Modelling the Human Brain: Resting and Task Evoked Activity

The emergence of functional connectivity in spontaneous and evoked brain activity

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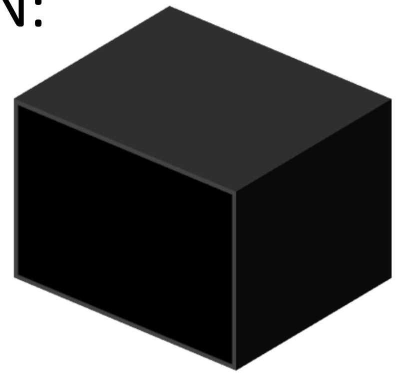
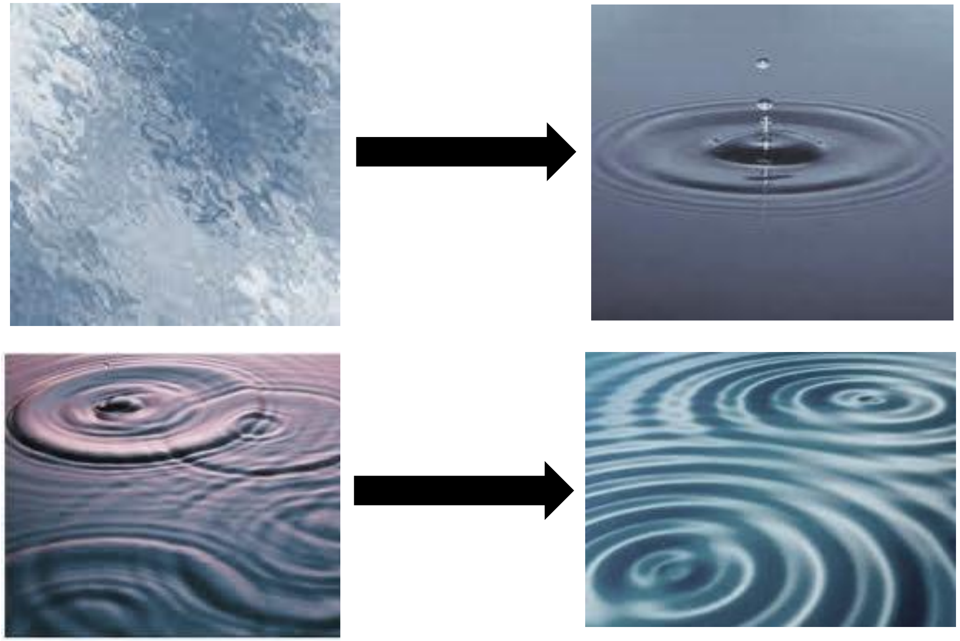
Basal and evoked states

The BRAIN:

Input



Output
(signal + “noise”)

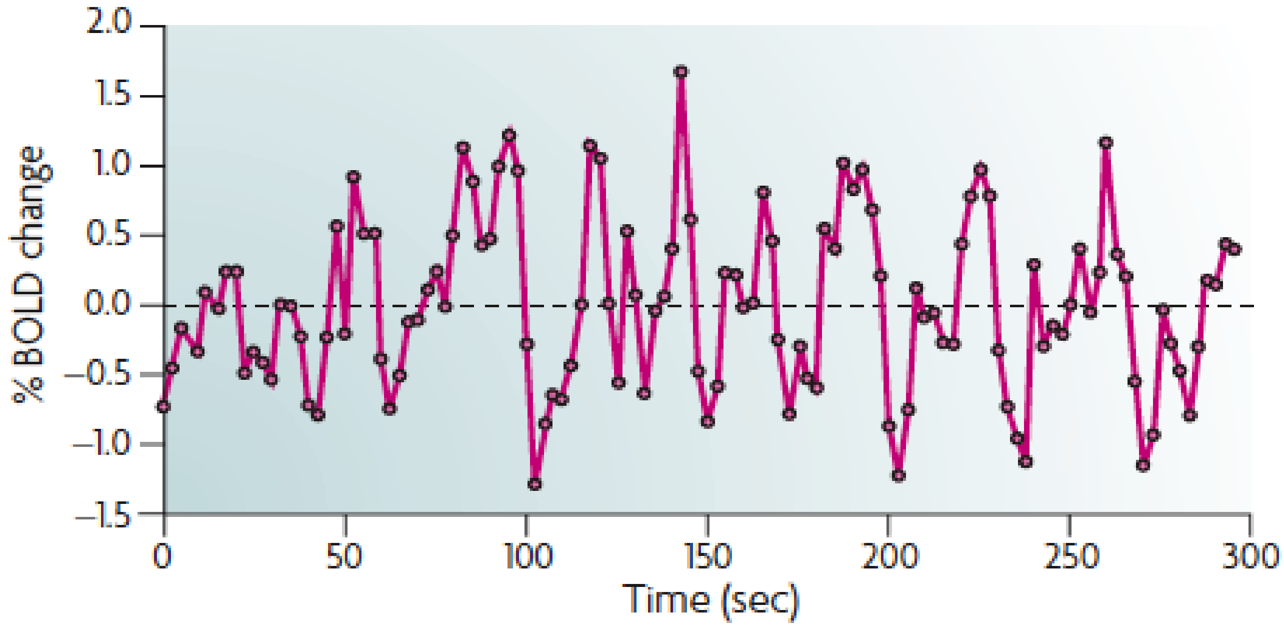


fMRI: new paradigm

Spontaneous fluctuations and functional connectivity

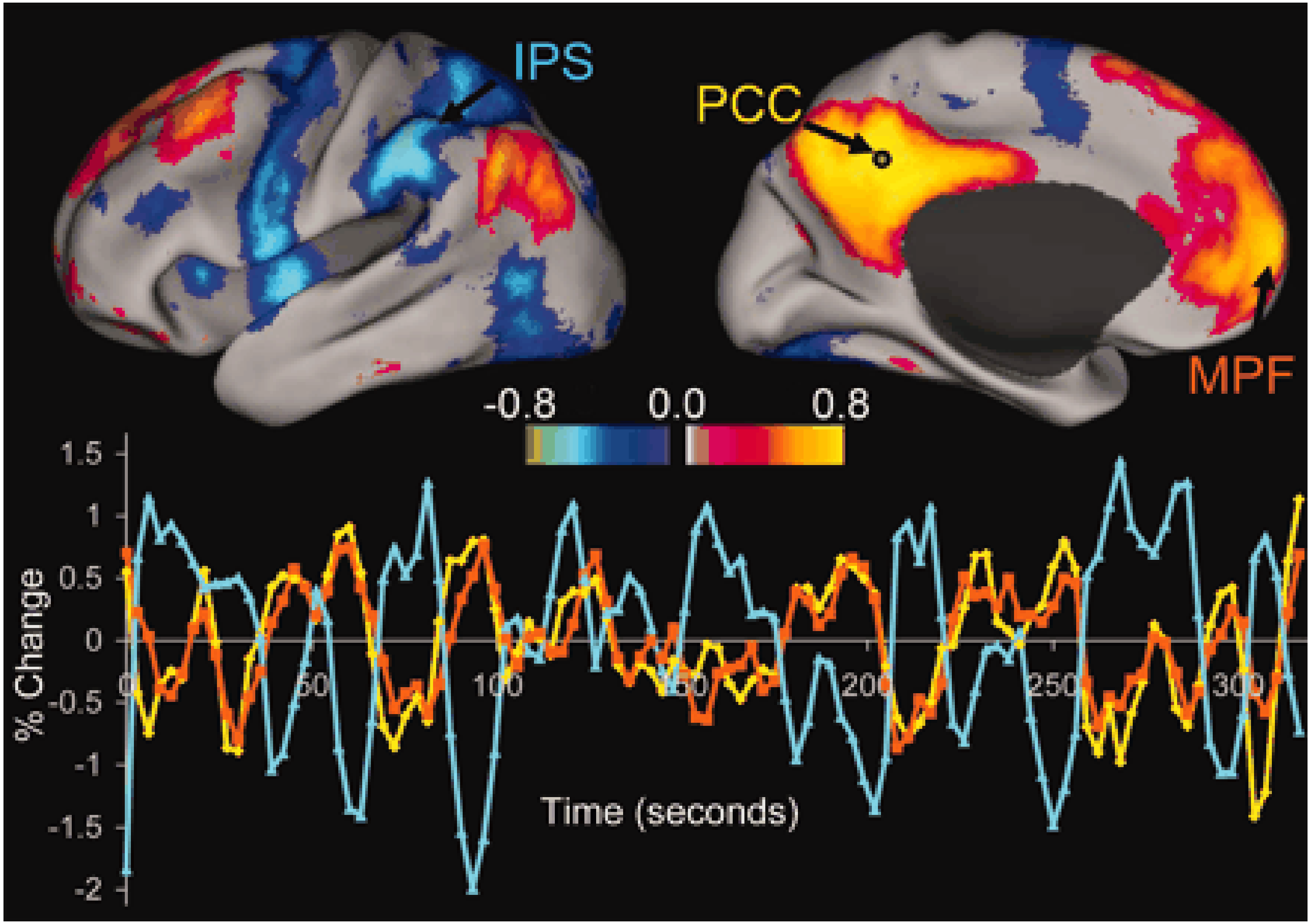
(Biswal et al., 1995)

Noise?

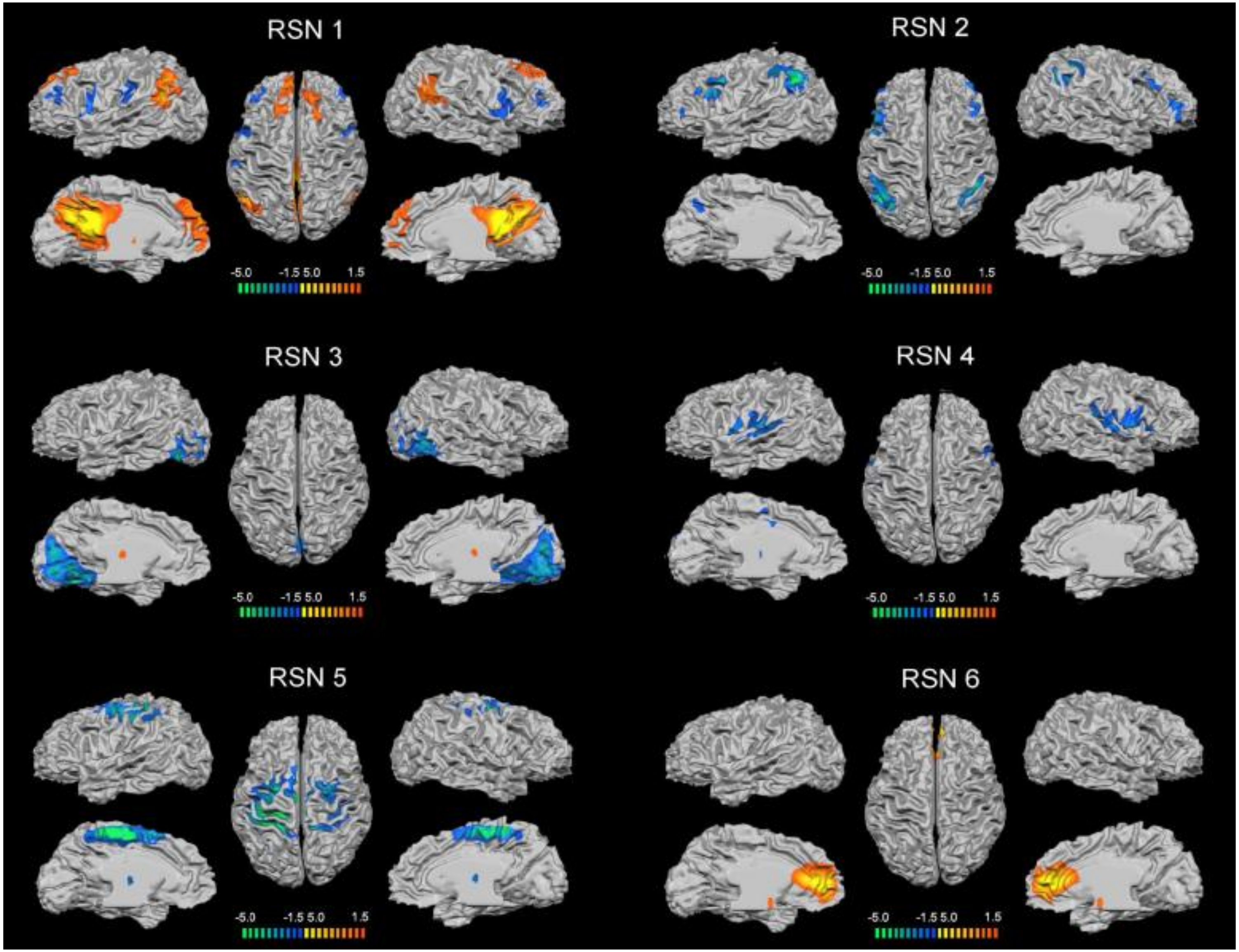


Low frequency (< 1 Hz) BOLD fluctuations in resting brain were observed to correlate within and between brain regions composing functional networks.

