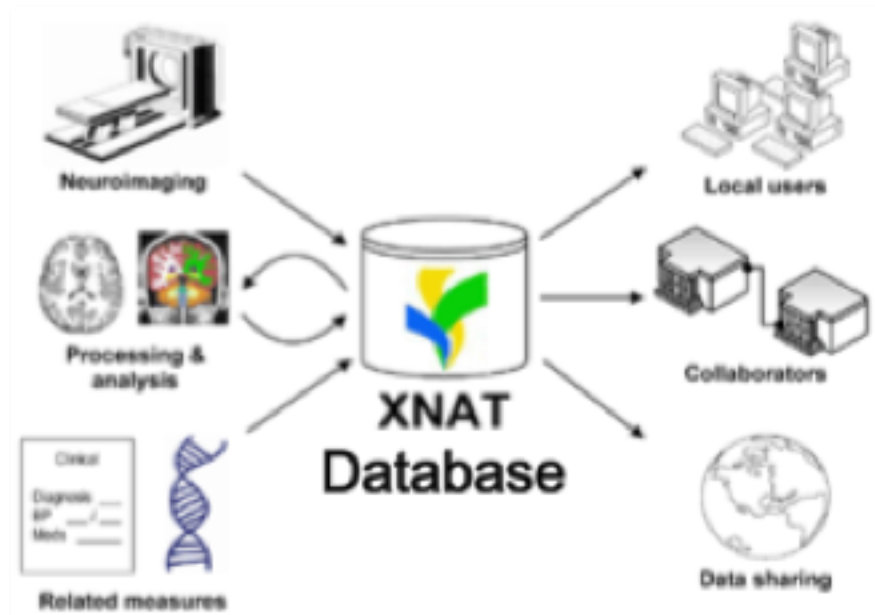
If the brain is a network, how do we study it?



Functional neuroimaging

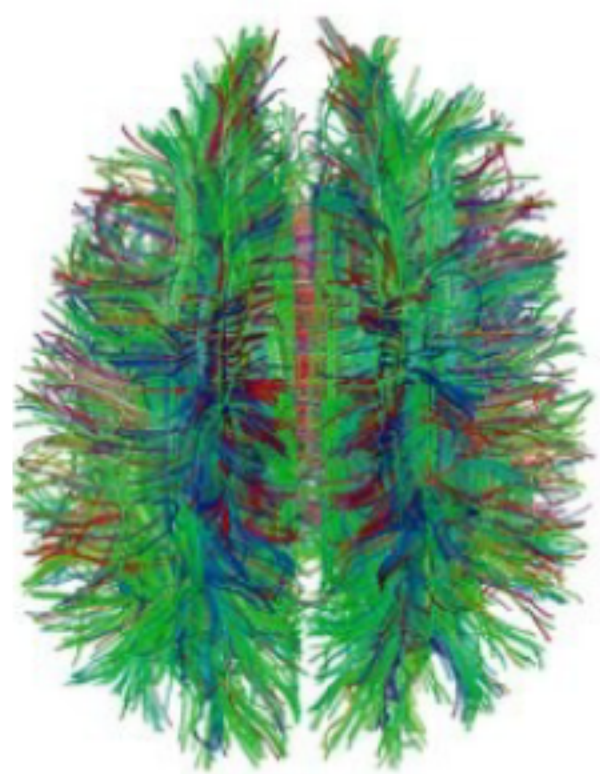


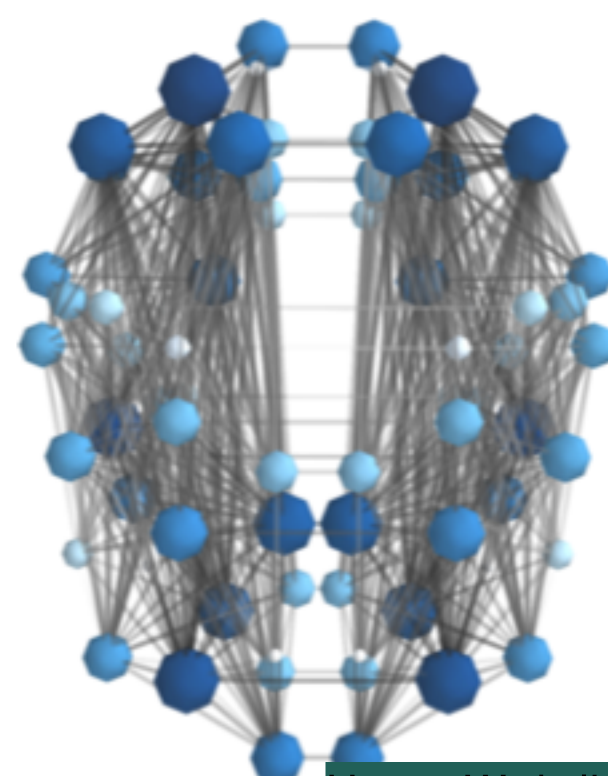
Structural neuroimaging



Neuroinformatics

Need for a large-scale network-based thinking

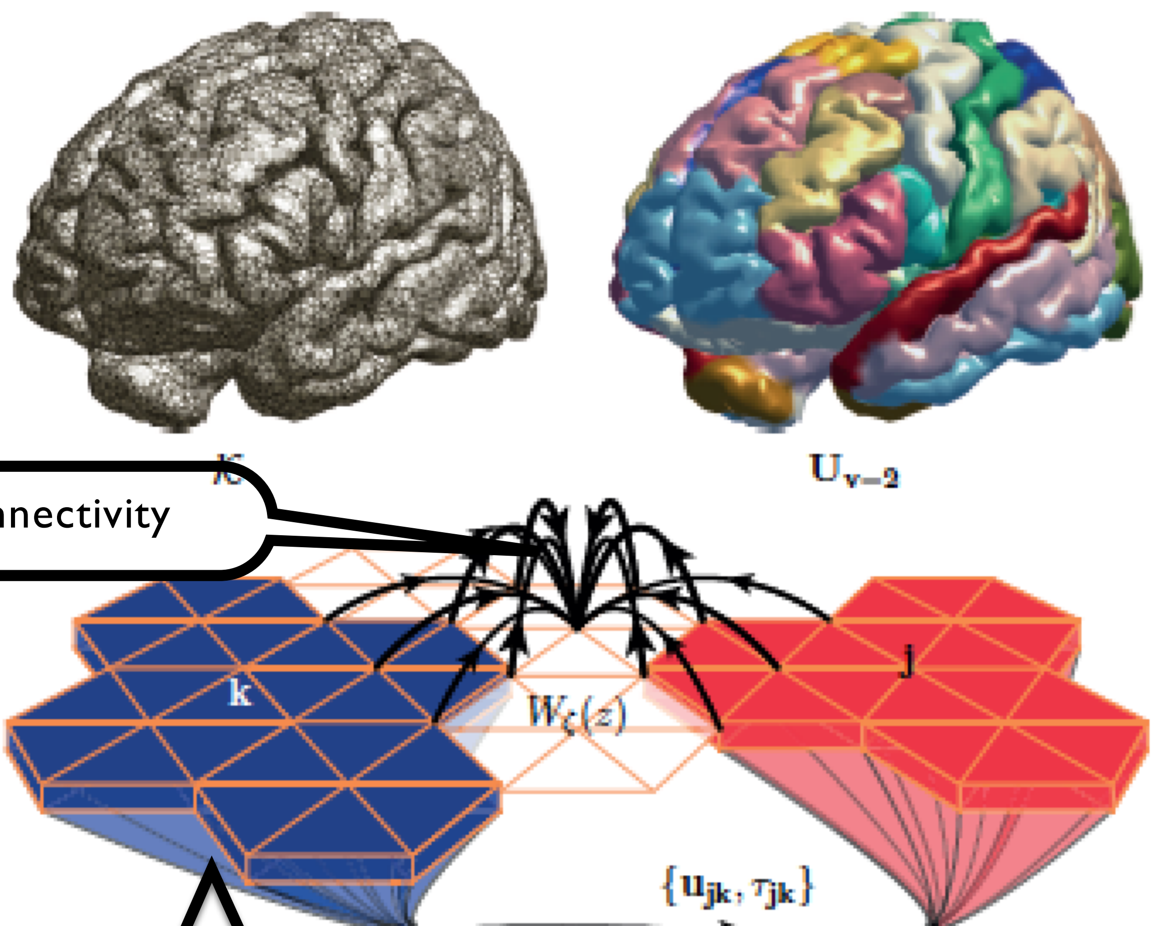




Ursus Wehrli «Kunst aufräumen»

Need for a large-scale network-based thinking

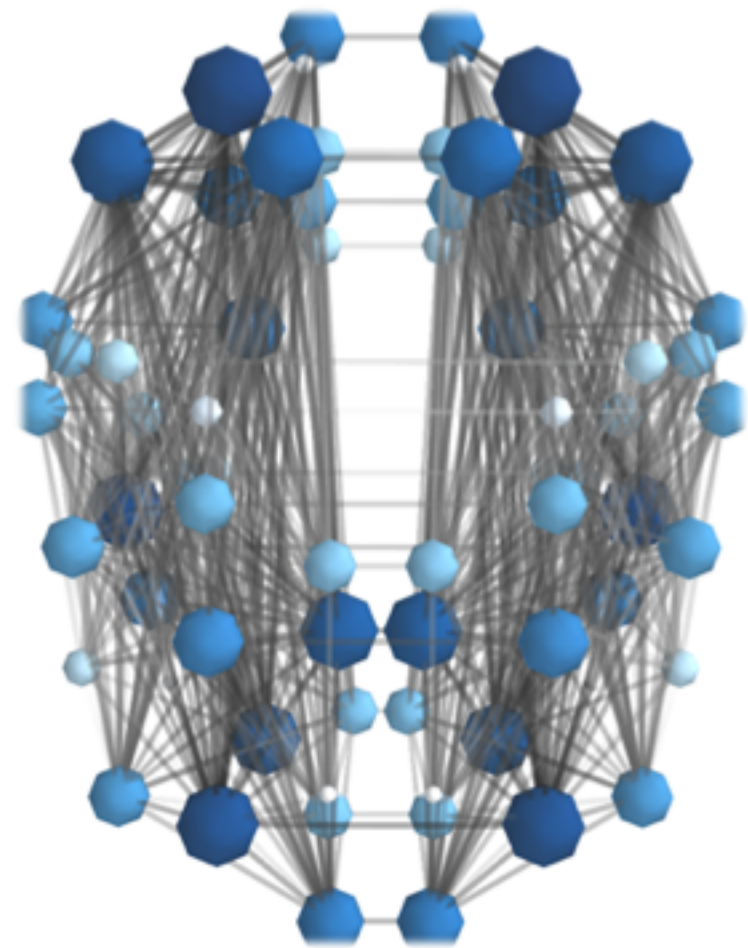
Large-scale brain networks



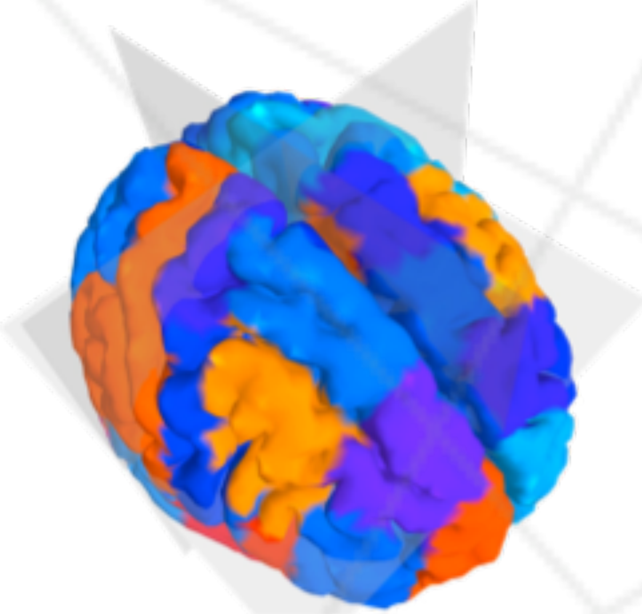
local connectivity

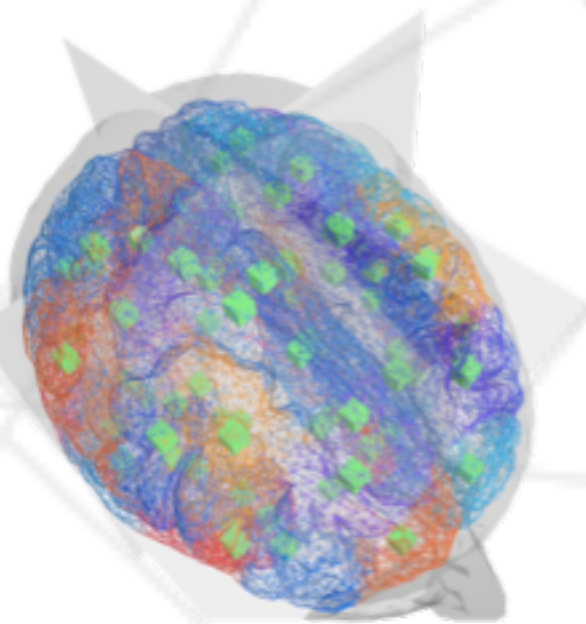
neural mass

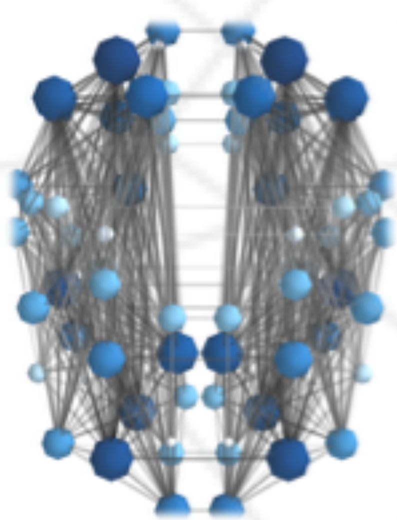
time delays via long range connections



Large-scale brain network modeling







Nunez 1974 Jirsa-Haken 1996, 1997, 1998	Homogeneous approximation/assumption
Robinson et al. 1997, 1998, 2001 Coombes 2010	First extensions to address inhomogeneity

Homogeneous

Jirsa & Kelso 2000	Two point connection
Jirsa et al 2002	Full brain system dynamics
Stephan, Kötter, et al 2000	Cocomac

Heterogeneous

Ghosh et al 2006, 2008	Cocomac based brain dynamics
Honey et al. 2007 Izhikevich et al 2008 Deco, Jirsa, et al 2009 Bojak et al 2009	DTI based full-brain dynamics "Resting state dynamics"
Deco, Jirsa & McIntosh 2011, 2013	Nature Neuroscience Review, TINS
Jirsa et al 2010; McIntosh et al. 2010	The Virtual Brain
Deco & Jirsa 2012 SfN 2012	Validation – resting state is critical TVB release

Connectome

Dominant strategies for modeling the brain

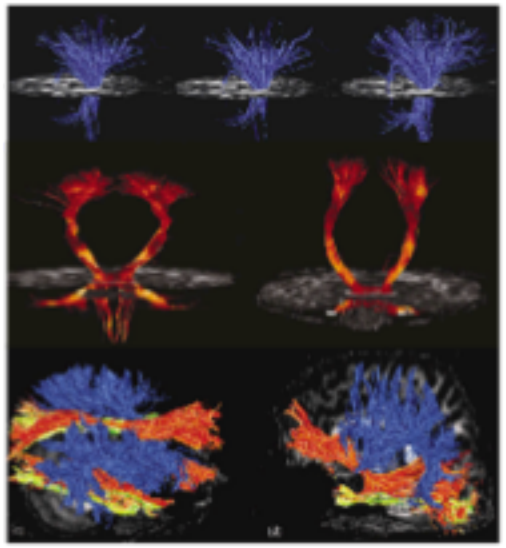
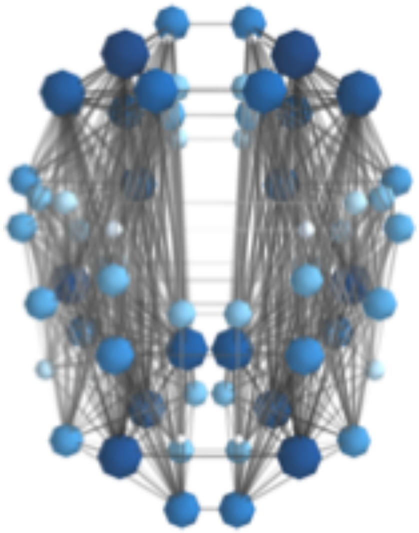
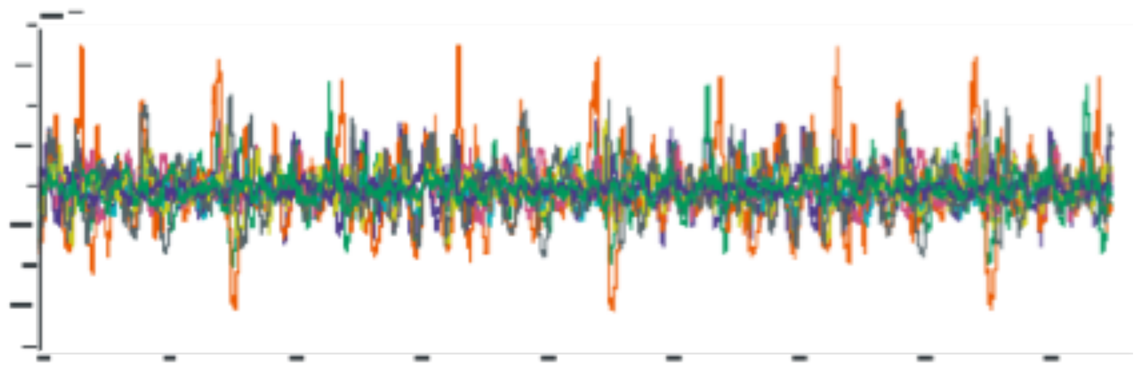
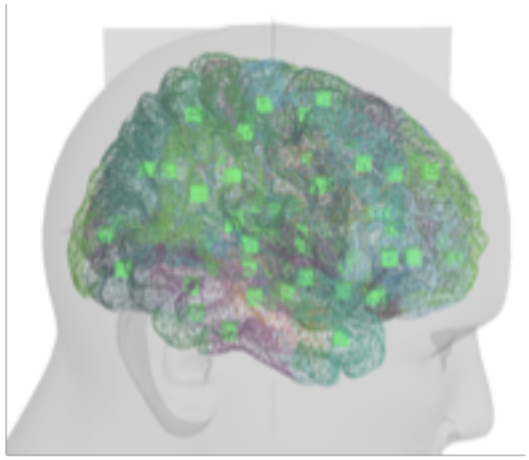
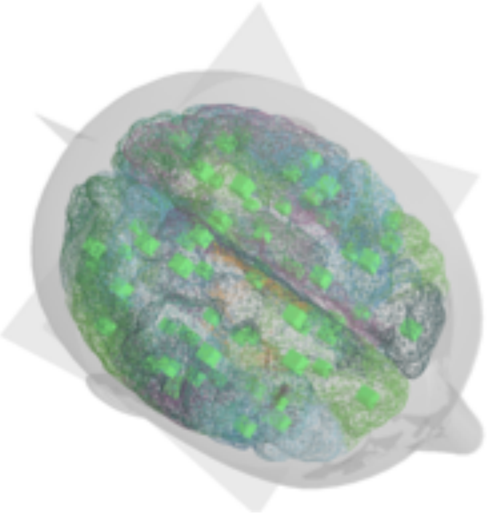
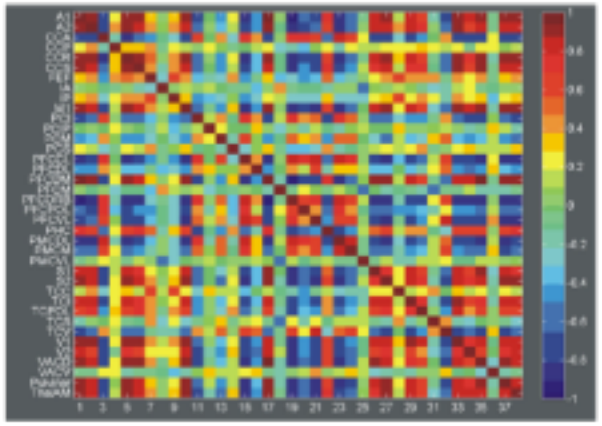
- Build a function and see if that’s how the brain does it
  - –Computer Science, Cognitive Models (PDP)
  - –Nengo/SPAUN
- Build a brain and see if it functions like a real one
  - –Human Brain Project (blue brain)
  - –The Virtual Brain

The software

Open source & ready to install

TVB: Synergy of competences

Structure	Function
Connectivity & geometry	Network dynamics & simulation


www.thevirtualbrain.org

Download: Windows, Mac, Linux

On-line Support

NEUROSCIENCE BRAINSIMULATOR NEWSWIRE TEAMWORK THEVIRTUALBRAIN.

- Software Downloads
- System Requirements
- Import & Export data
- Getting Help & Support
- Screenshots

Extensive support.
For scientists & developers.

Read the documentation

Discuss with peers

View the source code

Context-sensitive help & user guides

The software packages for The Virtual Brain contain **user guides** as PDF files (for users, developers and contributors). These can be found in the "docs" folder of the installation.

In the GUI, you can also use illustrated, **context-sensitive help** for entire sections or particular elements (e.g. variables for modeling parameters). The availability of context-sensitive help in the GUI is marked with a round "?" button.

Standard packages also contain a small set of **demo data** to play with.

Online documentation & tutorials

We offer a dedicated documentation website under → docs.thevirtualbrain.org. It covers almost every imaginable topic, from installation to step-by-step tutorials to developer guides for modifying and contributing code.

The documentation website also offers downloads for **bulky demo data sets** which are used in the online tutorials. These are a great start for new users to work with actual data.

Discussion forum and mailing list

If you have specific questions, also about how to use TVB for your current research activity, you can use our → public discussion forum, which doubles as a mailing list if you prefer this channel.

Talk with experts

We're happy to help you when your struggle with the TVB software. Please understand that we can't give programming lessons or scientific consulting.

For anything else like **errors** you encounter, **suggested improvements** or **feature requests**, we're eager to hear from you!

General TVB support

For general issues

On-Line Support

THEVIRTUALBRAIN.

Home | Install | Tutorials | Demos | Gui Guide | Console Guide | Developers | next | modules | index

Overview of *TheVirtualBrain*

TheVirtualBrain is a framework for the simulation of the dynamics of large-scale brain networks with biologically realistic connectivity. *TheVirtualBrain* uses tractographic data (DTI/DSI) to generate connectivity matrices and build cortical and subcortical brain networks. The connectivity matrix defines the connection strengths and time delays via signal transmission between all network nodes. Various neural mass models are available in the repertoire of *TheVirtualBrain* and define the dynamics of a network node. Together, the neural mass models at the network nodes and the connectivity matrix define **the Virtual Brain**. *TheVirtualBrain* simulates and generates the time courses of various forms of neural activity including Local Field Potentials (LFP) and firing rate, as well as brain imaging data such as EEG, MEG and BOLD activations as observed in fMRI.

TheVirtualBrain is foremost a scientific simulation platform and provides all means necessary to generate, manipulate and visualize connectivity and network dynamics. In addition, *TheVirtualBrain* comprises a set of classical time series analysis tools, structural and functional connectivity analysis tools, as well as parameter exploration facilities by launching parallel simulations on a cluster.

Download

To download it, check out the TVB download site.

To get in touch with other users and developers, please head over to the mailing list.

Some more documents and artefacts for TVB can be found in this share area (e.g. documentation from TVB Node# meetings, some team pictures).

We are grateful to

- our contributors (check their names on GitHub)
- our sponsors (check their names on the our sponsors page
- all 3rd party tools that we used (licenses are also included in TVB_Distribution)
- JetBrains for PyCharm IDE
- Hudson team for their continuous integration tool
- Atlassian company for Jira software
- and to you for reading these :-)

python™ Atlassian JIRA PyCharm SUBVERSION GitHub Hudson

Table Of Contents

Next topic

Installing the Application

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Enter search terms or a module, class or function name.

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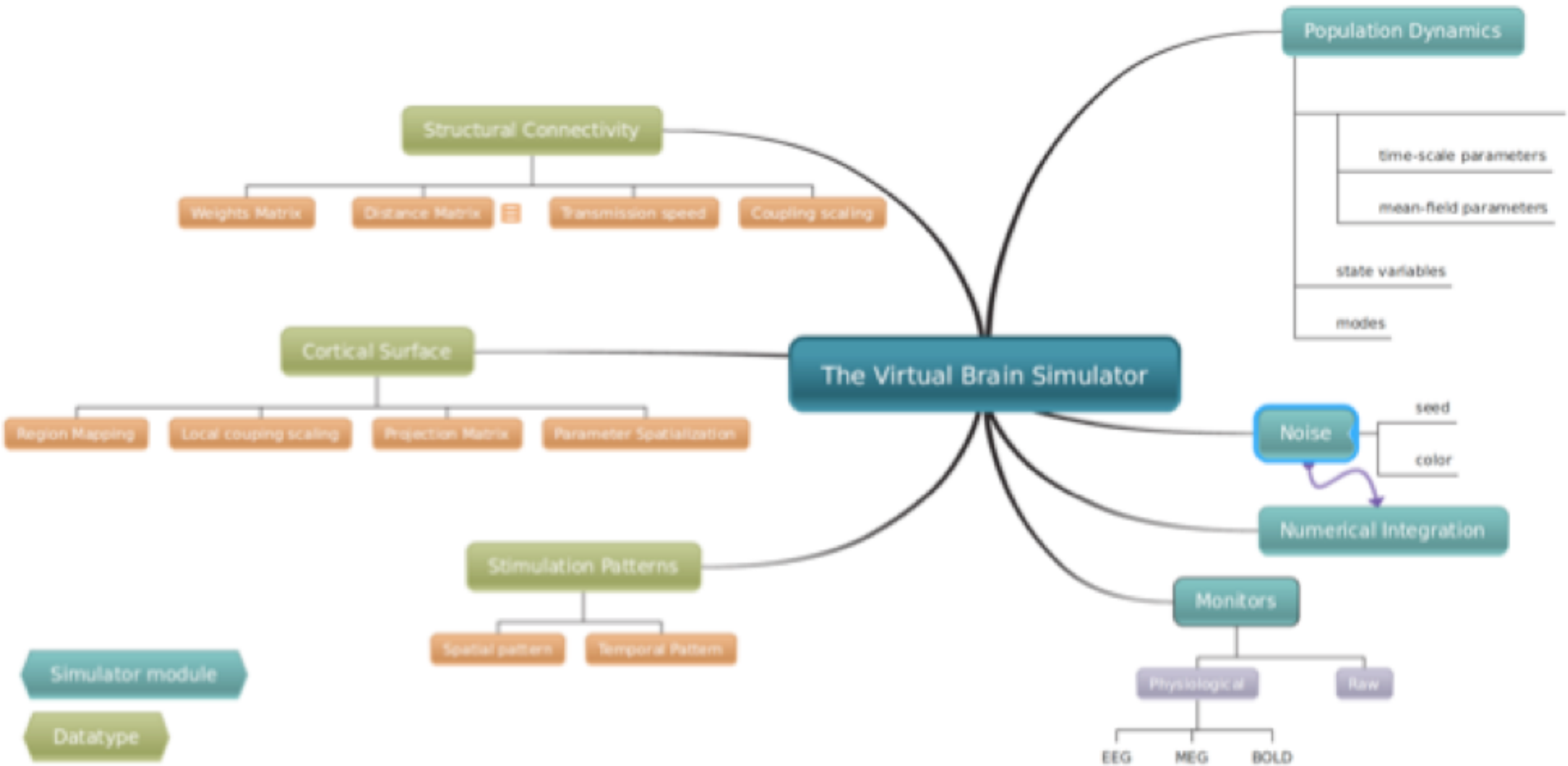
TVB: The system architecture



Written in Python	Scales from laptop to cluster
Open Source GPLv2	Highly modular
On GitHub	Runs on Windows, Mac, Linux

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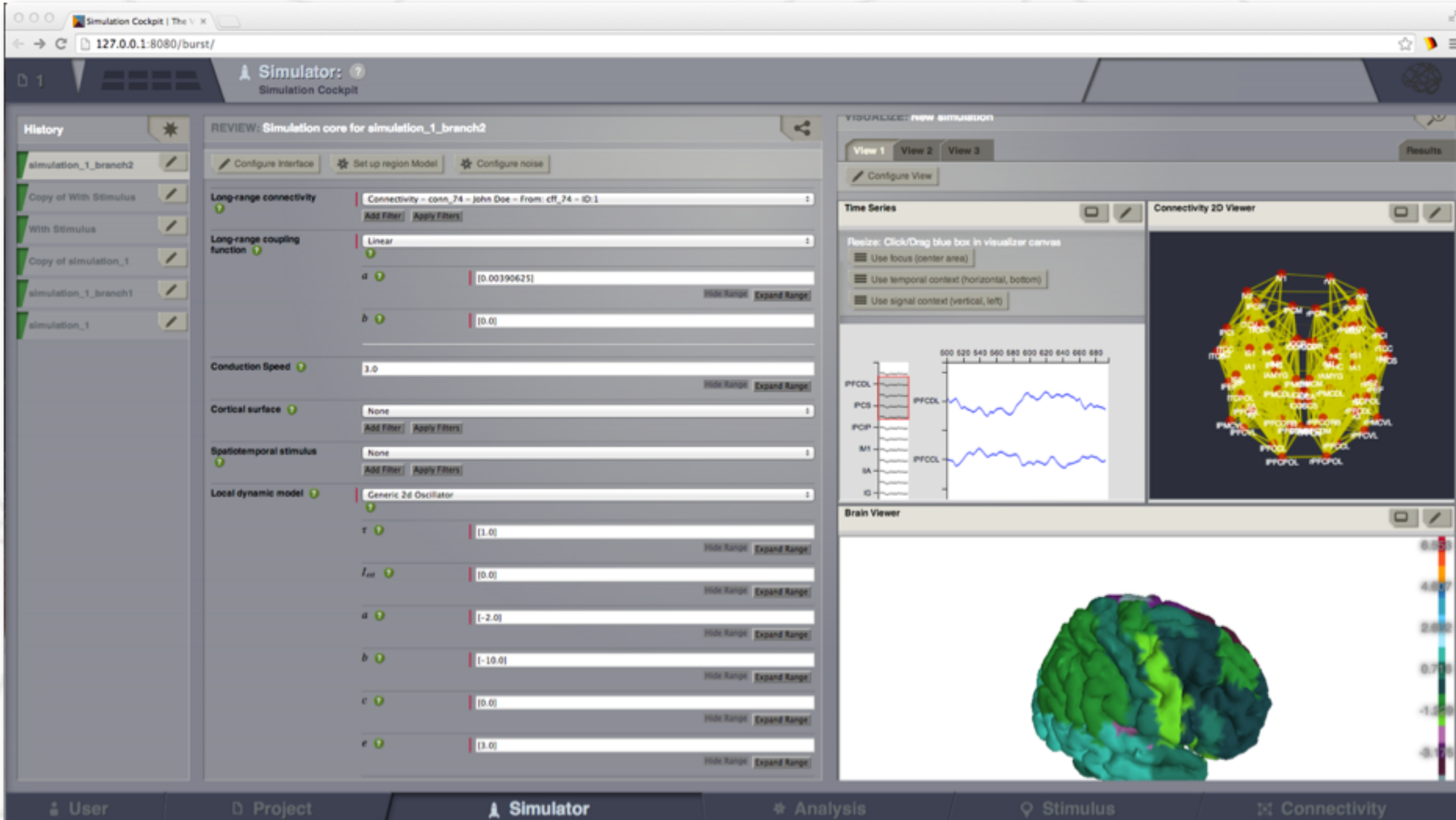
The software

