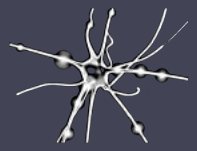
C3NL Computational, Cognitive & Clinical Neuroimaging Laboratory



Computational Neurodynamics Group
Department of Computing

Effects of lesions on dynamics in cortical networks

František Váša

fv247@cam.ac.uk

@frantisekvasa

Imperial College London

Cambridge Connectome Consortium

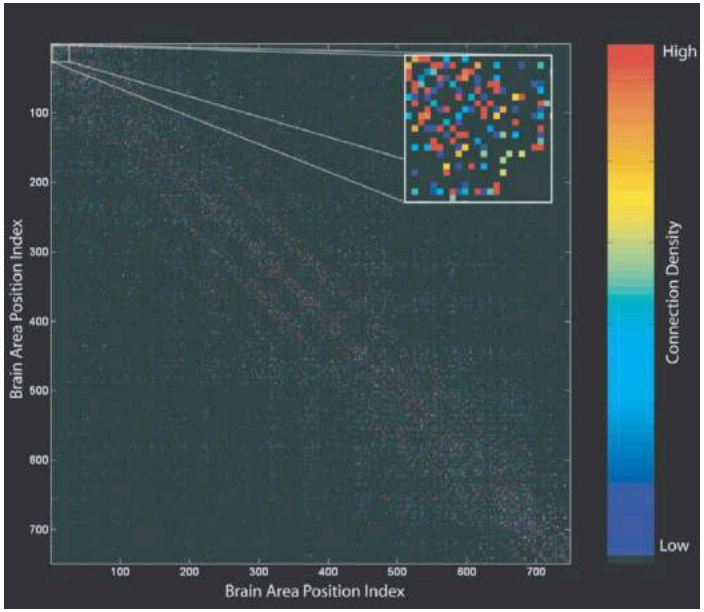
24th May 2016

UNIVERSITY OF CAMBRIDGE

Framework - The “Connectome”

Sporns et al. *PLoS Comp. Biol.* 2005 + Hagmann *PhD Thesis* 2005

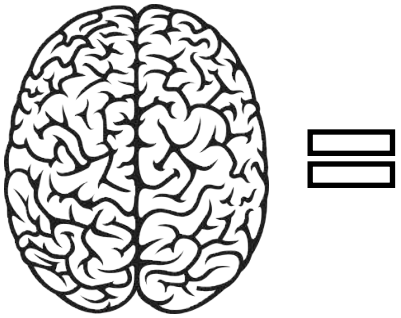
- “An obvious […] use of the human connectome would be providing structural information that can be implemented as part of large-scale computational models”
- “Most importantly, the connectome will provide an important tool for mechanistic modeling and interpretation of human functional brain data.”



Neural dynamics

- Coherence matters, as does its variability
  - Fries *Trends. Cog. Sci.* 2005 communication through coherence

- Neural dynamics are not stable, but "metastable"
  - Deco et al. *PNAS* 2009 "resting brains never rest"
  - Shanahan *Chaos* 2011 metastability metric



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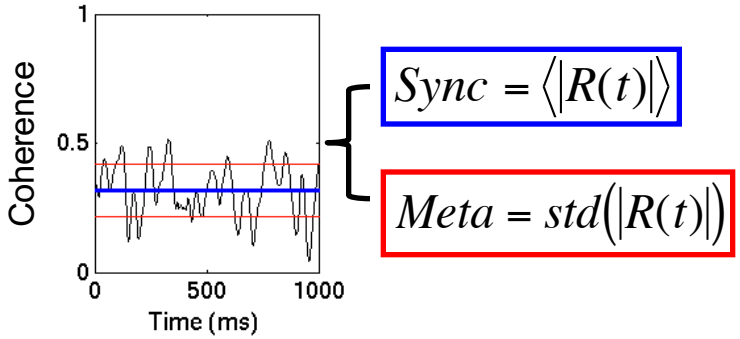


- Formally: stability ≠ multistability ≠ metastability

Synchronisation in coupled systems

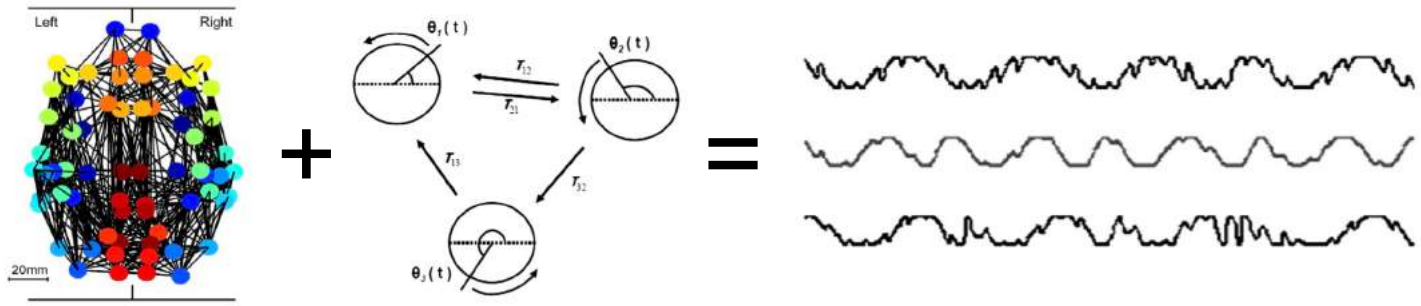
Video at: https://www.youtube.com/watch?v=JWToUATLGzs

Background: dynamics

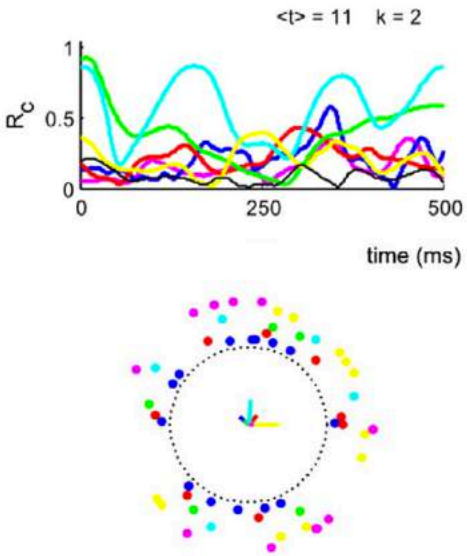
Neuroimage 2011

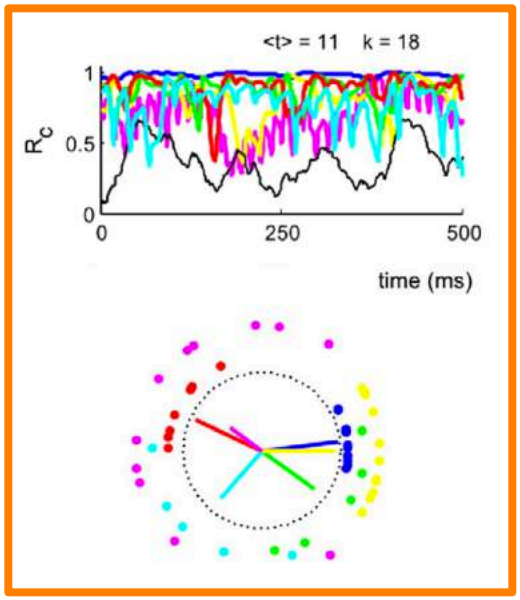
Role of local network oscillations in resting-state functional connectivity

Joana Cabral [a,*,1], Etienne Hugues [a,1], Olaf Sporns [b], Gustavo Deco [a,c]

