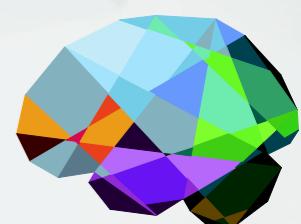


NODE #7 WORKSHOP

AUGUST 7-8, 2018 | MONTREAL, CANADA

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

*Randy McIntosh
Rotman Research Institute - Baycrest
Univ of Toronto*



Outline

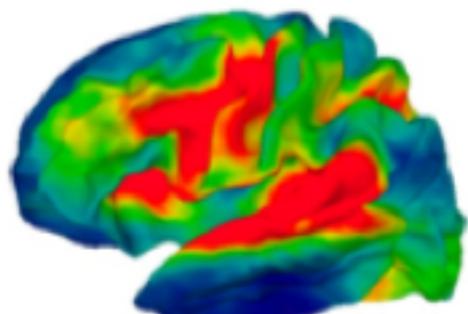
- Motivation for The Virtual Brain
- The Virtual Brain Platform
 - Architecture and access
 - Dynamics
 - Geometry & Connectivity
 - Simulations & Data Generation
- Examples



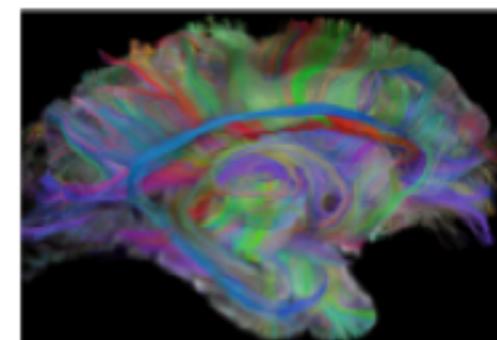
Brain Connectivity

Structure, dynamics and function

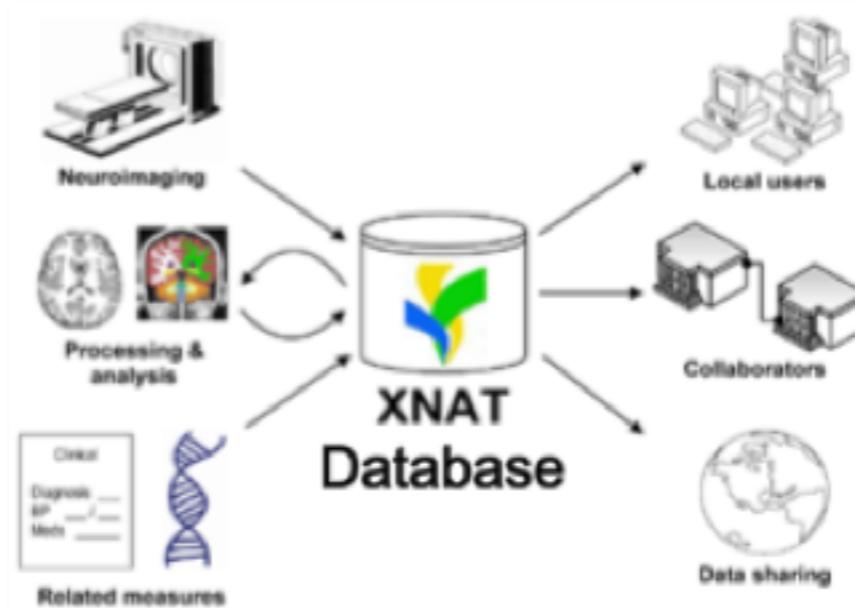
If the brain is a network, how do we study it?



Functional neuroimaging



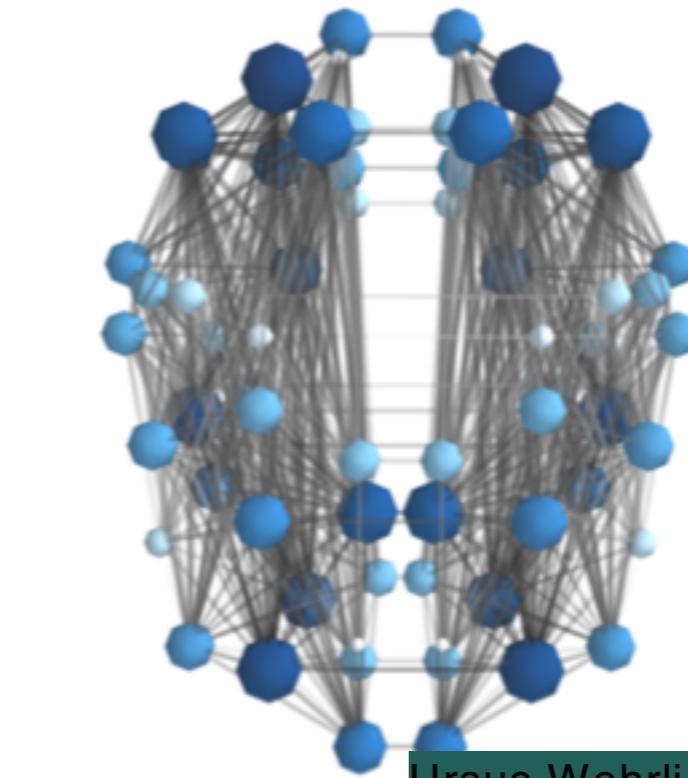
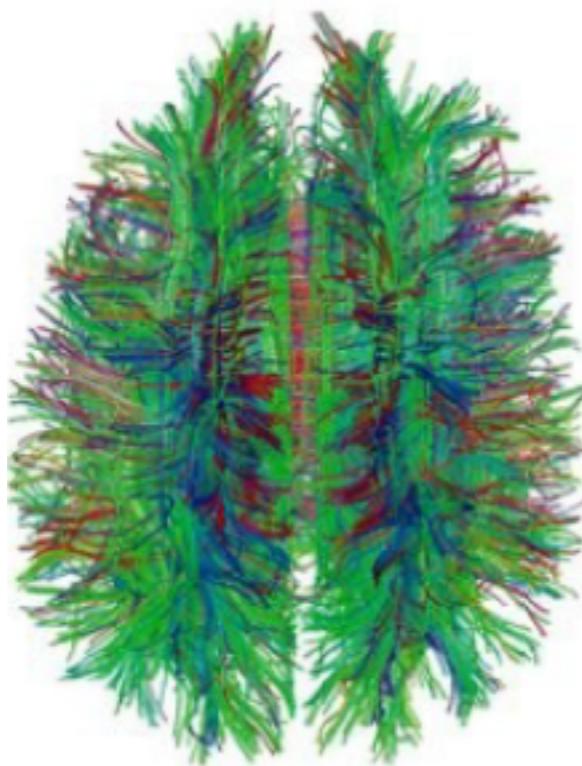
Structural neuroimaging



Neuroinformatics



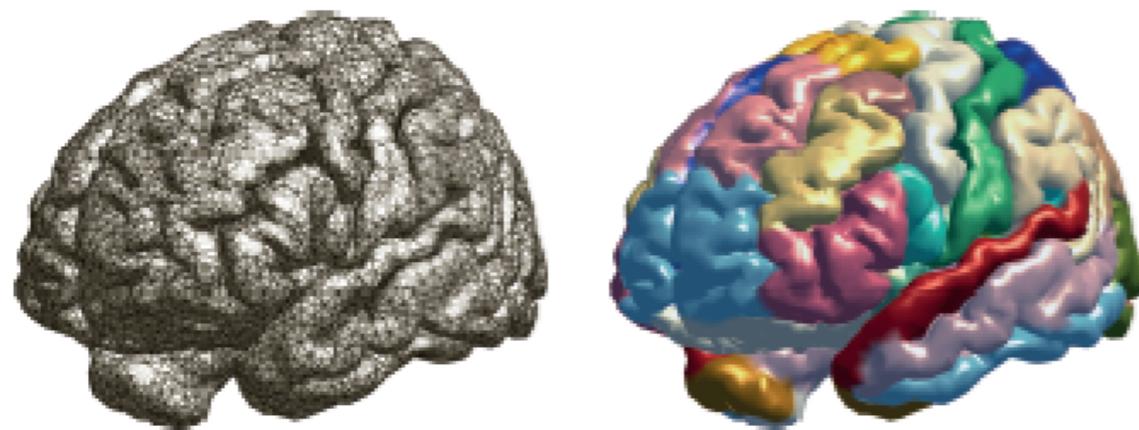
Need for a large-scale network-based thinking



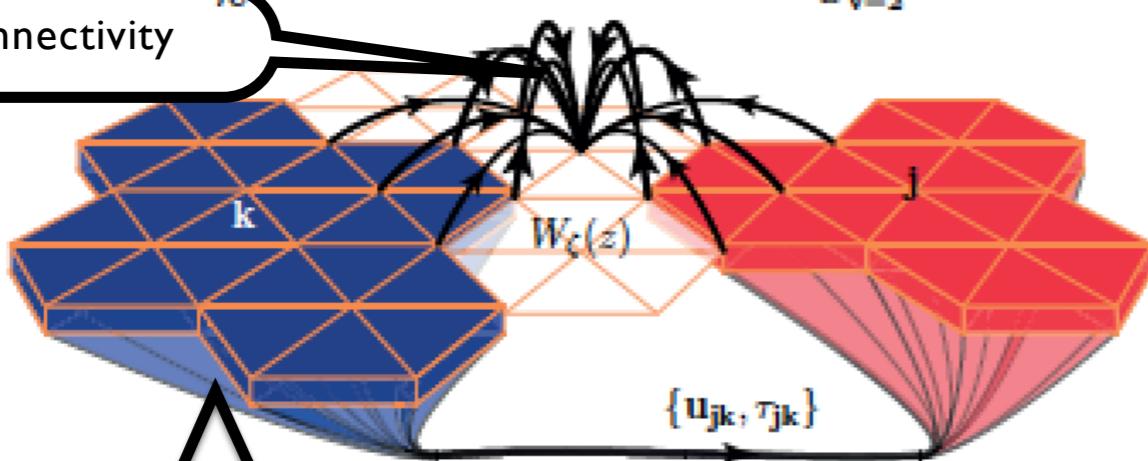
Ursus Wehrli «Kunst
aufräumen»

Need for a large-scale network-based thinking

Large-scale brain networks

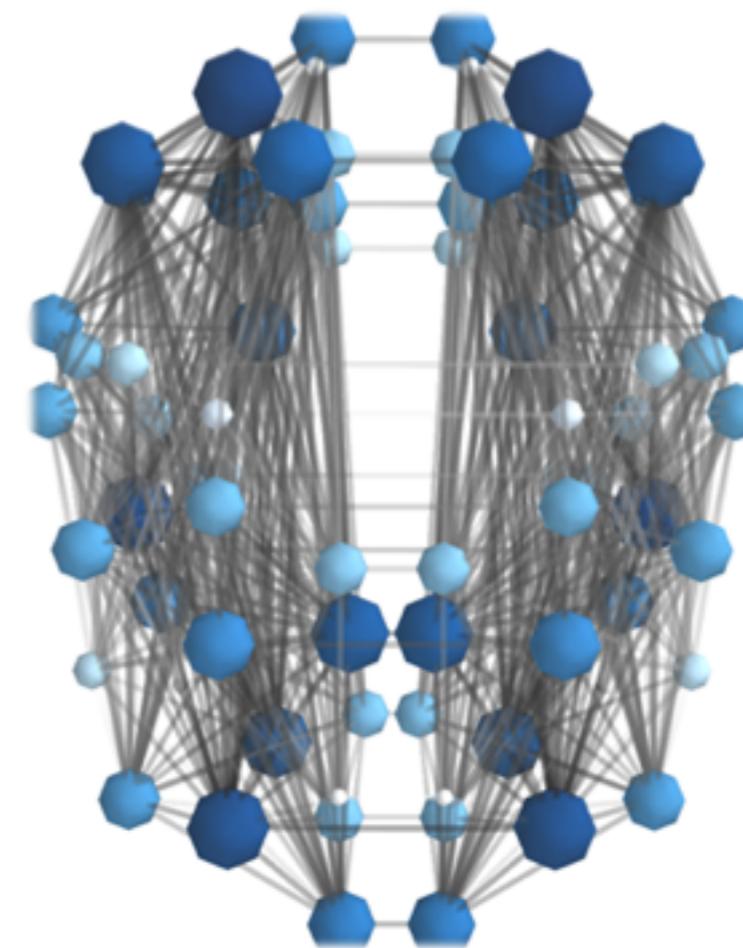


local connectivity

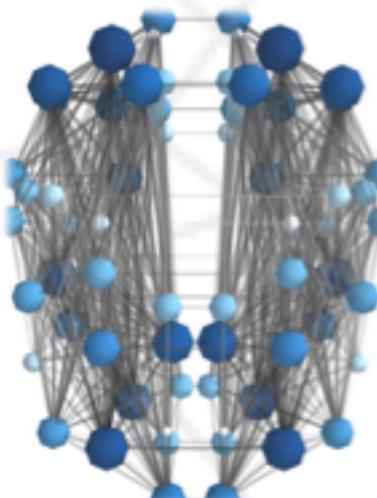
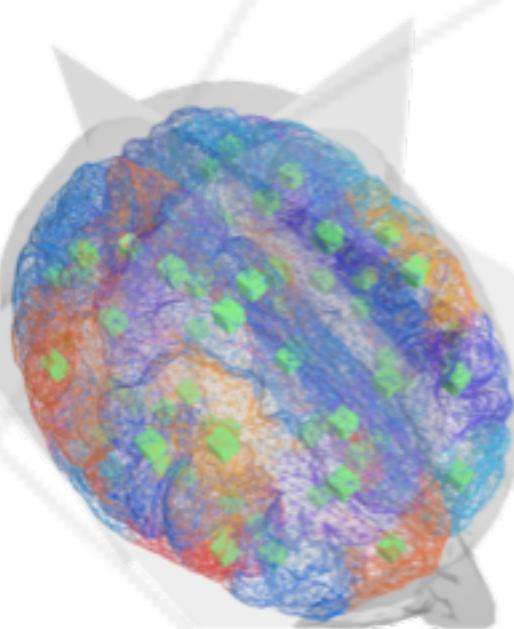
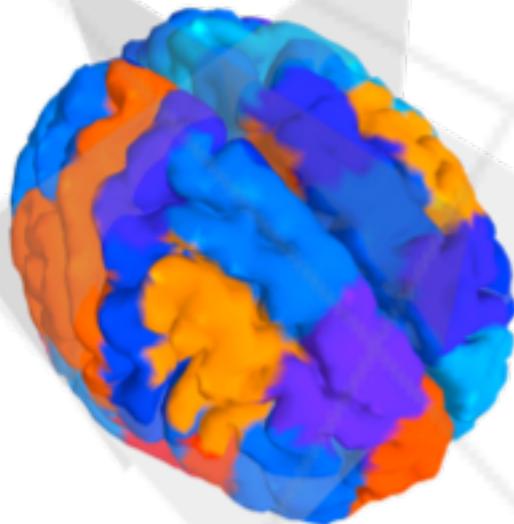


neural mass

time delays via long range connections



Large-scale brain network modeling



Nunez 1974
Jirsa-Haken 1996, 1997, 1998

Robinson et al. 1997, 1998, 2001
Coombes 2010

Homogeneous
approximation/assumption

First extensions to address
inhomogeneity

Homogeneous

Jirsa & Kelso 2000

Jirsa et al 2002

Stephan, Kötter, et al 2000

Two point connection

Full brain system dynamics

Cocomac

Heterogeneous

Ghosh et al 2006, 2008

Honey et al. 2007
zhikovich et al 2008
Deco, Jirsa, et al 2009
Bojak et al 2009

Cocomac based brain dynamics

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



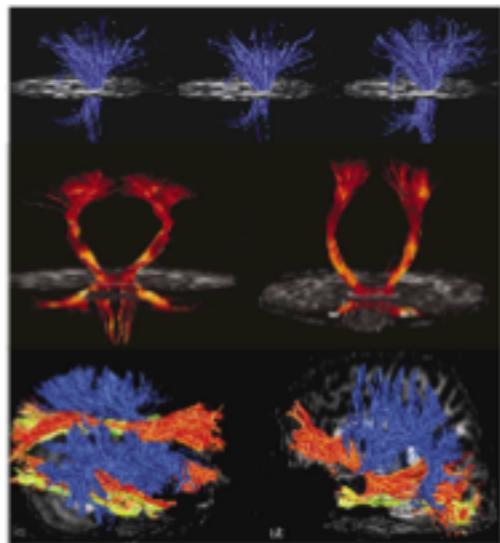
The software

Open source & ready to
install

TVB: Synergy of competences

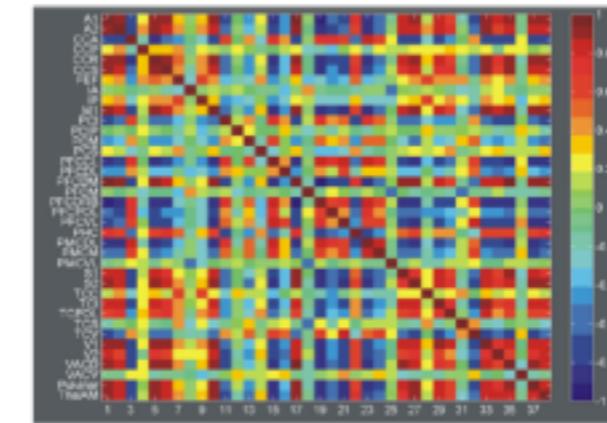
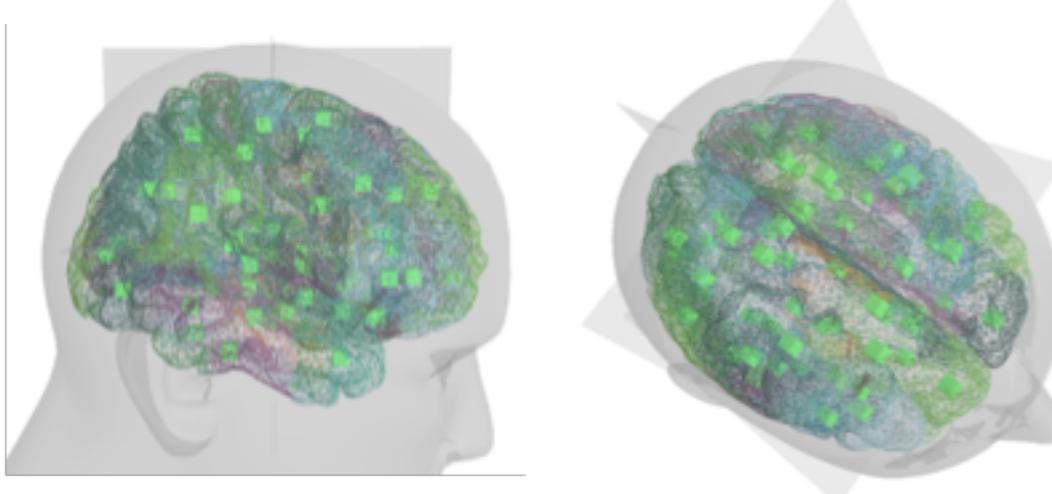
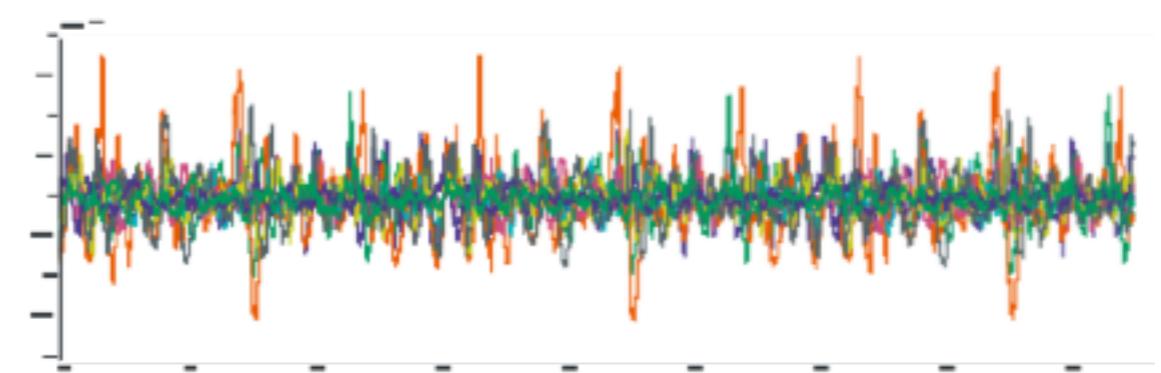
Structure

Connectivity & geometry



Function

Network dynamics & simulation



NEUROSCIENCE

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TEAMWORK

THEVIRTUALBRAIN

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Simulate a human brain, right on your PC!
FREE DOWNLOAD: WINDOWS / MAC / LINUX

Delivering practical results. For novel clinical applications.

Coming up: Workshop: TVB:Node#6

For over 20 years, bright minds and ambitious projects have attempted to emulate the human brain across various scales of organization. Despite impressive efforts to bring in the latest and greatest computing power of massively parallel hardware, success hasn't yielded practical applications yet.

To get practicality sooner, The Virtual Brain takes a network approach on the largest scale. By manipulating network parameters, in particular the brain's connectivity, The Virtual Brain simulates its behavior as it is commonly observed in clinical scanners (e.g. EEG, MEG, fMRI).

Though The Virtual Brain incorporates the complex world of neuro-chemistry only to a small degree, it gains a lot by not becoming as complex as the brain itself.

Instead, The Virtual Brain embraces and extends novel concepts from computational, cognitive and clinical neuroscience in order to drastically reduce the model's complexity while still keeping it sufficiently realistic – and delivering the same output as clinical brain-scanners.

Upcoming events

- NOV 26** **Workshop: TVB:Node#6**
Berlin, Germany: Get up to speed about the fundamental principles of full brain network modeling using
- NOV 15** **TVB Poster Series @ SfN 2017**
Washington DC, USA: TVB Poster Series @ SfN 2017 Don't miss the TVB poster series at SfN where you can
- NOV 11** **See TVB live at SfN 2017!**
Washington DC, USA: The Virtual Brain team will exhibit at the Annual Meeting of the Society for Neuro
- MAY 15** **Workshop: TVB:Node#5**
Marseille, France: Get up to speed about the fundamental principles of full brain network modeling using
- MAR 21** **Workshop: TVB:Node#4**
Toronto, Canada: Get up to speed about the fundamental principles of full brain network modeling using
- NOV 12** **See TVB live at SfN 2016!**
San Diego, USA: The Virtual Brain team will exhibit at the Annual Meeting of the Society for Neuroscience
- AUG 24** **Long Night of Museums**
Berlin, Germany: During Long Night of Museums on August 27, the Brain-Modes Berlin team participates with

Latest publications

- Inferring multi-scale neural mechanisms with brain network modelling
eLife 2018
- Structural and functional, empirical and modeled connectivity in the cerebral cortex of the rat.
NeuroImage
- The Virtual Mouse Brain: A Computational Neuroinformatics Platform to Study Whole Mouse Brain Dynamics.
eNeuro

New developments

- 10,000 installations of The Virtual Brain: Thank you!**
January 10: On the quiet Saturday morning
- TVB at 5th HBP School on Brain Disease Neuroscience in Austria**
January 6: Members
- Congratulations Dr. Petra Ritter!**
October 23: Petra Ritter has been appointed as a Lifetime Professor
- TVB @ TEDx Padova**
October 23: Dr. Petra Ritter presents an original talk about TVB at TEDx Padova, about

Download: Windows, Mac, Linux

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THEVIRTUALBRAIN

Software Downloads

System Requirements

Import & Export data

Getting Help & Support

Screenshots

Download The Virtual Brain for free! For Windows, Mac and Linux.

3520 Downloads Last 30 days **+368** Updated 162 days ago **v1.5**

WIN 55% of downloads **MAC** 31% of downloads **LINUX** 14% of downloads

687 MB **436 MB** **601 MB**

What you are getting

We offer ready-made packages which were tested for all major, 64-bit desktop platforms. If you wish to install a 32-bit version of TVB, you can still do so from the → source code on GitHub.

These packages work equally well for new installations or for updating existing installations. After unpacking, it's a good idea to look into the included README and Tutorial files, as well as our extensive → documentation website. Besides that, we provide ample → help and support for the software.

Our brain simulator software requires modern hardware, operating systems and web browsers. Please see our → technical requirements for details. While the TVB software itself is open source with a → GPLv2 license, we include some → 3rd party packages with different licenses.

Release notes

- JUN 21** **Version 1.5 [build 8028]**
2018 64 changes
New functionality related to simulation and visualizers
- SEP 22** **Version 1.4.1 (build 7595)**
2015 58 changes
Fixes for importing old projects and new Connectivity Annotations Viewer
- JUL 16** **Version 1.4 [build 7410]**
2015 50 changes
Improved default dataset and monitors; IPython notebooks included

Download & register as a TVB scientist!

Join our growing global community of over 2,000 registered TVB scientists and be among the first to learn about educational events in your area, receive news about research conducted with TVB and the latest plans for software updates and new features!

First name	<input type="text"/>
Last name	<input type="text"/>
Email address	<input type="text"/>
Organization	<input type="text"/>
Area of work	<input type="text"/>
How did you hear about The Virtual Brain?	<input type="text"/>
Register now!	

Registering is easy and secure

On-line Support



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THEVIRTUALBRAIN.

**Extensive support.
For scientists & developers.**

Software Downloads

System Requirements

Import & Export data

Getting Help & Support

Screenshots

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.

Read the documentation

Discuss with peers

View the source code

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



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 :-)



[Home](#) | [Install](#) | [Tutorials](#) | [Demos](#) | [Gui Guide](#) | [Console Guide](#) | [Developers](#) |

[next](#) | [modules](#) | [index](#)

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Table Of Contents

Overview of *TheVirtualBrain*

- [Download](#)
- [We are grateful to](#)