Resting State: Fox et al 2005 (PNAS)

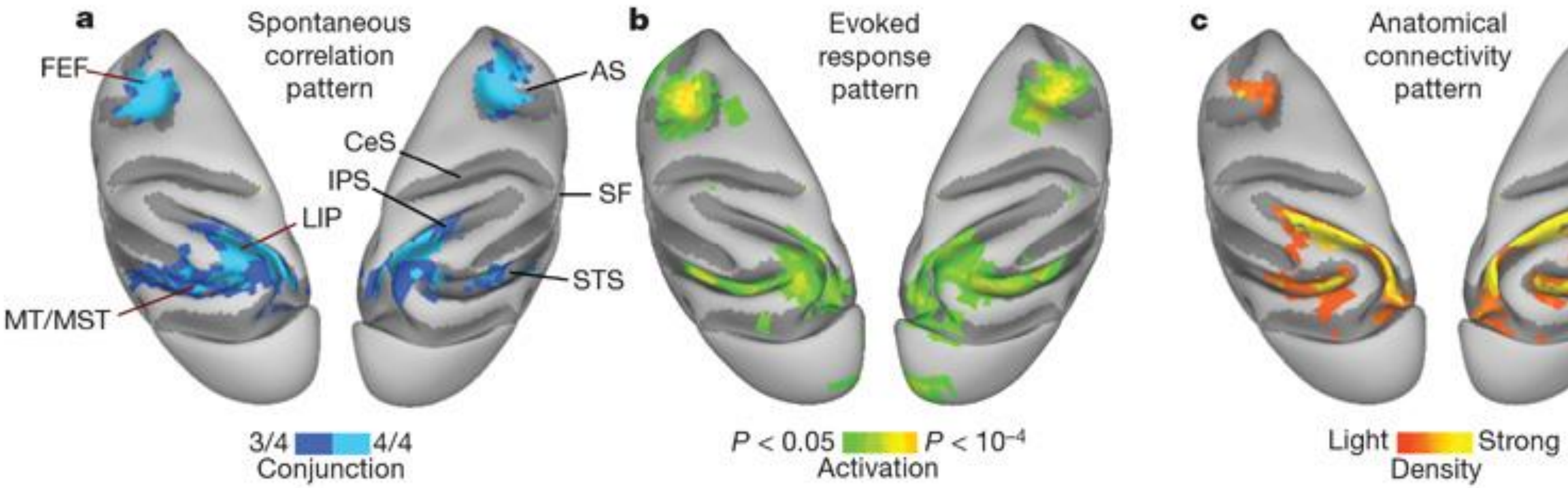


Resting-State Networks



Mantini et al. 2007

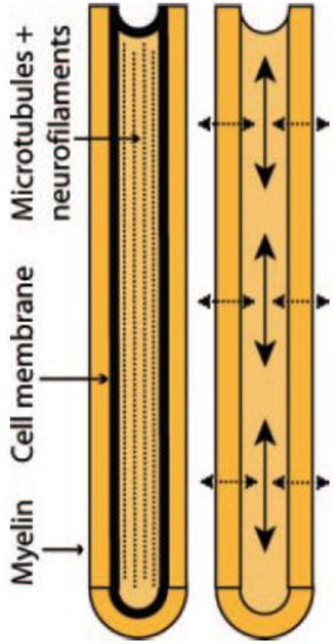
Resting-State Networks, Evoked Networks, Anatomical Networks

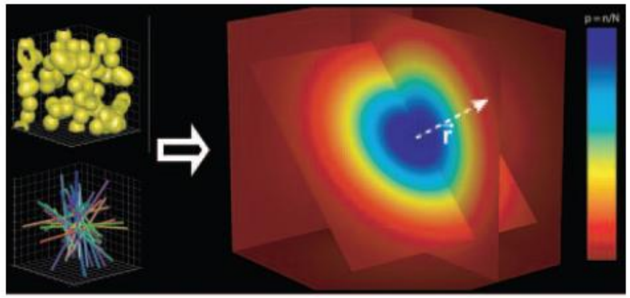


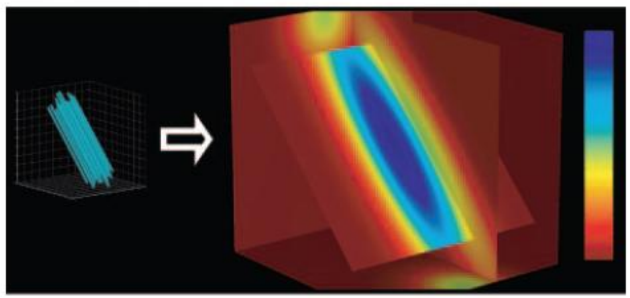
Vincent et al. (2007) Nature.

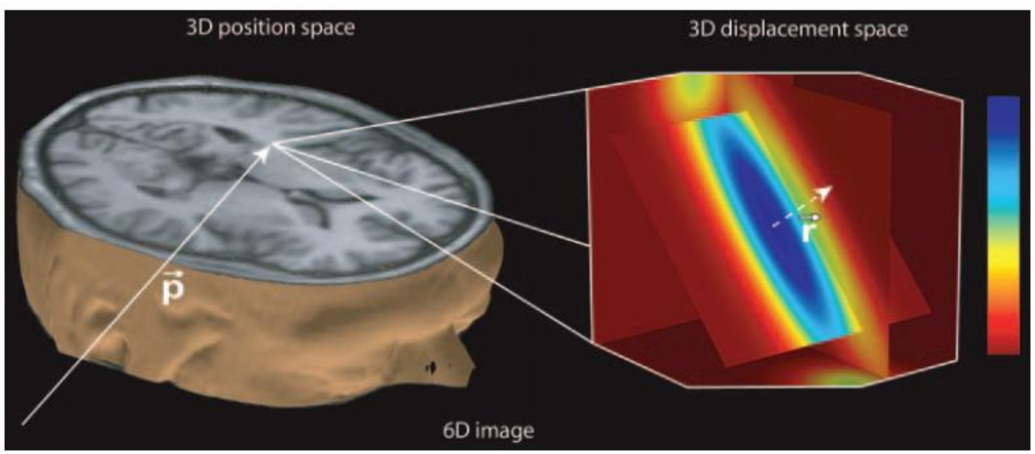
Relation between anatomical connectivity and resting/evoked functional connectivity?

Estimating the anatomical connectivity using Diffusion Imaging

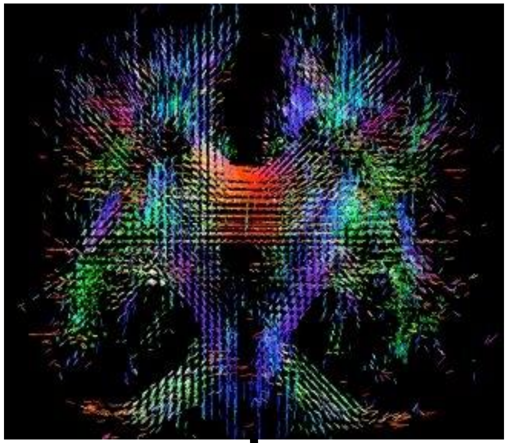




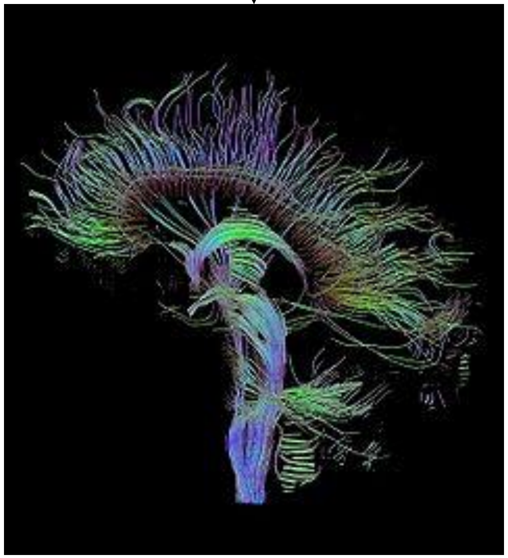




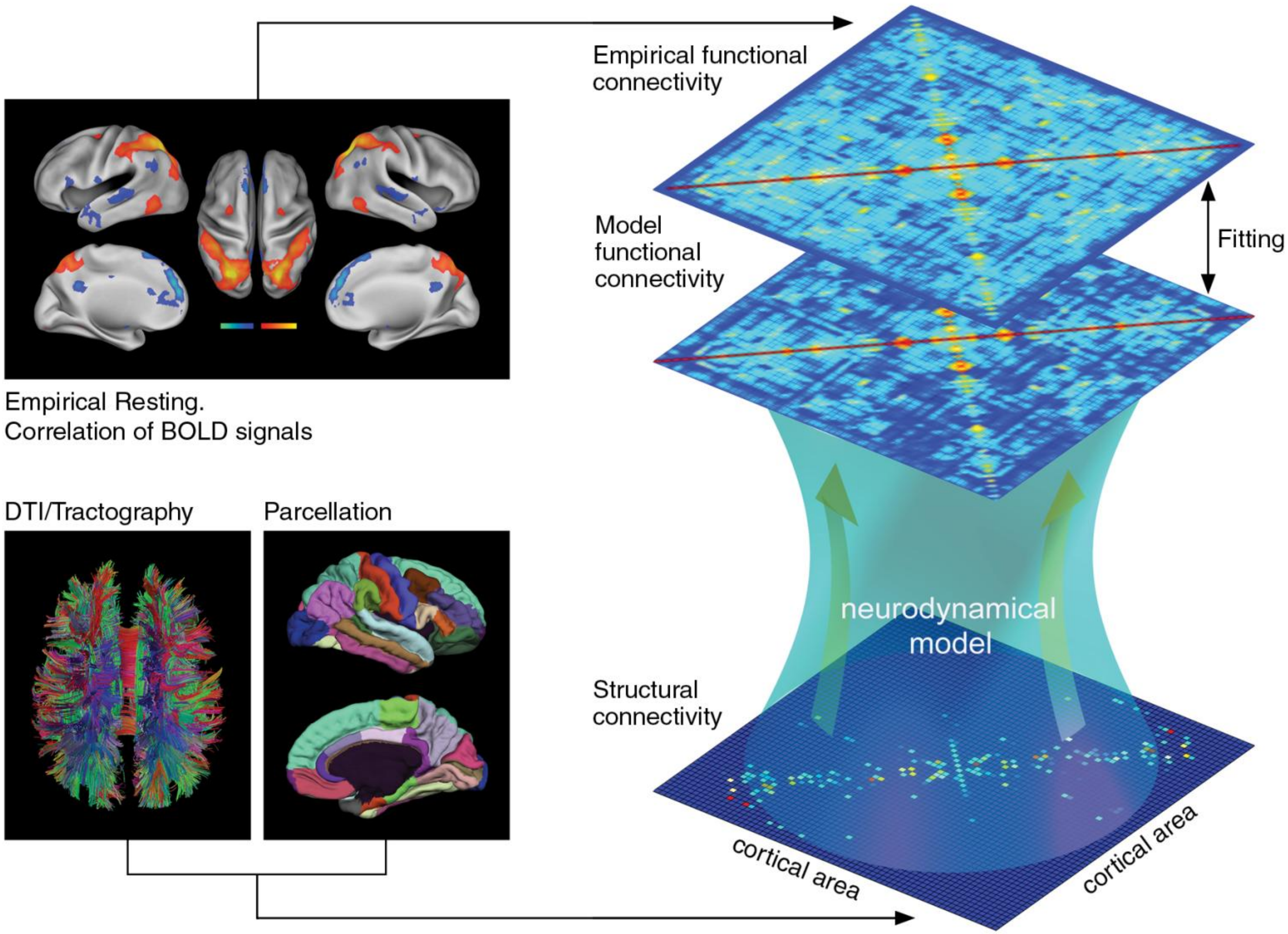
Hagmann et al. (2007)



Tractography



Modelling strategy



Deco, Ponce-Alvarez et al. (2013) J Neurosci.

