

Institut de
Neurosciences des
Systèmes

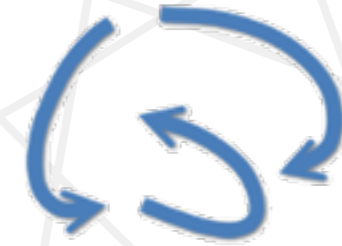
Beyond graph theory: *Alterations of the human structural and functional connectomes through aging*

Demian Battaglia

Institut de Neurosciences des Systèmes

UMR1106 INSERM, Université Aix-Marseille, France





Institut de
Neurosciences des
Systèmes

OLDER, SLOWER, HARDER,
(BETTER?)

Demian Battaglia

Institut de Neurosciences des Systèmes

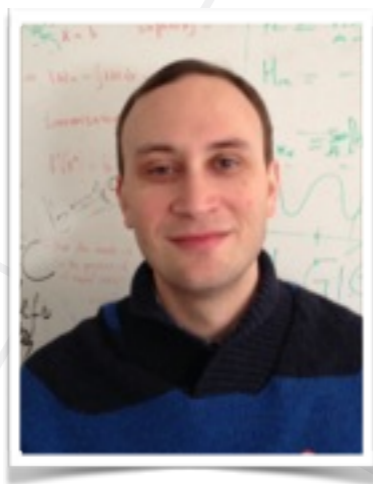
UMR1106 INSERM, Université Aix-Marseille, France



freely inspired to
“Harder, Better, Faster, Stronger”
world-famous French hit...



Viktor Jirsa
(INS, Marseille)



Enrique Hansen
(INS → FIAS,
Frankfurt)



Thomas Boudou
(INS, Marseille &
ENSTA ParisTech)

*but much
younger!*



Petra Ritter
(Charité, Berlin)



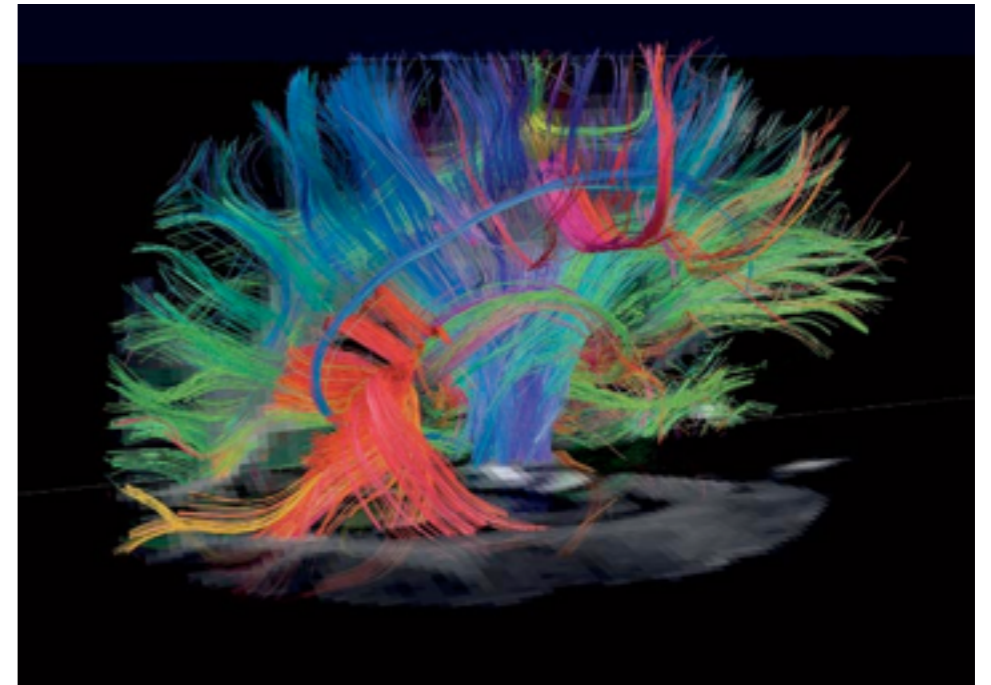
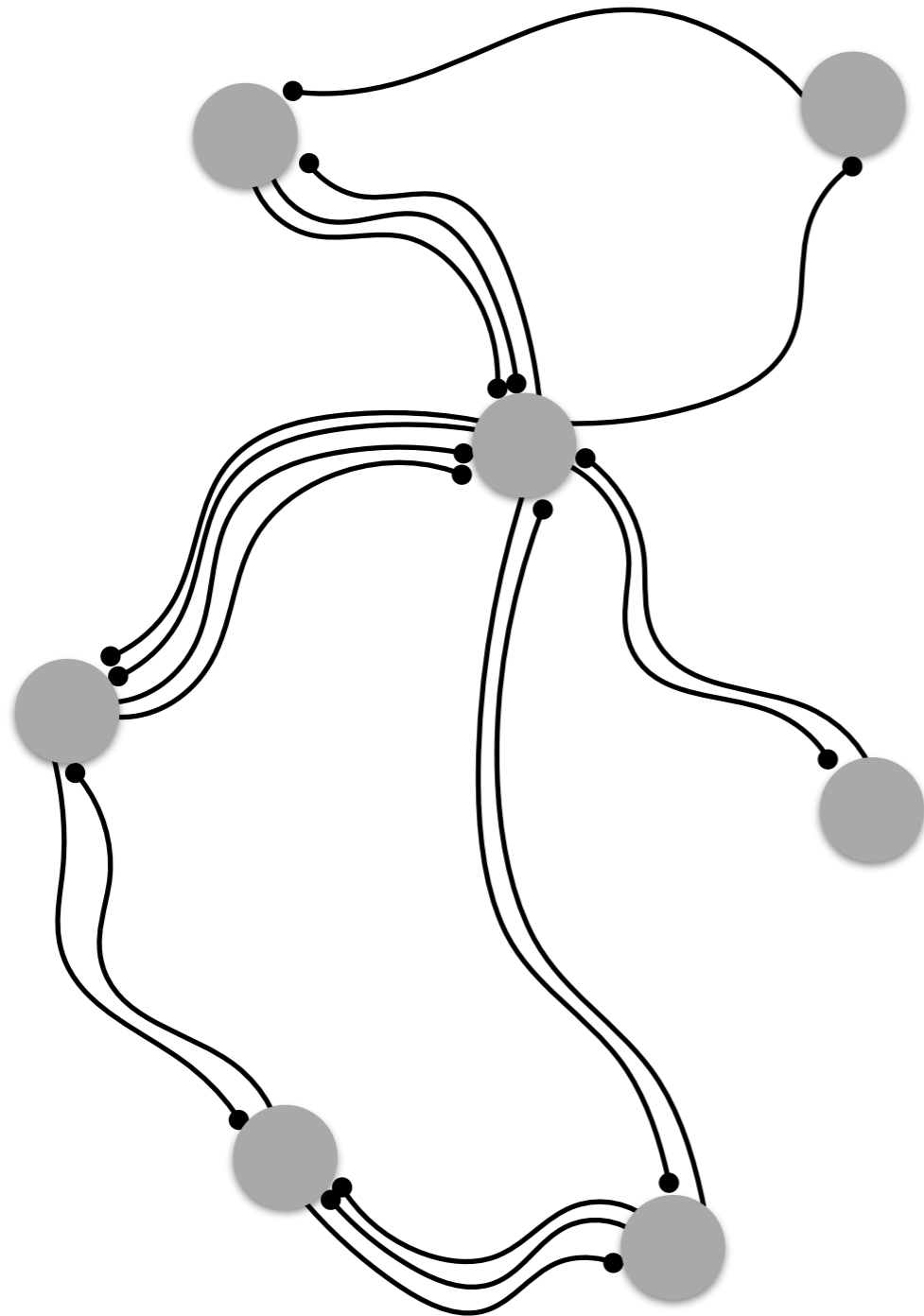
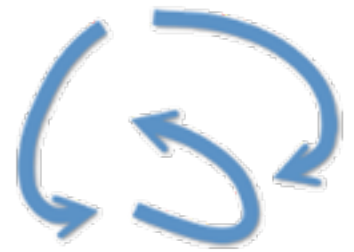
Francesco Vaccarino

(ISI foundation, Turin)



Giovanni Petri

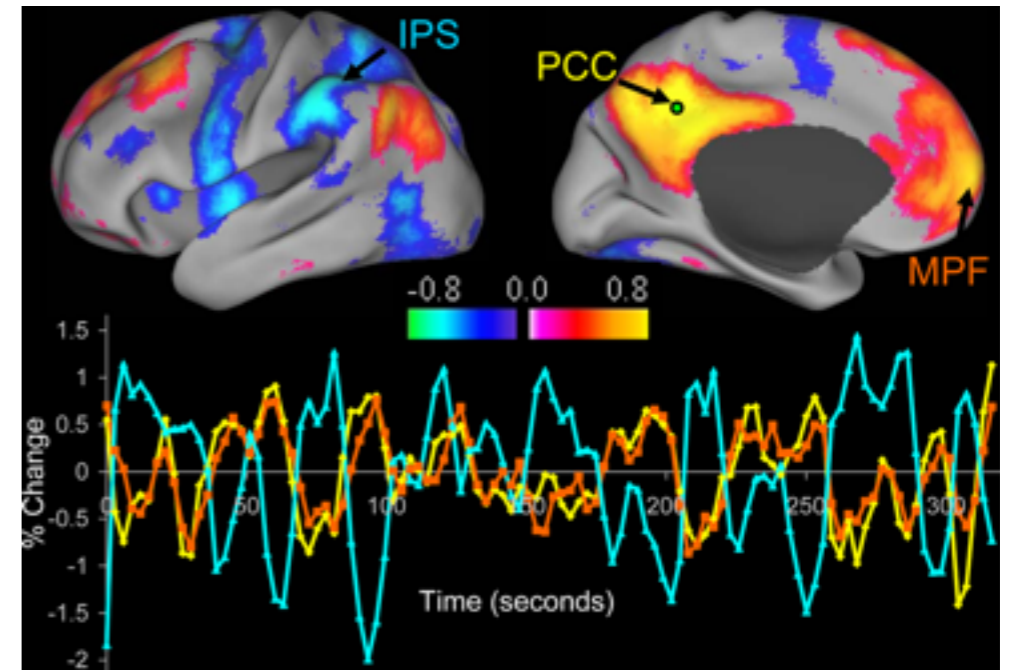
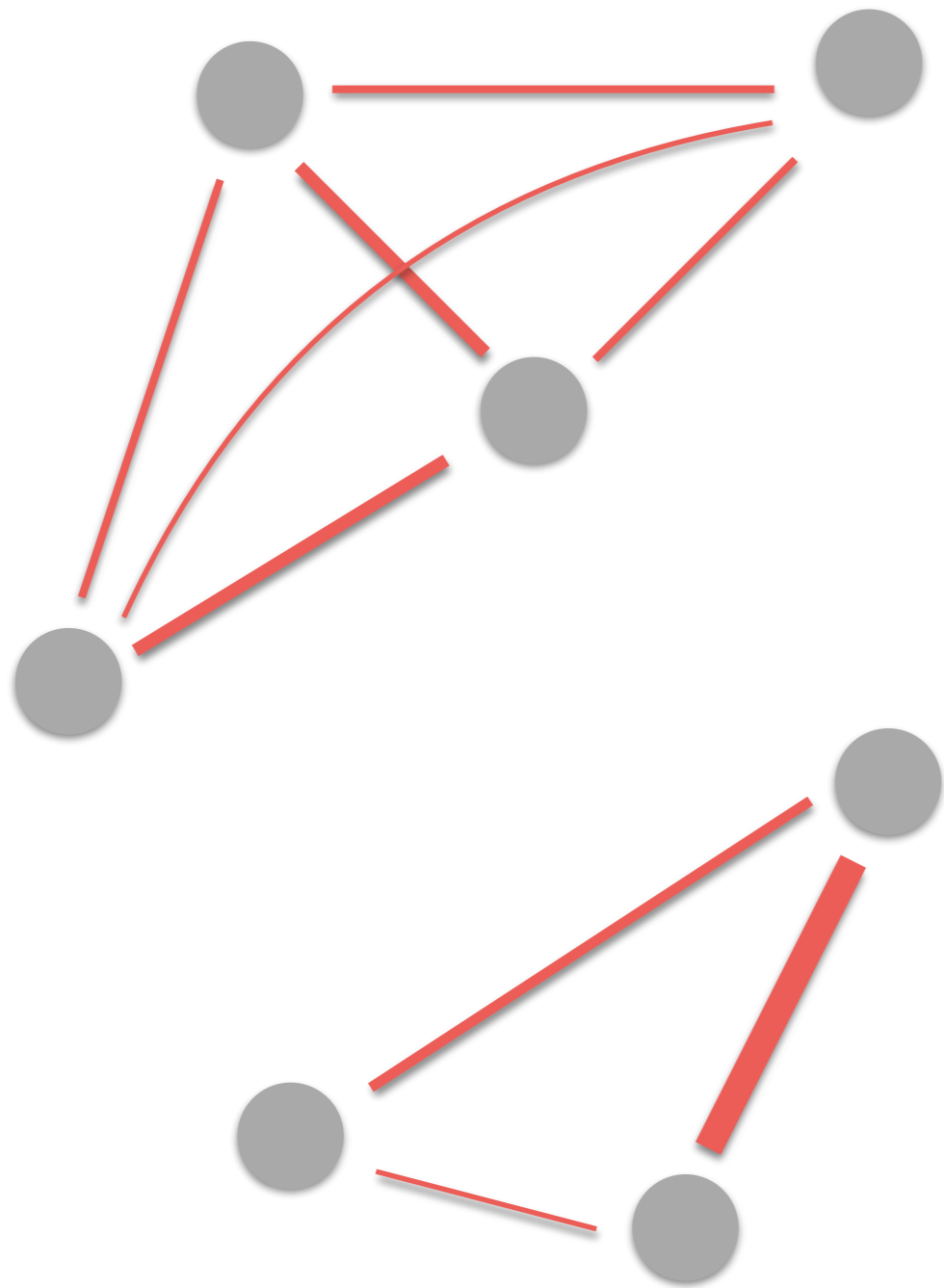
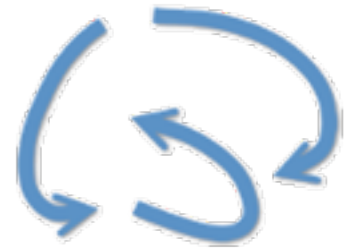
Structural connectome



Brain tractography by DTI (Filler 2009)

Inter-areal anatomical connections (SC)

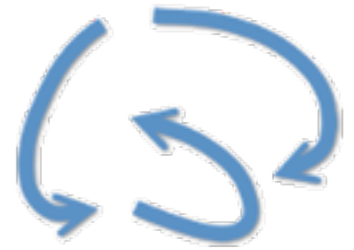
Functional connectome



Resting state fluctuations (Fox & Greicius 2010)

*Multi-areal activity
correlation patterns (FC)*

Aging

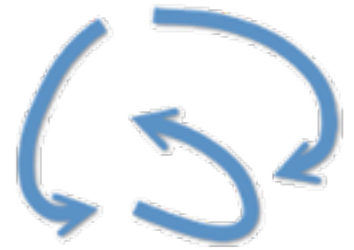


Titiano, *Le Età dell'Uomo*

- Effects on cognitive performance and behavior...
 - ➔ *Selective attention, attention switching*
 - ➔ *Working memory content manipulation*
 - ➔ *Salthouse's theory of information processing slowing down*
- but also, **structural alterations**
 - ➔ *e.g., decreased path-efficiency, "disconnection"*
- Resting state **functional connectivity alterations**
 - ➔ *Within and between RSNs*



More Omes?



From the connectome to the “dynome”

(Kopell et al. 2014)



Connect
Gnome

Neuron
Perspective

Beyond the Connectome: The Dynome

Nancy J. Kopell,^{1,*} Howard J. Gritton,² Miles A. Whittington,³ and Mark A. Kramer¹

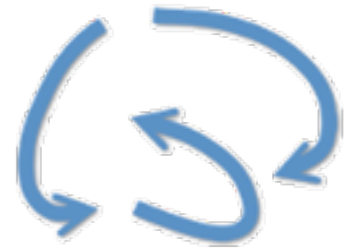
¹Department of Mathematics and Statistics, Boston University, Boston, MA 02215, USA
²Department of Biomedical Engineering, Boston University, Boston, MA 02215, USA
³The Hull York Medical School, University of York, Heslington, York YO10 5DD, UK
*Correspondence: nk@math.bu.edu
<http://dx.doi.org/10.1016/j.neuron.2014.08.016>



Dyn
Gnome



Chronnect
Gnome



From the “dynome” to the “chronnectome”

(Calhoun et al. 2014)



Connect
Gnome

The Chronnectome: Time-Varying Connectivity Networks as the Next Frontier in fMRI Data Discovery

Vince D. Calhoun,^{1,2,*} Robyn Miller,¹ Godfrey Pearlson,⁴ and Tulay Adalı³

¹The Mind Research Network & LBERI, Albuquerque, NM 87106, USA

²Department of ECE, University of New Mexico, Albuquerque, NM 87131, USA

³Department of CSEE, University of Maryland, Baltimore County, Baltimore, MD 21250, USA

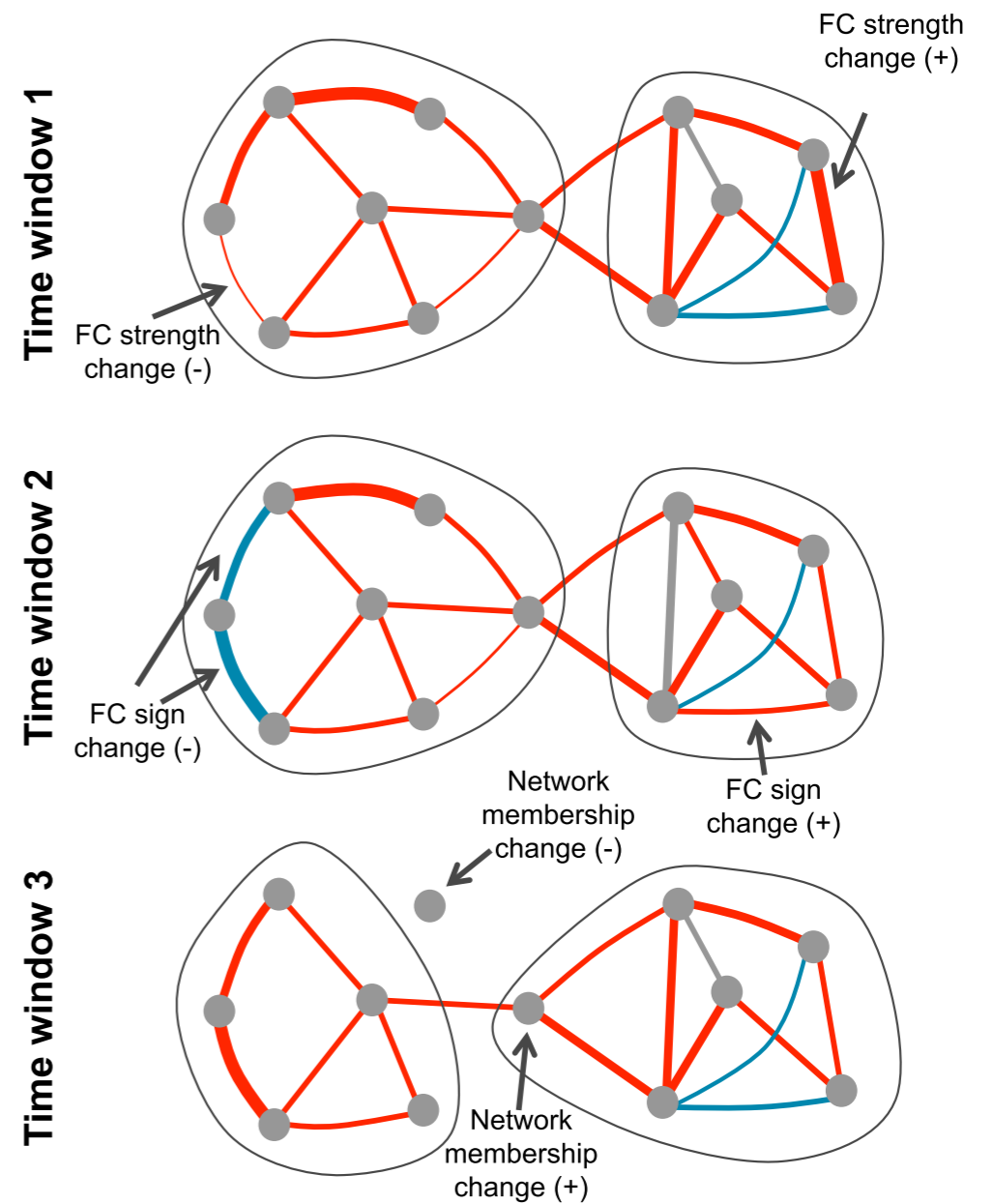
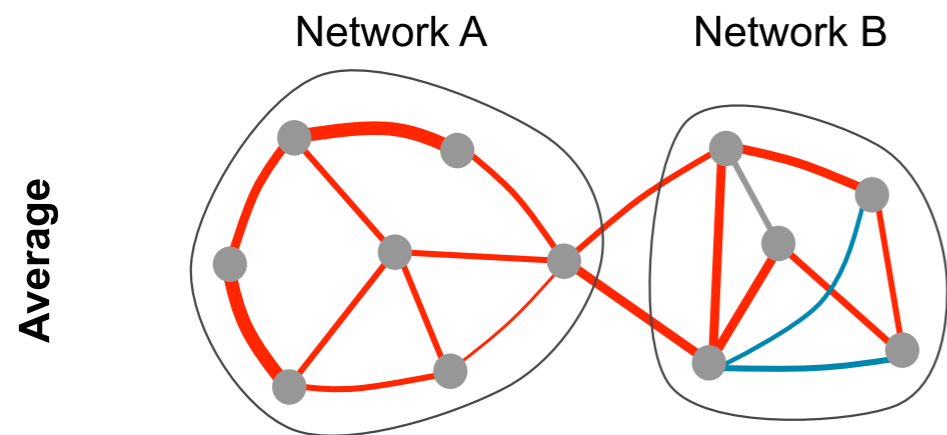
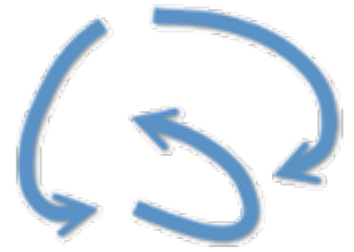
⁴Olin Neuropsychiatry Research Center, Hartford, CT 06114, USA