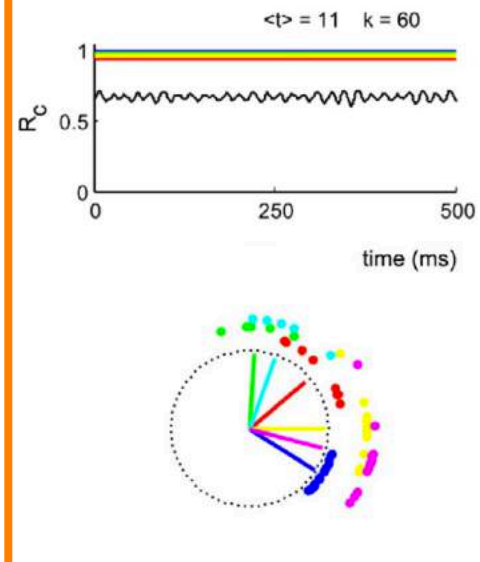


low coupling





high coupling



Background: dynamics

Neuroimage 2011

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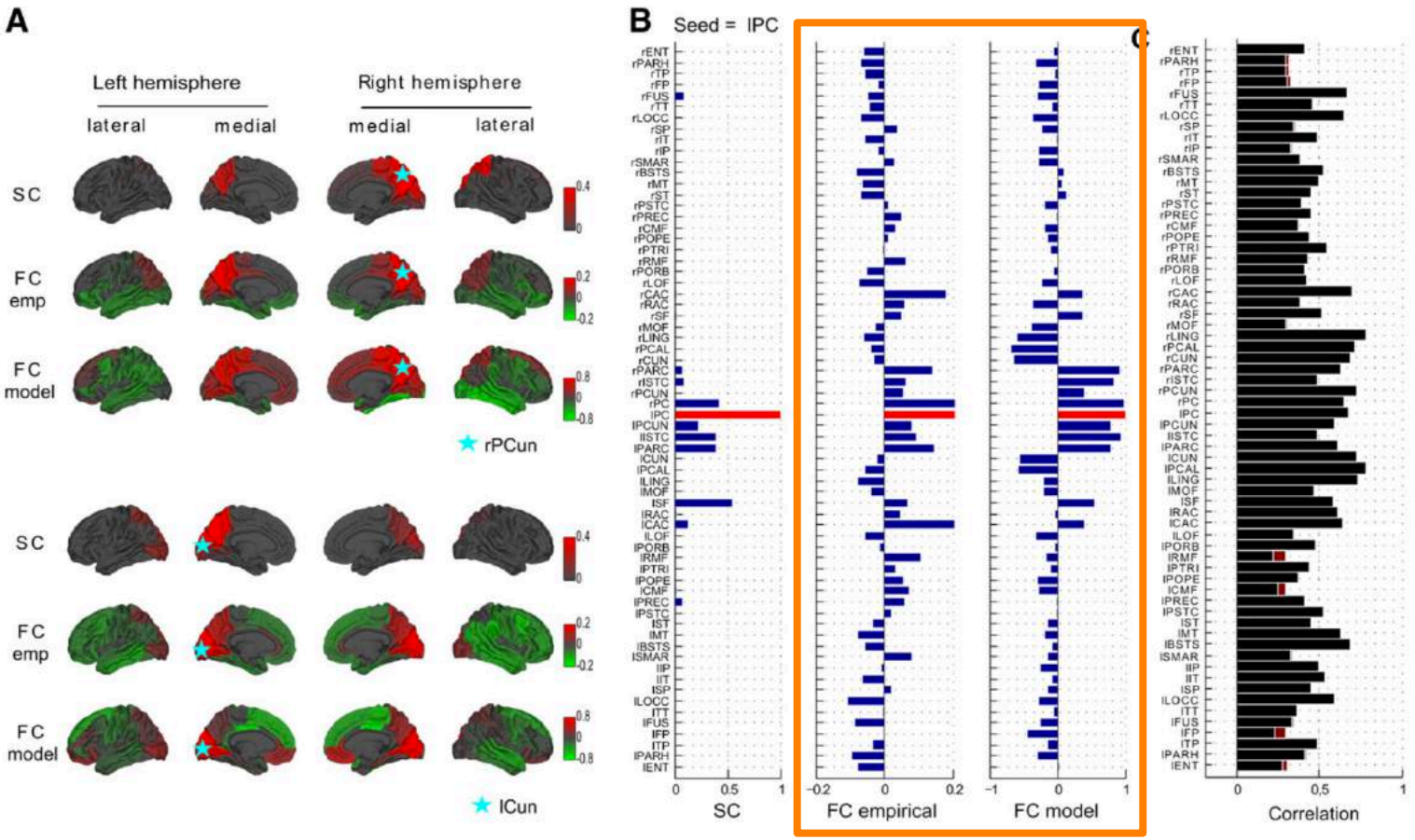
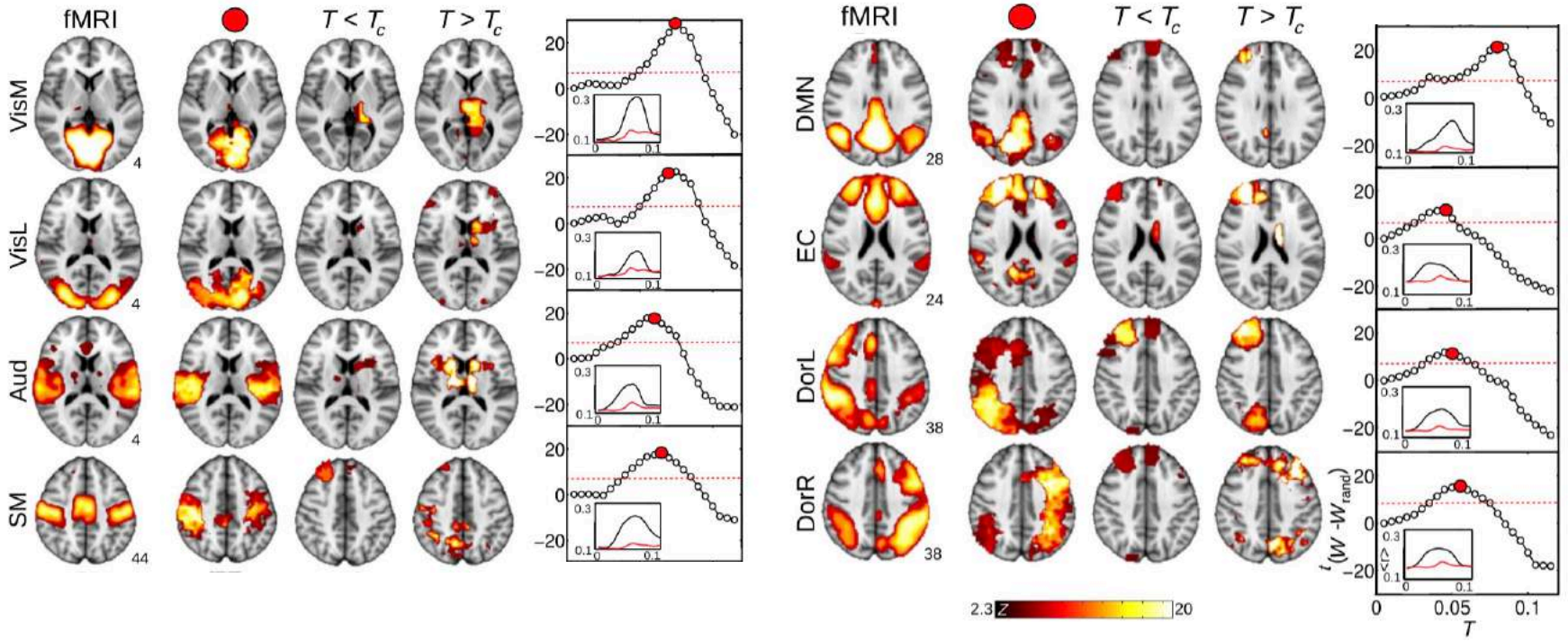


Background: dynamics

Phys. Rev. Lett. 2013

Brain Organization into Resting State Networks Emerges at Criticality on a Model of the Human Connectome

Ariel Haimovici,[1,2] Enzo Tagliazucchi,[3] Pablo Balenzuela,[1,2] and Dante R. Chialvo[2,4,5]



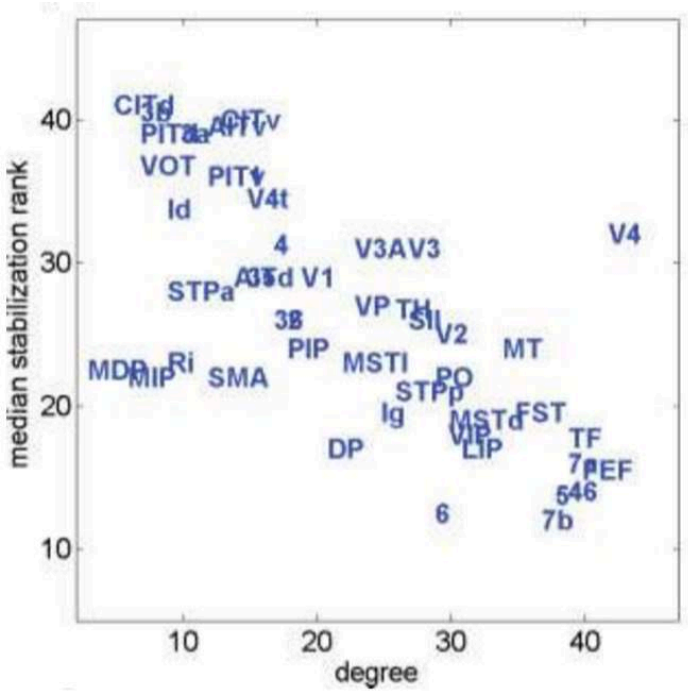
see also Kitzbichler et al. *PLoS Comp. Biol.* 2009

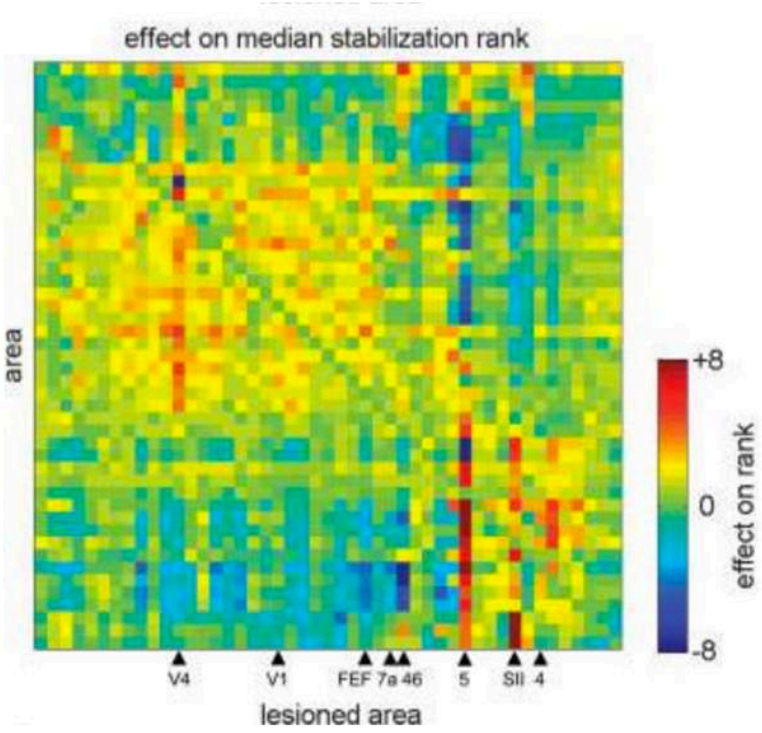
Background: virtual lesions

Hum. Brain Mapp. 2008

Dynamical Consequences of Lesions in Cortical Networks

Christopher J. Honey and Olaf Sporns*





Background: virtual lesions

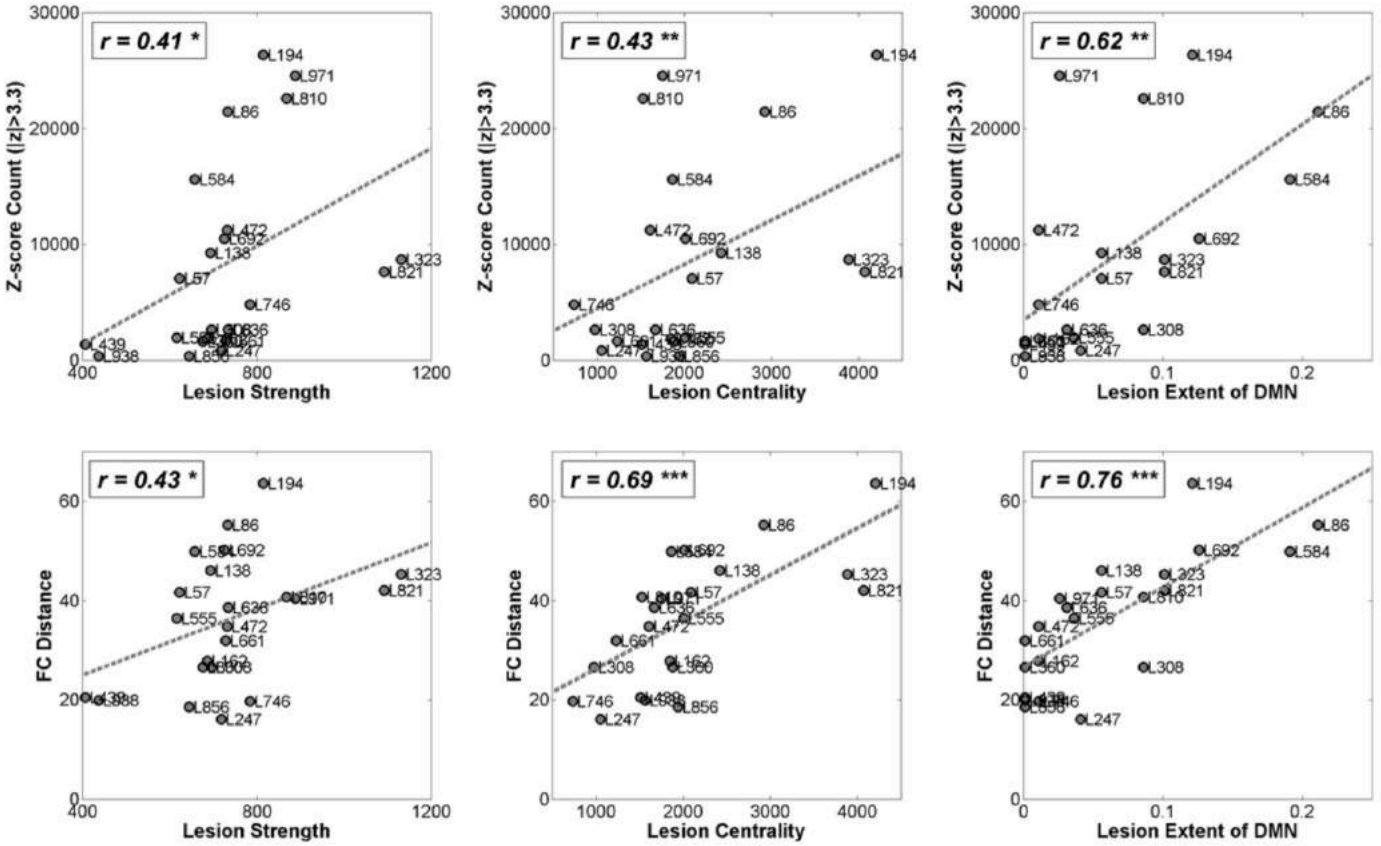
PLoS Comp. Biol. 2009

Modeling the Impact of Lesions in the Human Brain

Jeffrey Alstott[1], Michael Breakspear[2,3,4,5], Patric Hagmann[6,7], Leila Cammoun[6,7], Olaf Sporns[1,8]*

importance of lesioned nodes

impact on simulated FC



Aims

Q: What is the relationship between the structure of the connectome and (the metastability of) its dynamics?