Single-node models:

Oscillatory dynamics

Ghosh et al. 2008

Deco et al. 2009

Cabral et al. 2011

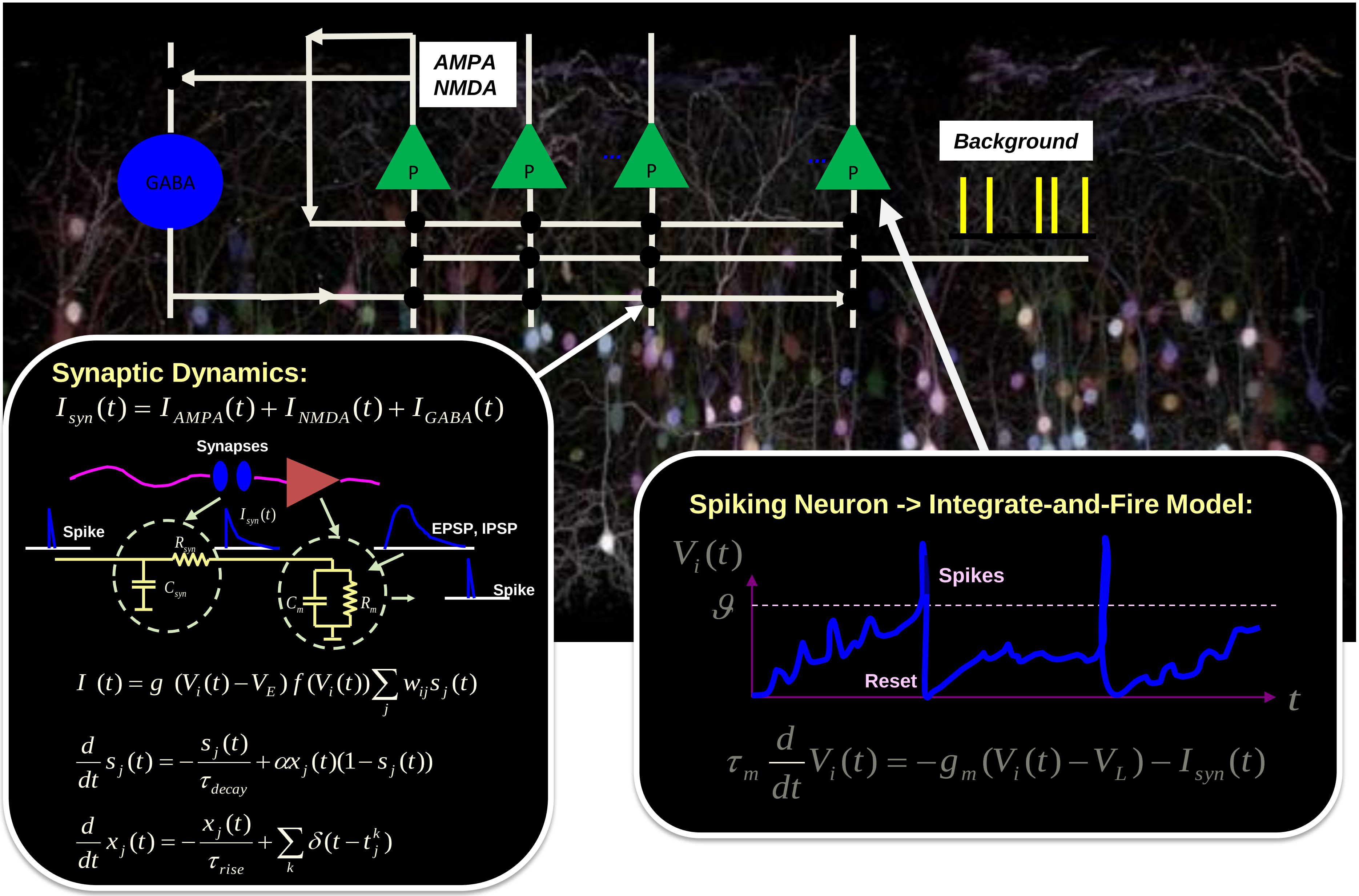
Fixed stable point

Honey et al. 2007

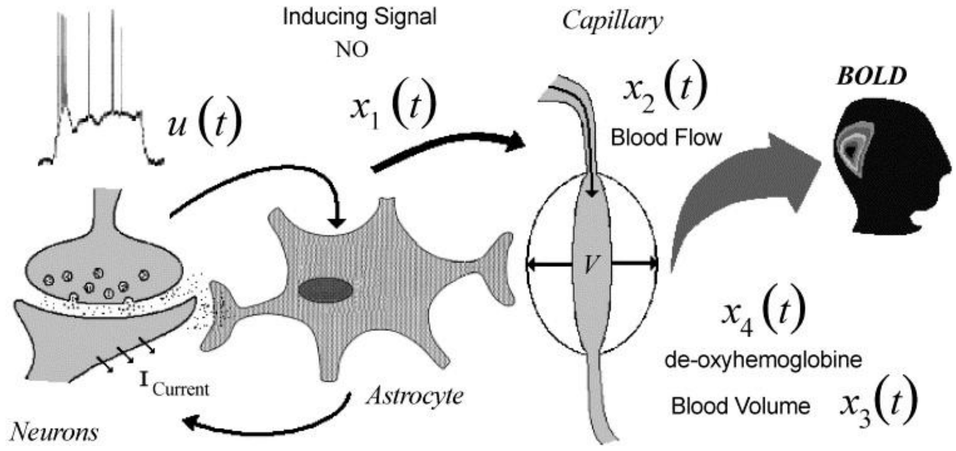
Detailed spiking networks of excitatory and inhibitory populations coupled through synaptic dynamics

Deco and Jirsa 2012

Local cortical networks



The Balloon-Windkessel model



Vessel ~ inflatable balloon

Riera et al. (2004)

$$\dot{x}_i = z_i - k_i x_i - \gamma_i \quad f_i - 1$$

$$\dot{f}_i = x_i$$

$$\tau_i \dot{v}_i = f_i - v_i^{1/\alpha}$$

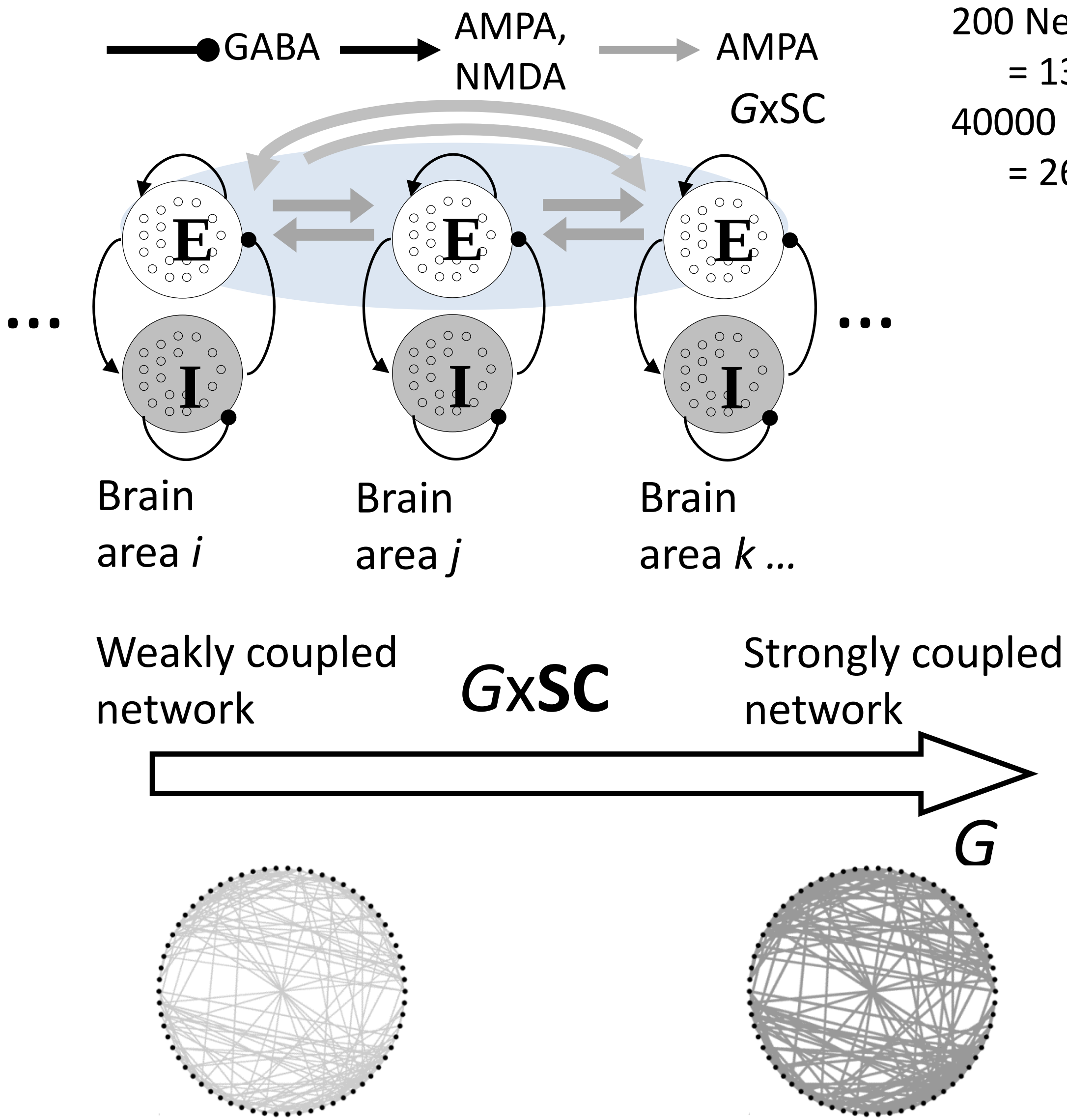
$$\tau_i \dot{q}_i = \frac{f_i}{\rho}\left[1 - \ 1 - \rho \ ^{1/f_i}\right] - q_i v_i^{1/\alpha - 1}$$

$$BOLD_i = V_0\left[k_1(1-q_i) + k_2(1-q_i/v_i) + k_3 \ 1 - v_i \ \right]$$

For the *i*-th region, **synaptic activity z_i** causes an increase in a **vasodilatory signal x_i**. **Inflow f_i** responds to this signal with changes in blood **volume v_i** and **deoxyhemoglobin content q_i**.