*Correspondence: vcalhoun@unm.edu



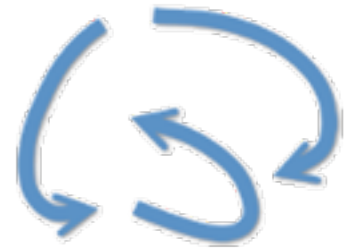
Dyn
Gnome

Time-varying FC

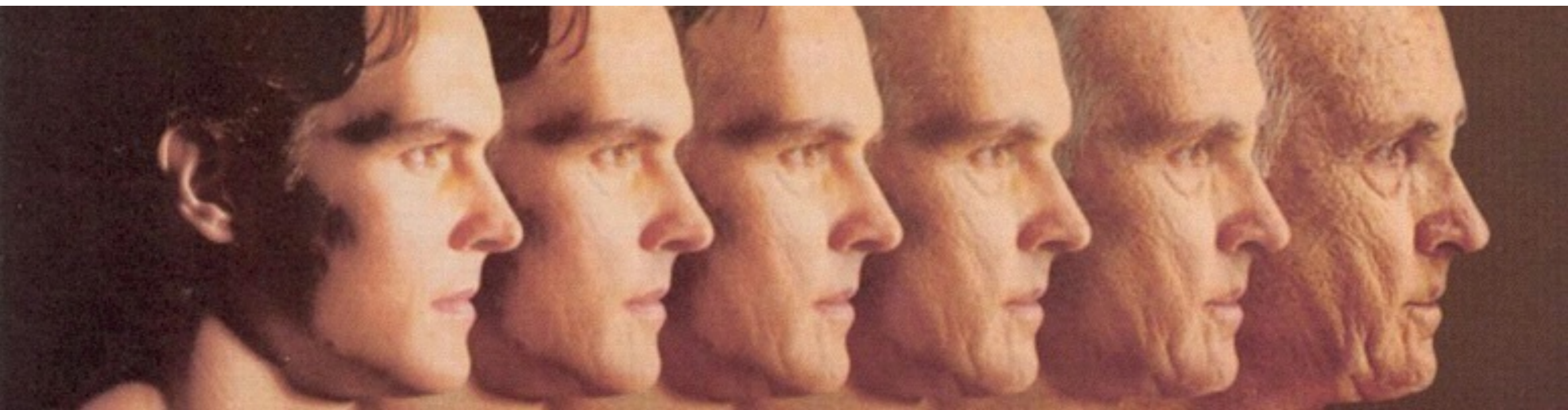


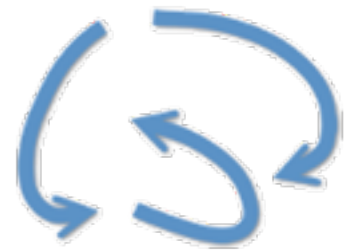
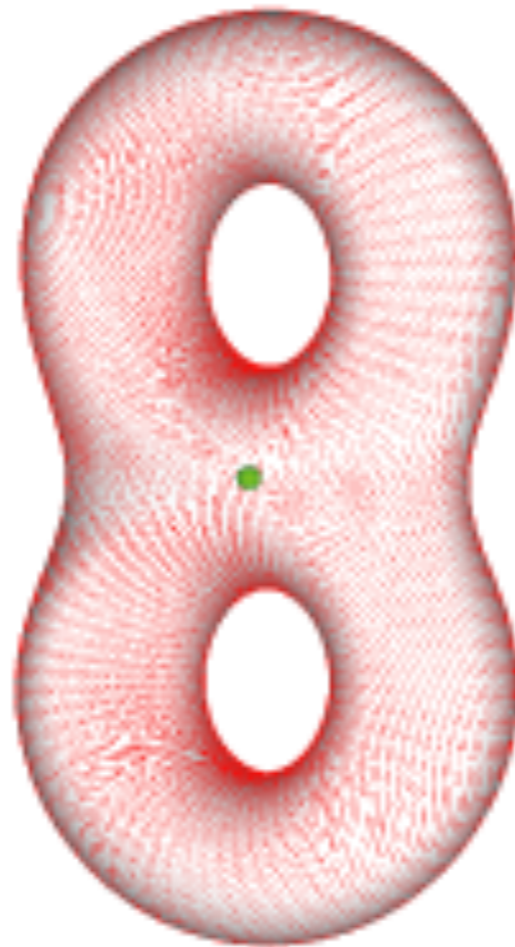
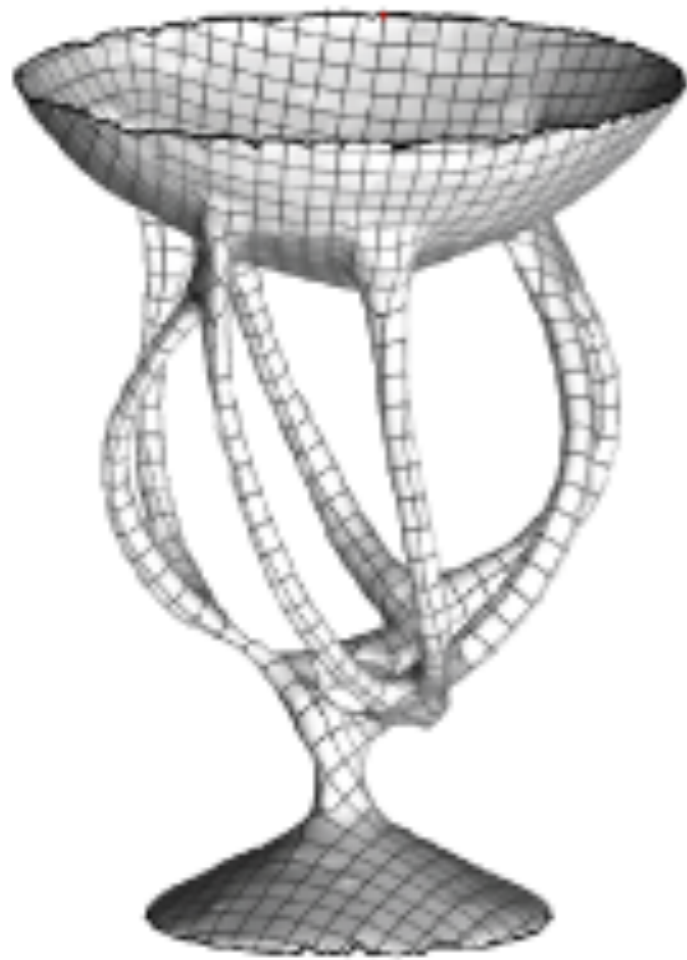
Functional Connectivity Dynamics, FCD

adapted from (Hutchison et al. 2013)



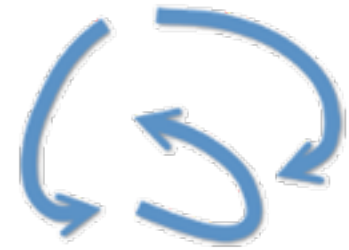
Does Functional
Connectivity Dynamics
provide better
biomarkers of aging?





The topolome
does not exist yet,
but...





Extracting insights from the shape of complex data using topology

P. Y. Lum¹, G. Singh¹, A. Lehman¹, T. Ishkanov¹, M. Vejdemo-Johansson², M. Alagappan¹, J. Carlsson³ & G. Carlsson^{1,4}

SUBJECT AREAS:
APPLIED MATHEMATICS
COMPUTATIONAL SCIENCE
SCIENTIFIC DATA
SOFTWARE

¹Ayasdi Inc., Palo Alto, CA, ²School of Computer Science, Jack Cole Building, North Haugh, St. Andrews KY16 9SX, Scotland, United Kingdom, ³Industrial and Systems Engineering, University of Minnesota, 111 Church St. SE, Minneapolis, MN 55455, USA, ⁴Department of Mathematics, Stanford University, Stanford, CA, 94305, USA.

Received
13 September 2012

Accepted
6 December 2012

Published
7 February 2013

This paper applies topological methods to study complex high dimensional data sets by extracting shapes (patterns) and obtaining insights about them. Our method combines the best features of existing standard methodologies such as principal component and cluster analyses to provide a geometric representation of complex data sets. Through this hybrid method, we often find subgroups in data sets that traditional methodologies fail to find. Our method also permits the analysis of individual data sets as well as the analysis of relationships between related data sets. We illustrate different kinds of data, namely gene expression from the House of Representatives and player performance data from the data which are more refined than those produced by

Ayasdi company website

Lum et al., Scientific Reports 2013

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The secret sauce behind Ayasdi's machine intelligence platform is Topological Data Analysis. TDA is the most powerful technique ever developed for advanced analytics of big data and complex data.

START WITH ANSWERS



Clique topology reveals intrinsic geometric structure in neural correlations

Chad Giusti^{a,b}, Eva Pastalkova^c, Carina Curto^{b,d,1}, and Vladimir Itskov^{b,d,1,2}

^aWarren Center for Network and Data Science, Departments of Bioengineering and Mathematics, University of Pennsylvania, Philadelphia, PA 19104; ^bDepartment of Mathematics, University of Nebraska, Lincoln, NE 68588; ^cJanelia Research Campus, Howard Hughes Medical Institute, Ashburn, VA 20147; and ^dDepartment of Mathematics, The Pennsylvania State University, University Park, PA 16802

Edited by William Bialek, Princeton University, Princeton, NJ, and approved September 23, 2015 (received for review April 28, 2015)

Detecting meaningful structure in neural activity and connectivity data is challenging in the presence of hidden nonlinearities, where traditional eigenvalue-based methods may be misleading. We introduce a novel approach to matrix analysis, called clique topology, that extracts features of the data invariant under nonlinear monotone transformations. These features can be used to detect both random and geometric structure, and depend only on the relative ordering of matrix entries. We then analyzed the activity of pyramidal neurons in rat hippocampus, recorded while the animal was exploring a 2D environment, and confirmed that

should be invariant under matrix transformations of the following form:

$$C_{ij} = f(A_{ij}), \quad [1]$$

where f is a nonlinear monotonic function (Fig. 1A). In the case of hippocampal place cells, f captures the manner in which pairwise correlations C_{ij} decrease with distance between place field centers (3). In less studied contexts, the represented stimuli—and the function f —may be completely unknown



Insights into Brain Architectures from the Homological Scaffolds of Functional Connectivity Networks

Louis-David Lord¹, Paul Expert², Henrique M. Fernandes^{1,3}, Giovanni Petri⁴, Tim J. Van Hartevelt^{1,3}, Francesco Vaccarino^{4,5}, Gustavo Deco^{6,7}, Federico Turkheimer² and Morten L. Kringelbach^{1,3*}

¹Hedonia Research Group, Department of Psychiatry, University of Oxford, Oxford, UK, ²Department of Neuroimaging, Institute of Psychiatry, King's College London, London, UK, ³Center for Music in the Brain, Aarhus University, Aarhus, Denmark, ⁴Institute for Scientific Interchange (ISI Foundation), Torino, Italy, ⁵Department of Mathematical Sciences, Politecnico di Torino, Torino, Italy, ⁶Center for Brain and Cognition, Universitat Pompeu Fabra, Barcelona, Spain, ⁷Institució Catalana de la Recerca i Estudis Avançats, Universitat Pompeu Fabra, Barcelona, Spain

In recent years, the application of network analysis to neuroimaging data has provided useful insights about the brain's functional and structural organization in both health and disease. This has proven a significant paradigm shift from the study of individual brain regions in isolation. Graph-based models of the brain consist of vertices, which



Cite this article: Petri G, Expert P, Turkheimer F, Carhart-Harris R, Nutt D, Hellyer PJ, Vaccarino F. 2014 Homological scaffolds of brain functional networks. *J. R. Soc. Interface* **11**: 20140873.
<http://dx.doi.org/10.1098/rsif.2014.0873>

Homological scaffolds of brain functional networks

G. Petri¹, P. Expert², F. Turkheimer², R. Carhart-Harris³, D. Nutt³, P. J. Hellyer⁴ and F. Vaccarino^{1,5}

¹ISI Foundation, Via Alassio 11/c, 10126 Torino, Italy
²Centre for Neuroimaging Sciences, Institute of Psychiatry, Kings College London, De Crespigny Park, London SE5 8AF, UK
³Centre for Neuropsychopharmacology, Imperial College London, London W12 0NN, UK
⁴Computational, Cognitive and Clinical Neuroimaging Laboratory, Division of Brain Sciences, Imperial College London, London W12 0NN, UK
⁵Dipartimento di Scienze Matematiche, Politecnico di Torino, C.so Duca degli Abruzzi no 24, Torino 10129, Italy

Networks, as efficient representations of complex systems, have appealed to scientists for a long time and now permeate many areas of science, including neuroimaging (Bullmore and Sporns 2009 *Nat. Rev. Neurosci.* **10**, 186–198. (doi:10.1038/nrn2618)). Traditionally, the structure of complex networks has been studied through their statistical properties and metrics concerned with

J Comput Neurosci (2016) 41:1–14
DOI 10.1007/s10827-016-0608-6

Two's company, three (or more) is a simplex Algebraic-topological tools for understanding higher-order structure in neural data

Chad Giusti^{1,2} · Robert Ghrist^{1,3} · Danielle S. Bassett^{2,3}

Closures and Cavities in the Human Connectome

Ann Sizemore^{1,2}, Chad Giusti¹, Richard F. Betzel¹, and Danielle S. Bassett^{1,3,*}

¹Department of Bioengineering, University of Pennsylvania, Philadelphia, PA 19041 USA
²Broad Institute, Harvard University and the Massachusetts Institute of Technology, Cambridge, MA 02142 USA
³Department of Electrical & Systems Engineering, University of Pennsylvania, Philadelphia, PA 19041 USA
*To whom correspondence should be addressed: dsb@seas.upenn.edu

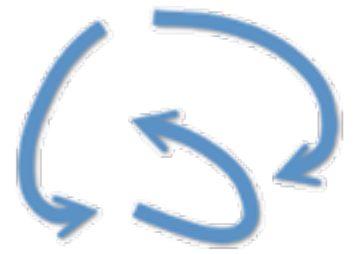


Biomedicine

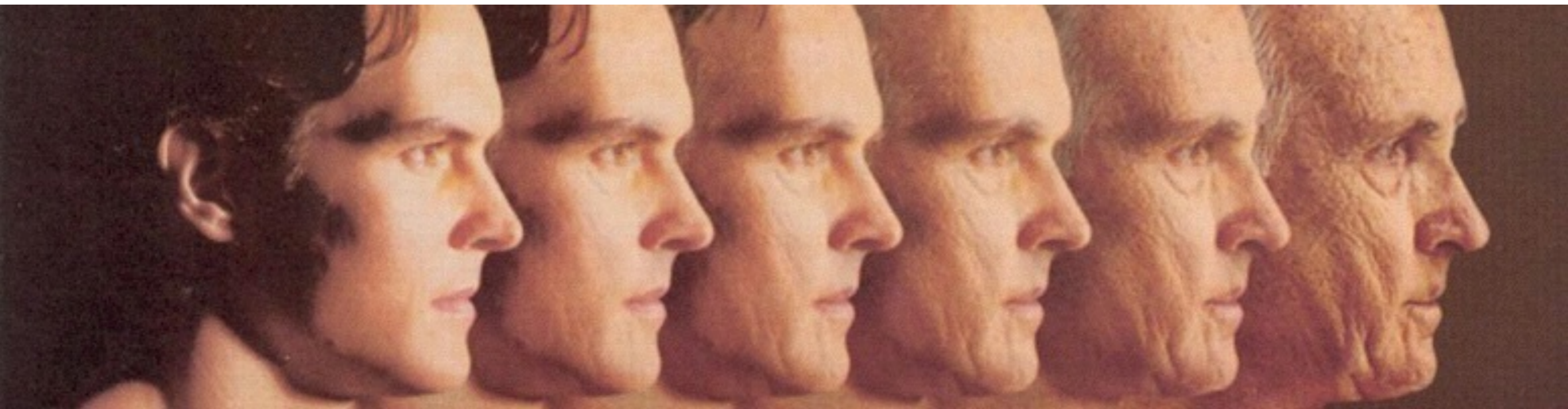
How the Mathematics of Algebraic Topology Is Revolutionizing Brain Science

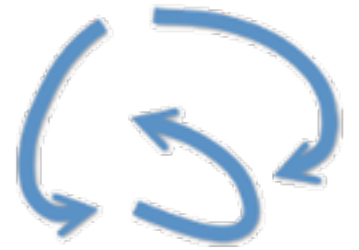
Nobody understands the brain's wiring diagram, but the tools of algebraic topology are beginning to tease it apart.

by Emerging Technology from the arXiv August 24, 2016

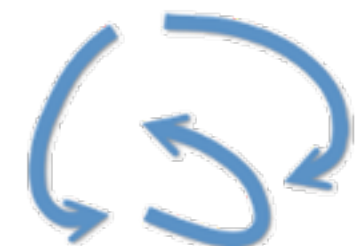


Does topological
techniques provide
better biomarkers of
aging?

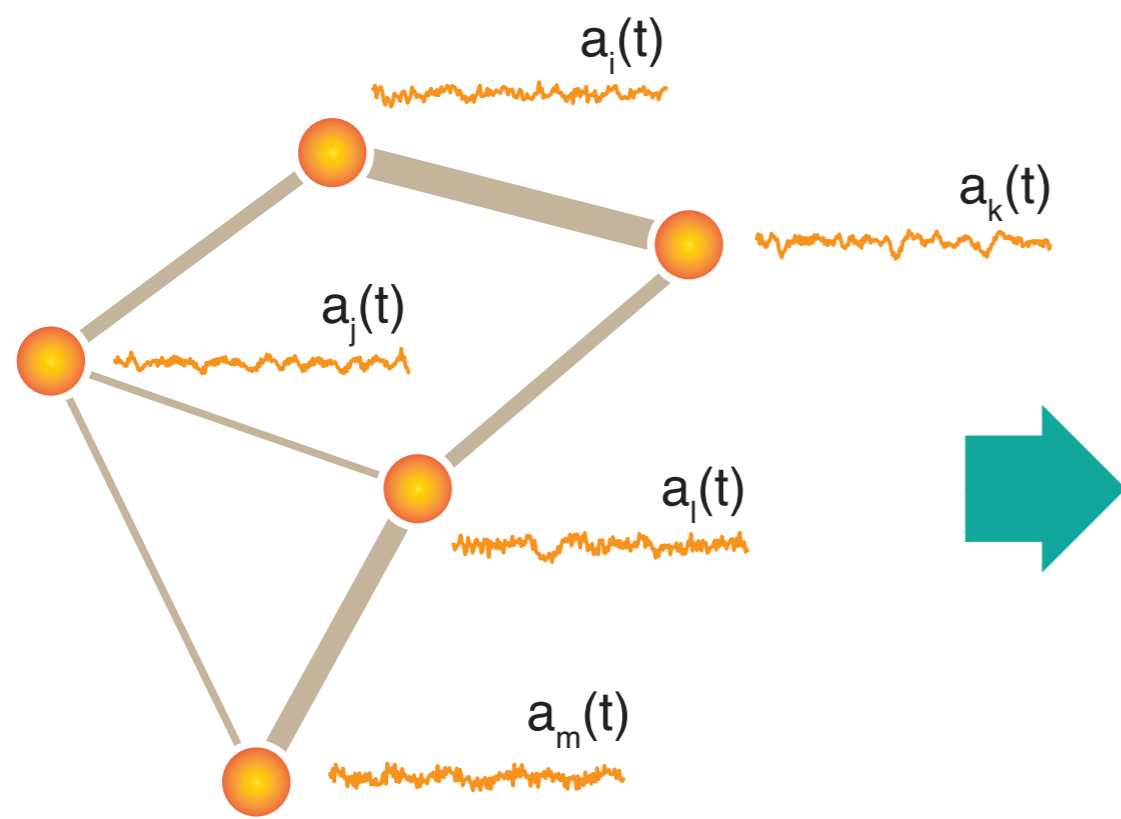




See later about the
meaning of “better”...

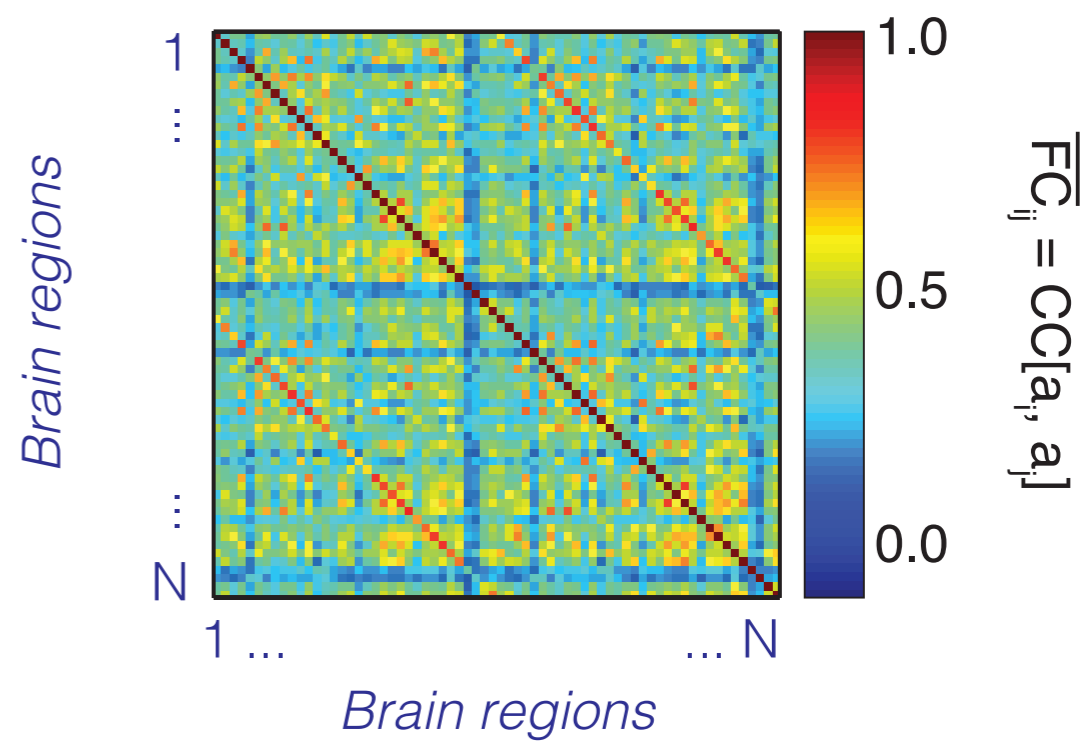


Time-series of **NODE** activity
(e.g. resting-state BOLD)

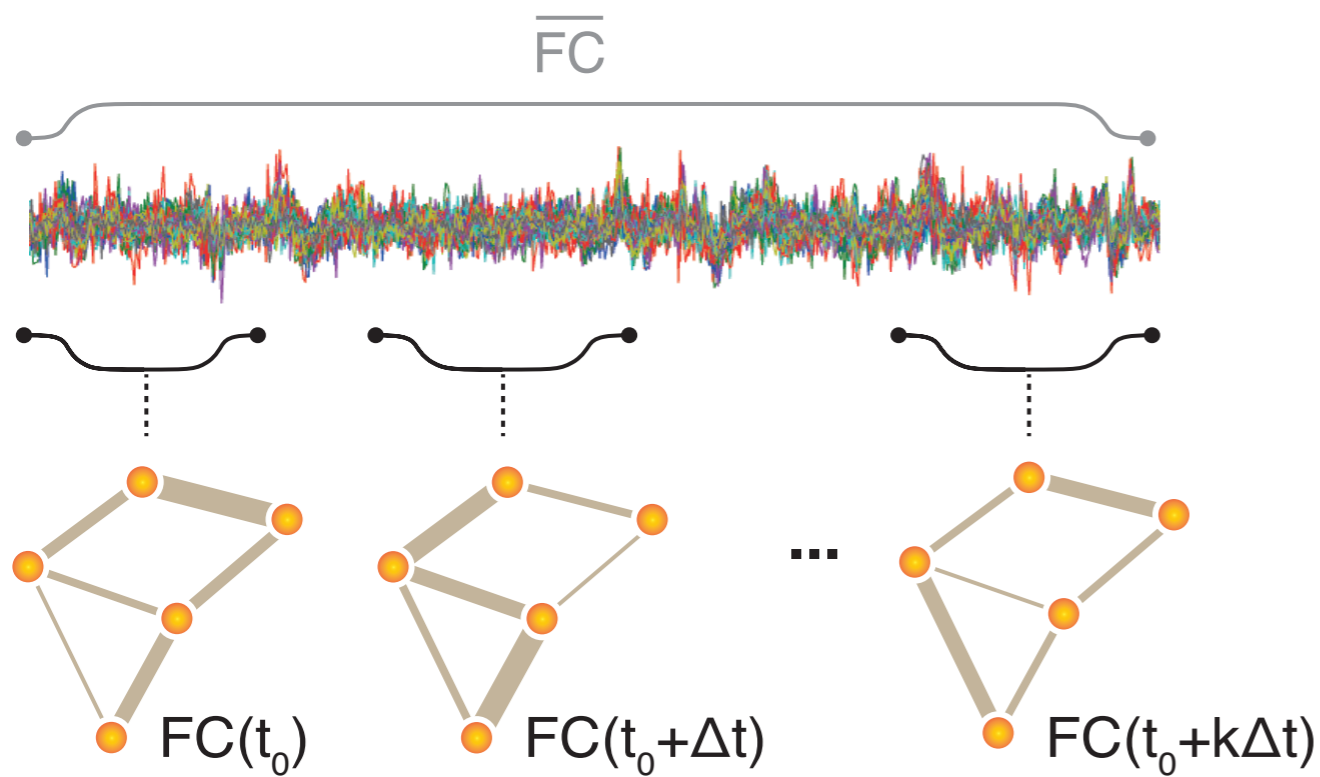


Link = correlation between
node time-series

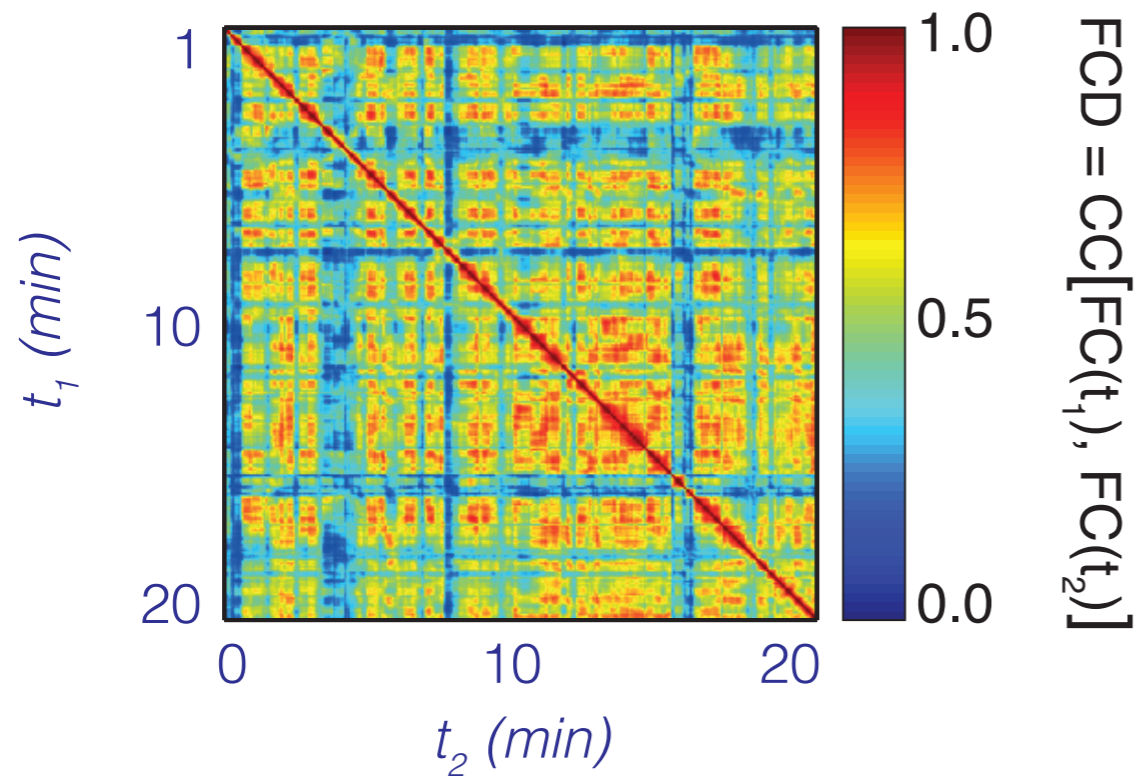
Functional Connectivity (FC)