Next topic

Installing the Application

This Page

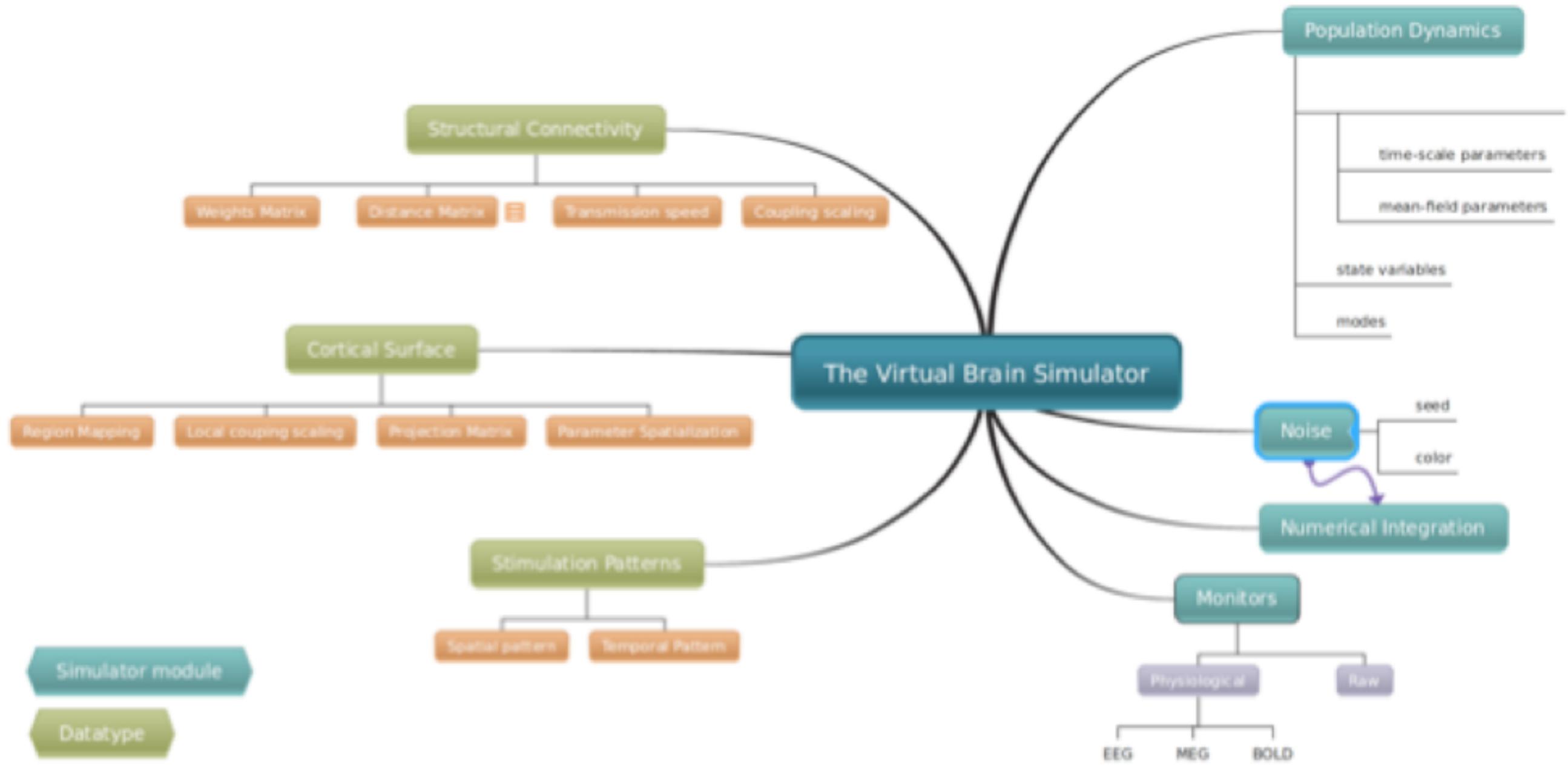
Show Source

Quick search

Go

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

TVB: The system architecture



Written in Python

Scales from laptop to cluster

Open Source GPLv2

Highly modular

On GitHub

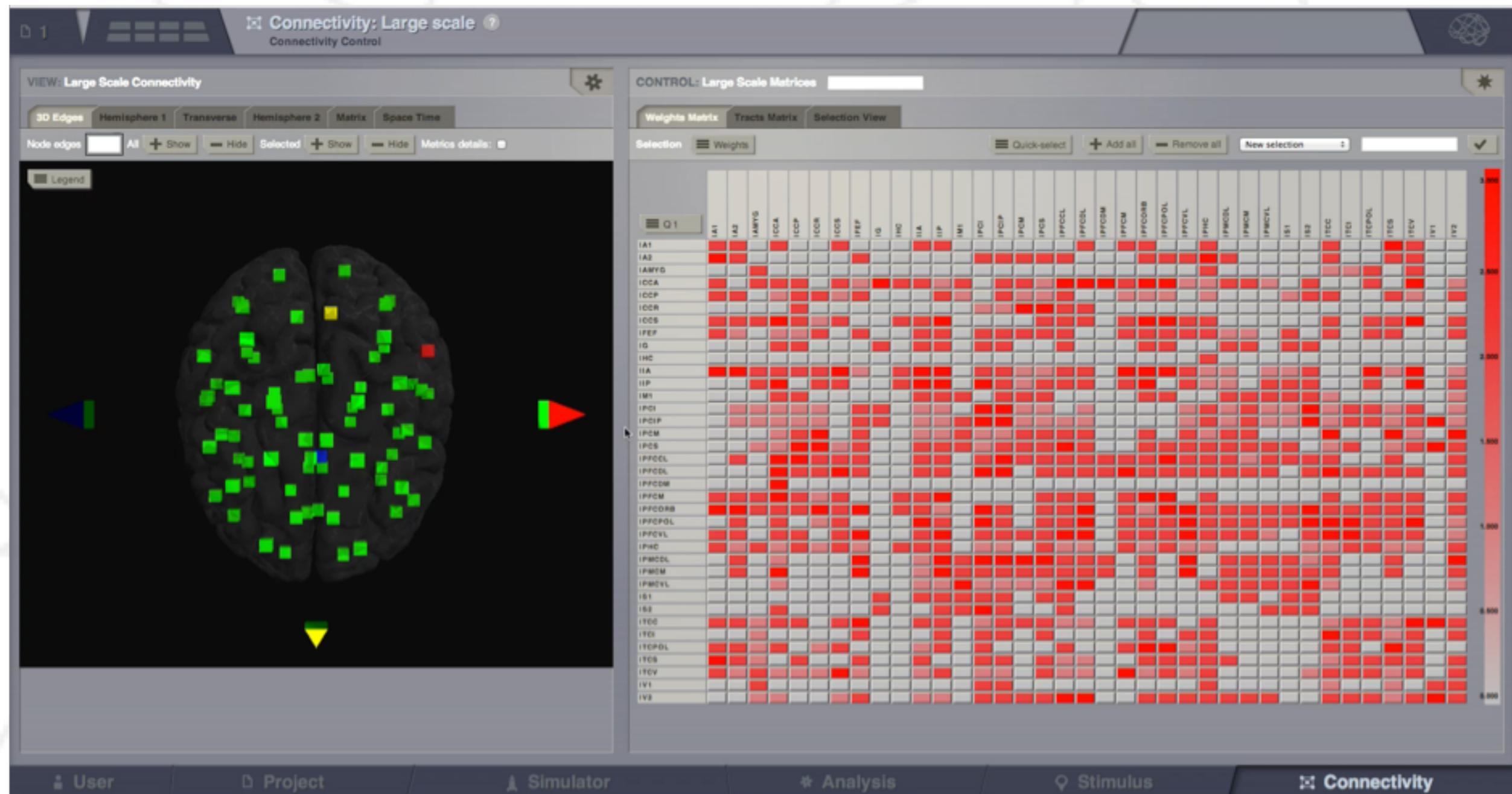
Runs on Windows, Mac, Linux



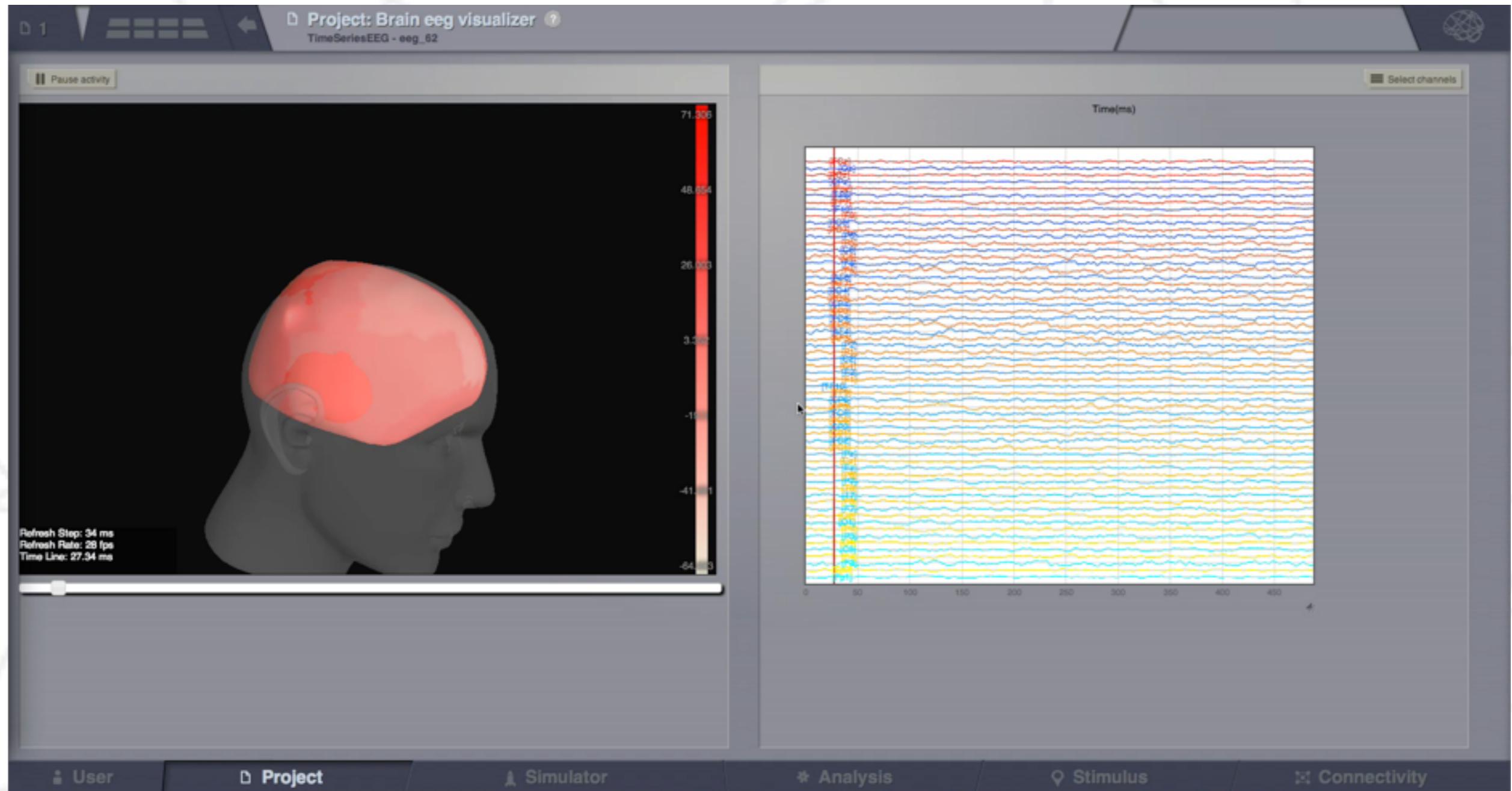
The software

Quick Tour









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 Transformation 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

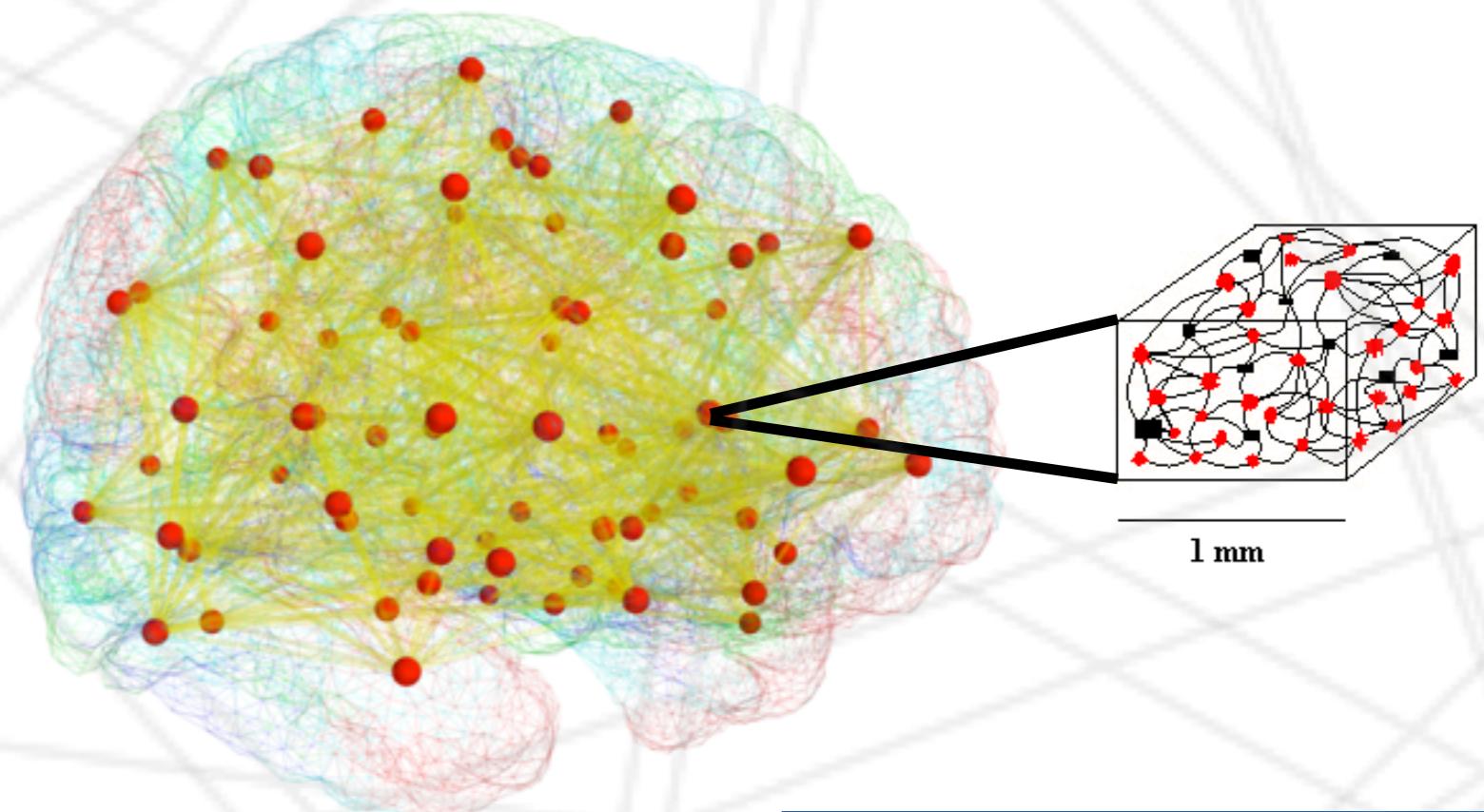
All models can be described by nonlinear dynamic systems via differential equations

Hodgkin-Huxley

Morris-Lécar

In TVB

Local Field Potential, synaptic activity



Stefanescu-Jirsa 2D

Stefanescu-Jirsa 3D

Wong-Wang

Firing rate

Phenomenological

Wilson-Cowan

Brunel-Wang

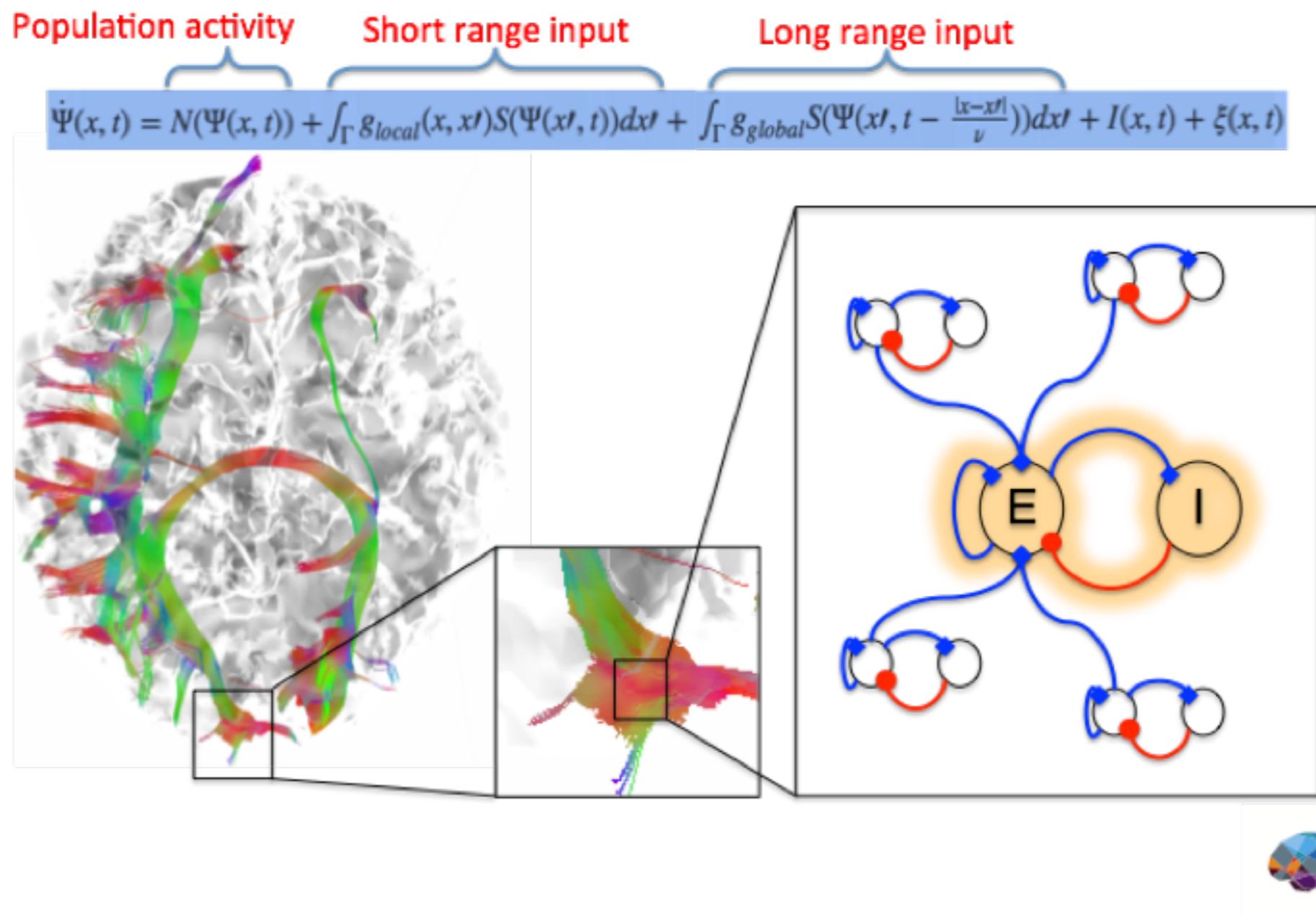
Jansen-Rit

Generic 2D

Kuramoto

Epileptor

Large-scale equation for The Virtual Brain



Evolution equation

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

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)

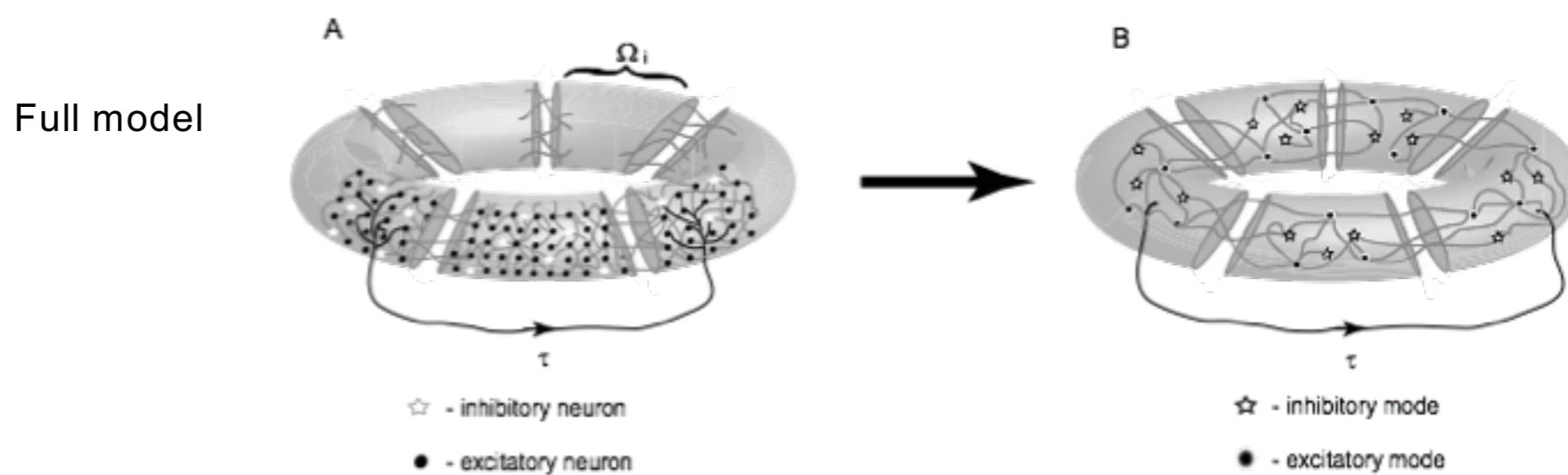
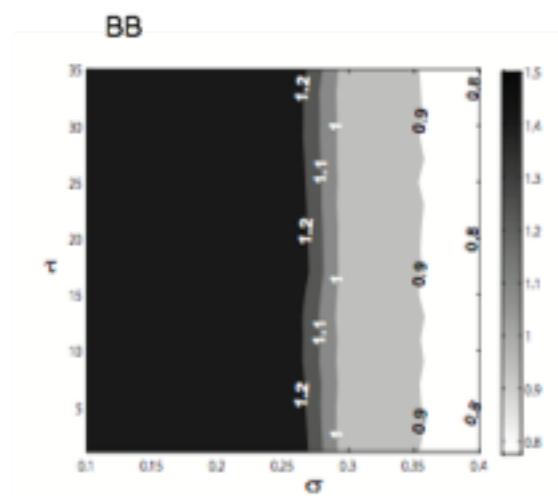
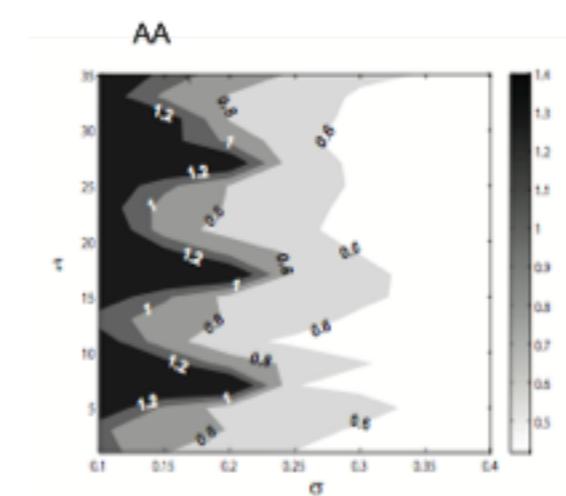
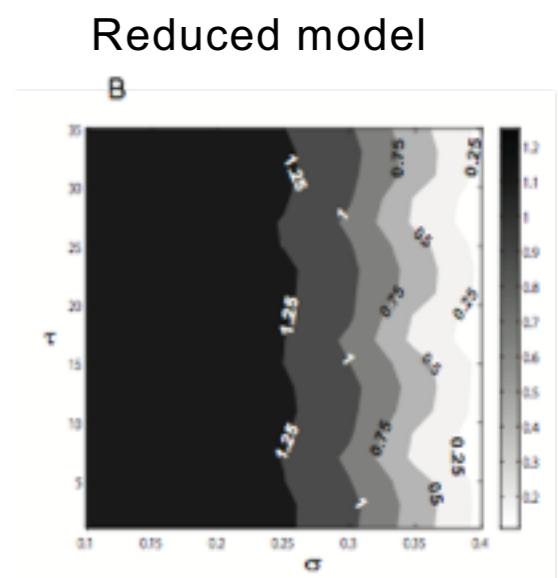
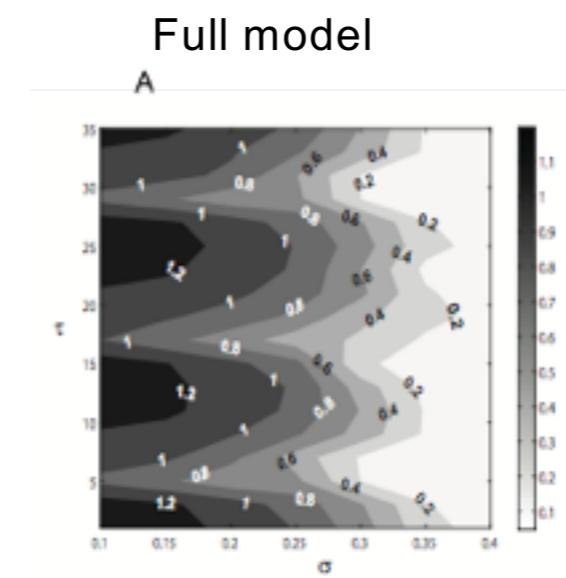
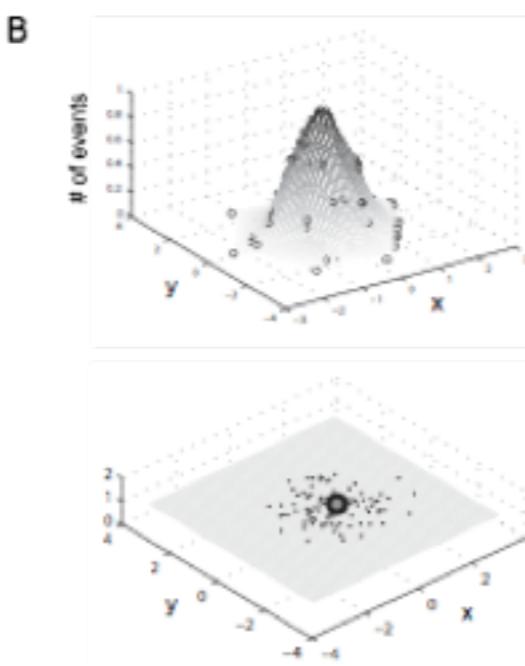
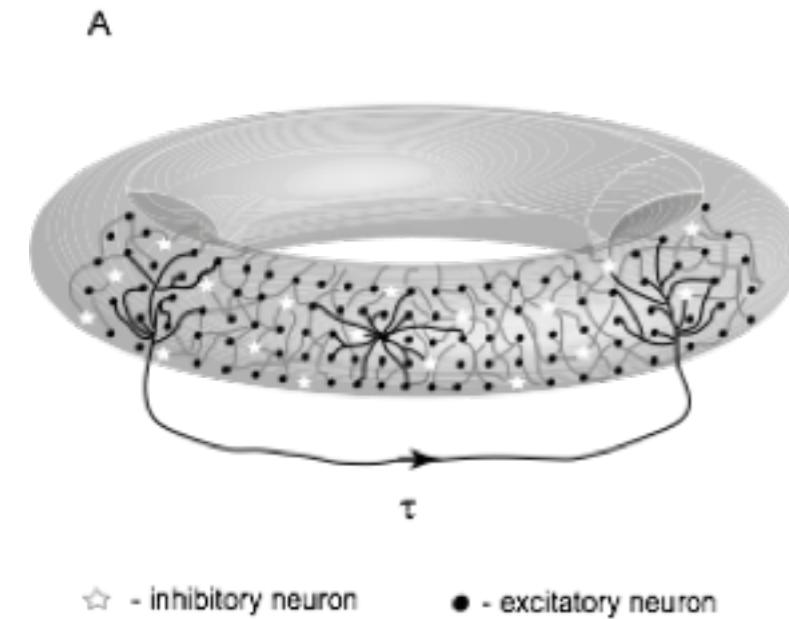
Time delays

Local connectivity

Injected input

Noise

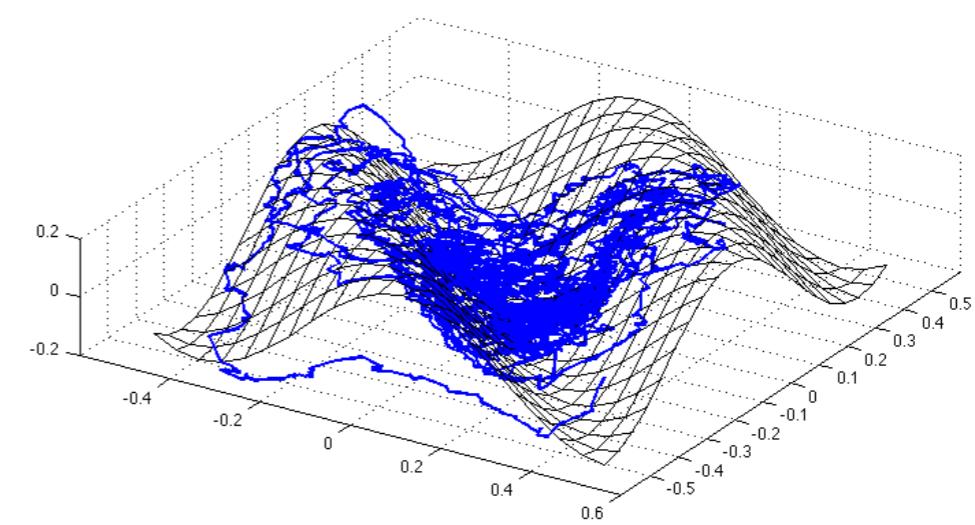
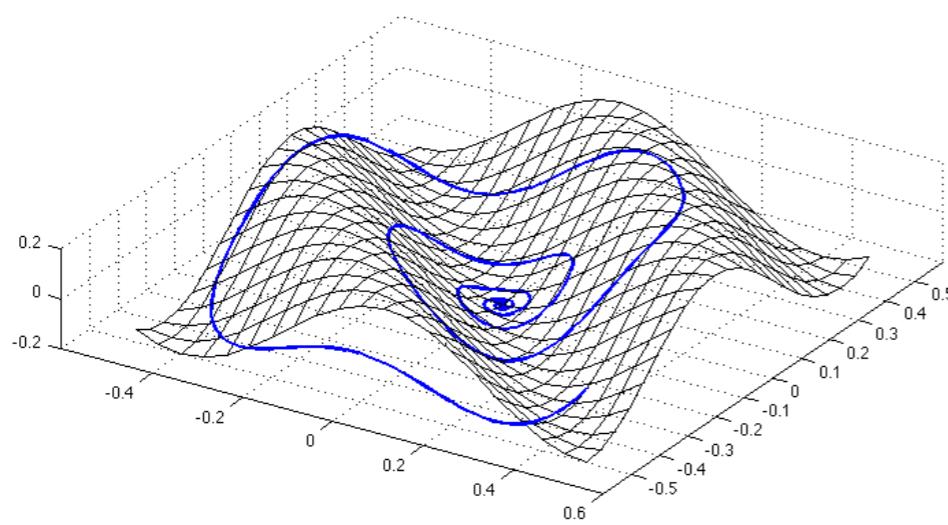
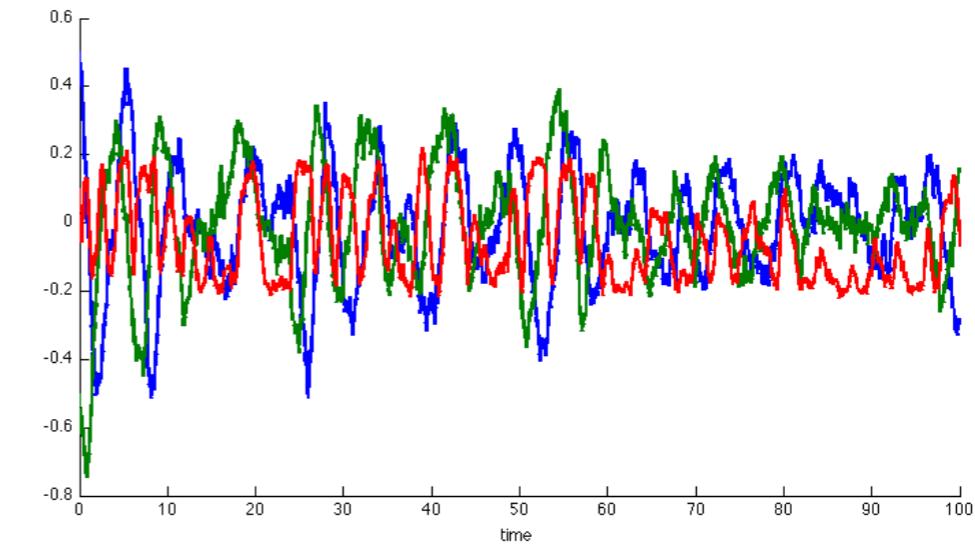
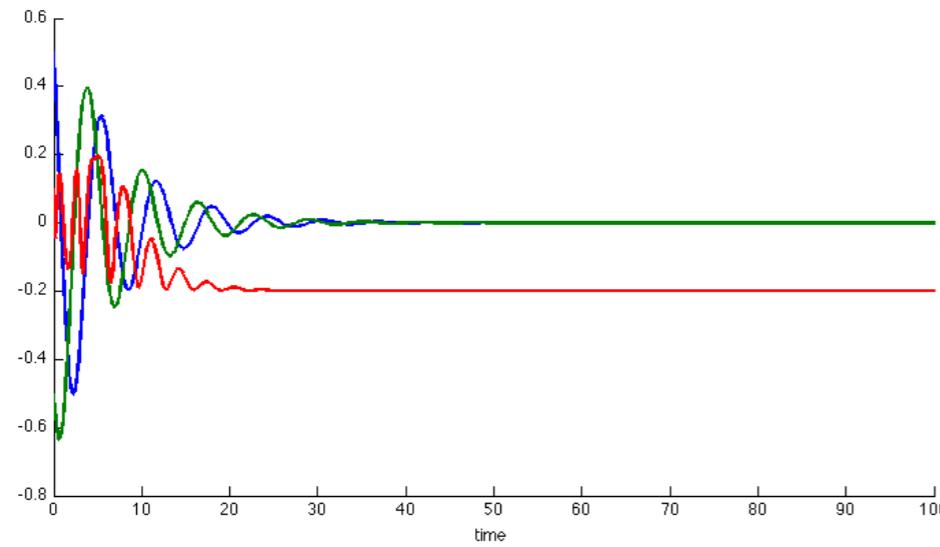
"Neurodegeneration" - diminishing numbers of neurons



Reduced model

Flows and Manifolds

Characterizing dynamics



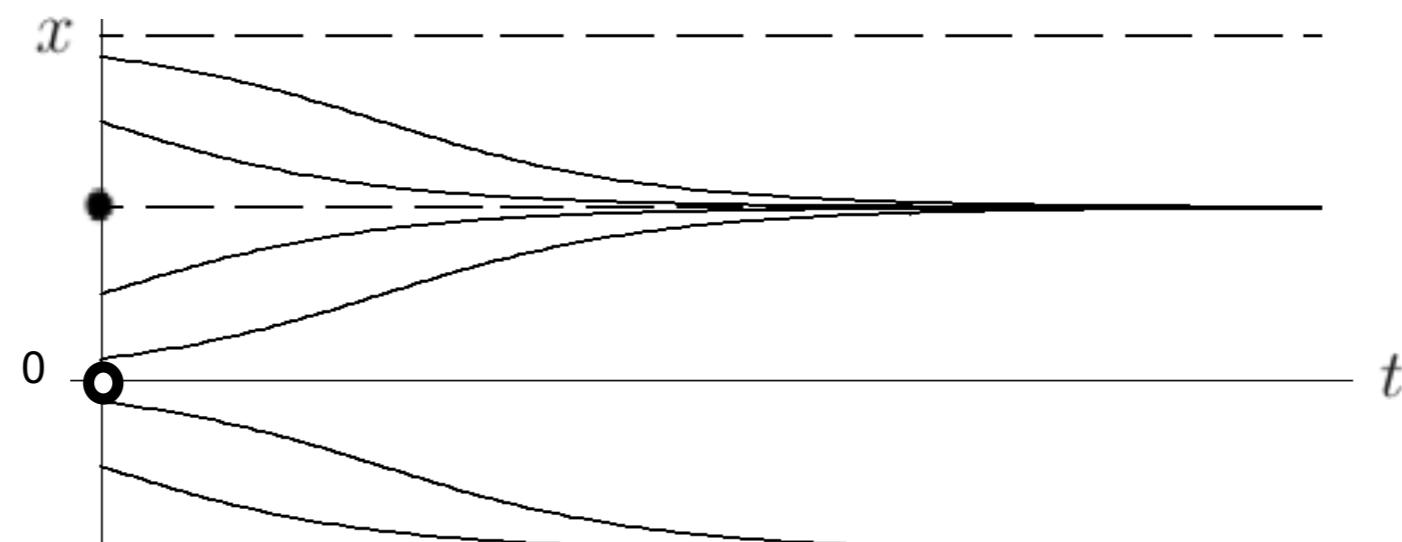
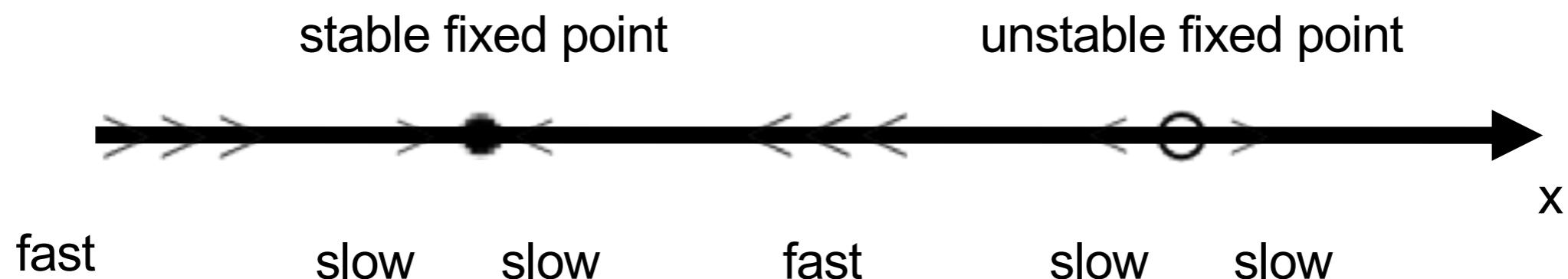
Coupled oscillators with no noise