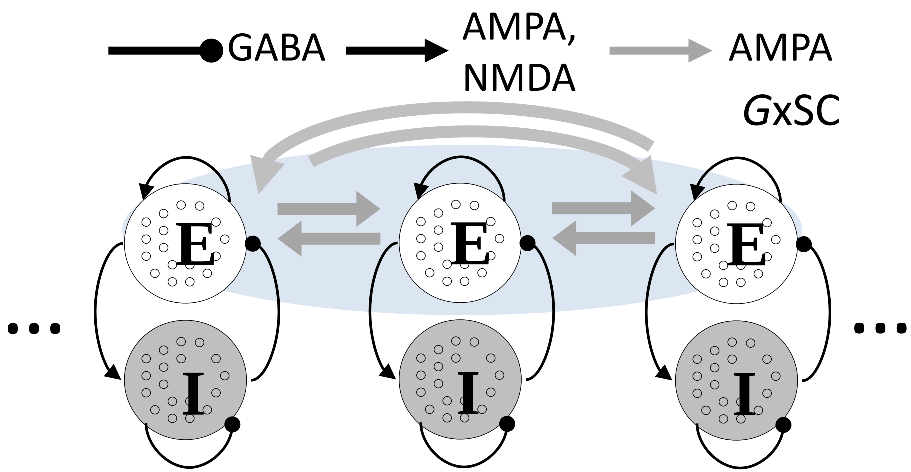
Friston et al. (2003)

Spiking Model



200 Neurons per area x 66 areas
= 13200 Spiking Neurons
40000 Synapses per area x 66 areas
= 2640000 synapses

Spiking Model



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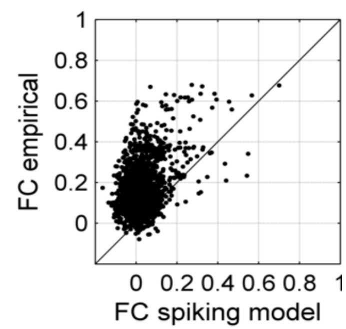

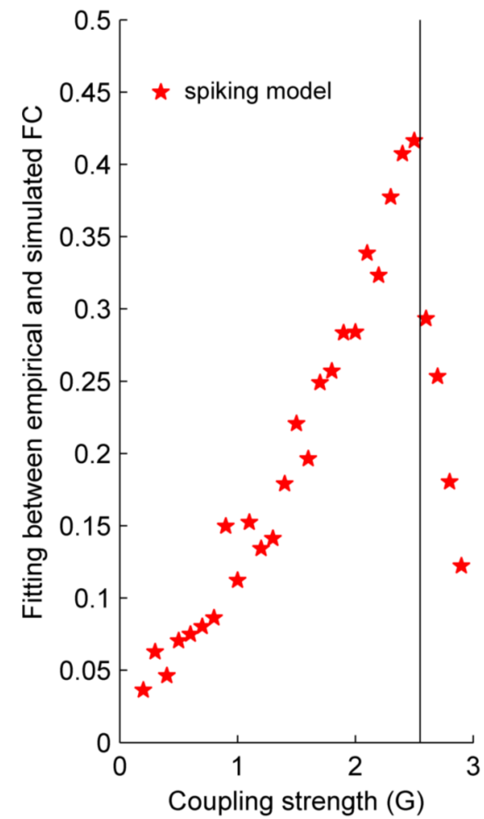

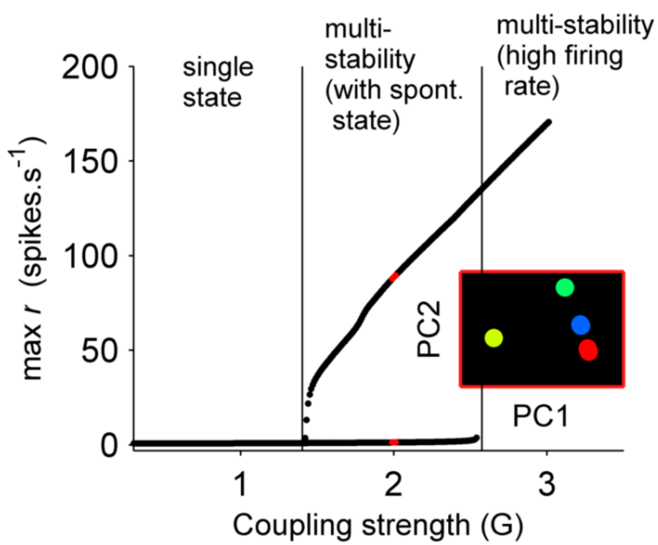

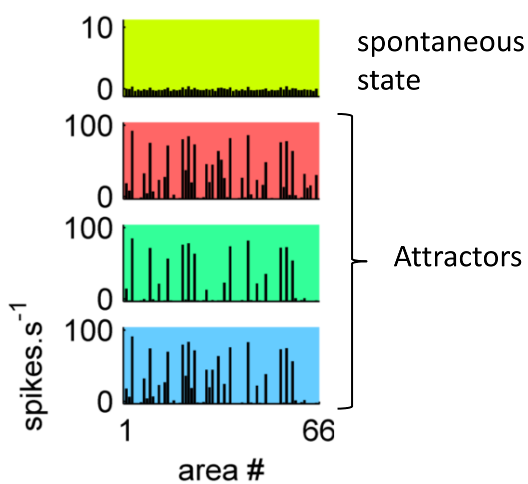

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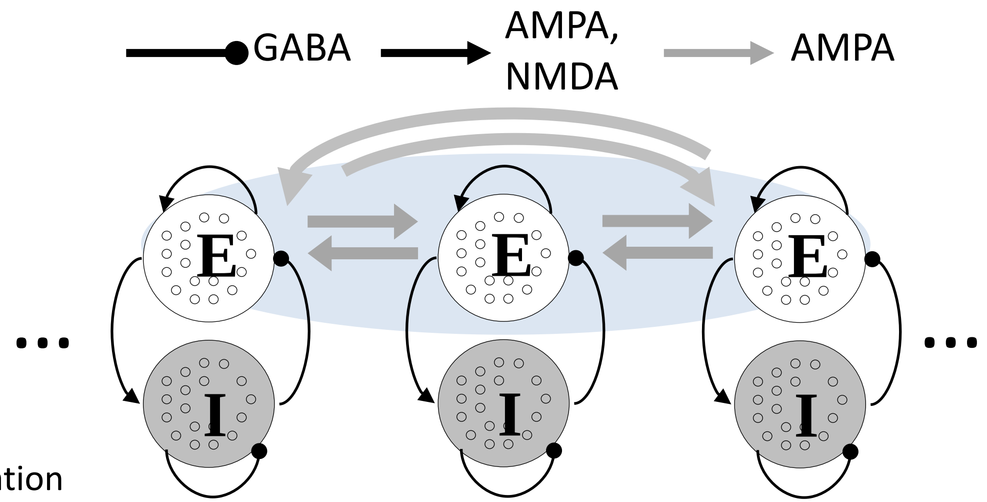
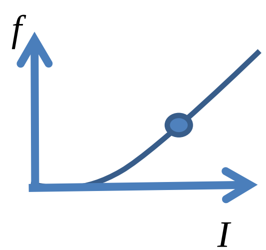
Mean Field Approximation



linear approximation
of the transfer function
of the inhibitory cells
(inhibitory cells typically fire between 8 –15 Hz.
Within this range, the F-I curve is almost linear)



Mean field approx.

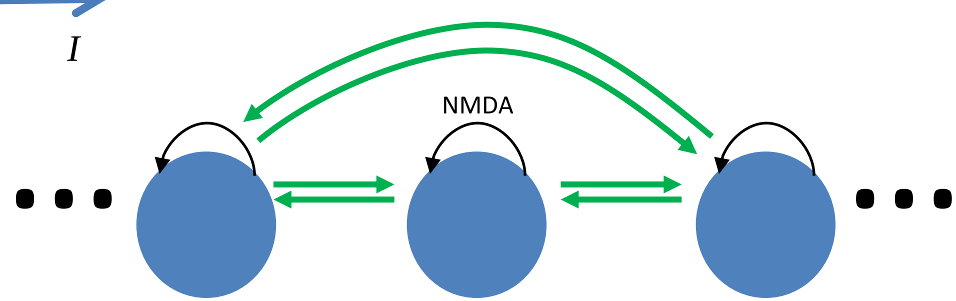
$$\tau_{NMDA} \gg \tau_{AMPA}, \tau_{GABA}$$

Wong and Wang (2006)

Neurons

Population synaptic activity

Reduced dynamic mean field model



Mean Field Approximation

The global brain dynamics of the network of inter-connected local networks is given by the following system of stochastic differential equations:

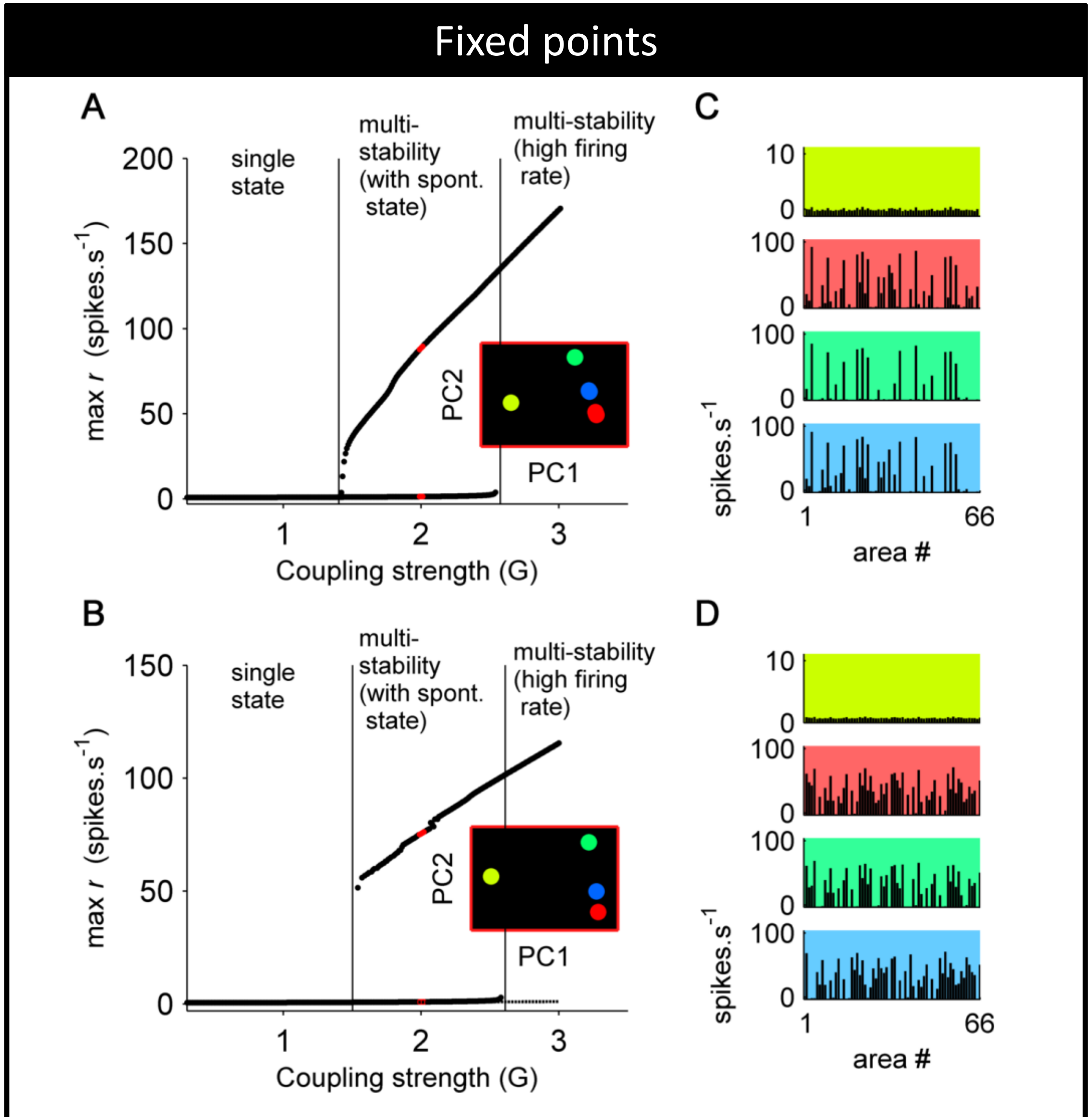
$$\frac{dS_i(t)}{dt} = -\frac{S_i}{\tau_S} + (1-S_i)\gamma H(x_i) + \sigma \upsilon_i(t)$$

$$H(x_i) = \frac{ax_i - b}{1-\exp(-d(ax_i - b))} \qquad (1)$$

$$x_i = wJ_N S_i + GJ_N \sum_j C_{ij} S_j + I_0$$

Where :		
	S_i	: synaptic gating variable at the local cortical area i
	$R_i = H(x_i)$	: average firing rate of population i
	$w = 0.9$	: local excitatory recurrence
	C_{ij}	: structural connectivity matrix expressing the neuroanatomical links between the areas i and j.
	$\tau_S = 100$ ms	: NMDA time constant
	$\upsilon_i(t)$	: uncorrelated Gaussian noise
	$\sigma = 0.001$ (nA)	: noise amplitude
	$I_0 = 0.3$ (nA)	: effective external input