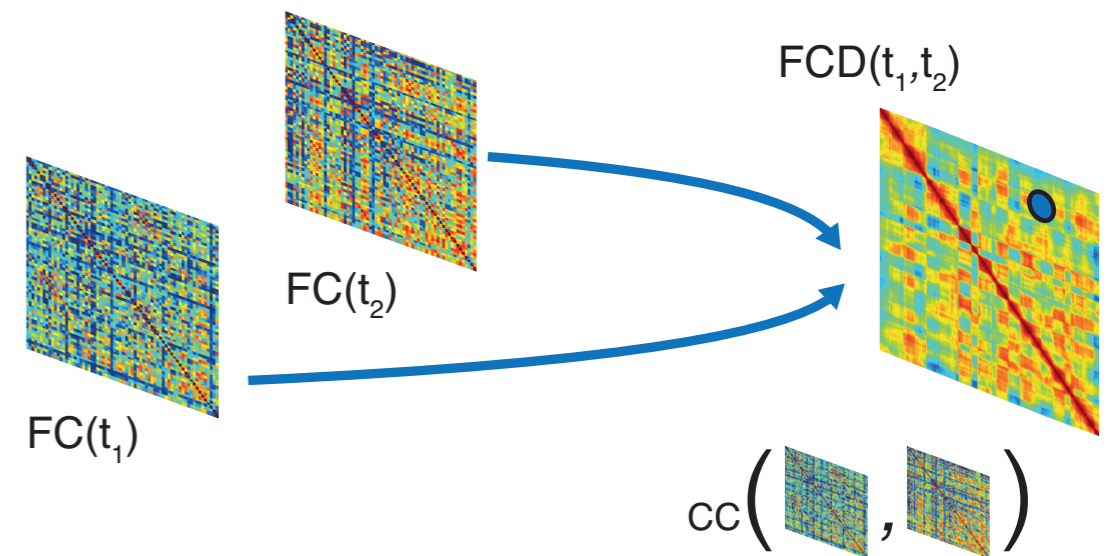
$N \times N$ matrix of
inter-node correlations



FC Dynamics



Time-series of
INTER-NODE CORRELATIONS

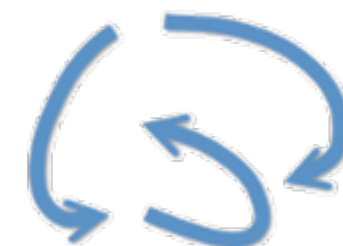


FUNCTIONAL CONNECTIVITY DYNAMICS
(FCD matrices)

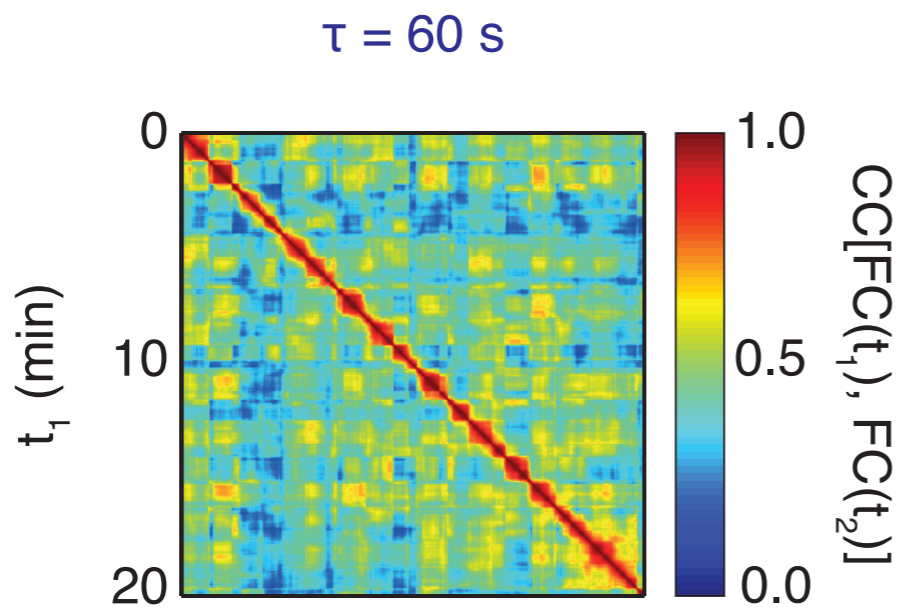
Correlation between networks at
different times

OLDER...

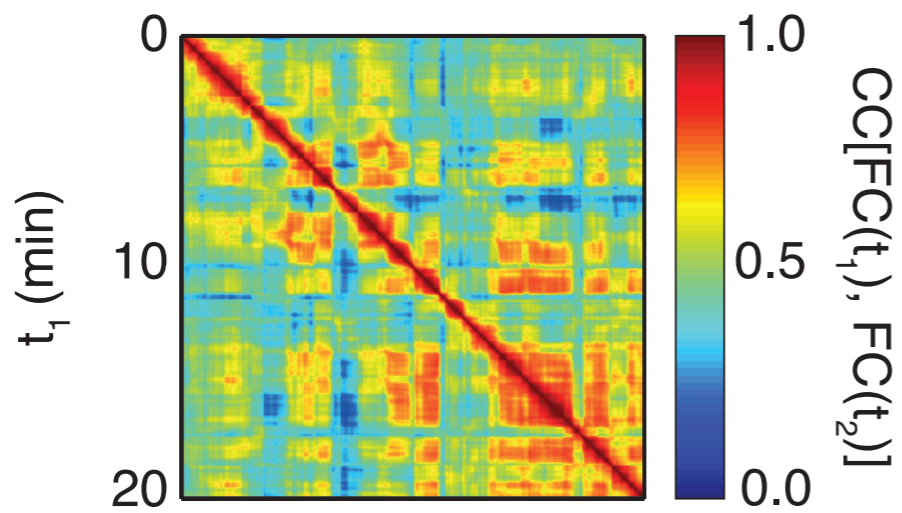




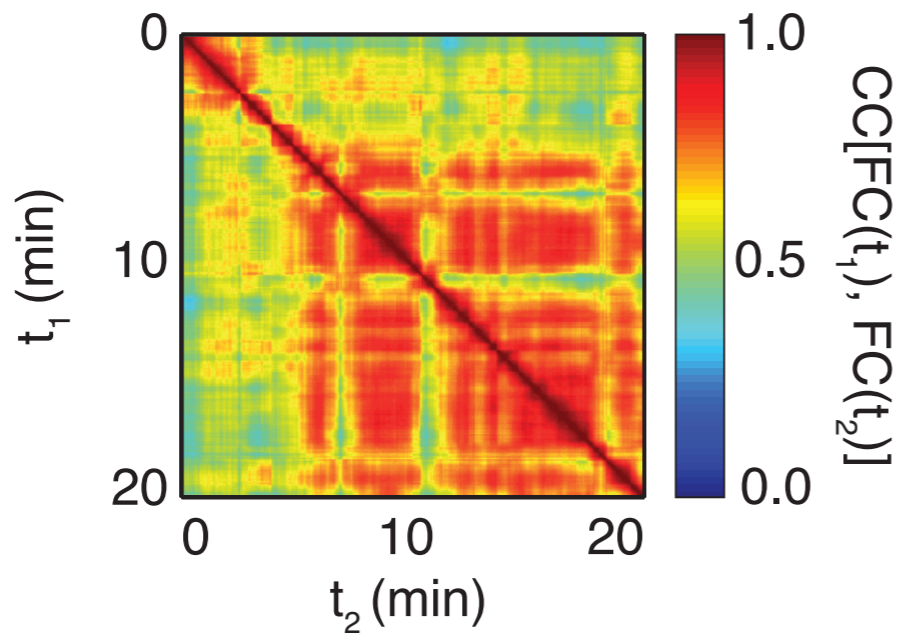
Subject A
(age 18 y)



Subject B
(age 56 y)



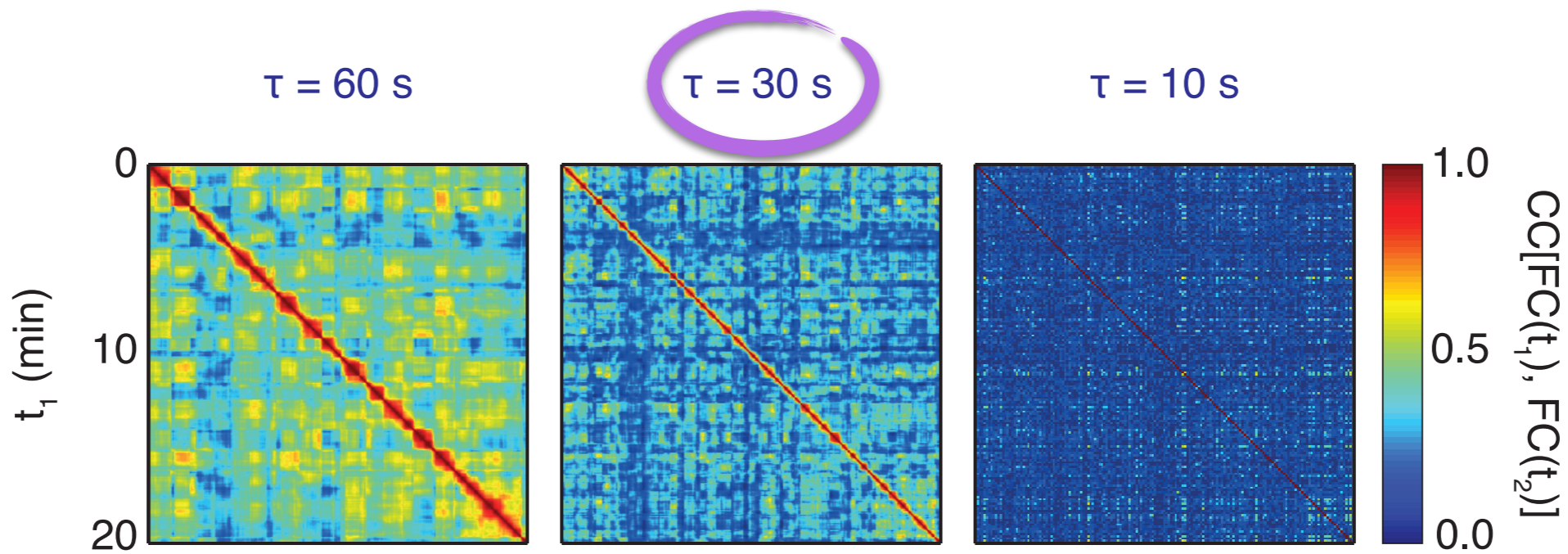
Subject C
(age 72 y)



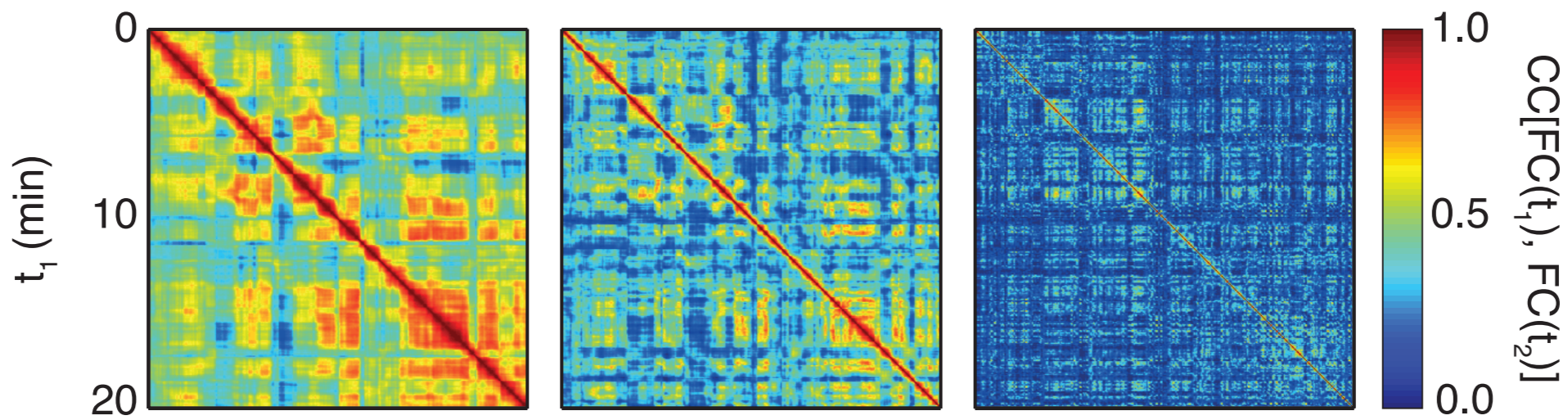
Petra Ritter
(Charité-BCCN, Berlin)

*DSI structural connectivity,
20 min rs BOLD
and simultaneous EEG
for 50 human subjects
through the adult lifespan*

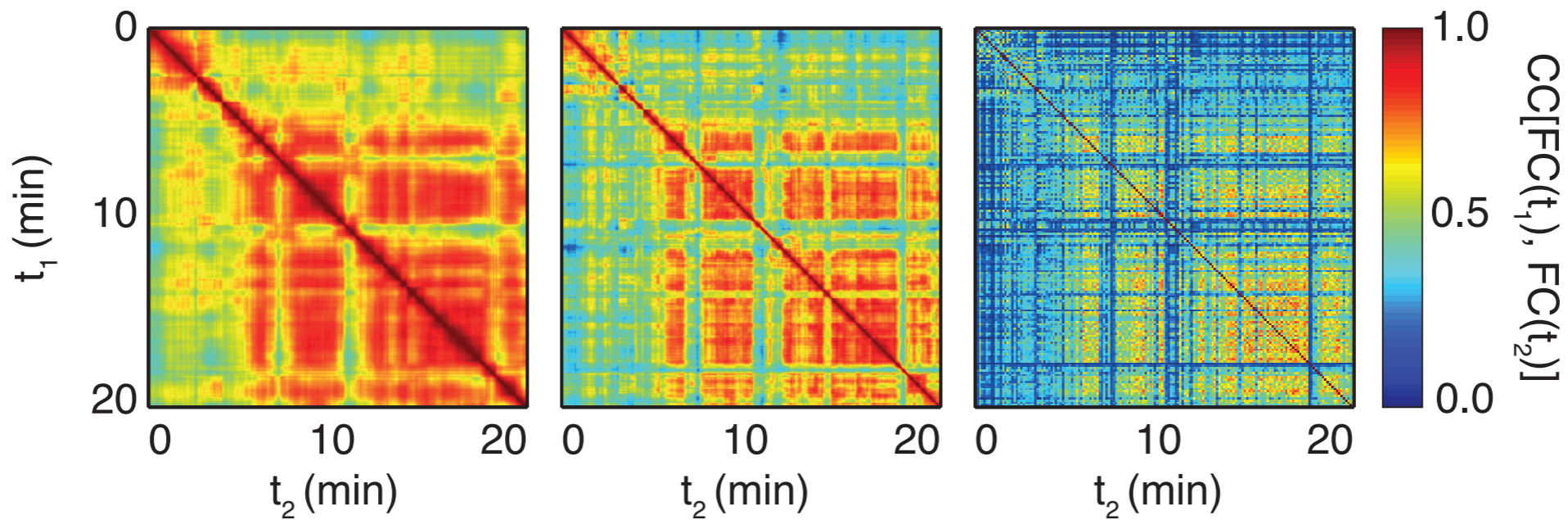
Subject A
(age 18 y)

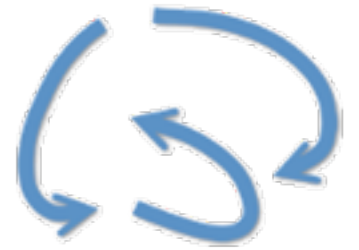


Subject B
(age 56 y)

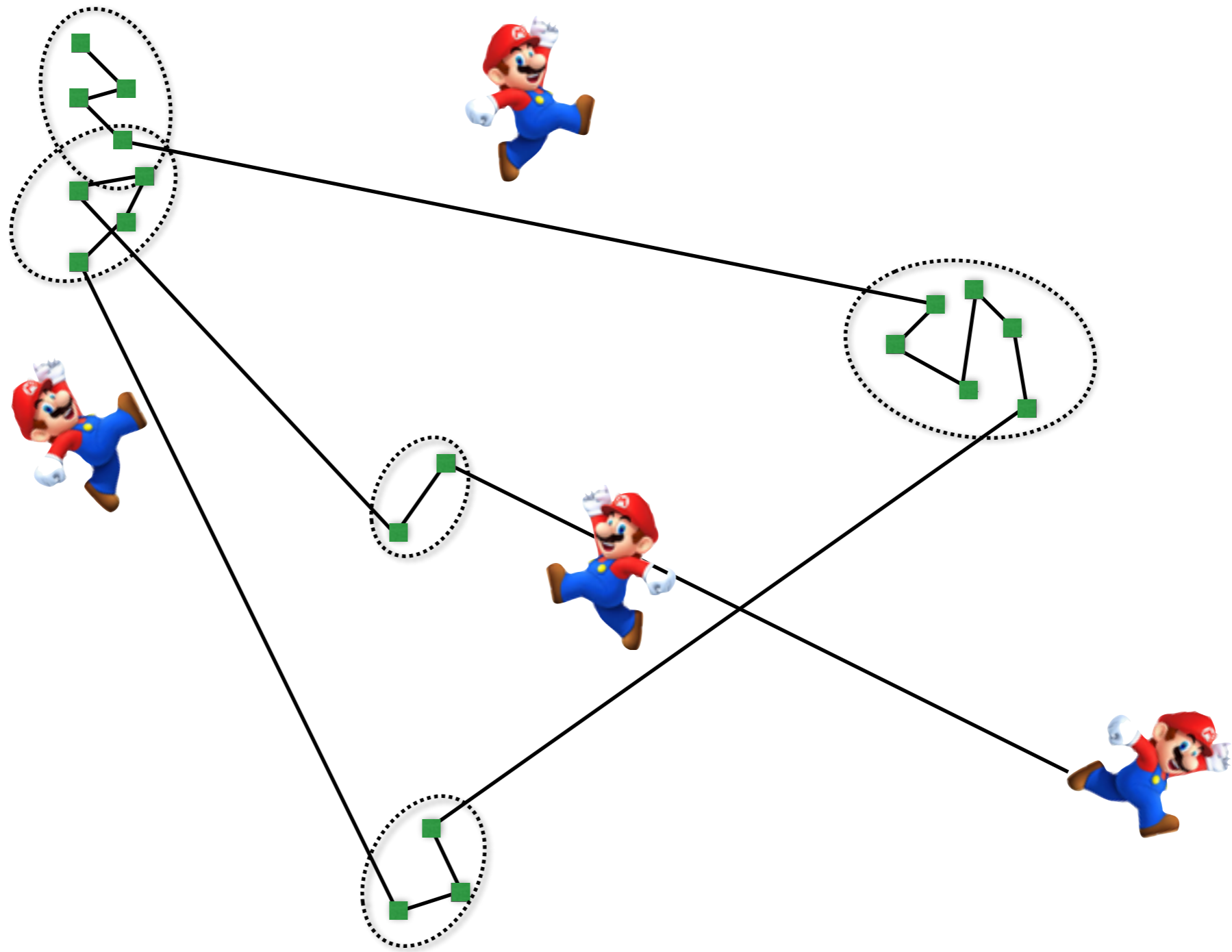


Subject C
(age 72 y)



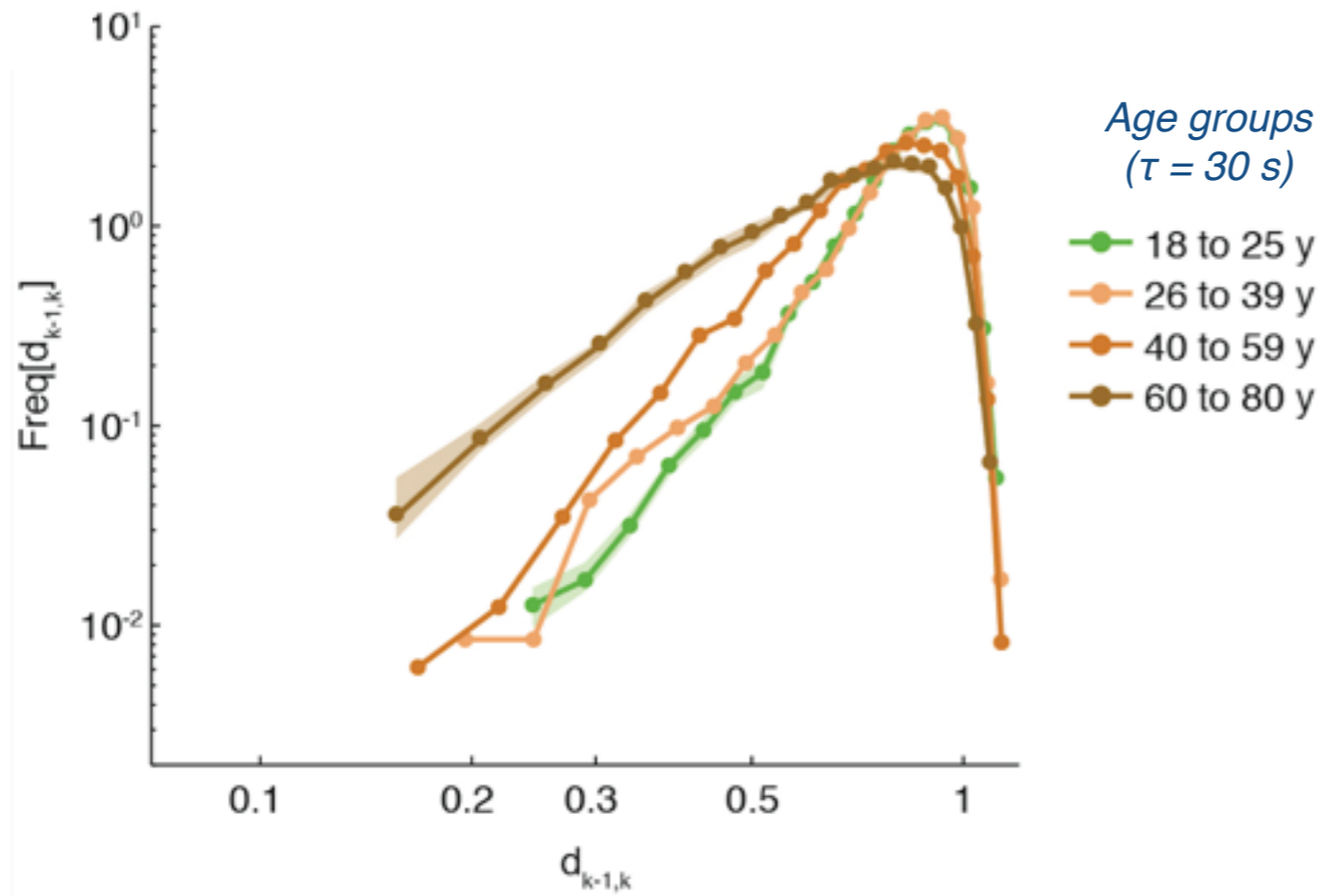


Let's quantify the reconfiguration of FC over time beyond visualization...