Coupled oscillators with noise

One-dimensional nonlinear flows

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

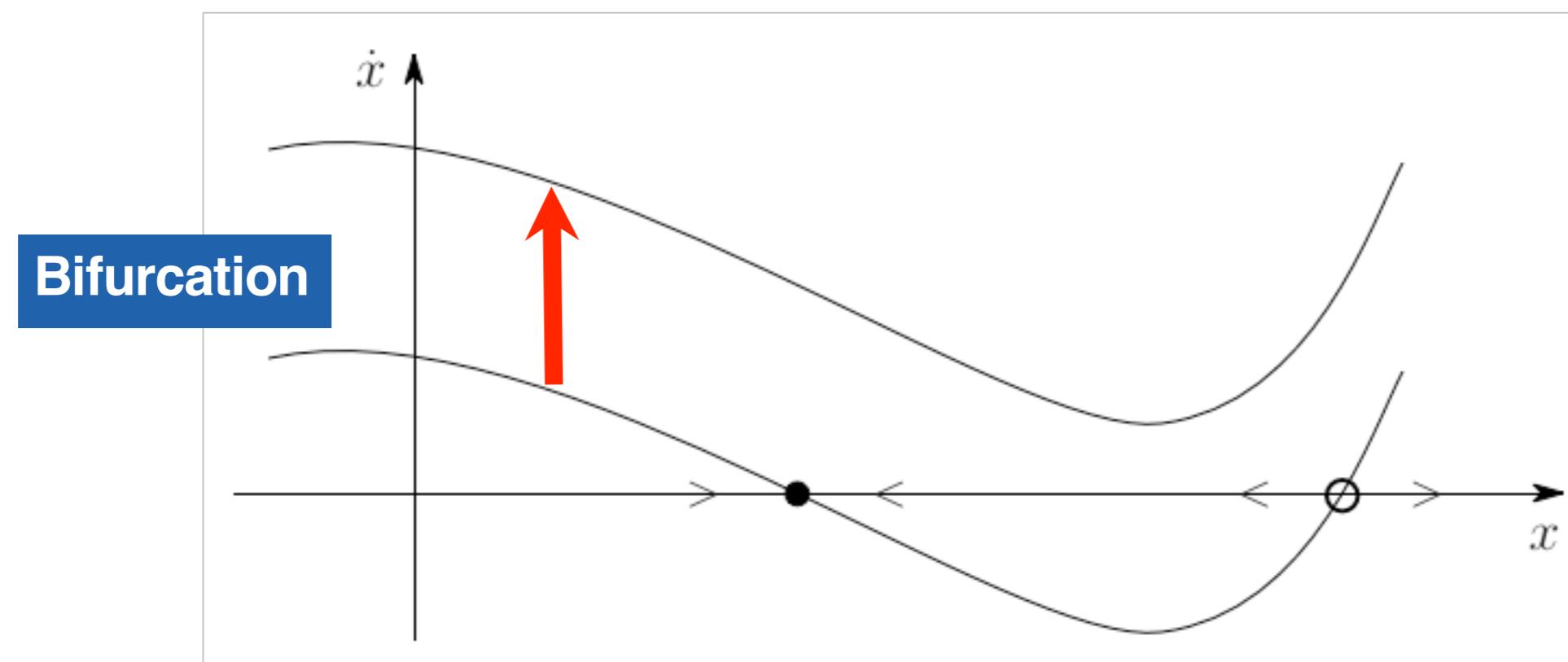
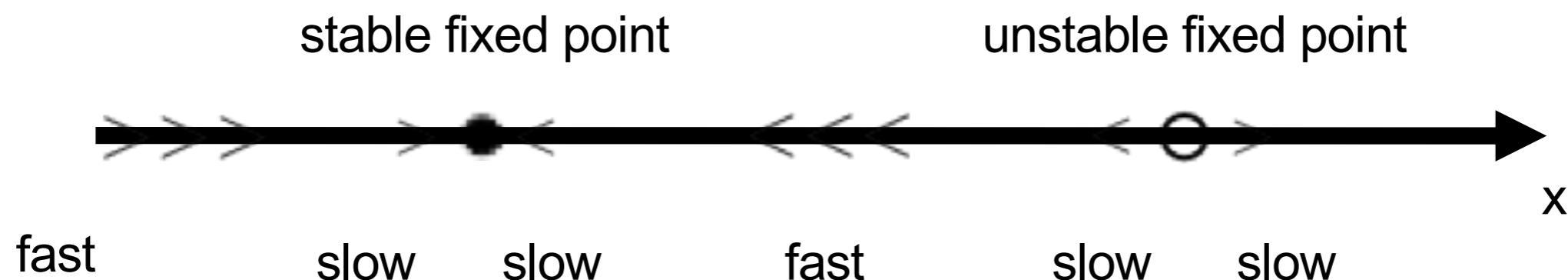
fixed point: $\dot{x}(t) = 0$



One-dimensional nonlinear flows

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

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



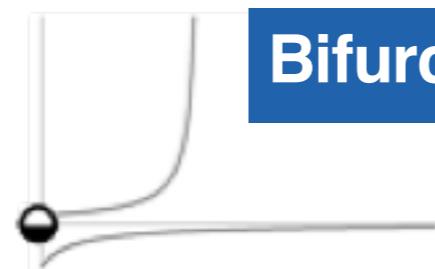
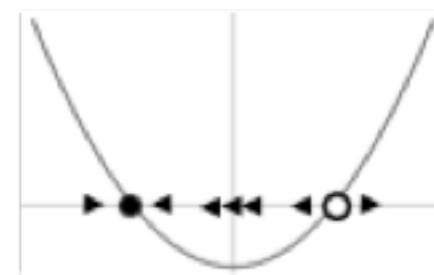
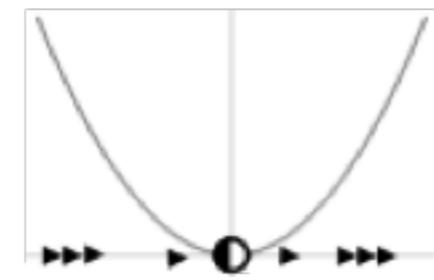
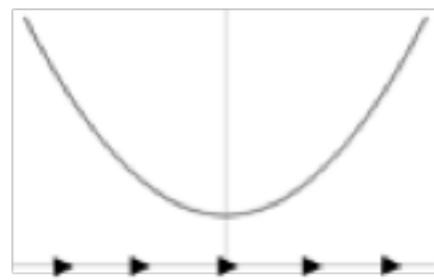
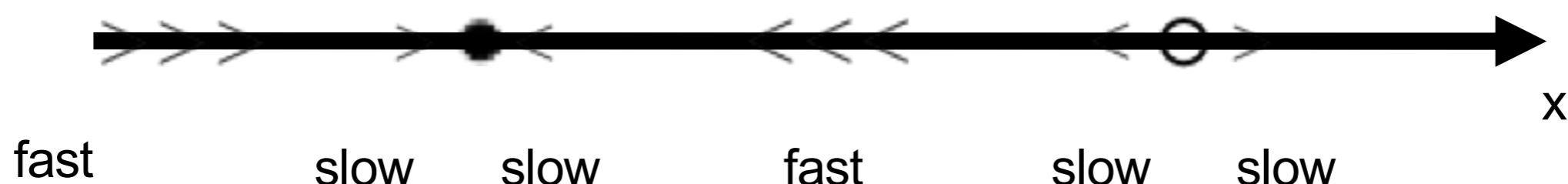
One-dimensional nonlinear flows

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

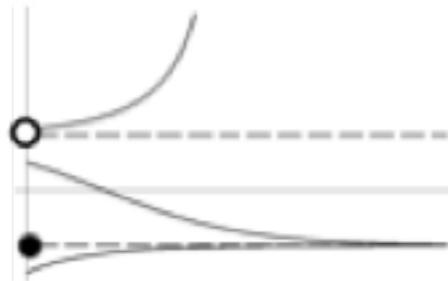
fixed point: $\dot{x}(t) = 0$

stable fixed point

unstable fixed point



Bifurcation



$$k > 0$$

$$k=0$$

$$k < 0$$

Two-dimensional nonlinear flows

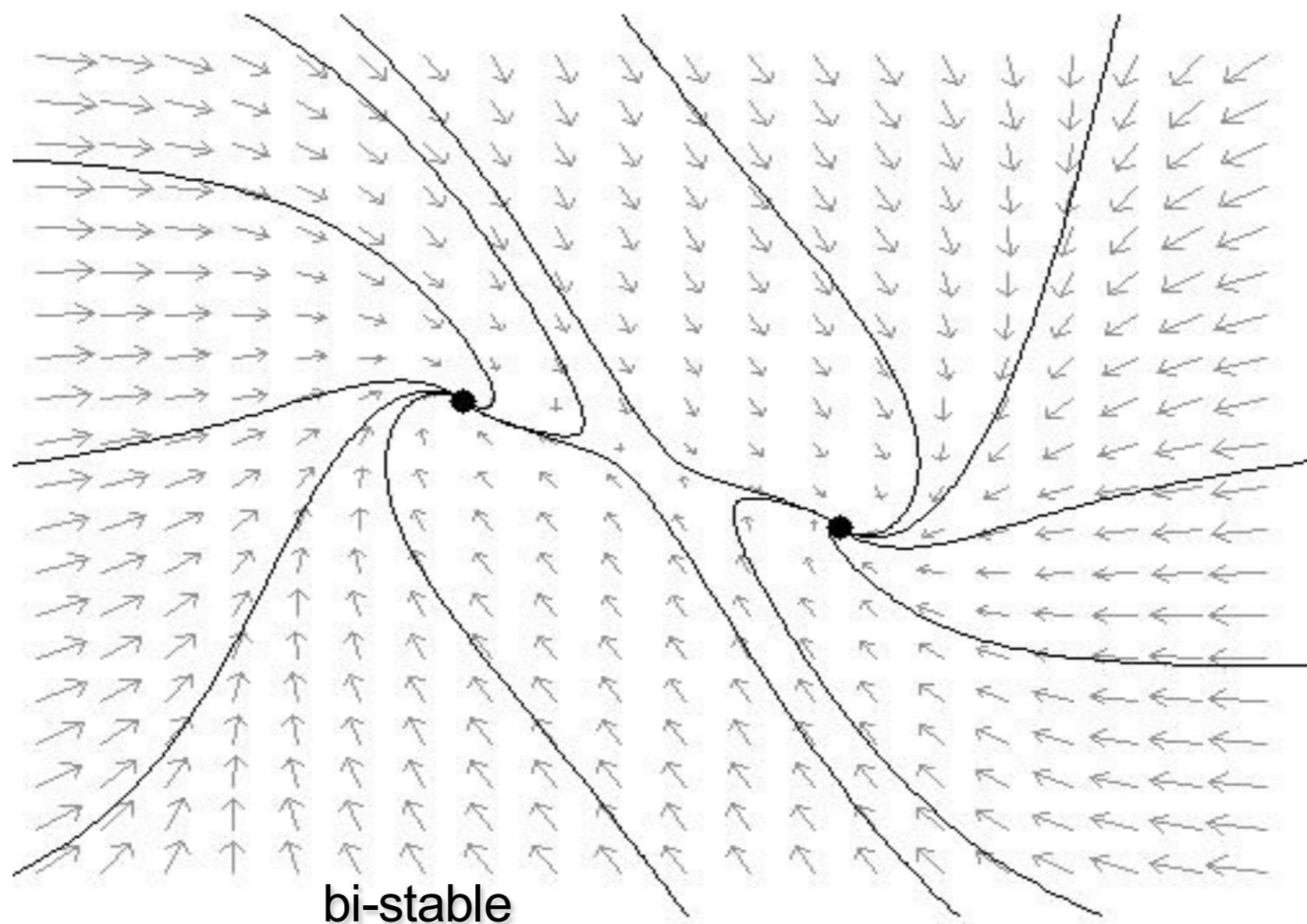
$$\dot{x}(t) = f(x(t), y(t), k)$$

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

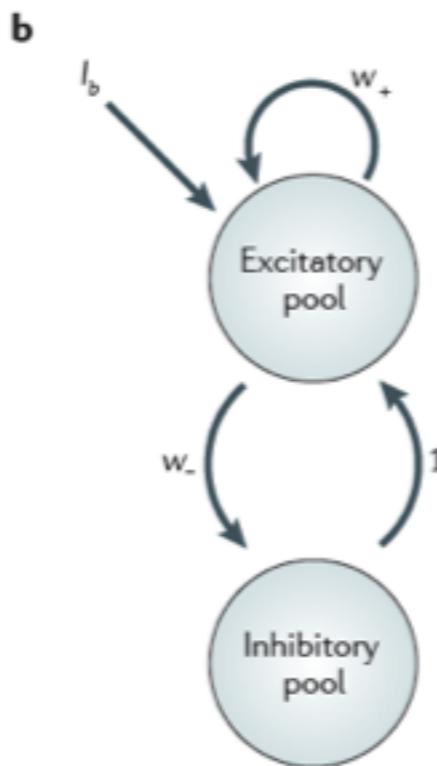
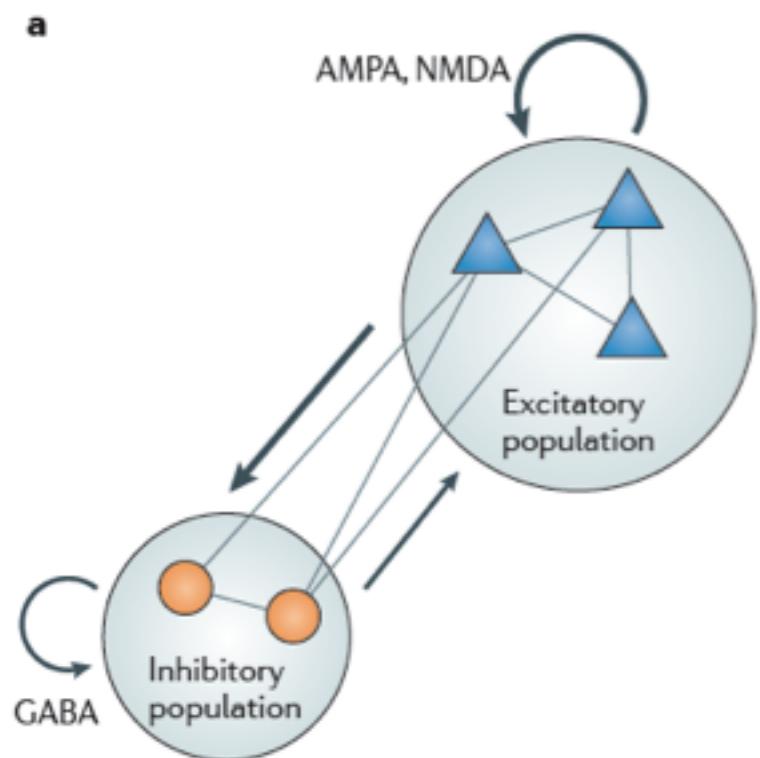
fixed point:

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

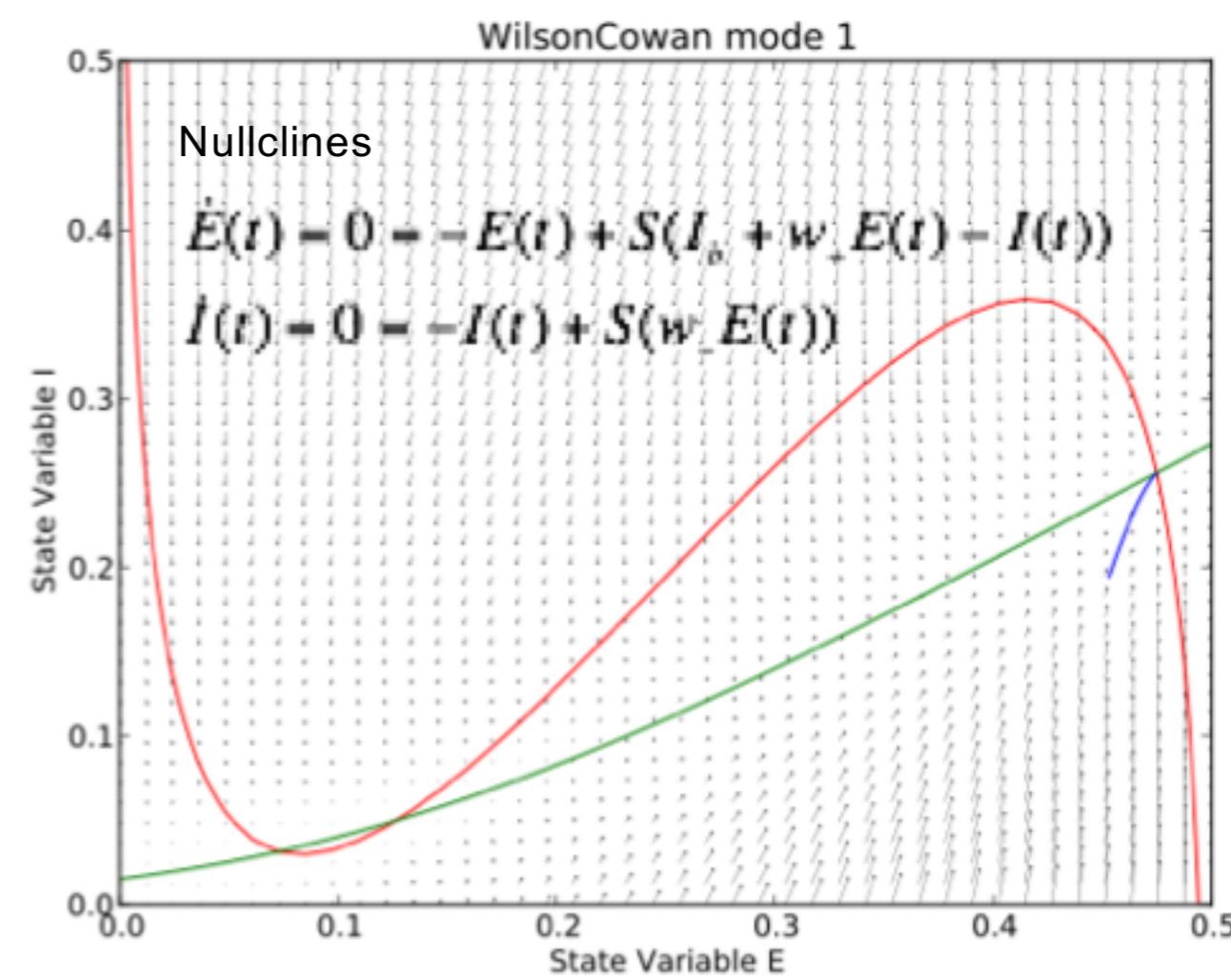
$$\dot{y}(t) = 0$$



The Wilson-Cowan model



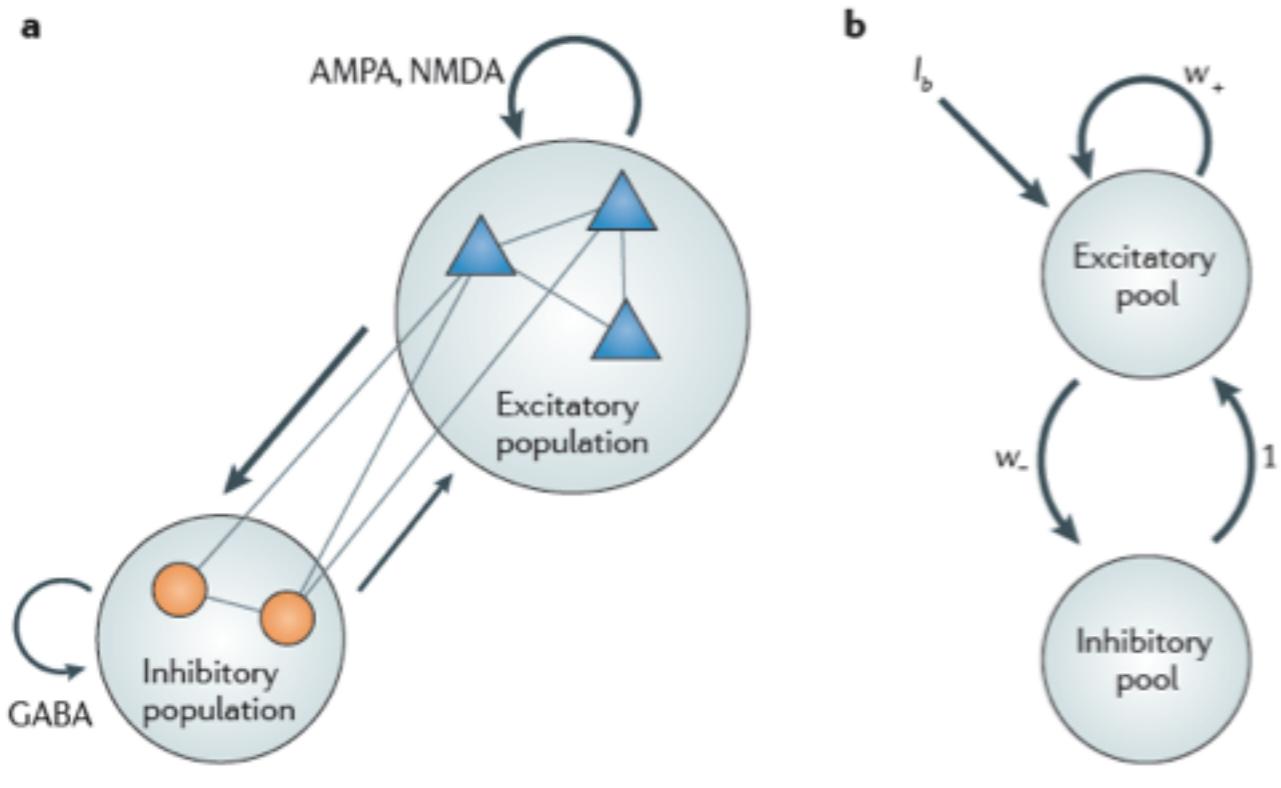
$$\dot{E}(t) = -E(t) + S(I_b + w_+ E(t) - I(t)) + \text{noise}$$
$$I(t) = -I(t) + S(w_- E(t)) + \text{noise}$$



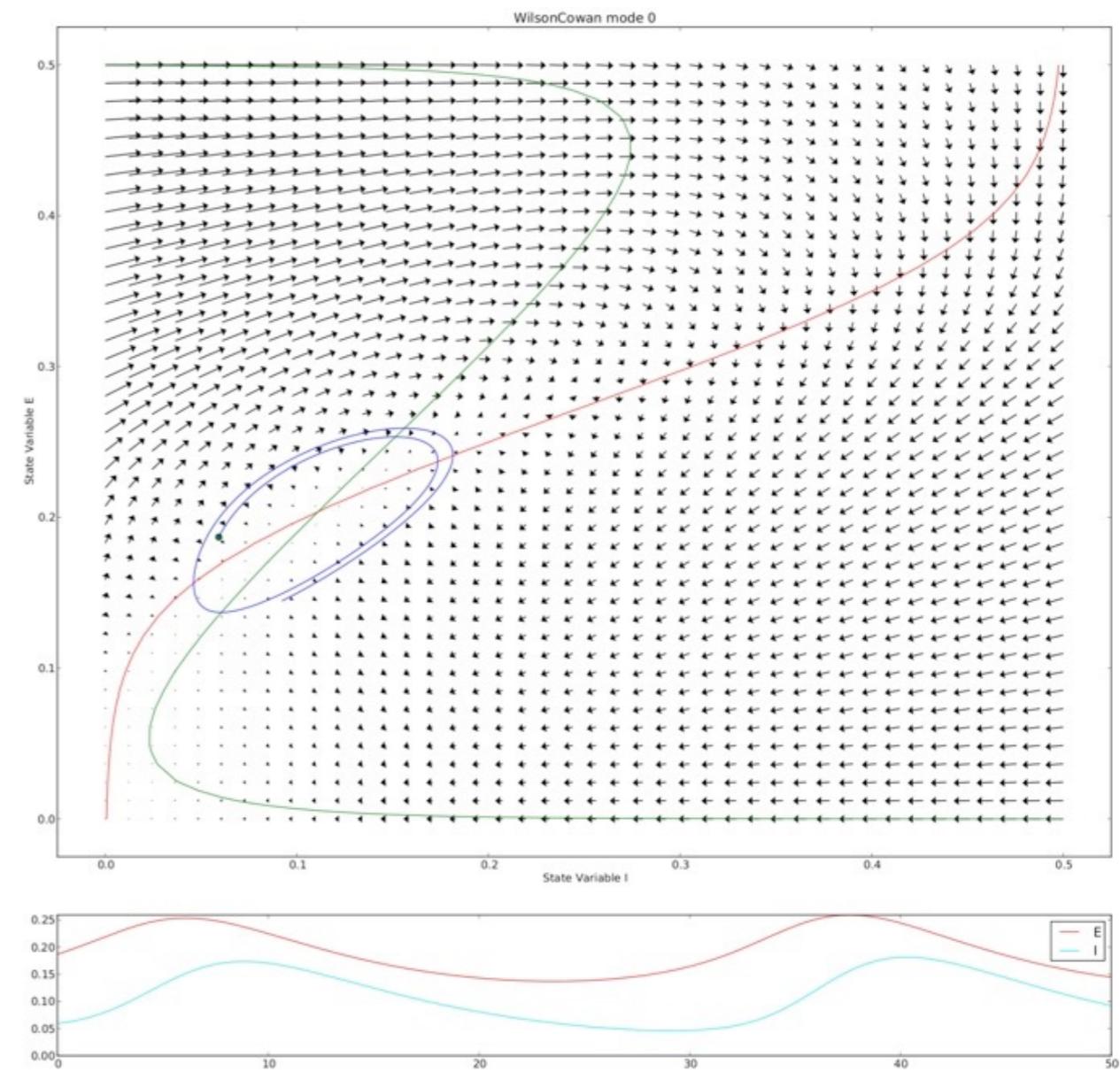
Key idea

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

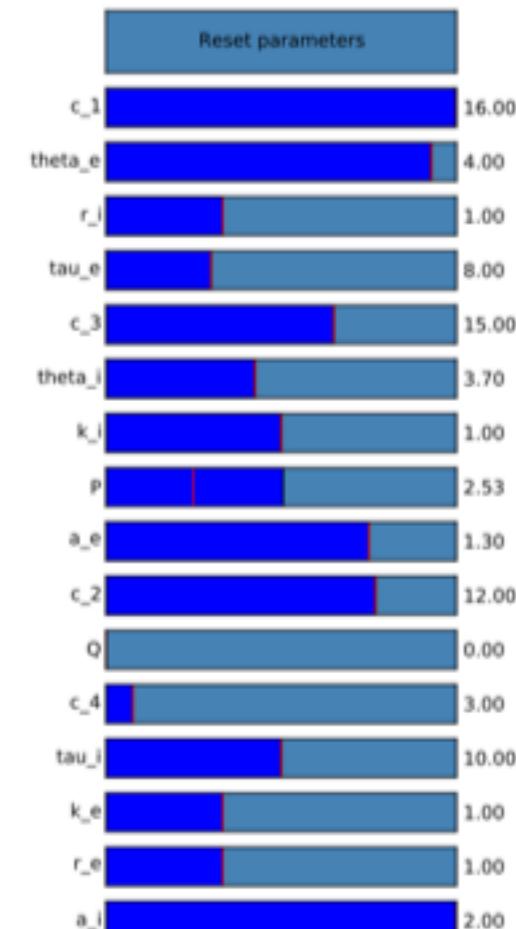
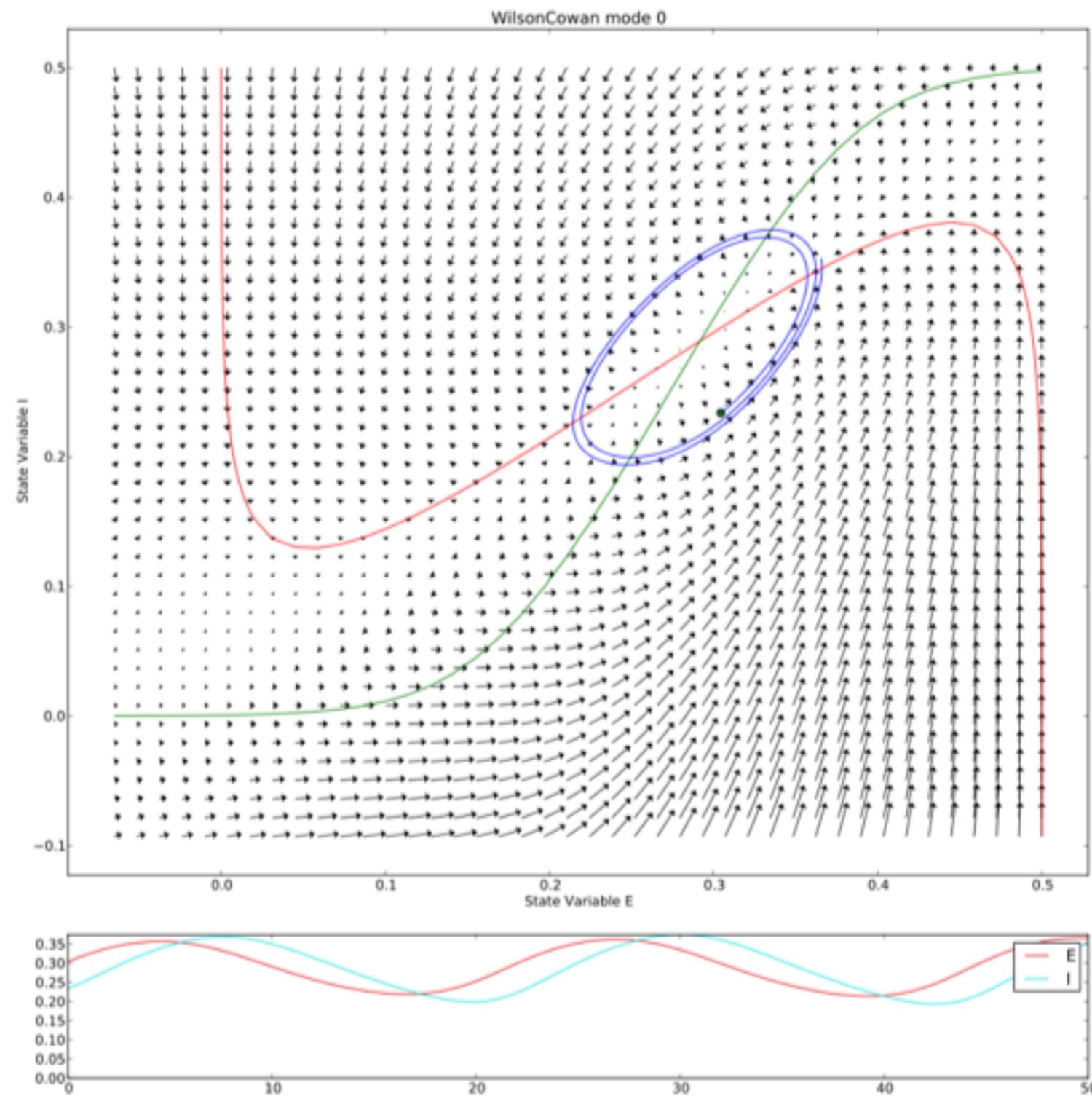
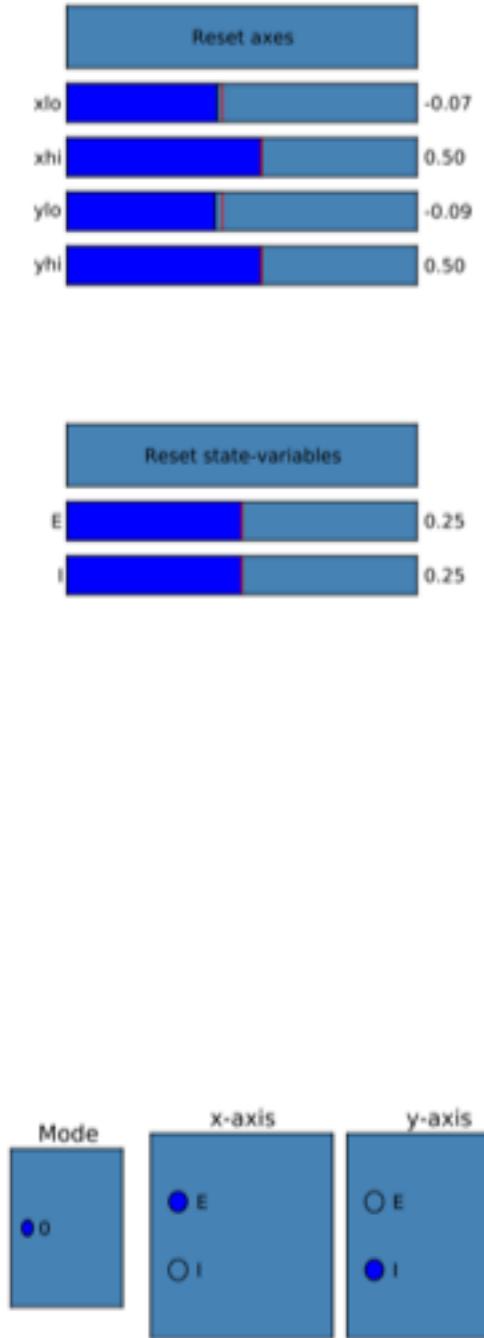
The Wilson-Cowan model