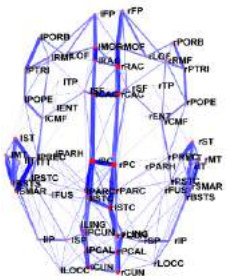
1) Calibrate Kuramoto model to match empirical fMRI data
2) Relate structure to dynamics using virtual lesions

(weak) Hypotheses

1) Structural importance of a node should relate to dynamical changes resulting from its removal
2) Effects of lesions most important in neighbourhood of lesioned node

+ unexpected relationship to several empirical studies…

Kuramoto oscillator model of neural synchrony (Kuramoto 1984)



Hagmann et al. (*PLOS Bio.* 2008)

inputs / parameters

$$\frac{d\theta_i}{dt} = \omega_i + \sum_{j=1}^{66} C_{ij} \sin(\theta_j(t - \tau_{ij}) - \theta_i(t)) + \eta_i(t)$$

phase: oscillator state
$(0 < \theta \leq 2\pi)$

frequency: periodic γ (60Hz) oscillations

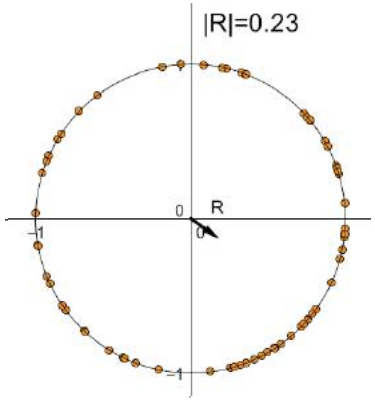
coupling: → **mean *k***

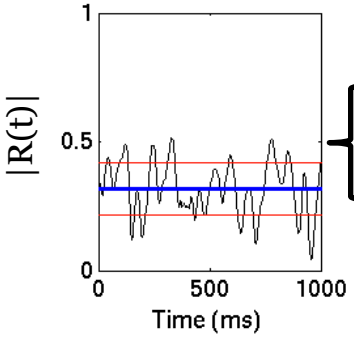
delay: → **mean τ**

Dynamics:

- Order parameter R(t)

$$R(t)e^{i\phi(t)} = \frac{1}{N}\sum_{n=1}^{N} e^{i\theta_n(t)}$$





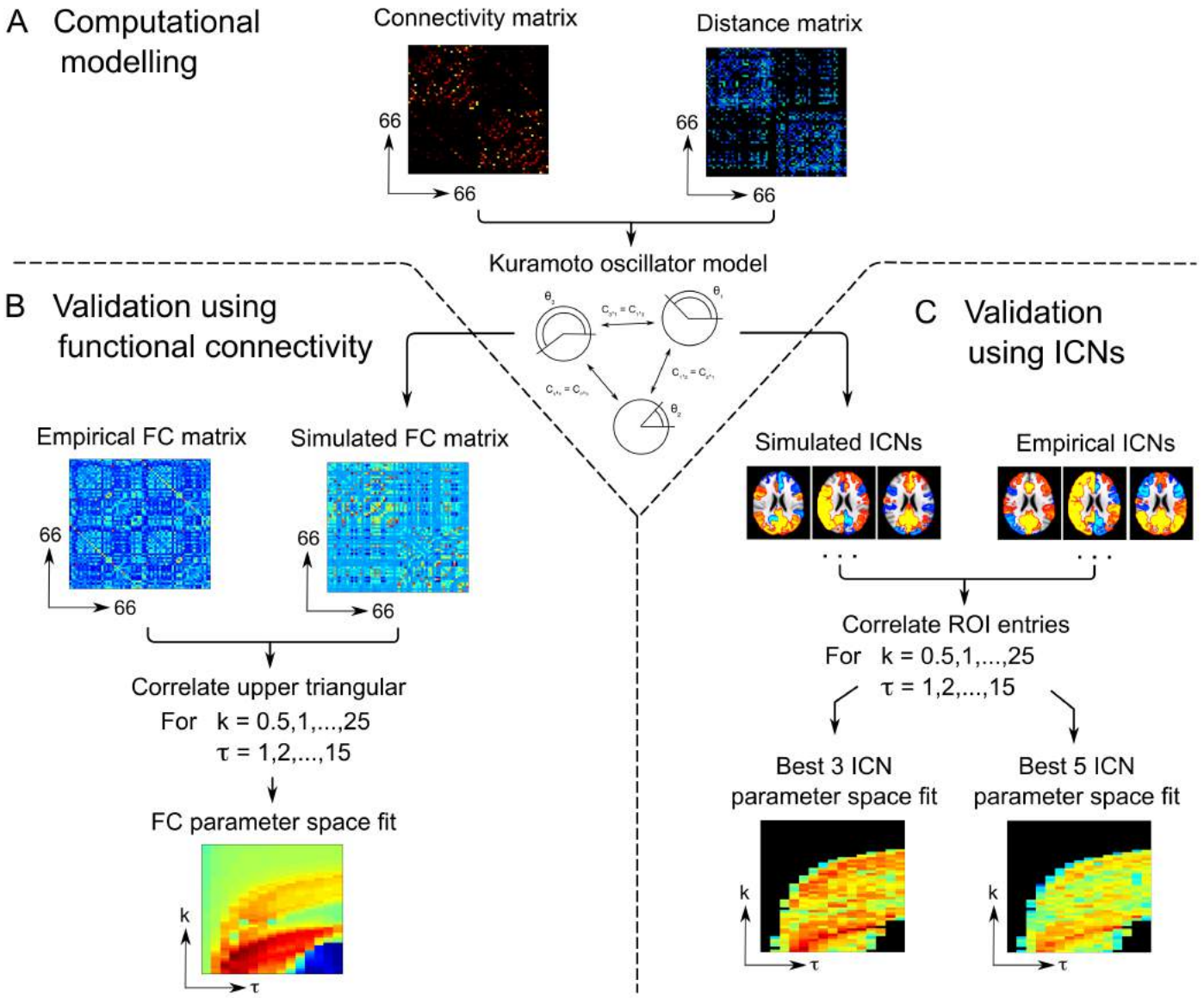
$$Sync = \langle |R(t)| \rangle$$

$$Meta = std(|R(t)|)$$

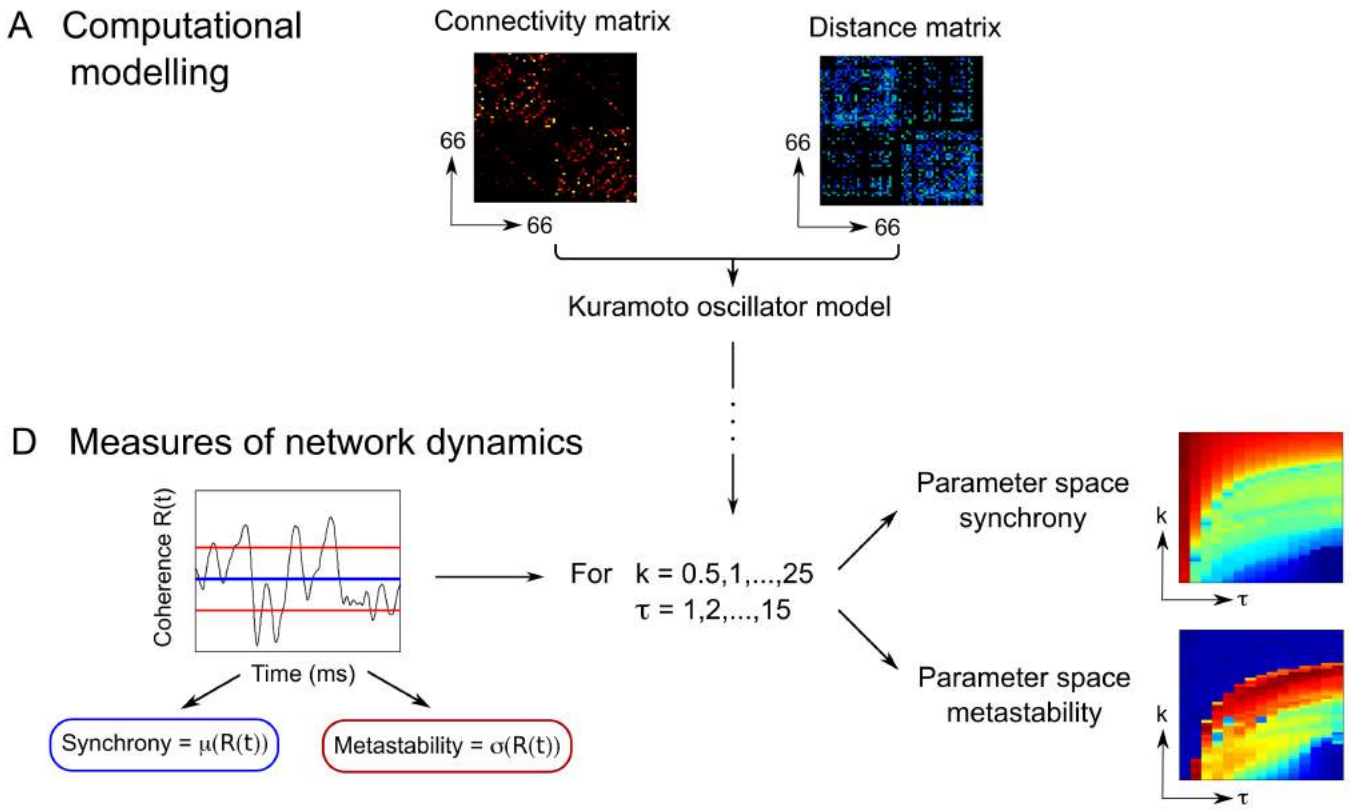
Shanahan (*Chaos* 2011)

- MATLAB, Euler method
- Conditions:
- Uniform → ω_i = 60 Hz for all i
- Noisy → ω_i - N(60,3) Hz + noise η_i = N(0,2) rad.