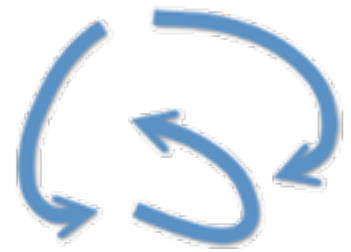
Steps in Functional
Connectivity space!

JUMP LENGTH DISTRIBUTION (for different age groups)

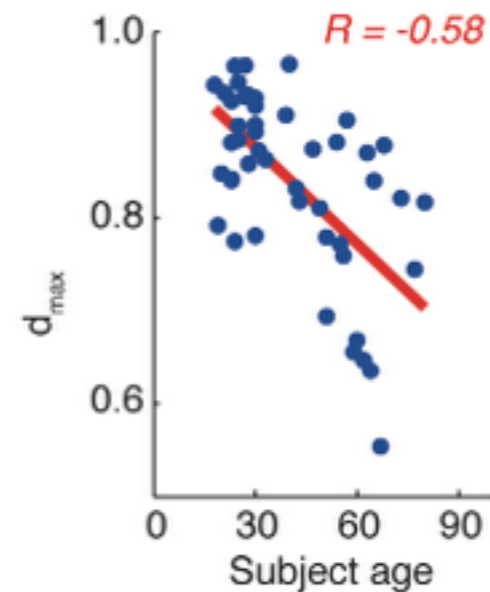
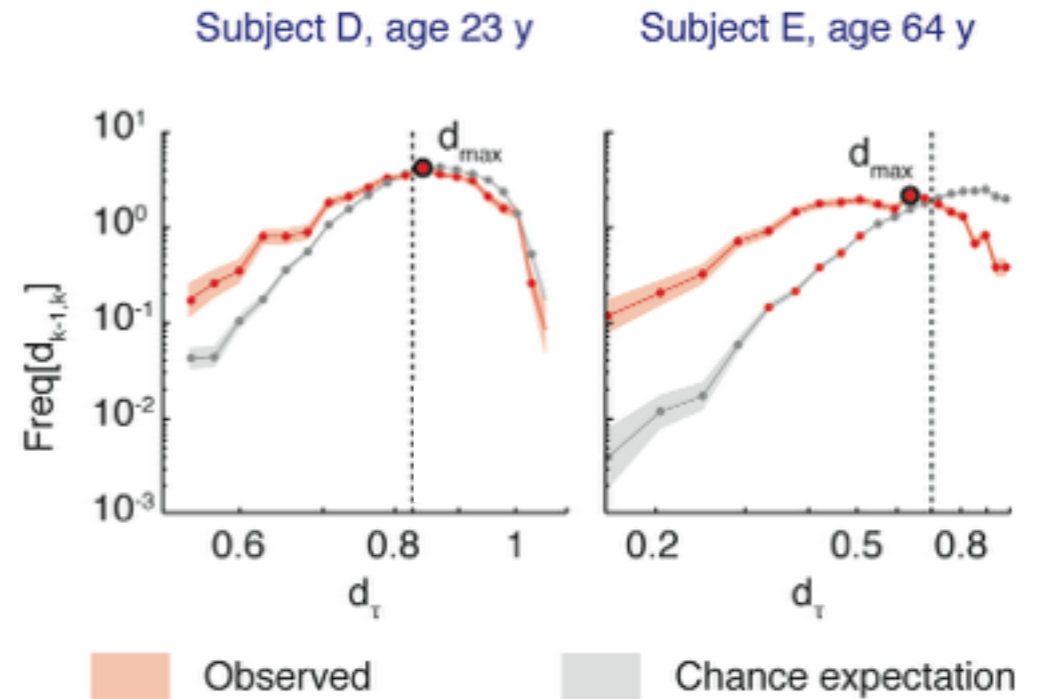


Step length distributions show a marked peak and (possibly) a "power-law" tail

TYPICAL STEP LENGTH



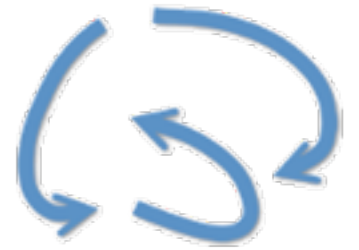
SINGLE-SUBJECT DISTRIBUTIONS



Typical step lengths anti-correlate with age

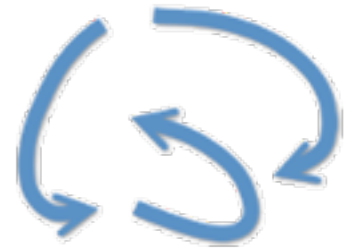
SLOWER...



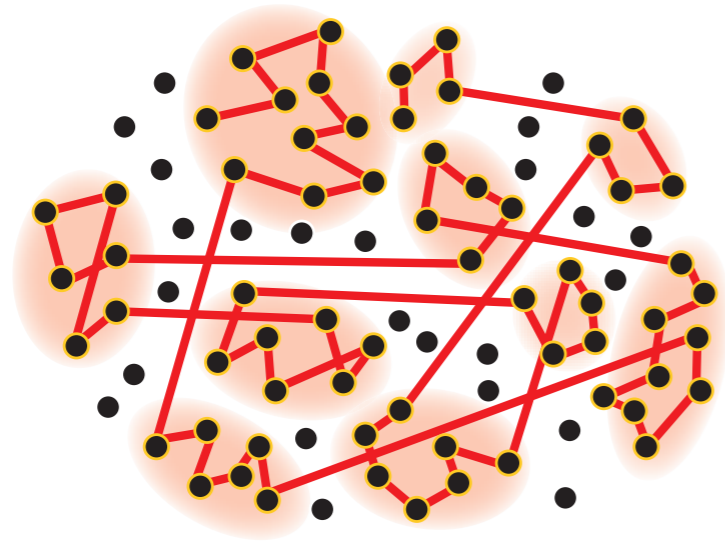


Conclusion 1

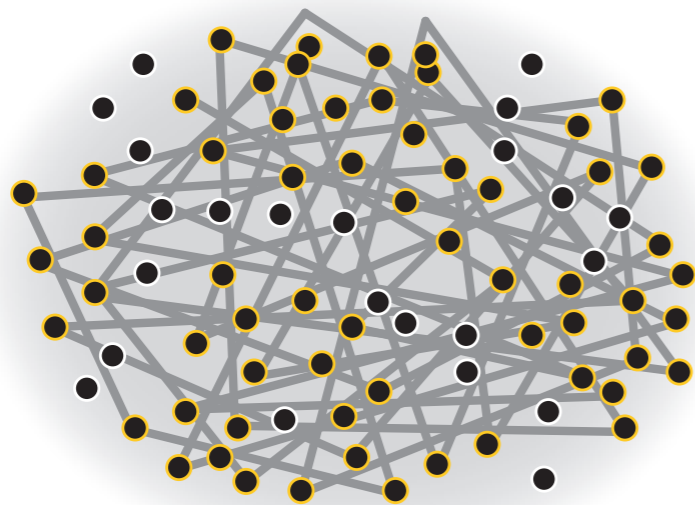
FCD slows down
with aging



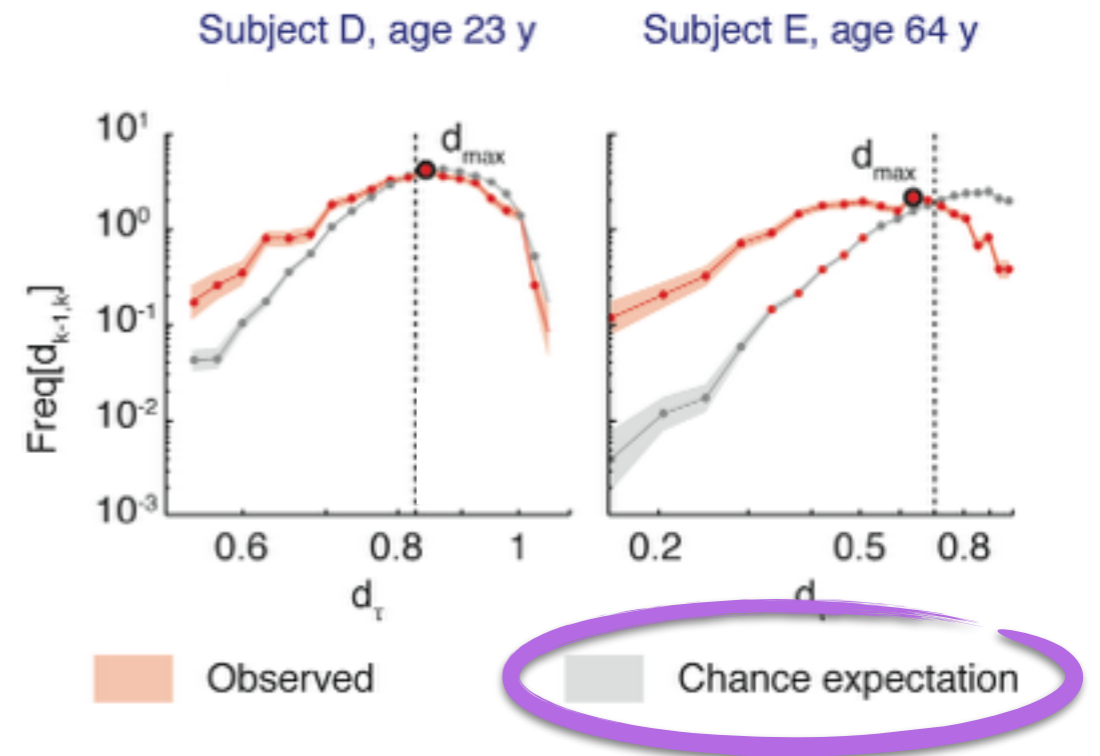
SINGLE-SUBJECT DISTRIBUTIONS



Empirical

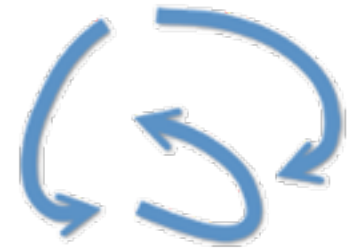


No seq.
correlations



*FC observations
preserved, but
destroyed sequential
correlations!*

Detrended Fluctuation analysis



Detrended fluctuation analysis

From Wikipedia, the free encyclopedia

Given a bounded [time series](#) x_t of length N , where $t \in \mathbb{N}$, integration or summation first converts this into an unbounded process X_t :

$$X_t = \sum_{i=1}^t (x_i - \langle x \rangle)$$

X_t is called cumulative sum or profile. This process converts, for example, an [i.i.d. white noise](#) process into a [random walk](#).

Next, X_t is divided into time windows of length n samples each, and a local [least squares](#) straight-line fit (the local trend) is calculated by minimising the least squared errors within each time window. Let Y_t be the series of straight line fits. Next, the root-mean-square deviation from the trend, the **fluctuation**, is calculated:

$$F(n) = \left[\frac{1}{N} \sum_{t=1}^N (X_t - Y_t)^2 \right]^{\frac{1}{2}}.$$

This detrending followed by fluctuation measurement process is repeated over a range of different window sizes n , and a [log-log graph](#) of n against $F(n)$ is constructed.

A straight line on this log-log graph indicates statistical [self-affinity](#) expressed as $F(n) \propto n^\alpha$. The scaling exponent α is calculated as the slope of a straight line fit to the log-log graph of n against $F(n)$ using least-squares. This exponent is a generalization of the [Hurst exponent](#). Because the expected displacement in an [uncorrelated random walk](#) of length N grows like \sqrt{N} , an exponent of $\frac{1}{2}$ would correspond to uncorrelated white noise. When the exponent is between 0 and 1, the result is [Fractional Brownian motion](#), with the precise value giving information about the series self-correlations:

- $\alpha < 1/2$: anti-correlated
- $\alpha \simeq 1/2$: uncorrelated, [white noise](#)
- $\alpha > 1/2$: correlated
- $\alpha \simeq 1$: 1/f-noise, [pink noise](#)
- $\alpha > 1$: non-stationary, unbounded
- $\alpha \simeq 3/2$: [Brownian noise](#)

Statistical self-affinity
Correlation function
as mean and
Fourier transform

Optimizing the success of random searches

G. M. Viswanathan*†‡, Sergey V. Buldyrev*, Shlomo Havlin*§, M. G. E. da Luz||¶, E. P. Raposo||# & H. Eugene Stanley*

* Center for Polymer Studies and Department of Physics, Boston University, Boston, Massachusetts 02215, USA

† International Center for Complex Systems and Departamento de Física Teórica e Experimental, Universidade Federal do Rio Grande do Norte, 59072-970, Natal-RN, Brazil

‡ Departamento de Física, Universidade Federal de Alagoas, 57072-970, Maceió-AL, Brazil

§ Gonda-Goldschmied Center and Department of Physics, Bar Ilan University, Ramat Gan, Israel

|| Lyman Laboratory of Physics, Harvard University, Cambridge, Massachusetts 02138, USA

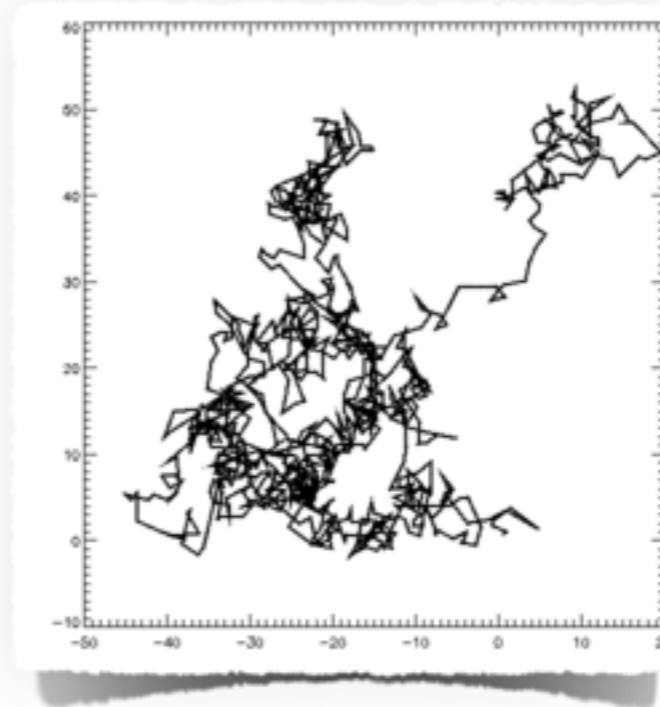
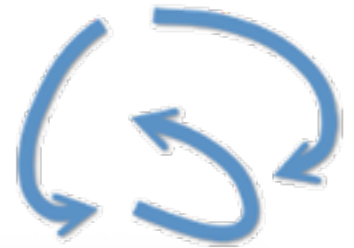
¶ Departamento de Física, Universidade Federal do Paraná, 81531-970, Curitiba-PR, Brazil

Laboratório de Física Teórica e Computacional, Departamento de Física, Universidade Federal de Pernambuco, 50670-901, Recife-PE, Brazil

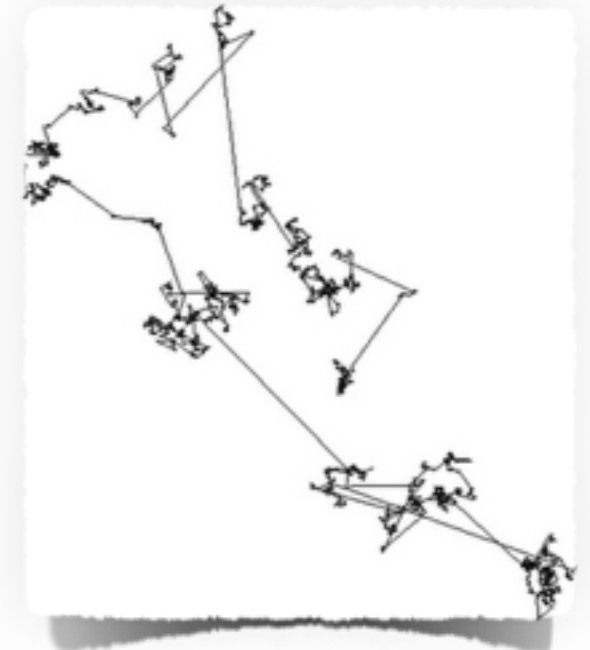
We address the general question of what is the best statistical strategy to adapt in order to search efficiently for randomly located objects ('target sites'). It is often assumed in foraging theory that the flight lengths of a forager have a characteristic scale: from this assumption gaussian, Rayleigh and other classical distributions with well-defined variances have arisen. However, such theories cannot explain the long-tailed power-law distributions^{1,2} of flight lengths or flight times³⁻⁶ that are observed experimentally. Here we study how the search efficiency depends on the probability distribution of flight lengths taken by a forager that can detect target sites only in its limited vicinity. We show that, when the target sites are sparse and can be visited any number of times, an inverse square power-law distribution of flight lengths, corresponding to Lévy flight motion, is an optimal strategy. We test the theory by analysing experimental foraging data on selected insect, mammal and bird species, and find that they are consistent with the predicted inverse square power-law distributions.

- $\alpha \simeq 1/2$: uncorrelated, white noise
- $\alpha > 1/2$: correlated
- $\alpha \simeq 1$: $1/f$ -noise, pink noise
- $\alpha > 1$: non-stationary, unbounded
- $\alpha \simeq 3/2$: Brownian noise

Random Fluctuation



“Classic” gaussian random walk



Levy-type walk

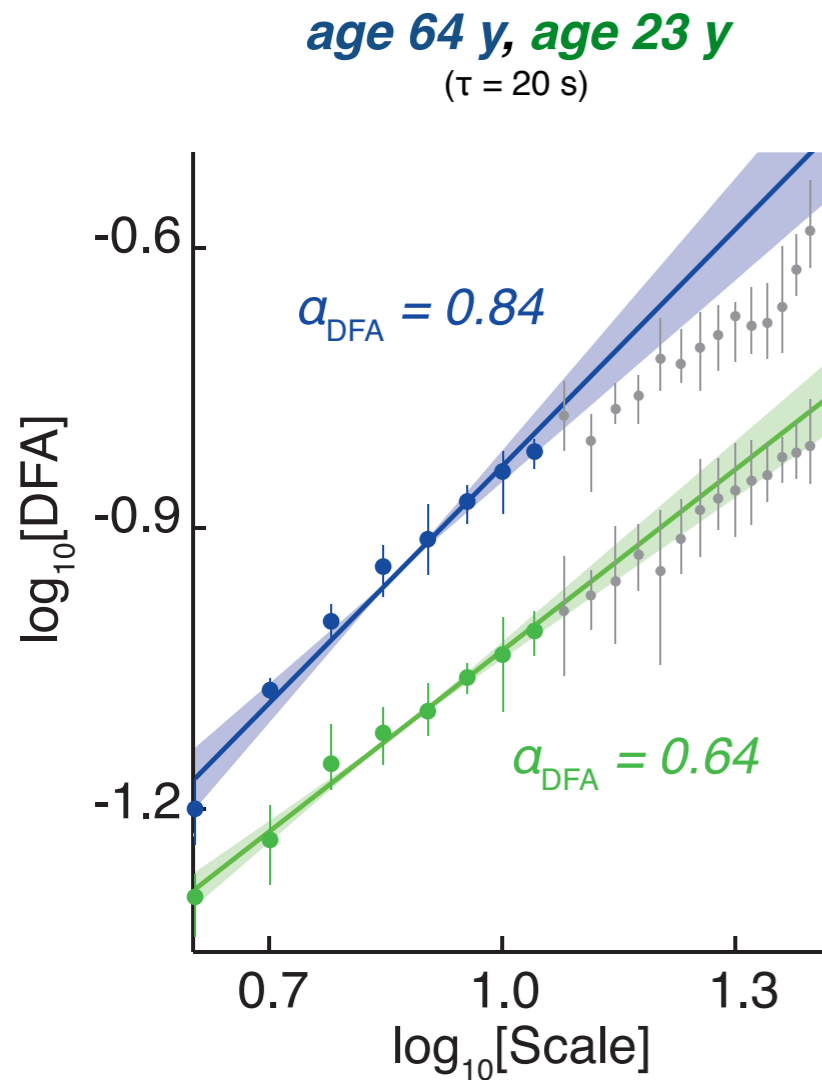
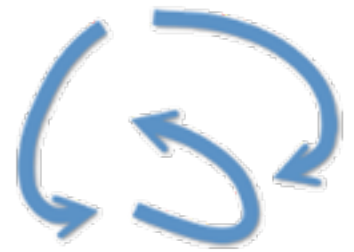


“Black death” in middle age

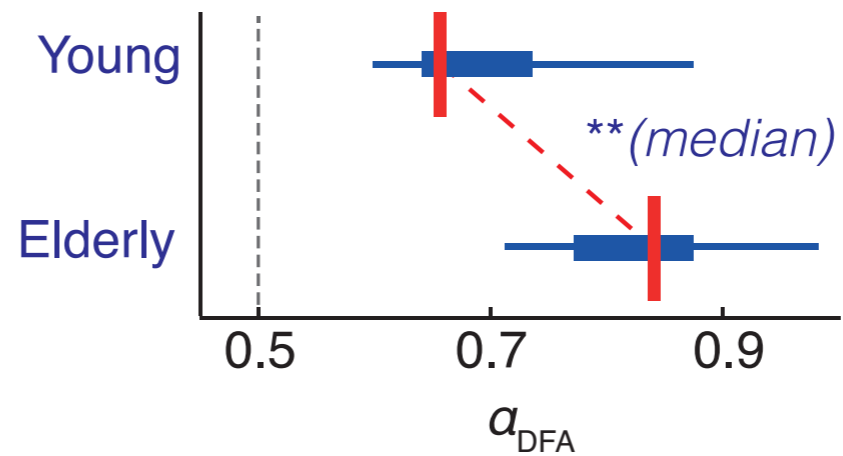


Contemporary epidemics

DFA of FCD and aging



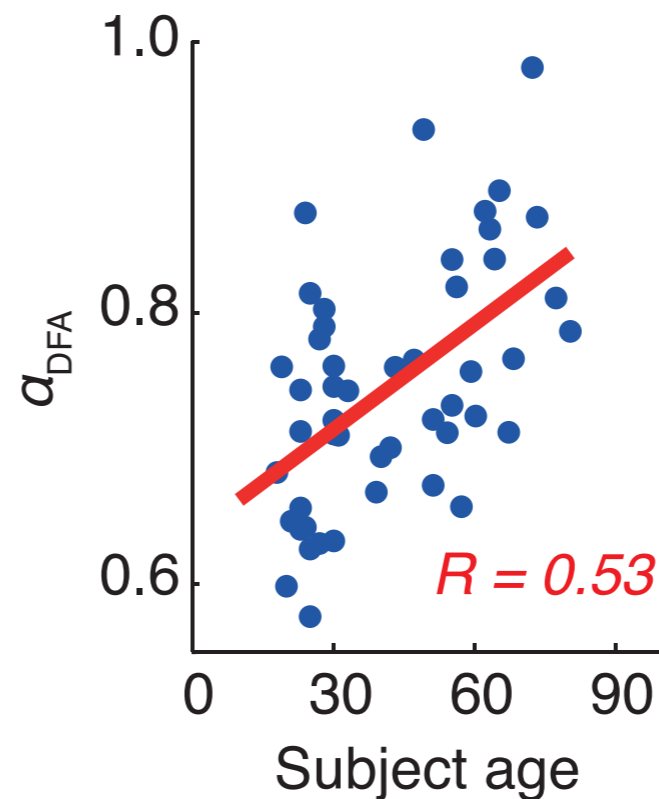
*Single-subject
DFA of FCD*



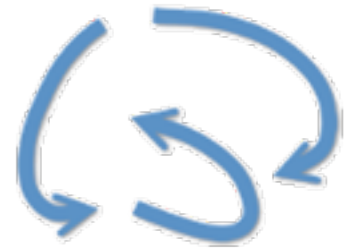
Inter-group comparison



*Thomas
Boudou*

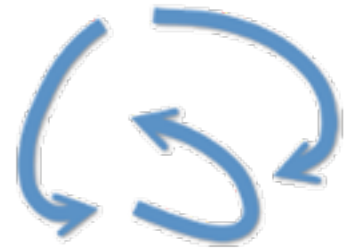


*Correlation
between DFA of FCD
exponent and age*

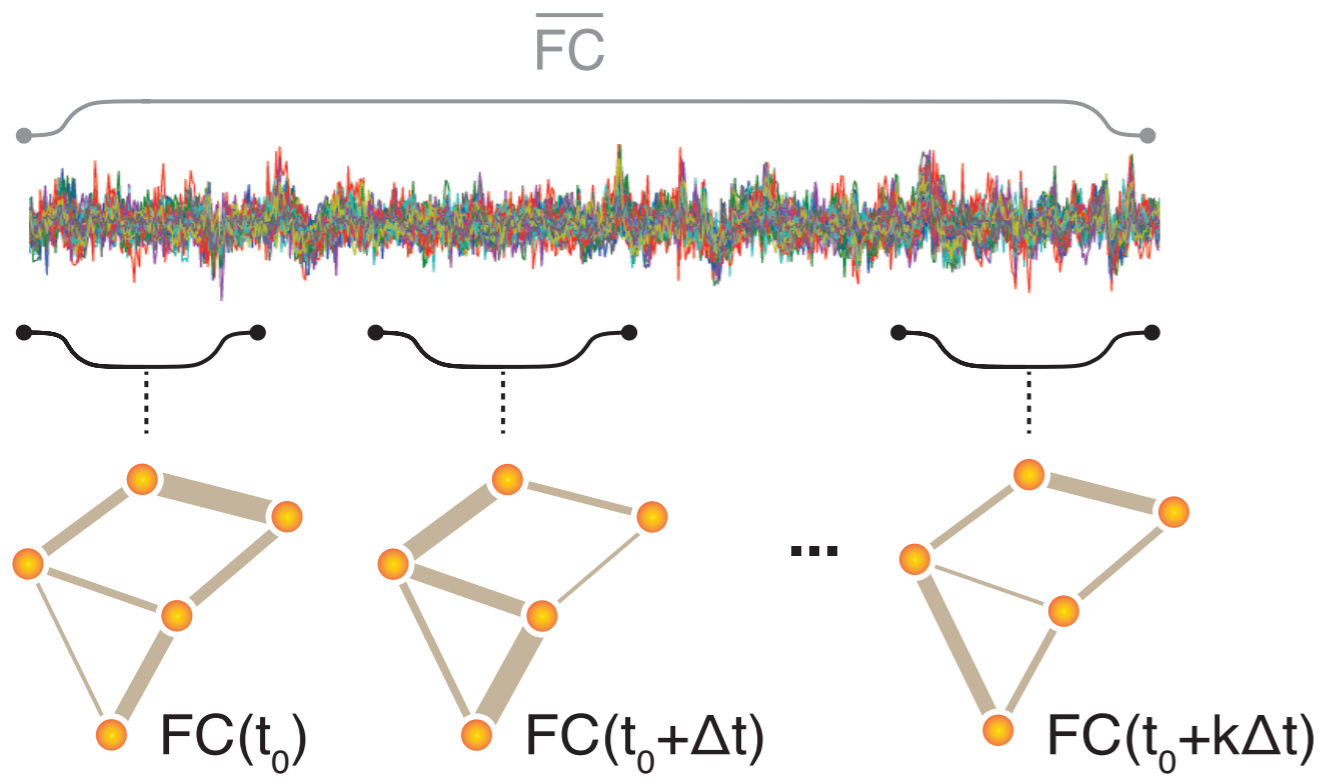


Conclusion 1b

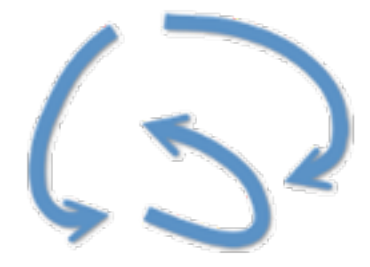
FCD become “less brownian” and “more Levy” with aging