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



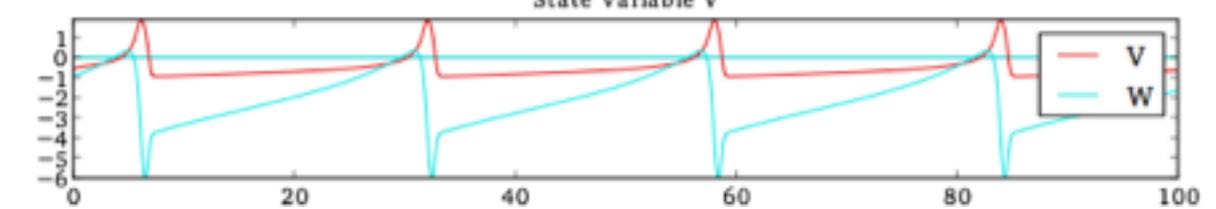
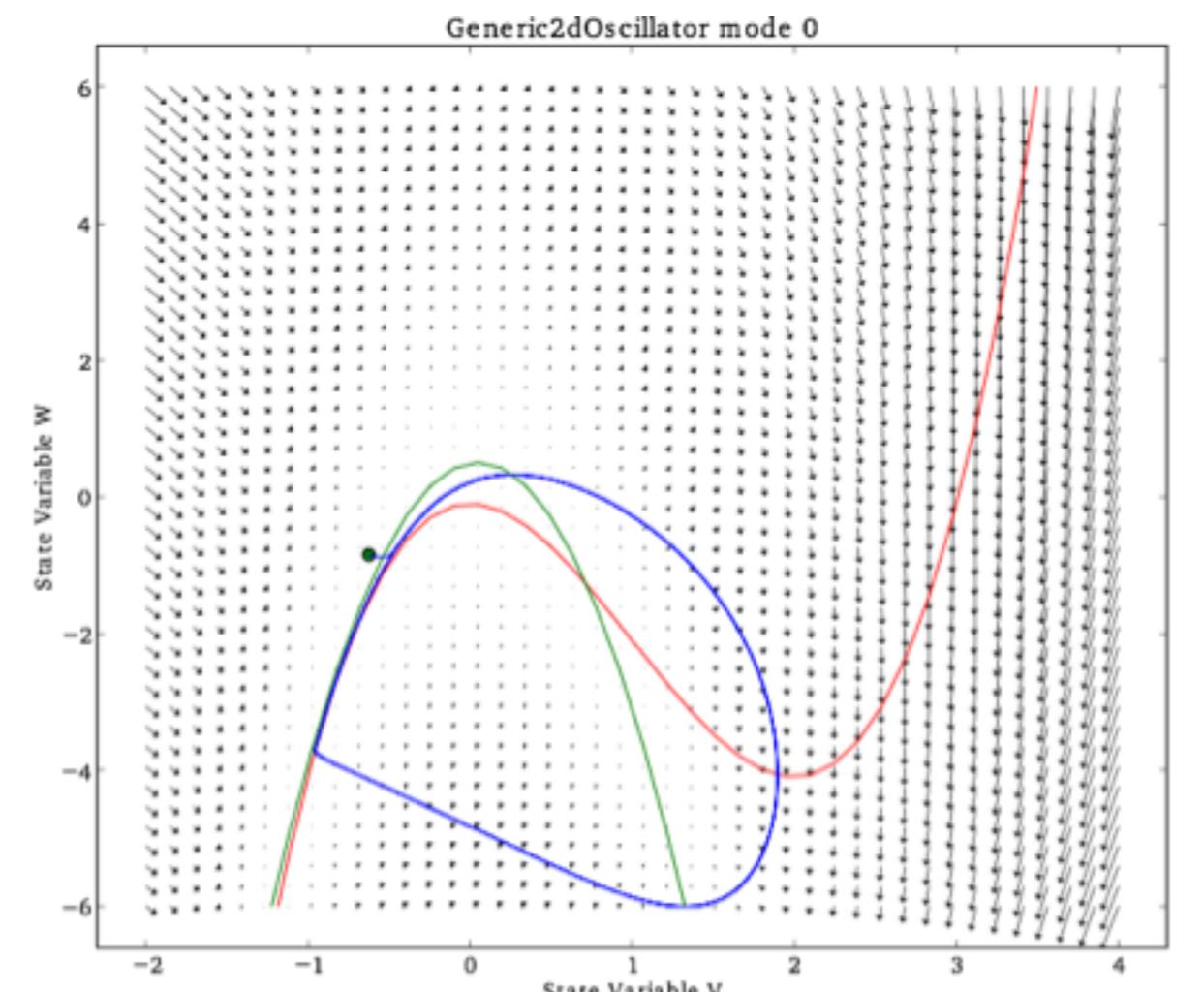
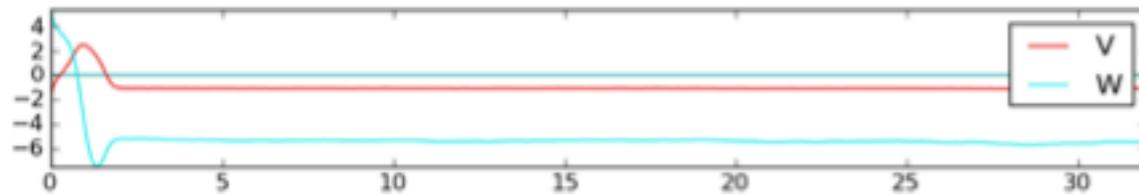
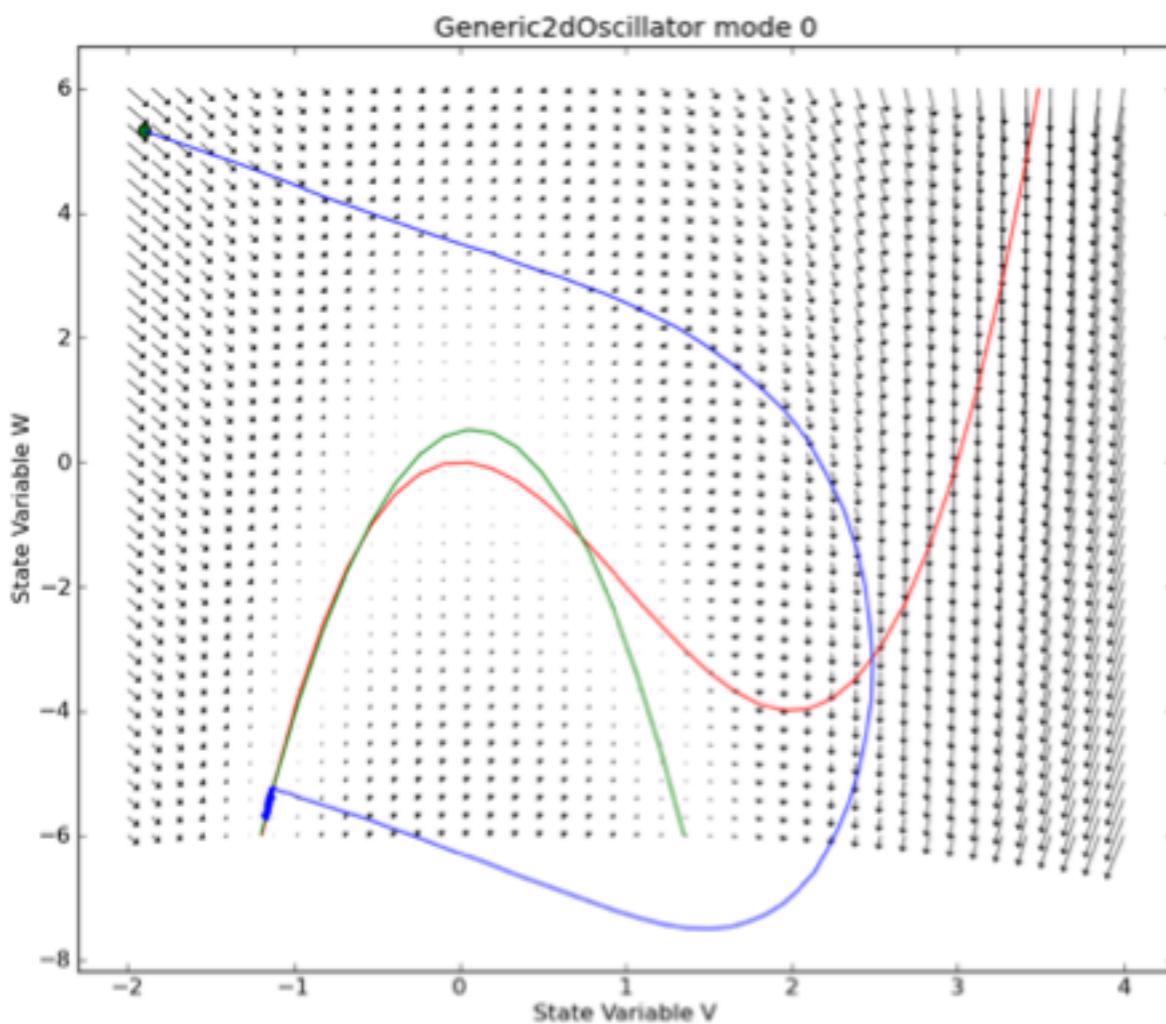
The Wilson-Cowan model



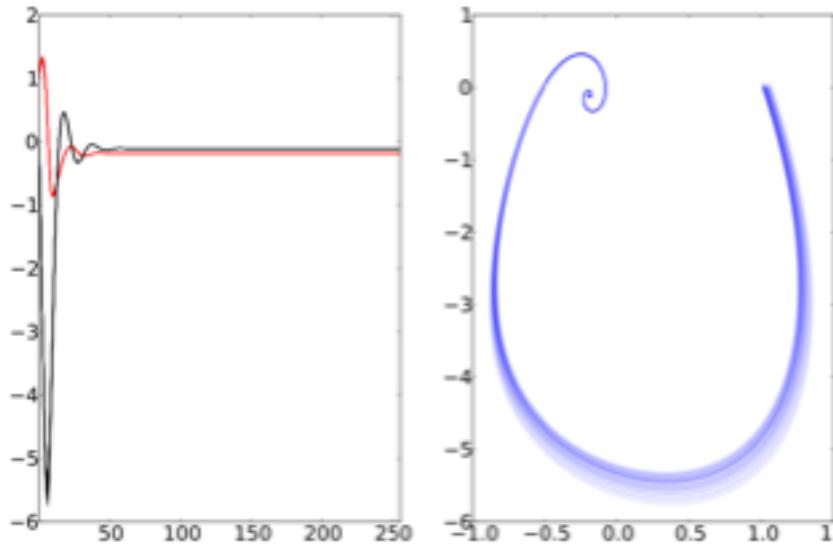
The Generic 2D oscillator model

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

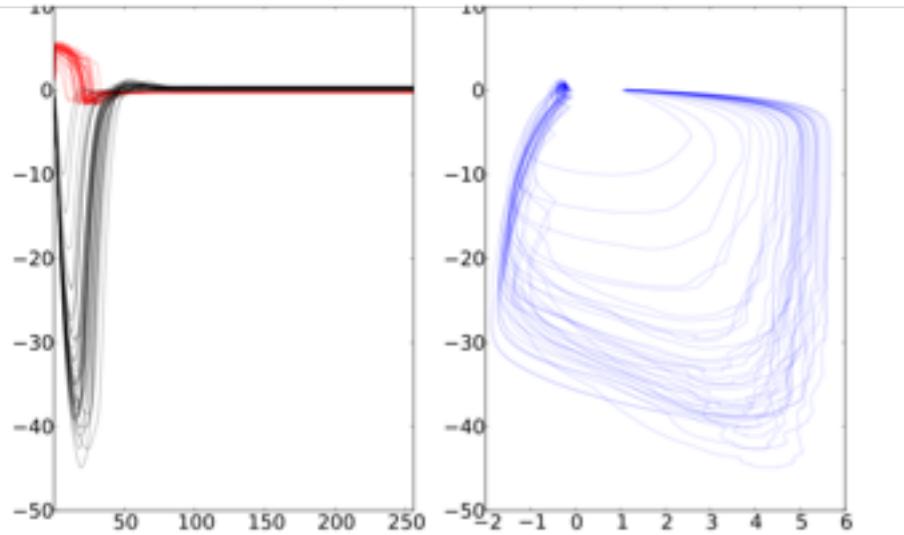
$$\dot{W}(t) = g(V(t), W(t)) + \text{noise}$$



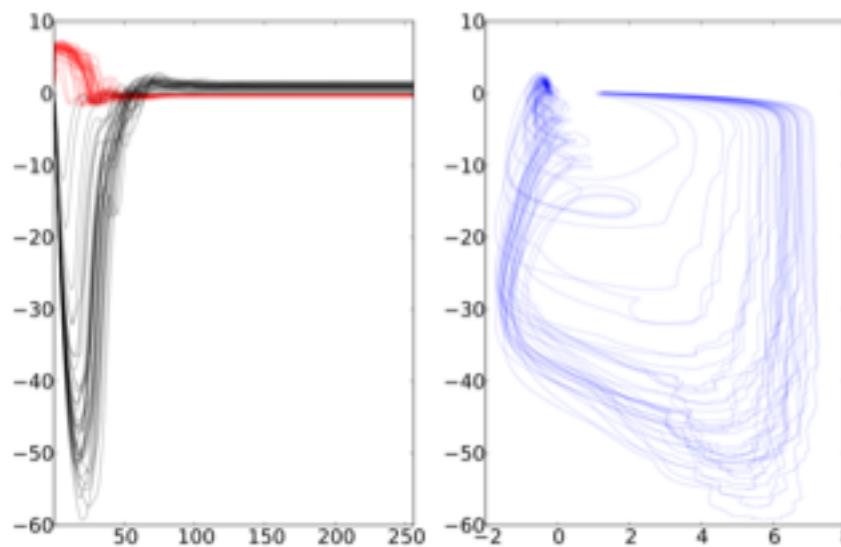
Generic 2D oscillators embedded in the network



No coupling



Weak coupling



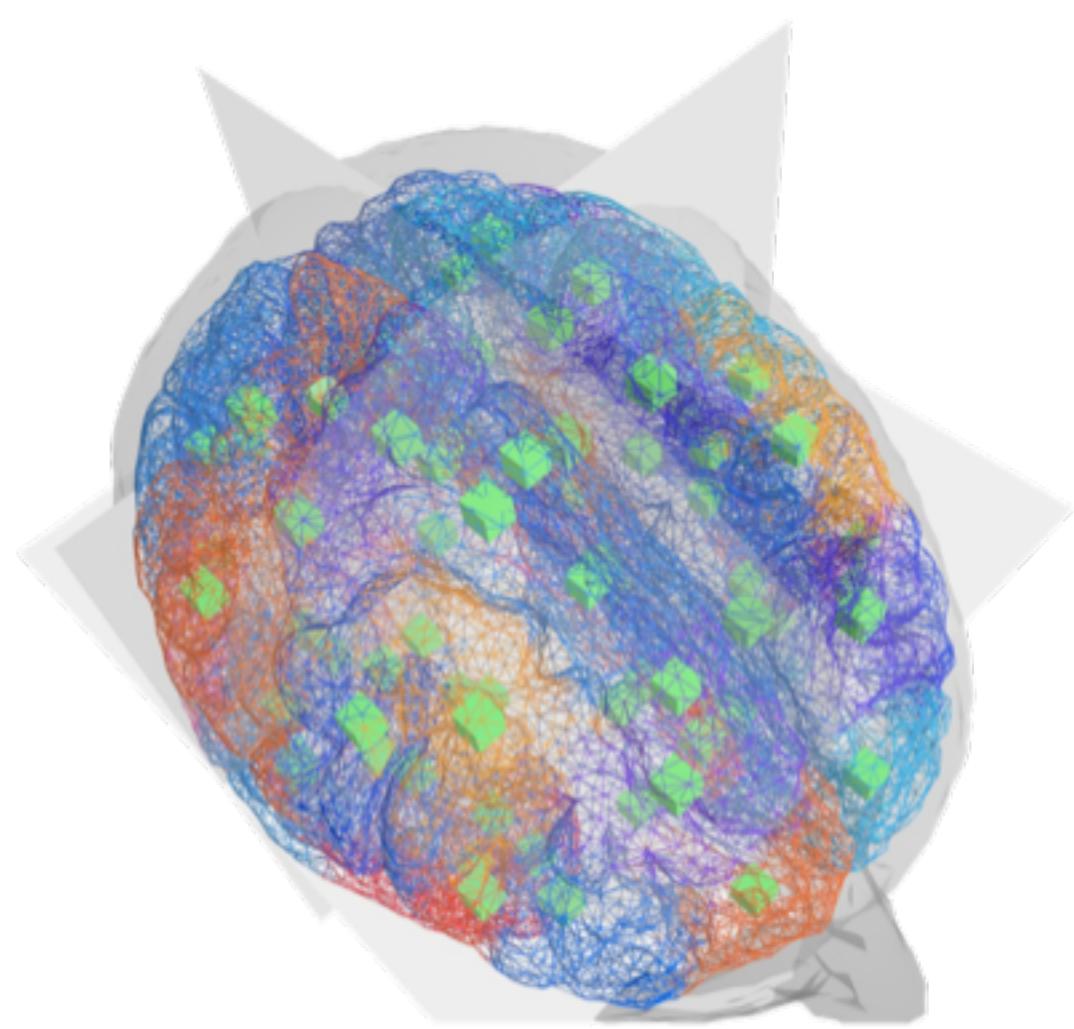
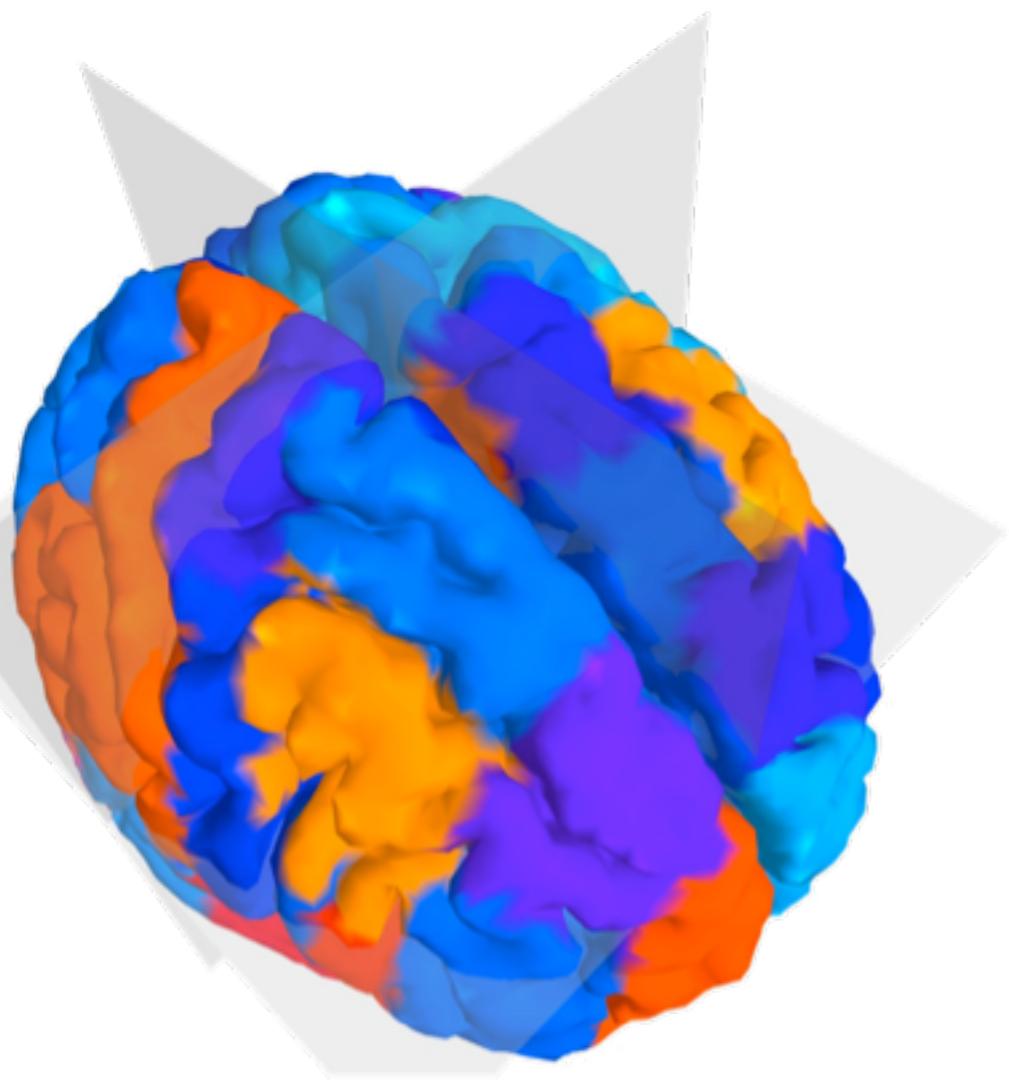
Strong coupling



TVB geometry

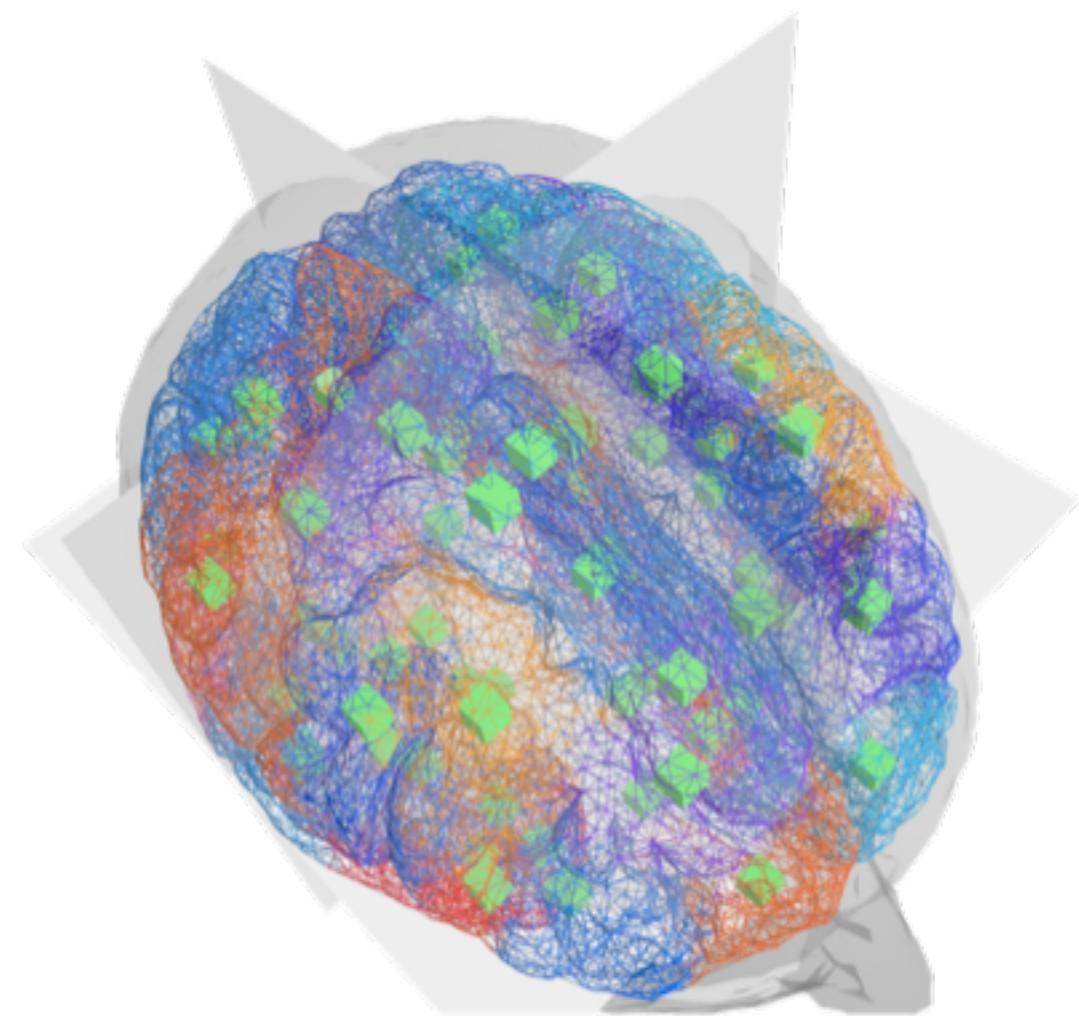
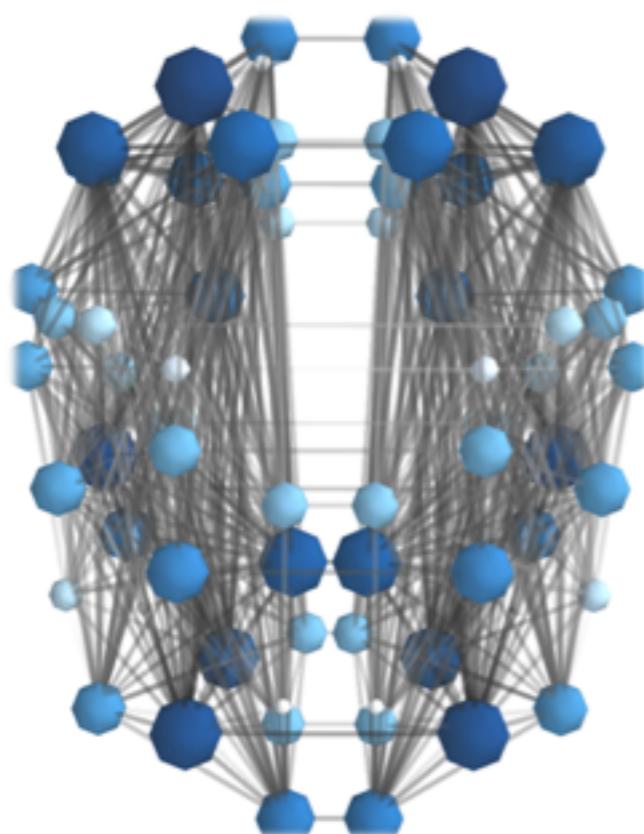
Topography of the brain

MNI brain geometry



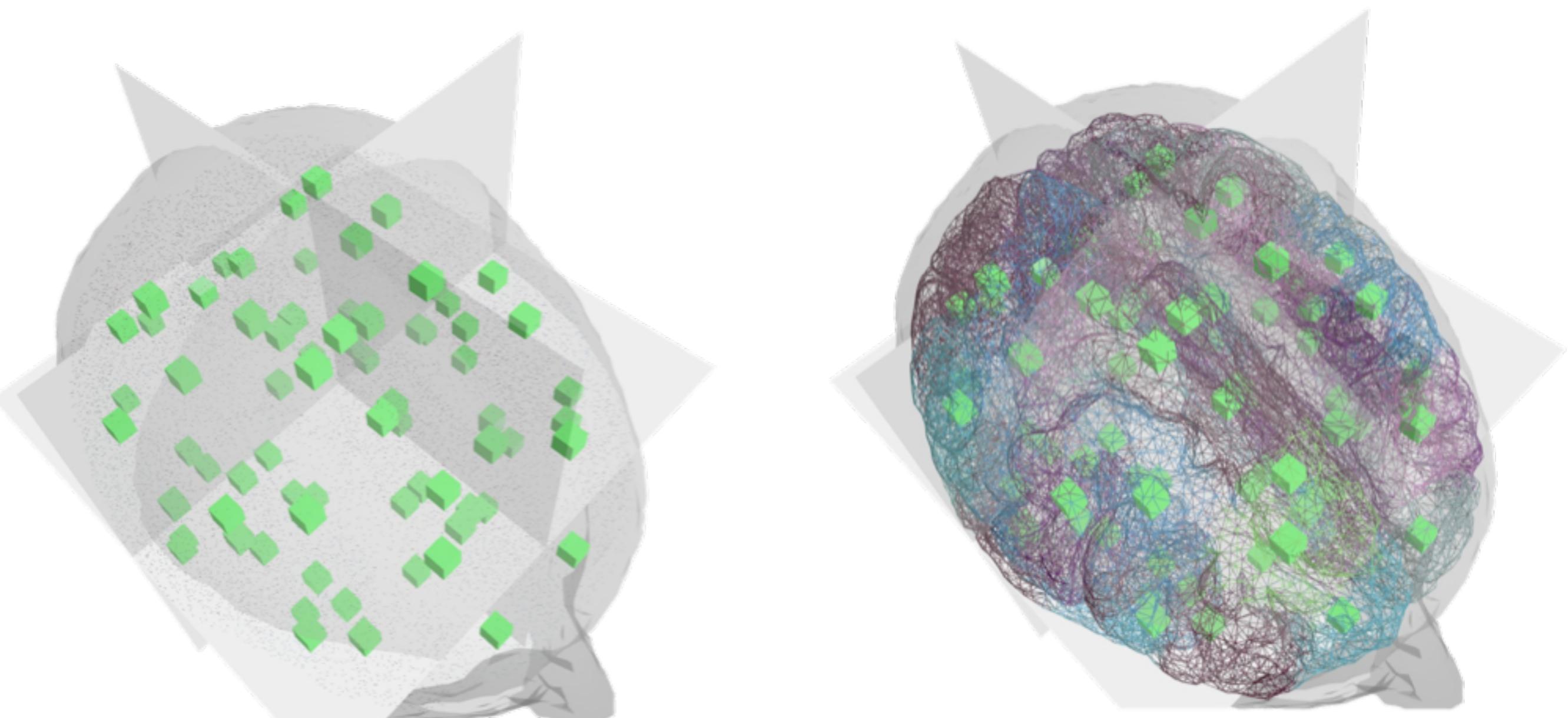
TVB topography

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



TVB topography

surface-based modeling (N=10000-140000)