Mean Field Approximation



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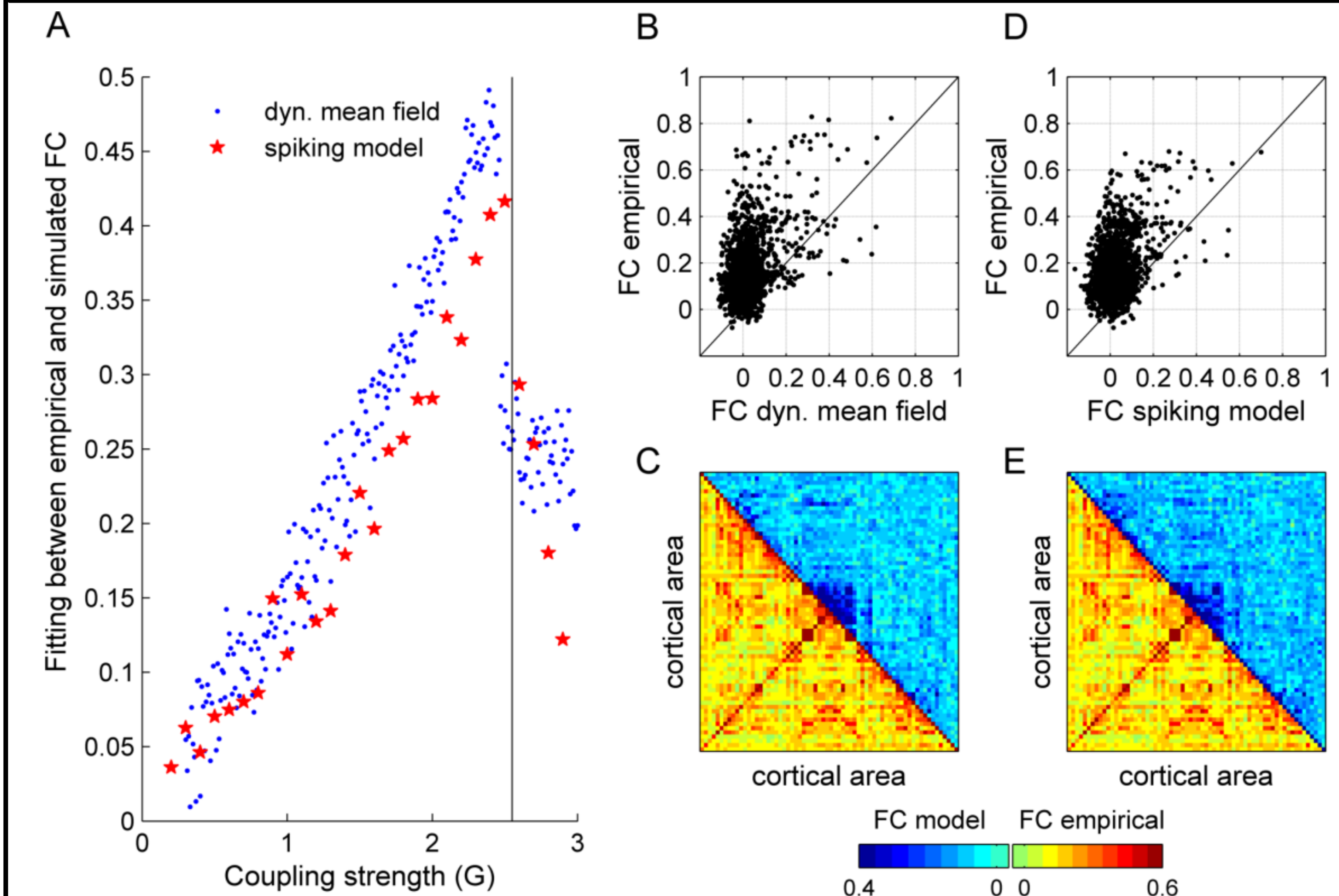
Mean Field Approximation

Model FC VS. empirical FC



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Moments reduction: Analytical relation between structure and function

We express the system of stochastic differential equations (1) in terms of means and covariances:

$$\mu_i(t) = \langle S_i(t) \rangle$$

$$P_{ij}(t) = \left\langle \left(S_i(t) - \mu_i(t) \right) \left[S_j(t) - \mu_j(t) \right] \right\rangle$$

Fokker-Plank equation for the distribution of gating variables:

Taylor expanding S_i around μ_i, i.e. $S_i = \mu_i + \delta S_i$, and keeping the terms up to $<\delta S_i \delta S_j>$:

$$\frac{d\mu_i}{dt} = f(\mu_i) = -\frac{1}{\tau_s}\mu_i + (1-\mu_i)\gamma H(\bar{x}_i)$$

$$\frac{dP}{dt} = JP + PJ^T + Q_n$$

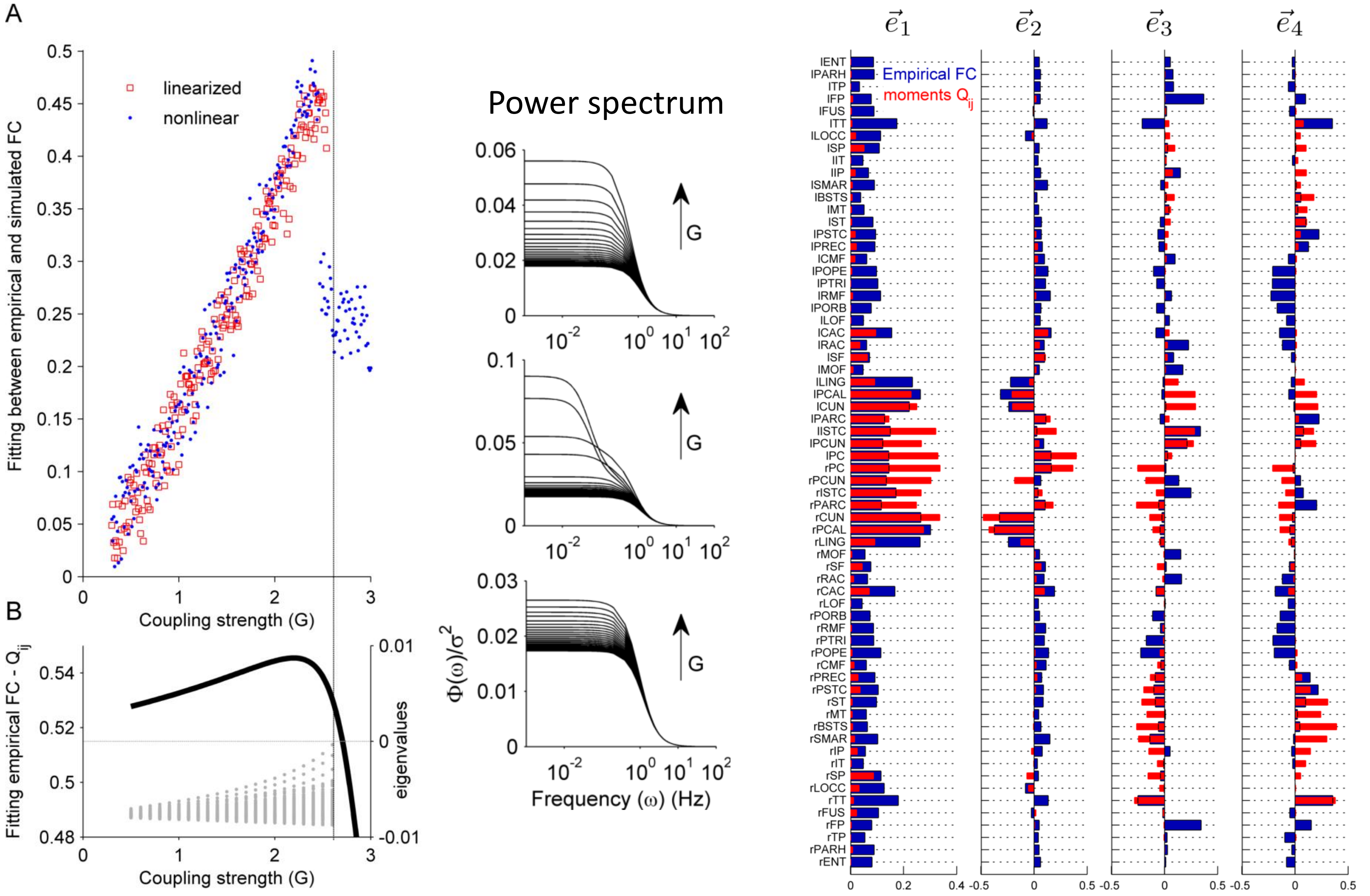
J : Jacobian matrix $J_{ij} = \dfrac{\partial f}{\partial S_j}(\mu_i)$

Q_n : noise covariance matrix

$$JP + PJ^T + Q_n = 0$$

Resting-State problem $\Longleftrightarrow$ $JP + PJ^T + Q_n = 0$

Moments reduction: Analytical relation between structure and function



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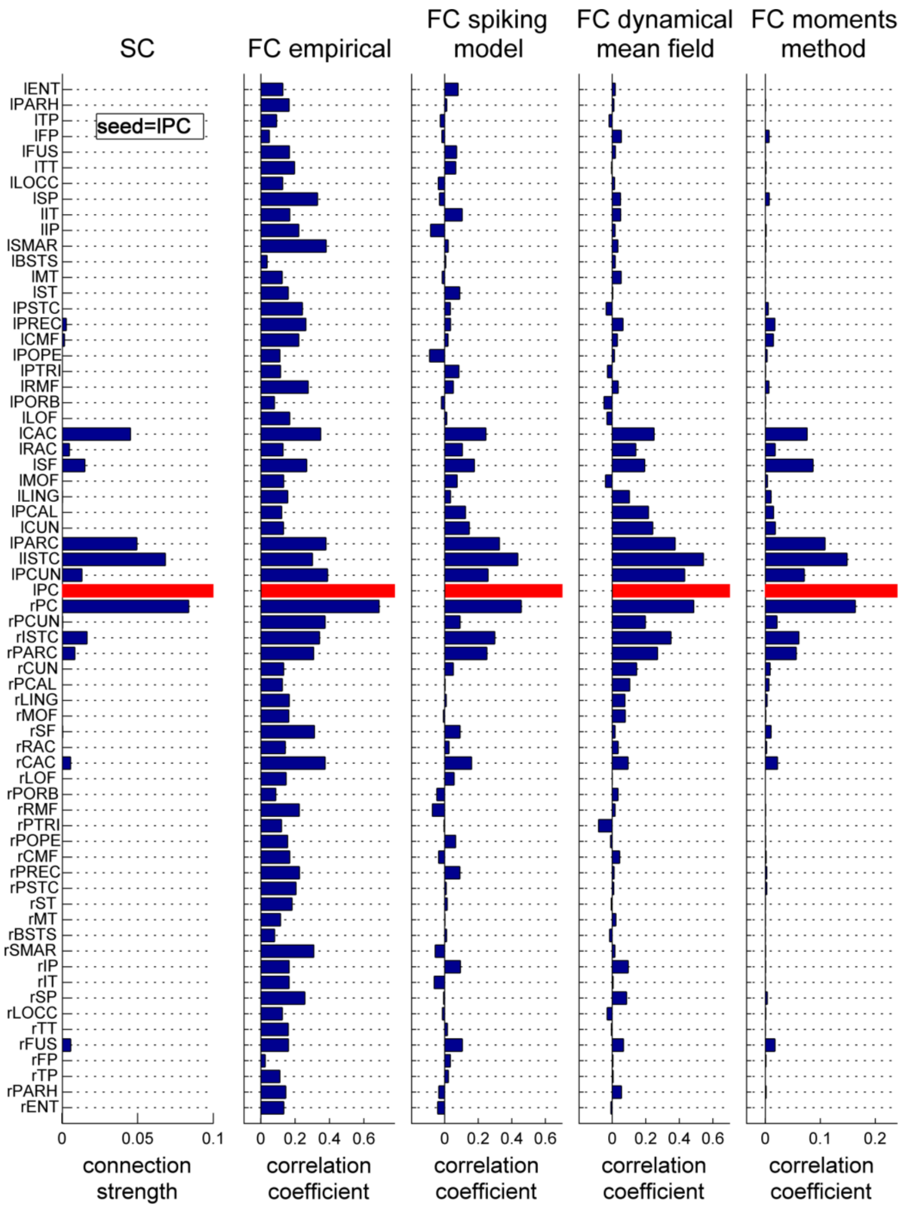