Quick Tour



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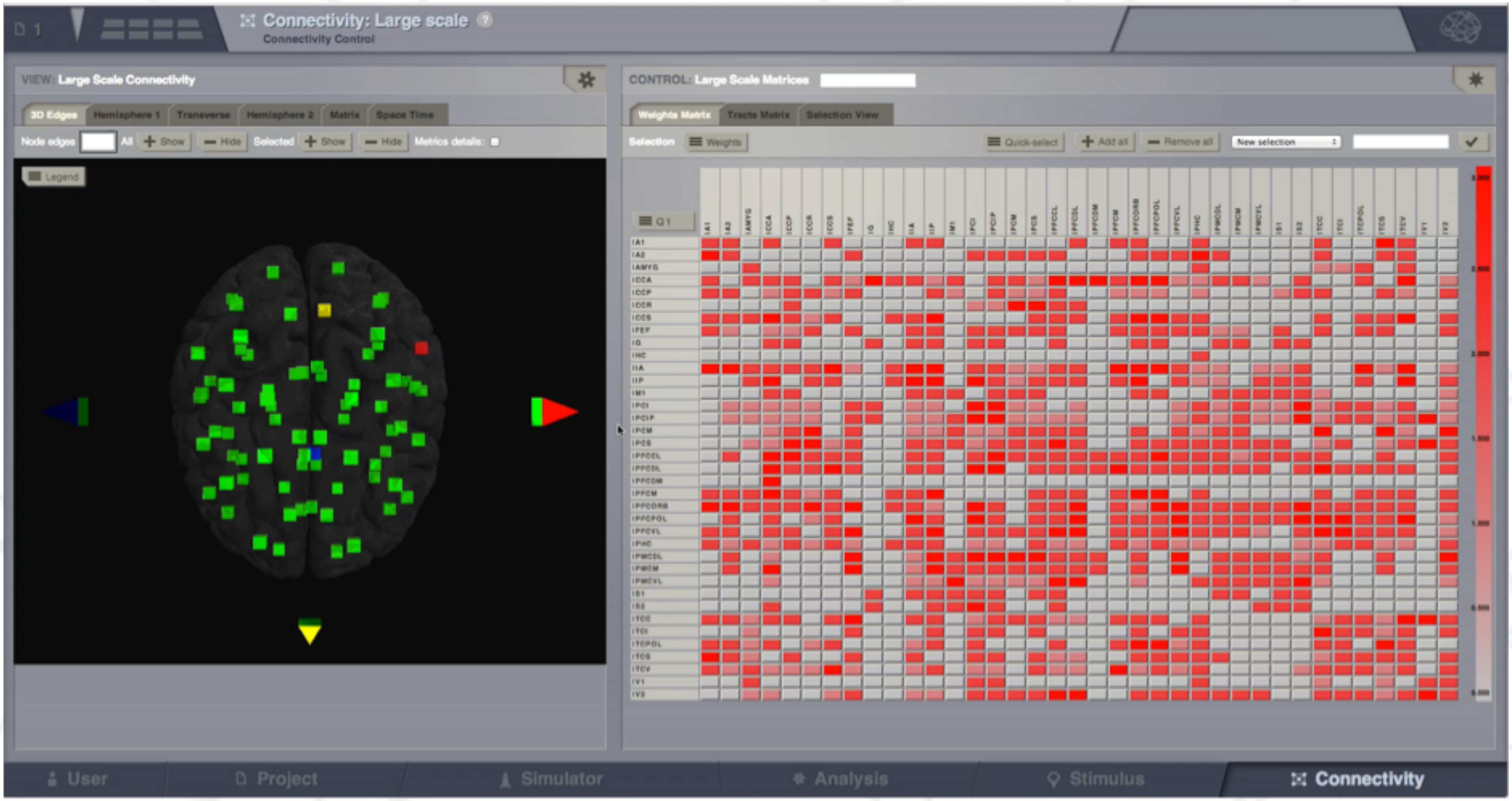

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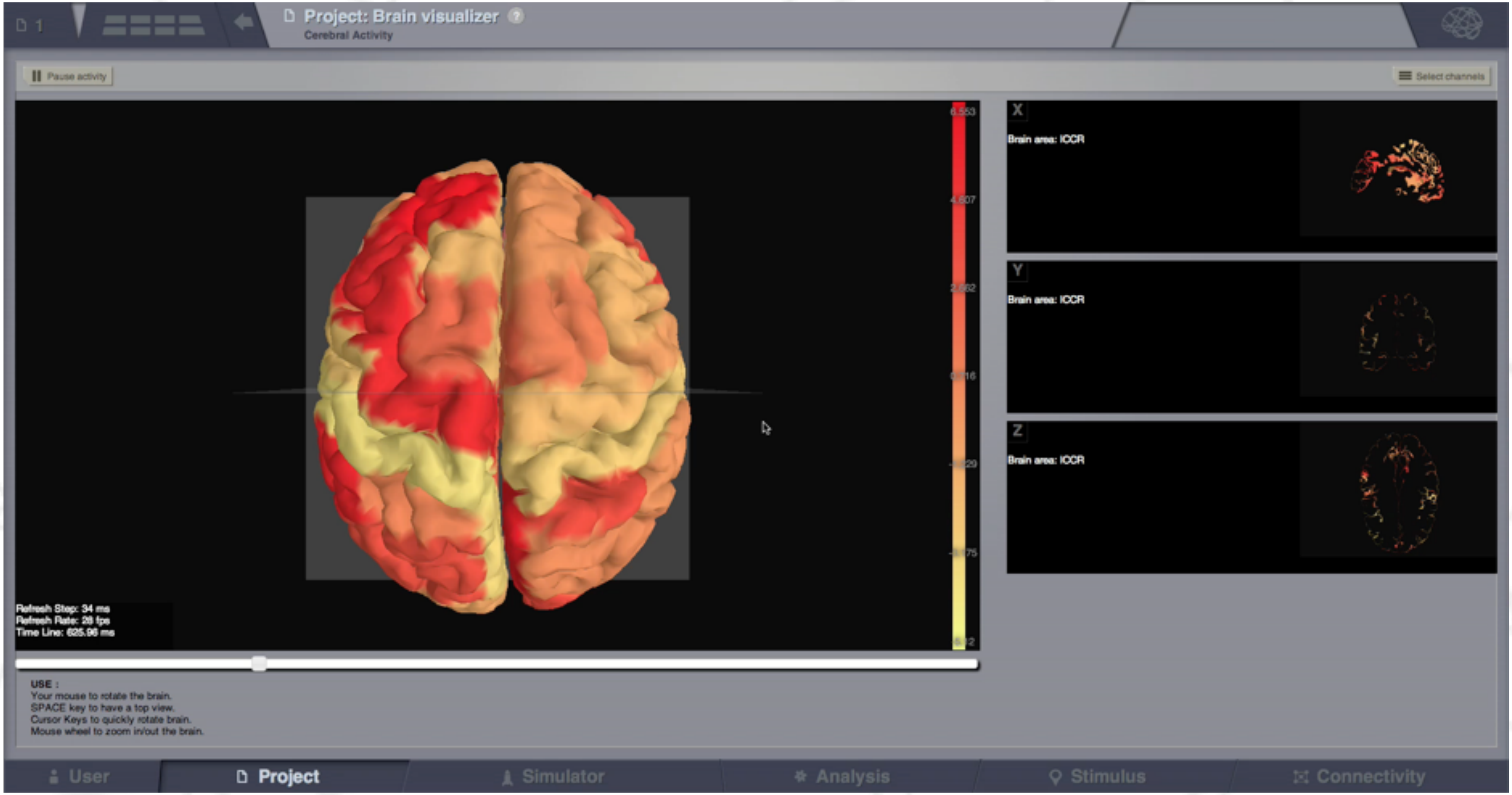

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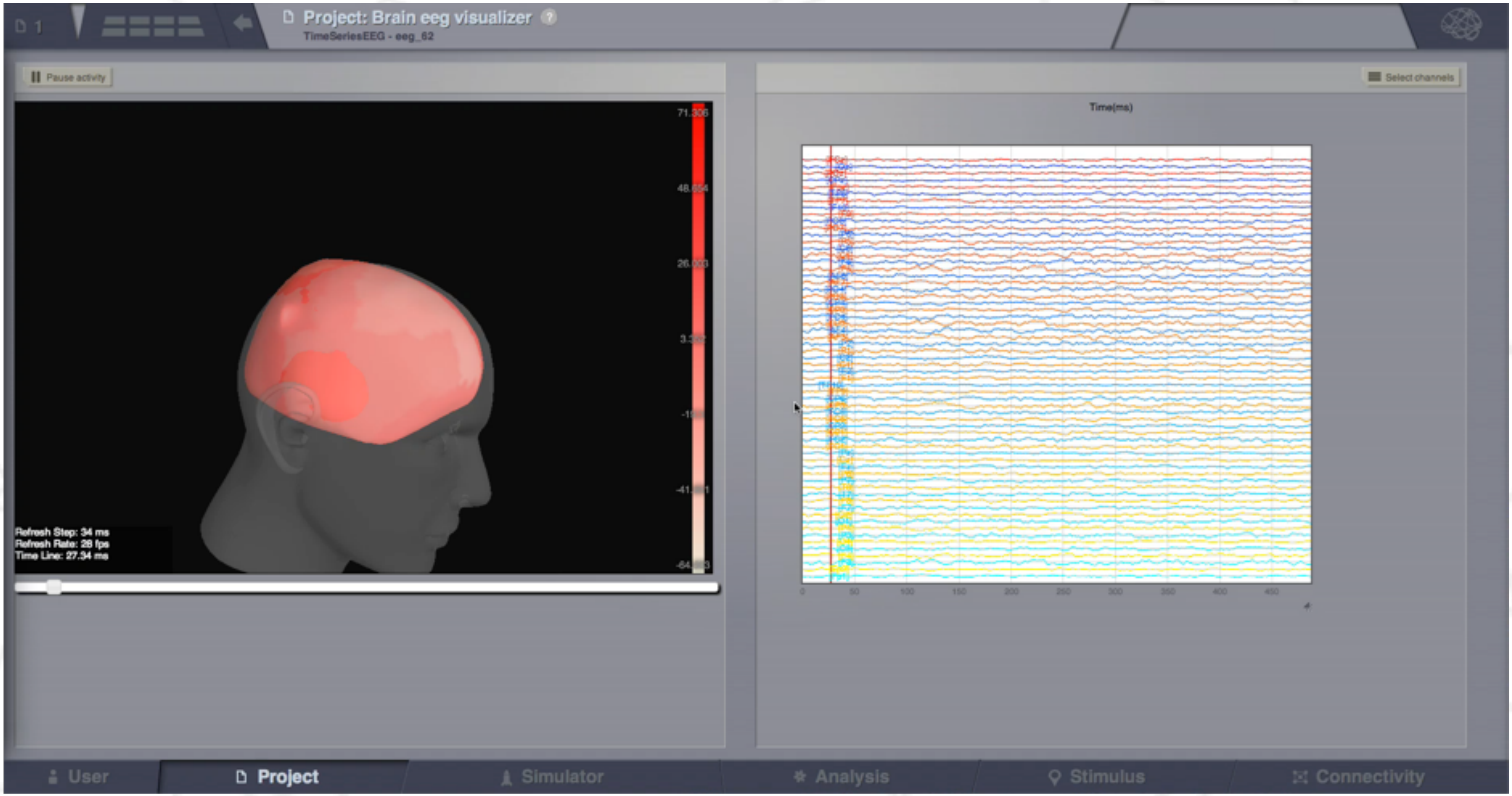

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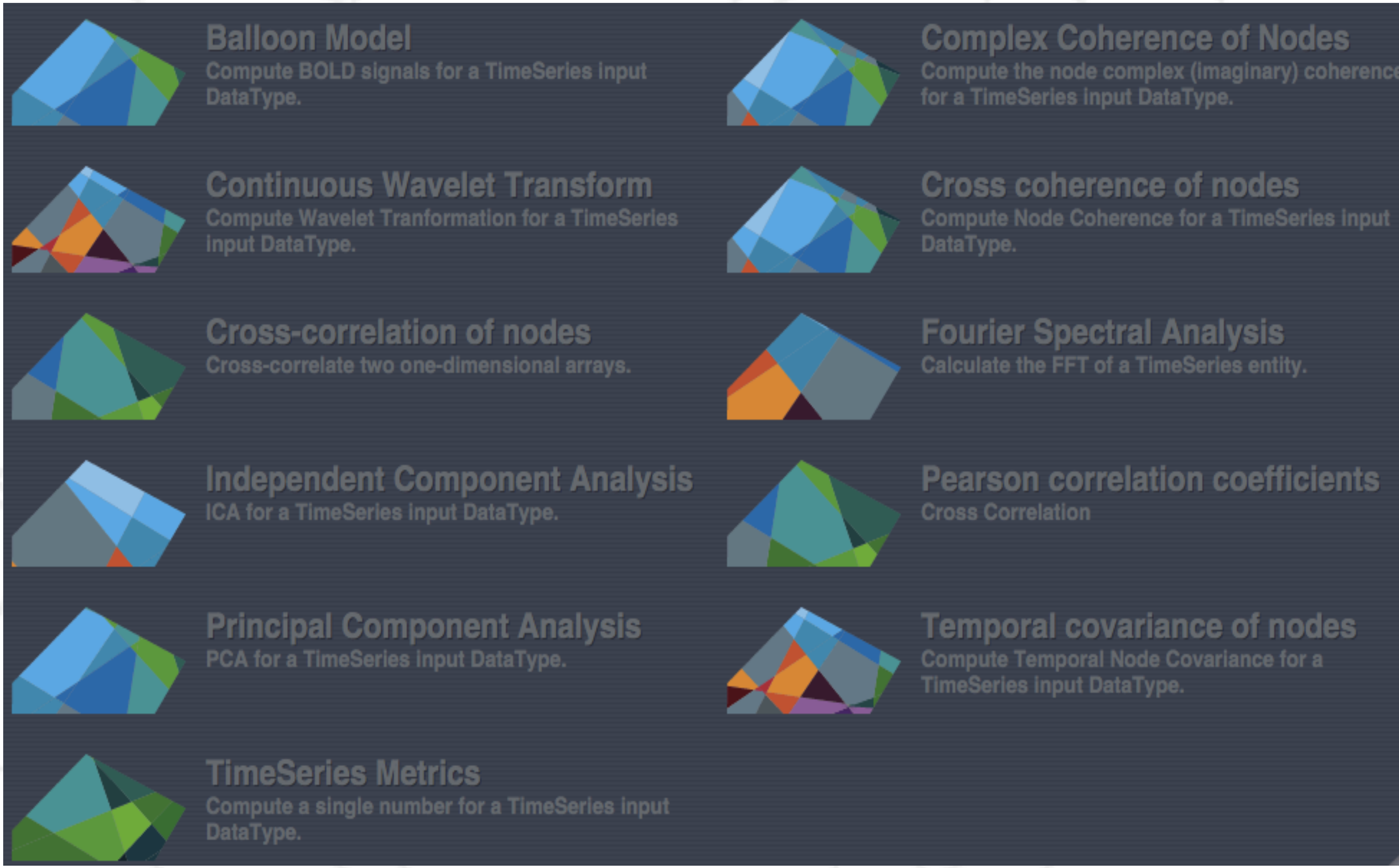
Analysis


Balloon Model
Compute BOLD signals for a TimeSeries input DataType.
Complex Coherence of Nodes
Compute the node complex (imaginary) coherence for a TimeSeries input DataType.
Continuous Wavelet Transform
Compute Wavelet Tranformation for a TimeSeries input DataType.
Cross coherence of nodes
Compute Node Coherence for a TimeSeries input DataType.
Cross-correlation of nodes
Cross-correlate two one-dimensional arrays.
Fourier Spectral Analysis
Calculate the FFT of a TimeSeries entity.
Independent Component Analysis
ICA for a TimeSeries input DataType.
Pearson correlation coefficients
Cross Correlation
Principal Component Analysis
PCA for a TimeSeries input DataType.
Temporal covariance of nodes
Compute Temporal Node Covariance for a TimeSeries input DataType.
TimeSeries Metrics
Compute a single number for a TimeSeries input DataType.

Neural mass models in TVB

Neural populations and fields...

Not in TVB

Cellular models

Hodgkin-Huxley

Morris-Lécar

In TVB

Local Field Potential, synaptic activity

Stefanescu-Jirsa 2D

Stefanescu-Jirsa 3D

Wong-Wang

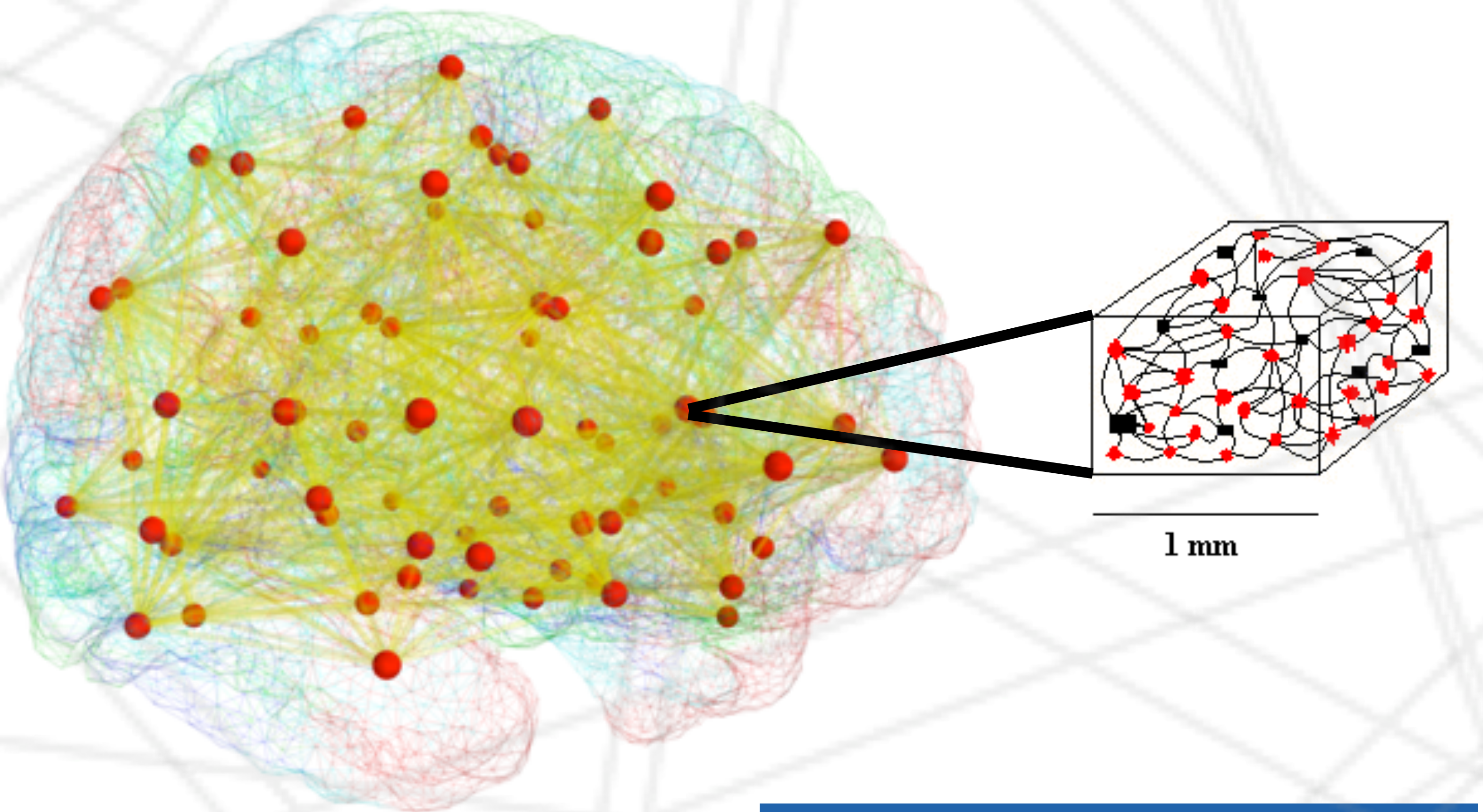
Firing rate

Wilson-Cowan

Brunel-Wang

Jansen-Rit

All models can be described by nonlinear dynamic systems via differential equations



Phenomenological

Generic 2D

Kuramoto

Epileptor

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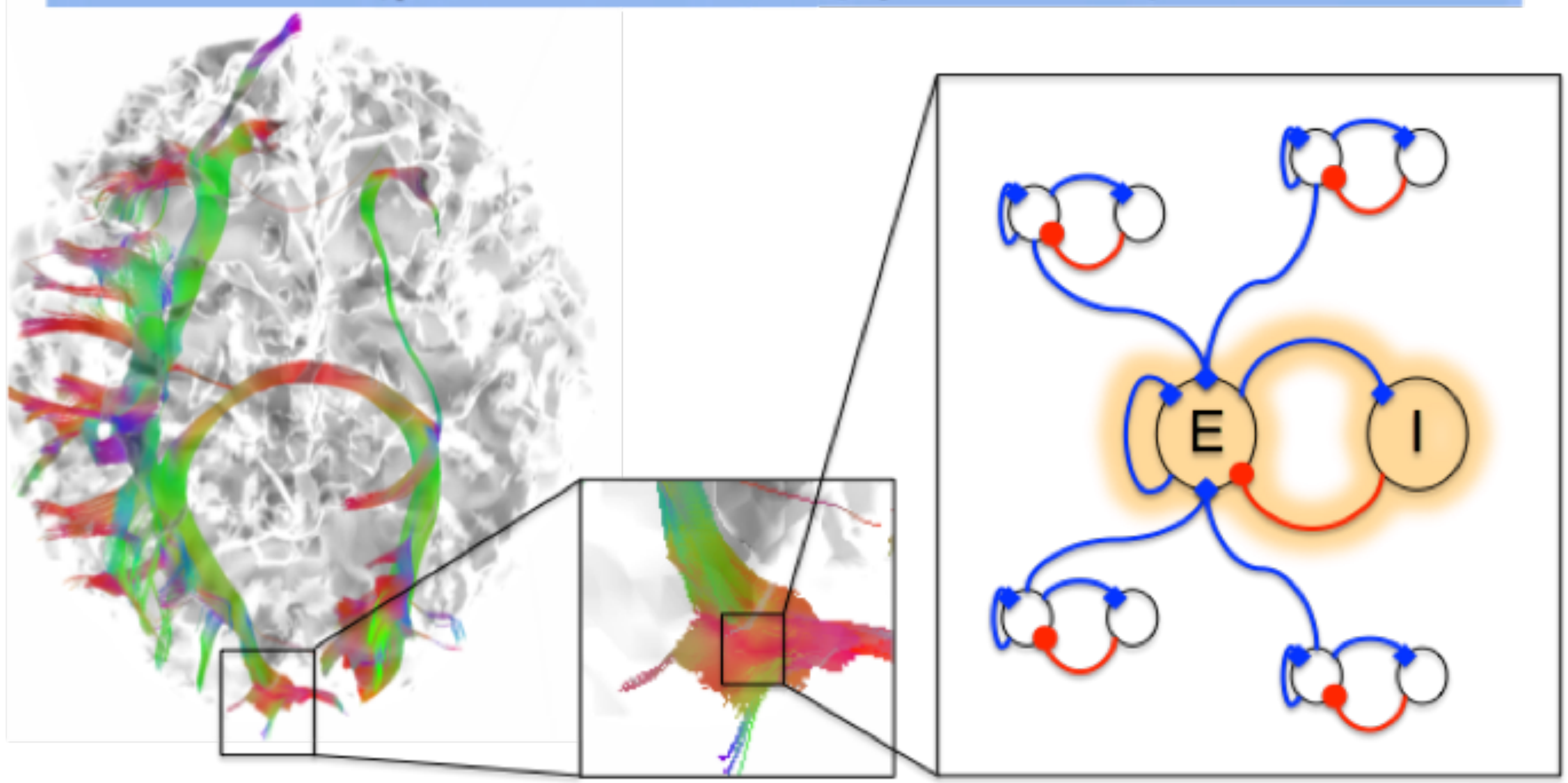
Large-scale equation for The Virtual Brain

$$\dot{\Psi}(x,t) = \overbrace{N(\Psi(x,t))}^{\text{Population activity}} + \overbrace{\int_\Gamma g_{local}(x,x')S(\Psi(x',t))dx'}^{\text{Short range input}} + \overbrace{\int_\Gamma g_{global}S(\Psi(x',t-\frac{|x-x'|}{v}))dx'}^{\text{Long range input}} + I(x,t) + \xi(x,t)$$



Evolution equation

$$\boxed{\frac{dx_i(t)}{dt}} = \boxed{N}(\boxed{x_i(t)}) + \boxed{G}\sum_j \boxed{SC_{ij}} x_j(t - \boxed{d_{ij}^{glob}}) + L\sum_j \boxed{LC_{ij}} x_j(t - d_{ij}^{loc}) + \boxed{I_i(t)} + \boxed{v_i(t)}$$

Differential operator that maps the system of equations into its derivatives

State operator for each neural mass i (i.e. neural mass model).

Vector of state variables for each region i, e.g., synaptic activity, firing rates, mean field, ...

Global coupling scaling factor

Structural connectivity matrix (global coupling)