Model validation (calibration)

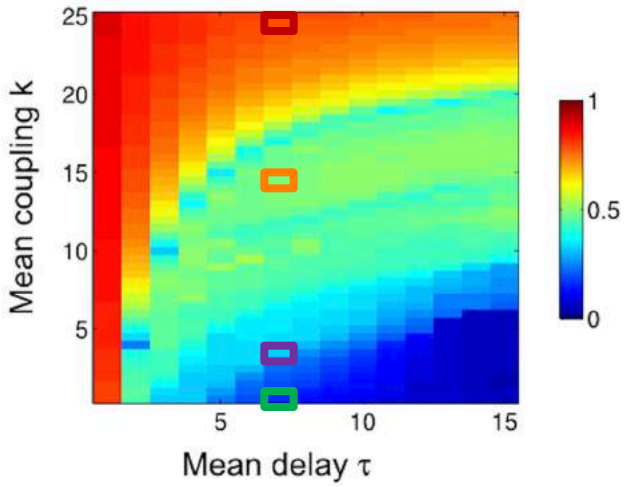


Model dynamics

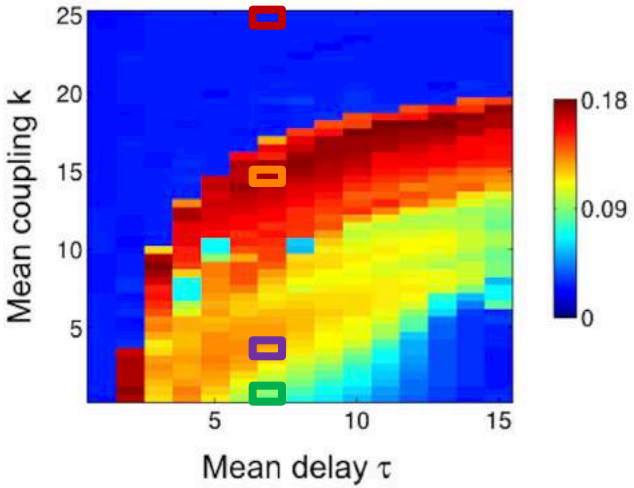


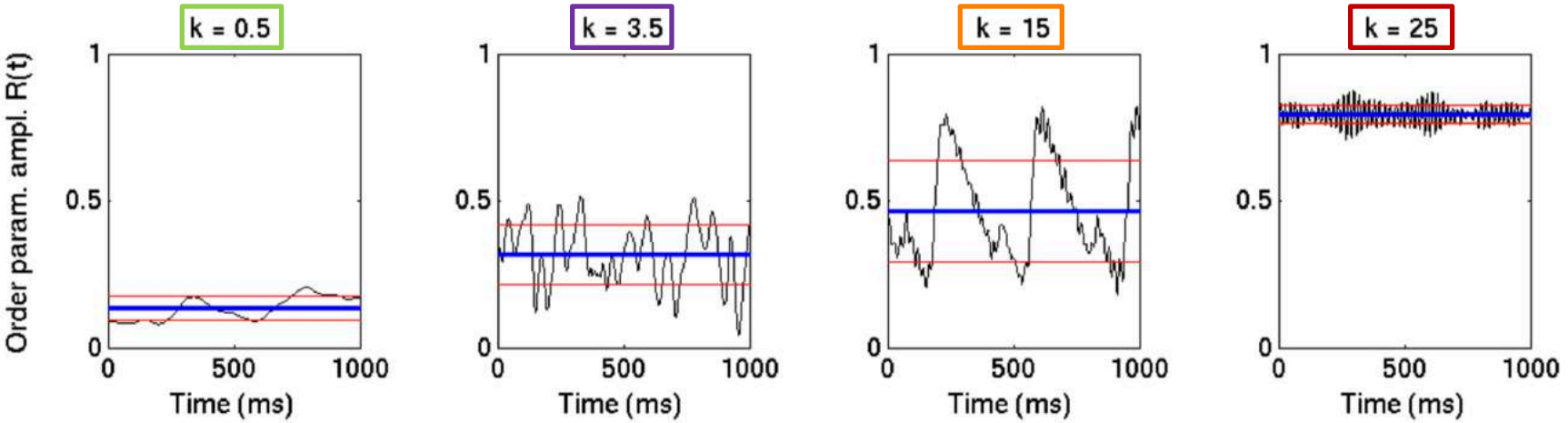
Model behavior along *k* axis

synchrony



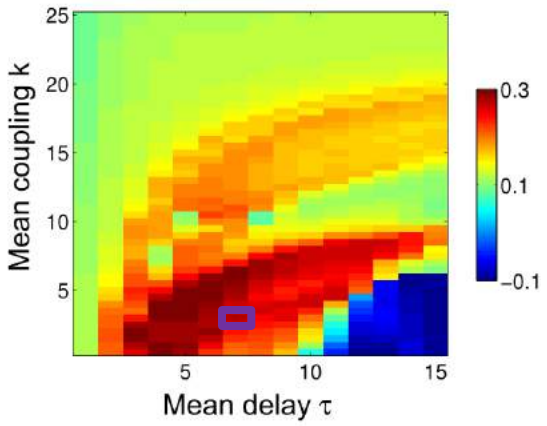
metastability



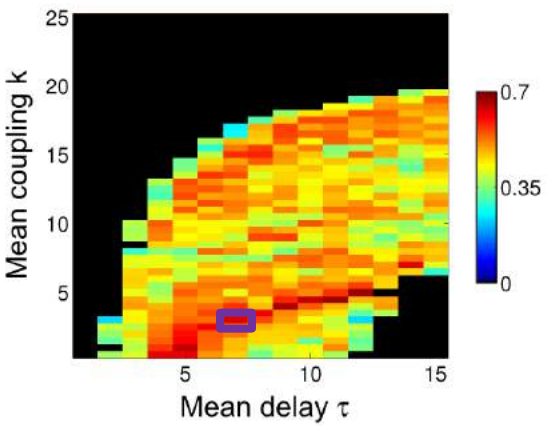


Model behavior across parameter space

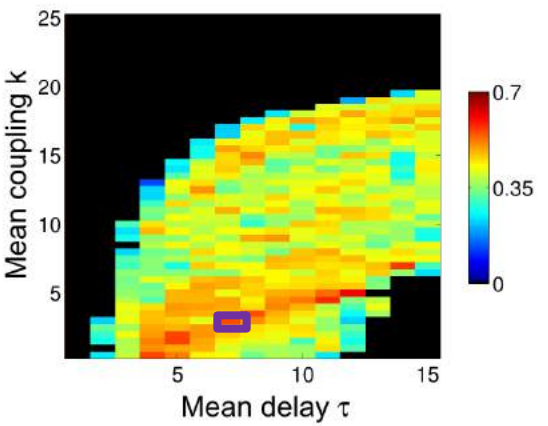
pairwise FC



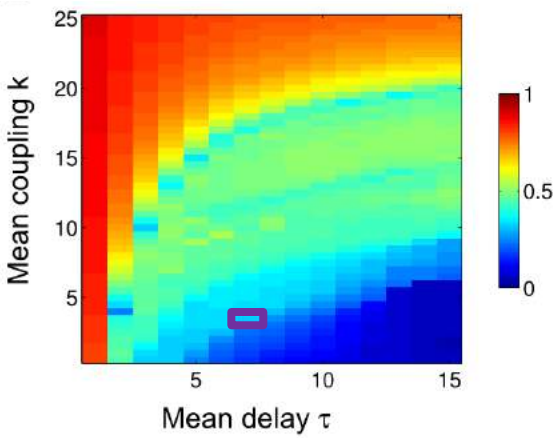
best 3 ICNs



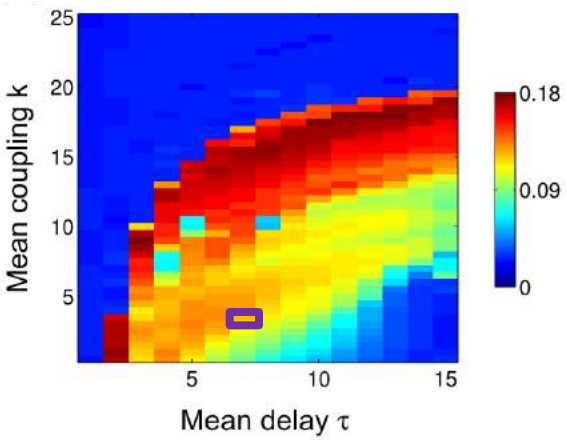
best 5 ICNs



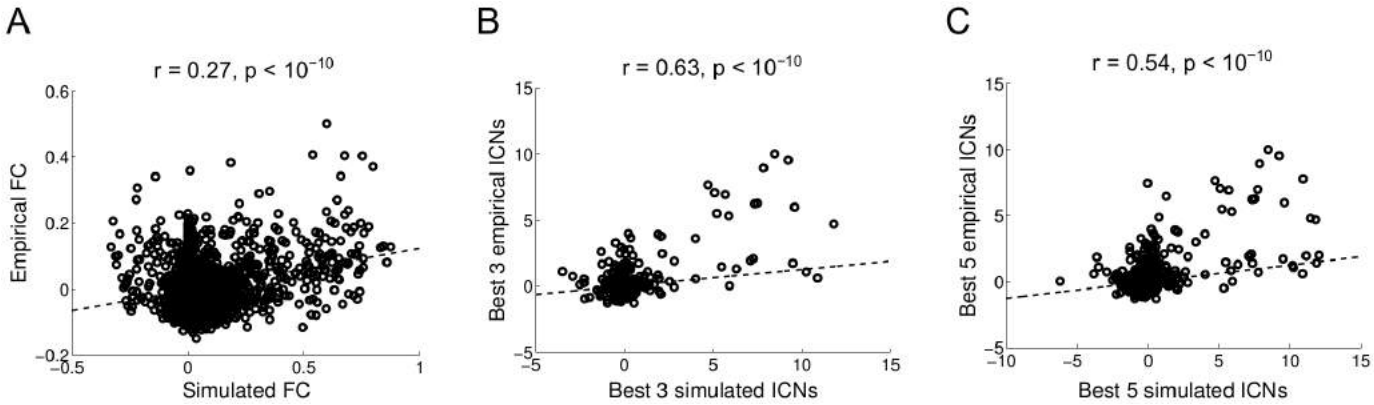
synchrony

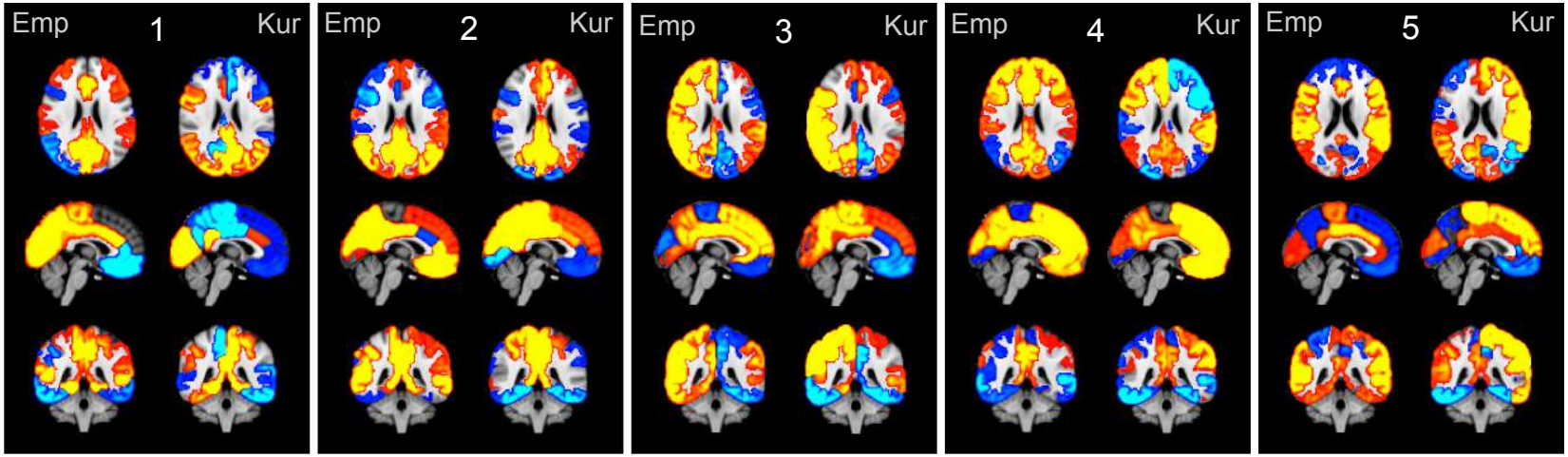


metastability



Working point



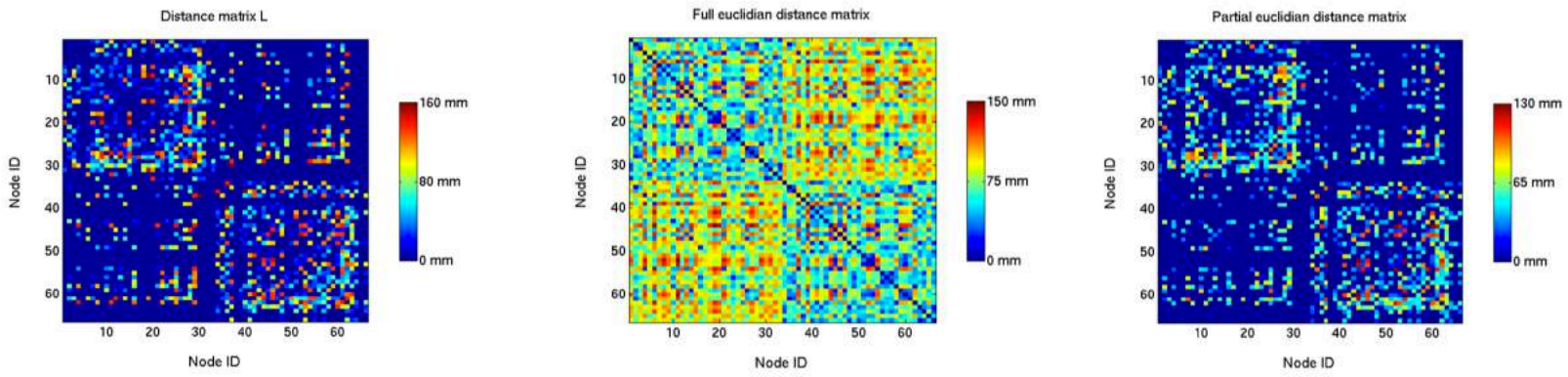