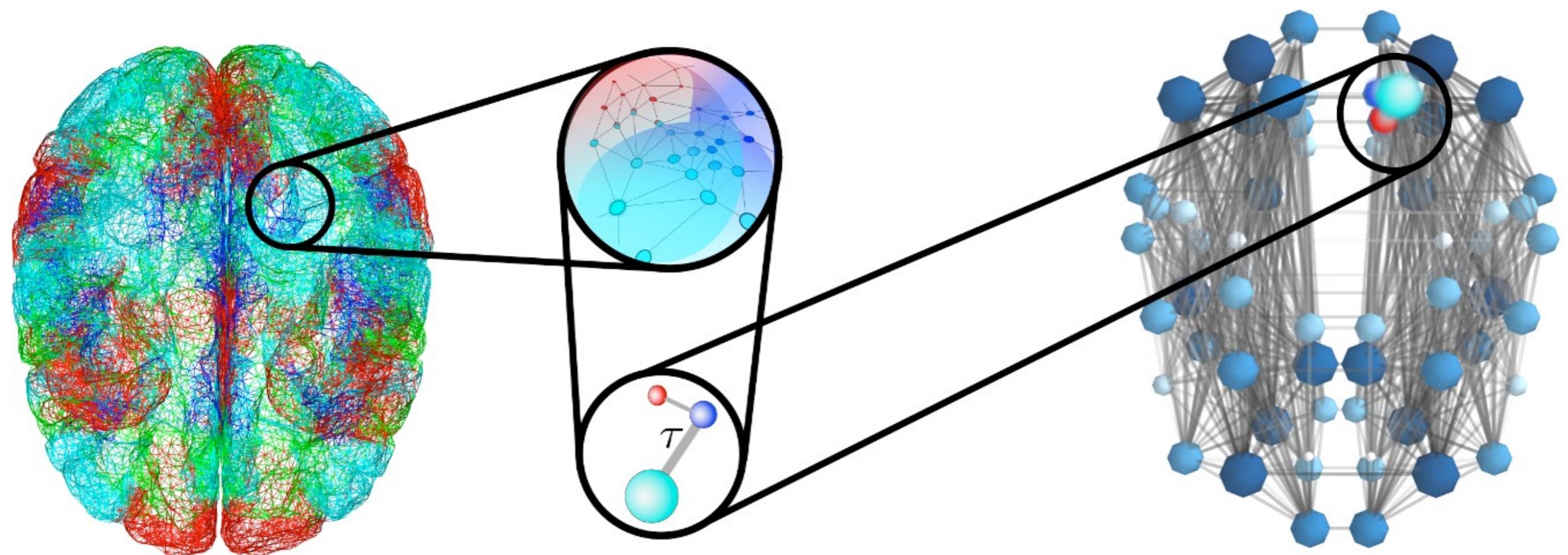


TVB connectivity

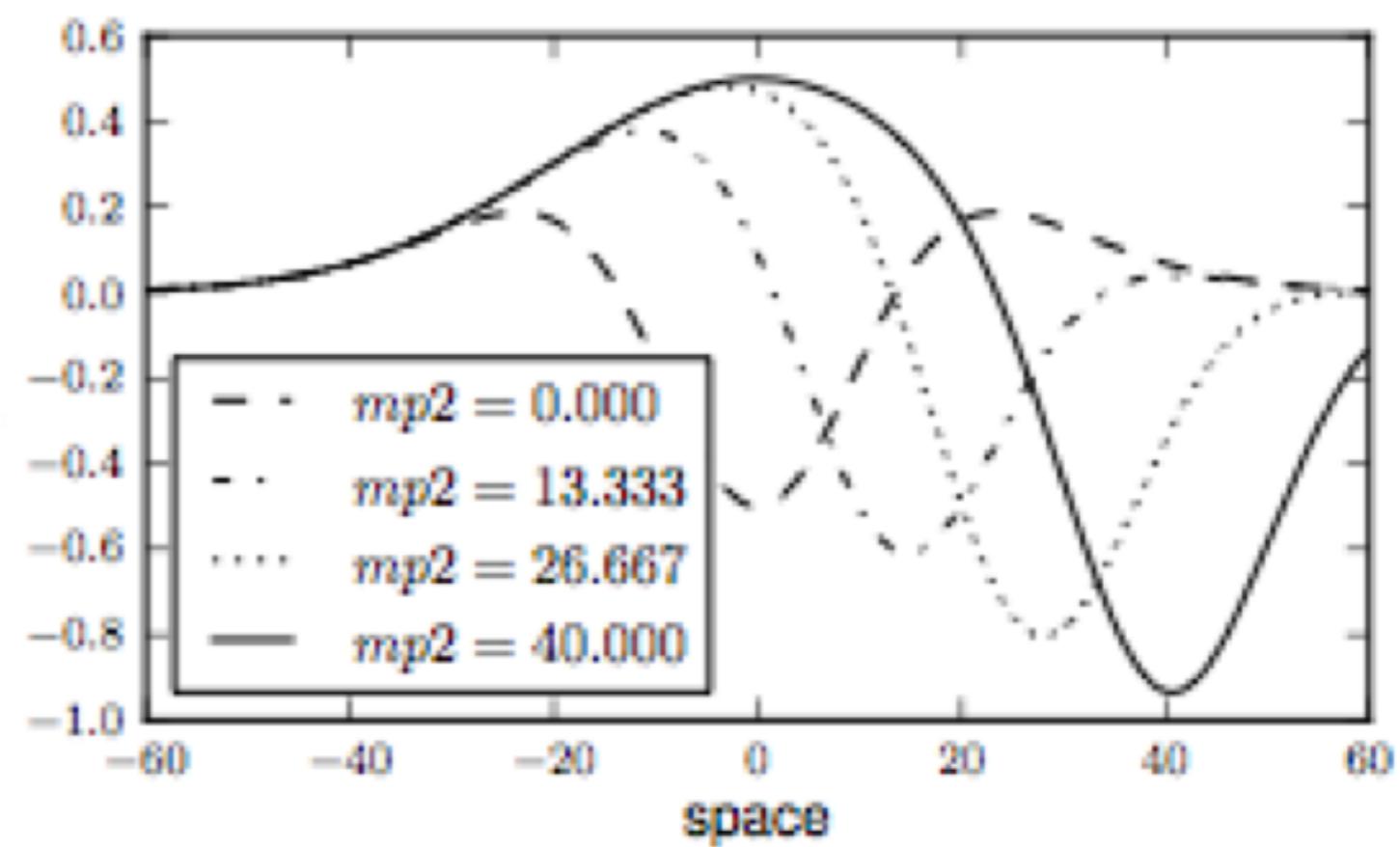
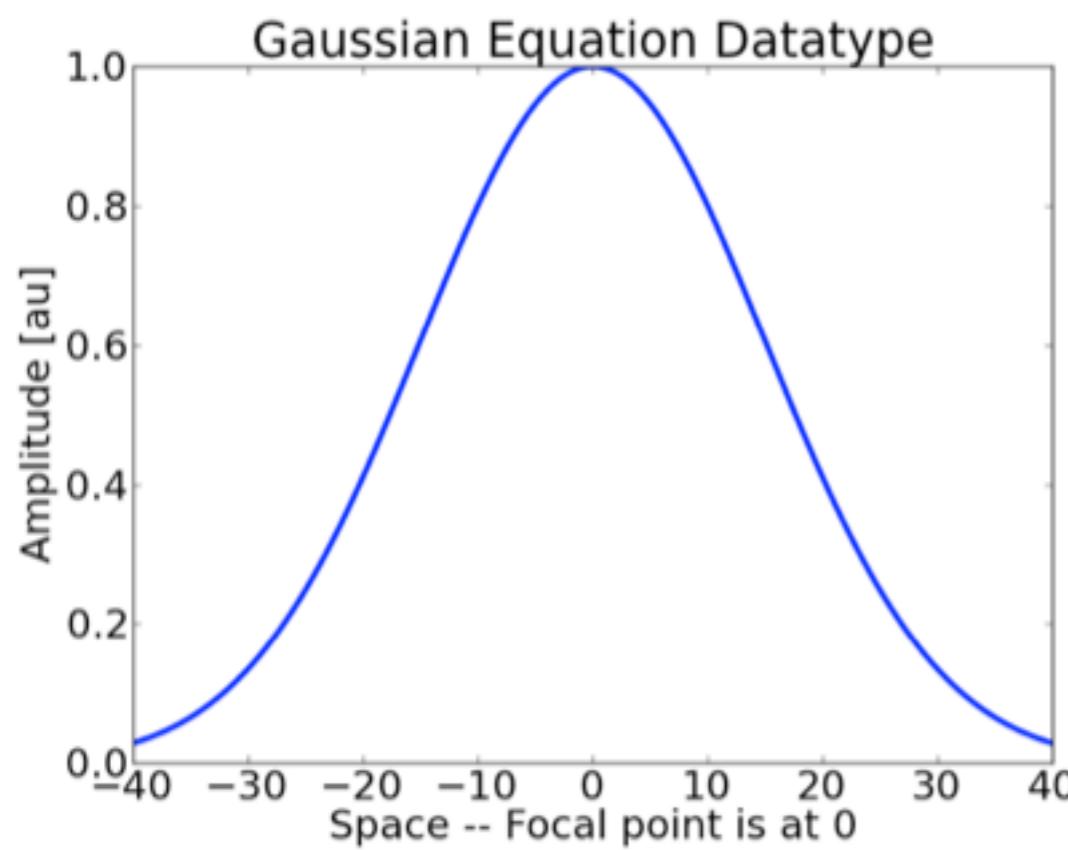
Topology of the brain

TVB connectivity

local coupling: surface-based modeling

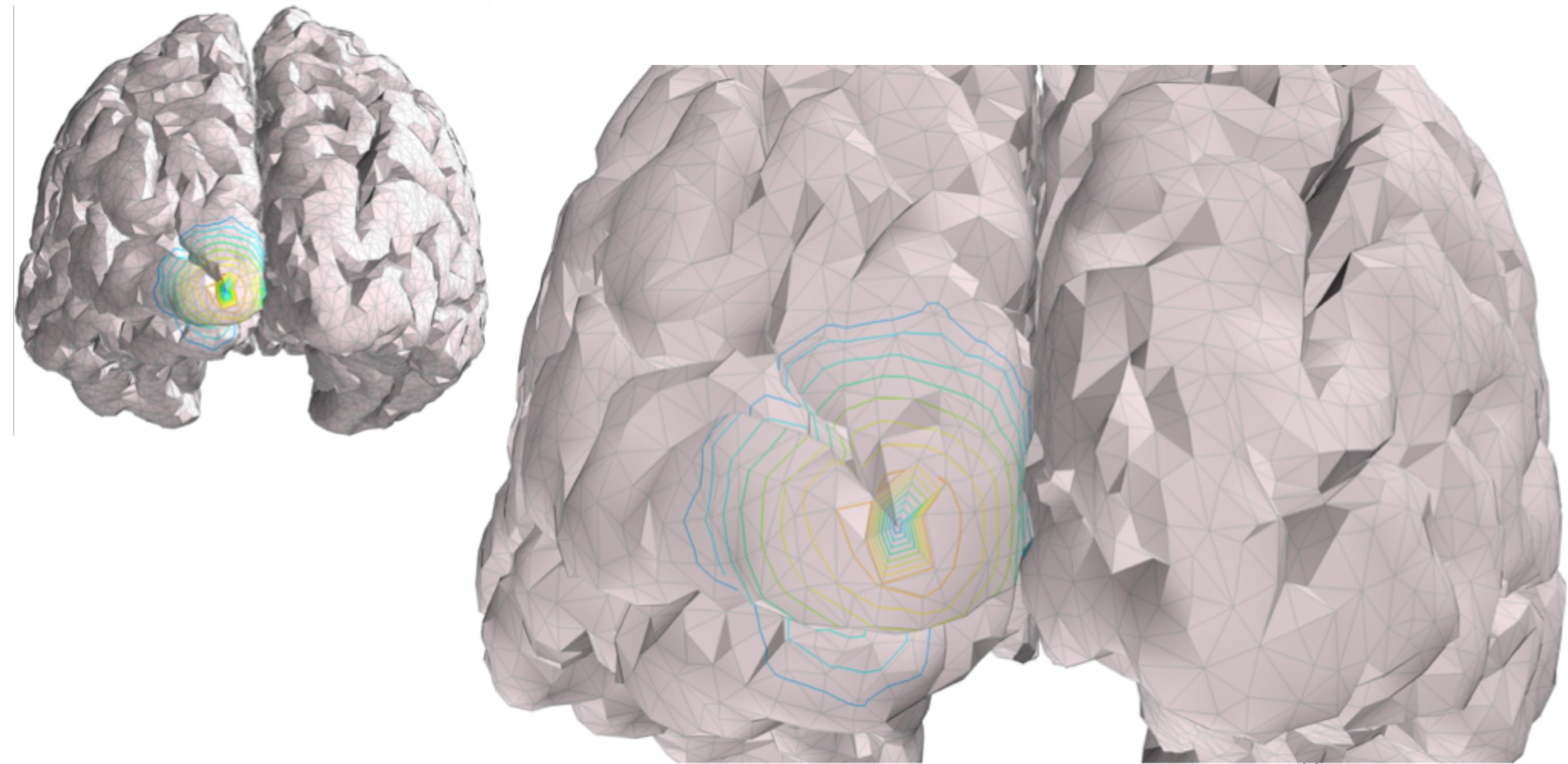


local coupling: surface-based modeling



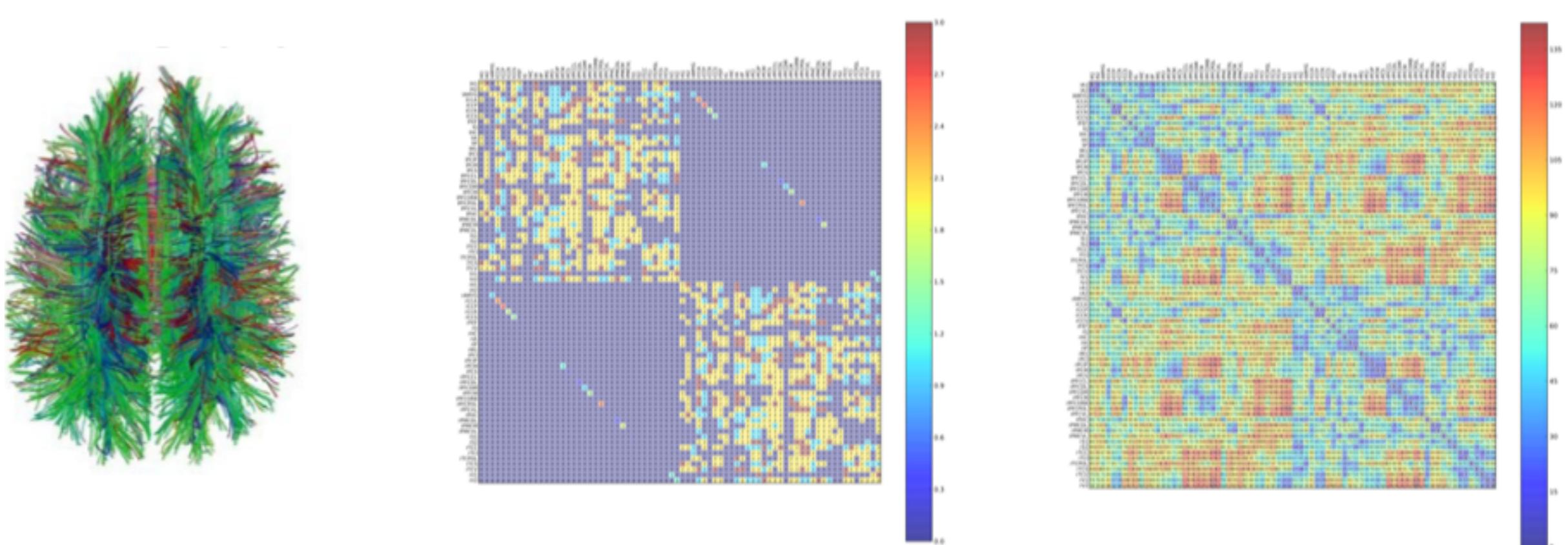
TVB connectivity

local coupling: surface-based modeling



space-time structure of connectivity

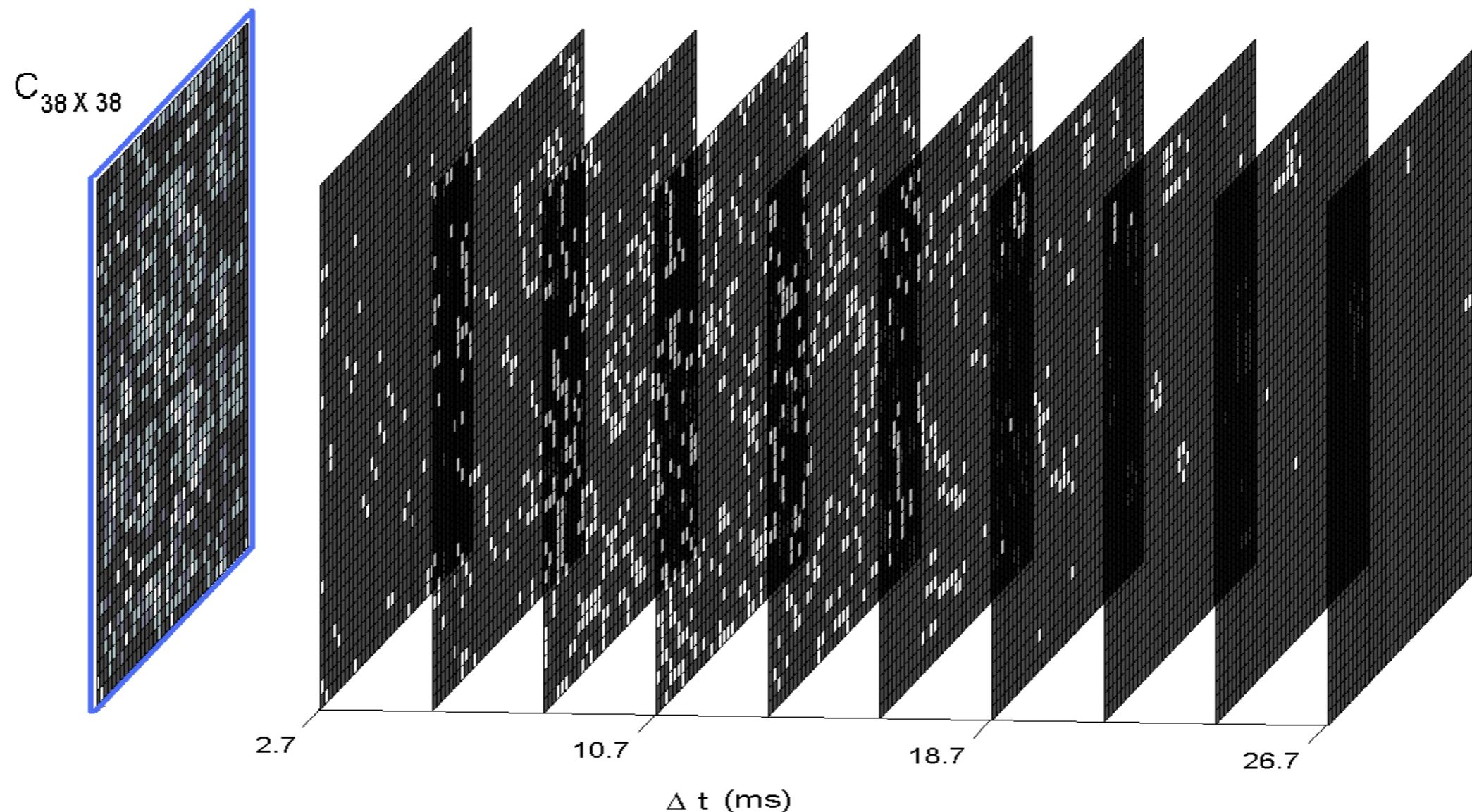
- no time delay for local coupling
- time delays for global coupling (default speed)
 - tract lengths
 - Euclidean distance in 3D