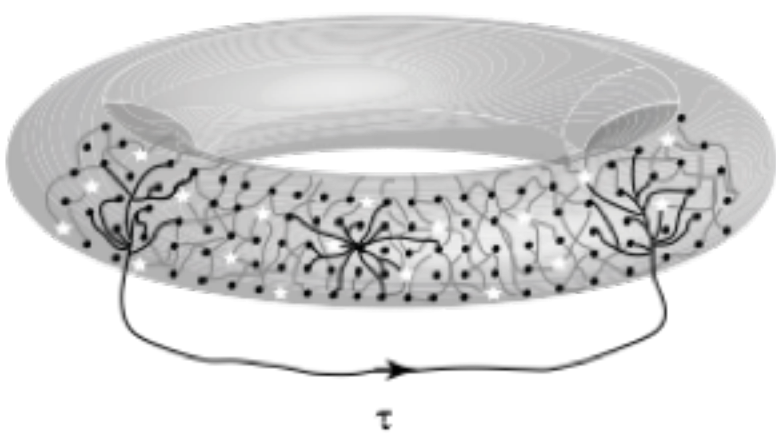
Time delays

Local connectivity

Injected input

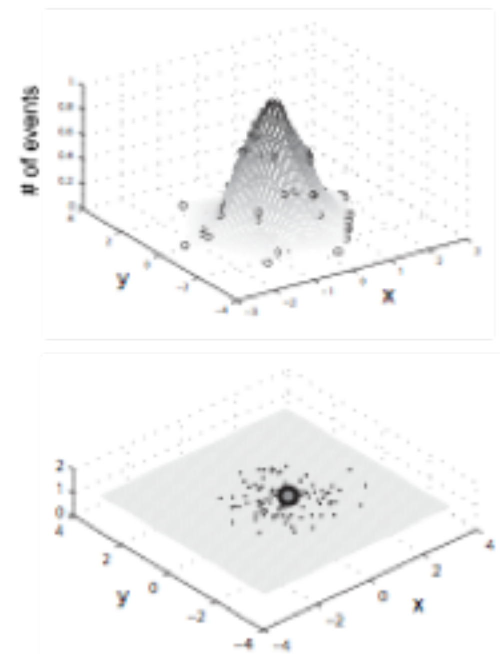
Noise

A

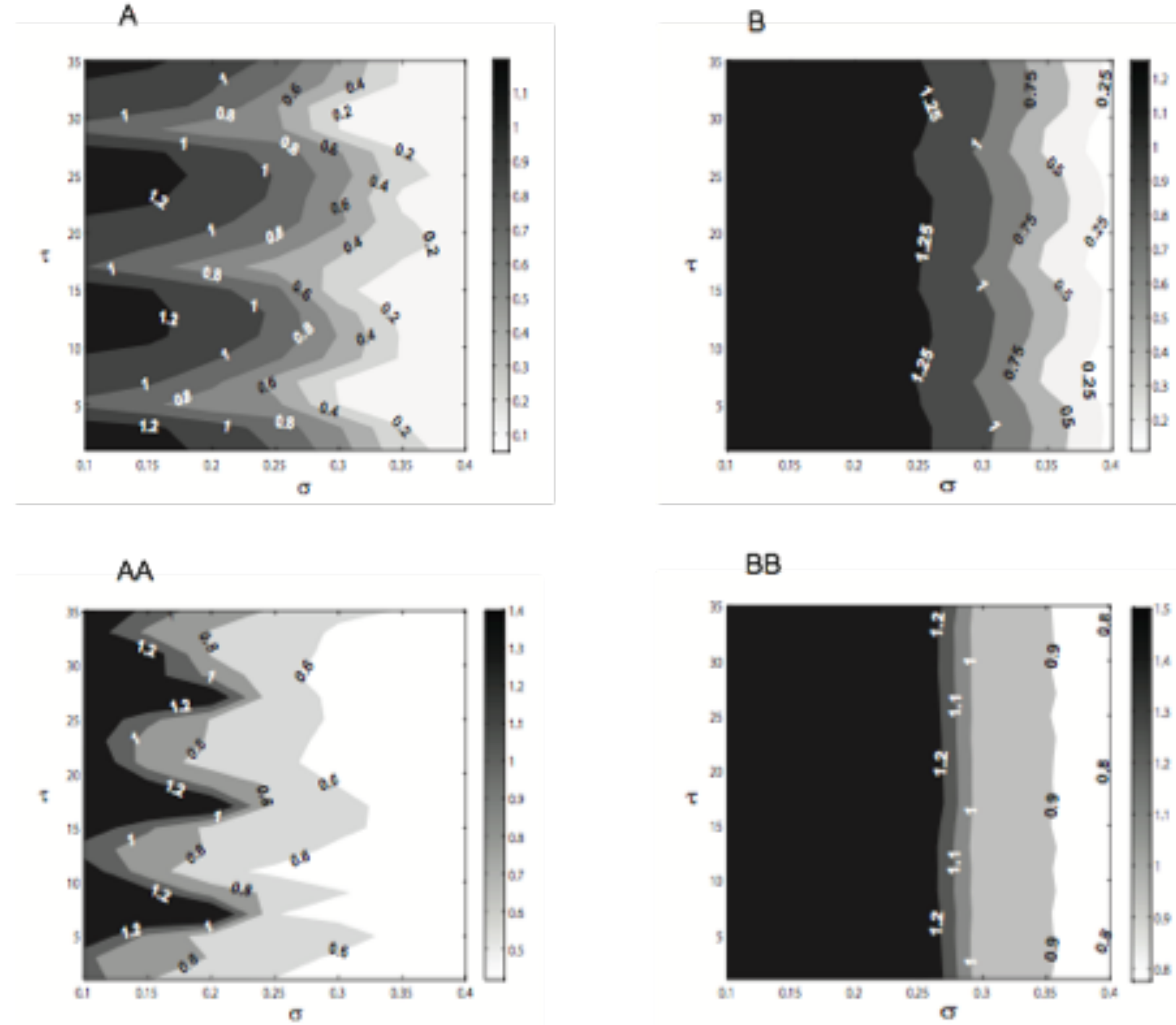


☆ - inhibitory neuron ● - excitatory neuron

B

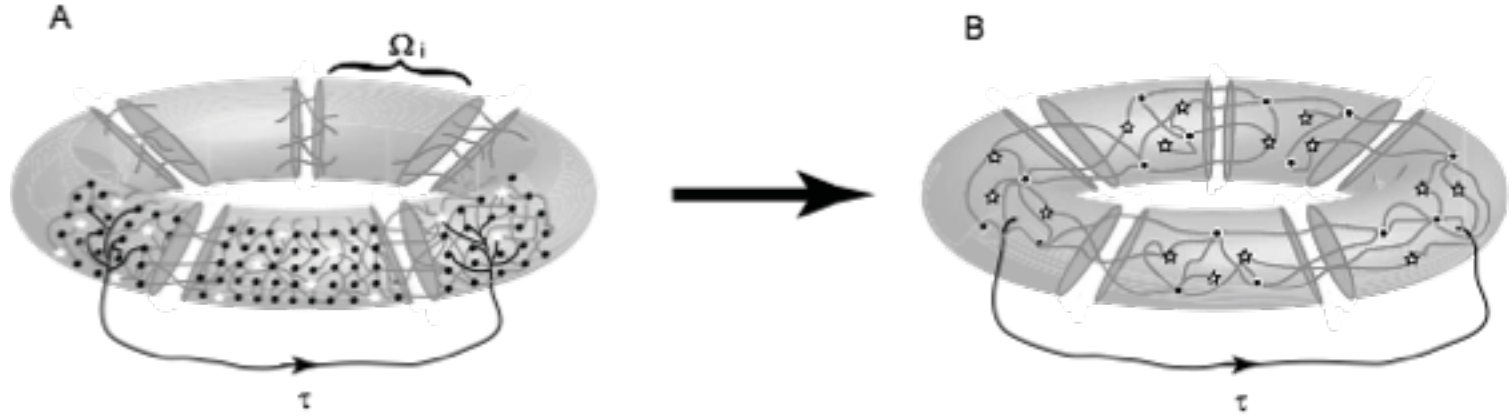


Full model Reduced model



A B

Full model



Reduced model

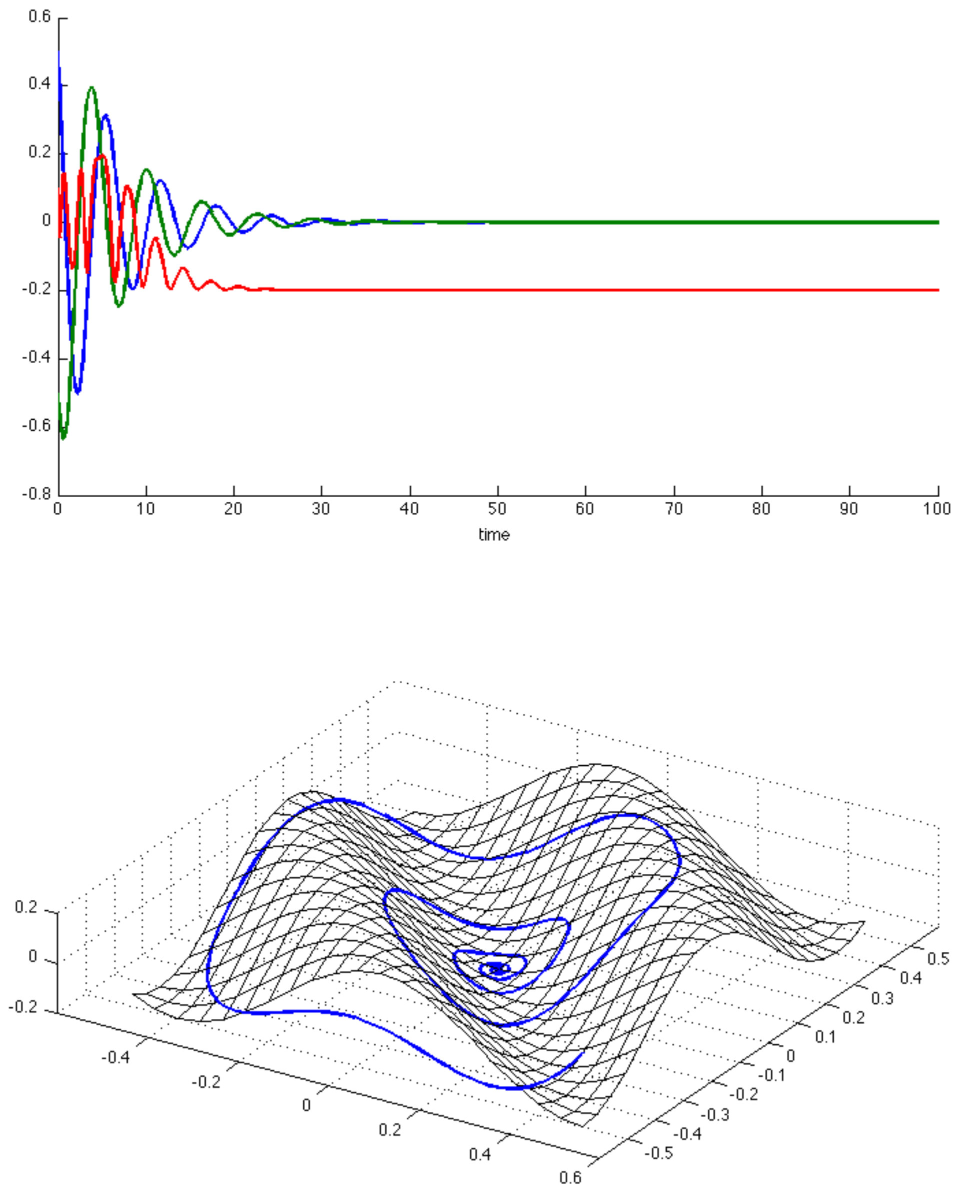
☆ - inhibitory neuron
● - excitatory neuron

☆ - inhibitory mode
● - excitatory mode

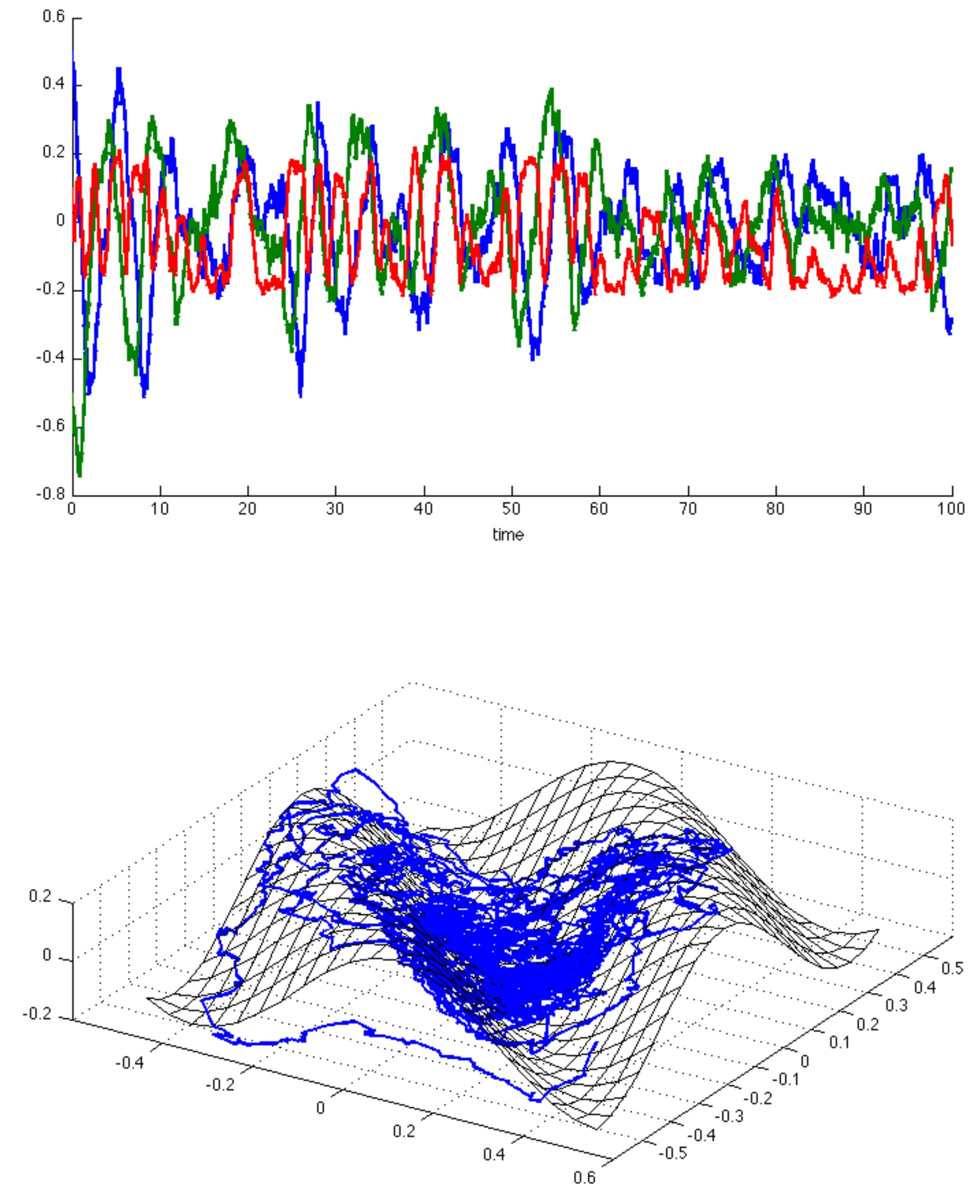
Stefanescu & Jirsa PLoS CB 2008; Stefanescu & Jirsa PRE 2011; Jirsa & Stefanescu Bull. Math. Biol. 2010

Flows and Manifolds

Characterizing dynamics



Coupled oscillators with no noise

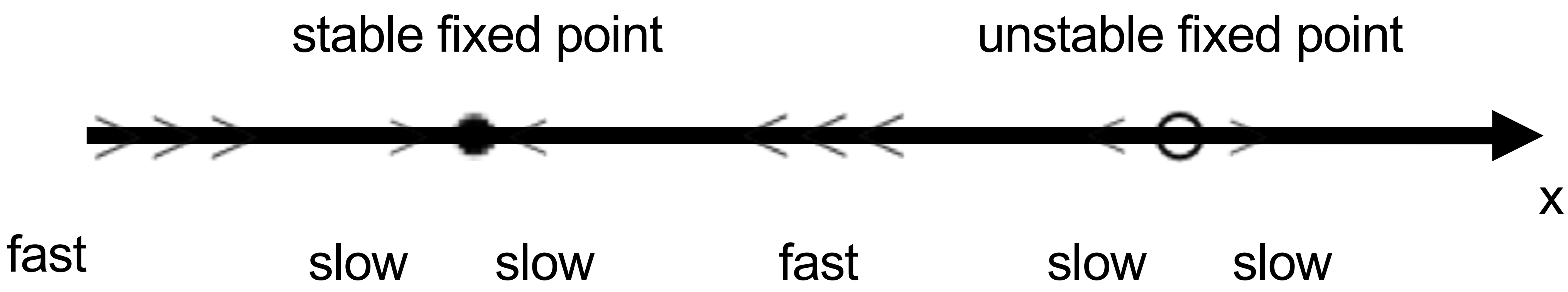


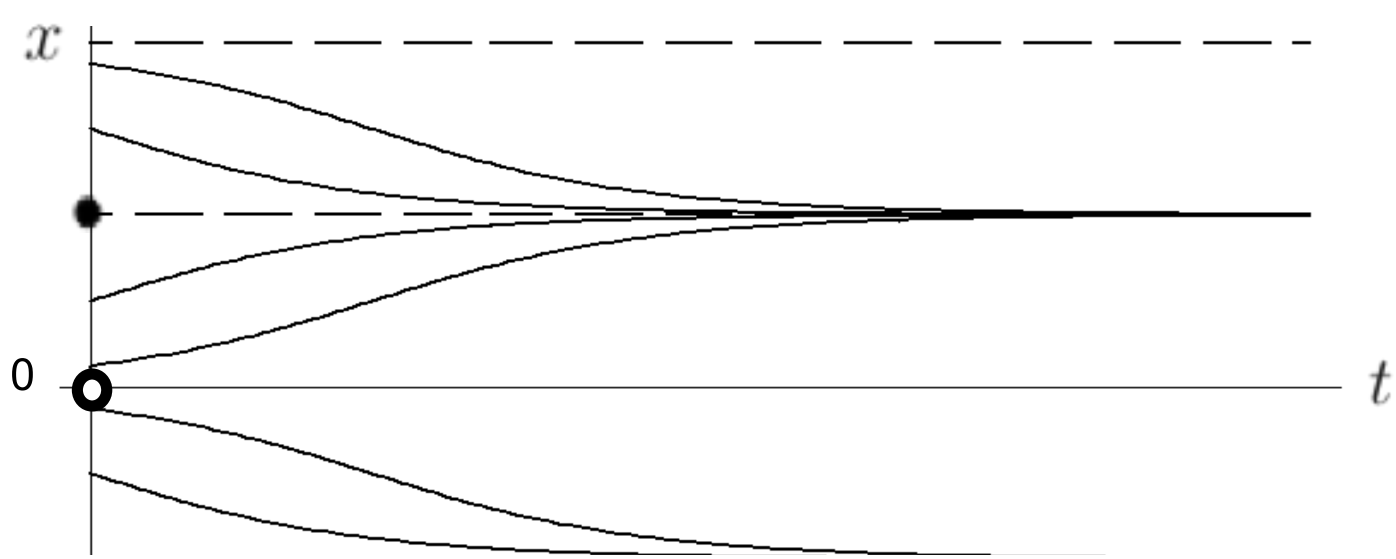
Coupled oscillators with noise

One-dimensional nonlinear flows

$$\dot{x}(t) = f(x(t), k)$$

fixed point: $\dot{x}(t) = 0$





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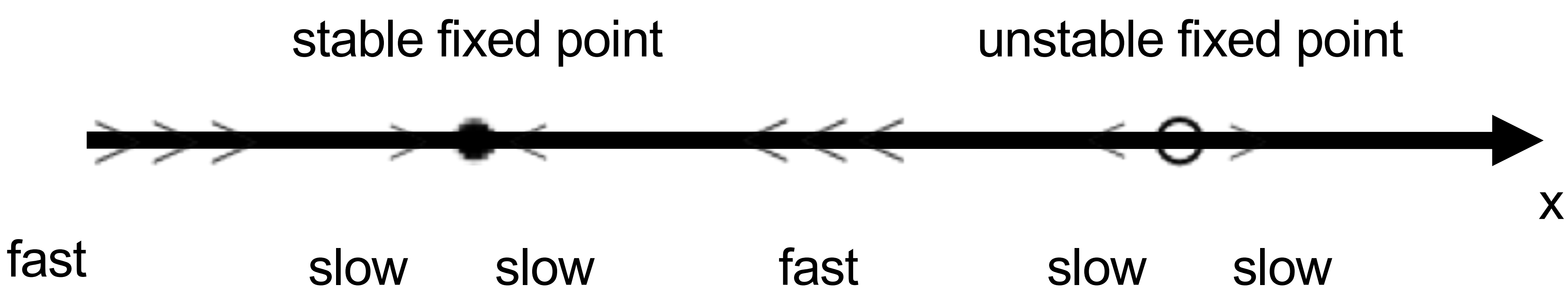
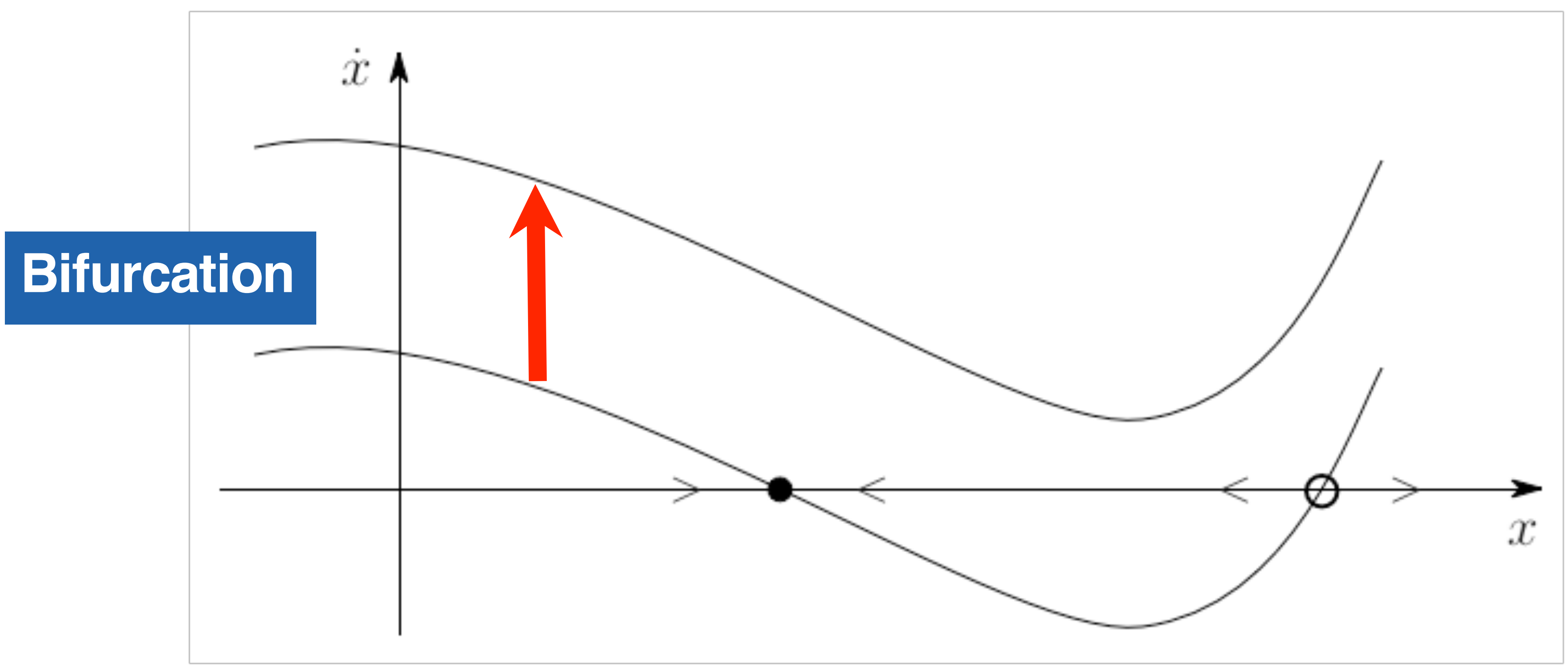


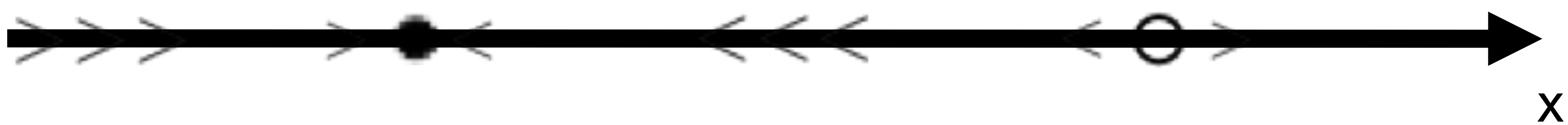


One-dimensional nonlinear flows

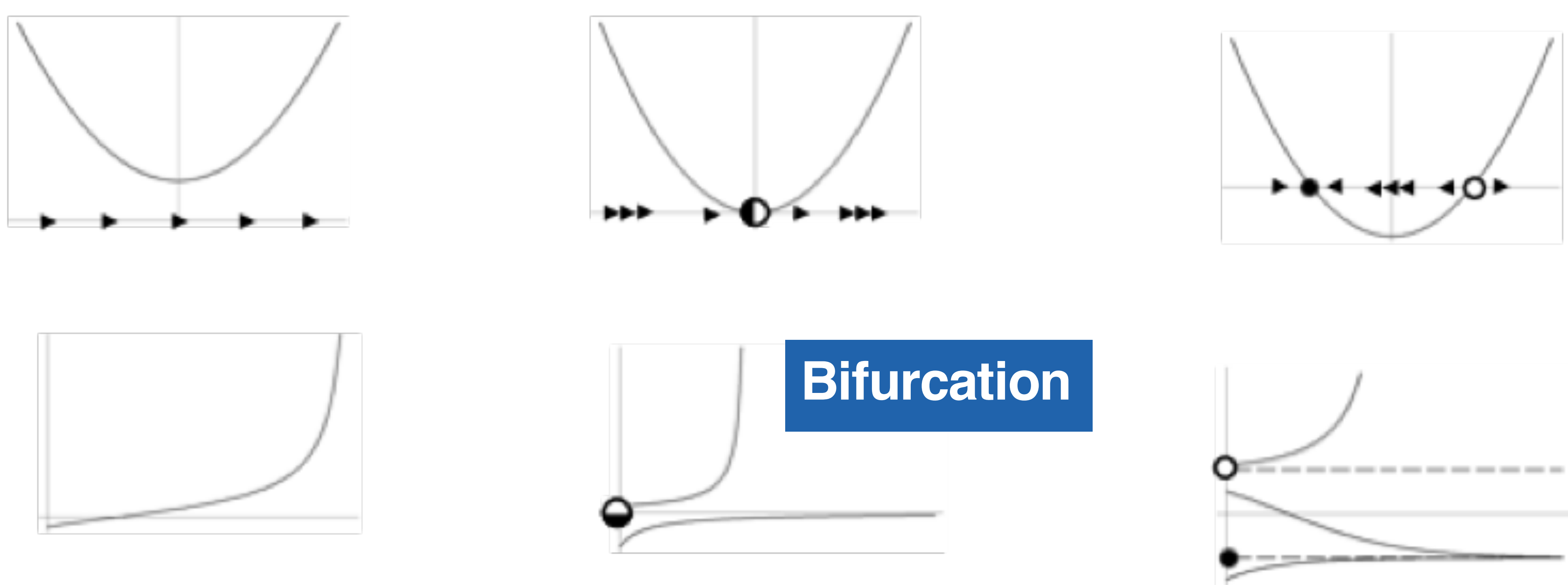
$$\dot{x}(t) = f(x(t),k)$$

fixed point: $\dot{x}(t) = 0$

stable fixed point unstable fixed point



fast slow slow fast slow slow



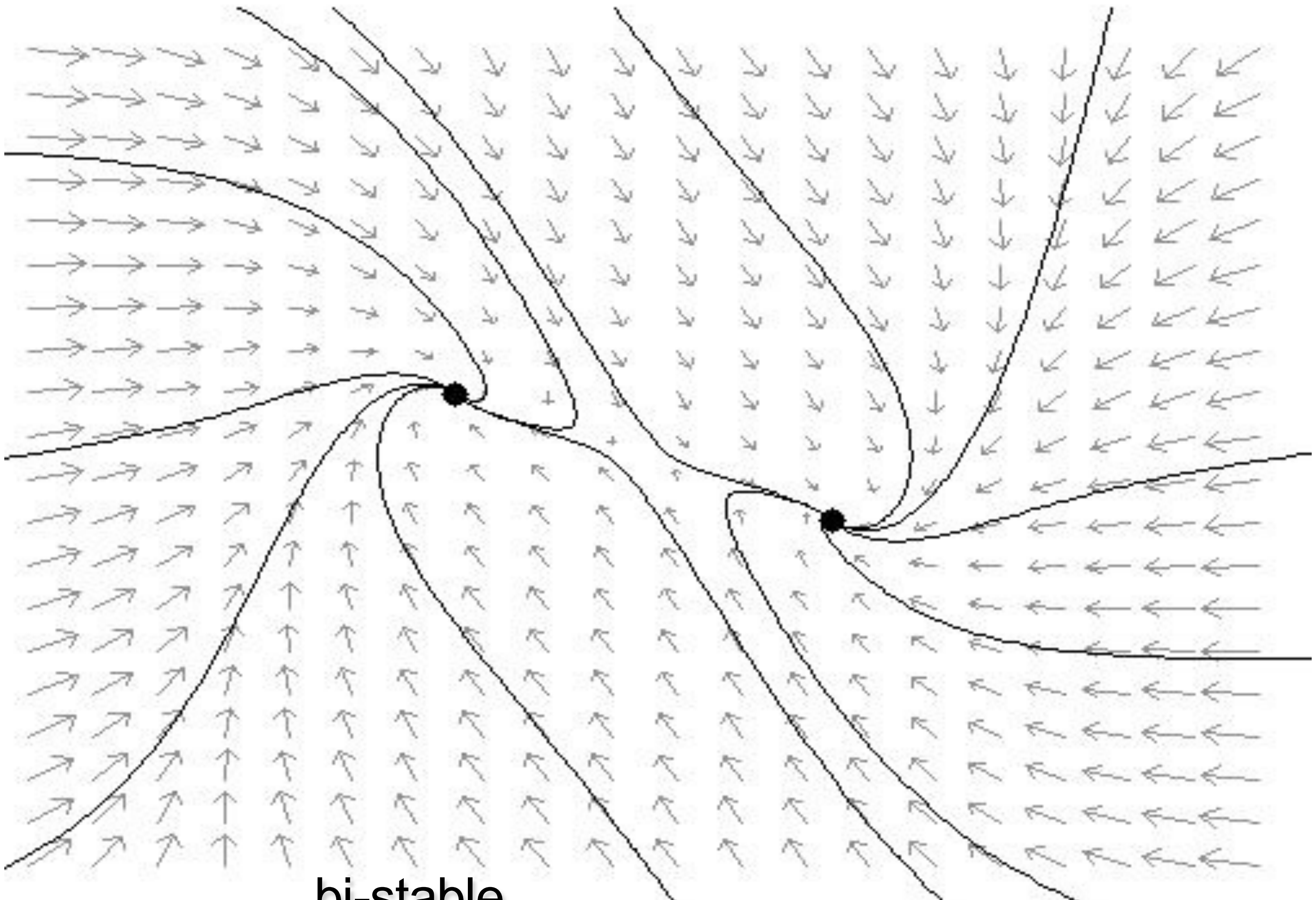
$k > 0$ $k = 0$ $k < 0$

Two-dimensional nonlinear flows

$$\dot{x}(t) = f(x(t), y(t), k)$$
$$\dot{y}(t) = f(y(t), x(t), k)$$

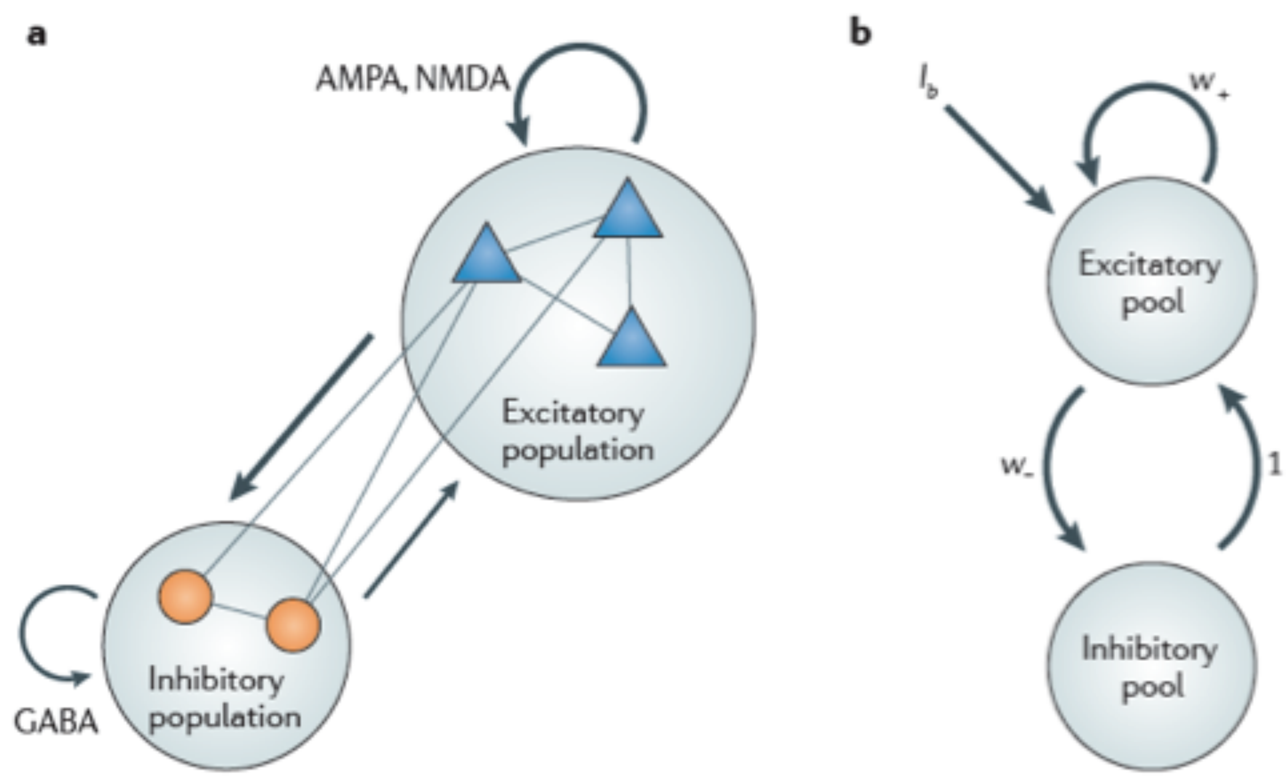
fixed point:

$$\dot{x}(t) = 0$$
$$\dot{y}(t) = 0$$

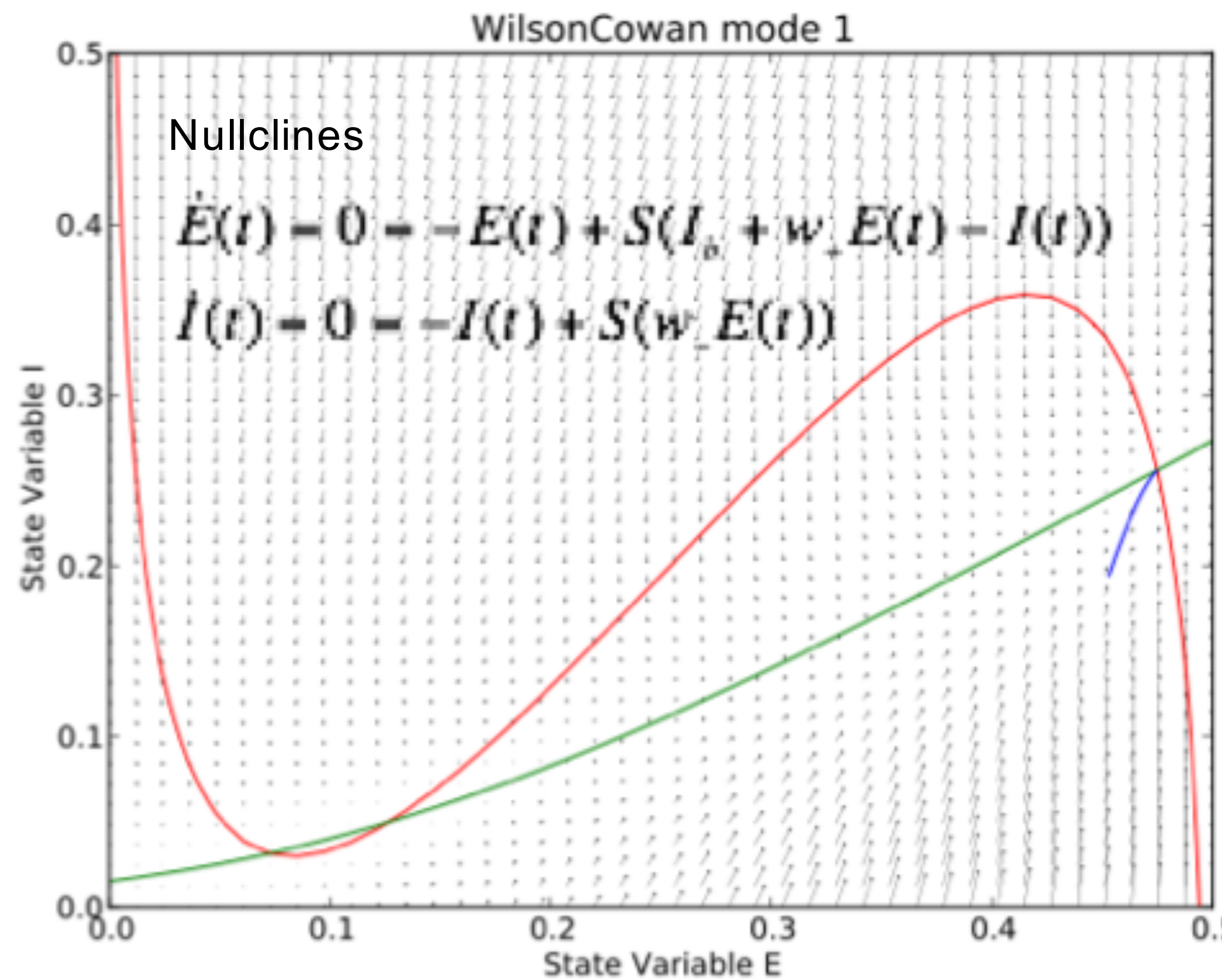


bi-stable

The Wilson-Cowan model



$$\dot{E}(t) = -E(t) + S(I_b + w_+ E(t) - I(t)) + noise$$
$$\dot{I}(t) = -I(t) + S(w_- E(t)) + noise$$