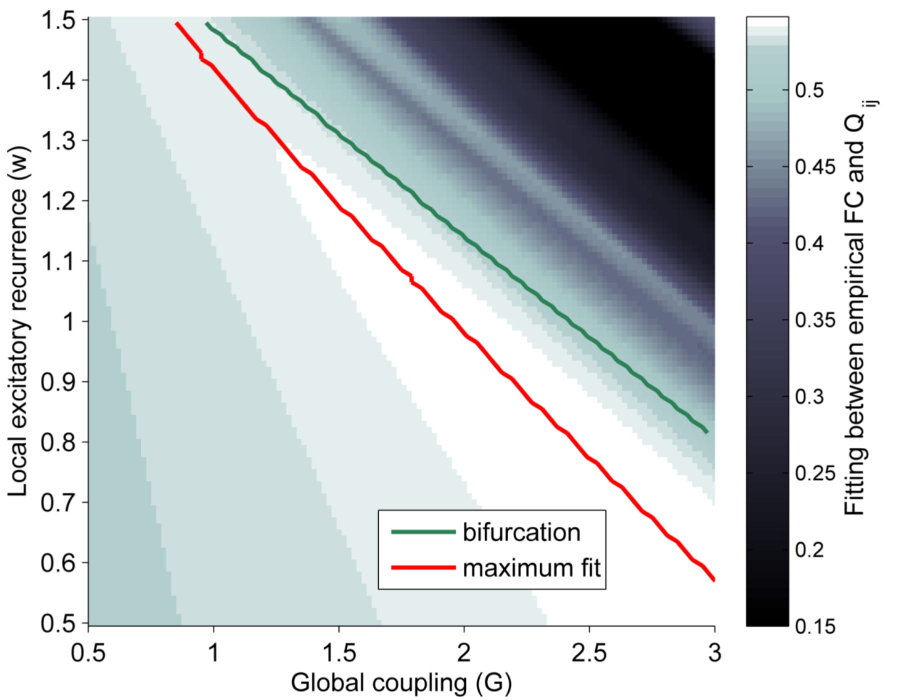

For a large range of parameters the best fit between model and data is close to the bifurcation

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Emergence of *effective* connectivity during task conditions

$$\frac{dP}{dt} = JP + PJ^T + Q_n$$

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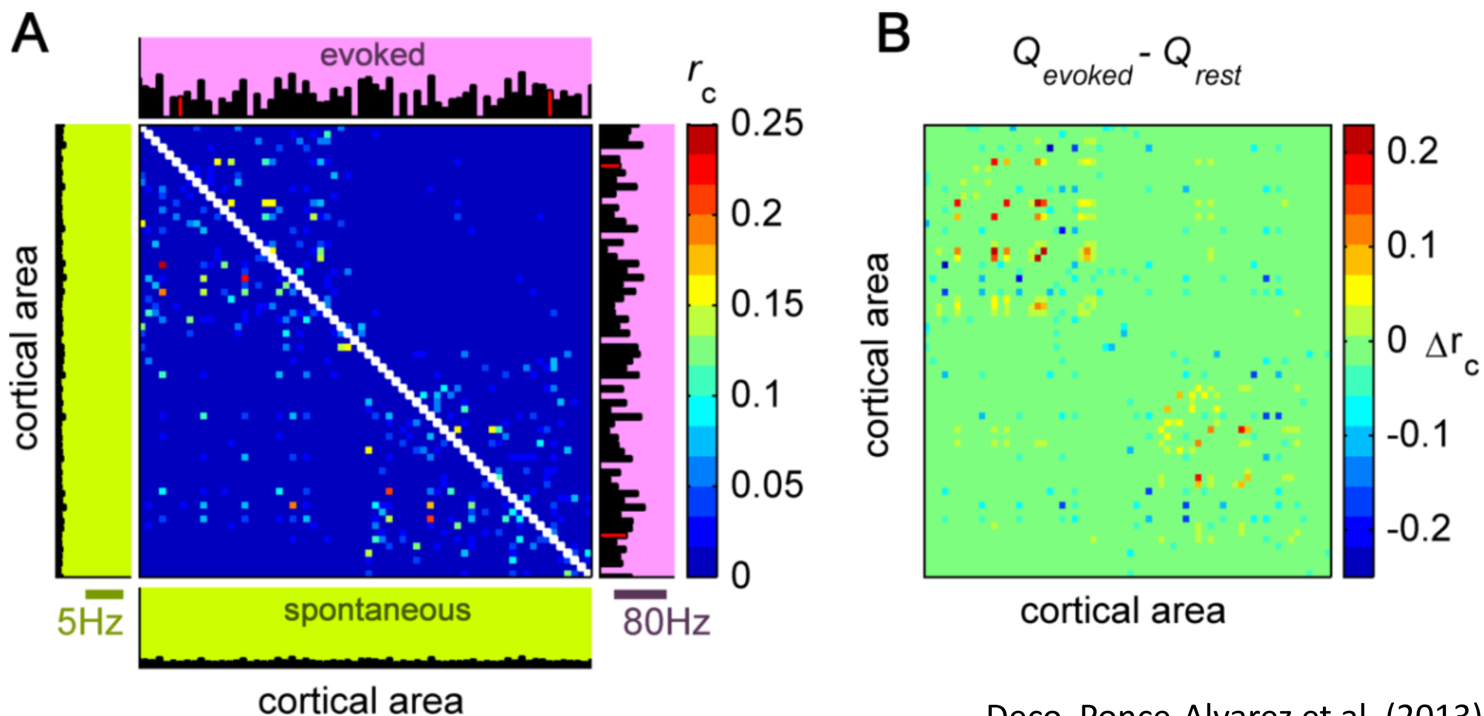
Q_n : noise covariance matrix

The covariance is <u>state-dependent</u>



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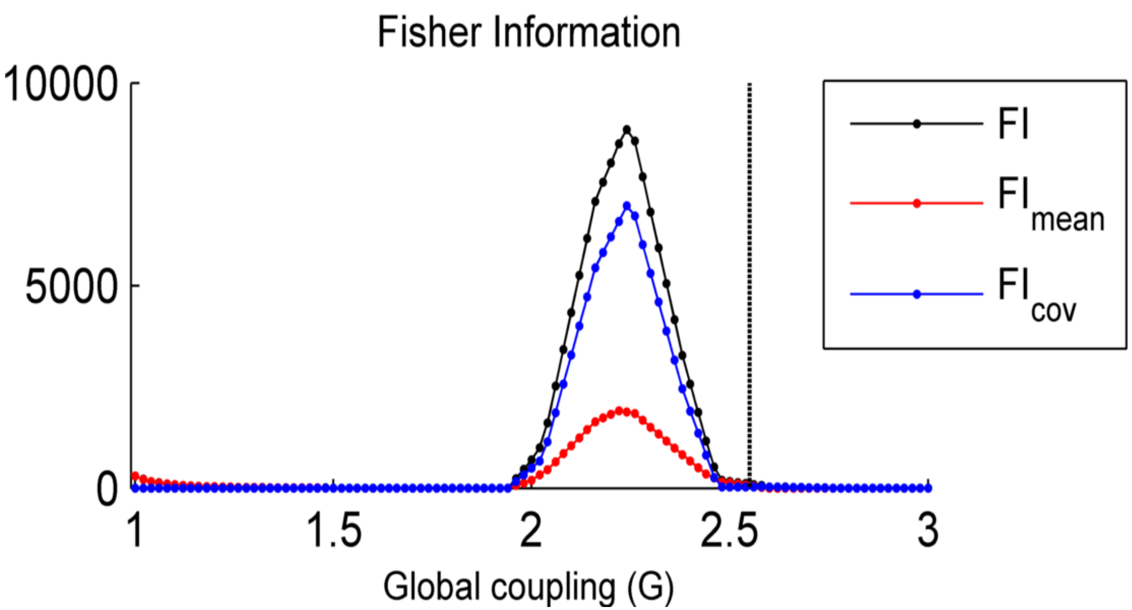
Emergence of *effective* connectivity during task conditions

The Fisher information (FI) gives an upper bound to the accuracy that any code can achieve. It takes into account the change of the mean activity and covariances with respect to a variation in the stimulus:

$$FI = FI_{\text{mean}} + FI_{\text{cov}}$$



$$FI_{\text{mean}} = r'(s)^T P(s)^{-1} r'(s)$$

$$FI_{\text{cov}}(s) = \frac{1}{2} \text{Trace} \left[P'(s) P(s)^{-1} \right]^2$$

s: stimulus
r(s): network mean response
P(s): network covariance

Conclusions

- We derived a simplified dynamical mean field model that summarizes the realistic dynamics of a detailed spiking and conductance-based synaptic large-scale model.

- With this reduction, we demonstrated that FC emerges as structured **linear** fluctuations around a stable low firing activity state close to destabilization (criticality).

- The model can be further and crucially simplified into a set of motion equations for statistical moments, providing a direct analytical link between anatomical structure, dynamics, and FC.

- FC arises from noise propagation and dynamical **slowing down** of fluctuations in the anatomically constrained dynamical system.

- The network's covariance is **state-dependent**: the interactions between cortical areas depend on the dynamical state of the global network at which the Jacobian matrix is evaluated
  → *effective connectivity*.

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Limitations

- Inter-hemispherical correlations in the model, because the DTI/DSI-tractography missed inter-hemispherical connections (due to fiber crossing issues).
- The anatomical matrix used here did not include subcortical routes that are known to play an important role in shaping the spontaneous activity of the brain (Robinson et al., 2001; Freyer et al., 2011)
- Model simplifying assumptions: all connections between brain areas are excitatory and instantaneous, thus neglecting the effects of feed-forward inhibition and conduction delays that are likely to shape spatial and temporal features of brain dynamics.
- Mesoscopic architecture (layers, functional maps, etc) were not considered.

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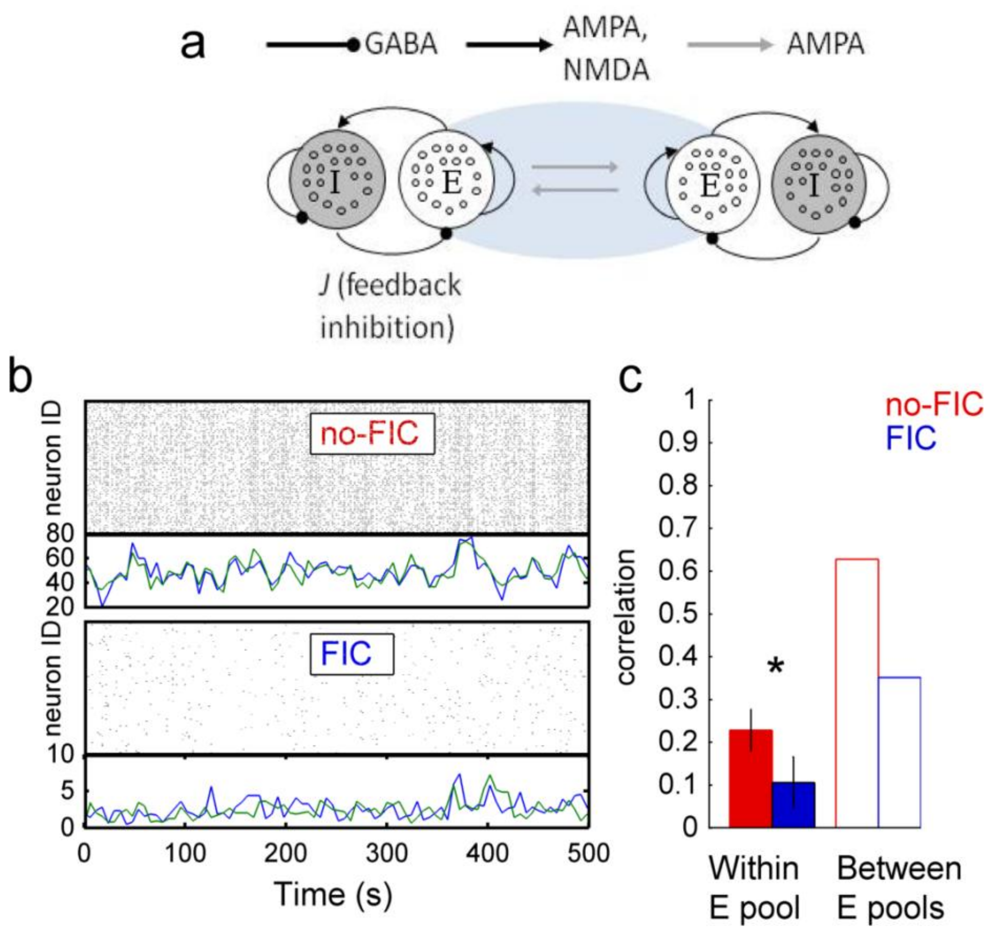
Balanced Networks