Jirsa Phil Trans Roy Soc 2009;
Sanz Leon et al Front
Neuroinformatics 2013

TVB connectivity

space-time structure of connectivity



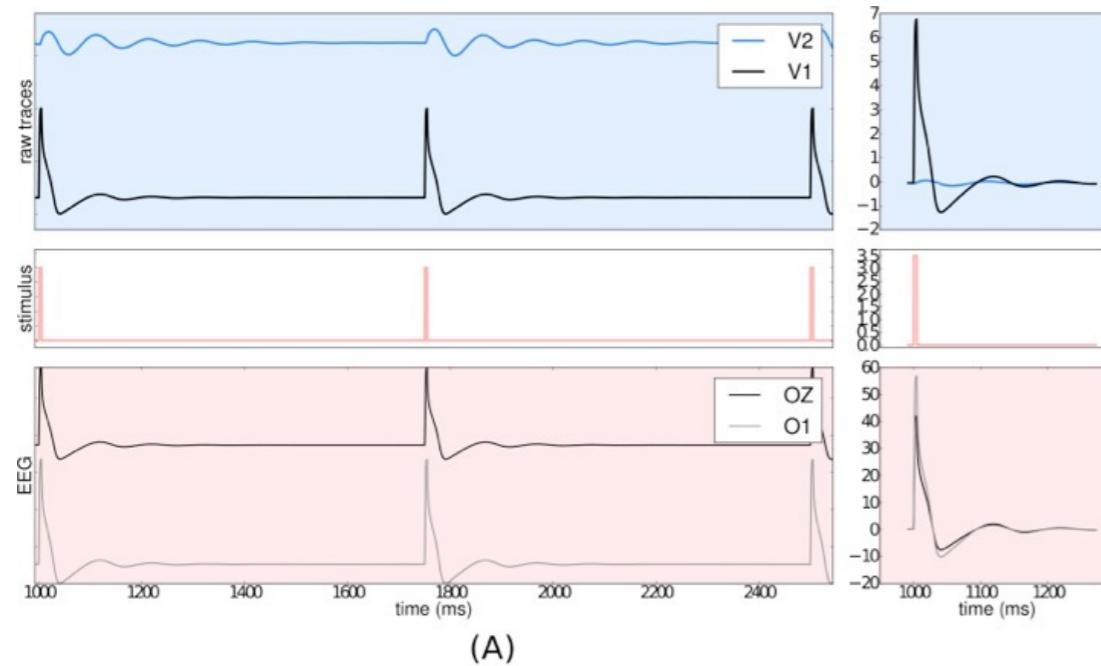


TVB stimulation

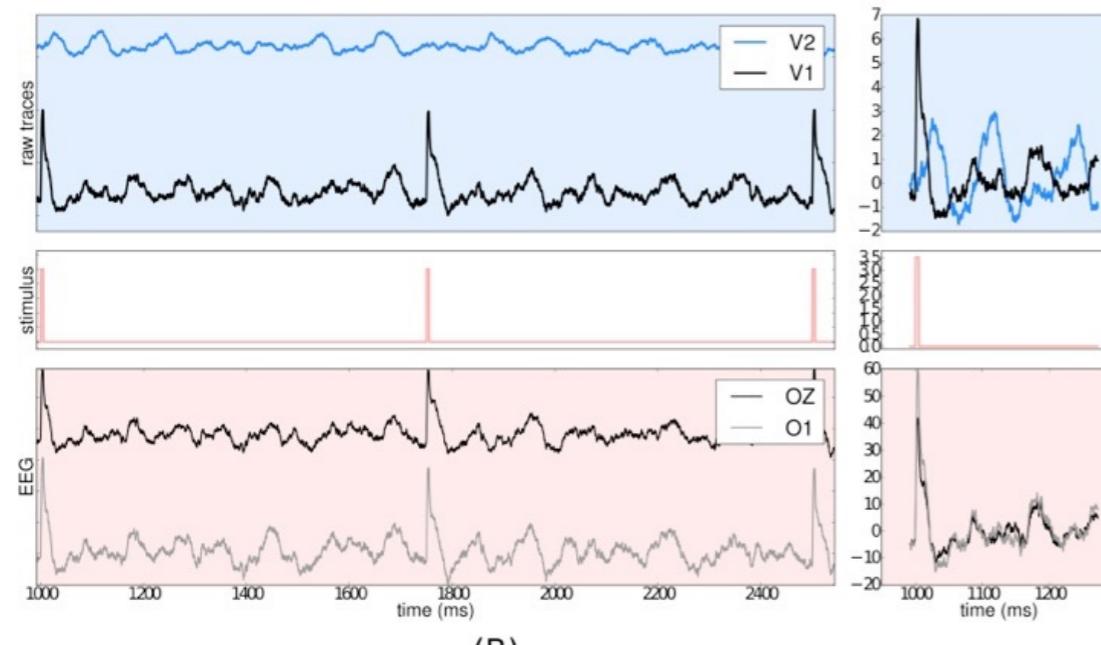
Dispersion in space and time

TVB stimulation

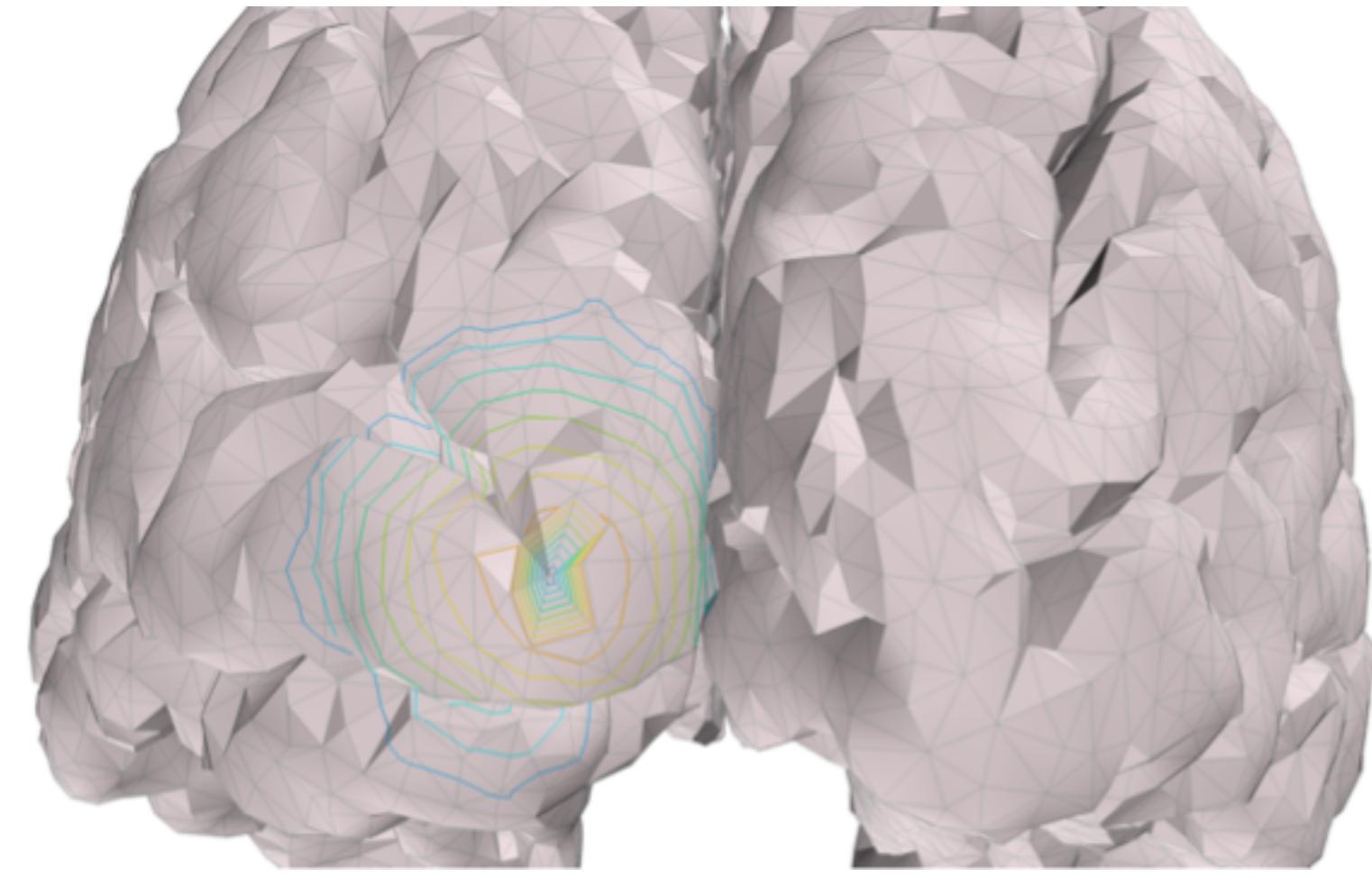
Stimulus = time course + spatial extent



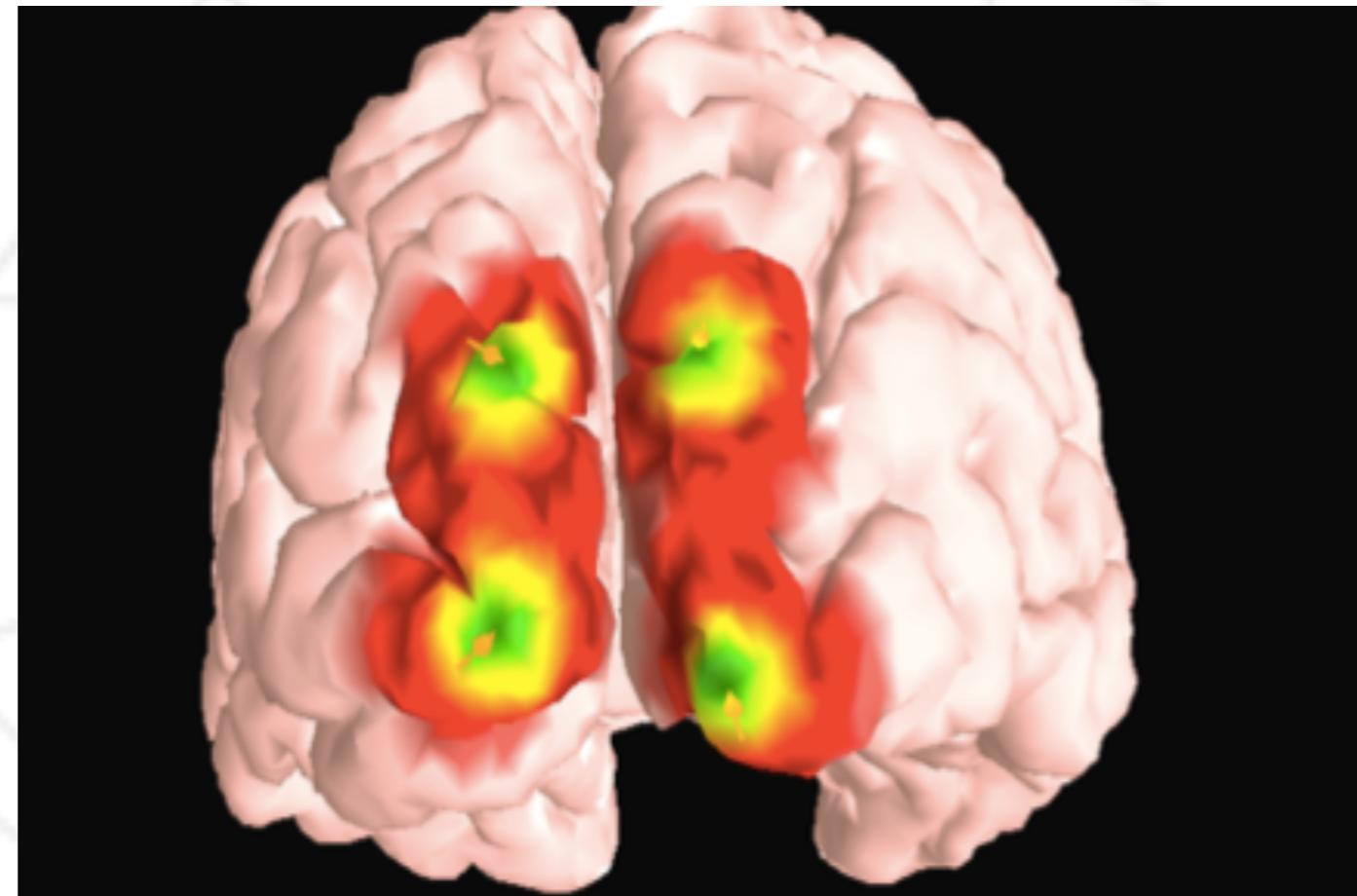
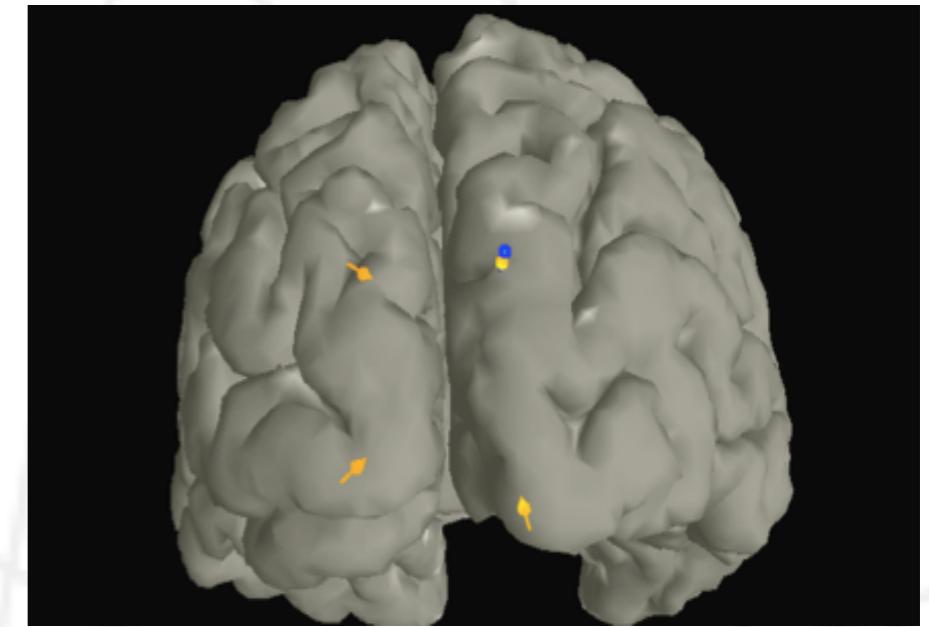
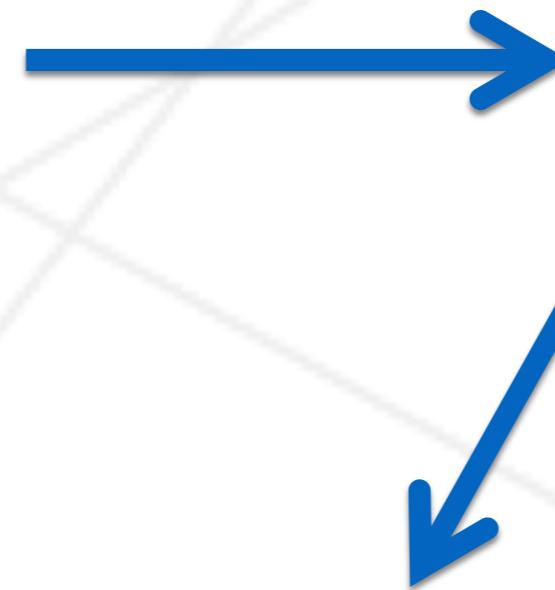
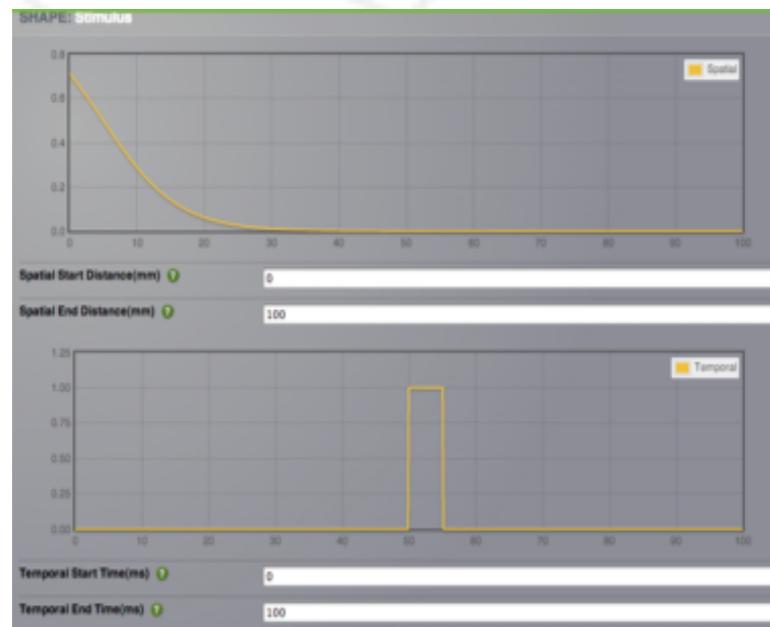
(A)



(B)



Stimulation





TVB monitors

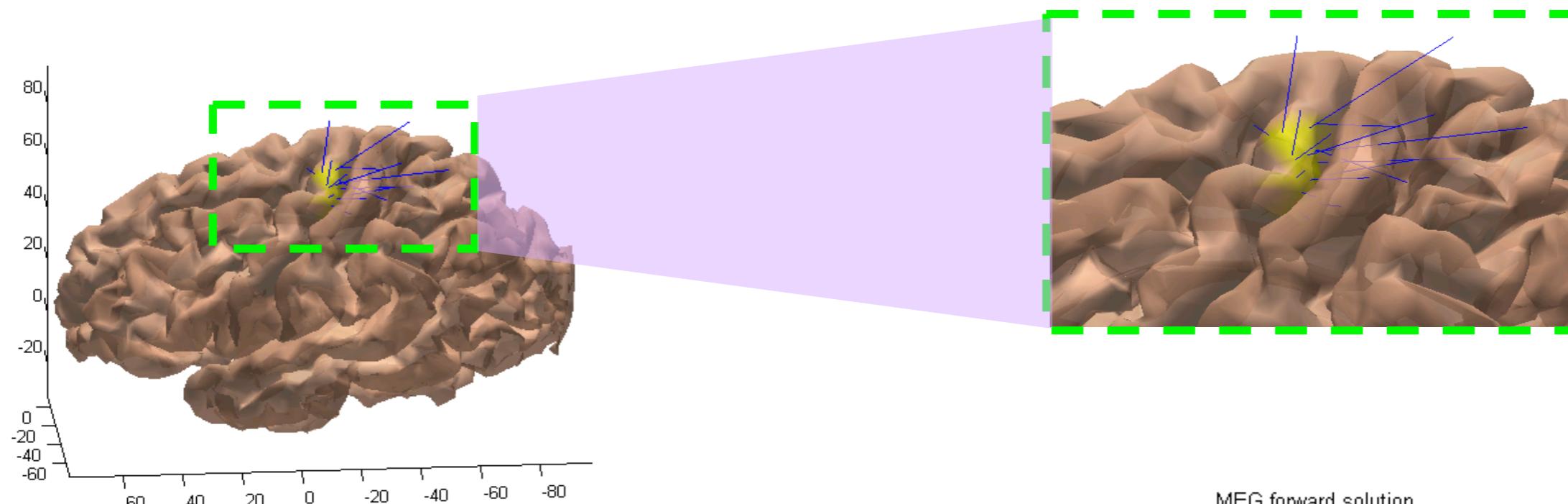
Non-invasive and invasive
imaging

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

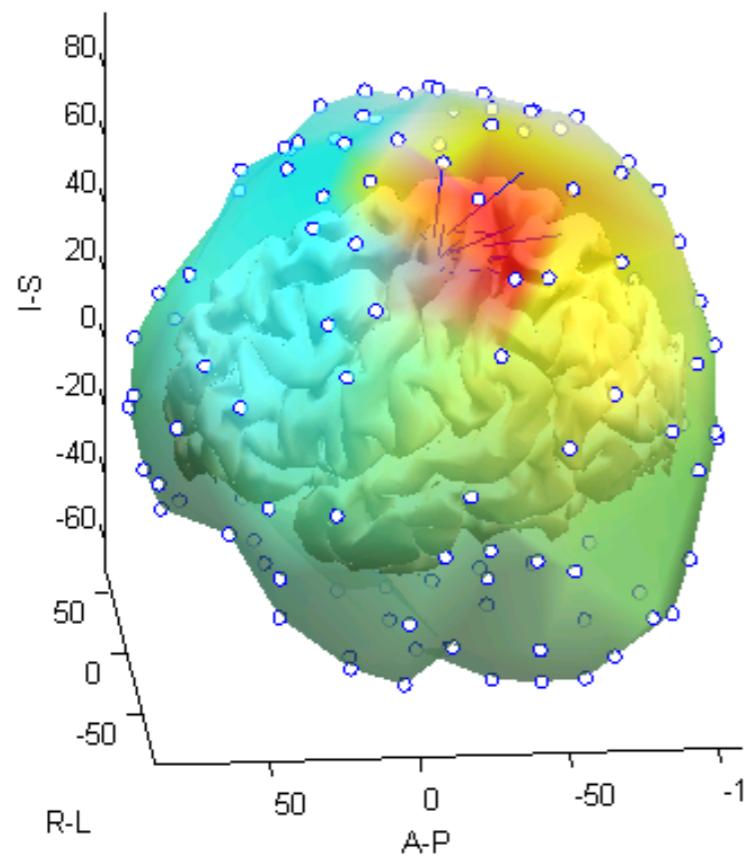
Raw signals (LFP, firing rate)

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

TVB monitors: EEG & MEG



EEG forward solution

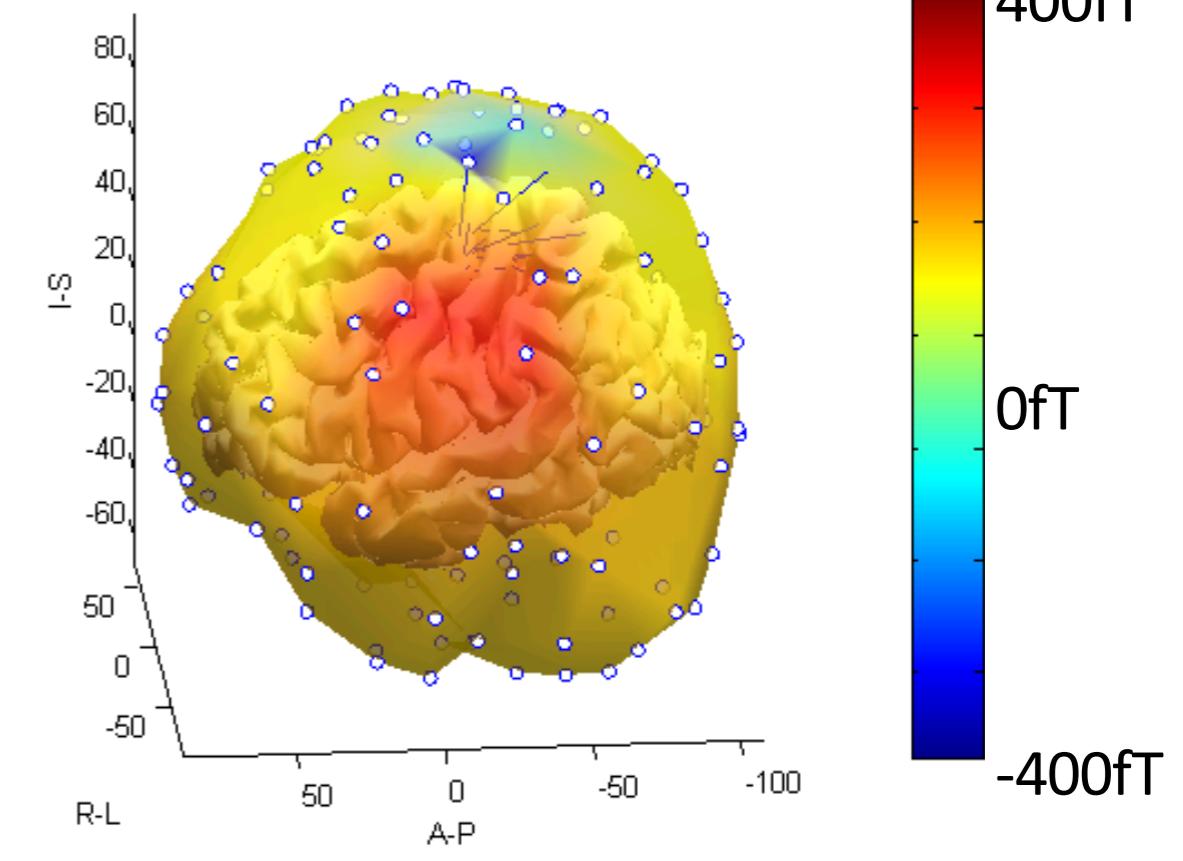


15uV

0 uV

-15uV

MEG forward solution

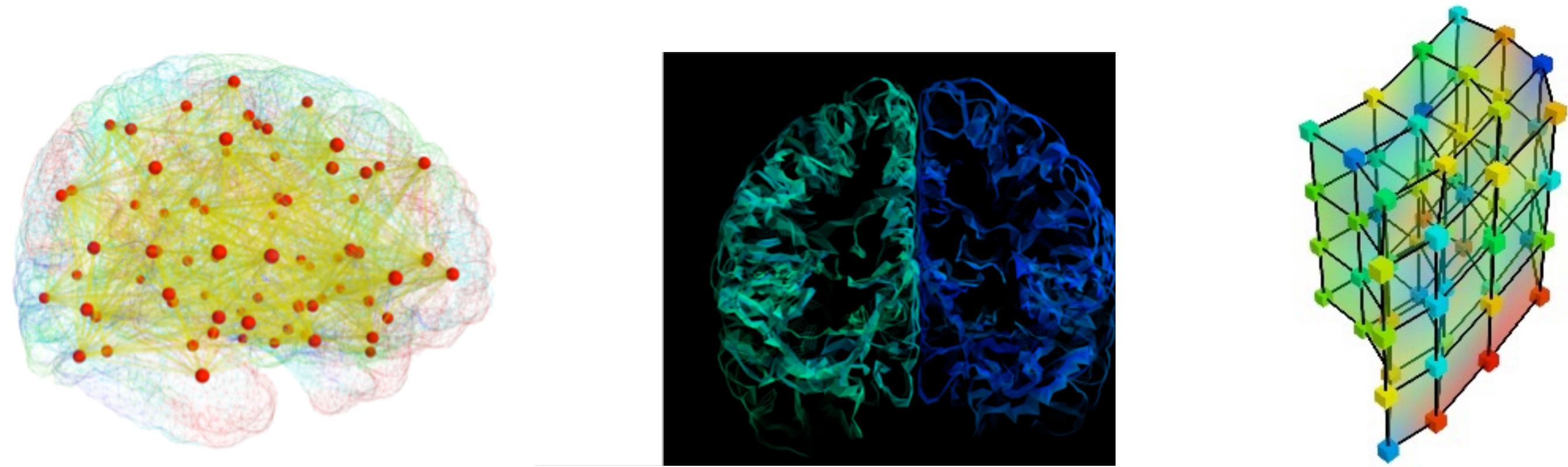


400fT

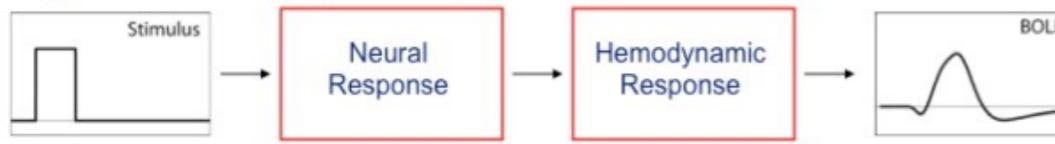
0fT

-400fT

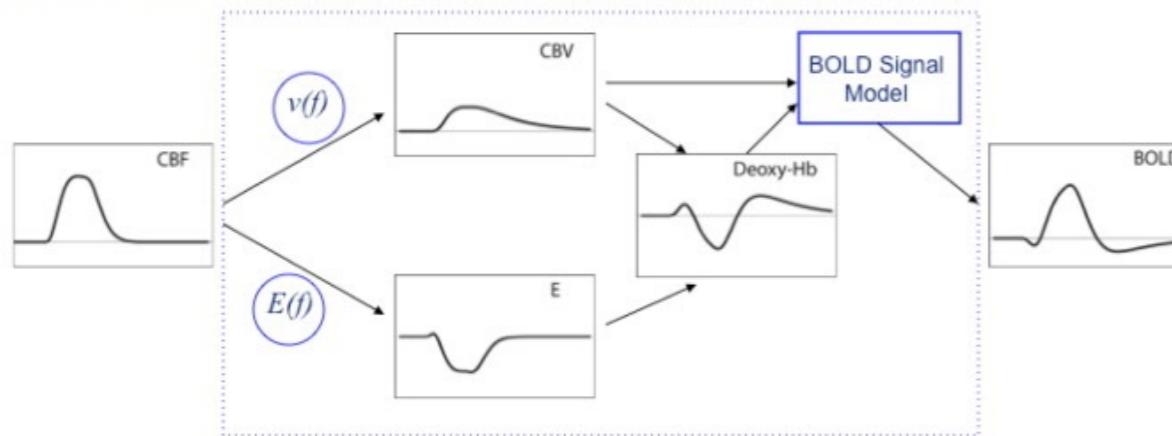
TVB monitors: Bold



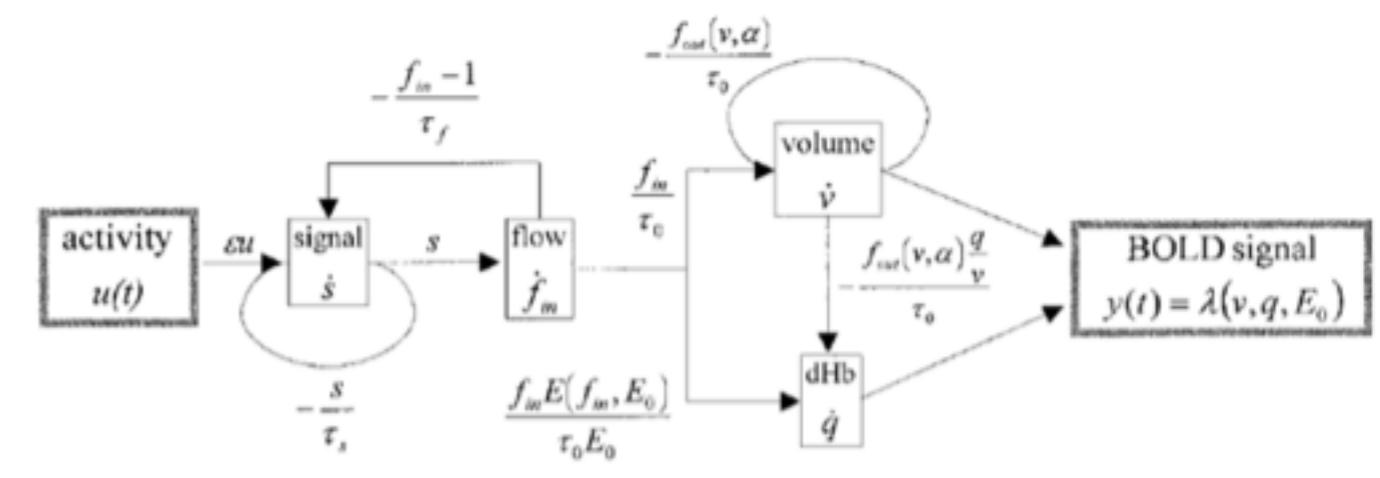
A. Early view of the BOLD response



B. Balloon model

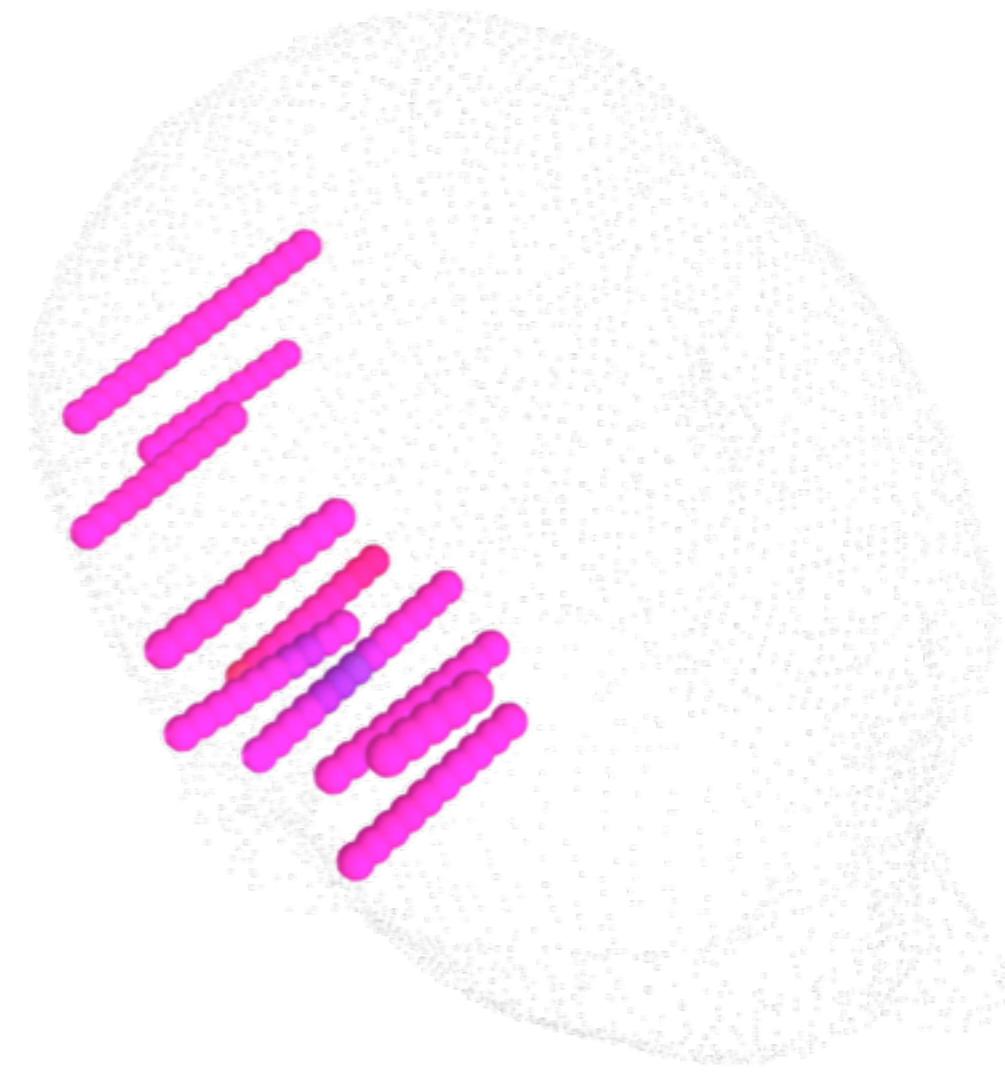
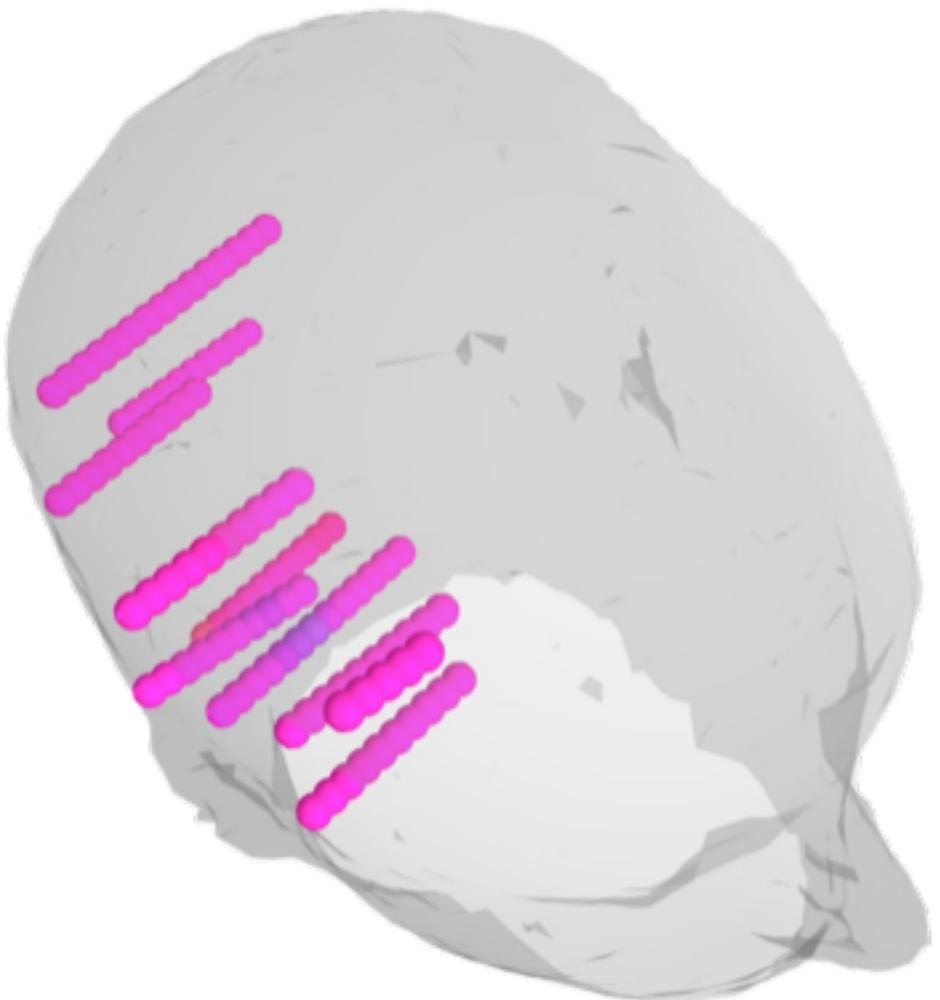


Reduced Balloon-Windkessel model



TVB monitors: stereotactic EEG

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



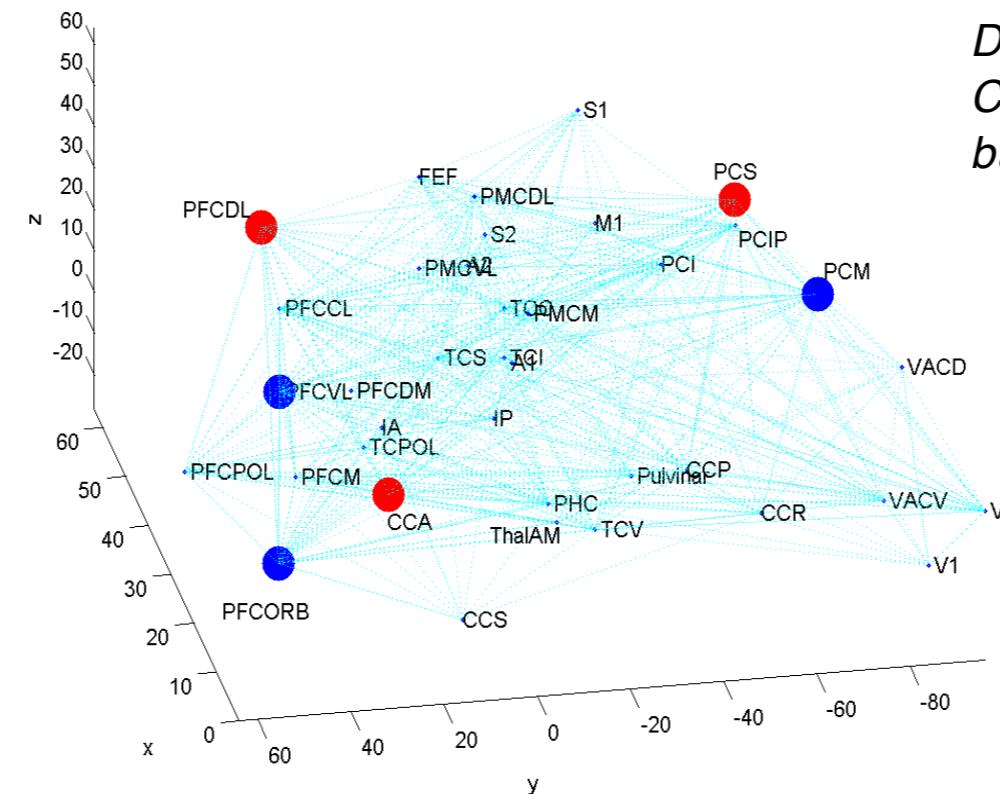


TVB Examples

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

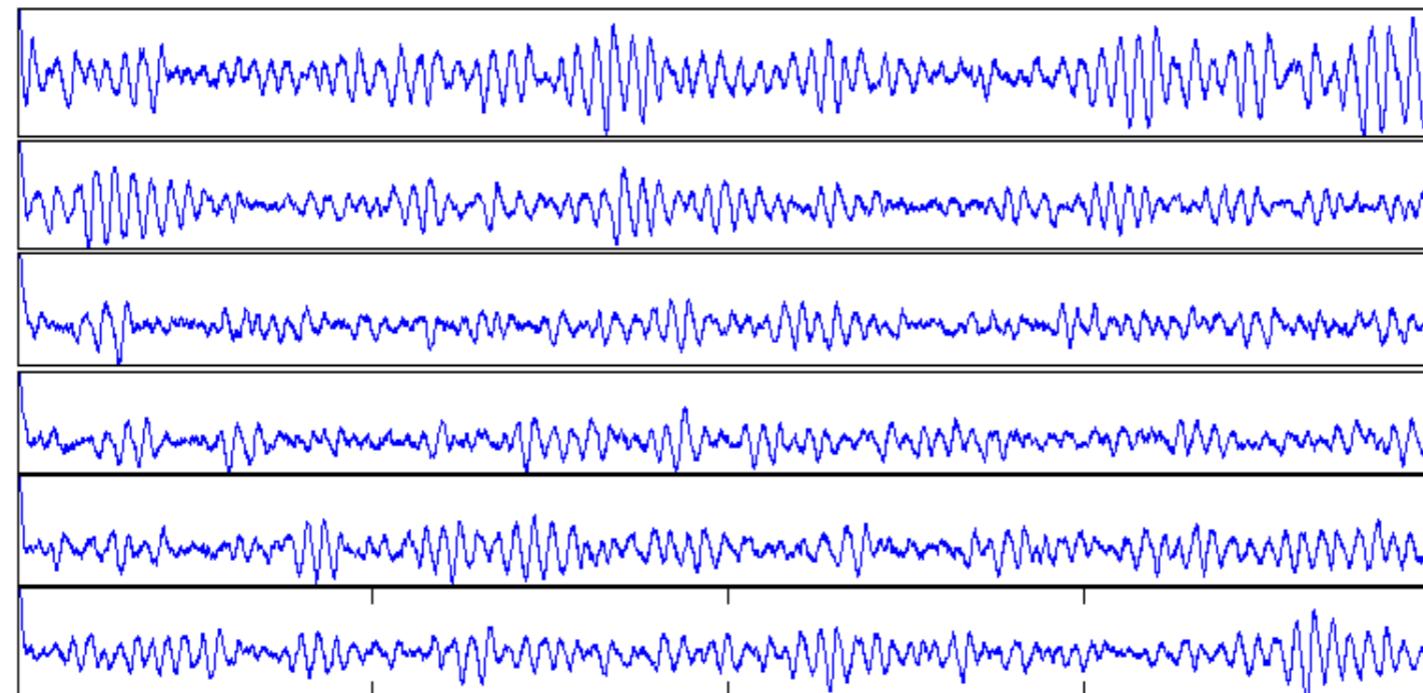
Intrinsic Dynamics (*Resting-State*) are driven by brain noise