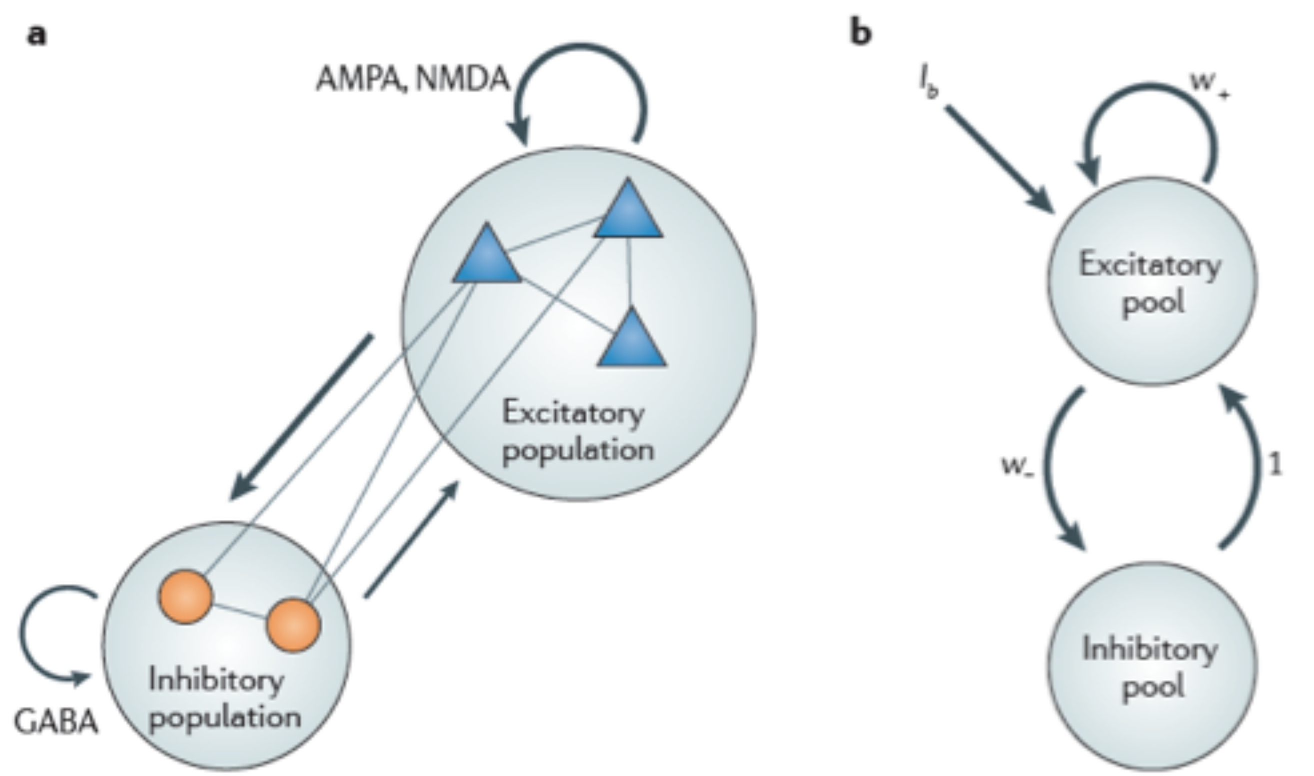


Key idea

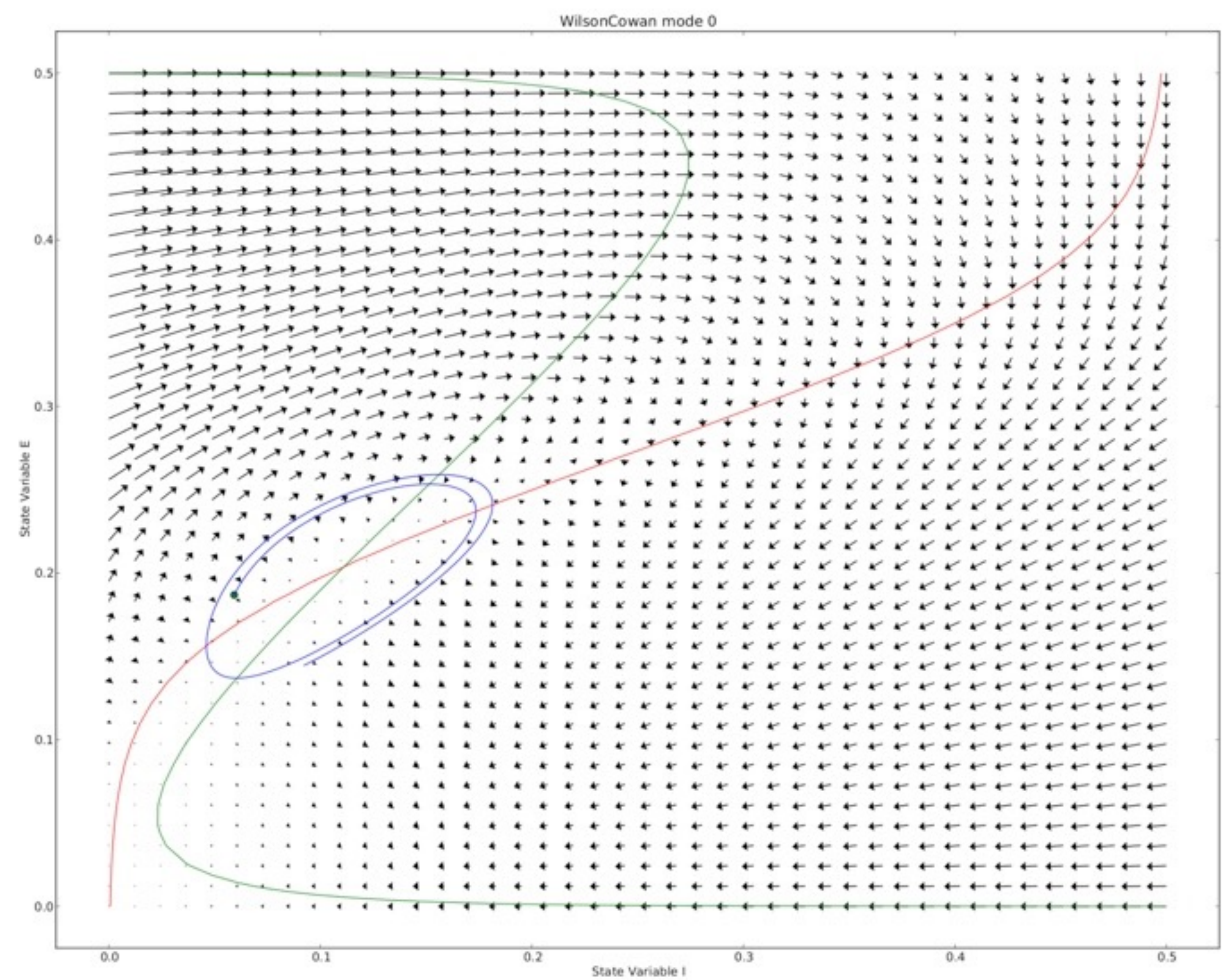
Spike timings of neurons are random and distributed following a Poisson distribution

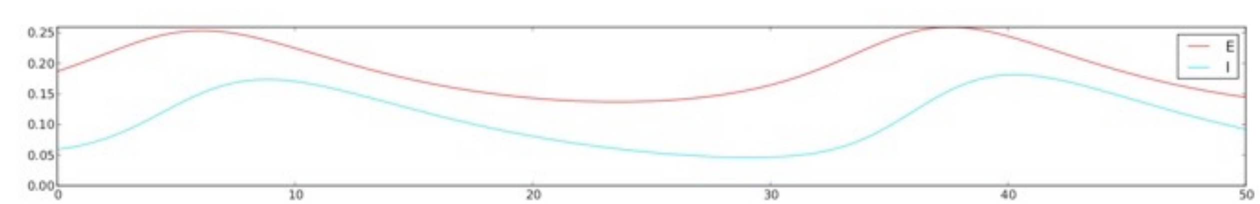
Wilson & Cowan Kybernetik 1972, 1973

The Wilson-Cowan model



$$\dot{E}(t) = -E(t) + S(I_b + w_+ E(t) - I(t)) + noise$$
$$\dot{I}(t) = -I(t) + S(w_- E(t)) + noise$$



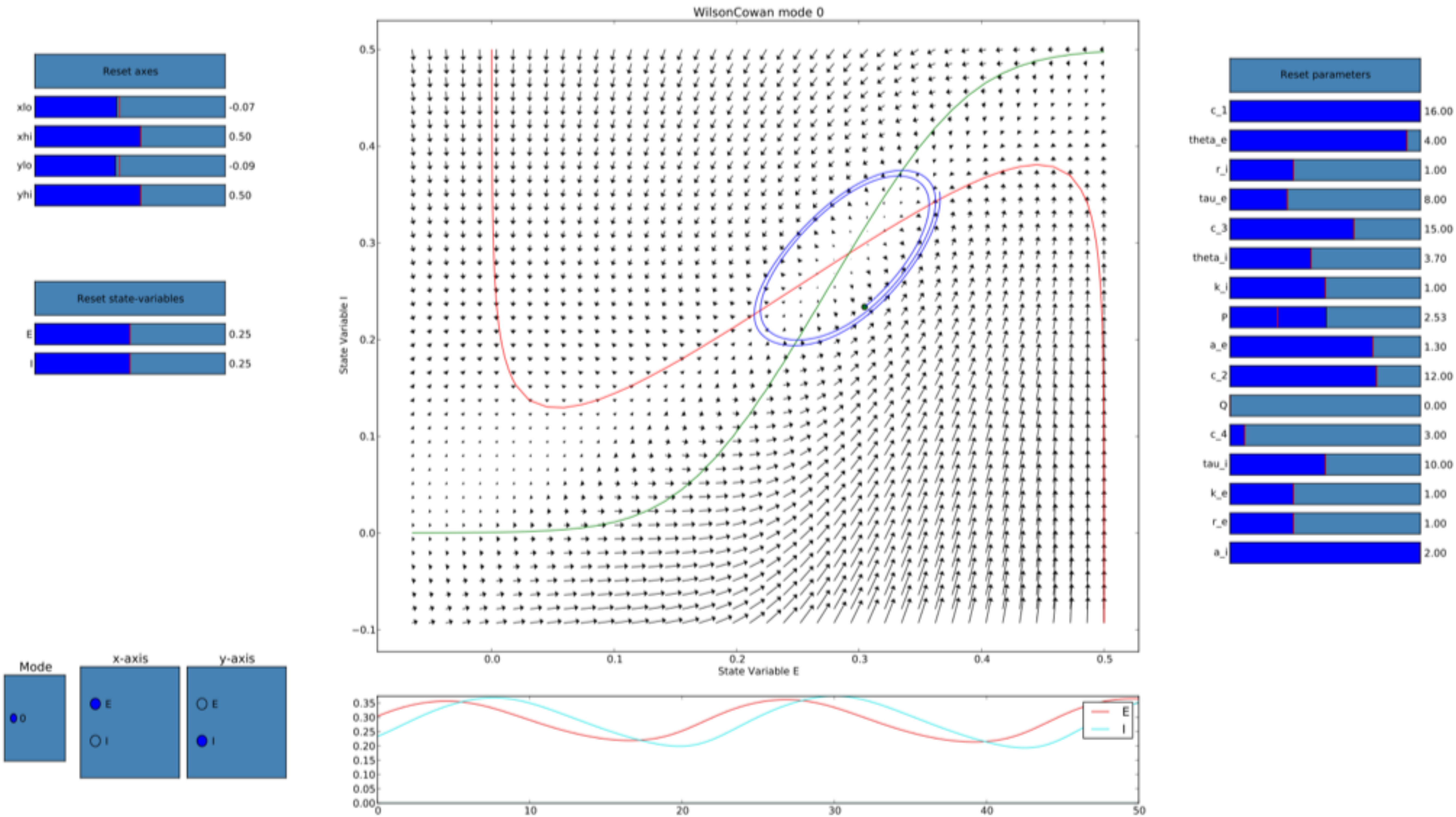


Key idea

Spike timings of neurons are random and distributed following a Poisson distribution

Wilson & Cowan Kybernetik 1972, 1973

The Wilson-Cowan model

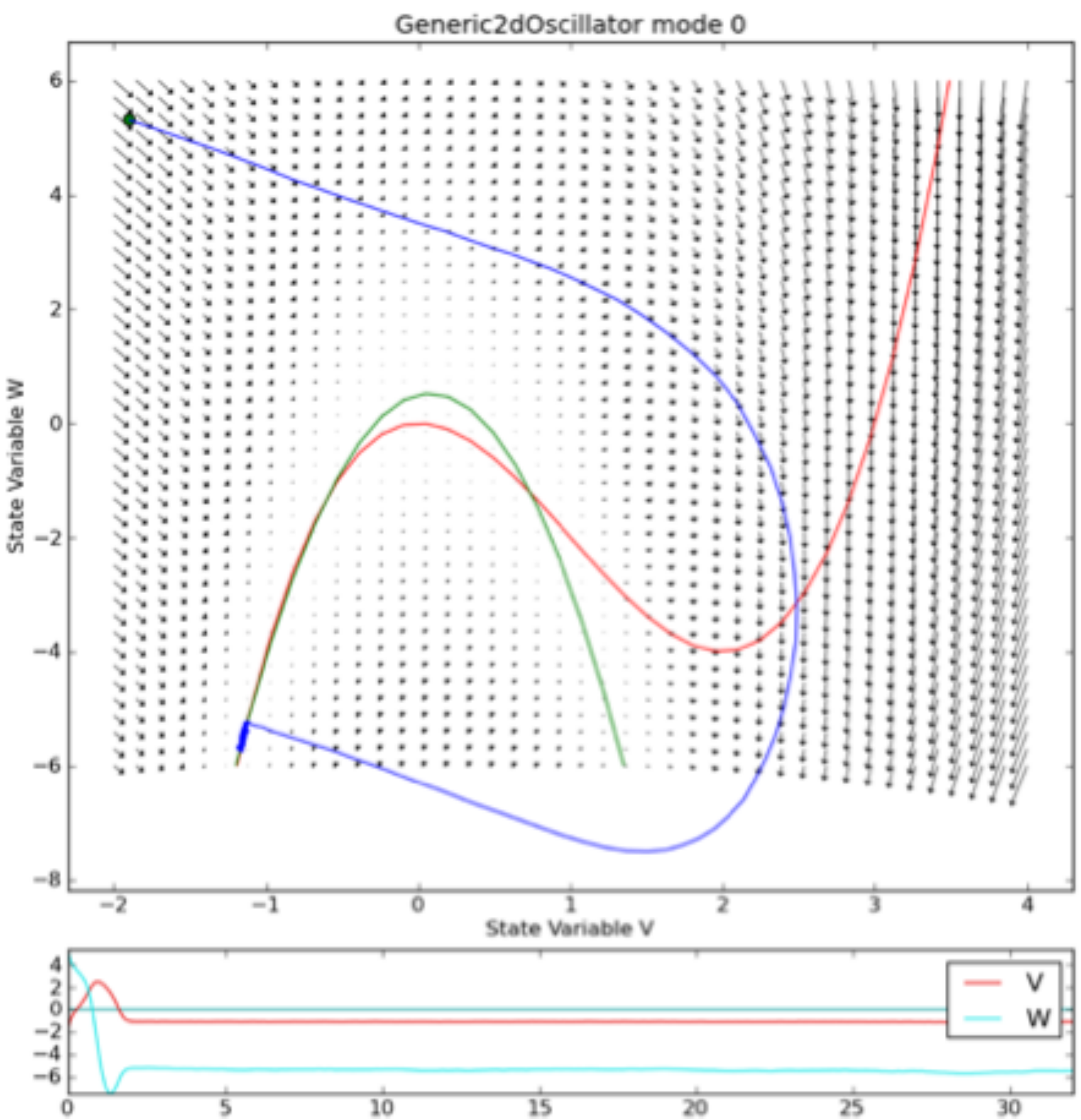


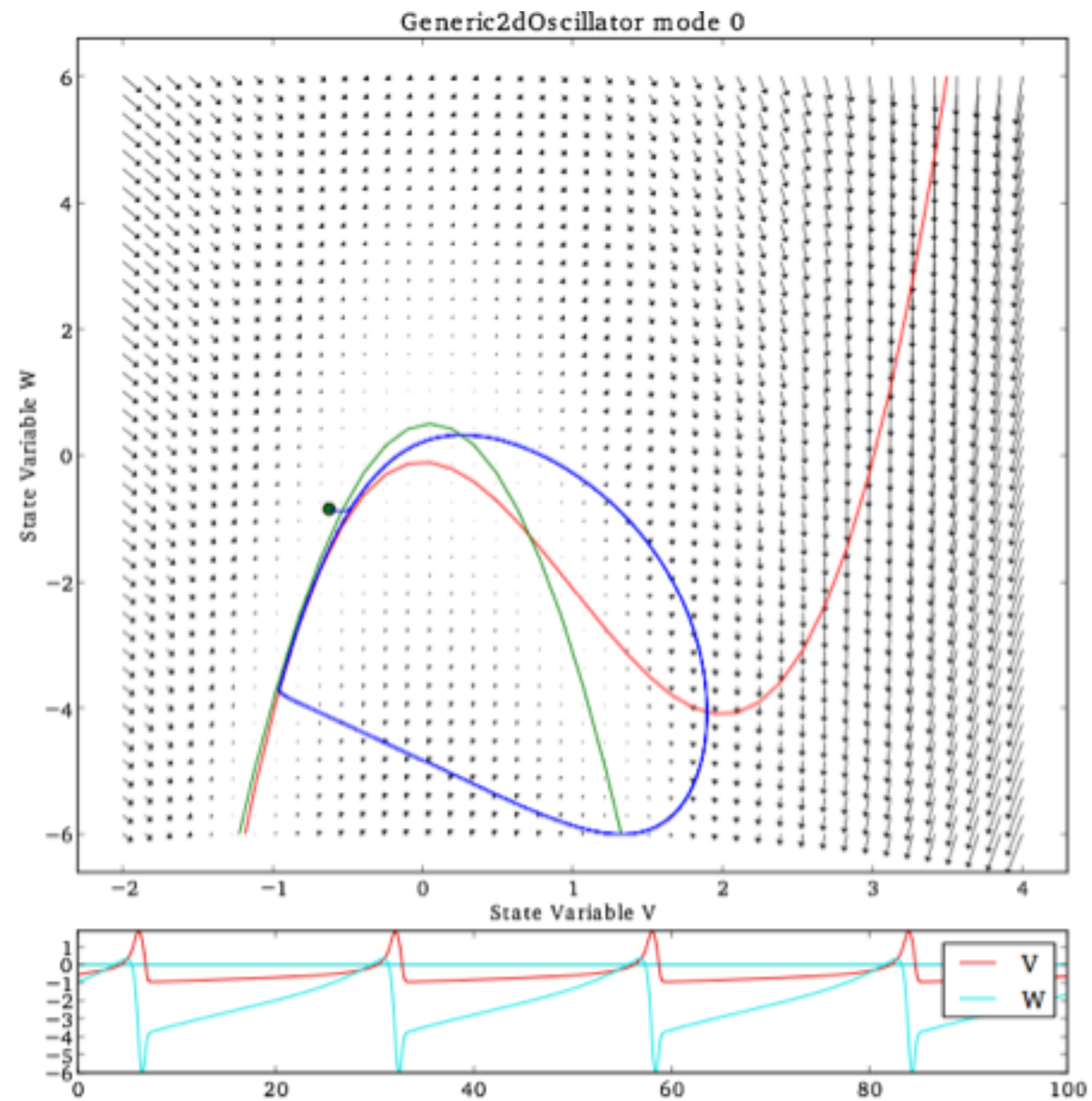
Wilson & Cowan Kybernetik 1972, 1973

The Generic 2D oscillator model

$$\dot{V}(t) = f(V(t), W(t)) + Input + noise$$

$$\dot{W}(t) = g(V(t), W(t)) + noise$$





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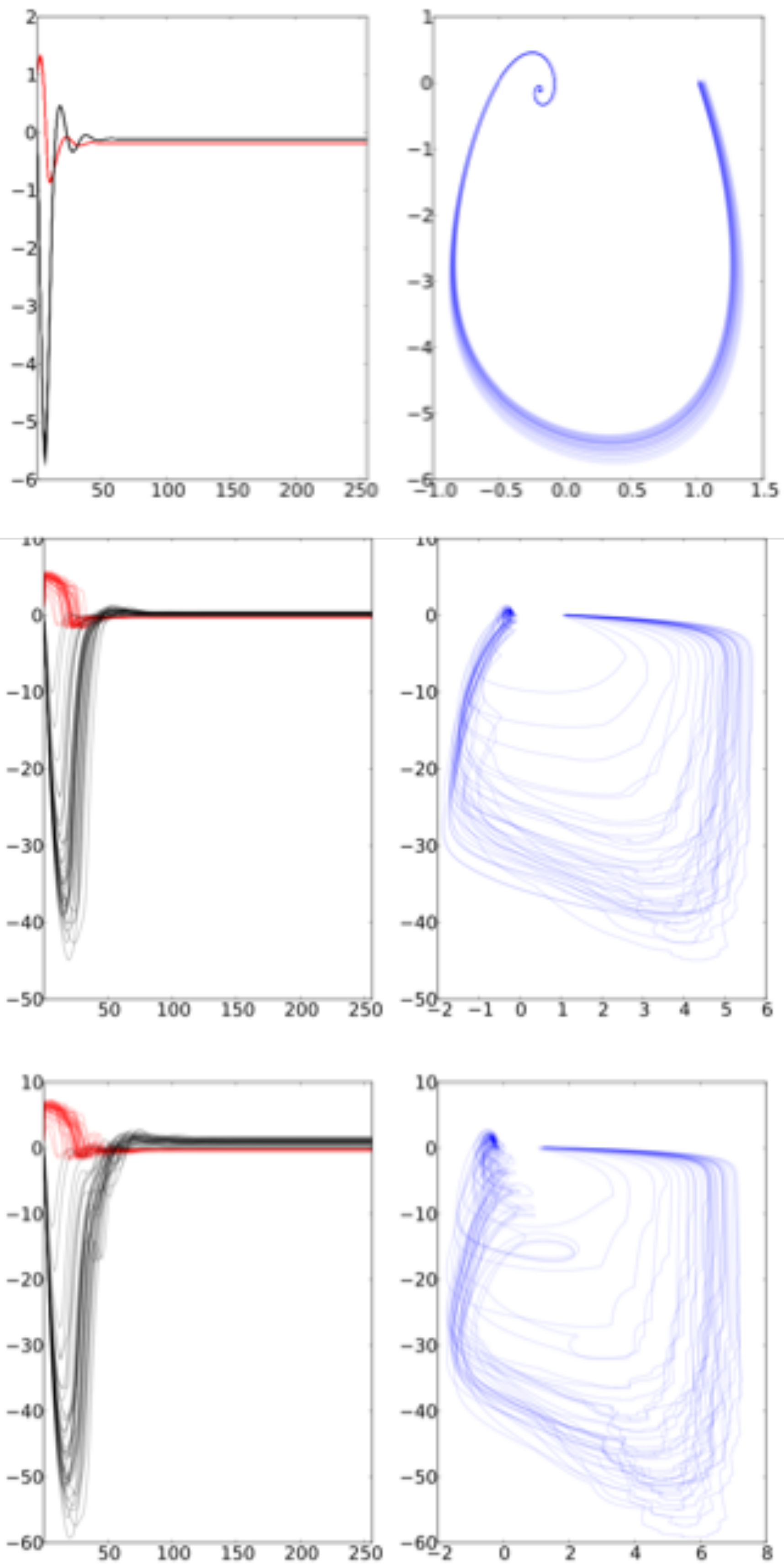
Generic 2D oscillators embedded in the network



No coupling

Weak coupling

Strong coupling

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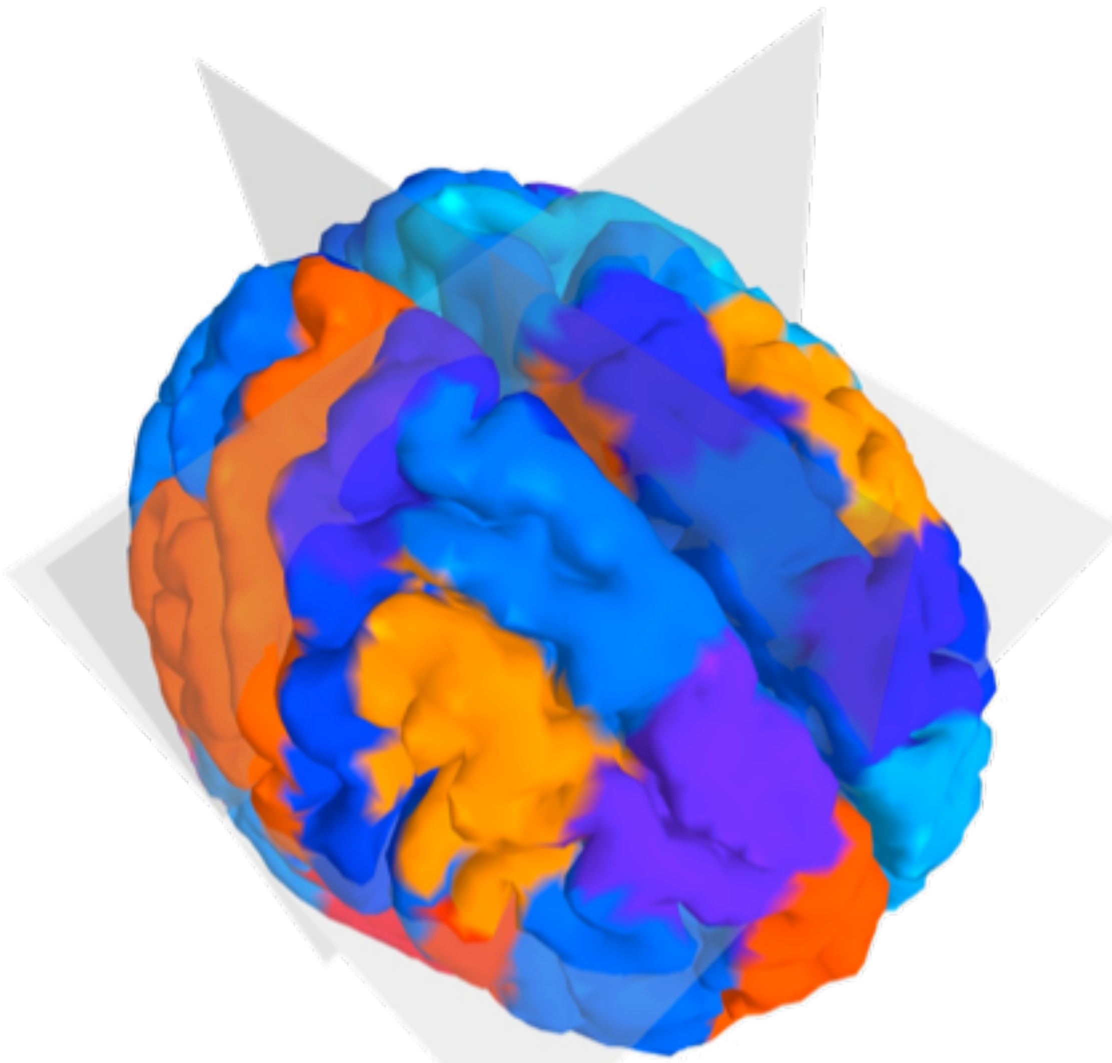
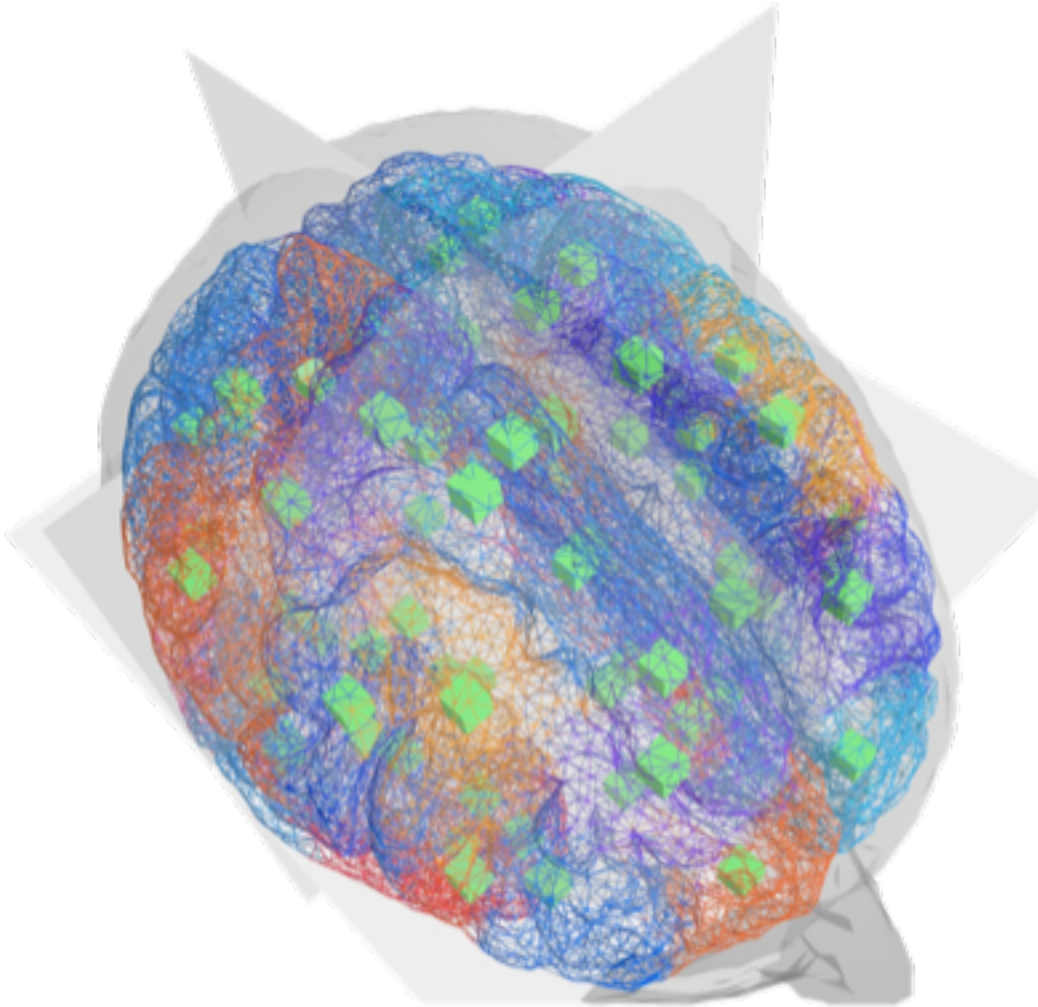
TVB geometry