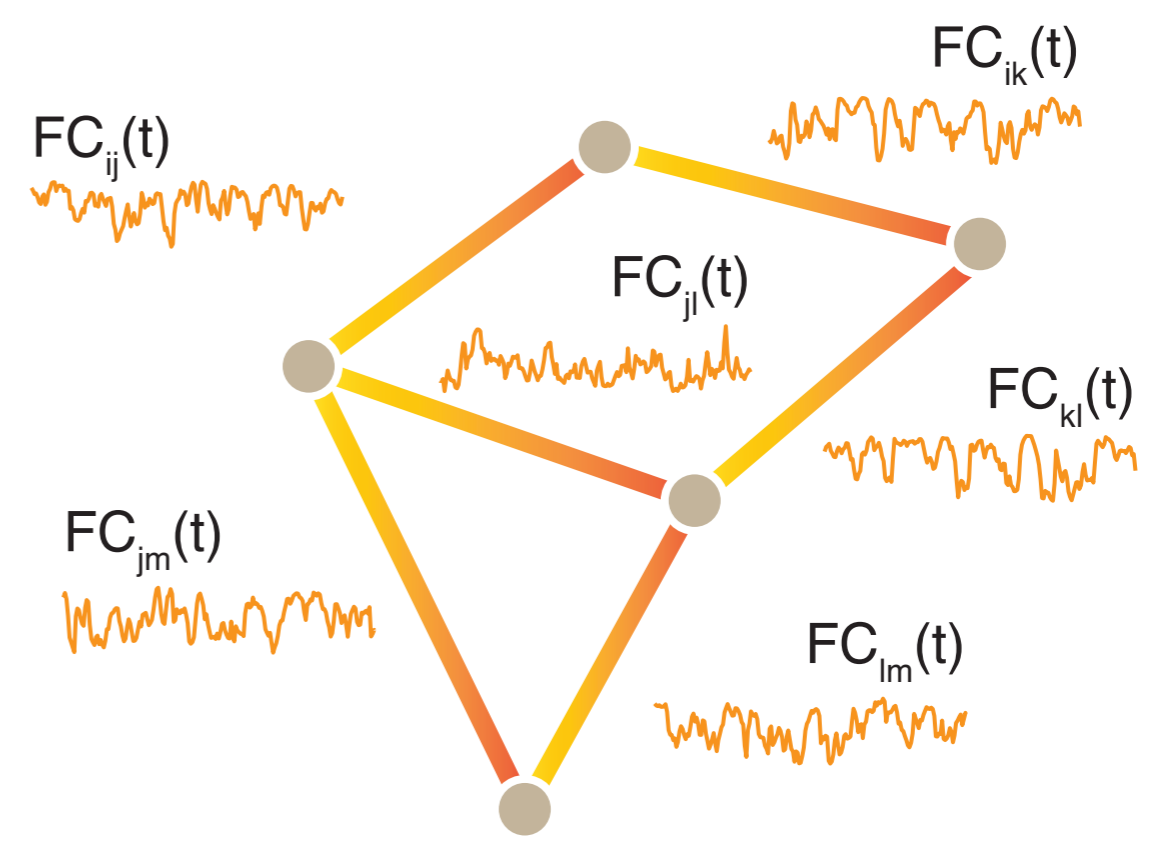
*Let's now introduce
an alternative description of FCD...*

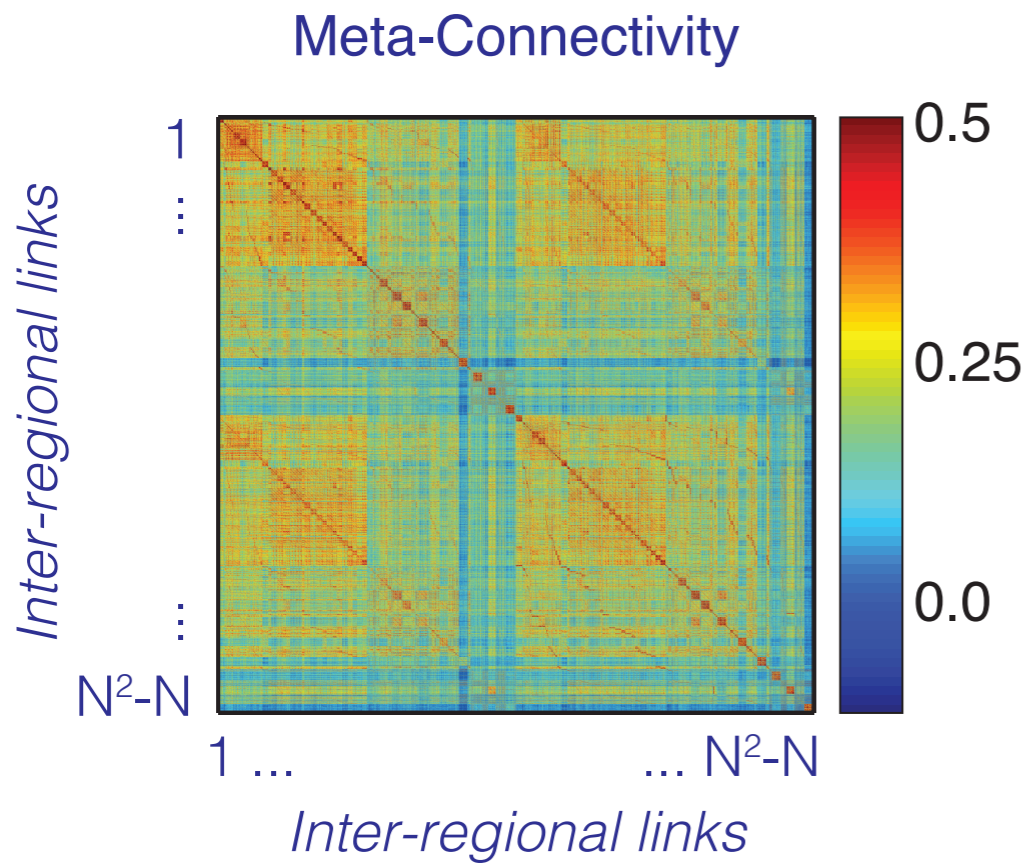


*Time-series of
INTER-NODE CORRELATIONS*



*Time-series of
LINK strengths*

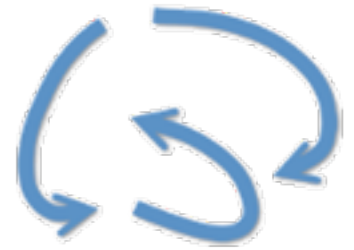




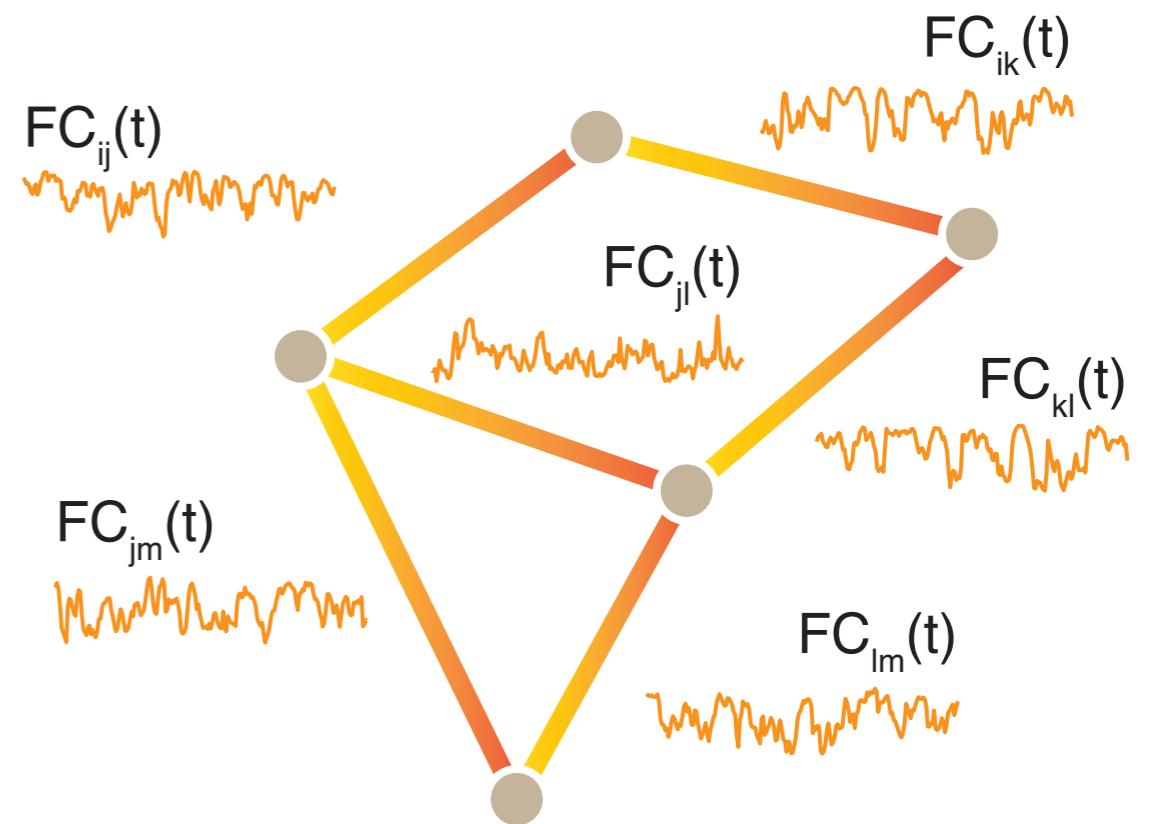
$$FmC_{ij,kl} = CC[(FC_{ij}, FC_{kl})]$$

FUNCTIONAL META-CONNECTIVITY (FMC matrices)

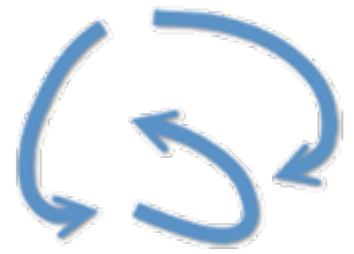
$N(N-1) \times N(N-1)$ matrix of
inter-link correlations



Time-series of
LINK strengths

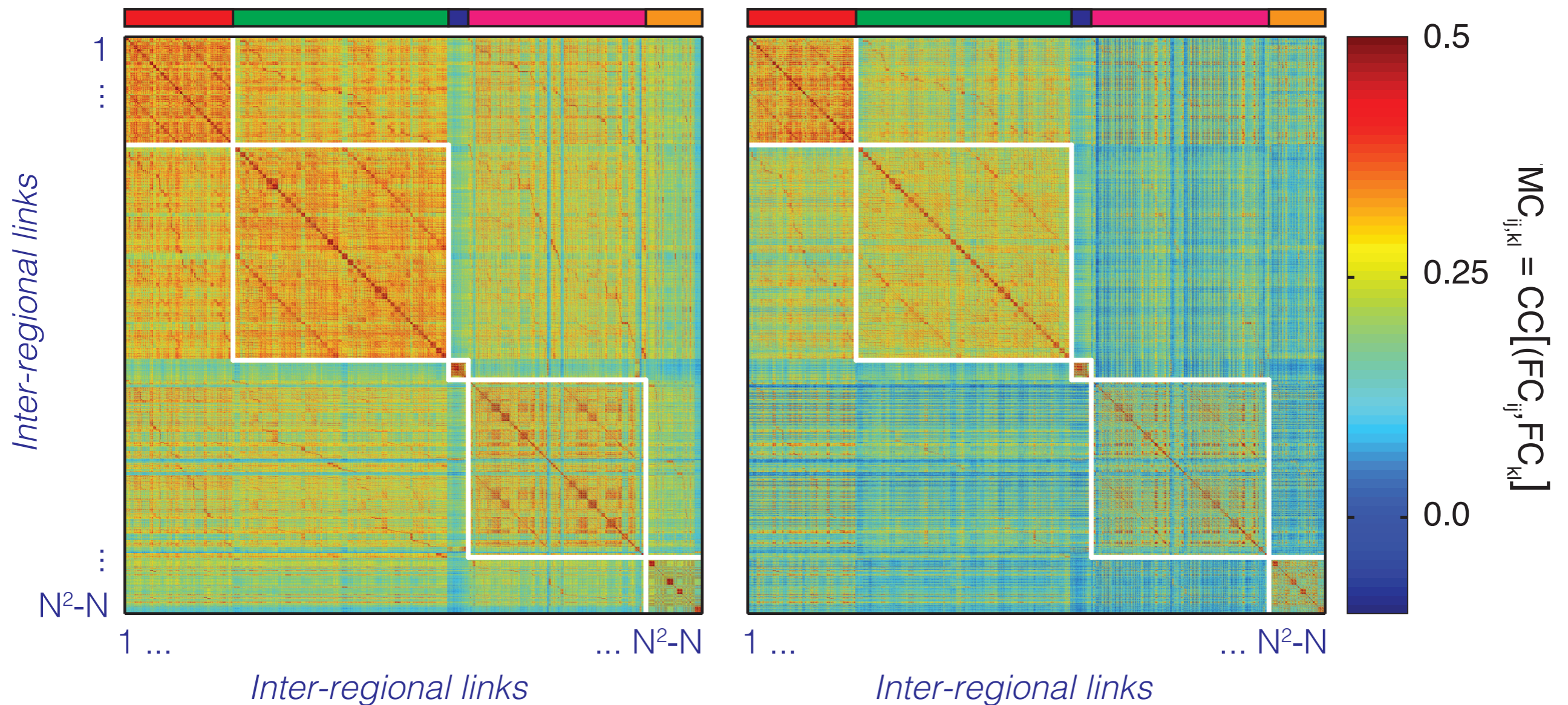


Aging alters Meta-connectivity too!



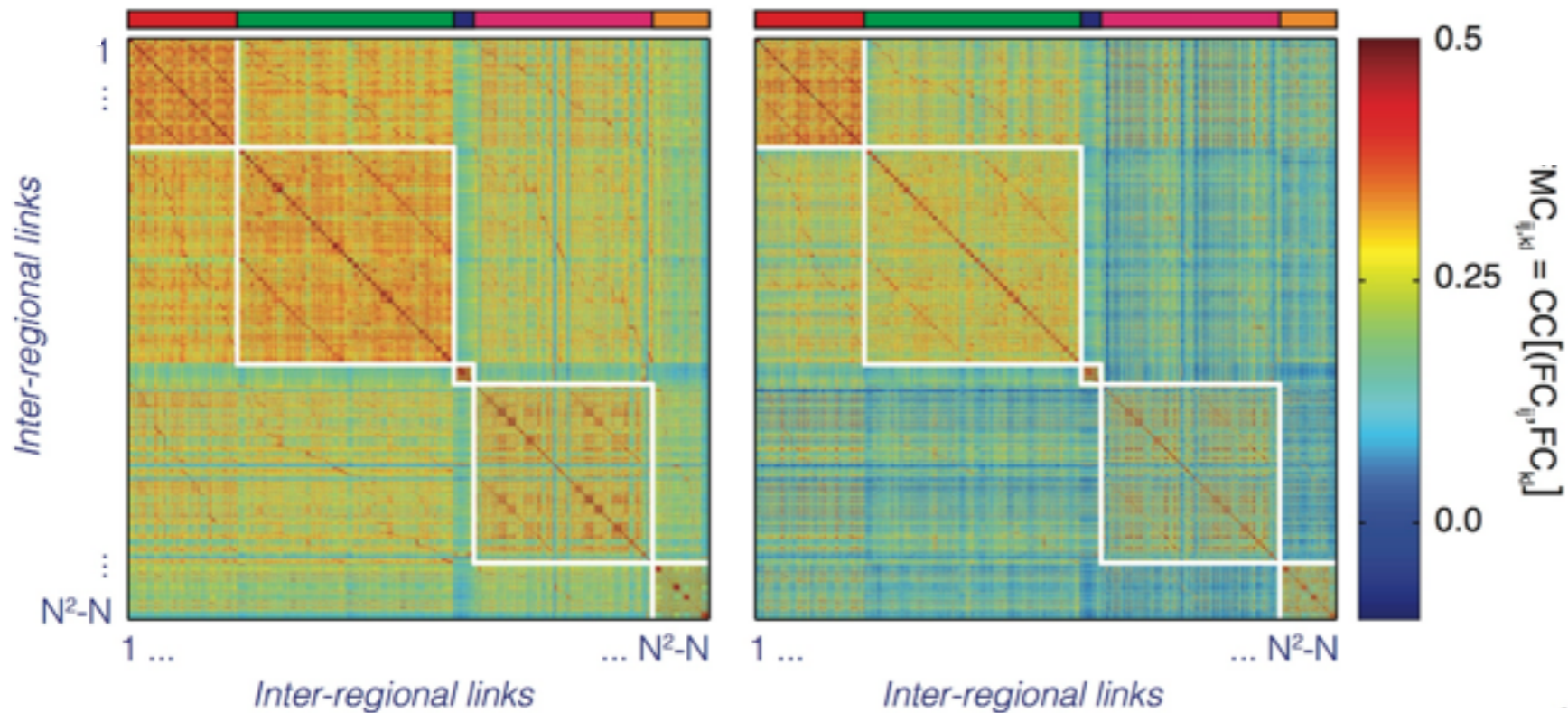
Young adults (18-25 y)

Elderly (60-80 y)



Young adults (18-25 y)

Elderly (60-80 y)

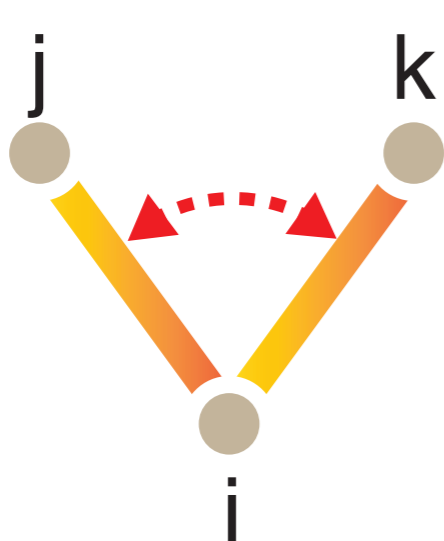


Communities of co-modulated links

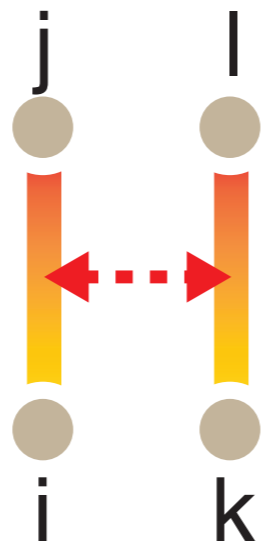
$$\{MC_{ij,kl}\}$$

U

$$\{MC_{ij,ik}\}$$



"Trimers"

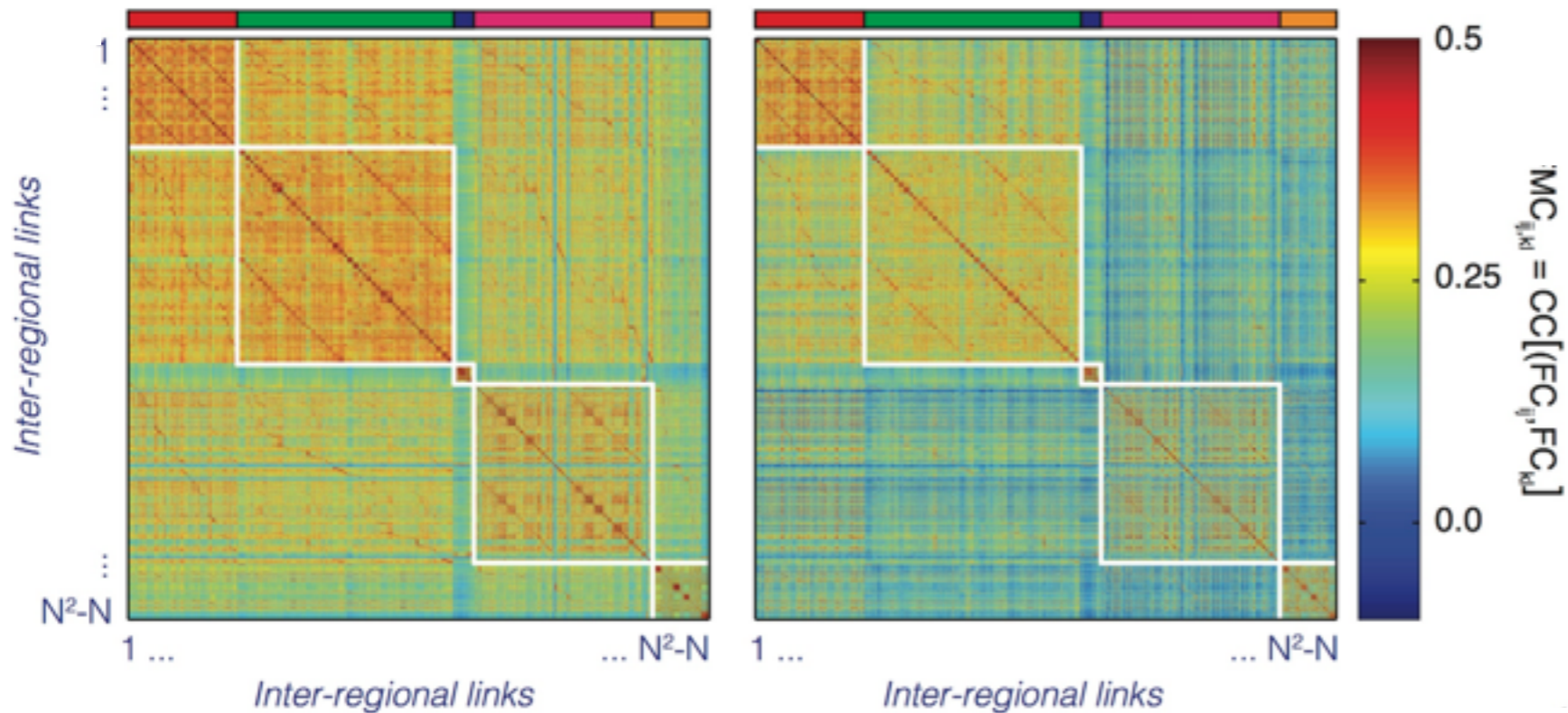


"Tetramers"

$$MC(i) = \sum_{j,k} MC_{ij,ik}$$

Young adults (18-25 y)