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



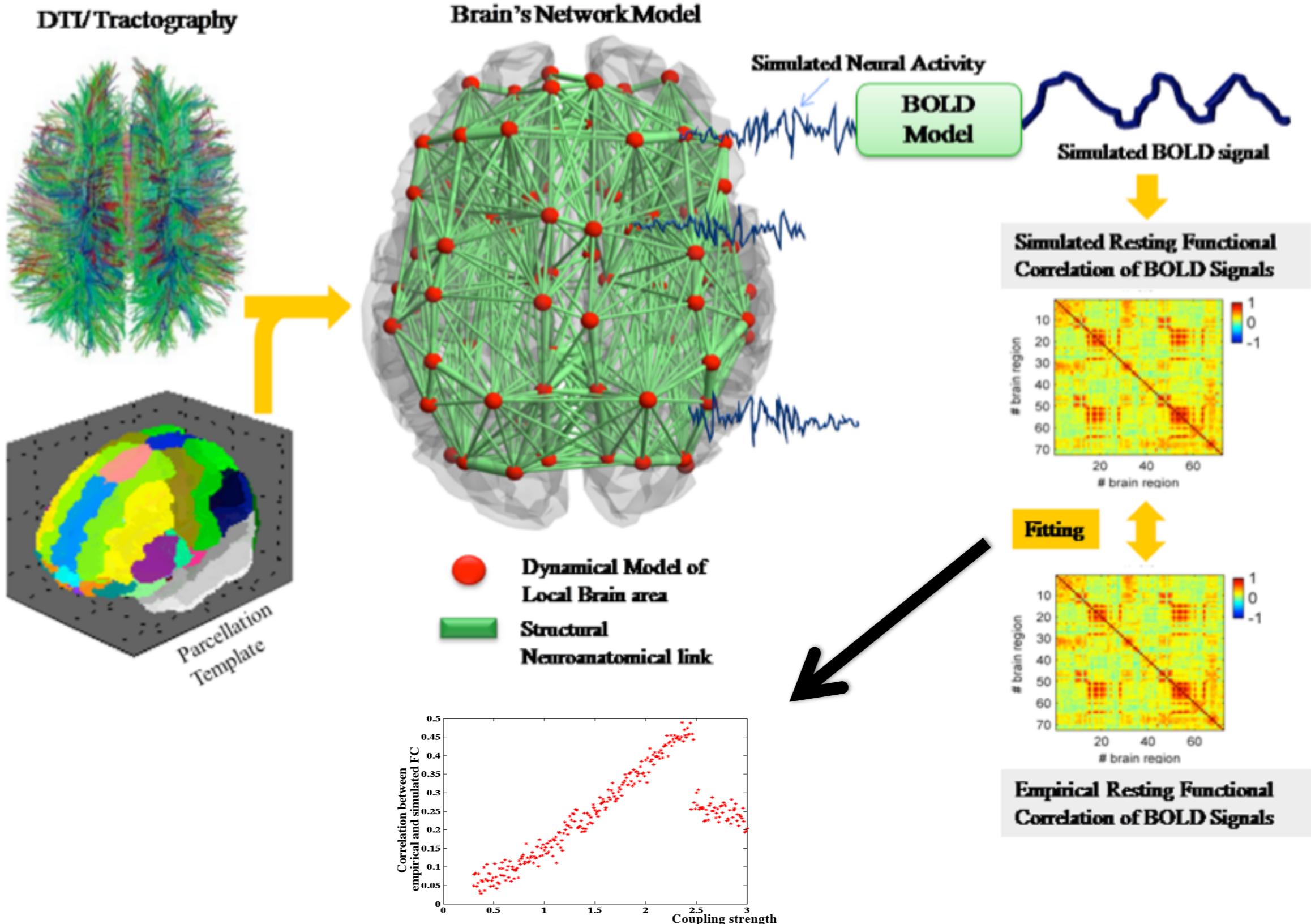
*Default Model in TVB
CoCoMac connectome with time delays based on distance in MNI template brain*

PFCorb
PFCvl
PCM
PCS
CCA
PFCdl



“Default mode regions” drive the system through instabilities

The modeling process of resting-state activity

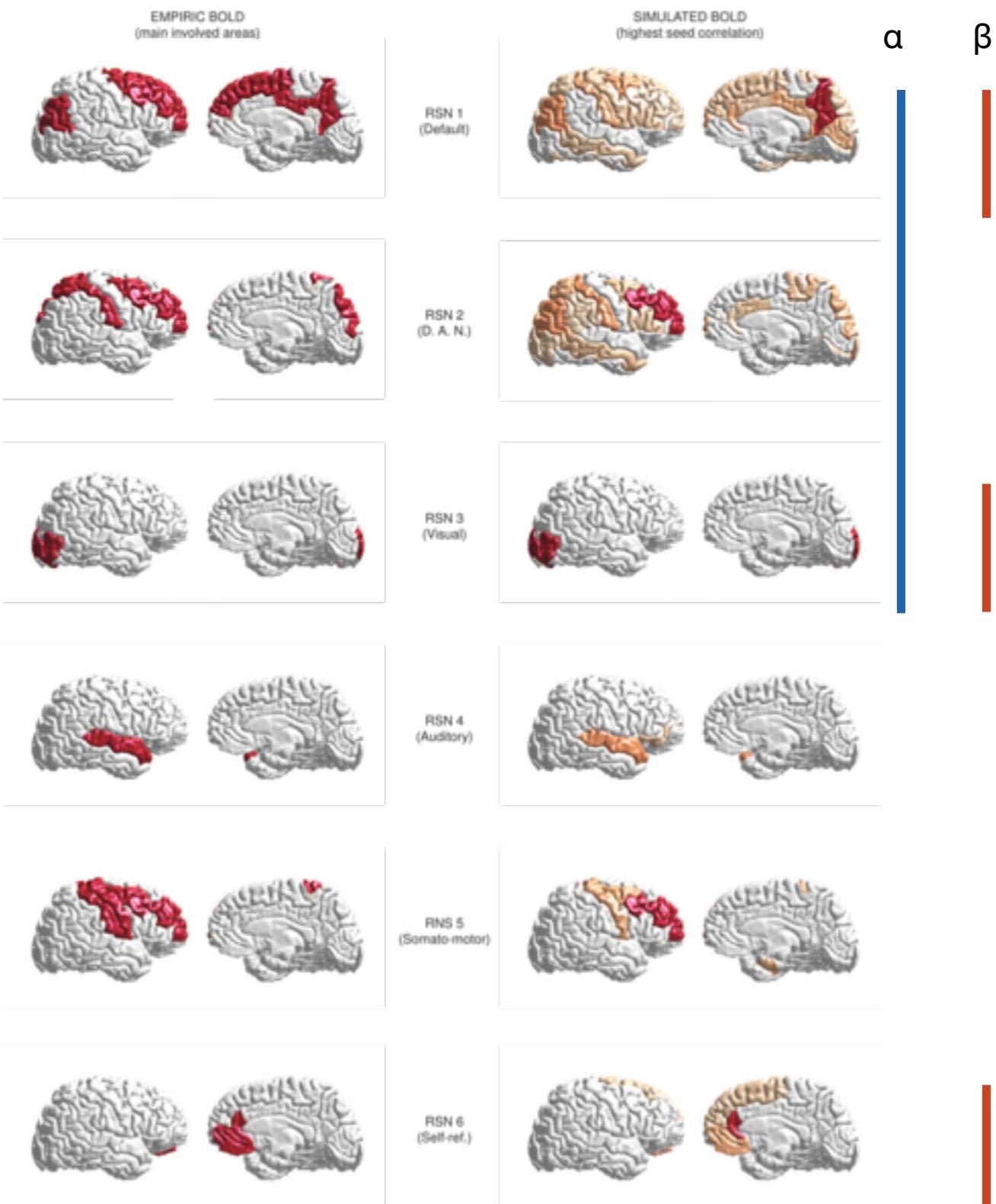
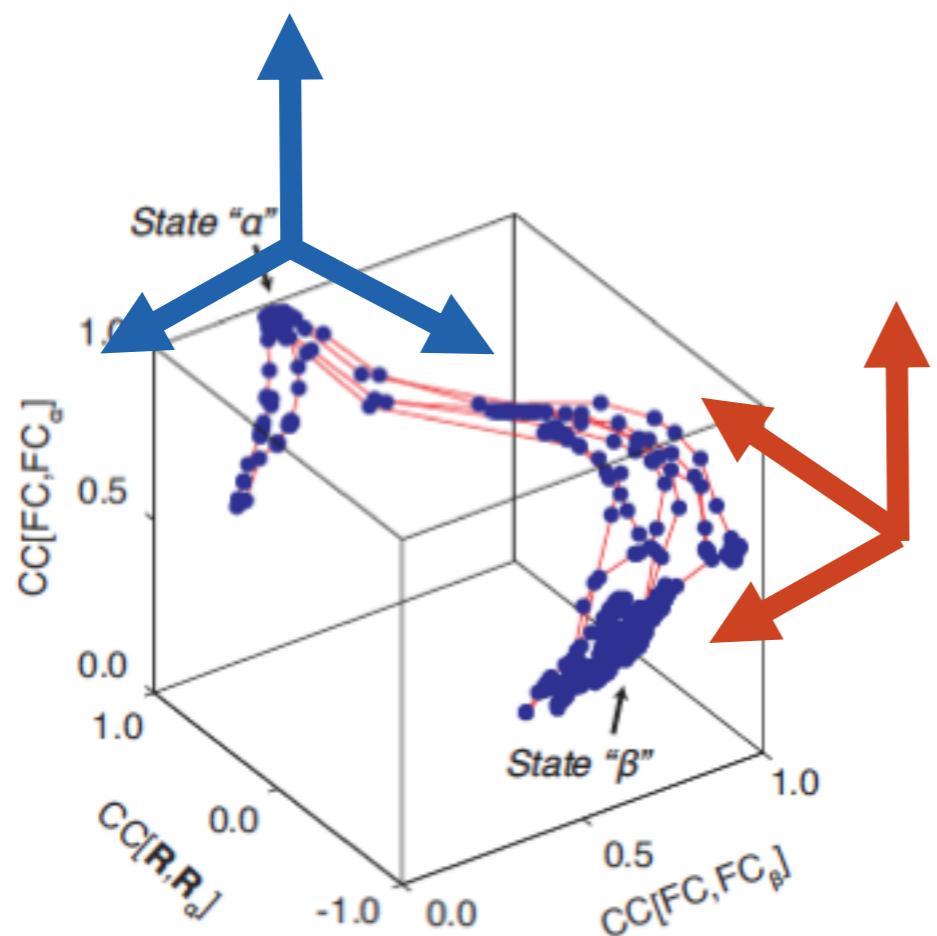


Gosh et al PLoS CB 2008; Deco, Jirsa & McIntosh et al PNAS 2009; Deco & Jirsa JNS (2012); Deco, Jirsa & McIntosh Nat Rev Neurosci (2011); Deco, Jirsa & McIntosh TINS (2013)

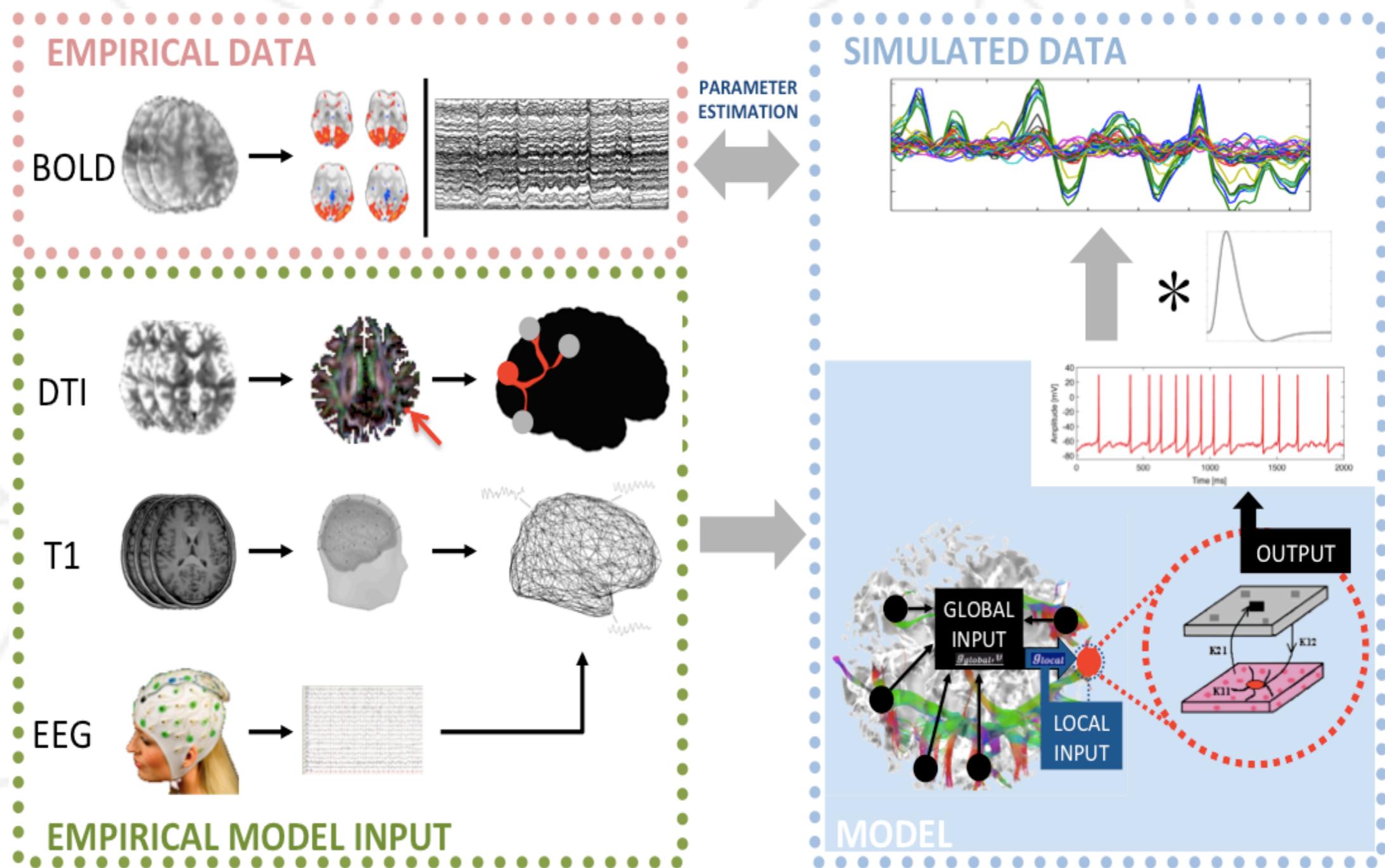
The modeling process of resting-state activity

Functional Connectivity Dynamics

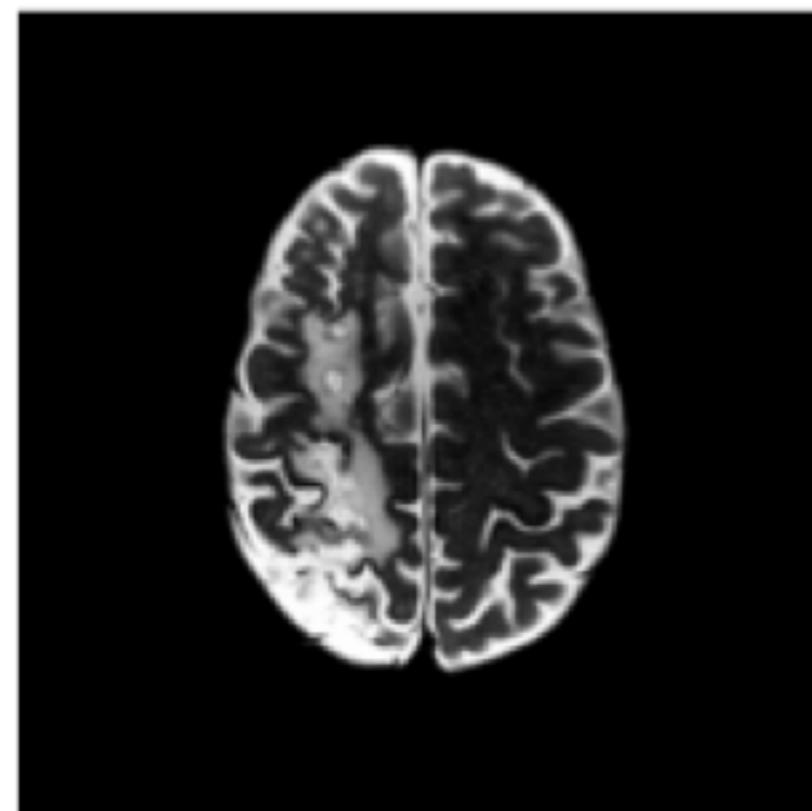
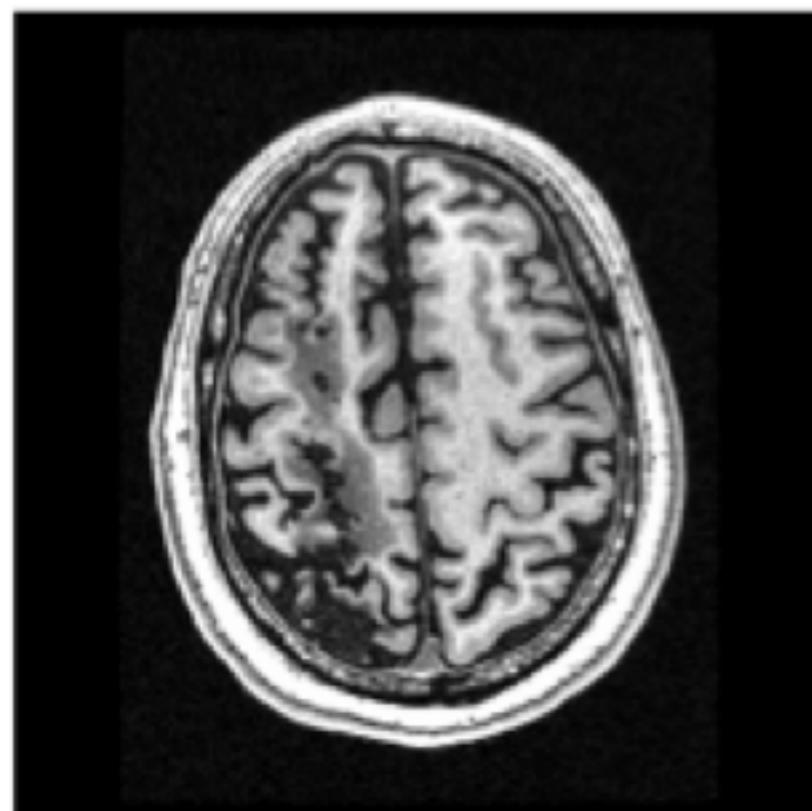
Epochs of invariant functional connectivity evolve dynamics in subspaces spanned by sets of resting state network patterns



Integration of EEG & fMRI



TVB model of Stroke Recovery



Left hemisphere stroke, Male 55yrs

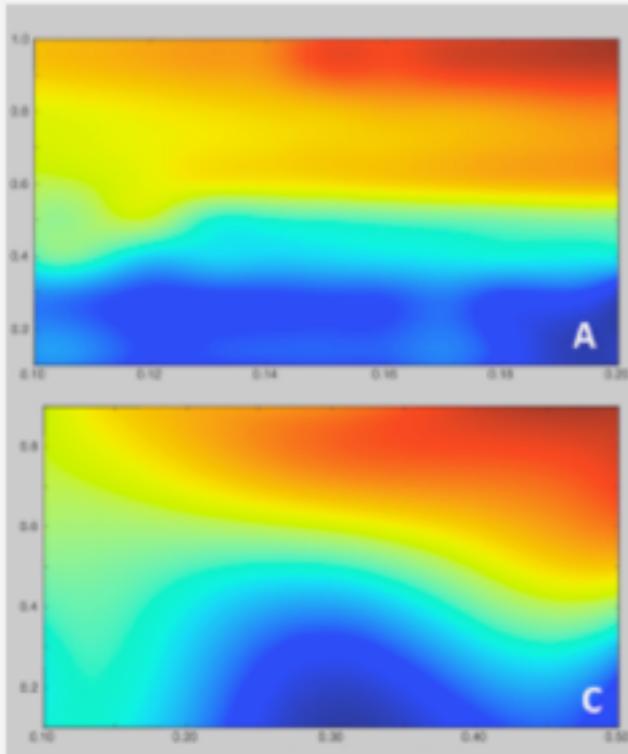


Global variance of state variable

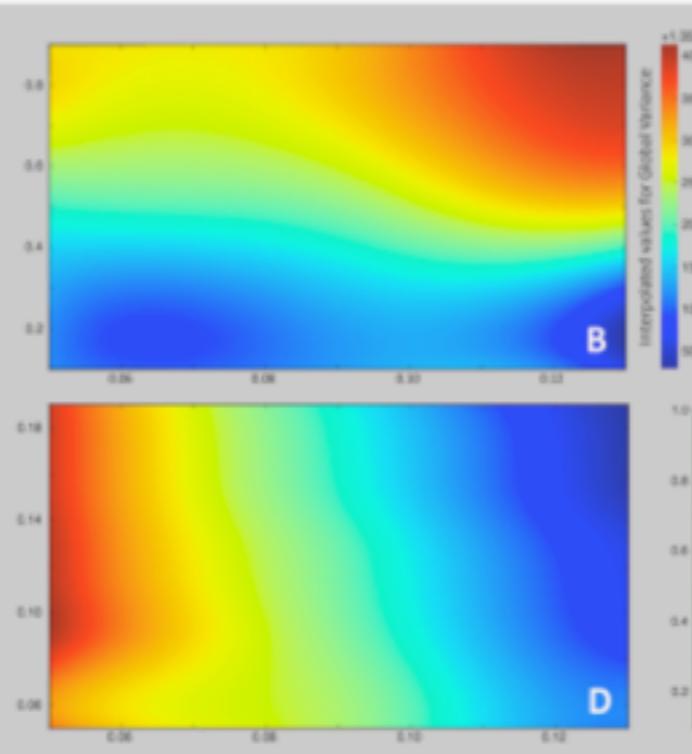
Healthy

Stroke

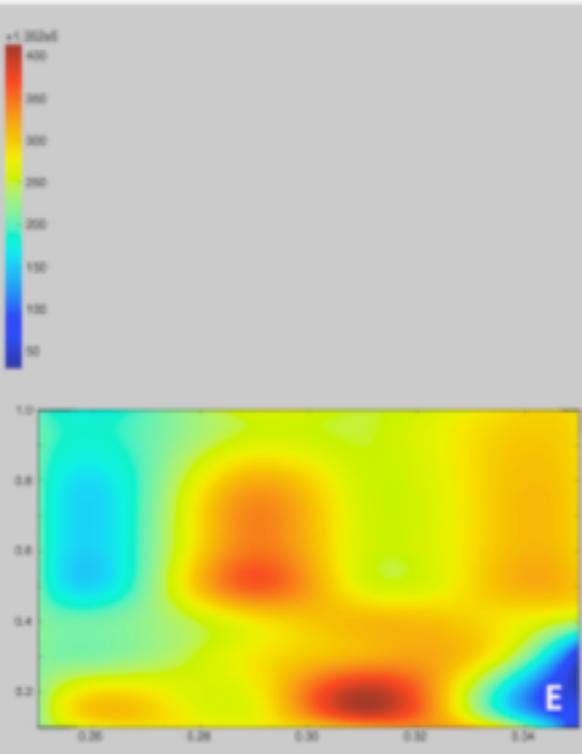
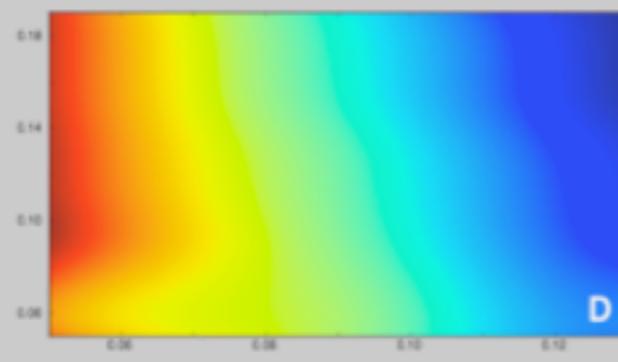
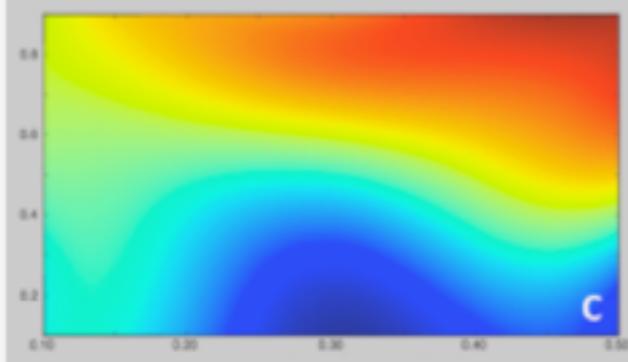
GABA coupling parameter



A



B

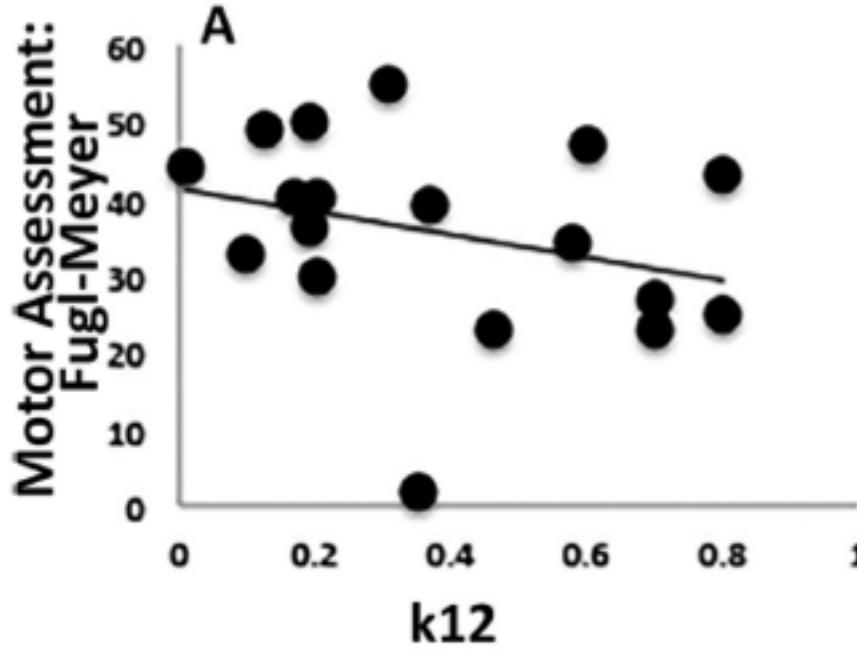


NMDA coupling parameter

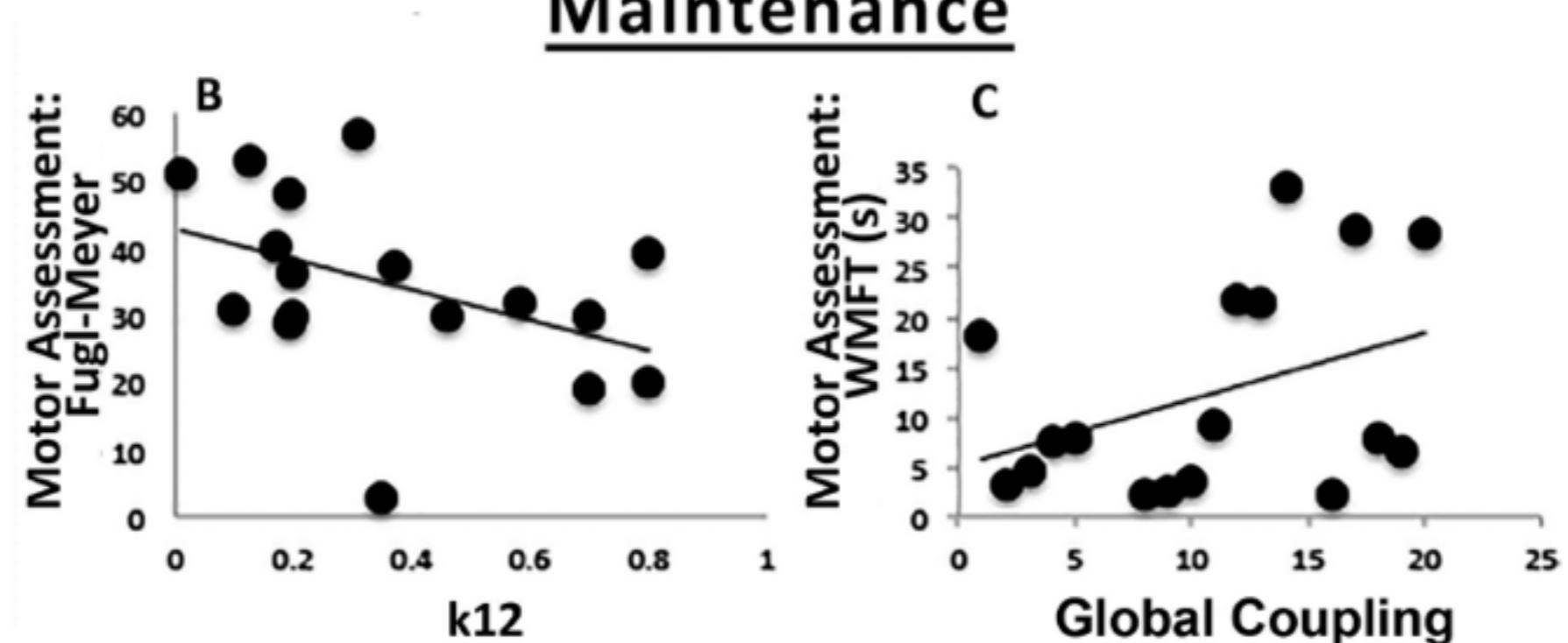
Falcon et al. 2015 Frontiers
Computational Neuroscience