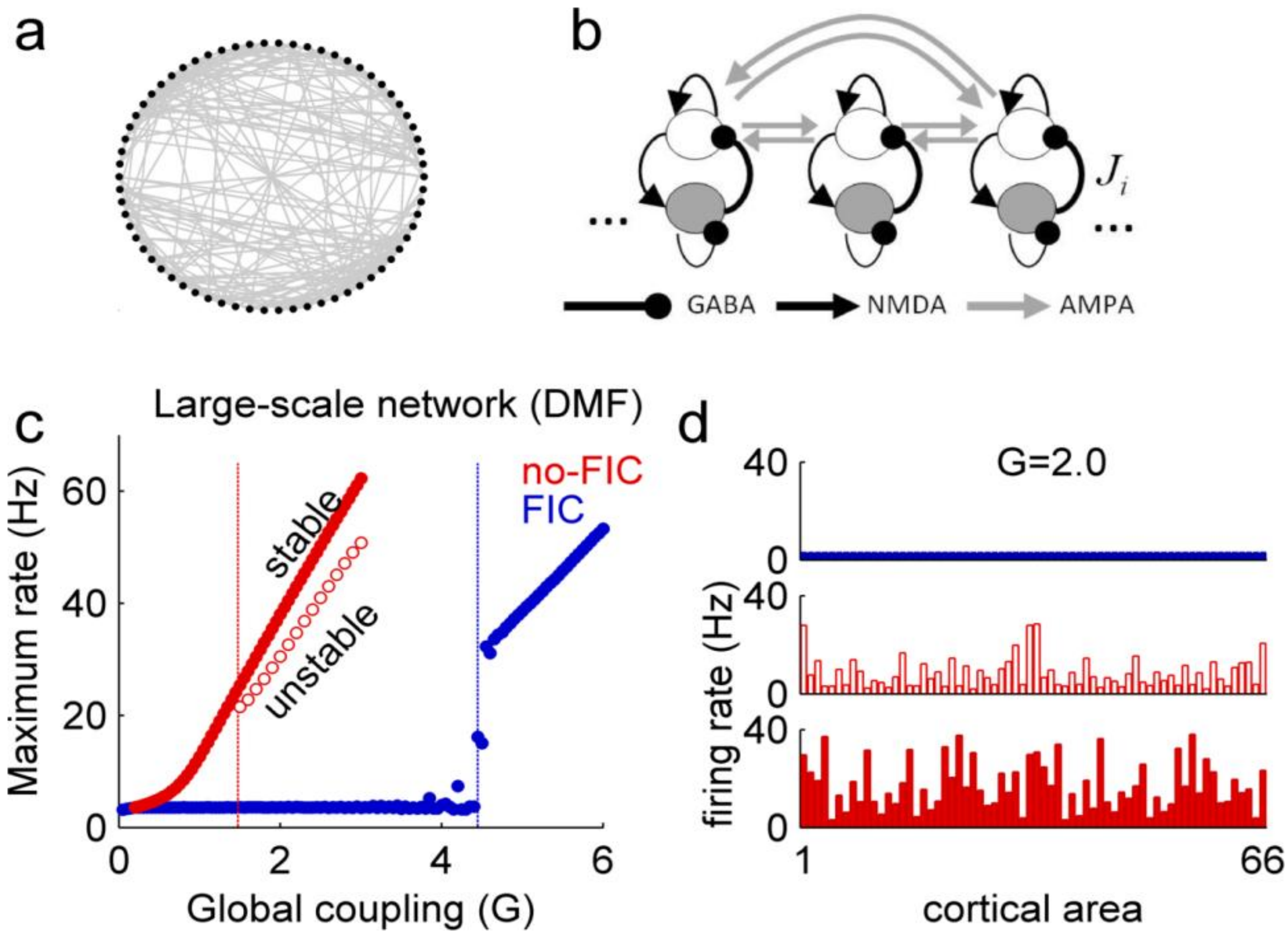
Is the working point of the brain fine tuned (critical) ?

Balanced Networks

- **Long-range** correlations are highly and strongly structured in spatio-temporal patterns (Resting State Networks)
- Neurophysiological reports show that **short-range** correlations between neighboring neurons are low, or even negligible (Ecker et al. 2010).
- One proposed mechanism of decorrelation: feedback inhibition (Tetzlaff et al., 2012).



Balanced Networks



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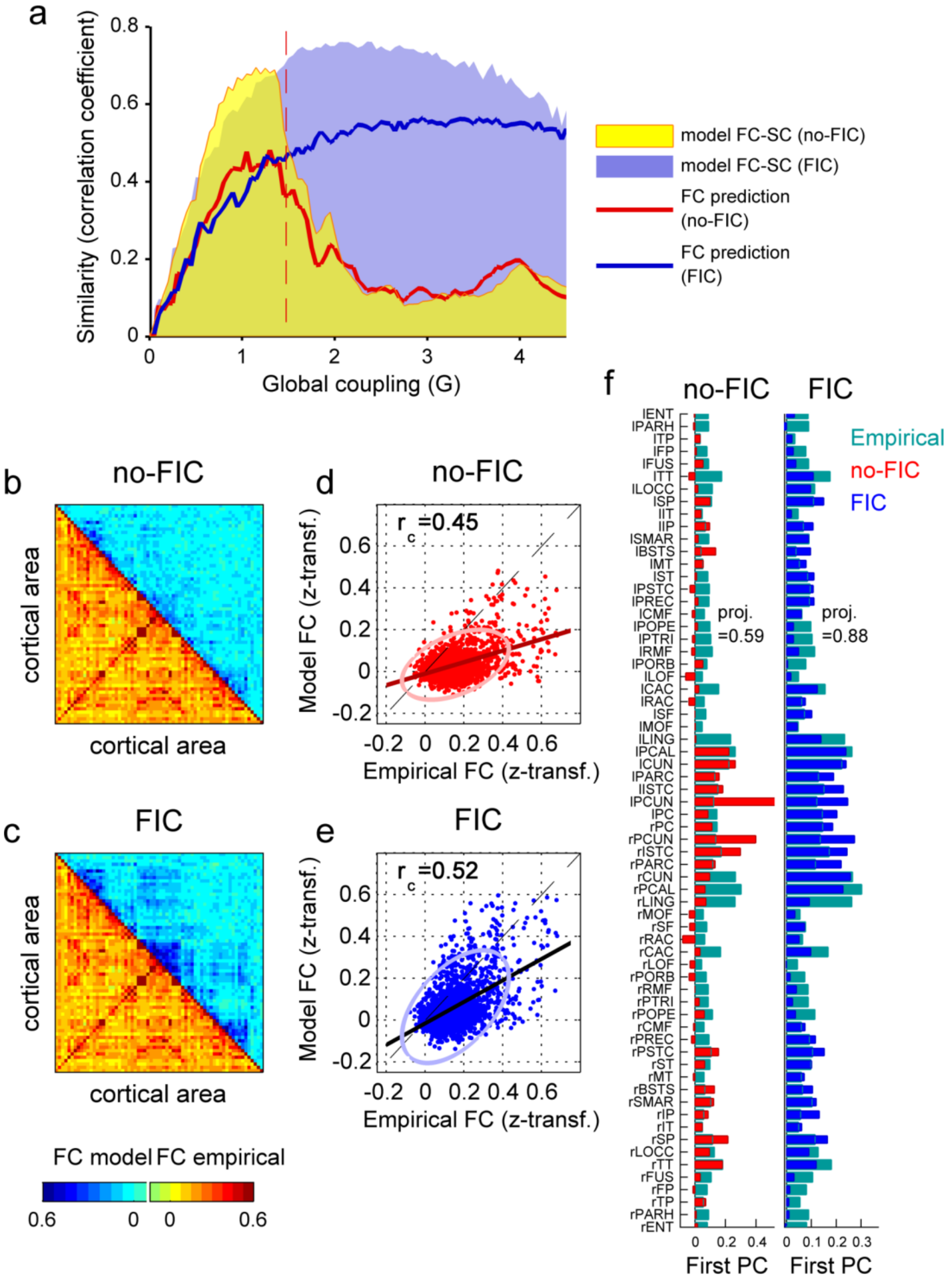
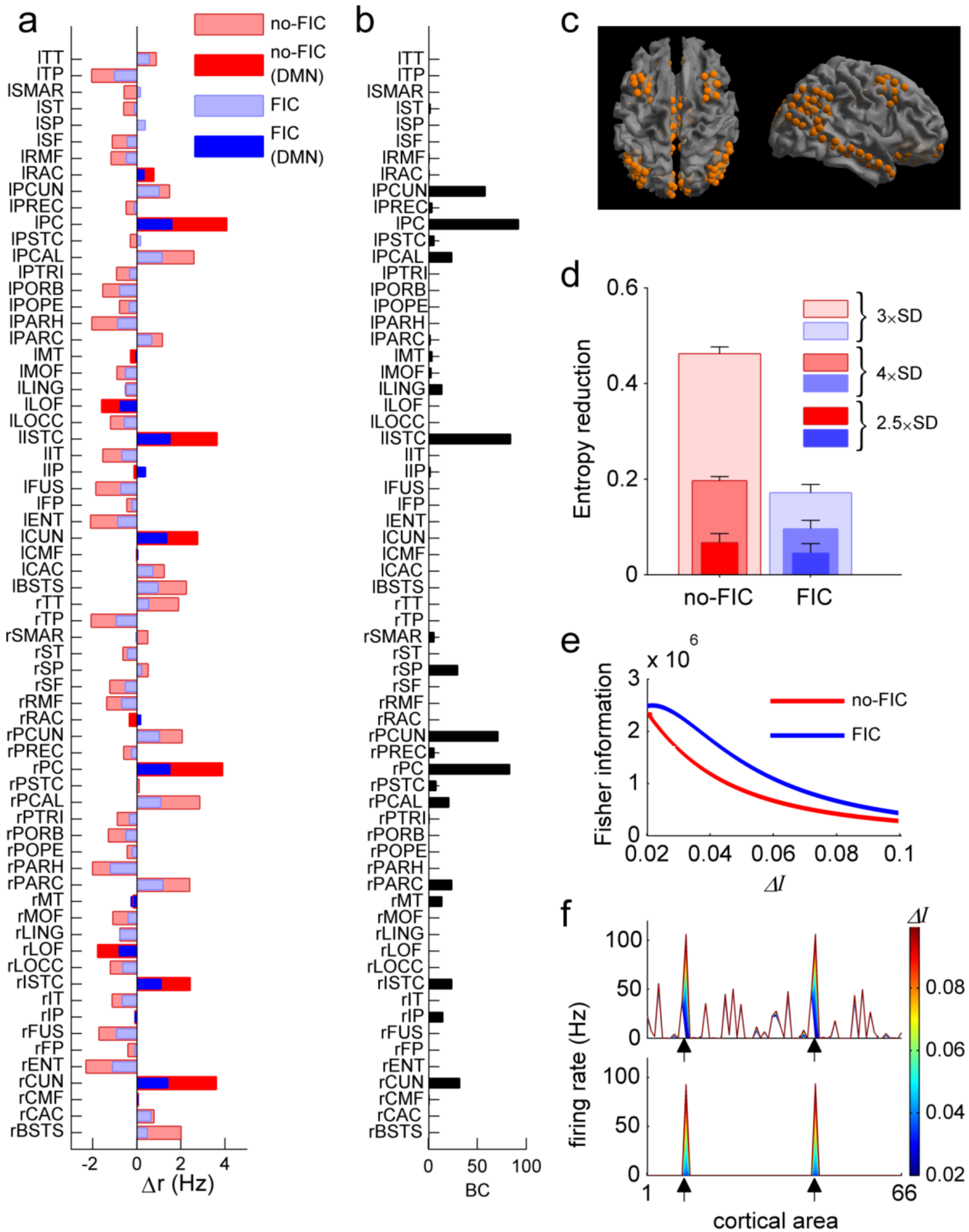


Local feedback inhibition control (FIC) provides a better and more robust prediction of Human empirical resting state connectivity.