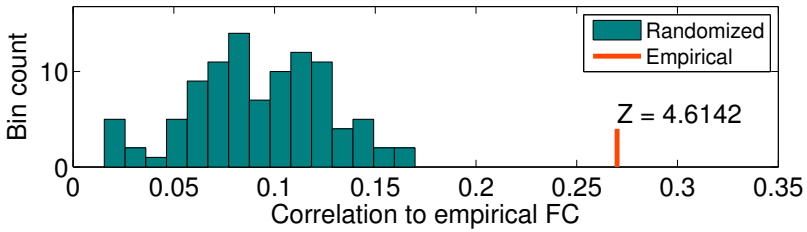
Working point:

$\boldsymbol{k} = 3.5$, $\boldsymbol{\tau} = 7$ ms

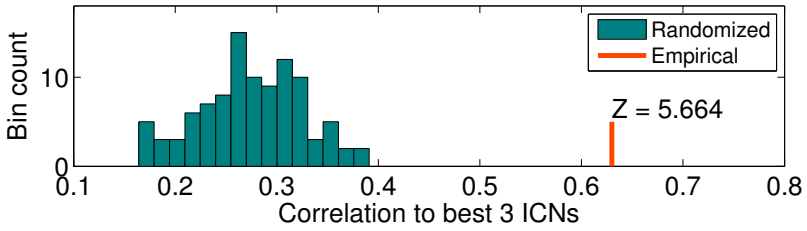
$$v = \frac{\overline{L}}{\overline{\tau}} = \frac{64.2\ mm}{7\ ms} \approx 9.2\ m/s$$

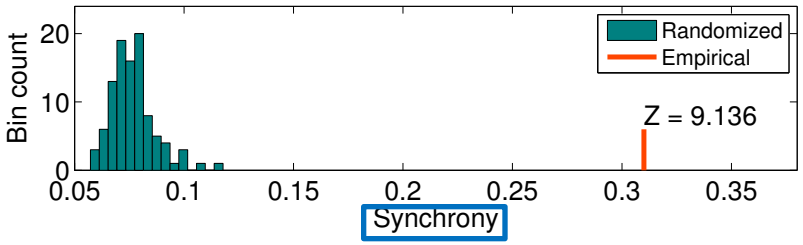
Null model – random network dynamics

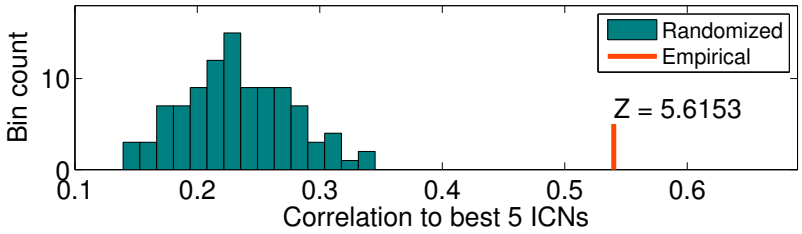


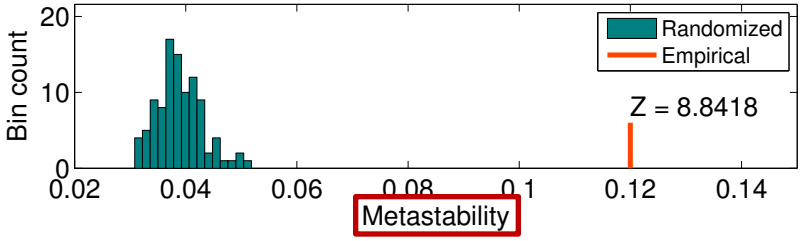


Pearson r = 0.72 ($p < 10^{-10}$)









Reminder - Aims

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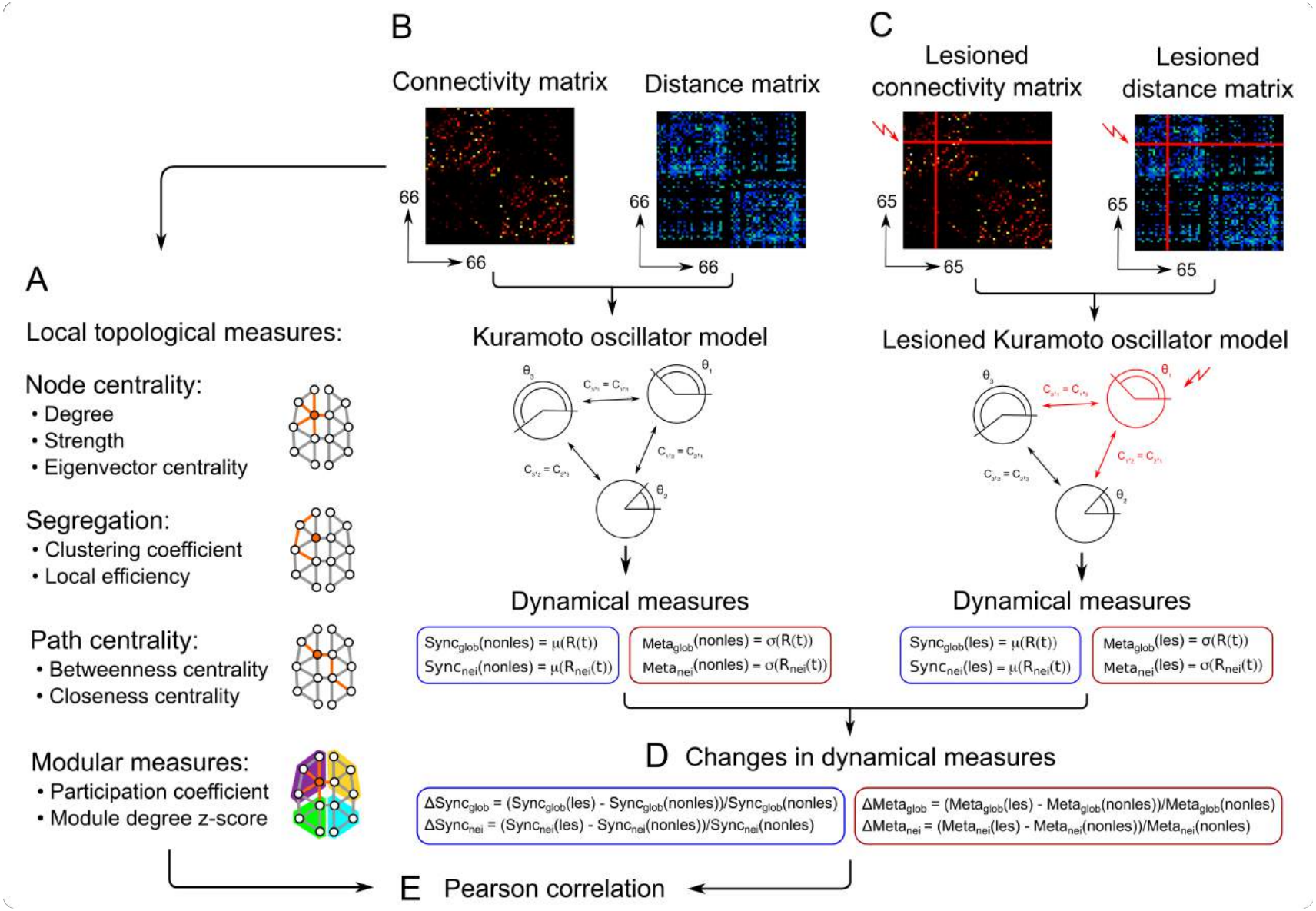
1) Calibrate Kuramoto model to match empirical fMRI data ✓
2) → Relate structure to dynamics using virtual lesions