Falcon et al. 2016 eNeuro

Post-Therapy

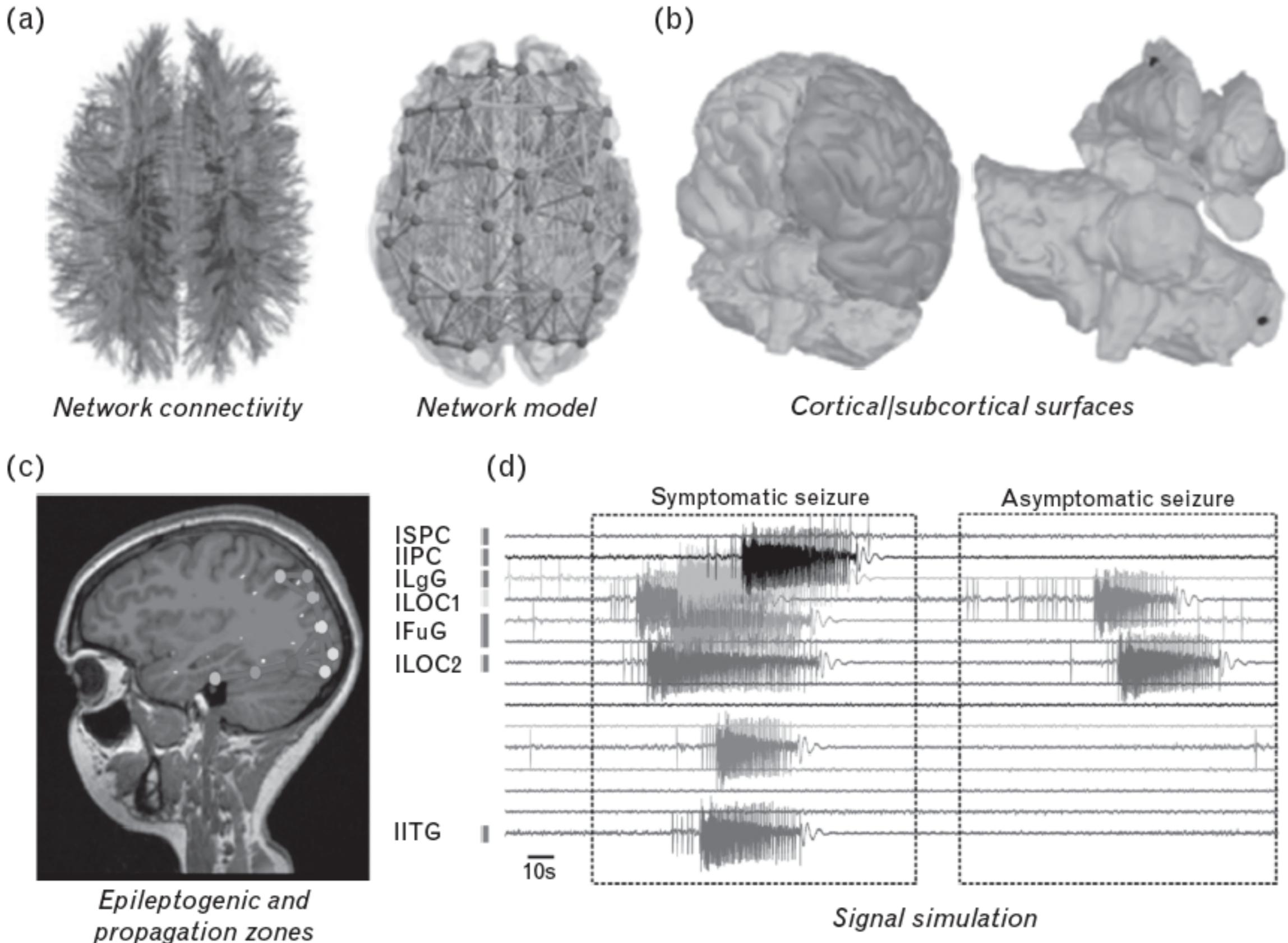


Maintenance



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

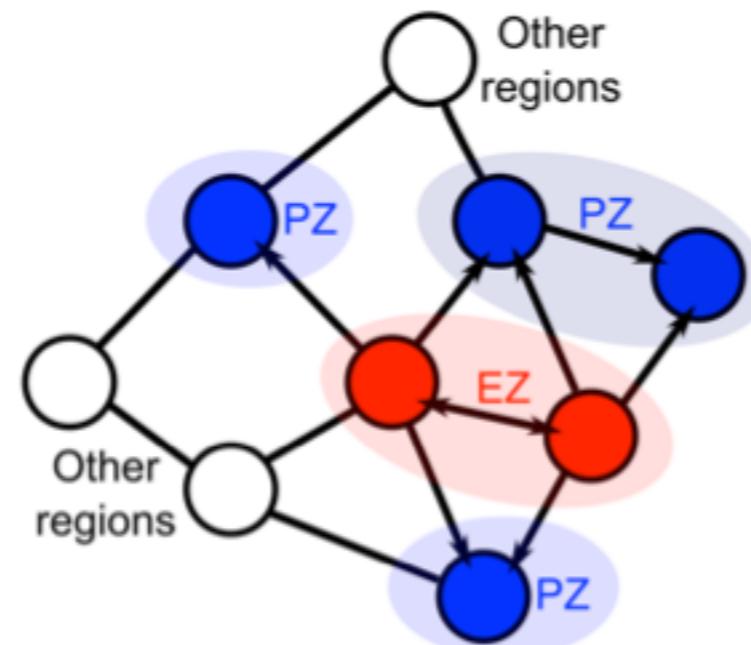
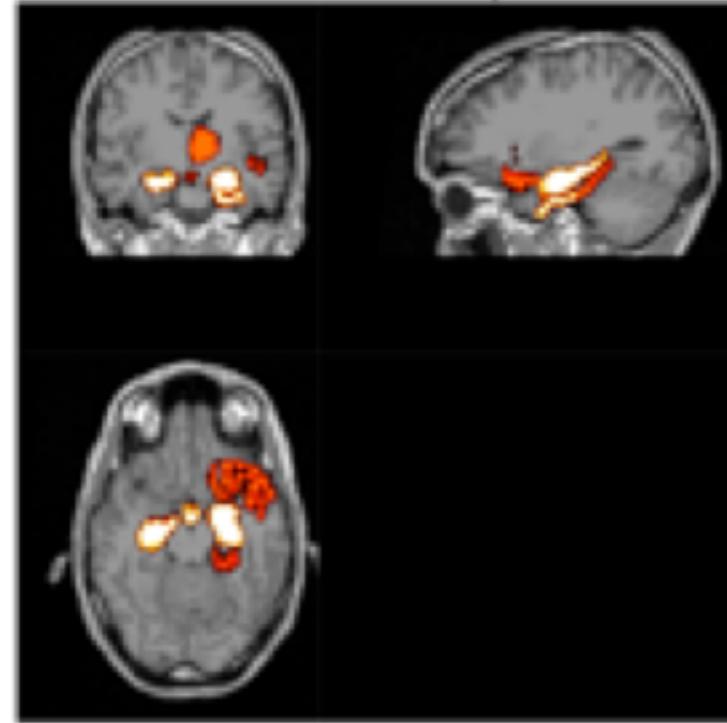
TVB modeling for epilepsy



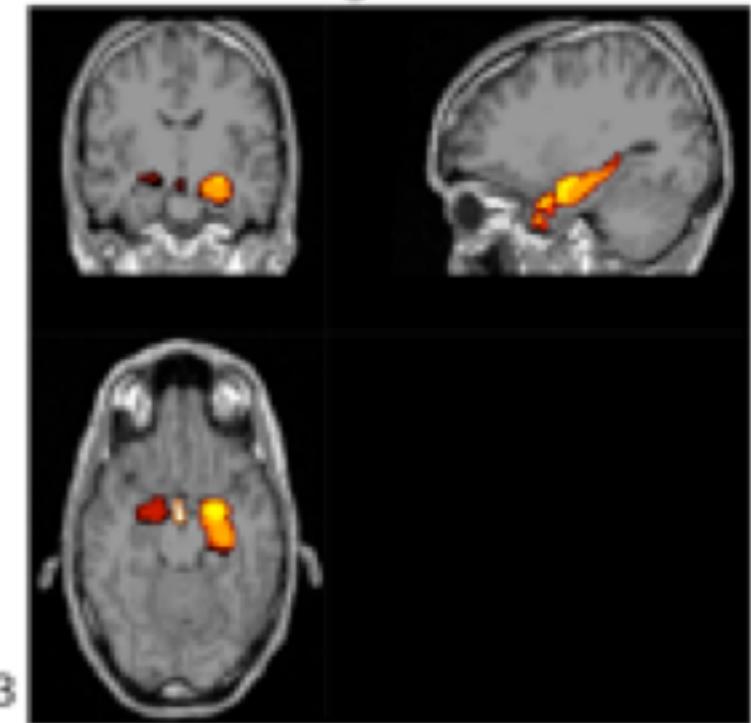


TVB & Epilepsy: Finger printing

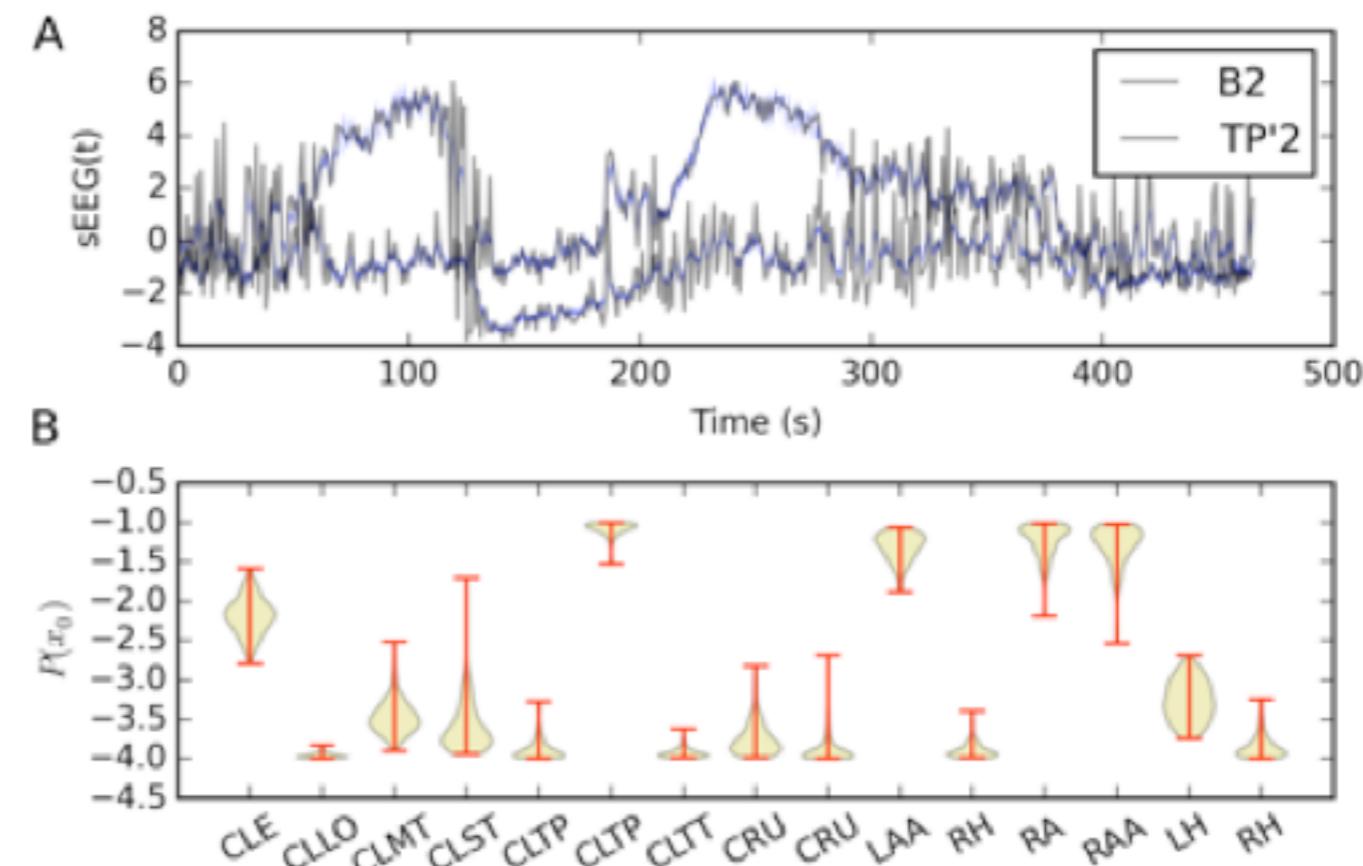
A Clinician EZ and PZ prediction



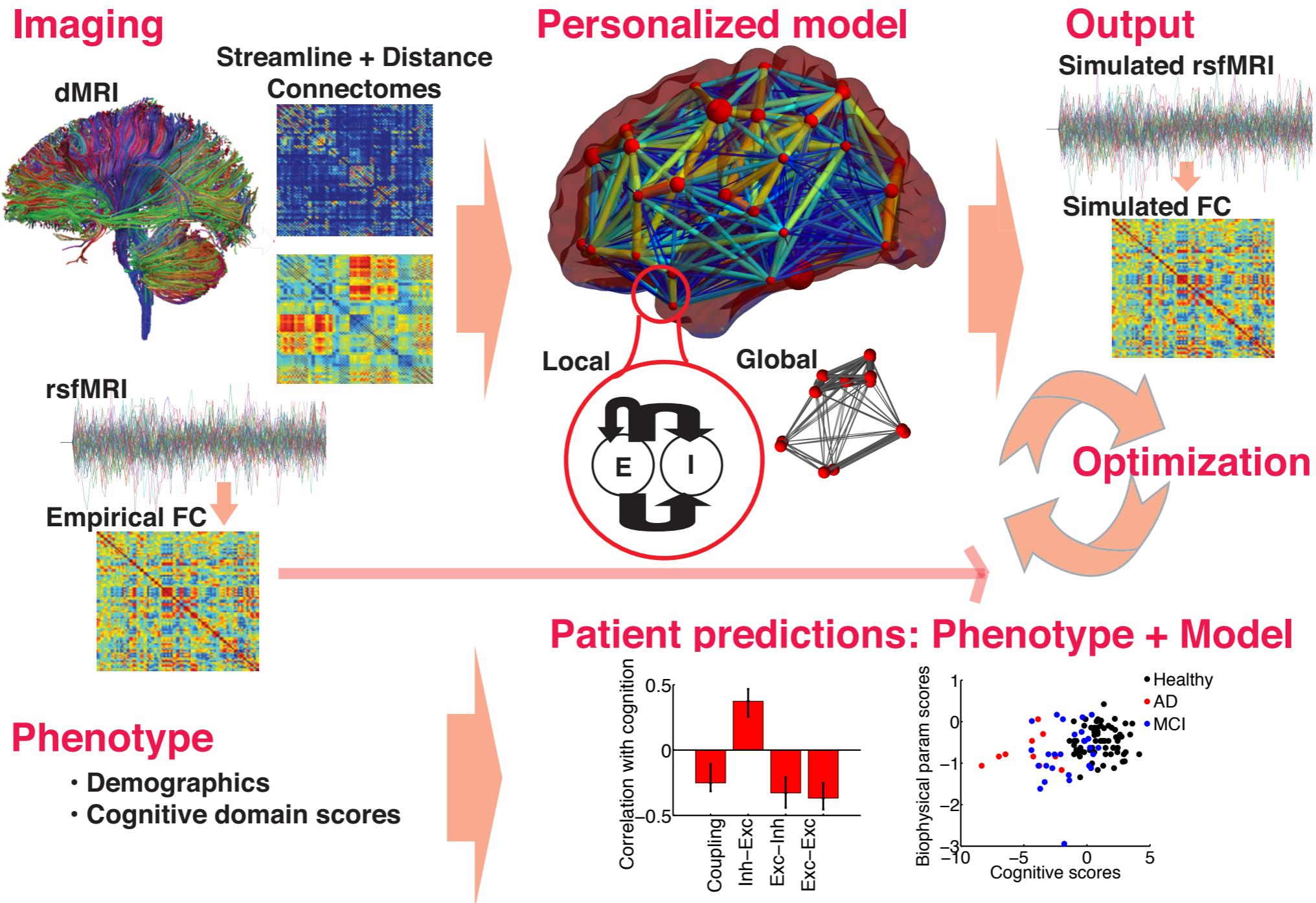
C Data fitting excitabilities



Model inversion using
Bayesian inference
framework



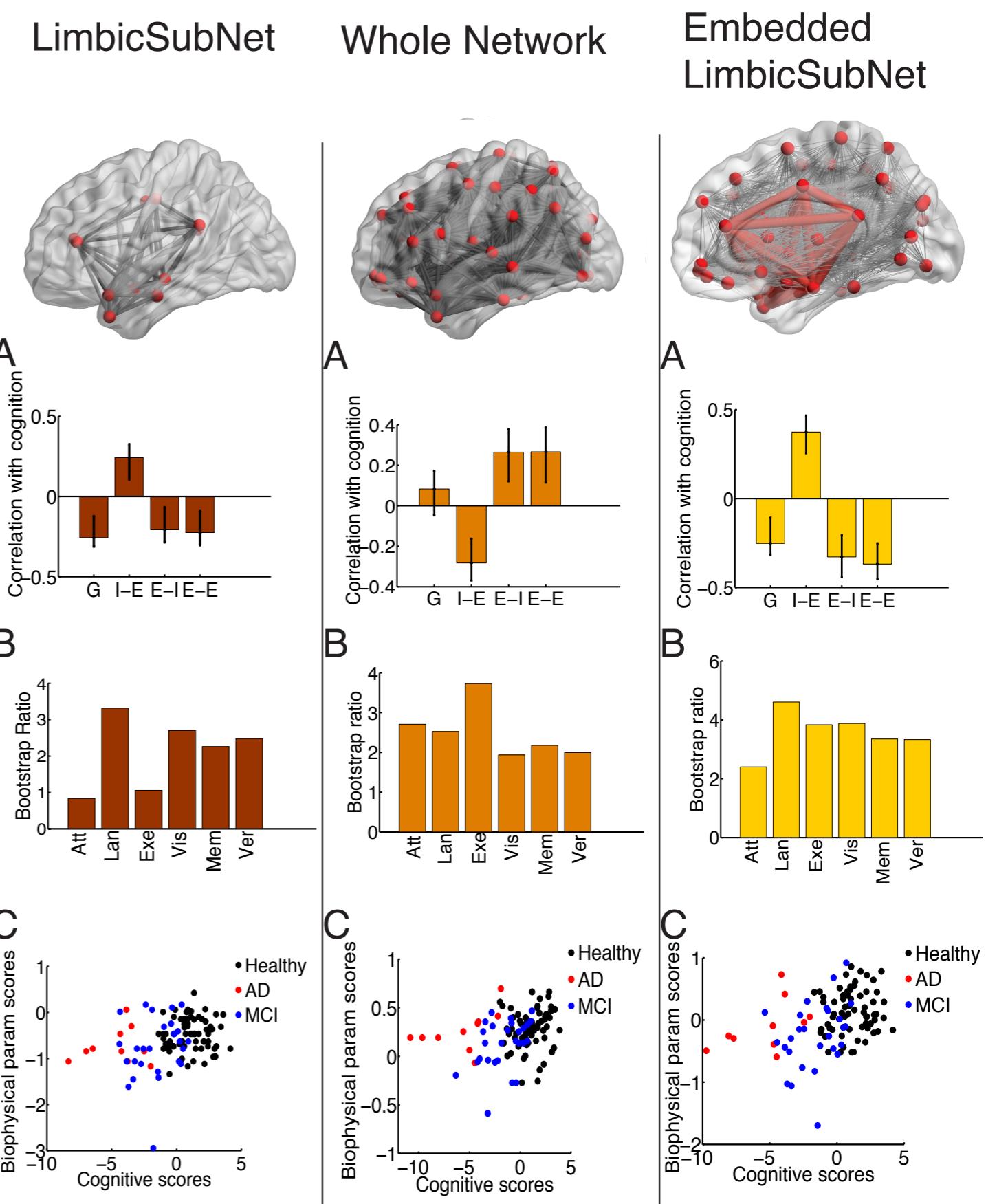
TVB modeling for Alzheimer's Dementia



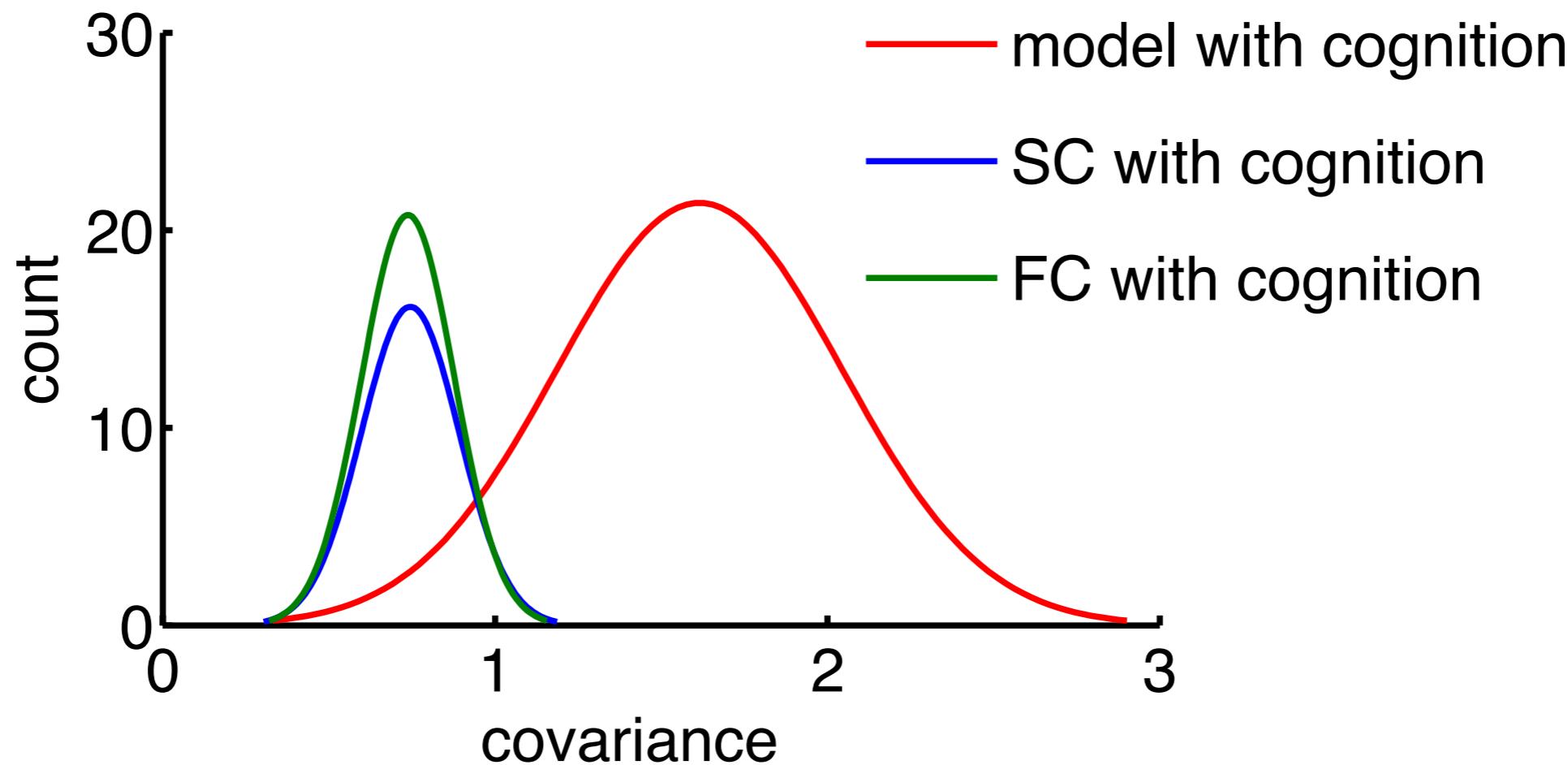
Prediction of cognitive status using TVB parameters

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



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

The Virtual Mouse Brain (TVMB) modeling

Local dynamics

Global dynamics

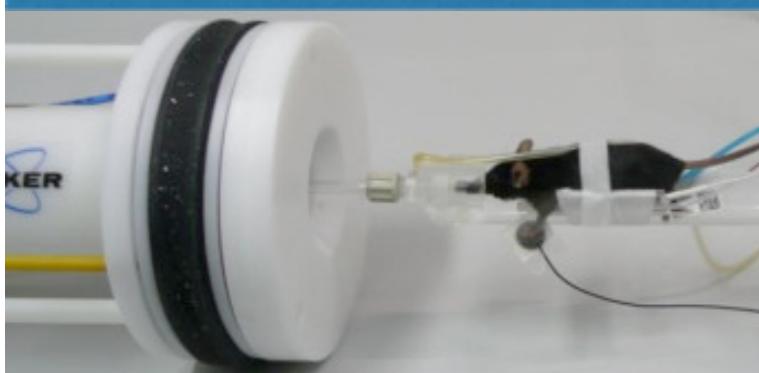
$$\psi(x,t) = N(\psi(x,t)) + \int_{local} g(x - x')S(\psi(x',t))dx' + \int_{global} G(x,x')S(\psi(x',t - \frac{|x - x'|}{v}))dx' + noise$$

Field potential Intrinsic activity

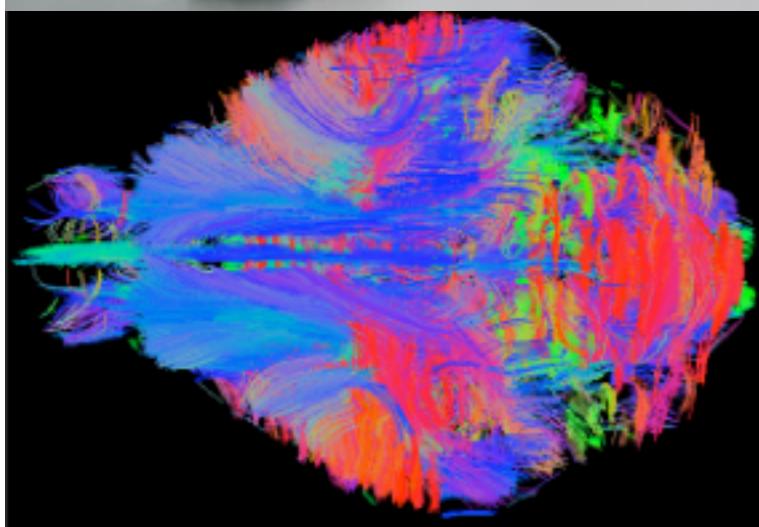
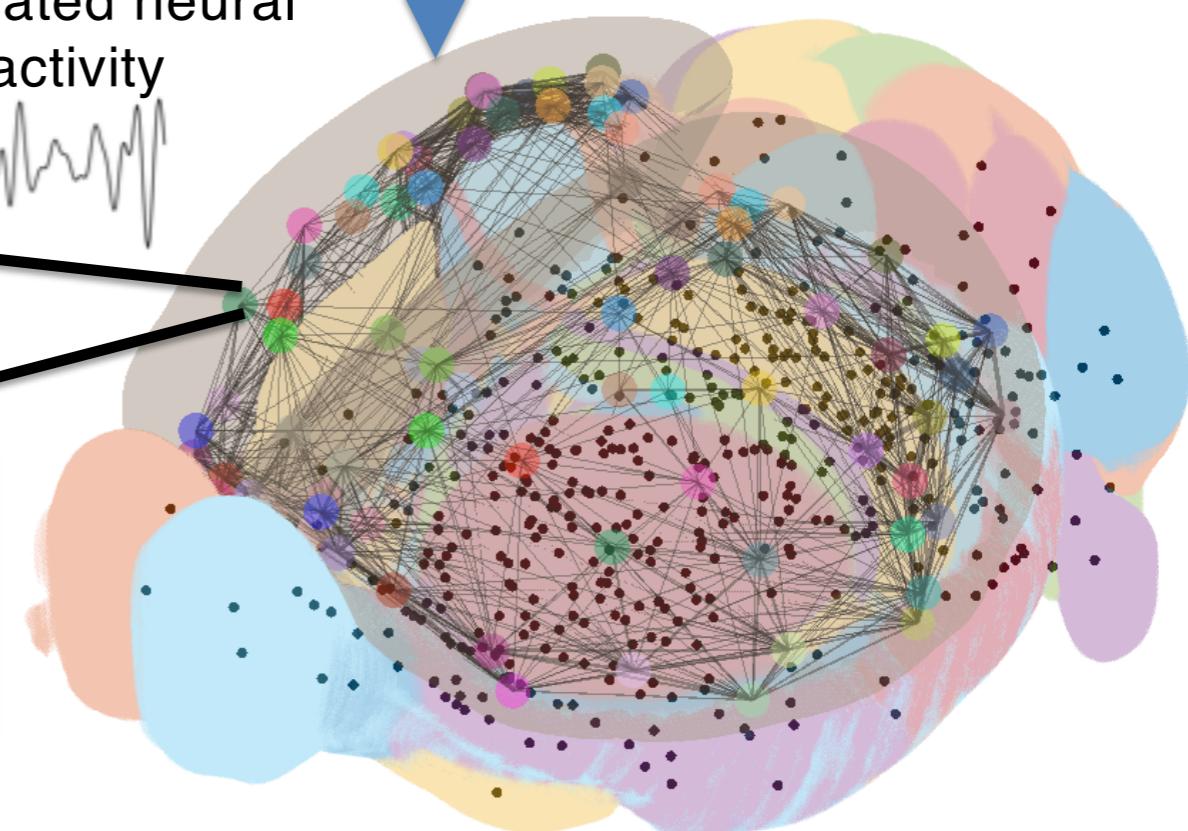
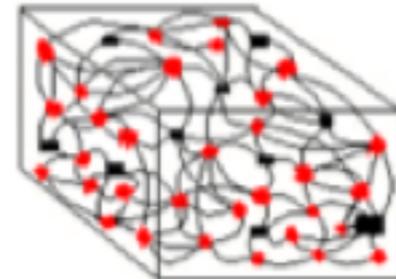
0.1-1mm

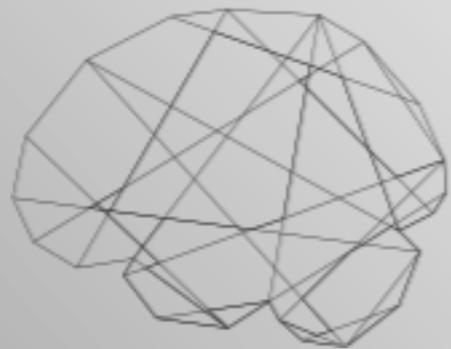
Simulated neural
activity

Tractography



Neuronal
population





THANK YOU
Play nice,
have fun