Topography of the brain

MNI brain geometry





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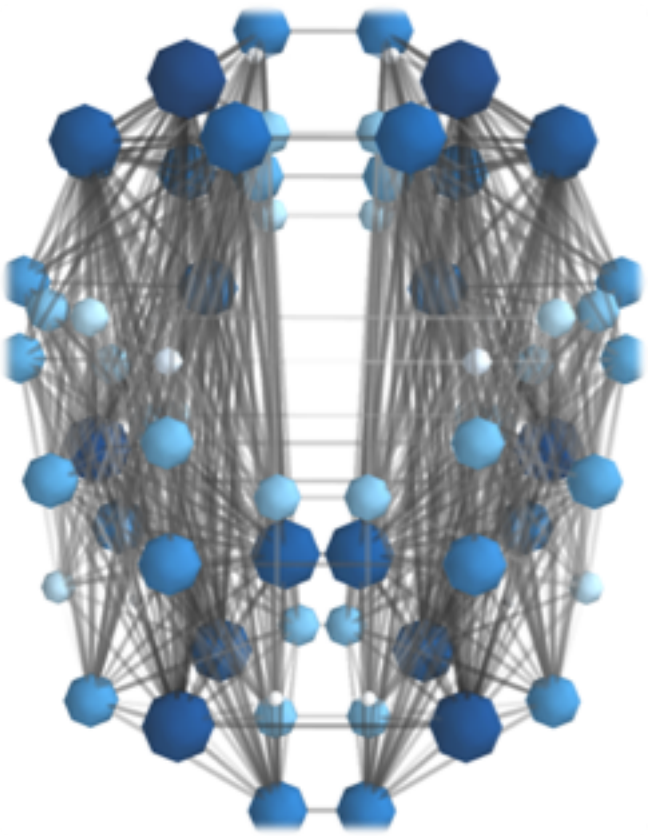
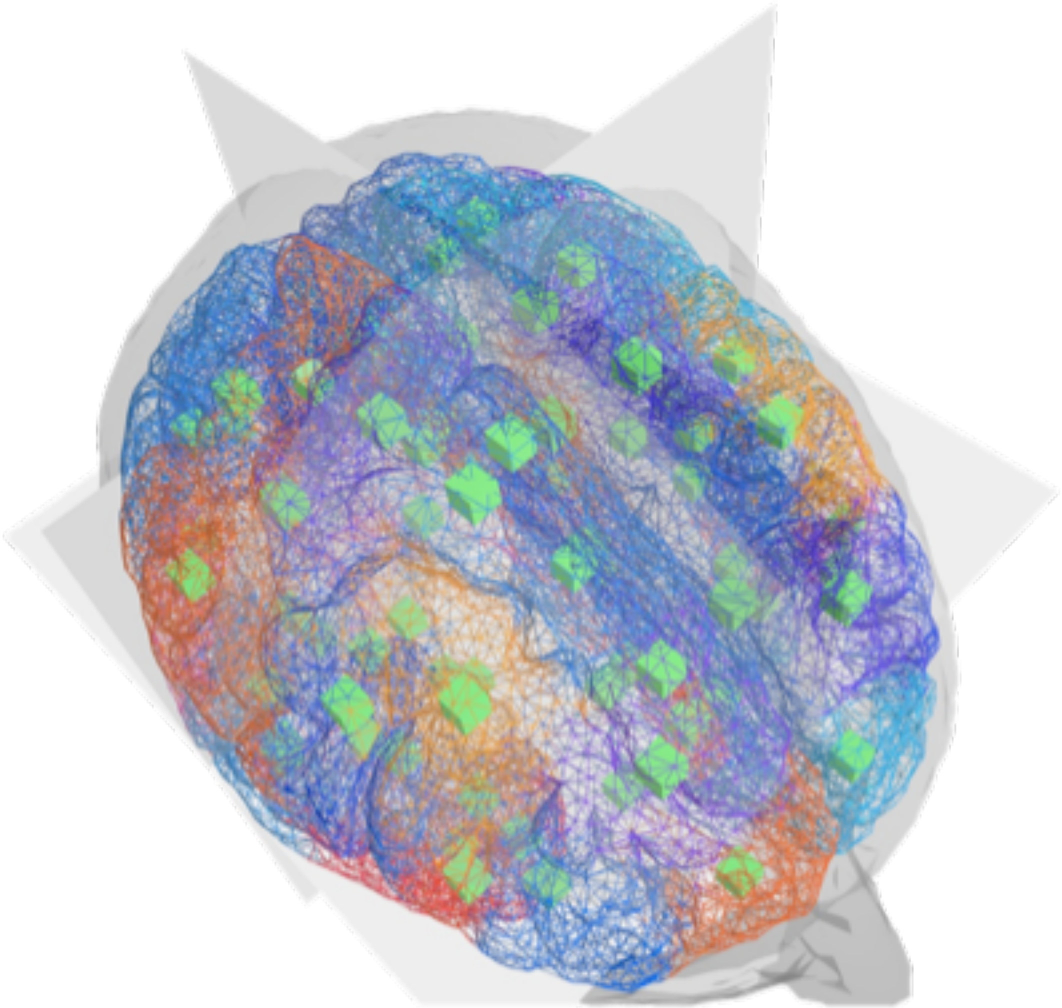
TVB topography

- region-based modeling (N=30-200)

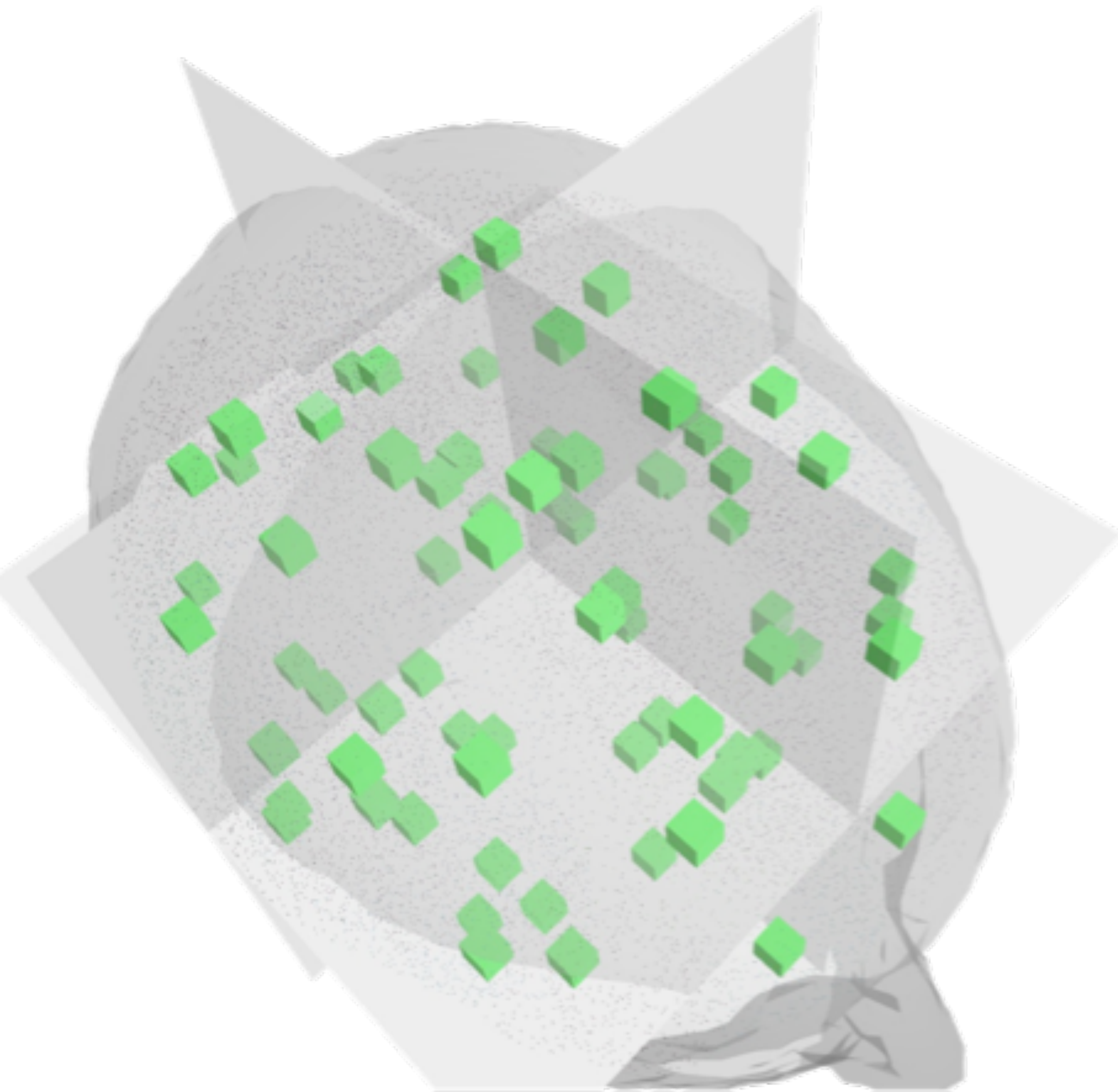


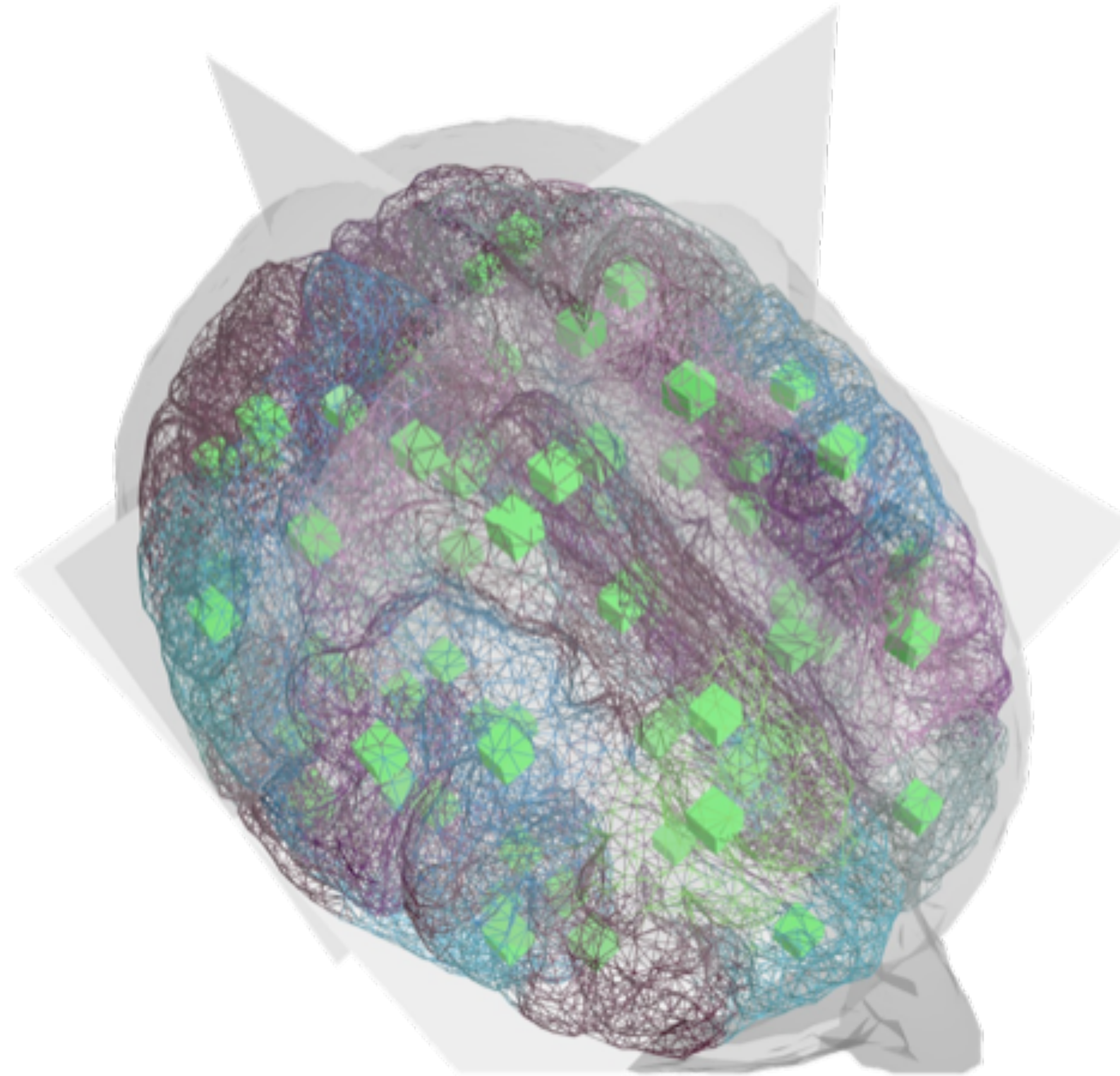


Sanz Leon et al Front NeuroInformatics 2013

TVB topography

surface-based modeling (N=10000-140000)



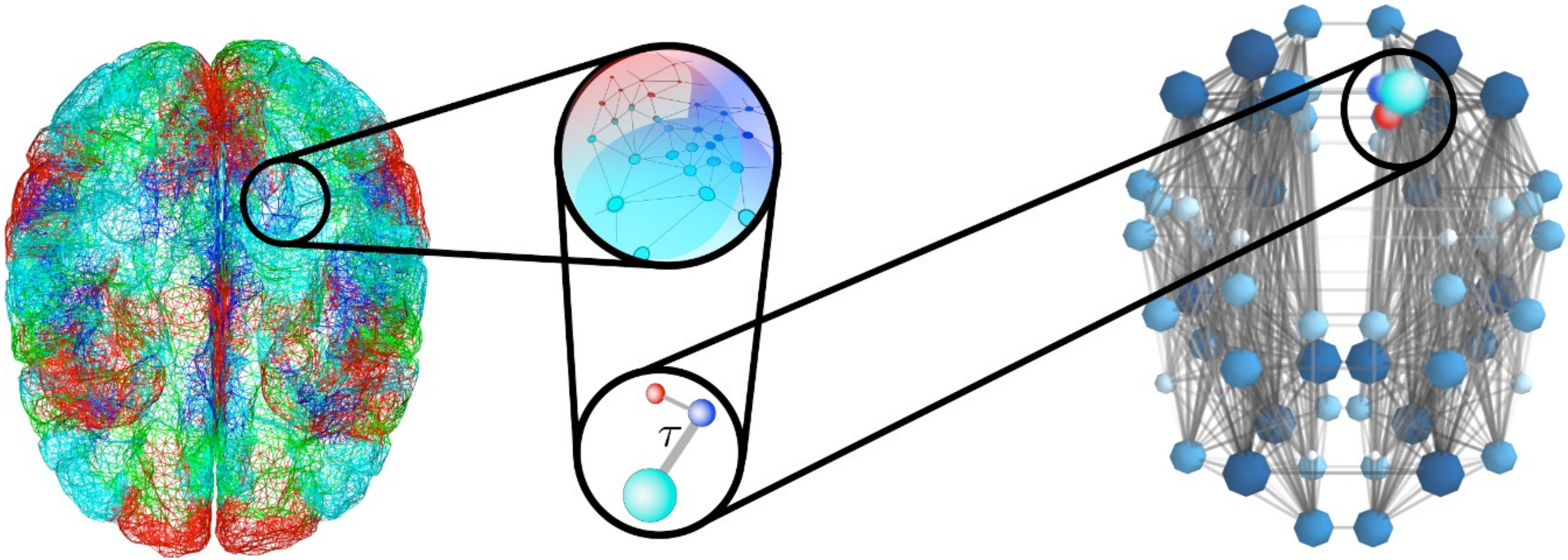


Sanz Leon et al Front NeuroInformatics 2013

TVB connectivity

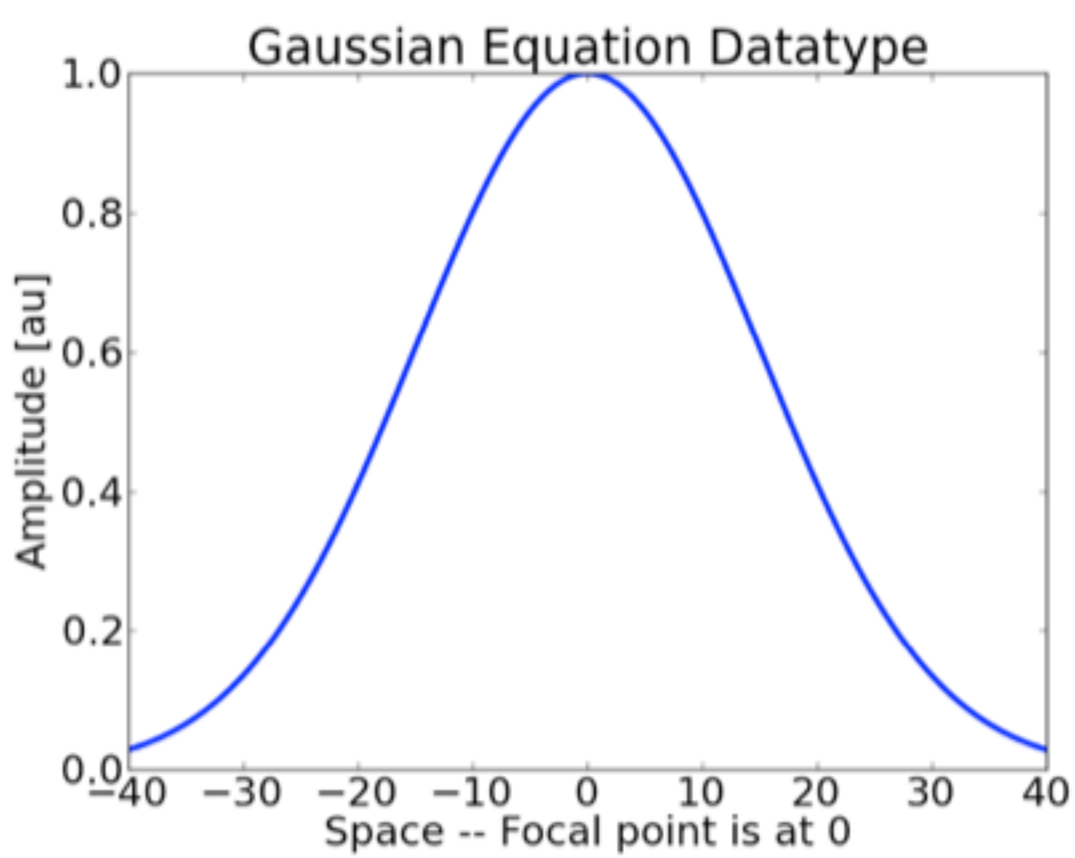
Topology of the brain

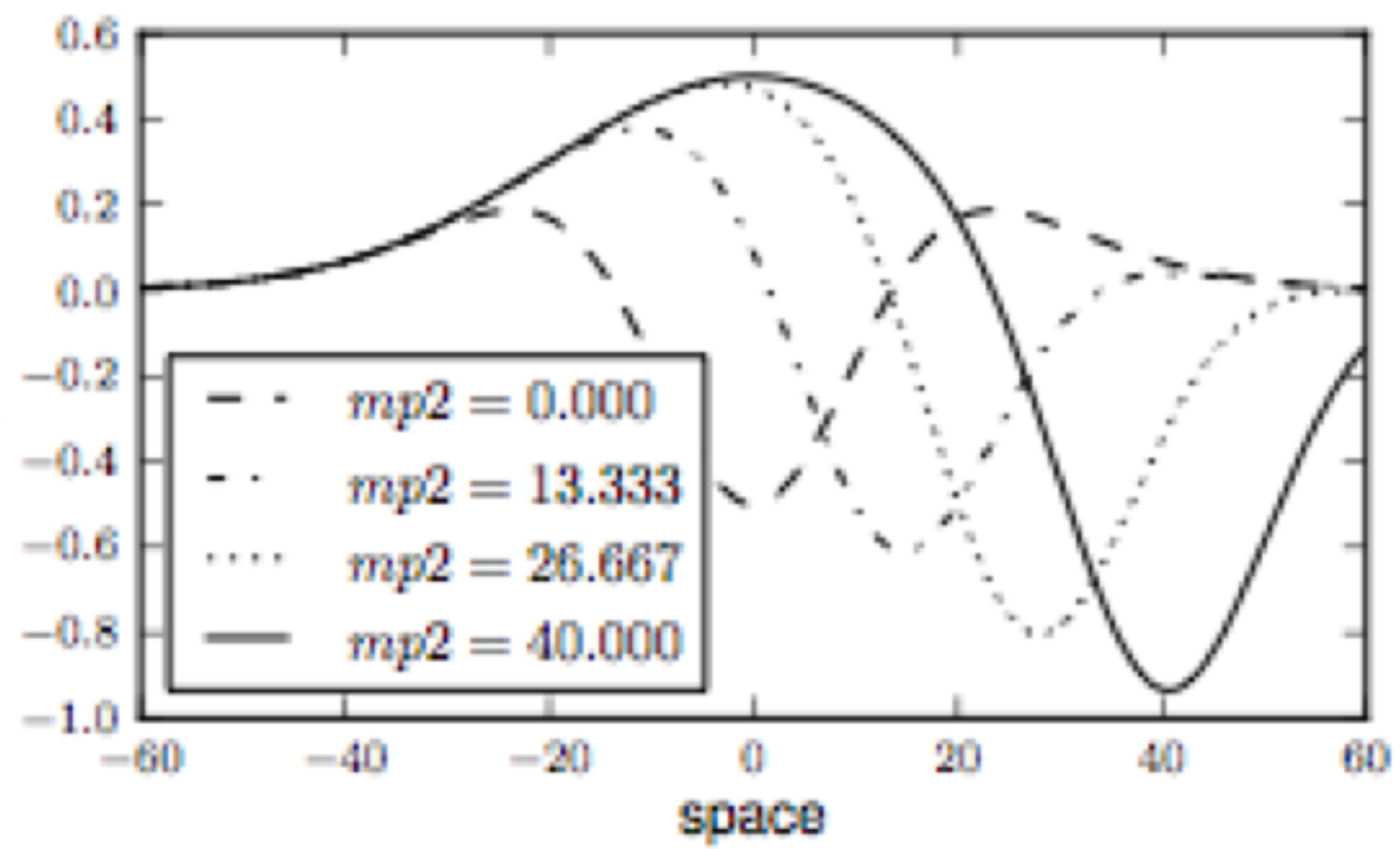
local coupling: surface-based modeling



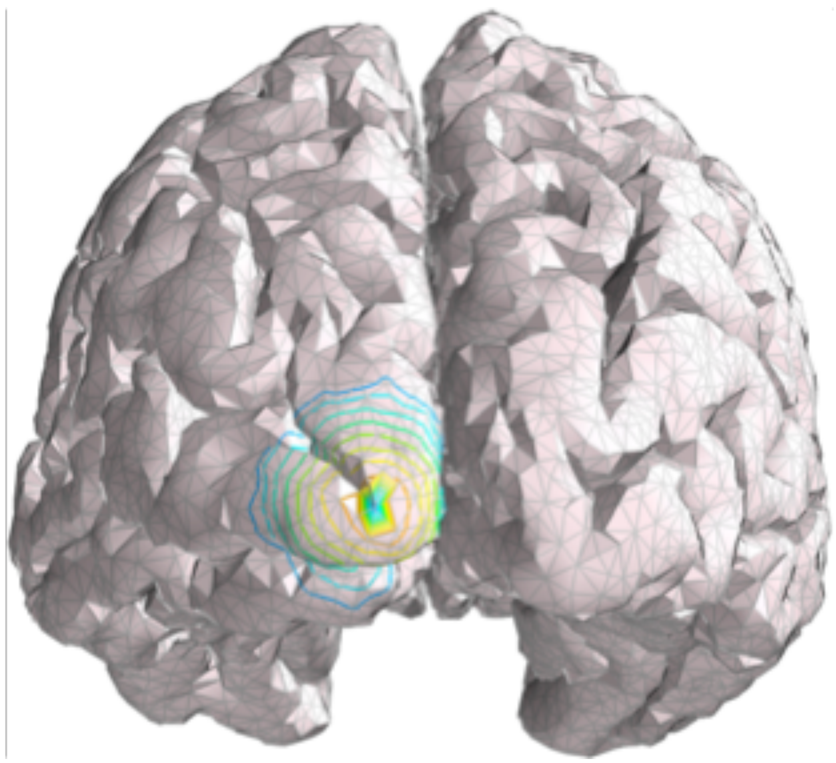
Sanz Leon et al Front NeuroInformatics 2013