Elderly (60-80 y)

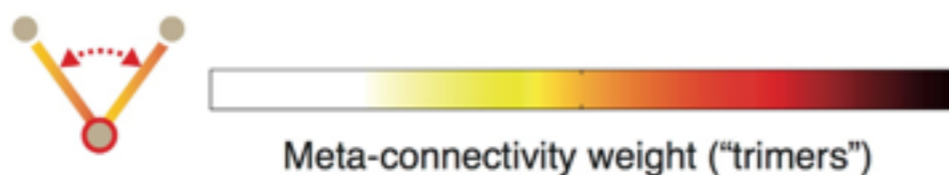
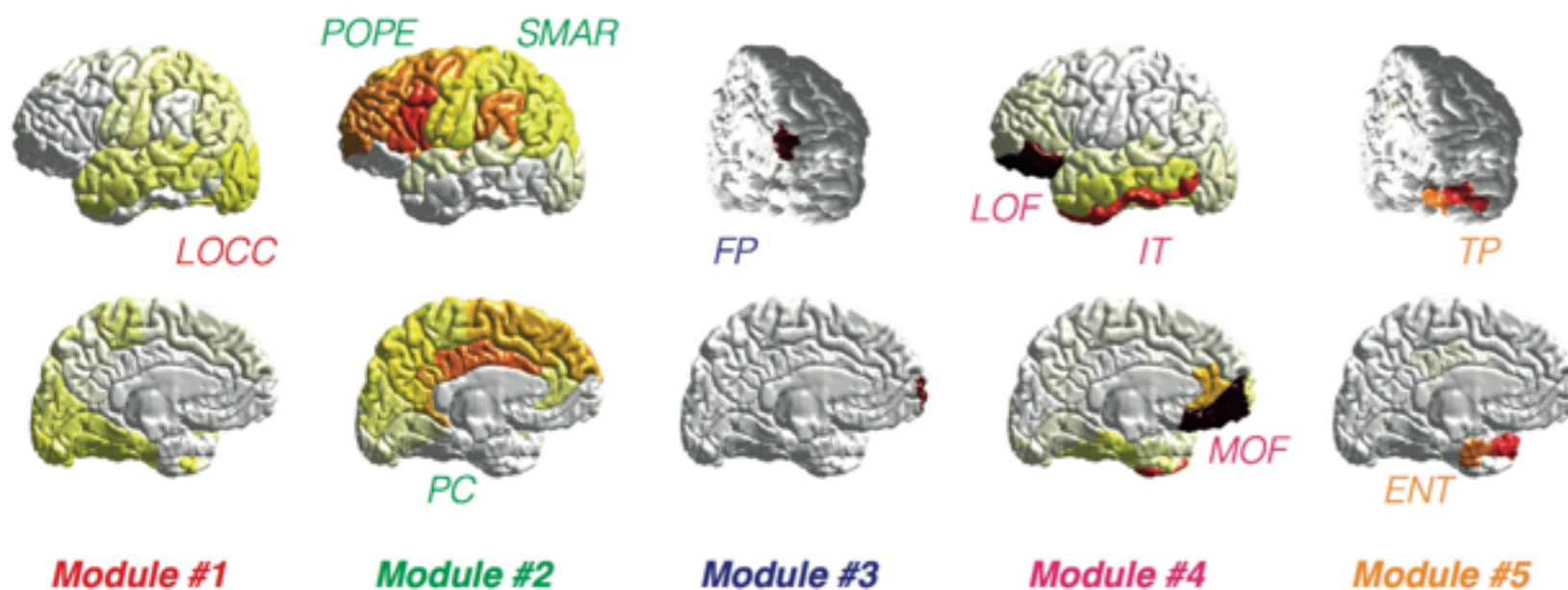


Communities of co-modulated links

$$\{MC_{ij,kl}\}$$

U

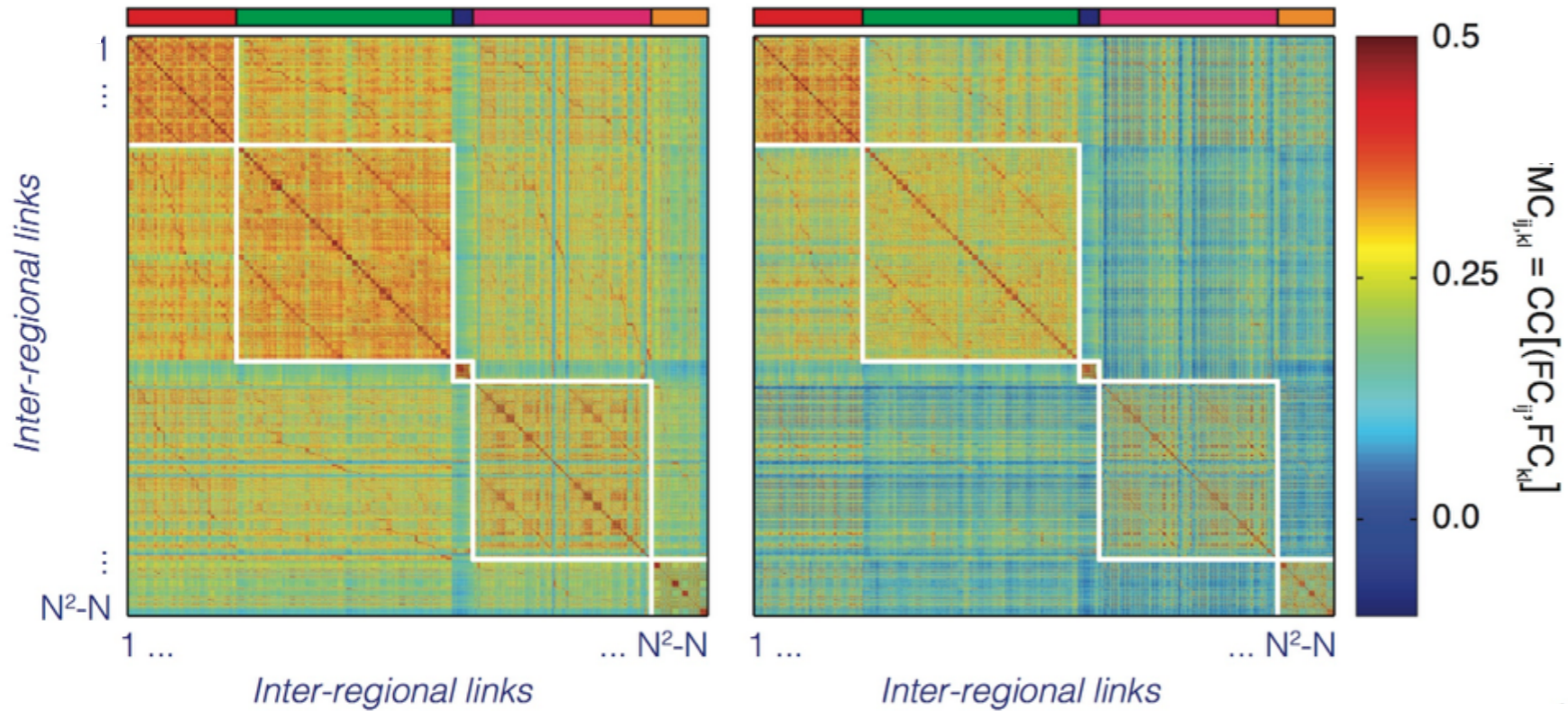
$$\{MC_{ij,ik}\}$$



$$MC(i) = \sum_{j,k} MC_{ij,ik}$$

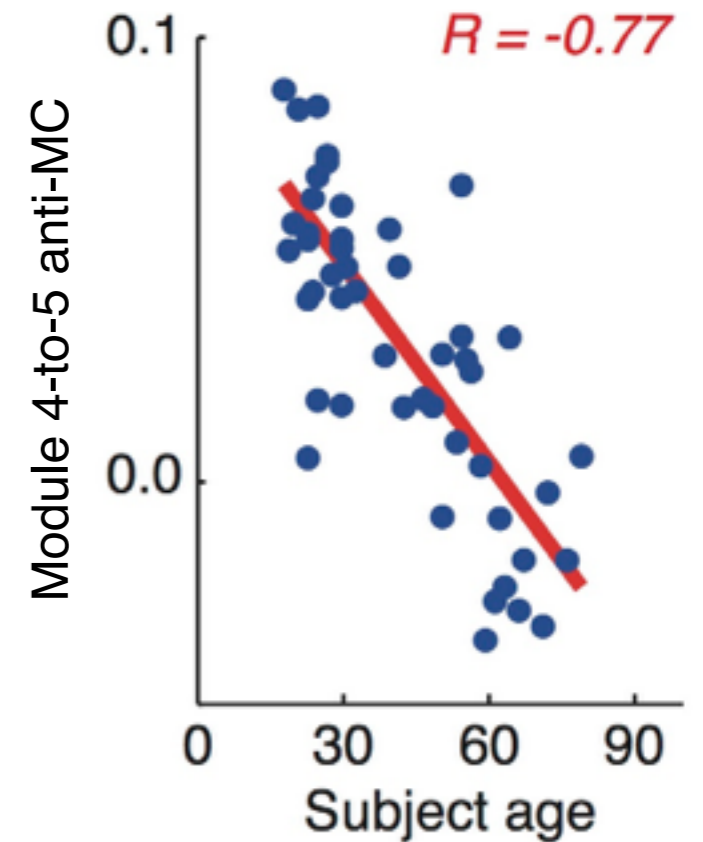
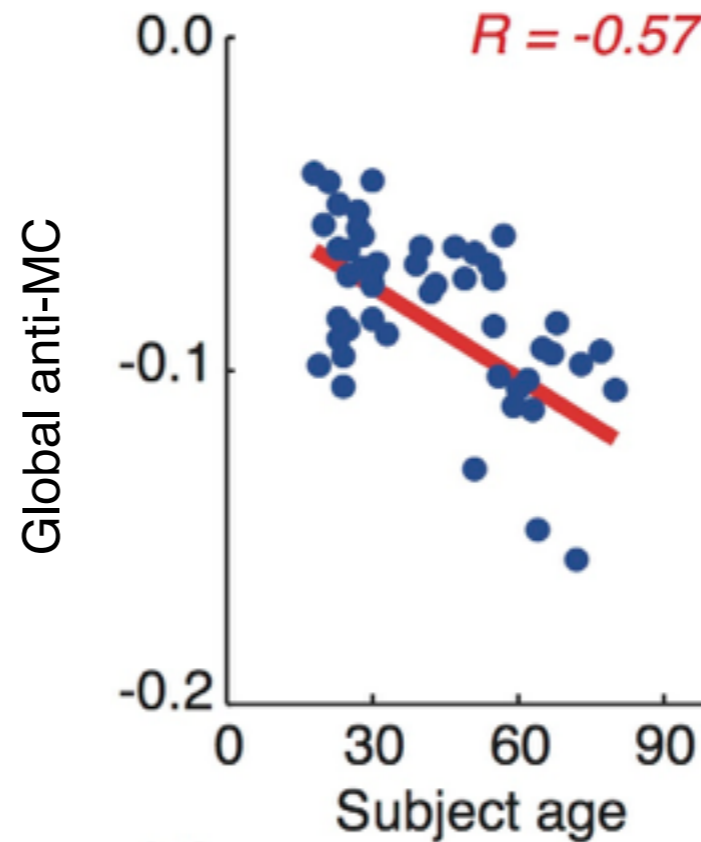
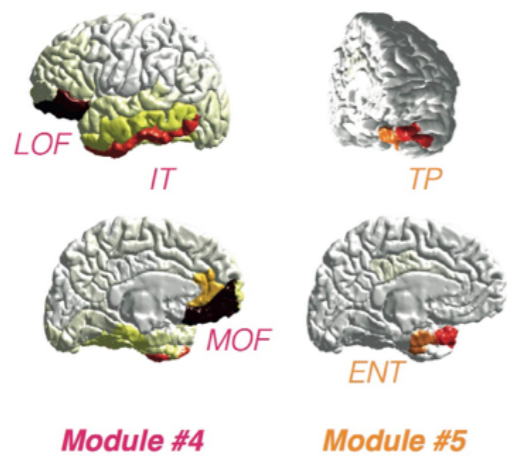
Young adults (18-25 y)

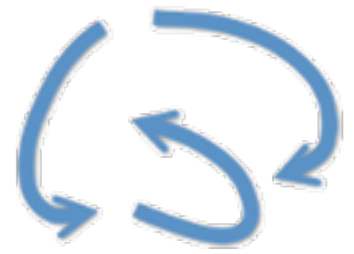
Elderly (60-80 y)



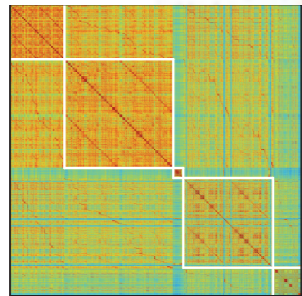
Communities of co-modulated links

Negative meta-connectivity develops with aging
 (“frustration”)



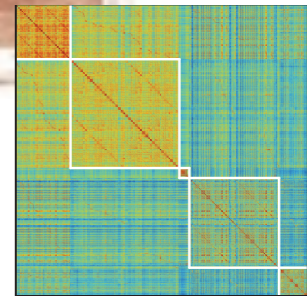


Trouvez l'erreur !



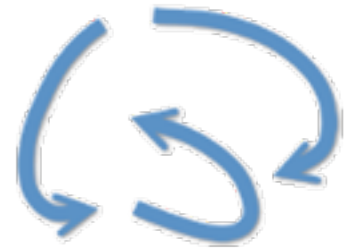
Young

Elderly



HARDEER...





Conclusion 2

FCD “choreography”
becomes more
constrained, less fluent
(increased competition)

FCD (seems to) correlate with cognitive performance



MONTREAL COGNITIVE ASSESSMENT (MOCA)

NAME: E.H. Beckhoff, 2000
 Ausbildung: ... Geburtsdatum: 22.11.2000
 Geschlecht: ... Datum: 27.02.2020

VISUOSPATIAL / EXEKUTIV
 Würfel nachzeichnen (1 Punkt)
 Eine Uhr zeichnen (Zehn nach elf) (1 Punkt)

BEWERTEN
 Löwe, Nashorn, Kamel (je 1 Punkt)

GEDÄCHTNIS
 Wörter vorlesen, wiederholen hören
 2 Durchgänge Nach 5 Minuten überprüfen (je 1 Punkt)

AUFPERSAMKEIT
 Zahlenreize vorlesen (1 Buchst./Sek.) Punkte für jeden Buchstaben „A“ mit der Hand klopfen. Neue Punkte für 2 oder mehr klopfen

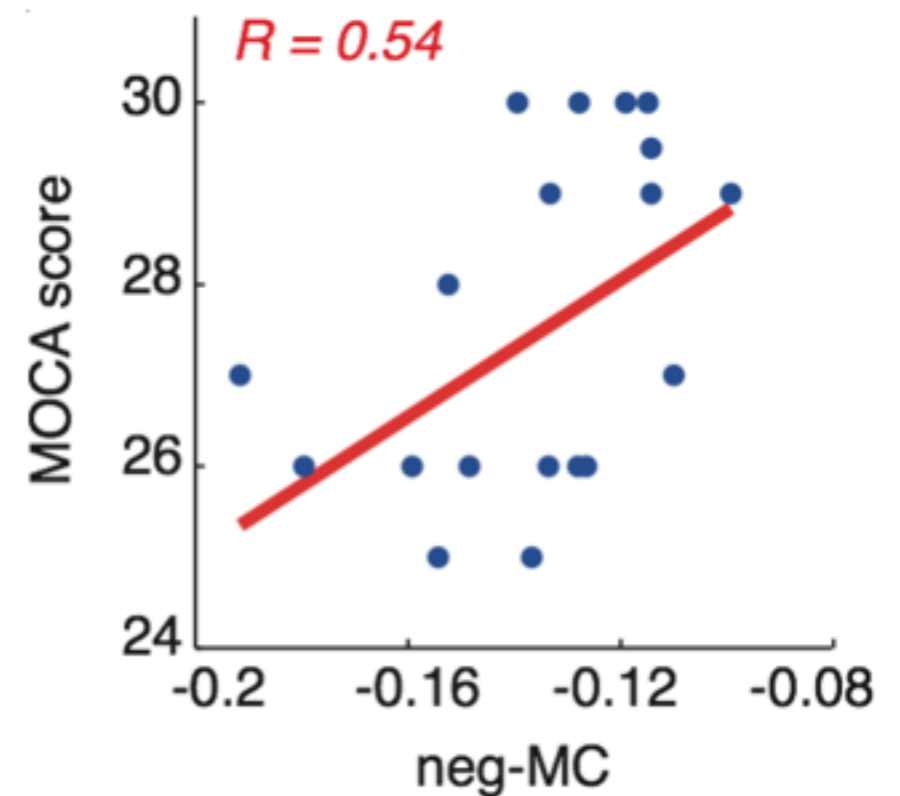
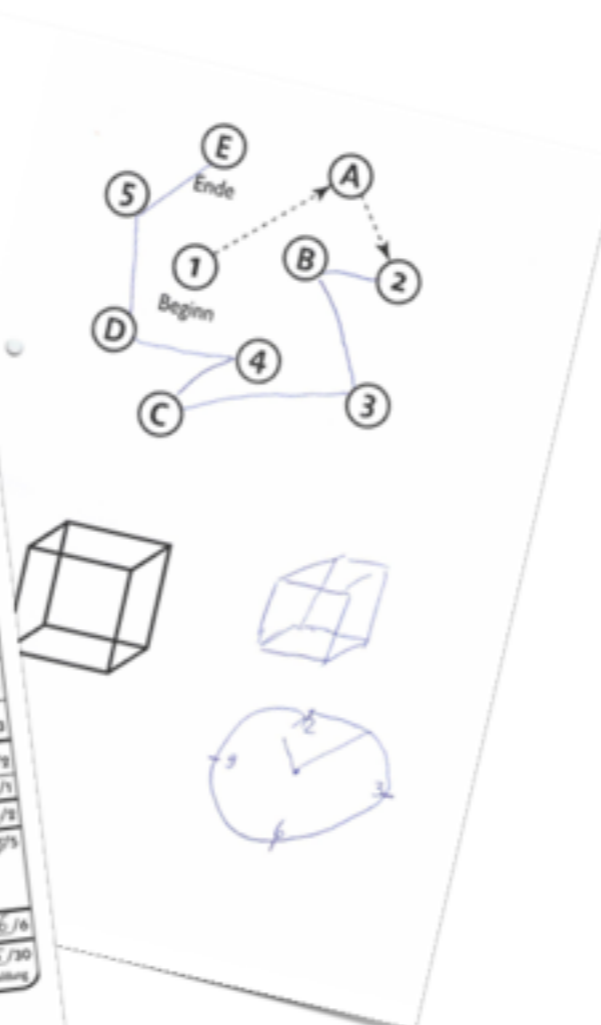
SPRACHE
 Wiederholen: „Ich weiß lediglich, dass Maria heute an der Bushaltestelle in der Nähe von ...“
 Die Karte verbindet sich immer unter der Couch, wenn die Hände im Zimmer waren“

ABSTRAKTION
 Gemeinsamkeit von 4 Bildern und 4 Buchstaben + Punkte

ERINNERUNG
 Wortschatz (je 1 Punkt)

ORIENTIERUNG
 Datum, Monat, Jahr, Uhrzeit, Ort

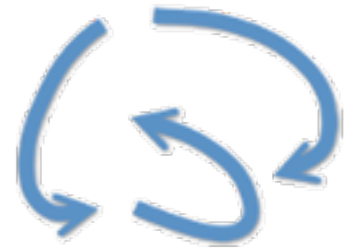
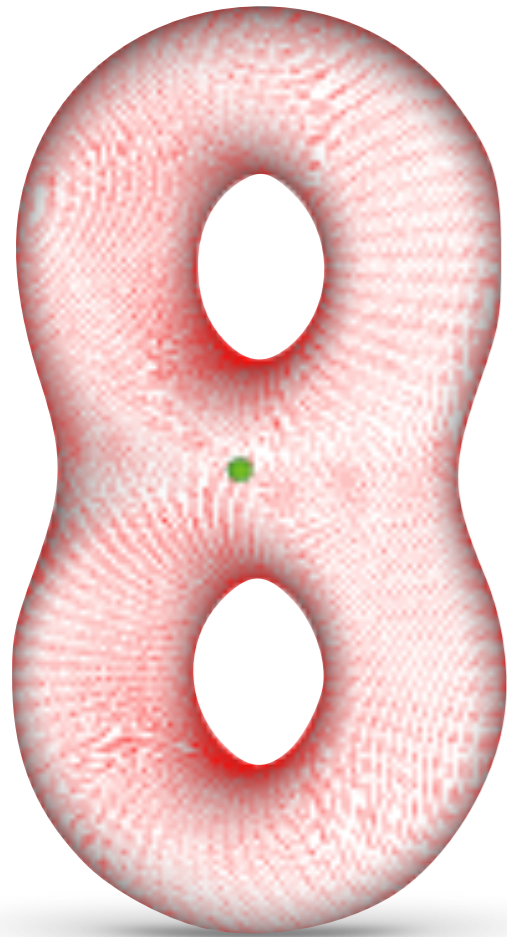
TOTAL
 25/30
 + 1 Punkt wenn < 10 Jahre Ausbildung



... correlate with MC frustration

Cognitive Assessment scores...

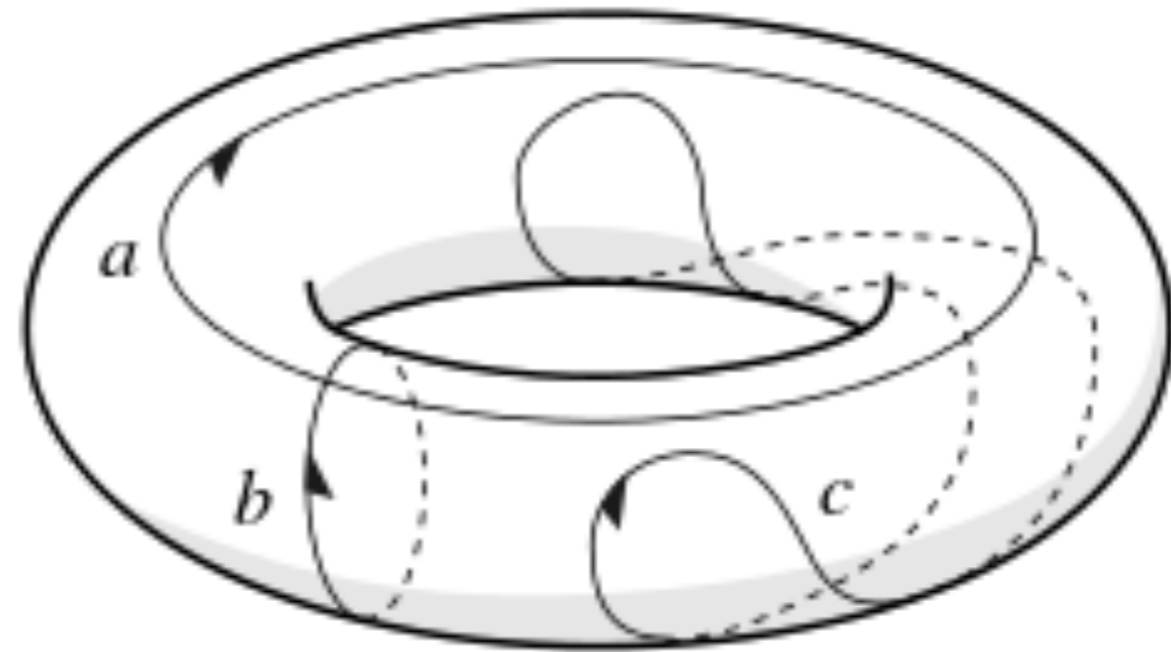
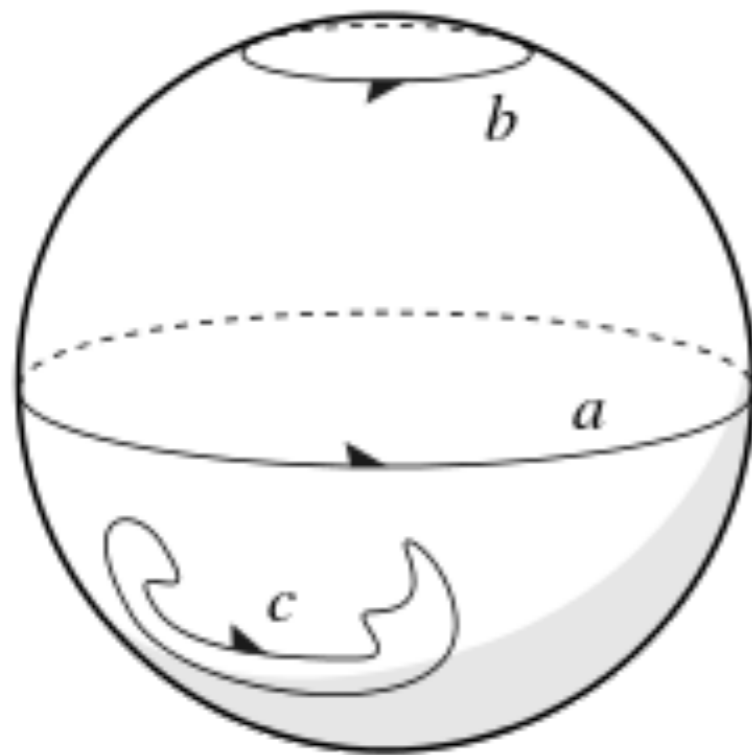
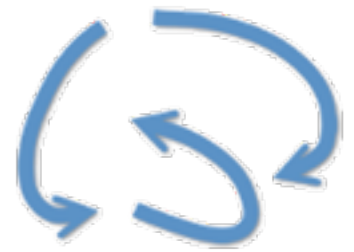
CC(neg-MC, MOCA | Age) = 0.51 (**)
 CC(neg-MC, MOCA-wm | Age) = 0.65 (***)



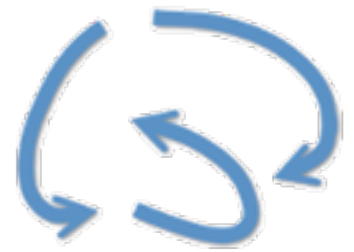
Topolome
and aging!