Balanced Networks

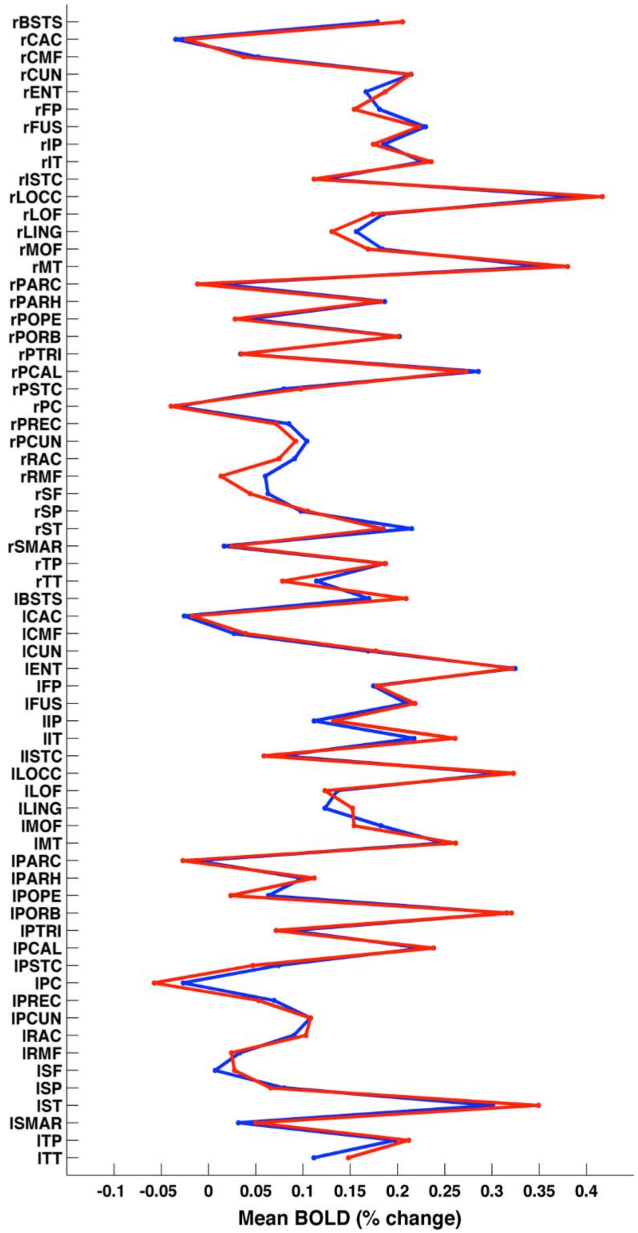


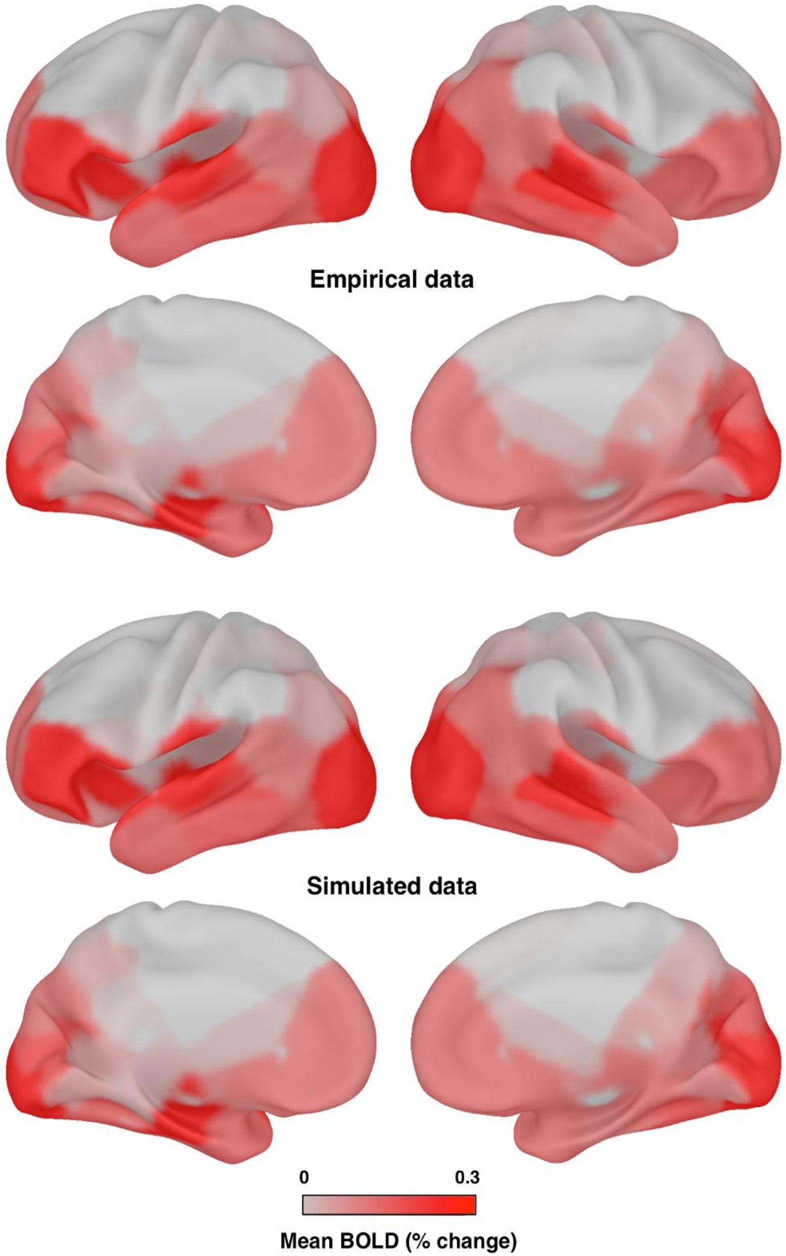
Regulating the local level of feedback inhibition in the brain has an important role at the global level:

- It attenuates the response of cortical areas in the default mode network.
- It increases the information capacity of the global network by increasing the entropy of the network's evoked responses.
- Ii increases the stimulus discriminability

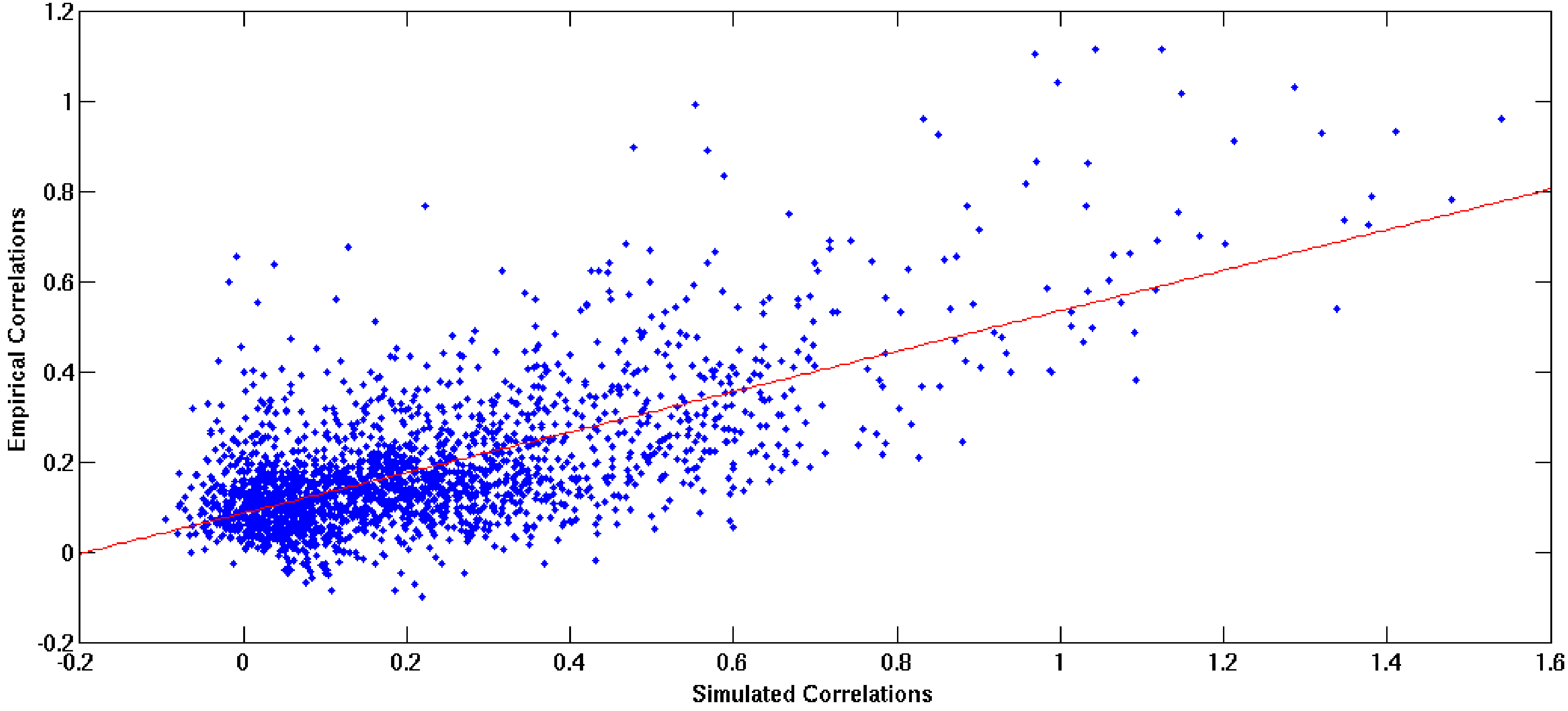
Effective dynamics

Model validation during movie watching





Effective dynamics



Acknowledgements

Functional data

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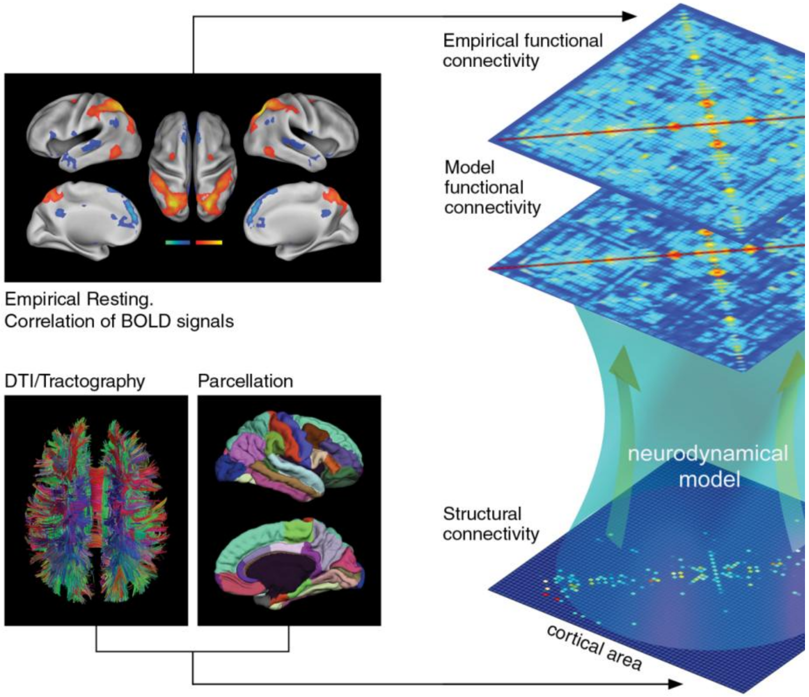
Structural data

Patric Hagmann
Alessandra Griffa — University of Lausanne, Switzerland.



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