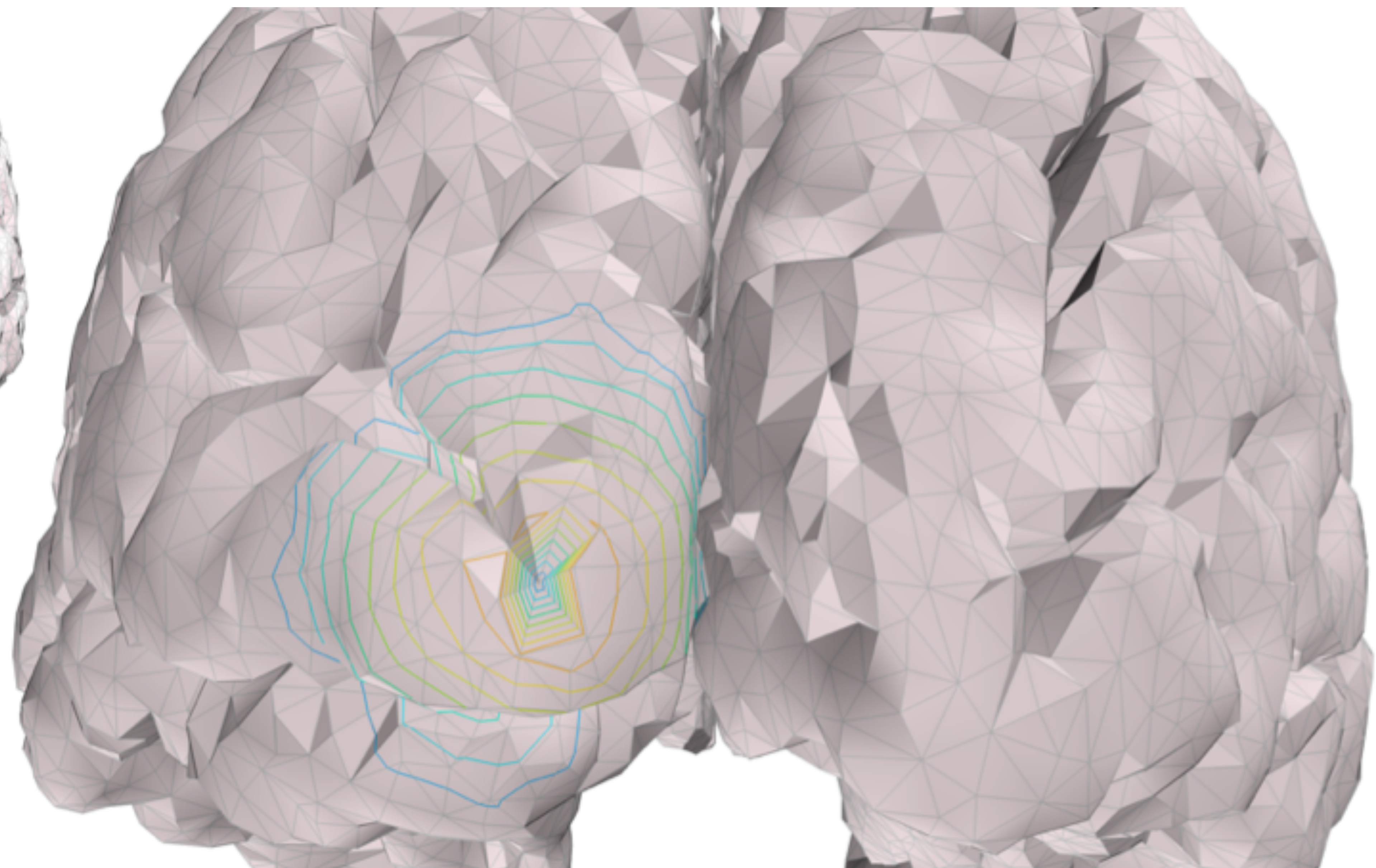
local coupling: surface-based modeling





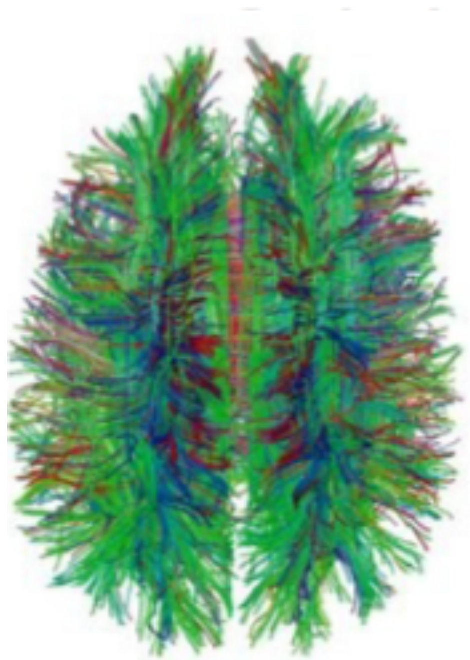
local coupling: surface-based modeling

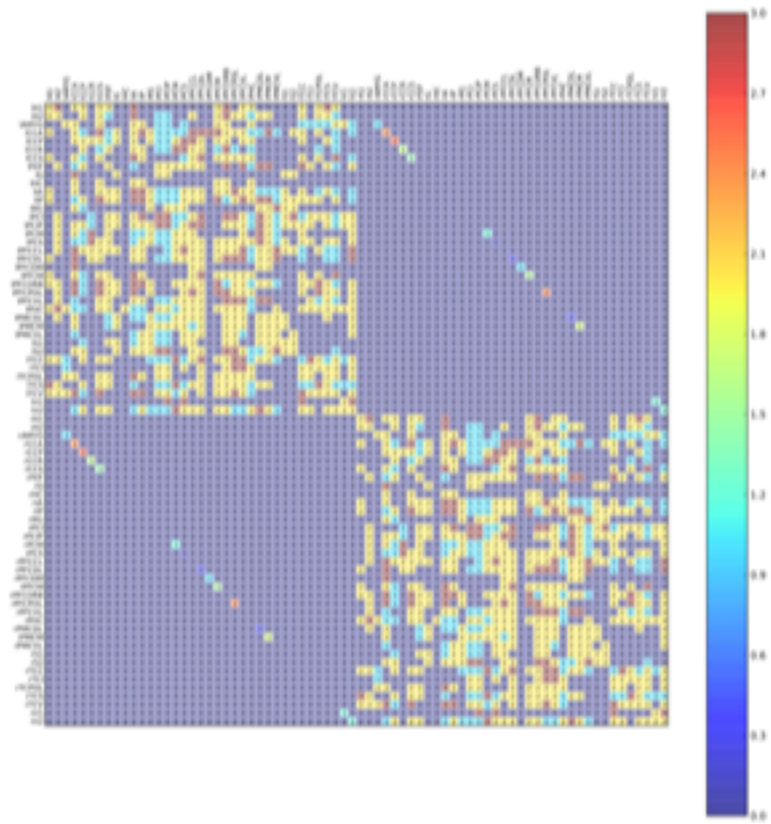


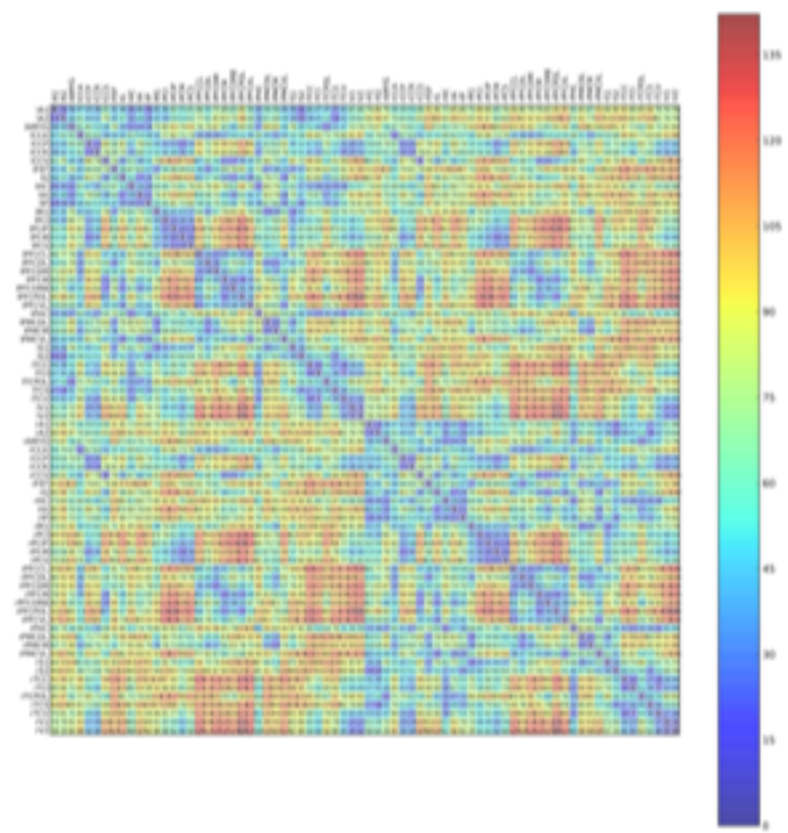


space-time structure of connectivity

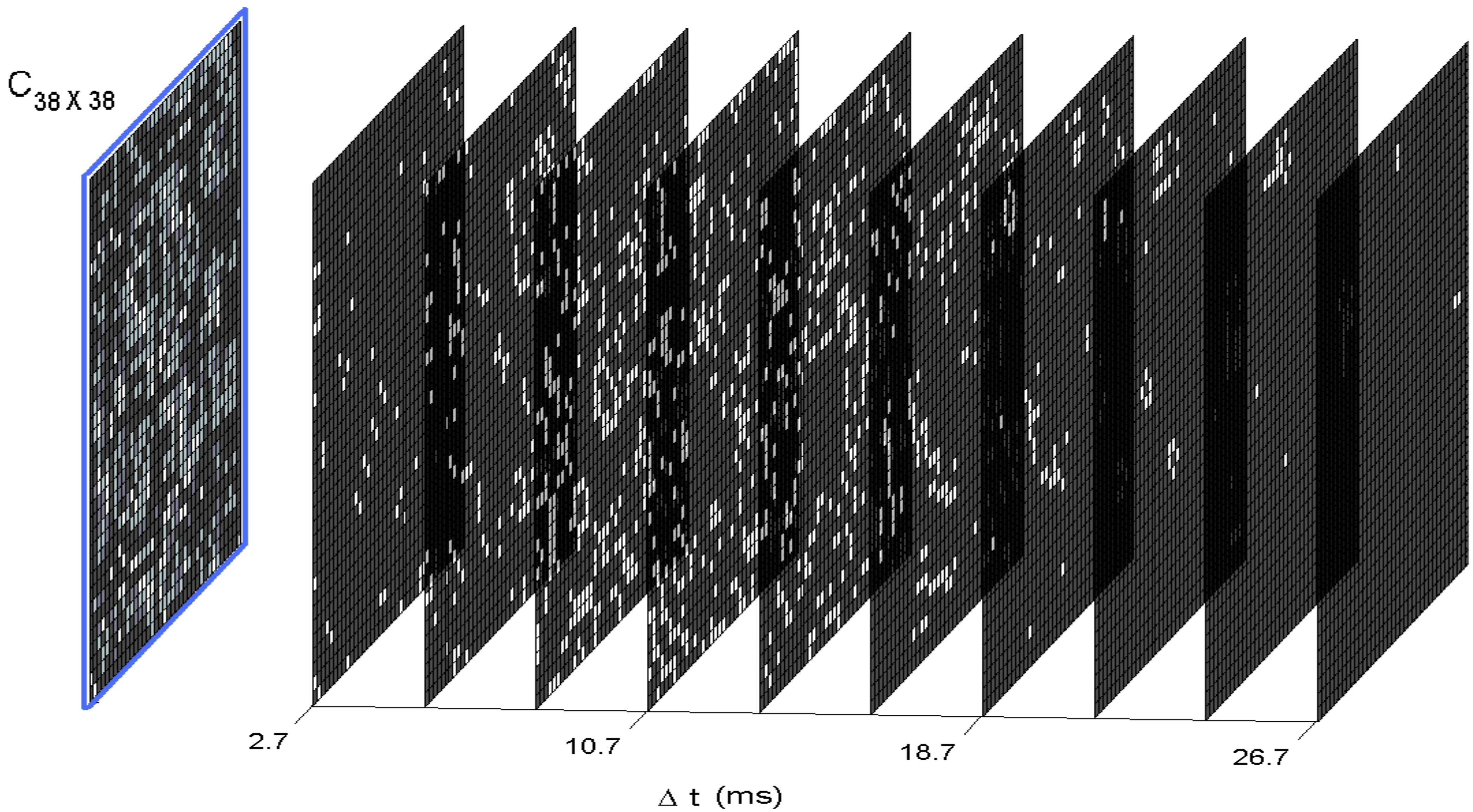
- no time delay for local coupling
- time delays for global coupling (default speed)
  - tract lengths
  - Euclidean distance in 3D







Jirsa Phil Trans Roy Soc 2009; Sanz Leon et al Front NeuroInformatics 2013 space-time structure of connectivity

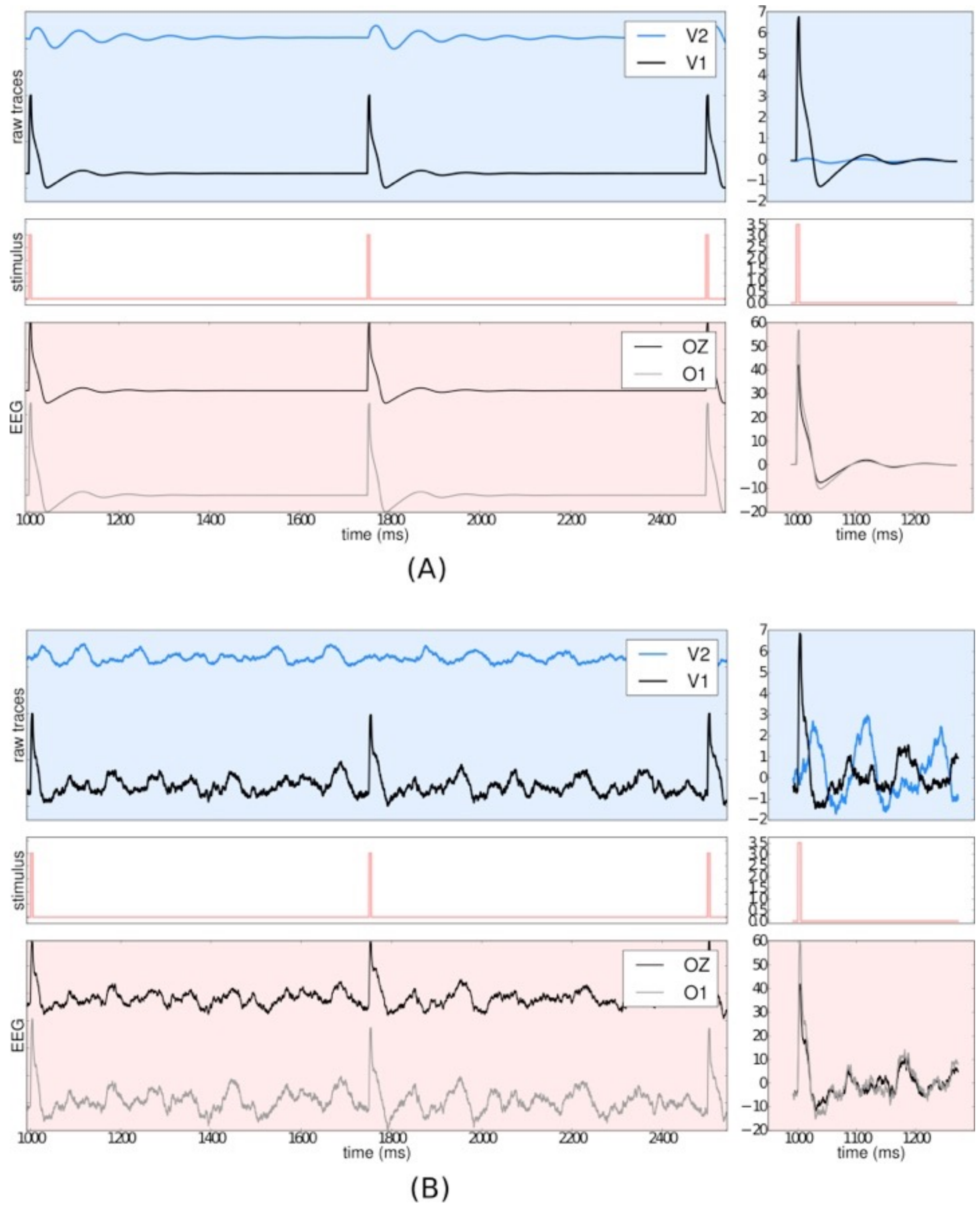


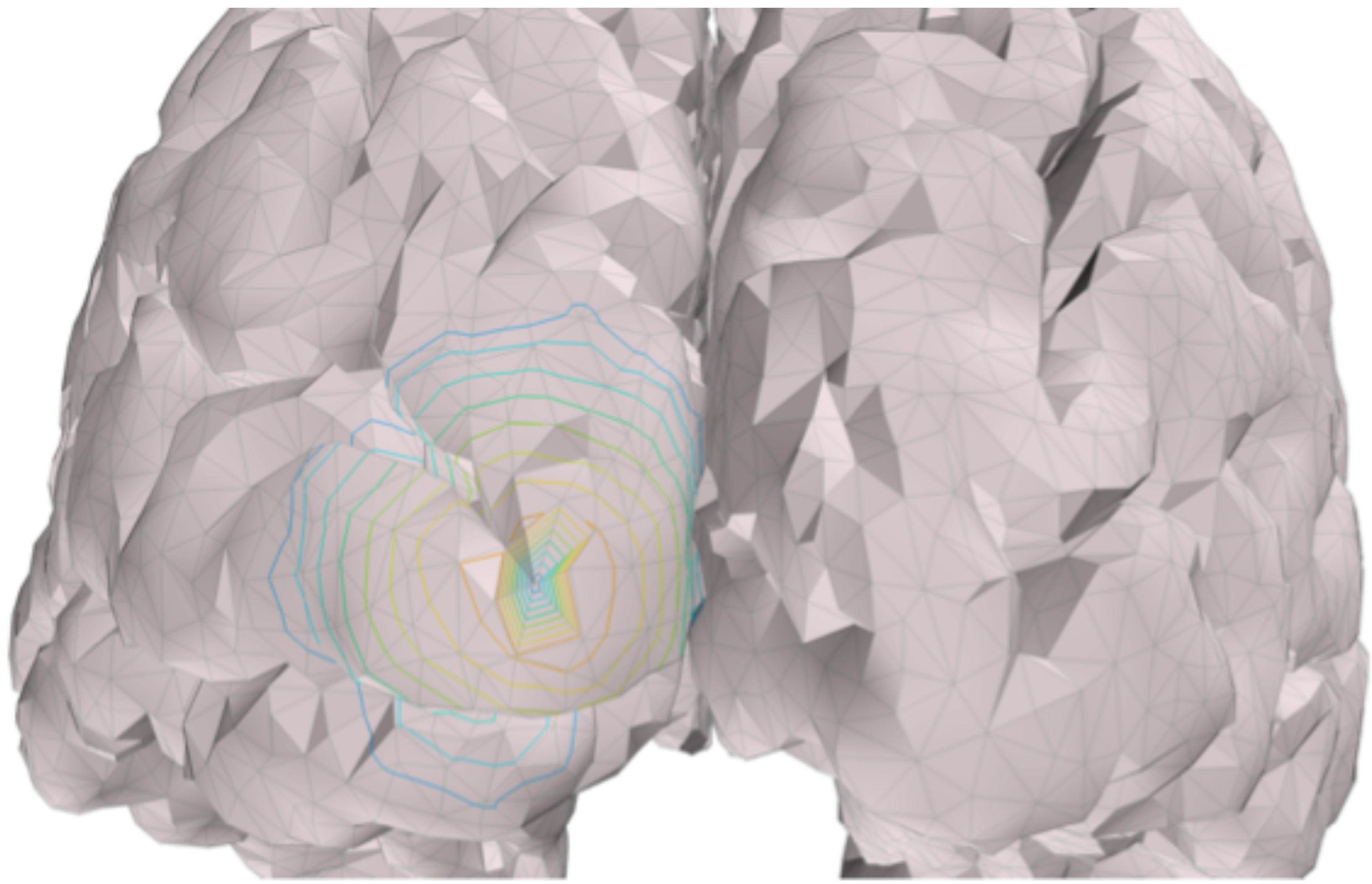
Ghosh et al PLoS CB 2008;
Jirsa Phil Trans Roy Soc 2009

TVB stimulation

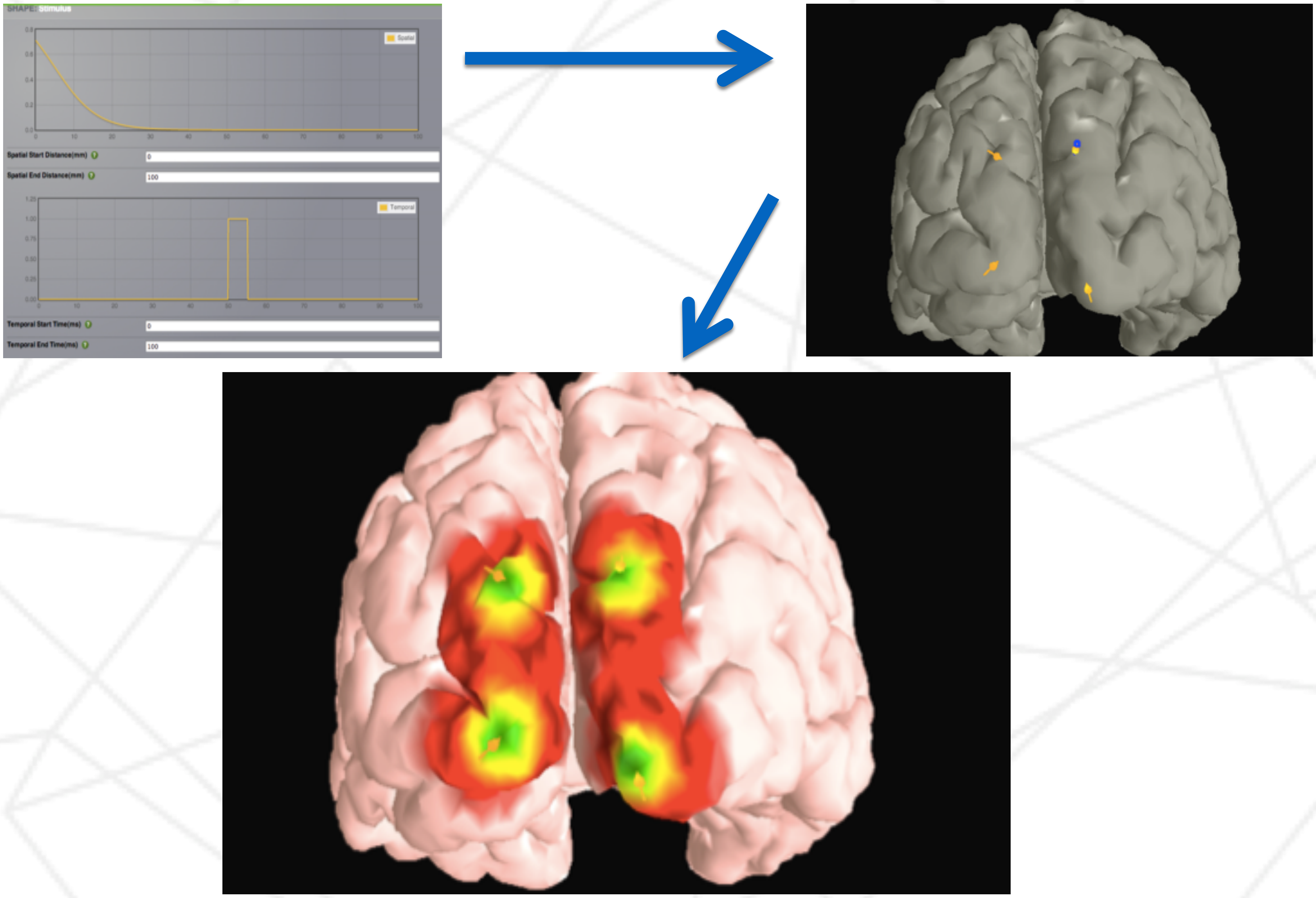
Dispersion in space and time

Stimulus = time course + spatial extent





Stimulation



TVB monitors

Non-invasive and invasive imaging

TVB monitors

- Raw signals from neural population models
- EEG and MEG
- Bold
- Stereotactic EEG

Sanz Leon et al Front NeuroInformatics 2013

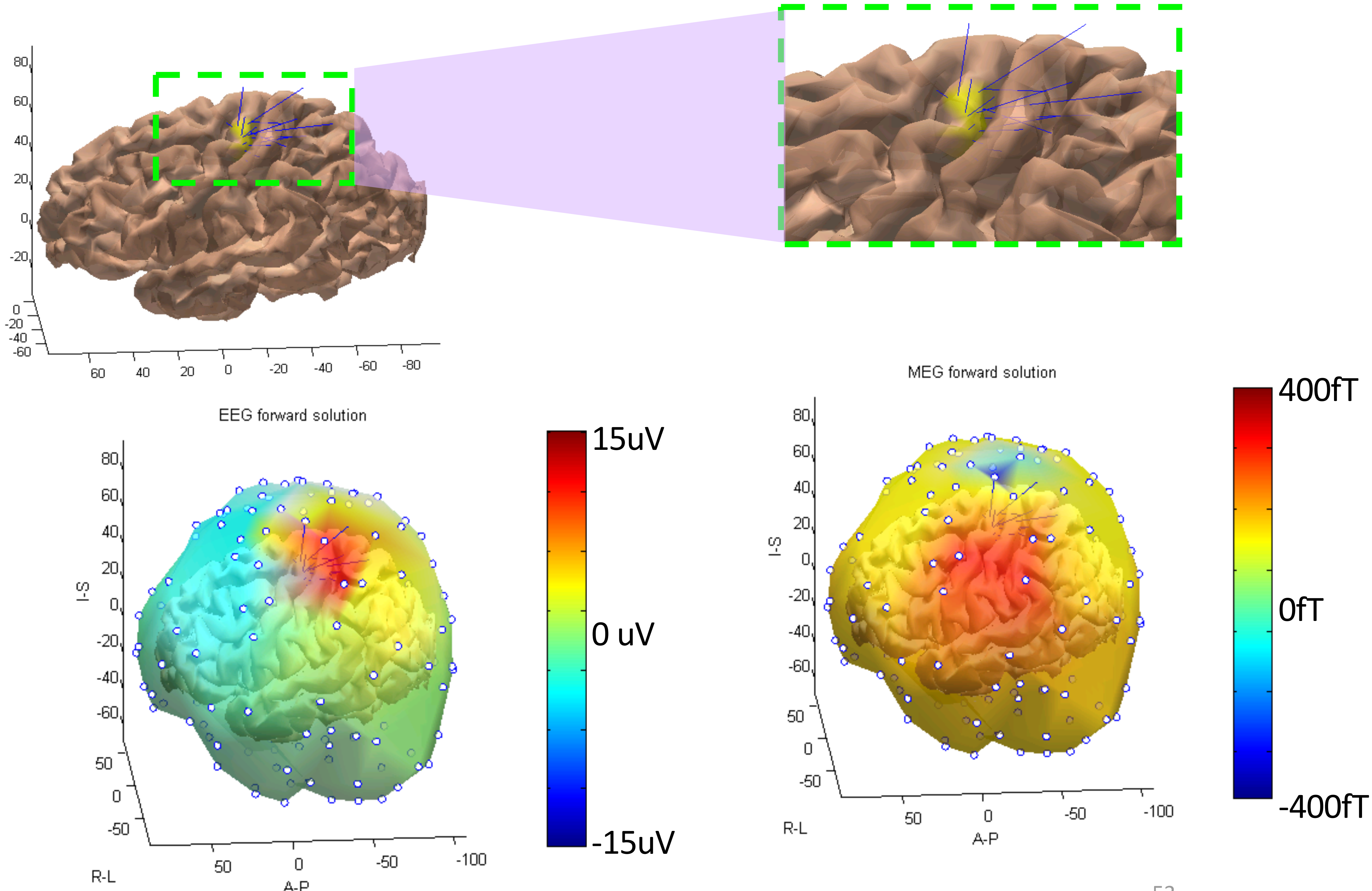
TVB monitors

Raw signals (LFP, firing rate)

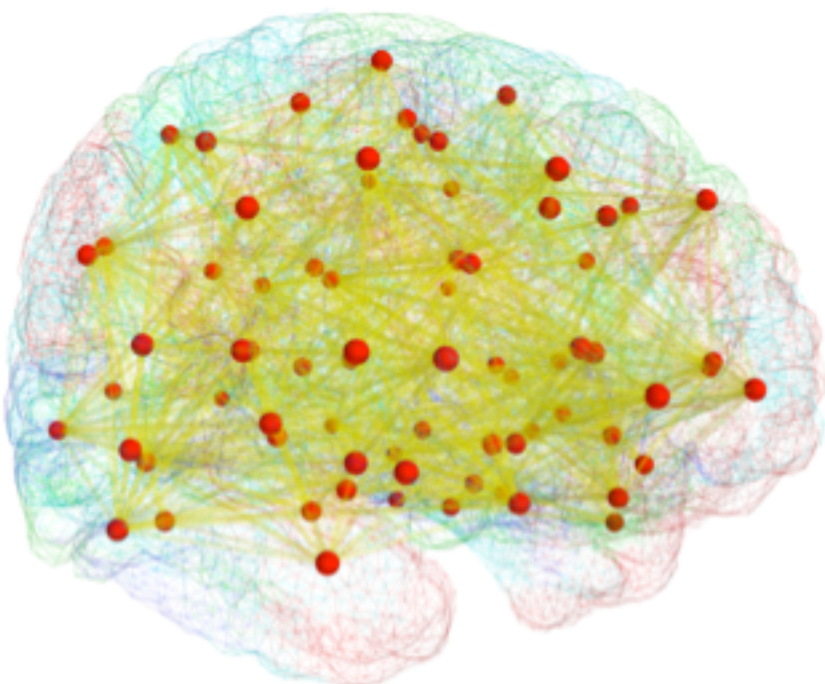
- all state variables are computed and can be saved
- state variables are model dependent

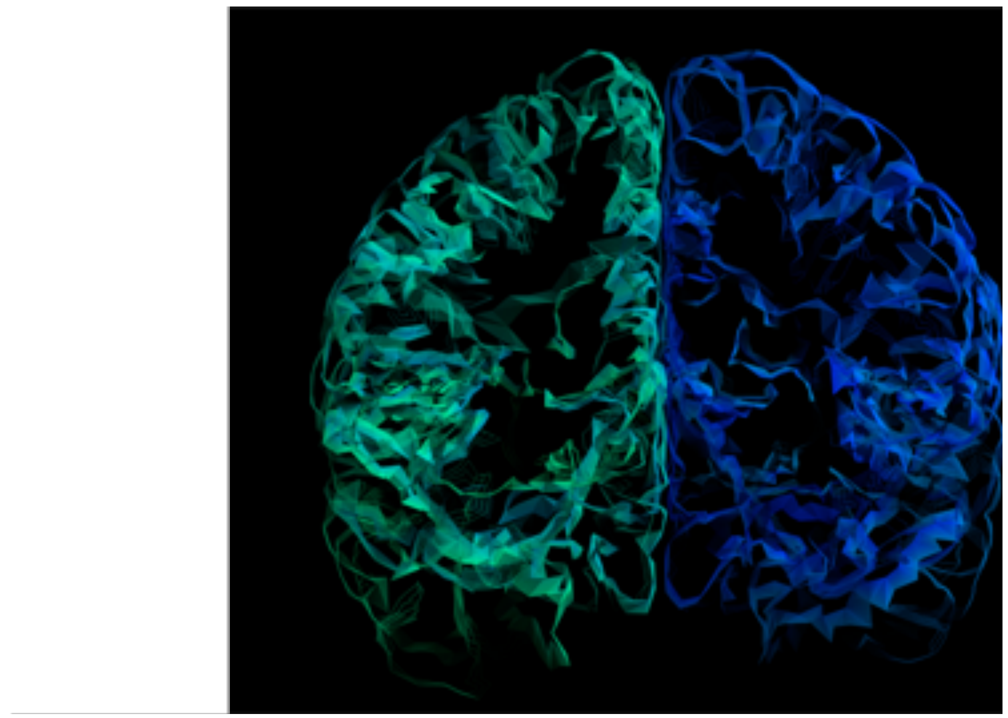
Sanz Leon et al Front NeuroInformatics 2013

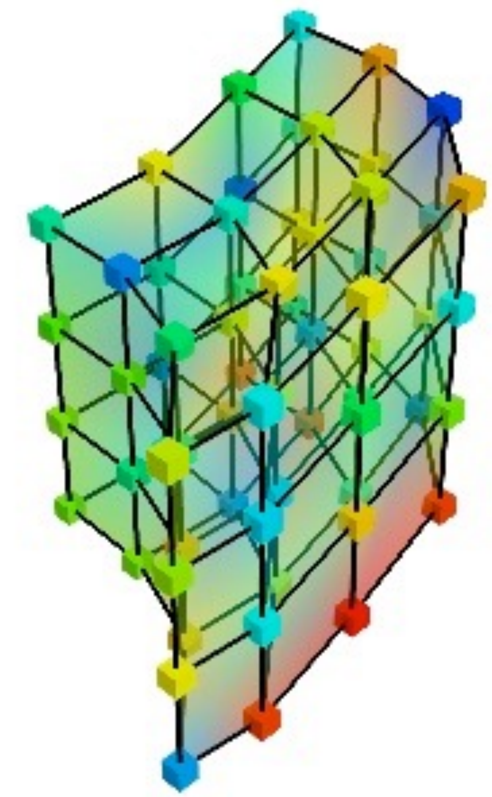
TVB monitors: EEG & MEG

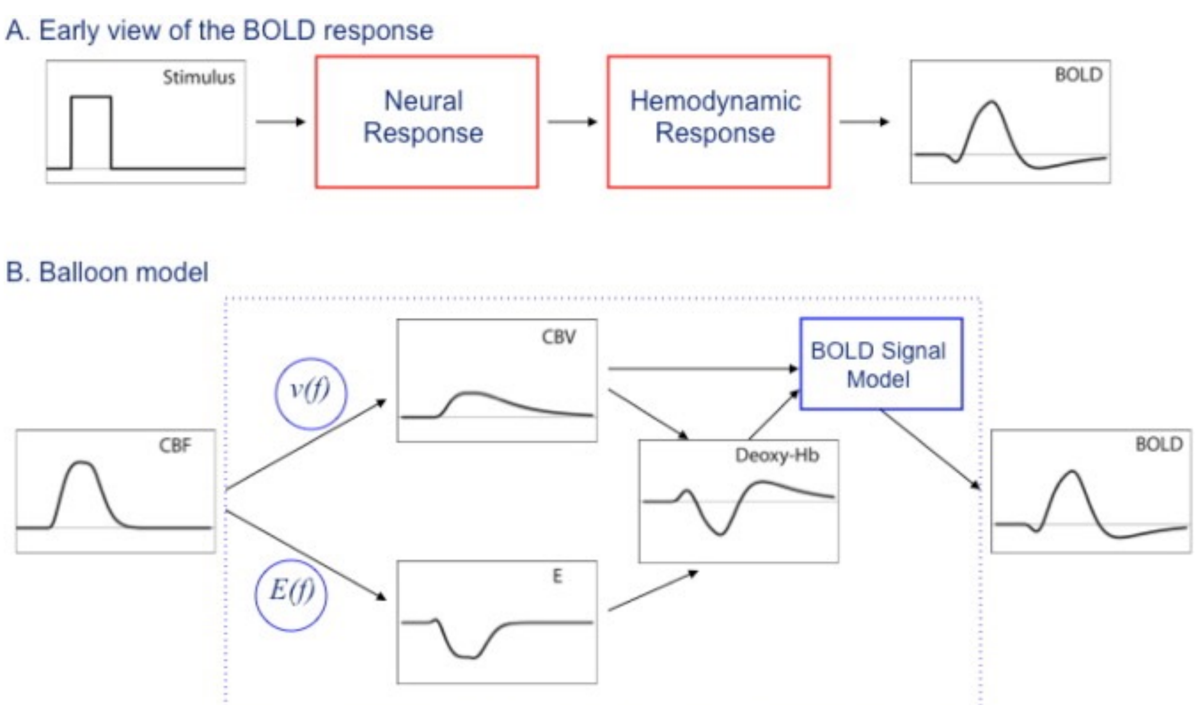


TVB monitors: Bold

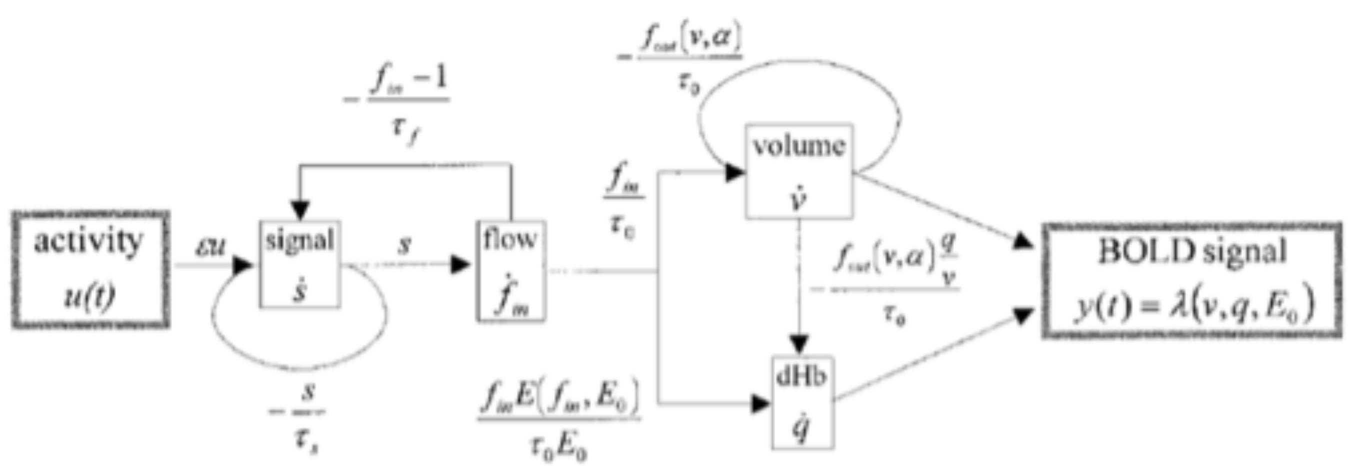






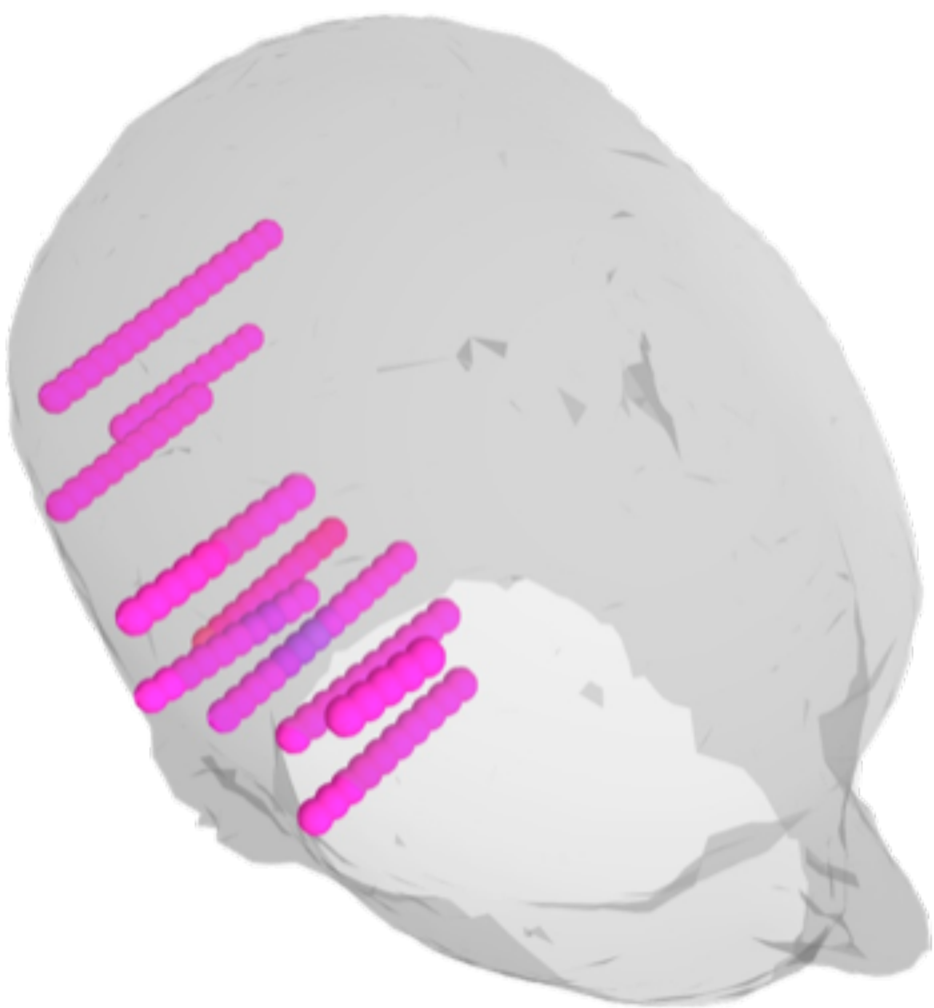


Reduced Balloon-Windkessel model



TVB monitors: stereotactic EEG

$$\mathbf{V}(\mathbf{r}) = \frac{1}{4\pi\sigma}\mathbf{Q} \cdot \frac{\mathbf{r} - \mathbf{r}_0}{|\mathbf{r} - \mathbf{r}_0|^3}$$