Homology



Persistent homology



SCIENTIFIC REPORTS

OPEN Extracting insights from the shape of complex data using topology

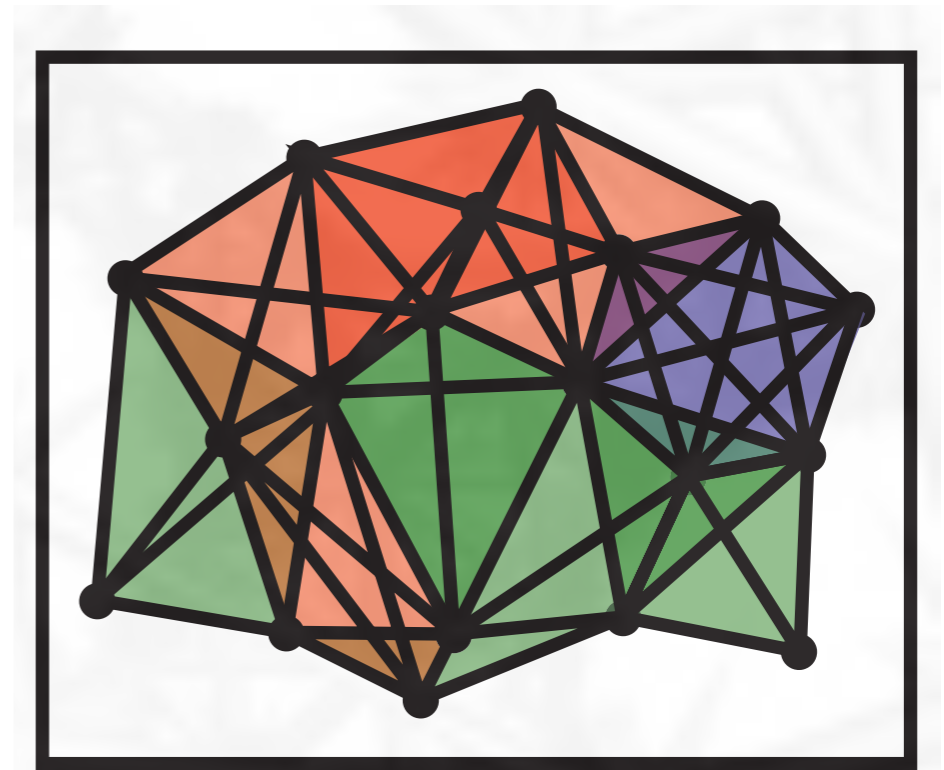
SUBJECT AREAS:
APPLIED MATHEMATICS
COMPUTATIONAL SCIENCE
SCIENTIFIC DATA
SOFTWARE

Received 13 September 2012
Accepted 6 December 2012
Published 7 February 2013

P. Y. Lum¹, G. Singh¹, A. Lehman¹, T. Ishkanov¹, M. Vejdemo-Johansson², M. Alagappan¹, J. Carlsson³ & G. Carlsson^{1,4}

¹Ayasdi Inc., Palo Alto, CA, ²School of Computer Science, Jack Cole Building, North Haugh, St. Andrews KY16 9SX, Scotland, United Kingdom, ³Industrial and Systems Engineering, University of Minnesota, 111 Church St. SE, Minneapolis, MN 55455, USA, ⁴Department of Mathematics, Stanford University, Stanford, CA, 94305, USA.

This paper applies topological methods to study complex high dimensional data sets by extracting shapes (patterns) and obtaining insights about them. Our method combines the best features of existing standard methodologies such as principal component and cluster analyses to provide a geometric representation of complex data sets. Through this hybrid method, we often find subgroups in data sets that traditional methodologies fail to find. Our method also permits the analysis of individual data sets as well as the analysis of relationships between related data sets. We illustrate the use of our method by applying it to three very different kinds of data, namely gene expression from breast tumors, voting data from the United States House of Representatives and player performance data from the NBA, in each case finding stratifications of the data which are more refined than those produced by standard methods.



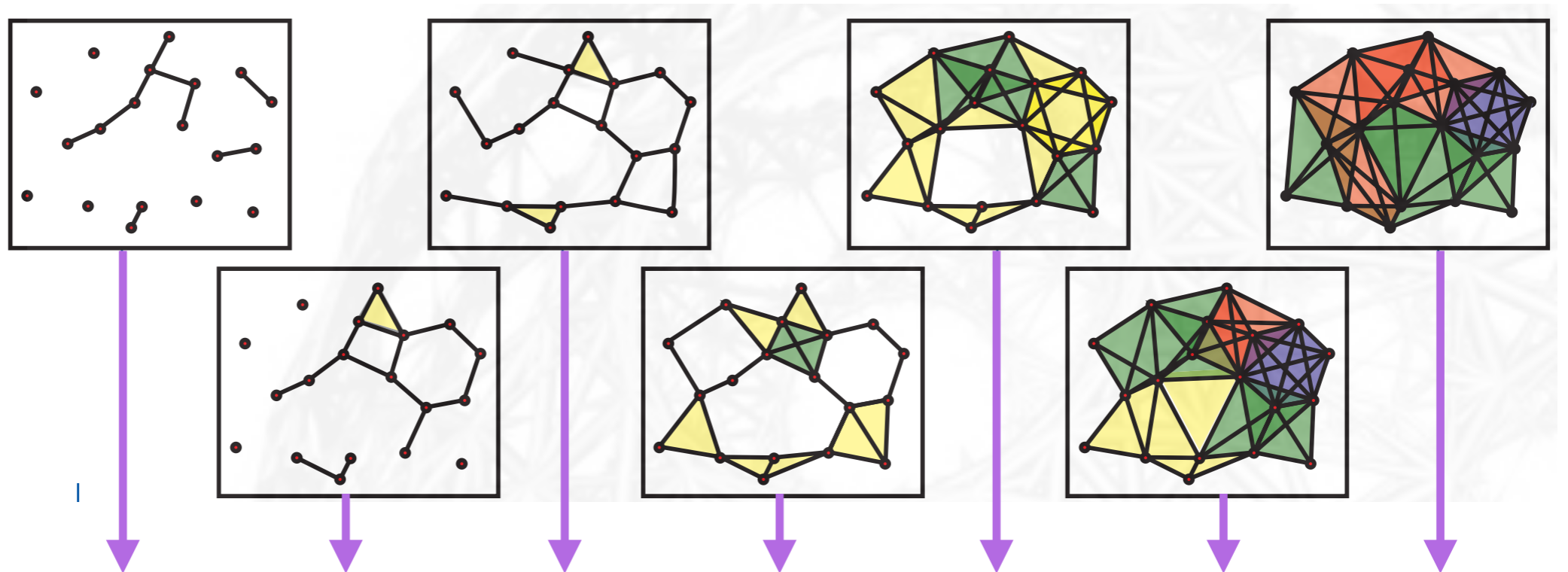
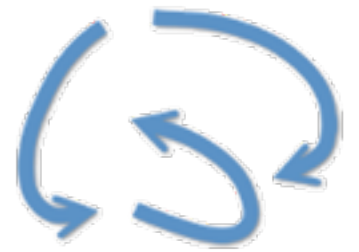
Francesco Vaccarino



Giovanni Petri

WARNING!
*Ask my pals mathematicians
for details!*

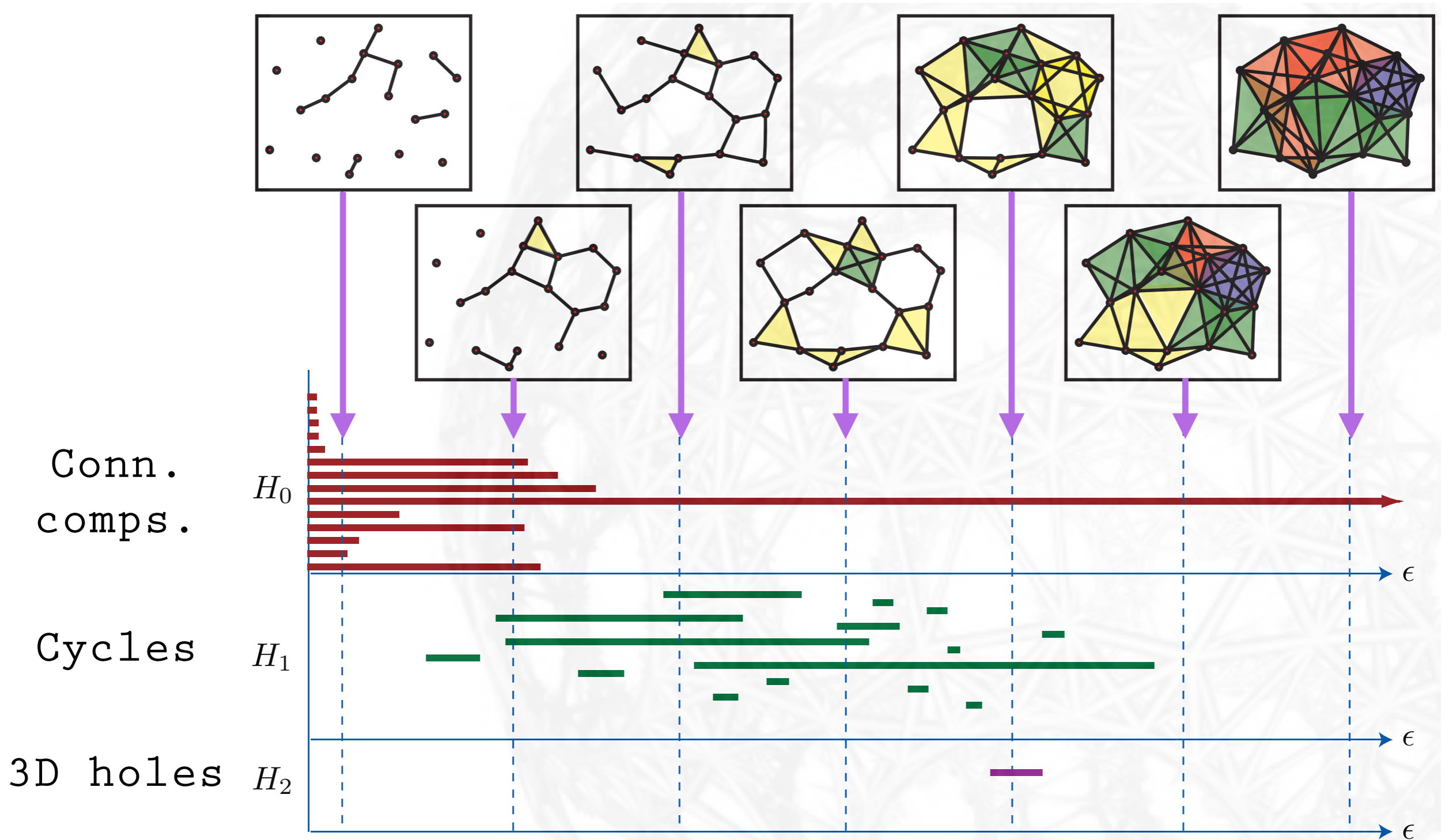
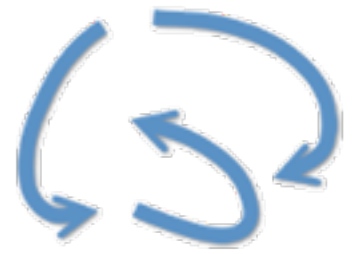
Persistent homology



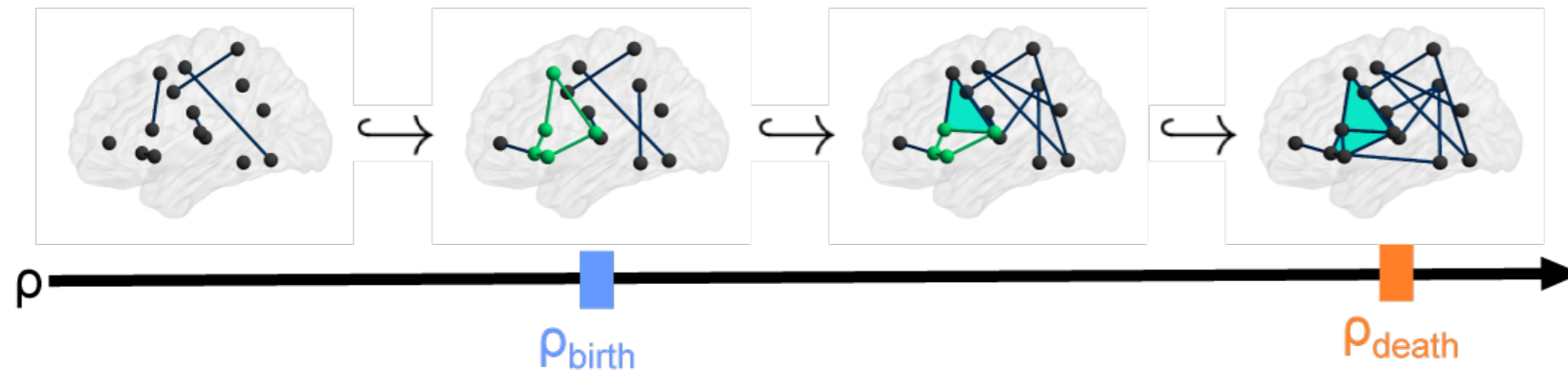
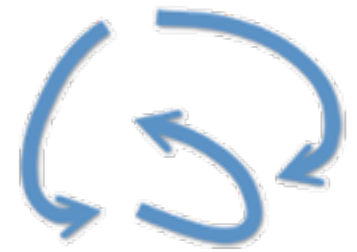
“Filtration”

Let's add (or remove) gradually nodes, e.g. in order of decreasing strength

Persistent homology

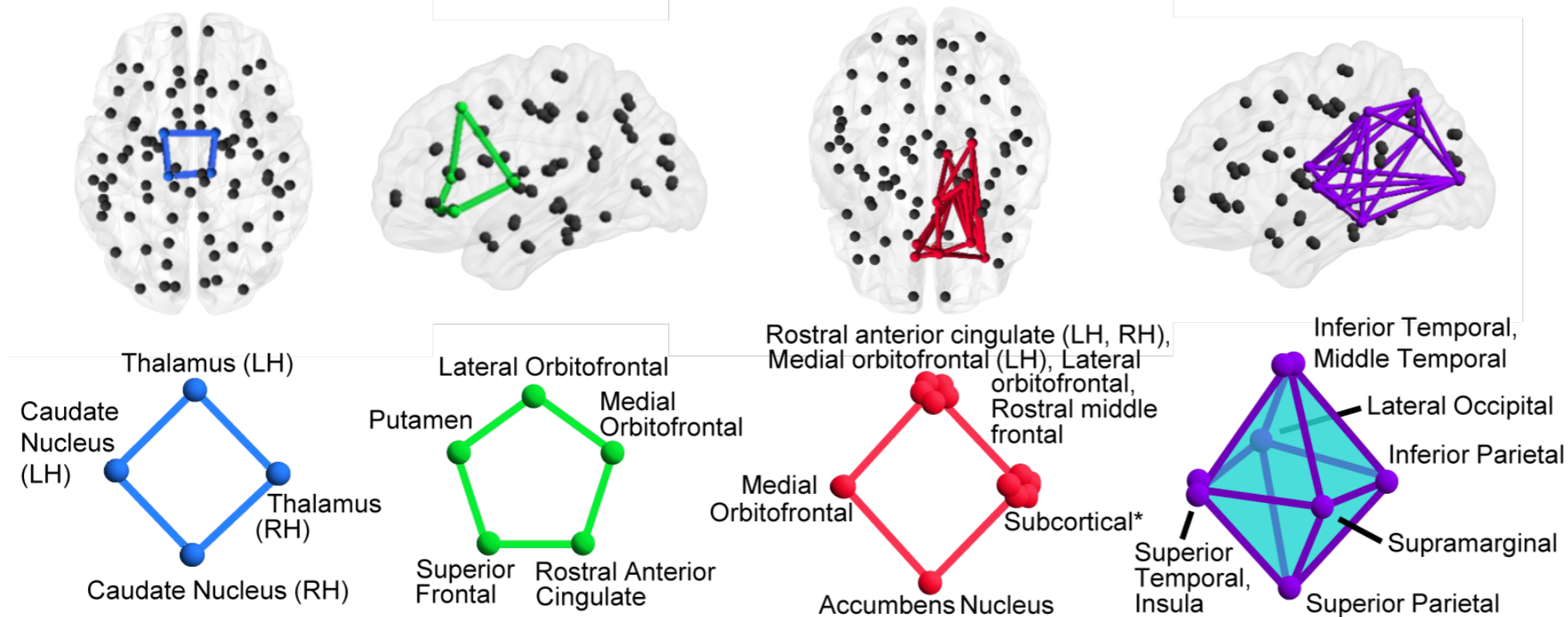


Cycles and "cavities"

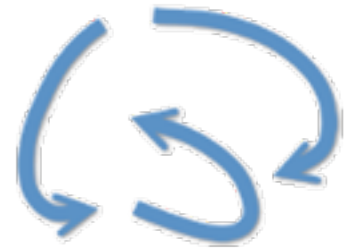


The most persistent cycles and holes

Adapted from
Sizemore, Giusti, Bassett,
arXiv (2016)



Persistence homology scaffold

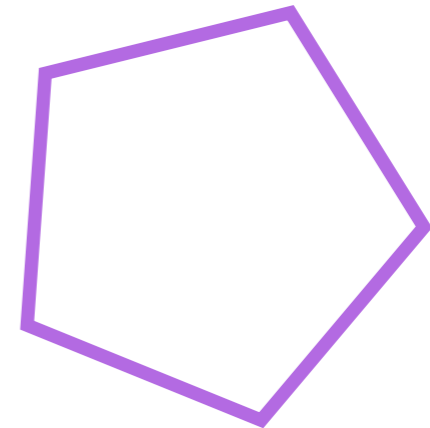


JOURNAL
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THE ROYAL
SOCIETY
Interface

rsif.royalsocietypublishing.org

Homological scaffolds of brain functional networks

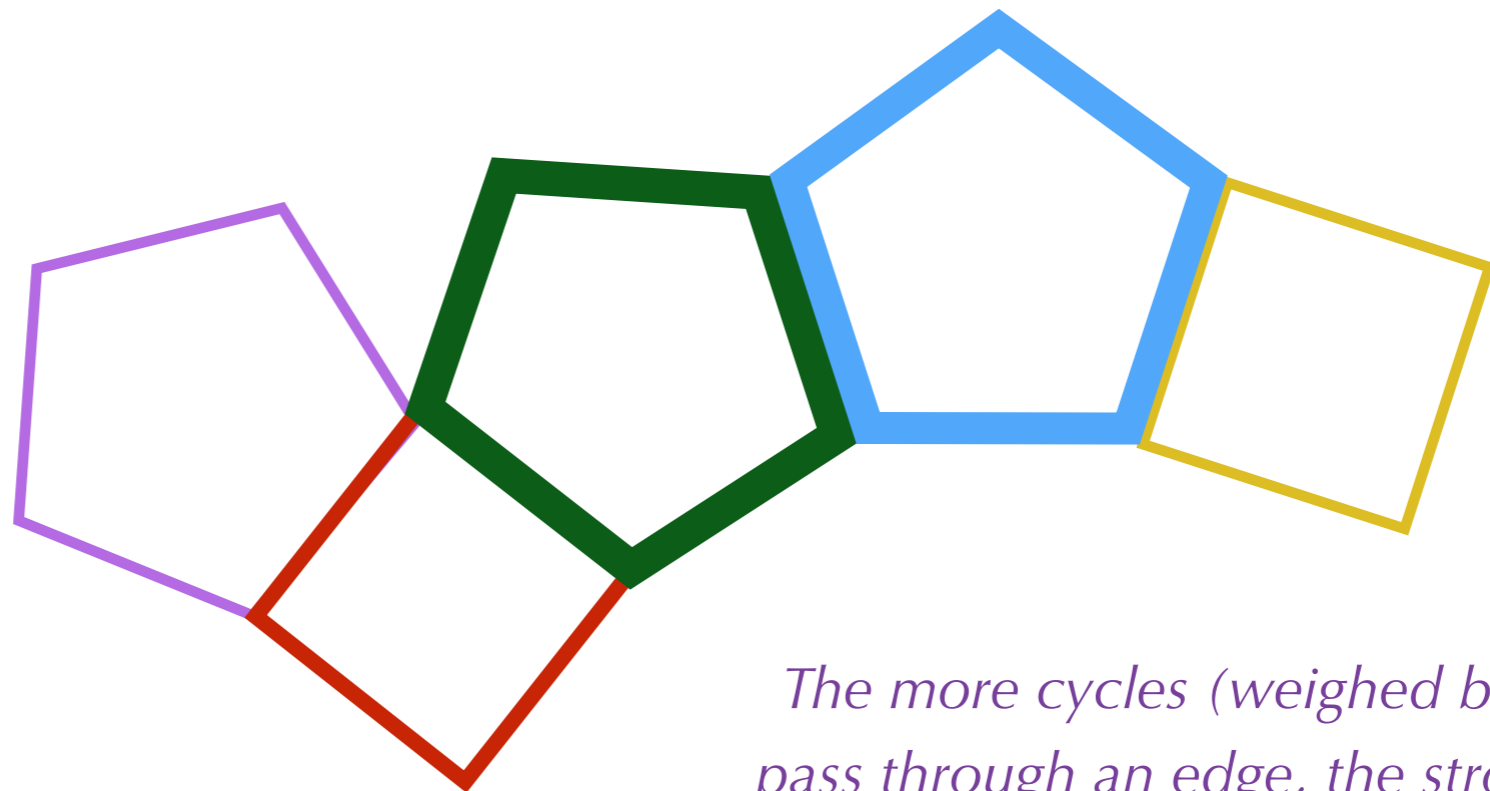
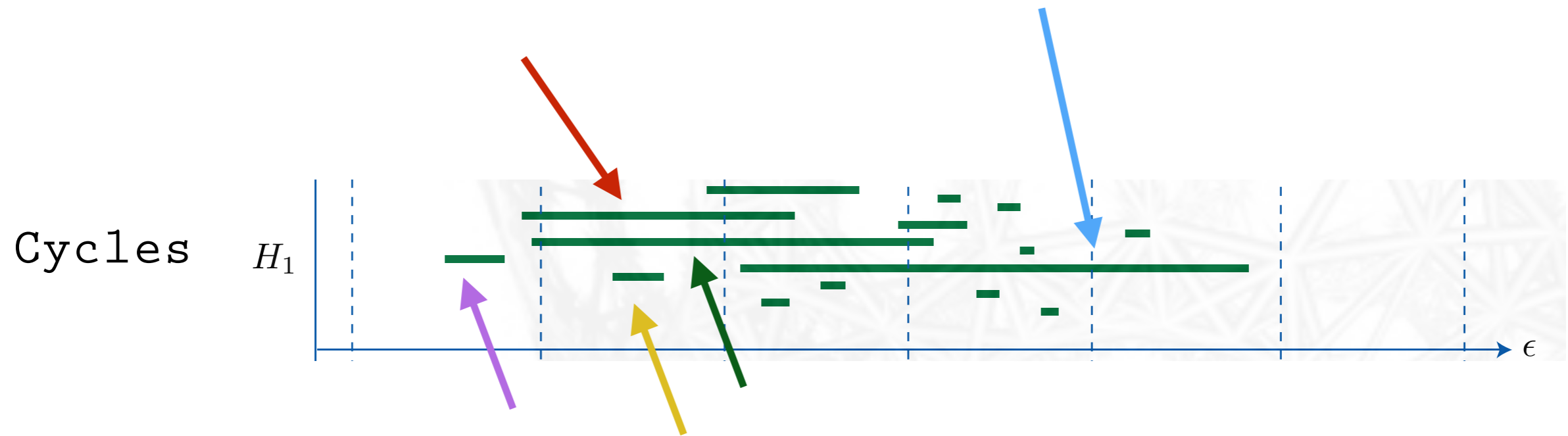
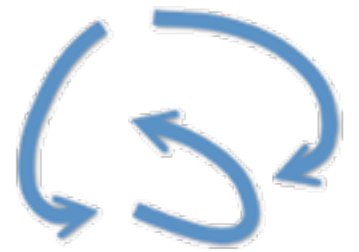
G. Petri¹, P. Expert², F. Turkheimer², R. Carhart-Harris³, D. Nutt³, P. J. Hellyer⁴
and F. Vaccarino^{1,5}