(weak) Hypotheses

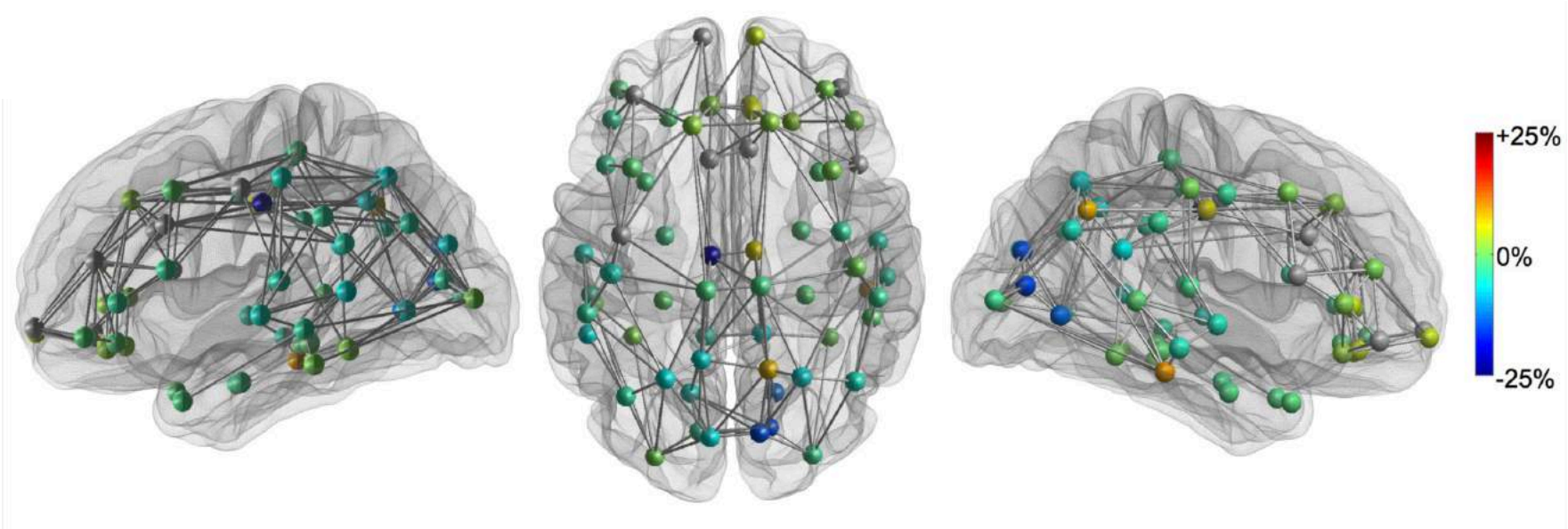
1) Structural importance of a node should relate to dynamical changes resulting from its removal
2) Effects of lesions most important in neighbourhood of lesioned node

Effects of lesions



Post-lesion Δ synchrony

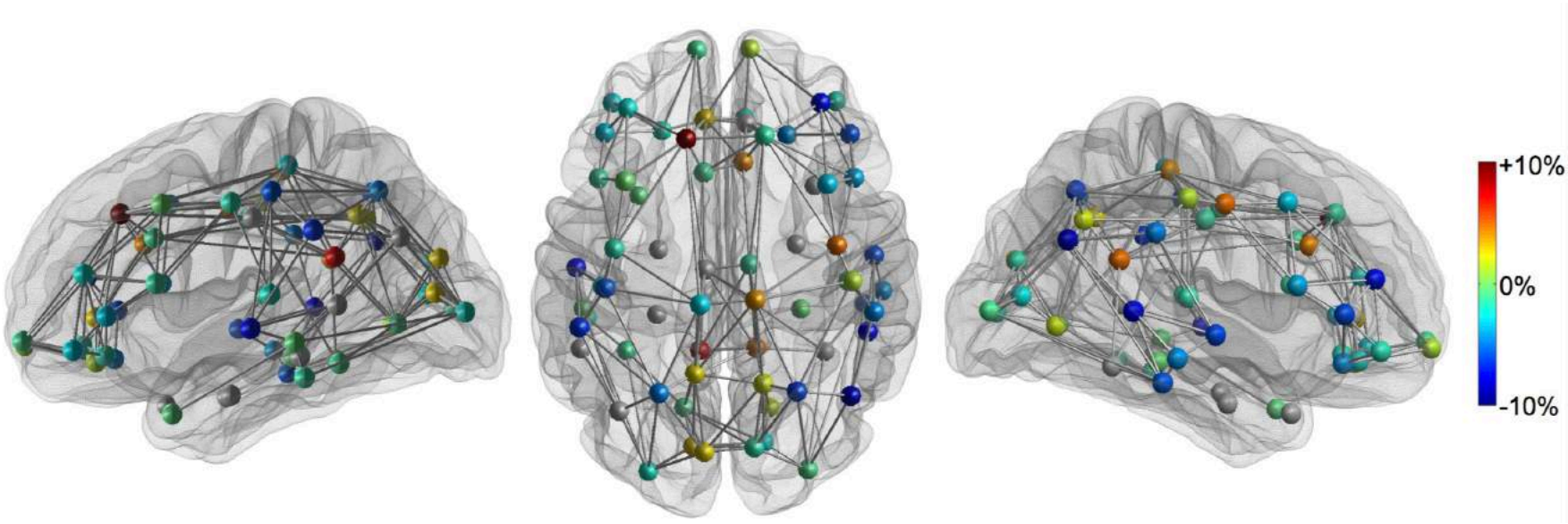
Global: μ [95% CI] = -1.7 [-3.0,-0.4] % (two-tailed T-test p = 0.017)



Neighbourhood: μ [95% CI] = -5.1 [-7.1,-3.1] % (two-tailed T-test p = $3.5 \cdot 10^{-6}$)

Post-lesion Δ metastability

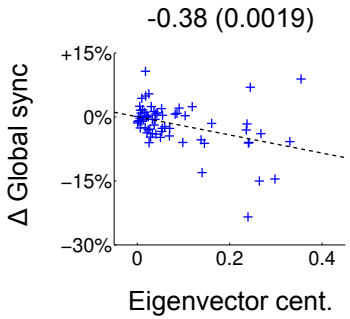
Global: μ [95% CI] = -0.9 [-1.8,-0.05] % (two-tailed T-test p = 0.035)

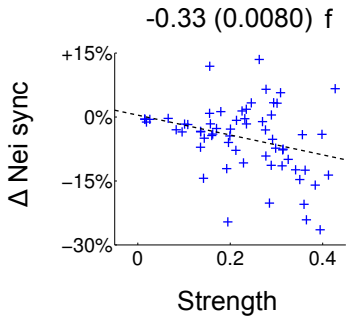


Neighbourhood: μ [95% CI] = +1.7 [-1.8,-0.05] % (two-tailed T-test p = 0.21)

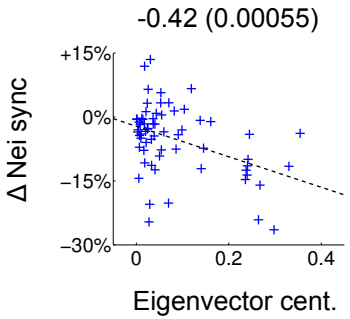
Structure VS Δdynamics

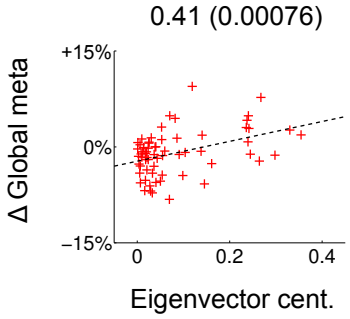
global

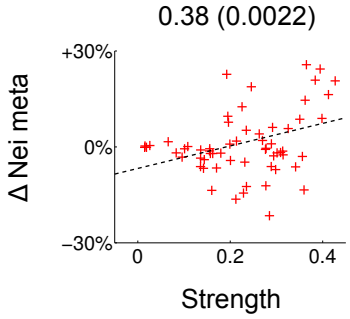


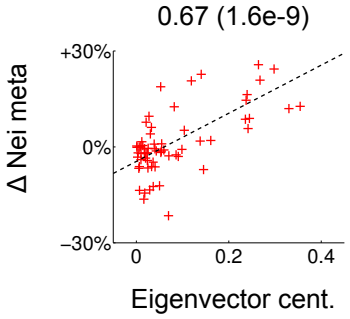


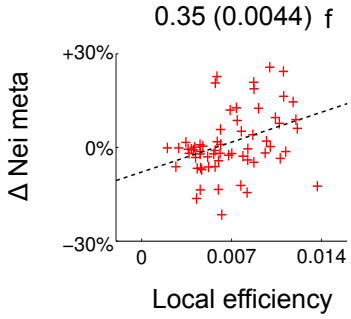
neighbourhood

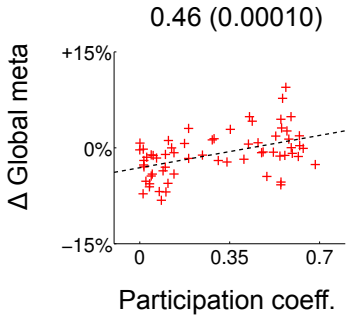


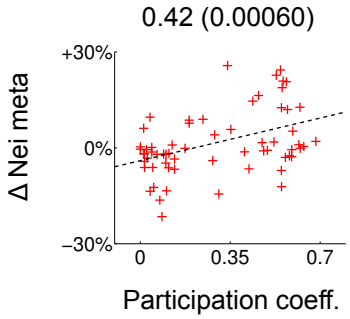


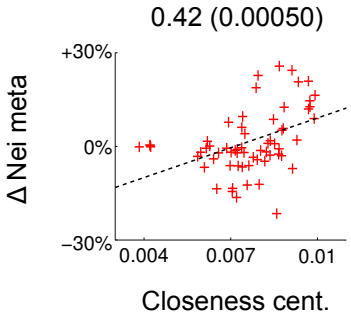










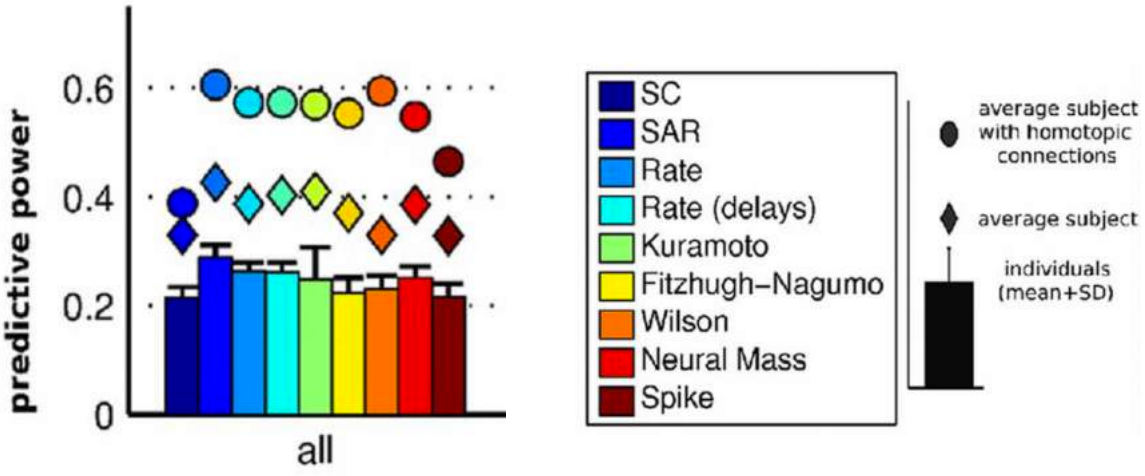


plot title =
Pearson r (p)

Fit between model and empirical data

Messé et al.