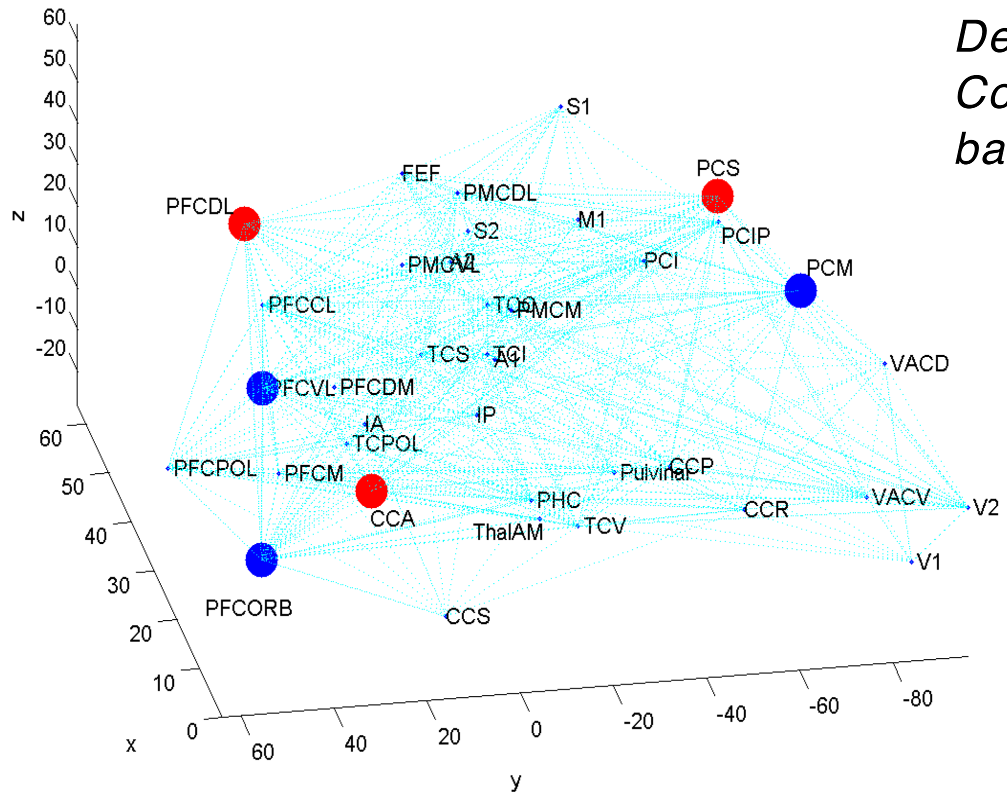


TVB Examples

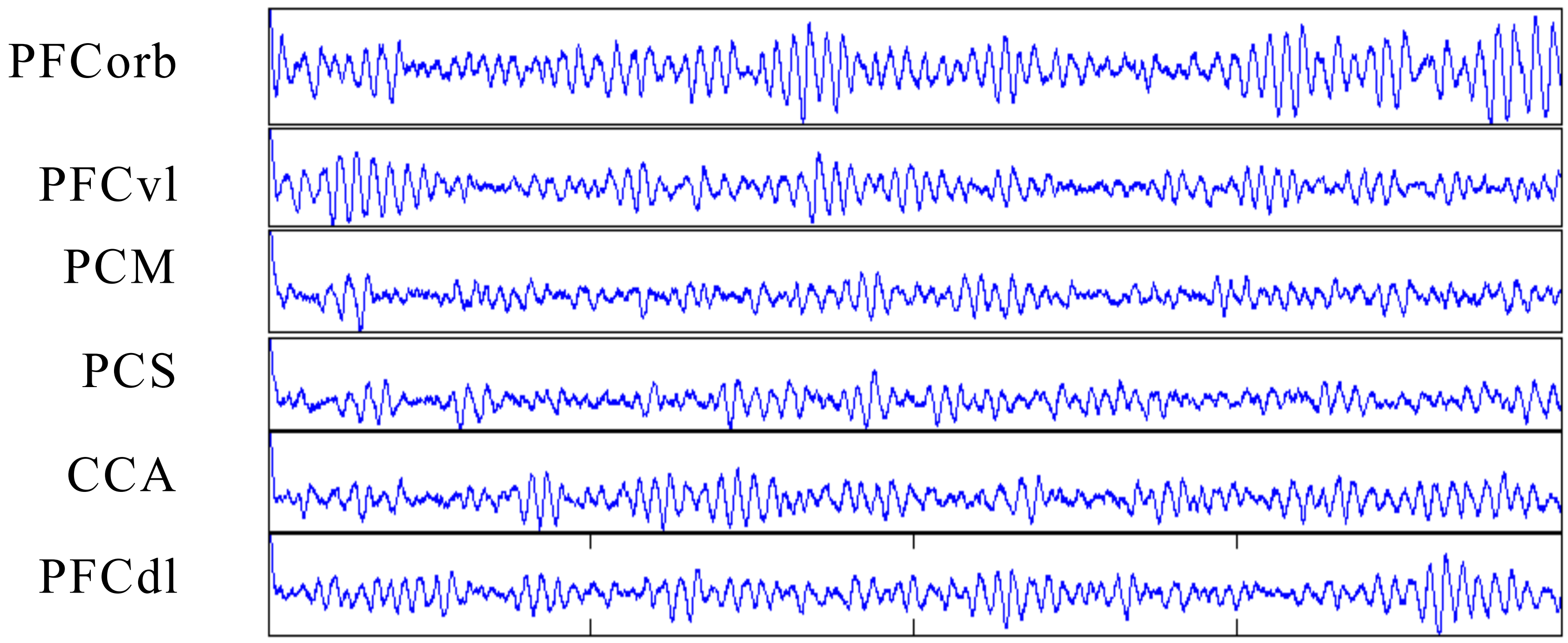
- Resting-State
- Stroke
- Epilepsy
- Dementia
- Mouse

Intrinsic Dynamics (*Resting-State*) are driven by brain noise

"Exploring the dynamic repertoire"
Optimal connection strength, conductivity and noise puts the system into a metastable state



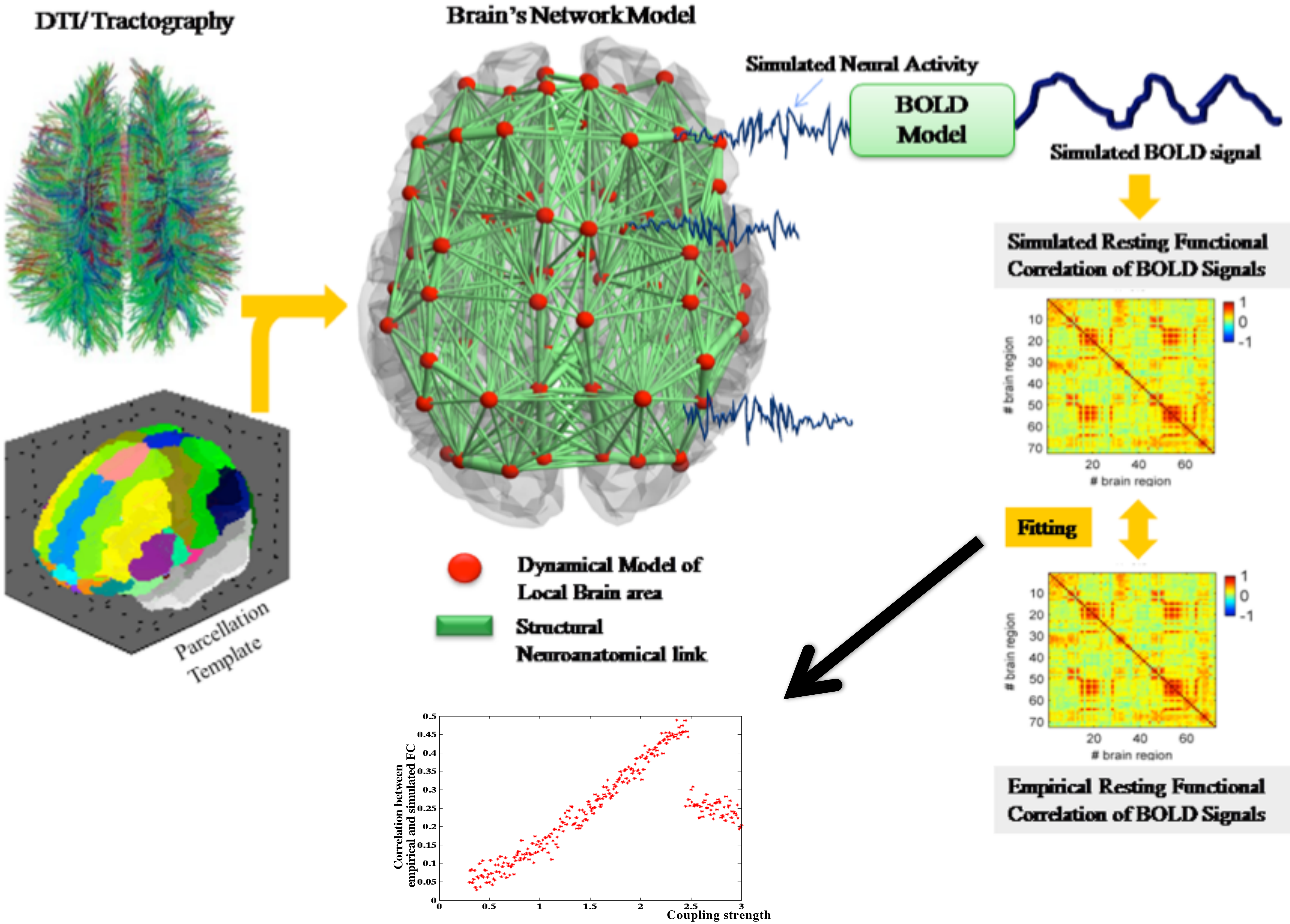
Default Model in TVB
CoCoMac connectome with time delays based on distance in MNI template brain



"Default mode regions" drive the system through instabilities

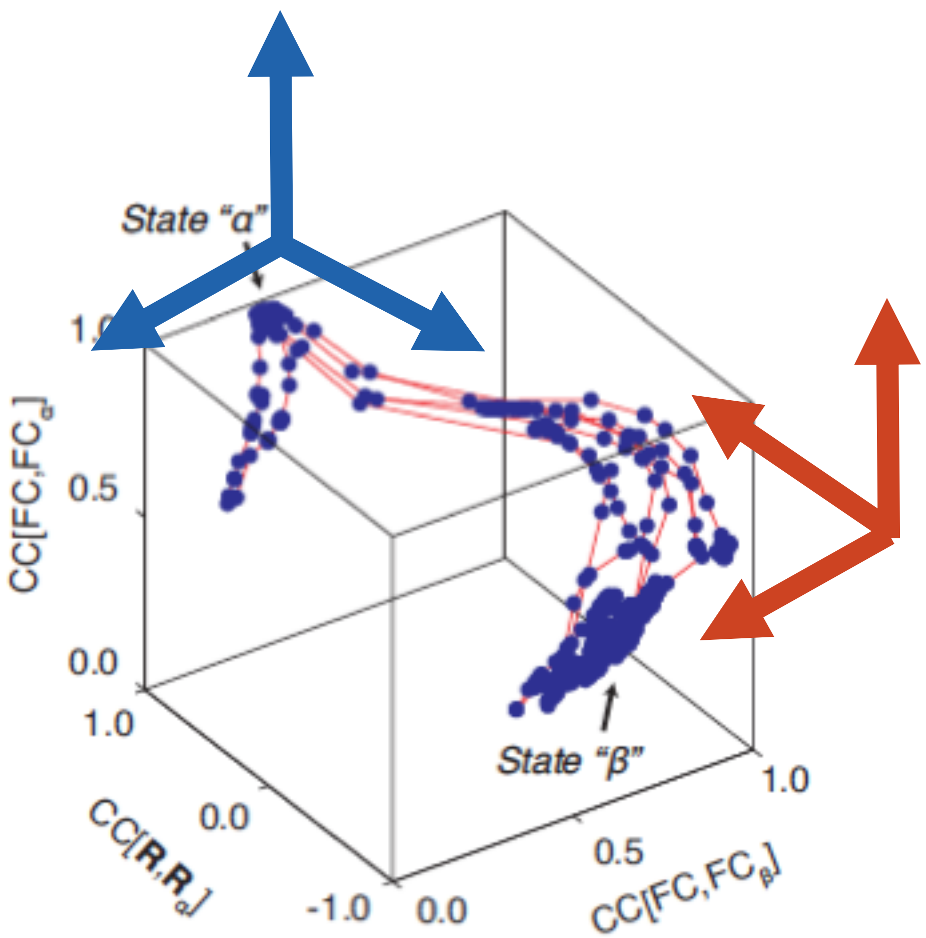
Ghosh, McIntosh, Kötter & Jirsa, PLoS CompBiol, 2008

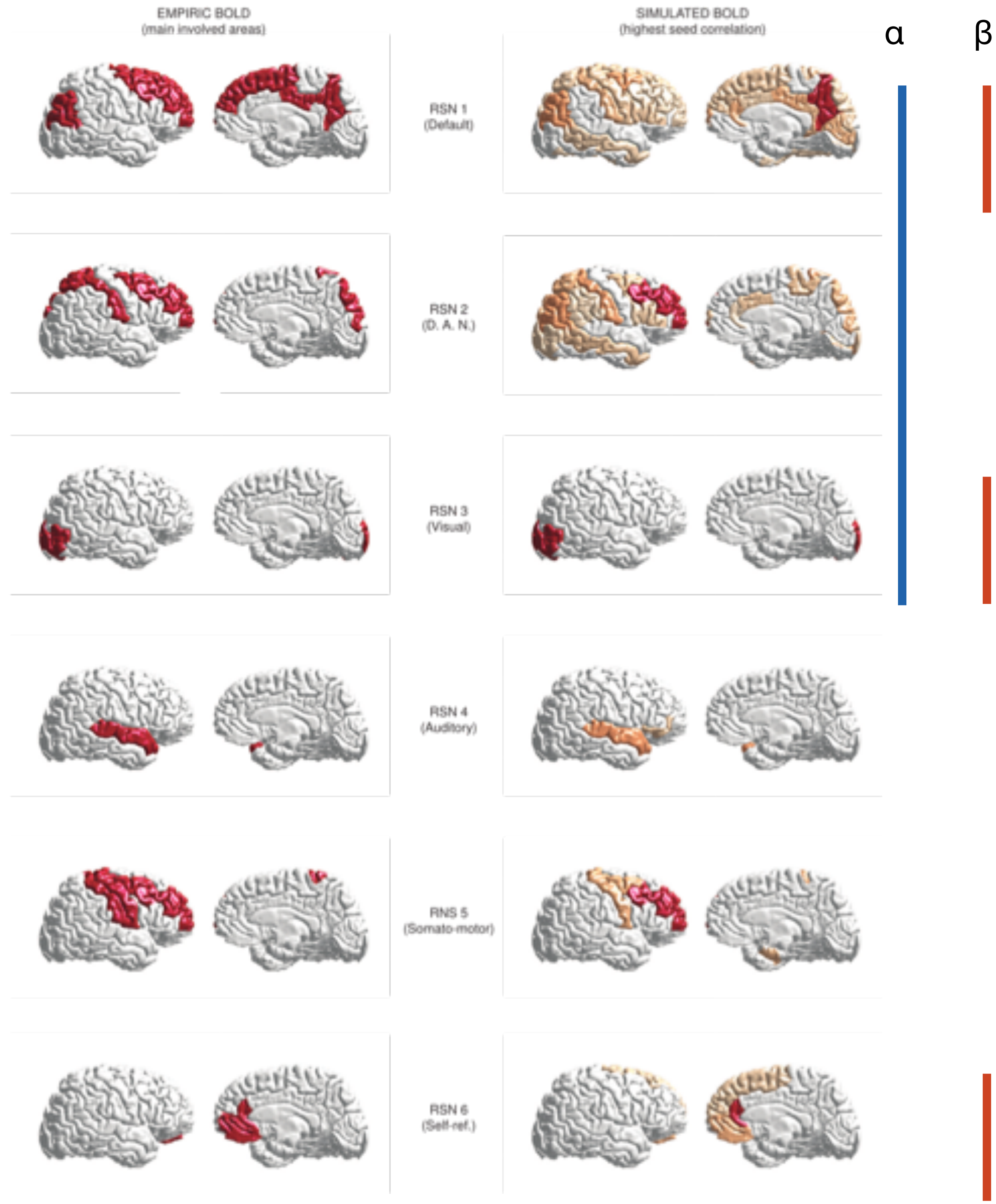
The modeling process of resting-state activity



Gosh et al PLoS CB 2008; Deco, Jirsa & McIntosh et al PNAS 2009; Deco & Jirsa JNS (2012); Deco, Jirsa & McIntosh Nat Rev Neurosci (2011); Deco, Jirsa & McIntosh TINS (2013)

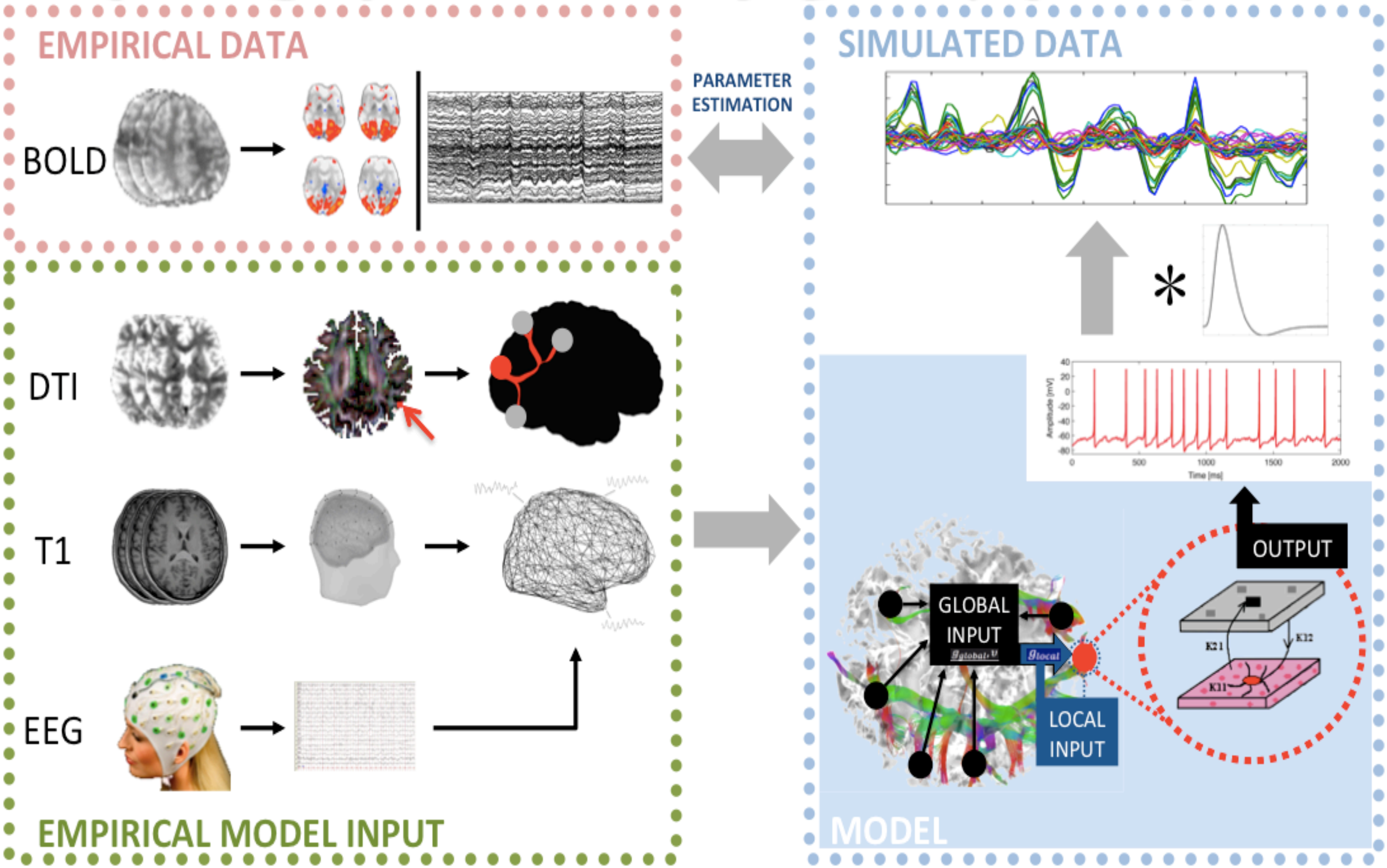
Epochs of invariant functional connectivity
evolve dynamics in subspaces
spanned by sets of resting state network patterns





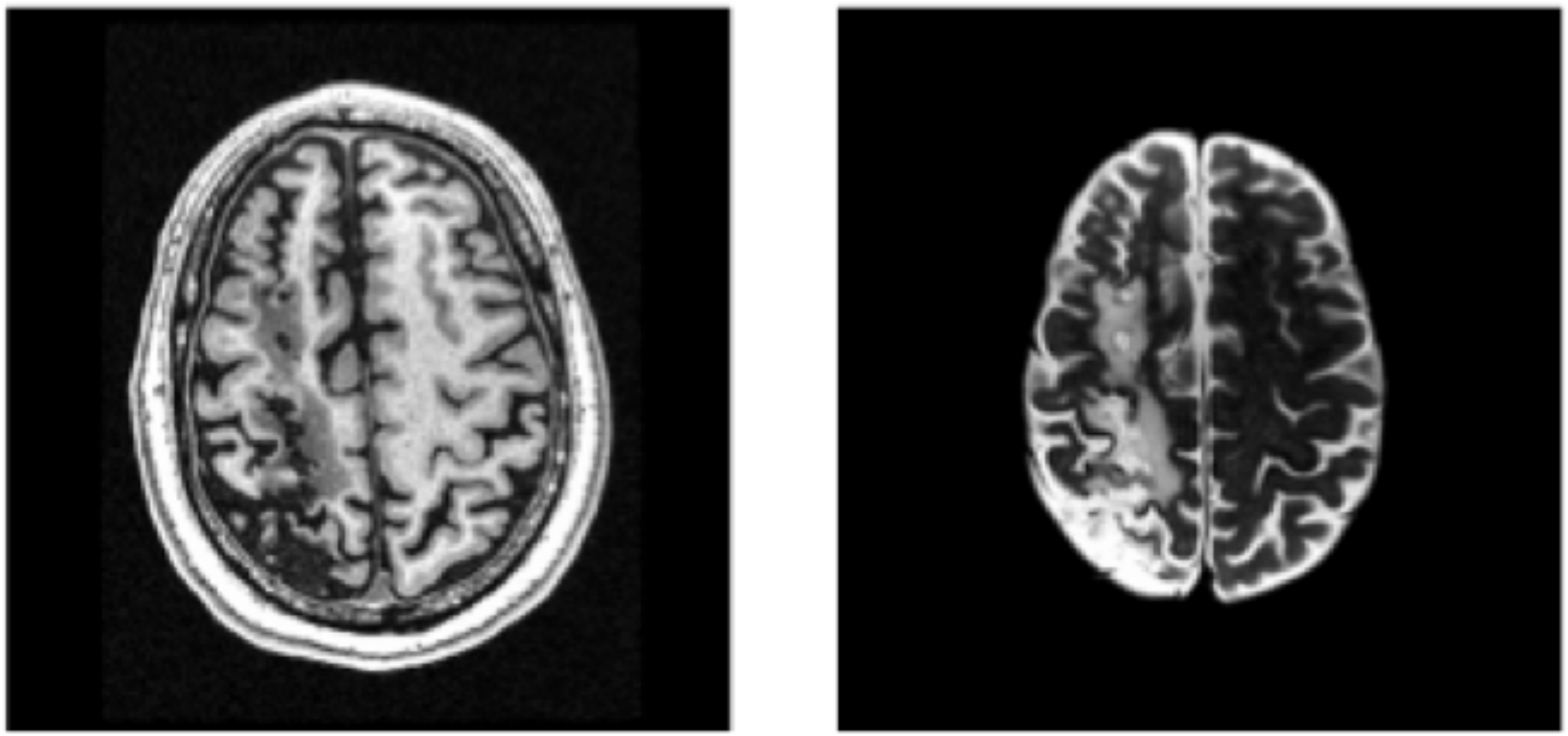
Hansen et al Neuroimage (2014)

Integration of EEG & fMRI



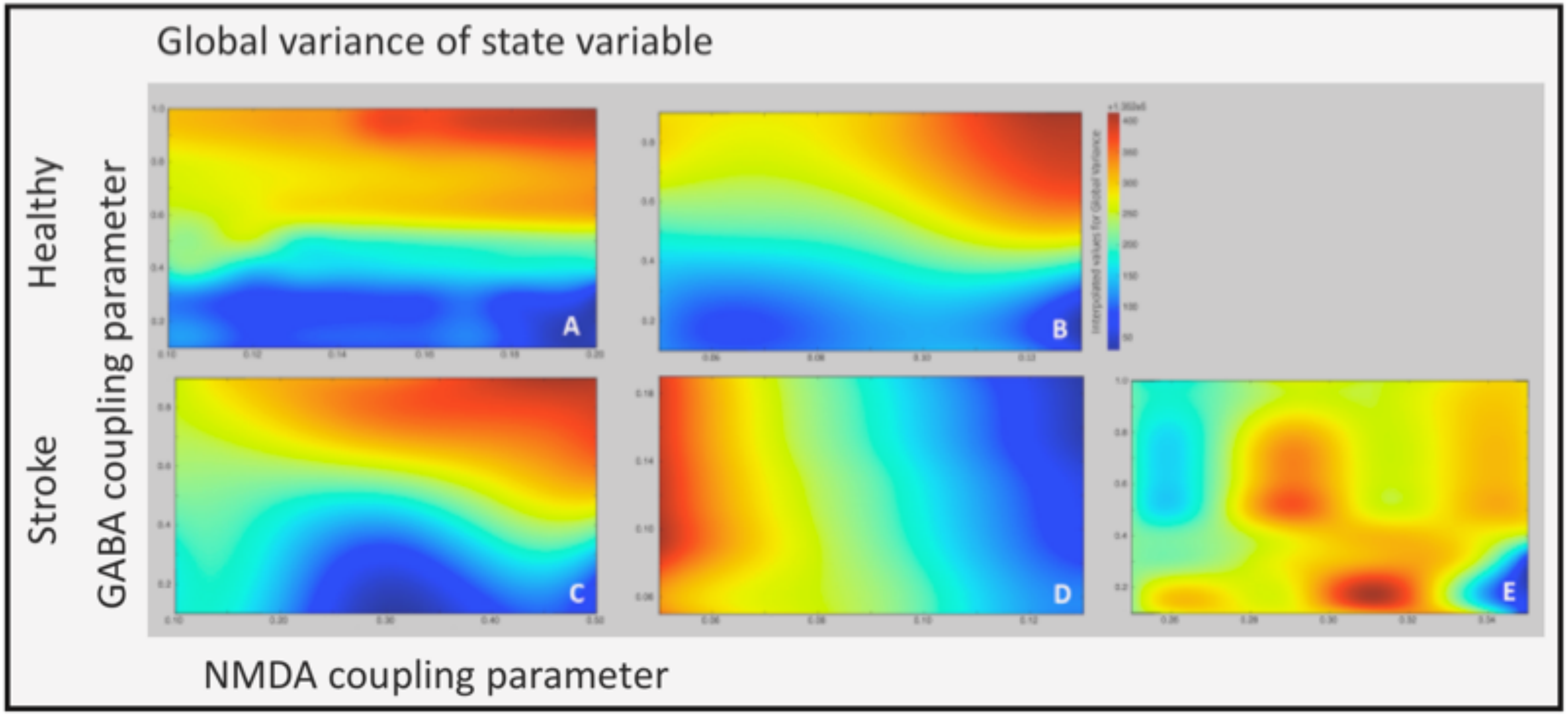
Schirner, McIntosh, Jirsa, Deco, Ritter, eLife, 2018

TVB model of Stroke Recovery



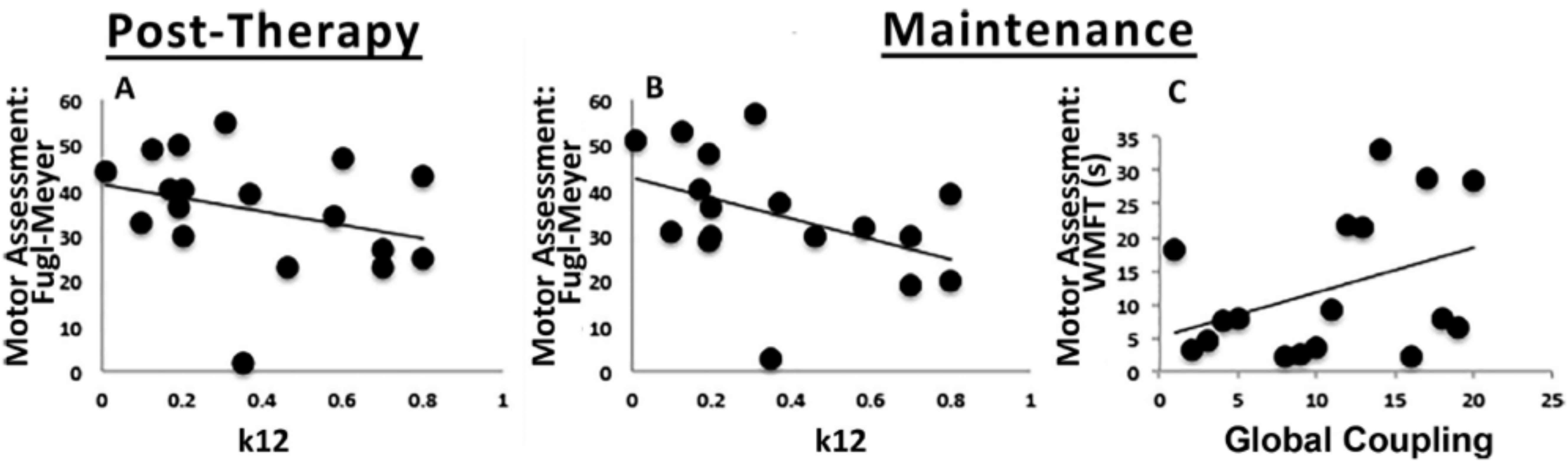
Left hemisphere stroke, Male 55yrs

Falcon et al. 2016 eNeuro



Falcon et al. 2015 Frontiers Computational Neuroscience

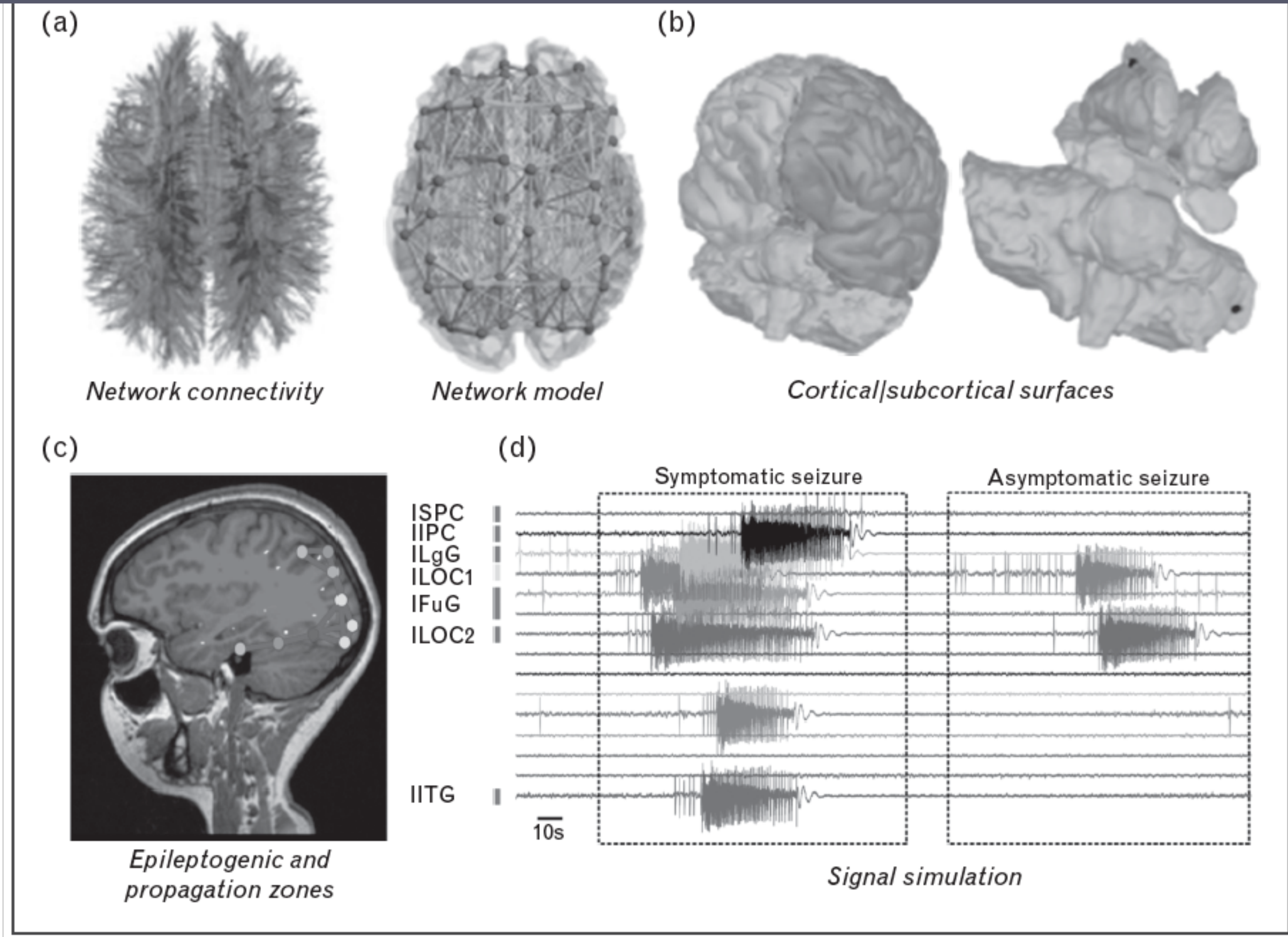
Falcon et al. 2016 eNeuro



Parameter values for from TVB in a patient also predict recovery of motor function!

Falcon et al. 2016
eNeuro

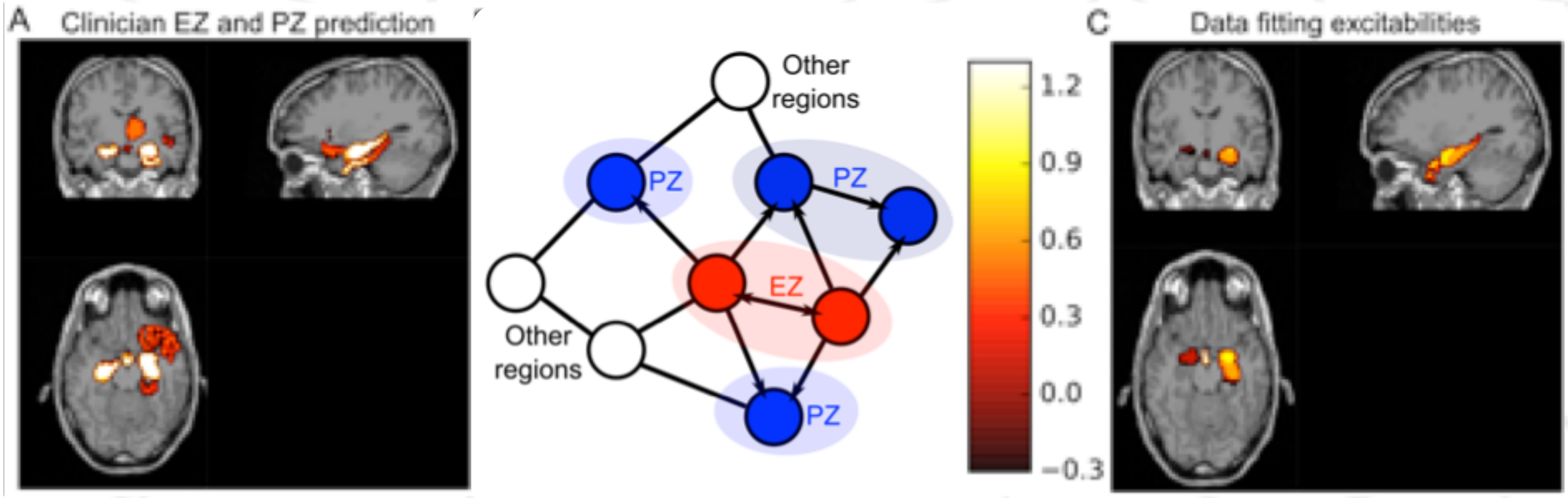
TVB modeling for epilepsy



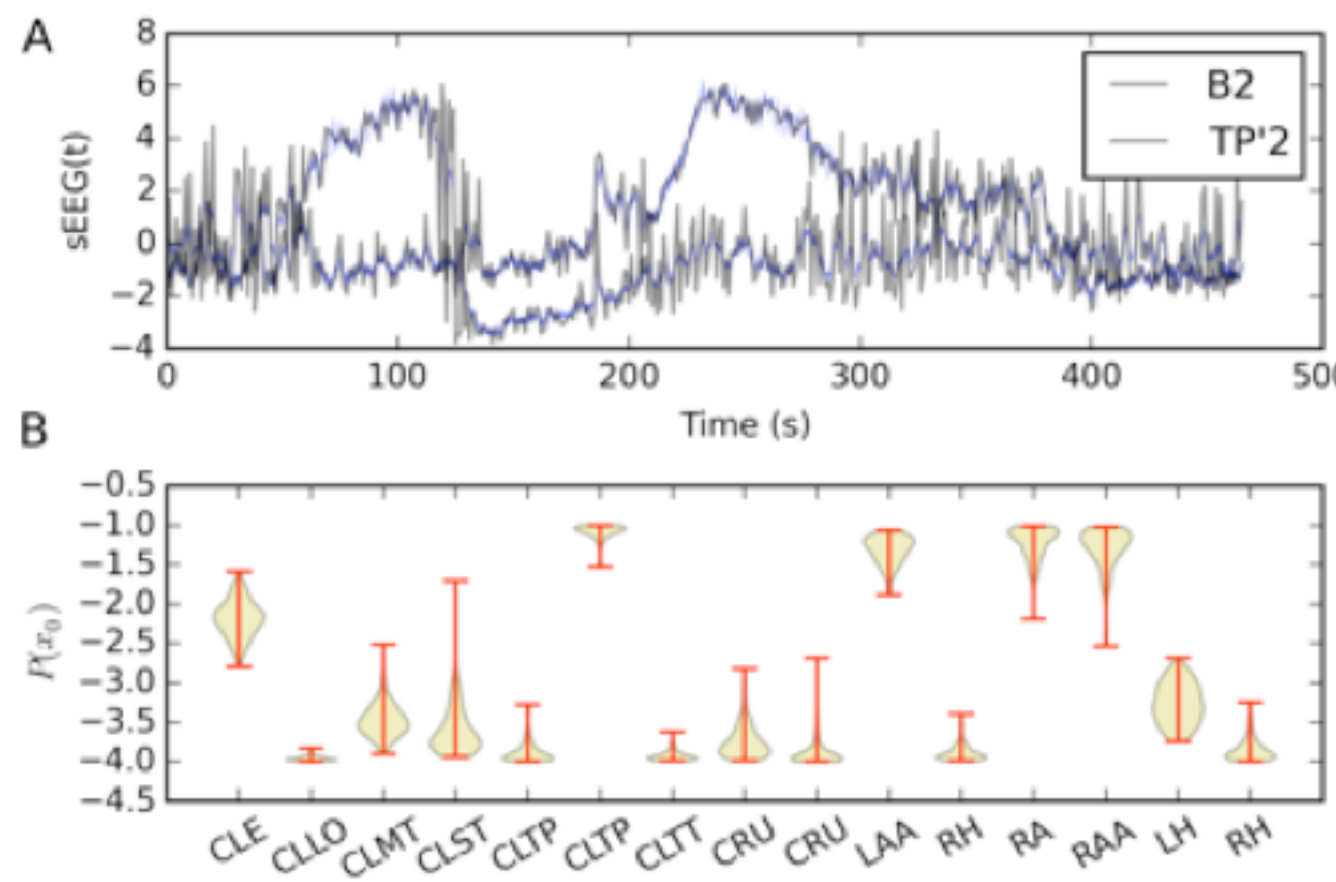
Proix et al. 2016 Neuroimage

Falcon et al. 2016 Current Opinion in Neurology

TVB & Epilepsy: Finger printing

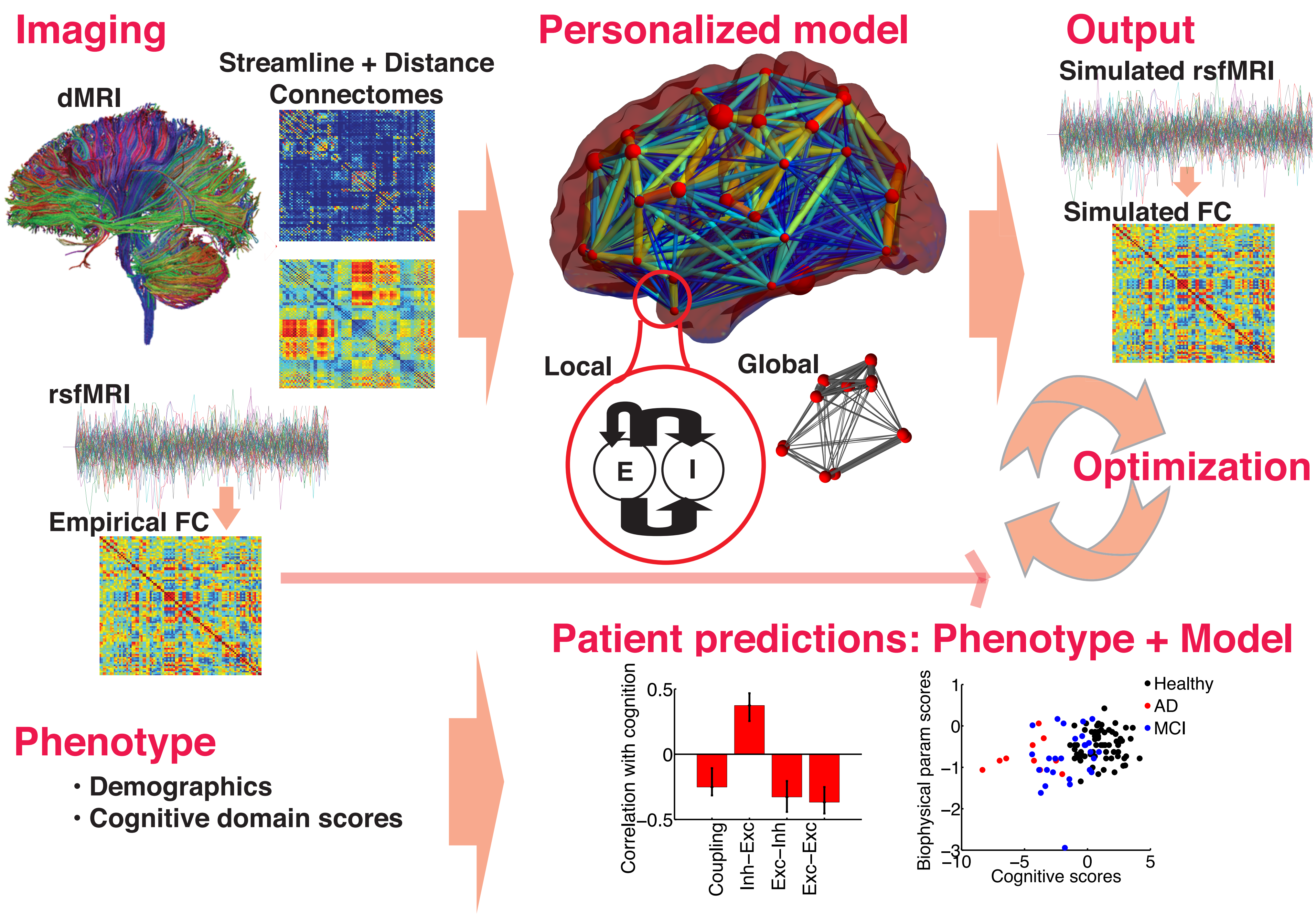


Model inversion using Bayesian inference framework



Jirsa et al. Neuroimage (2016)

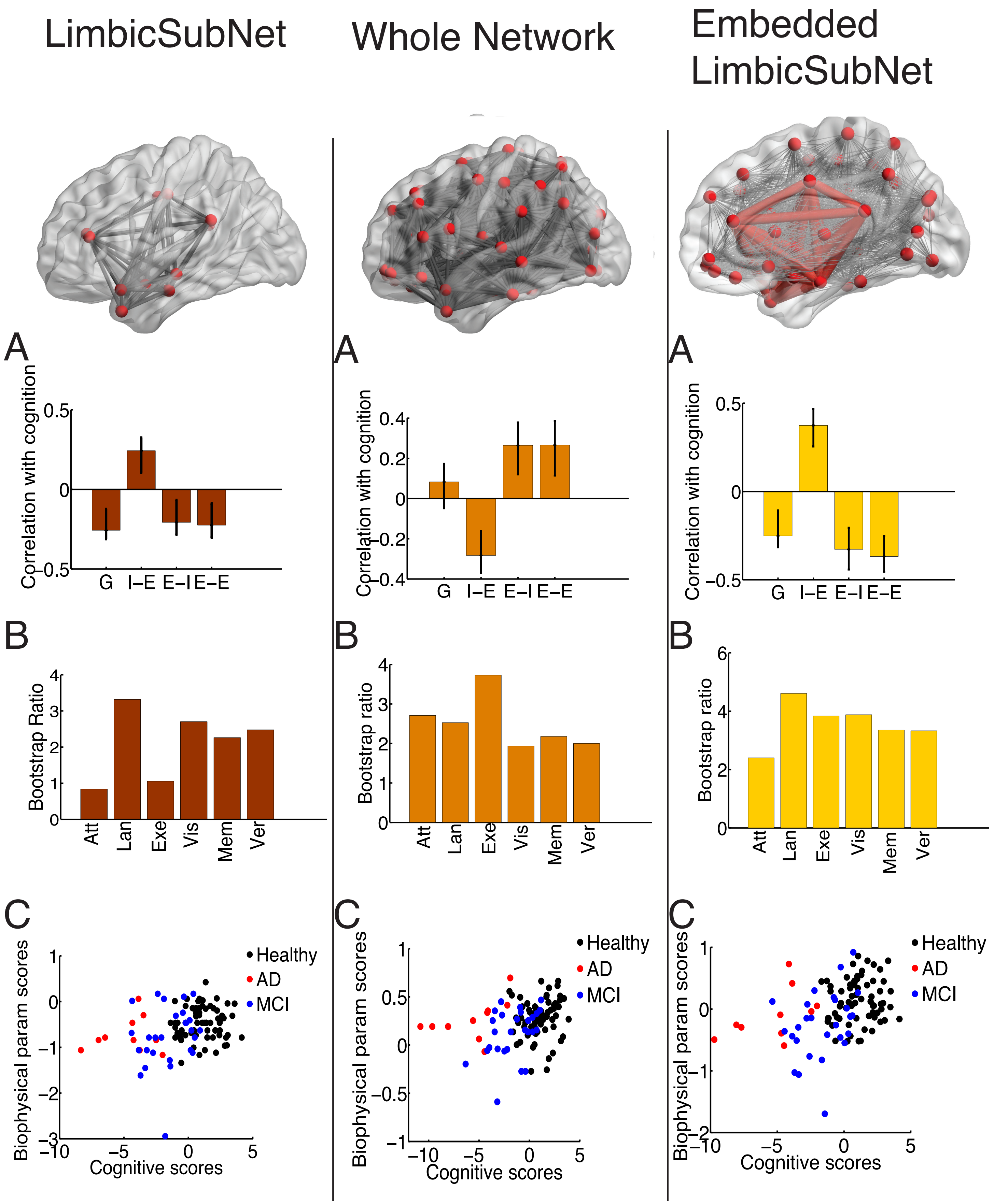
TVB modeling for Alzheimer's Dementia



Zimmemann et al Neuroimage Clinical 2018

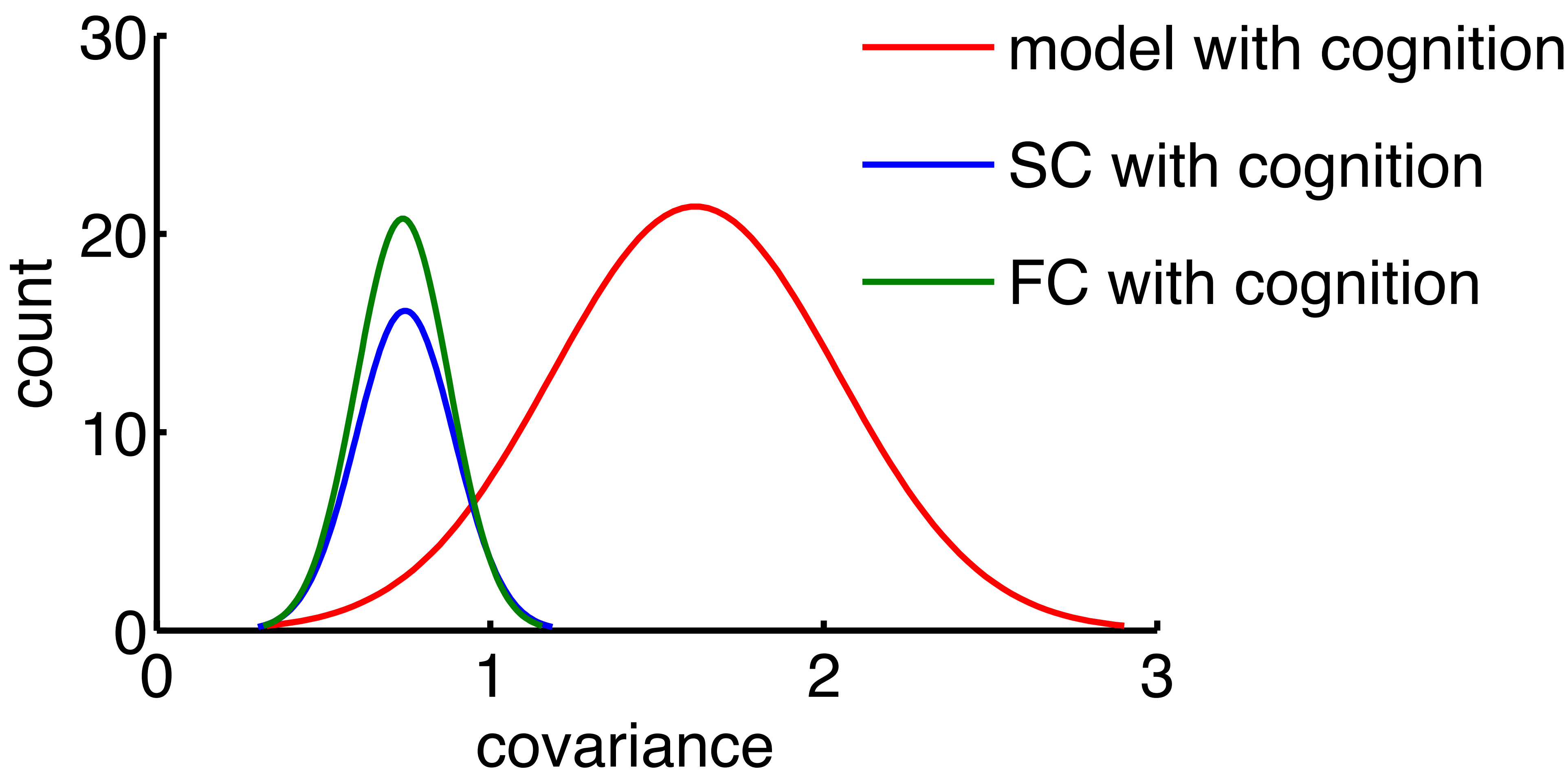
Prediction of cognitive status using TVB parameters

General correlation between local and global model parameters and cognitive scores
- The specific pattern dependent on network extent
- The more embedded the limbic network was the “better” the cognitive status



Zimmemann et al Neuroimage Clinical 2018

TVB parameters superior to structural or functional connectivity in predicting cognition



Also assessed whether the TVB model parameters were a better predictor of cognitive function than structural or functional connectivity (SC, FC)

- Bootstrap distributions show TVB model is a better predictor of cognition
- SC and FC are equivalent

Zimmemann et al Neuroimage Clinical 2018

The Virtual Mouse Brain (TVMB) modeling

Local dynamics

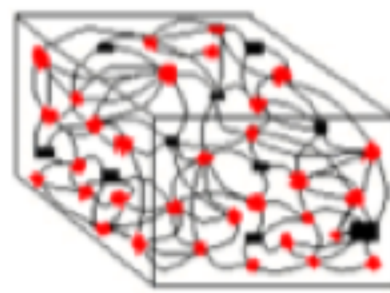
Global dynamics

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

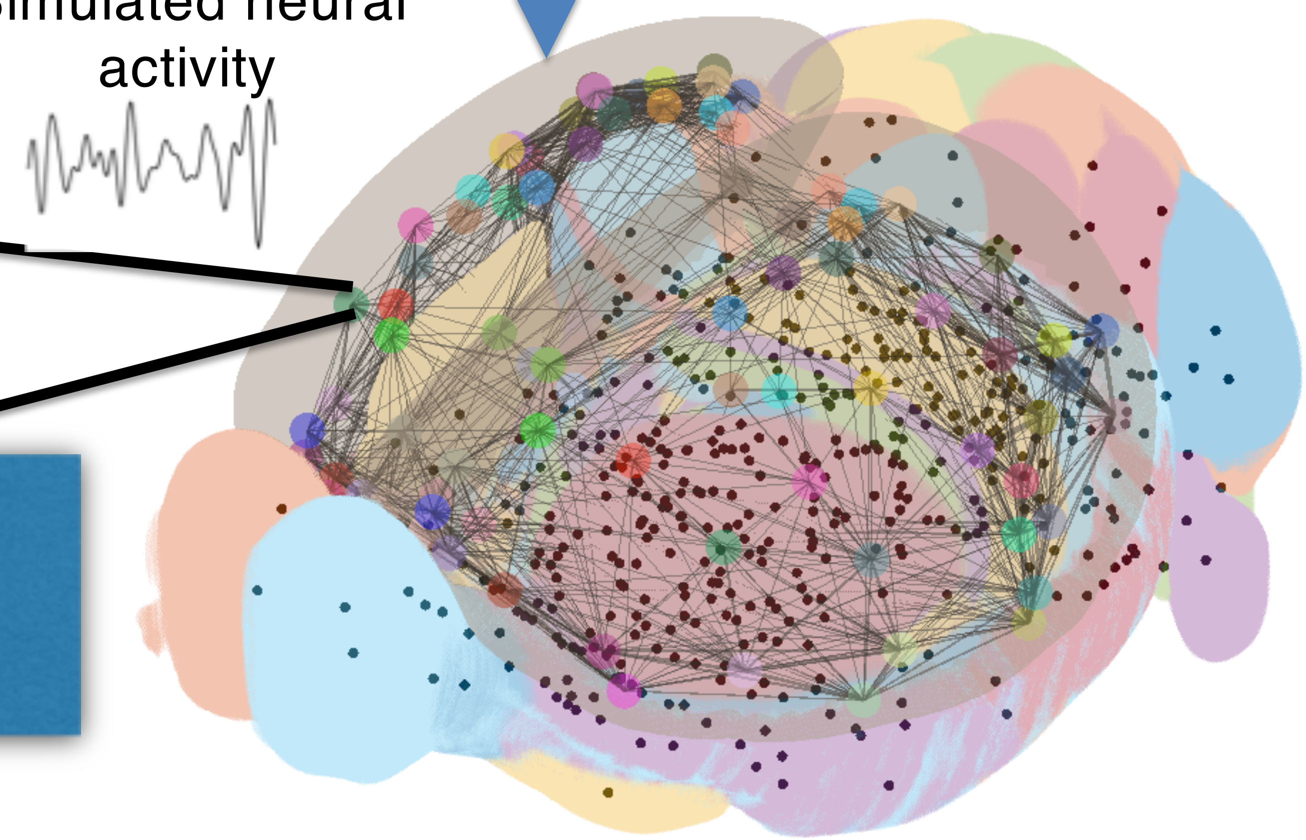
Field potential

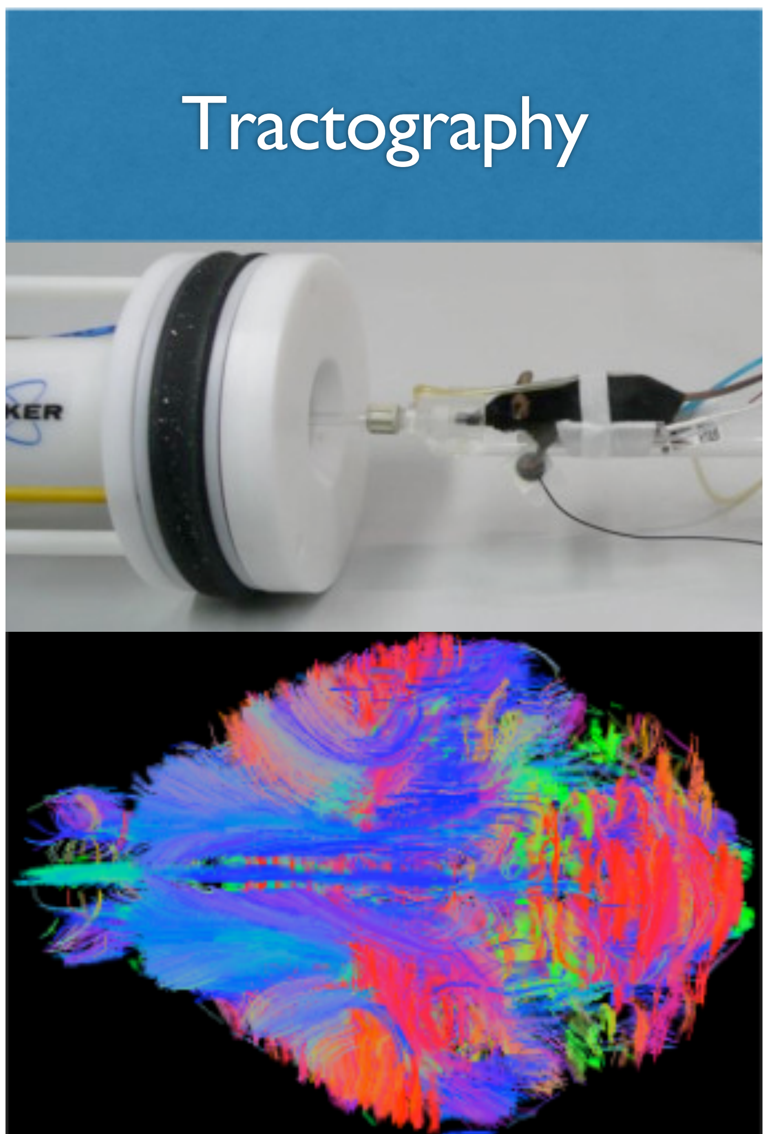
Intrinsic activity

0.1-1mm



Simulated neural activity

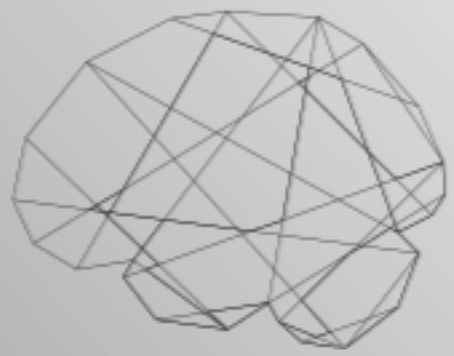




Neuronal population

Melozzi et al. eNeuro, 2017

Human Brain Project



THANK YOU
Play nice, have fun