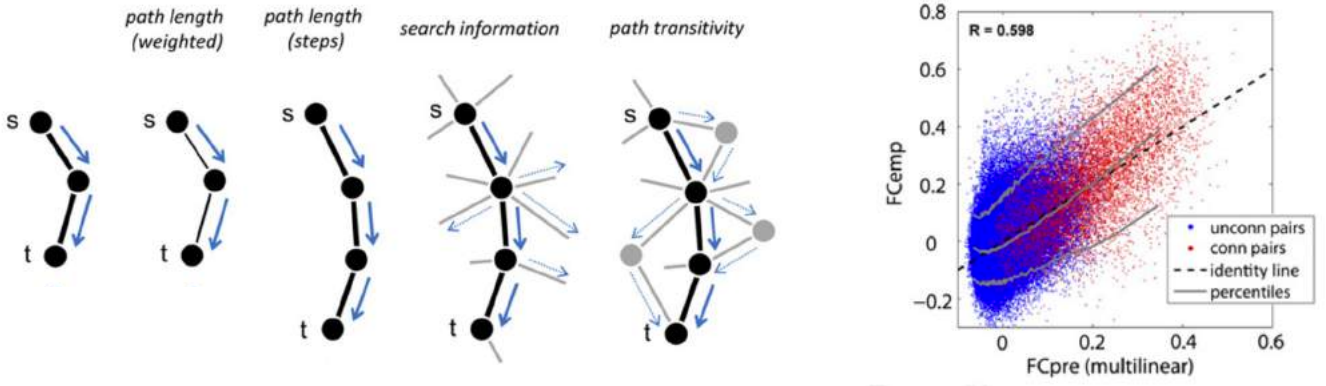
PLoS Comp. Biol. 2014



Deco et al. *J. Neurosci.* 2014

"A dramatic improvement of the fitting of the matrices was obtained with the addition of a small number of anatomical links, particularly cross-hemispheric connections"

Goñi et al.
PNAS 2014



Role of structural topology in shaping function

- Strength, eigenvector cent. predicitive of Δ dynamics; degree is not.
  - perturbing high-degree nodes affects dynamics most (Honey & Sporns *HBM* 2008)
  - structural degree important predictor of FC (Tewarie et al. *NeuroImage* 2014)

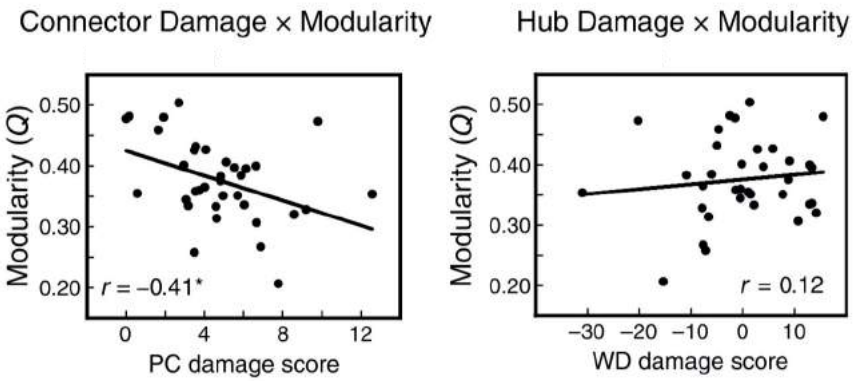
  → BUT both studies used binary structural connectomes
  - model correspondence to FC_{emp} + metastability destroyed if:
    - topology is randomised
    - connections are made equally important

  (Cabral et al. *NeuroImage* 2014)

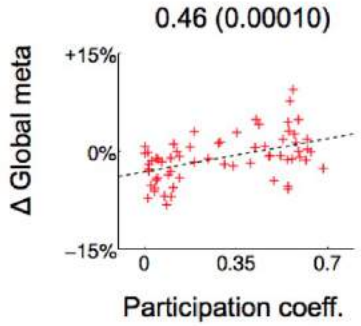
- Eigenvector centrality, participation coefficient strongest predictors
  - Likely members of the rich club (RC) (van den Heuvel & Sporns J. Neurosci. 2011)
  - RC = anatomical substrate for transmodal integration of ICNs (RSNs)
    - Leech et al. *J. Neurosci.* 2012, van den Heuvel & Sporns *J. Neurosci.* 2013
  - Dynamics: Rich nodes → slow + stable; Periphery → fast + unstable
    - Gollo et al. *Phil. Trans. R. Soc. B* 2015

Integrative hubs, modularity and cortical dynamics

Stroke: Gratton et al. *J. Cog. Neurosci.* 2012

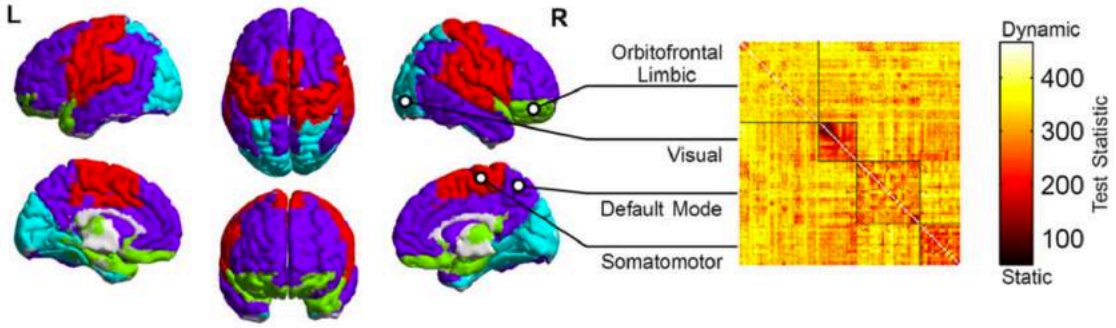


Váša et al. *NeuroImage* 2015



modularity VS integrative hubs ⟷ integrative hubs VS dyn. variability

modularity VS dyn. variability

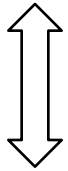


Functional dynamics: Zalesky et al. *PNAS* 2014

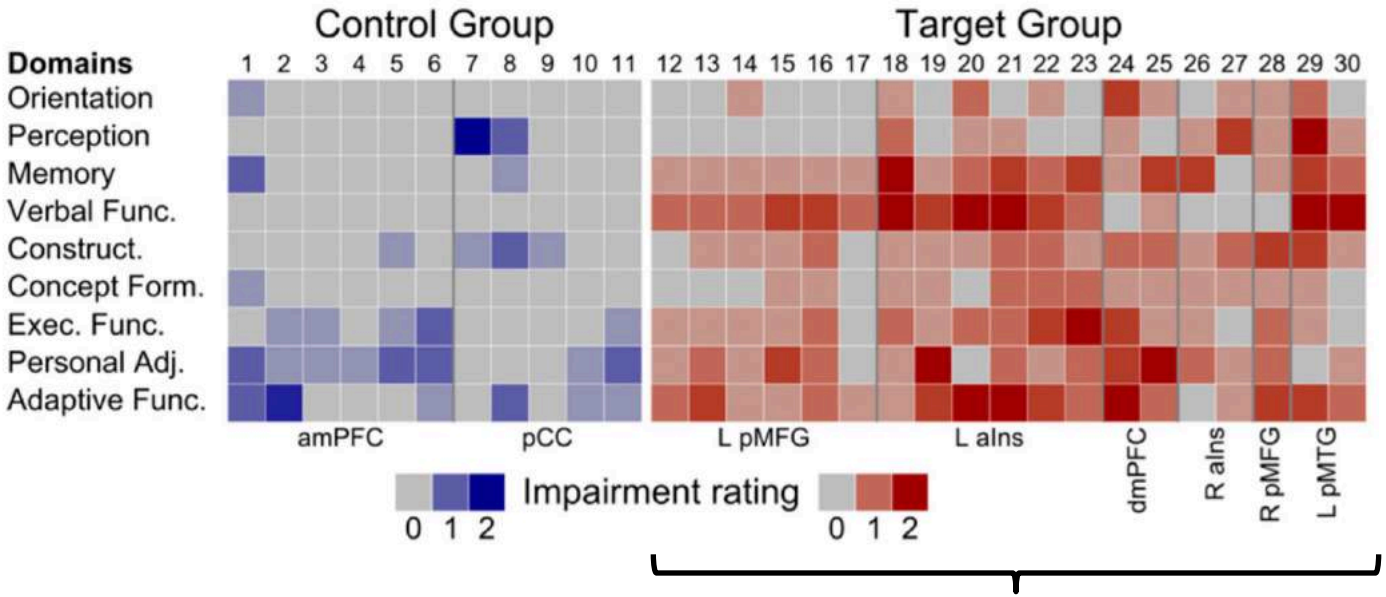
Integrative hubs, modularity and cortical dynamics

Stroke VS Cognition:

Warren et al. *PNAS* 2014

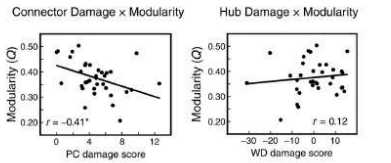


strokes at high-degree nodes strokes at high-participation nodes

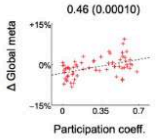


communication between disparate cognitive networks disrupted

Stroke: Gratton et al. *J. Cog. Neurosci.* 2012

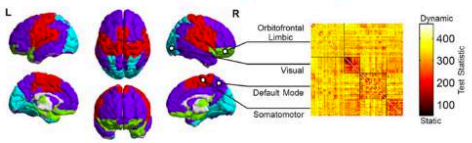


Váša et al. *NeuroImage* 2015



modularity VS integrative hubs ⟷ integrative hubs VS dyn. variability

modularity VS dyn. variability



Functional dynamics: Zalesky et al. *PNAS* 2014

Additional markers of cognitive impairment:

- Modularity
- Dynamical variability

Limitations / Future work

- Model simplicity / "stationarity" (Hansen et al. *NeuroImage* 2015)
- Dependence of ICN tuning on ICA dimensionality not explored
- Diffusion imaging tractography
  - "Anatomical accuracy of brain connections derived from diffusion MRI tractography is inherently limited" (Thomas et al. *PNAS* 2014)
- To improve relevance to stroke:
  - Add subcortical nodes; "majority of strokes were localized subcortically" (Corbetta et al. *Neuron* 2015)
  - Use lesion maps from clinical data (Falcon et al. eNeuro 2016)
  - Damaged areas may remain active (van Dellen et al. *NeuroImage* 2013)
  - Use more specific dynamical measure(s)

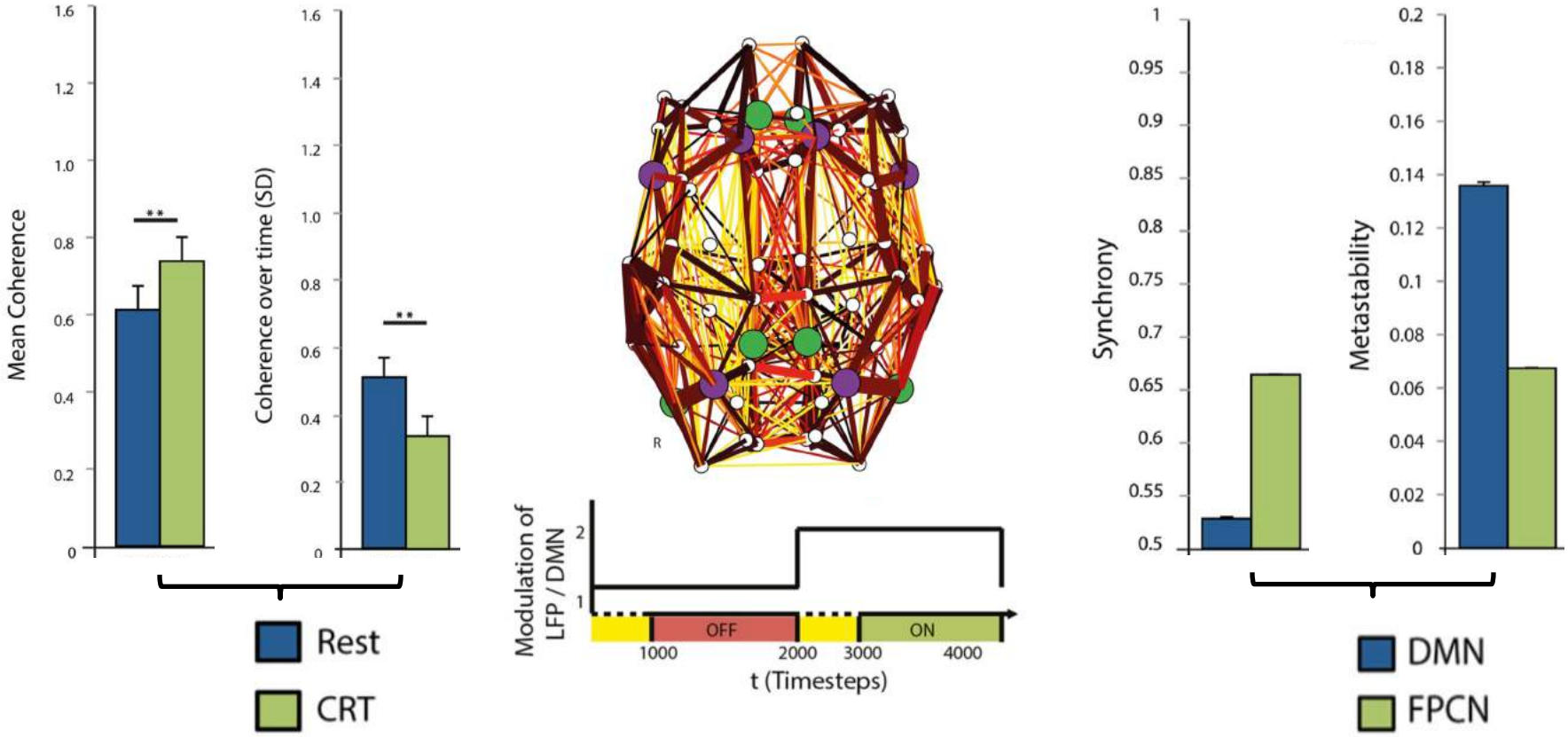
→ eg: global metastability too coarse to discern diaschisis

Relevance to cognition

J. Neurosci. 2014

The Control of Global Brain Dynamics: Opposing Actions of Frontoparietal Control and Default Mode Networks on Attention

Peter J. Hellyer,[1] Murray Shanahan,[2] Gregory Scott,[1] Richard J. S. Wise,[1] David J. Sharp,[1] and Robert Leech[1]



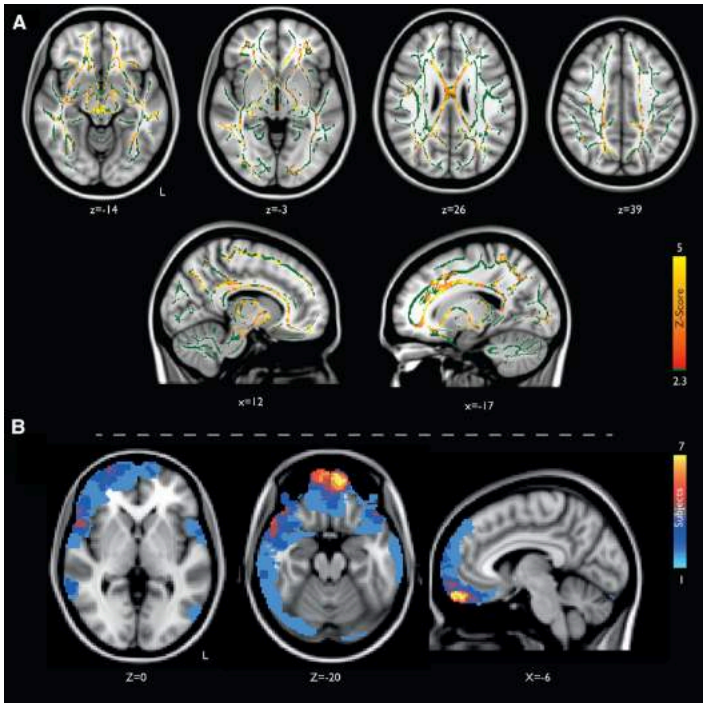
Relevance to disease

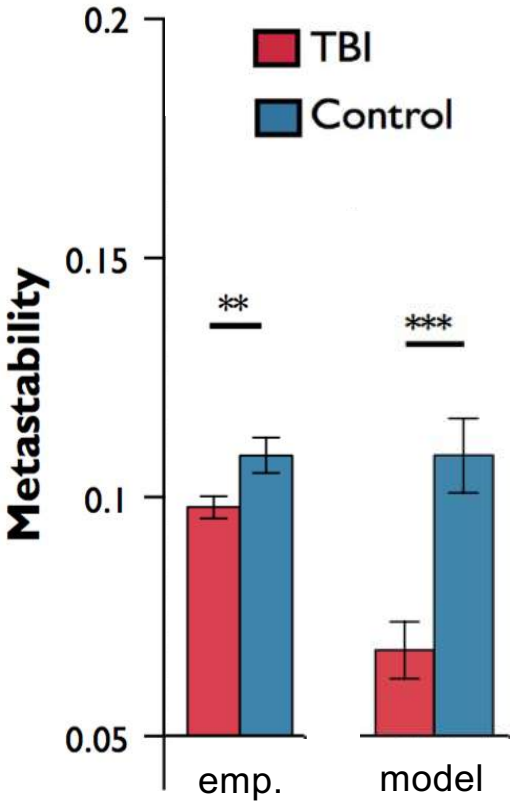
J. Neurosci. 2015

Cognitive Flexibility through Metastable Neural Dynamics Is Disrupted by Damage to the Structural Connectome

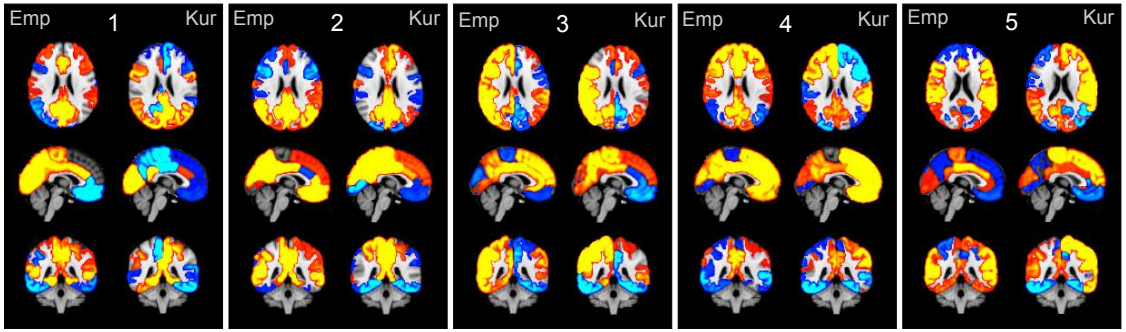
Peter J. Hellyer,[1,2*] Gregory Scott,[1*] Murray Shanahan,[3] David J. Sharp,[1] and Robert Leech[1]

Traumatic Brain Injury (TBI)

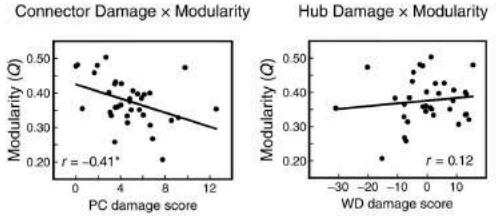




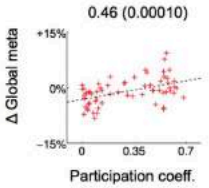
Summary



Stroke: Gratton et al. *J. Cog. Neurosci.* 2012

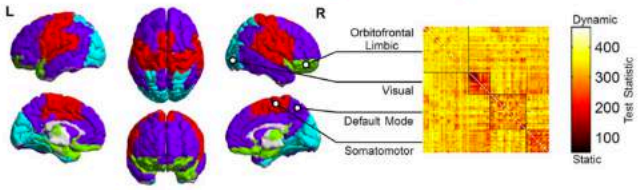


Váša et al. *NeuroImage* 2015



modularity VS integrative hubs ↔ integrative hubs VS dyn. variability

modularity VS dyn. variability



Functional dynamics: Zalesky et al. *PNAS* 2014

NeuroImage

Effects of lesions on synchrony and metastability in cortical networks

František Váša, Murray Shanahan, Peter J. Hellyer, Gregory Scott, Joana Cabral, Robert Leech

ARTICLE INFO

ABSTRACT

Introduction

Try it yourself!

see also Sanz-Leon et al. *Front. Neuroinform.* 2013; *NeuroImage* 2015

Thank you!

Robert Leech

Murray Shanahan

Peter Hellyer

Gregory Scott

Joana Cabral

Imperial College London

C3NL Computational, Cognitive & Clinical Neuroimaging Laboratory

Computational Neurodynamics Group
Department of Computing

Patric Hagmann

CHUV Centre hospitalier universitaire vaudois

GATES Cambridge

UNIVERSITY OF CAMBRIDGE