We exploit this to define two new objects, the *persistence* and the *frequency homological scaffolds* \mathcal{H}_G^p and \mathcal{H}_G^f of a graph G . The *persistence homological scaffold* is the network composed of all the cycle paths corresponding to generators weighted by their persistence. If an edge e belongs to multiple cycles g_0, g_1, \dots, g_s , its weight is defined as the sum of the generators' persistence:

$$\omega_e^\pi = \sum_{g_i | e \in g_i} \pi_{g_i}. \quad (4.1)$$

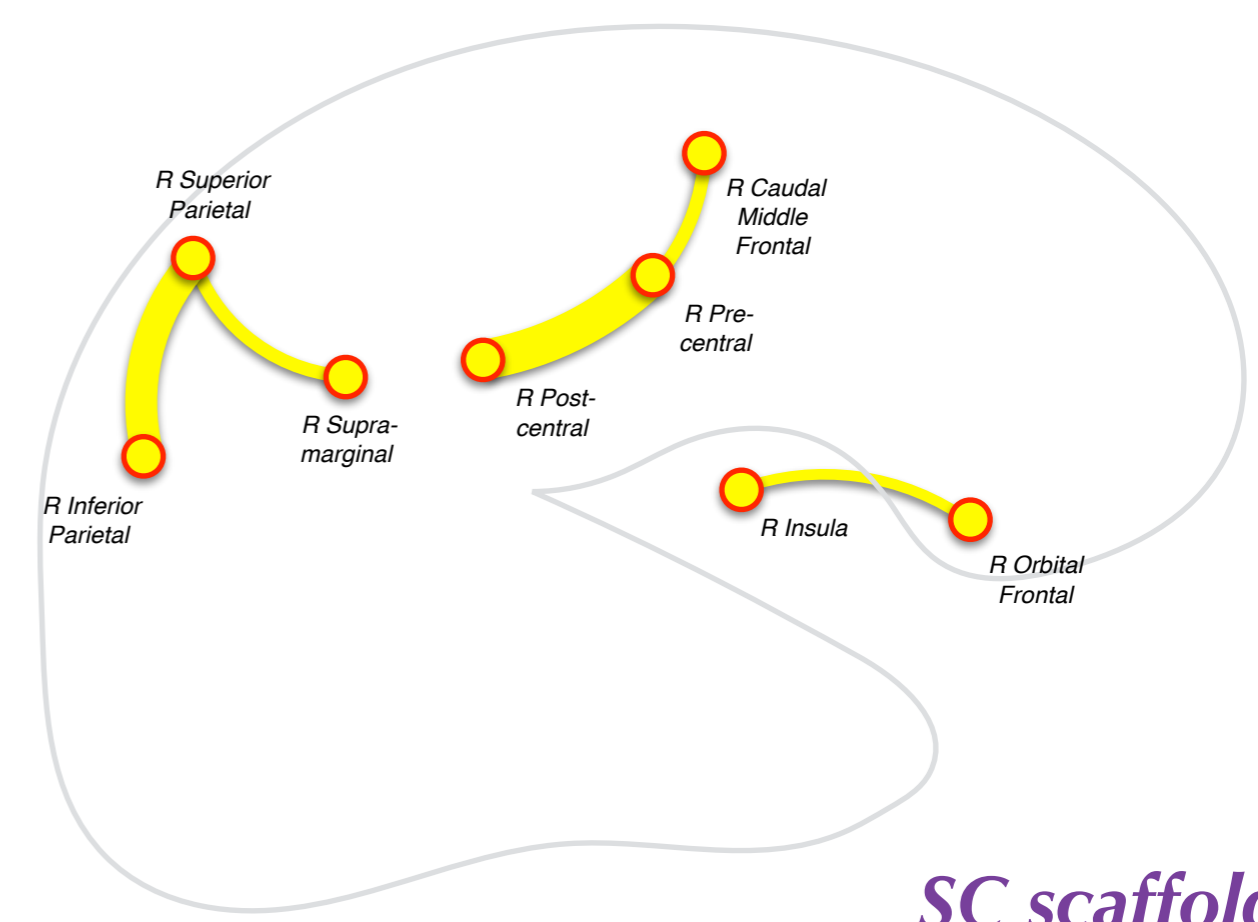
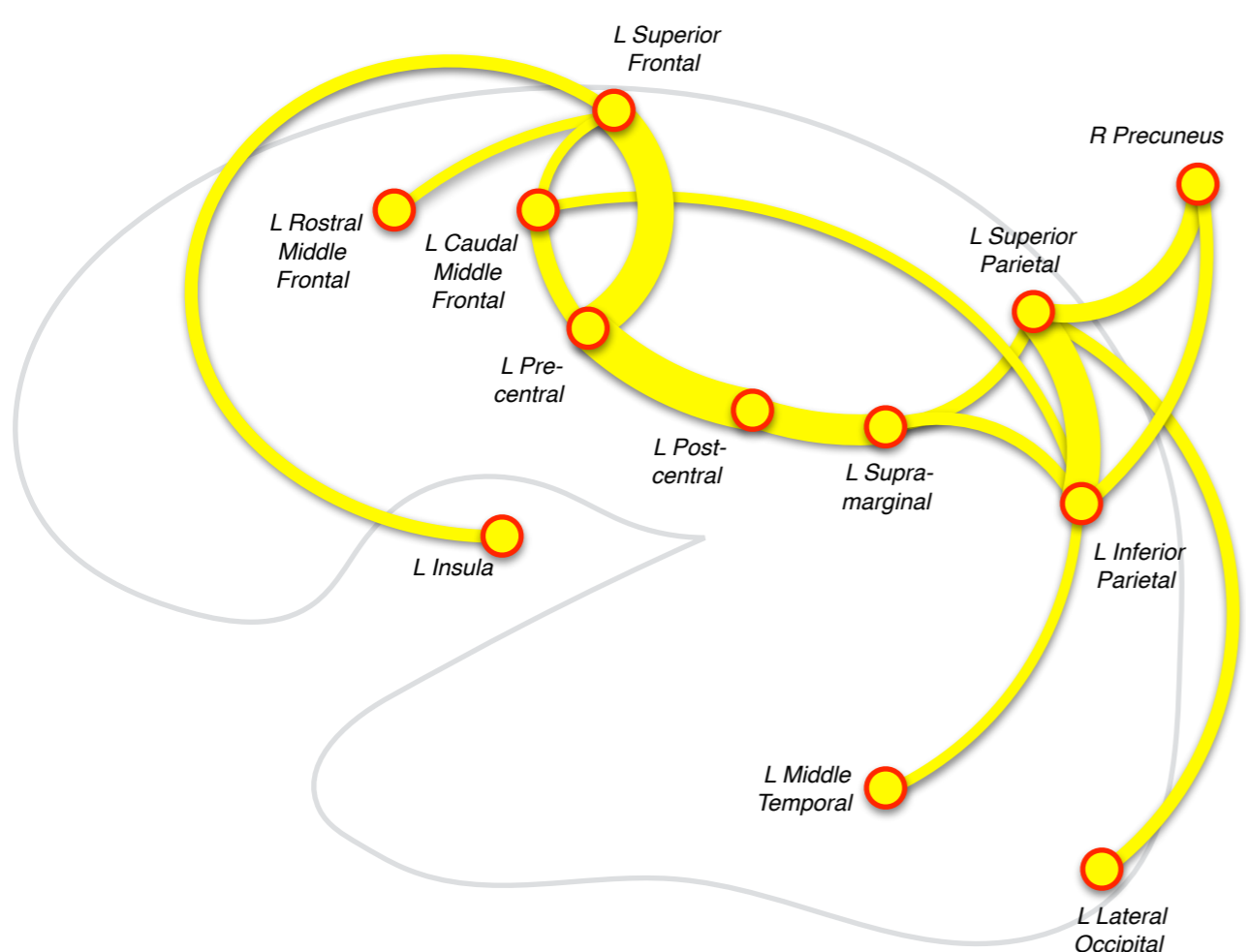
Persistence homology scaffold



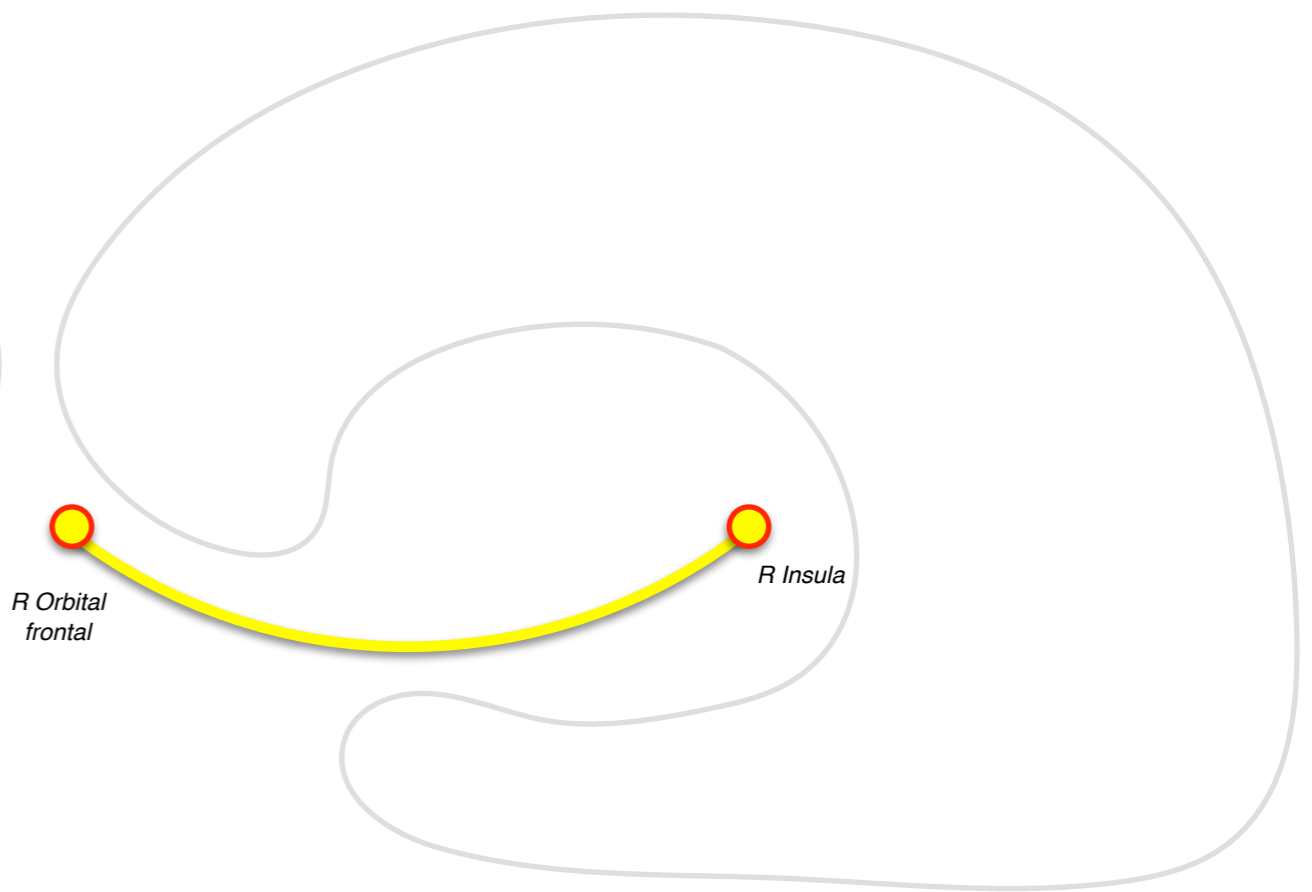
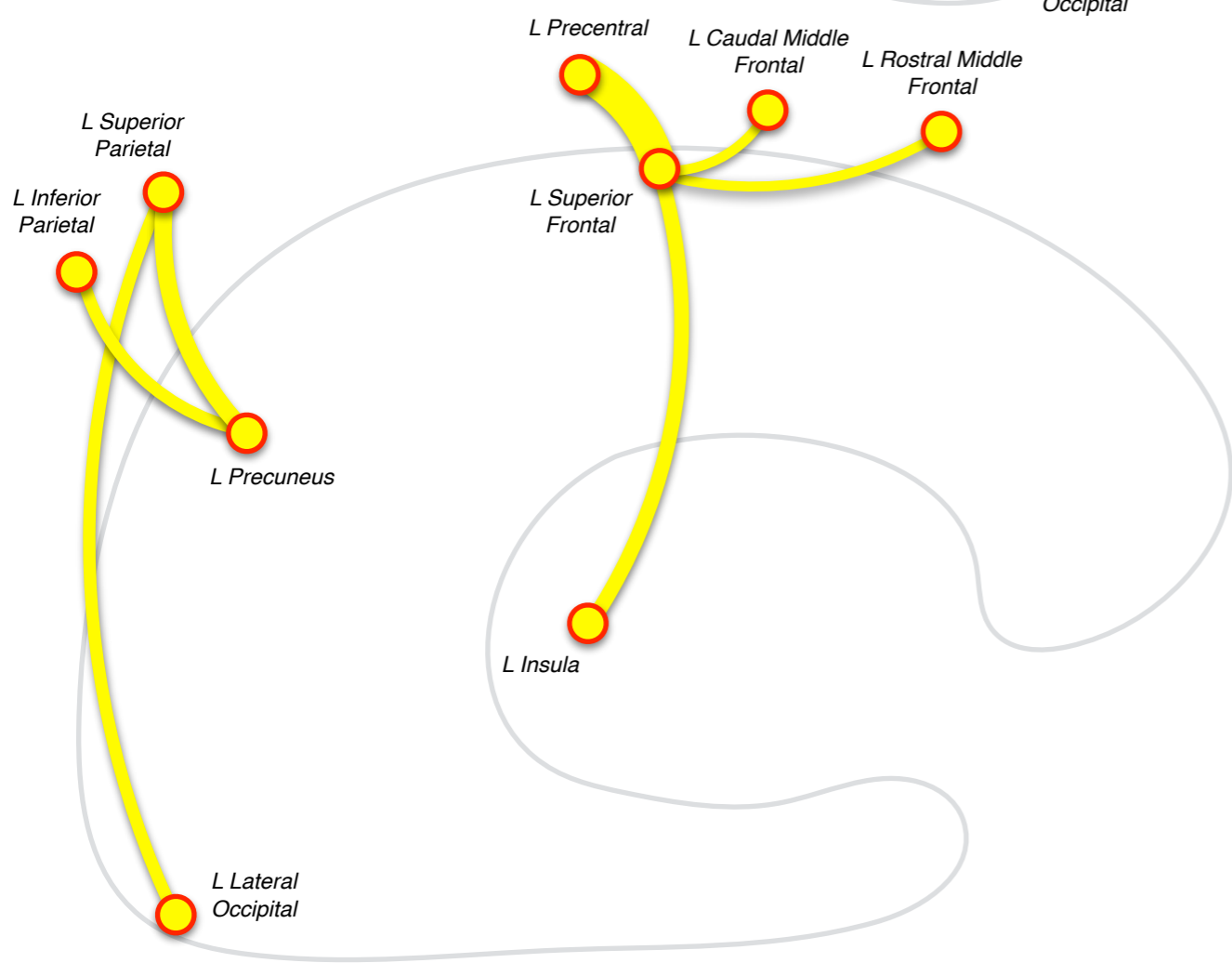
$$\omega_e^\pi = \sum_{g_i | e \in g_i} \pi_{g_i}$$

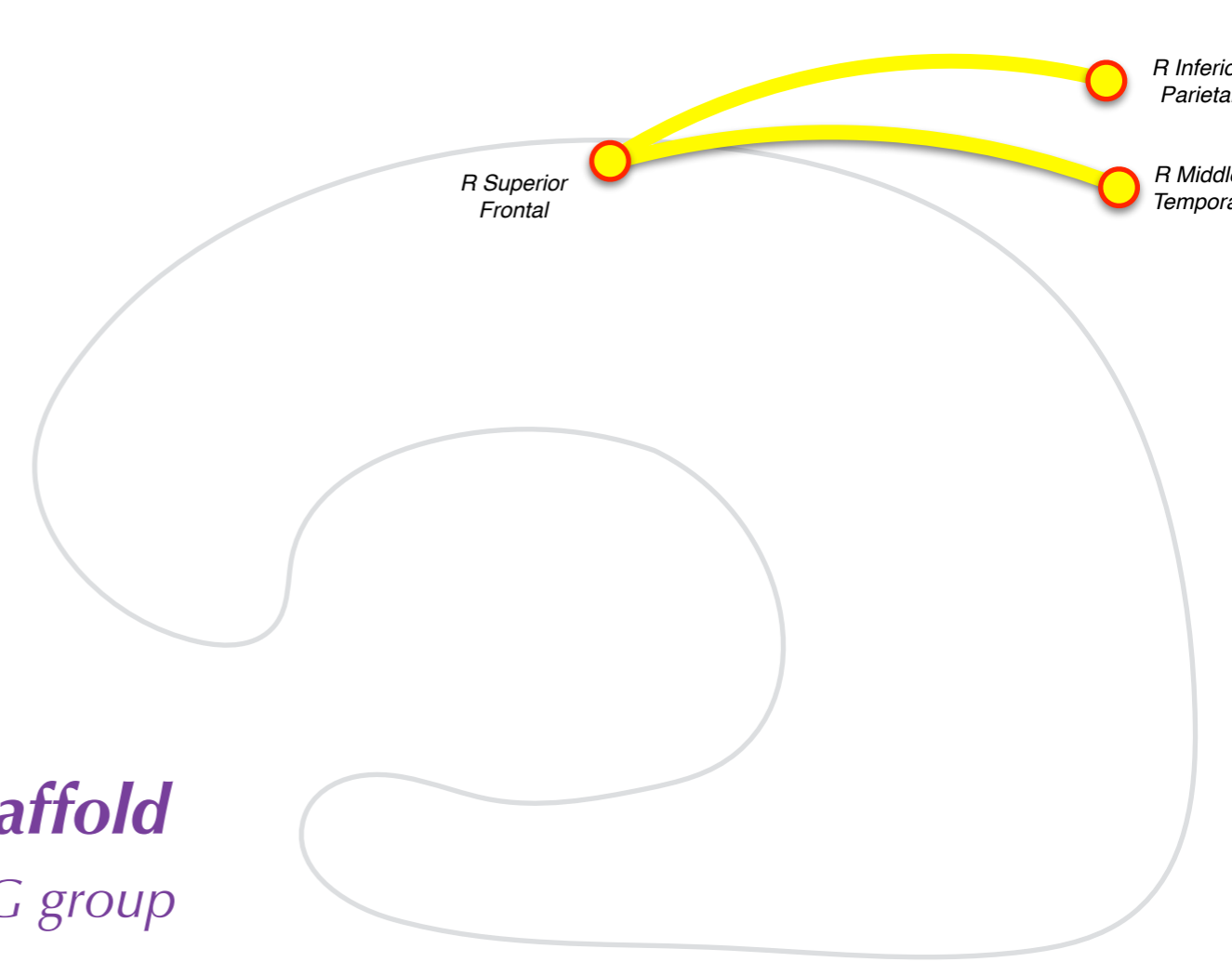
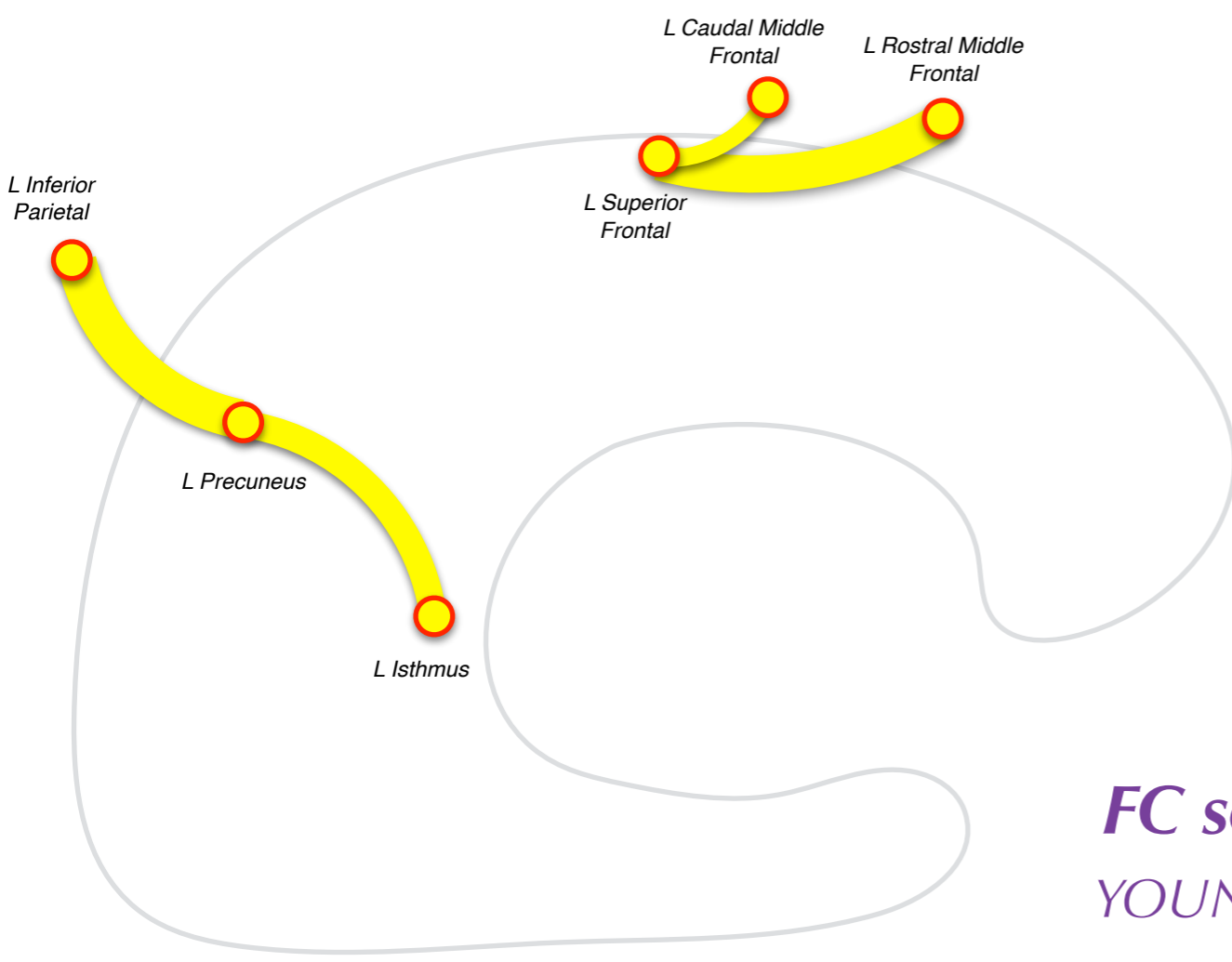
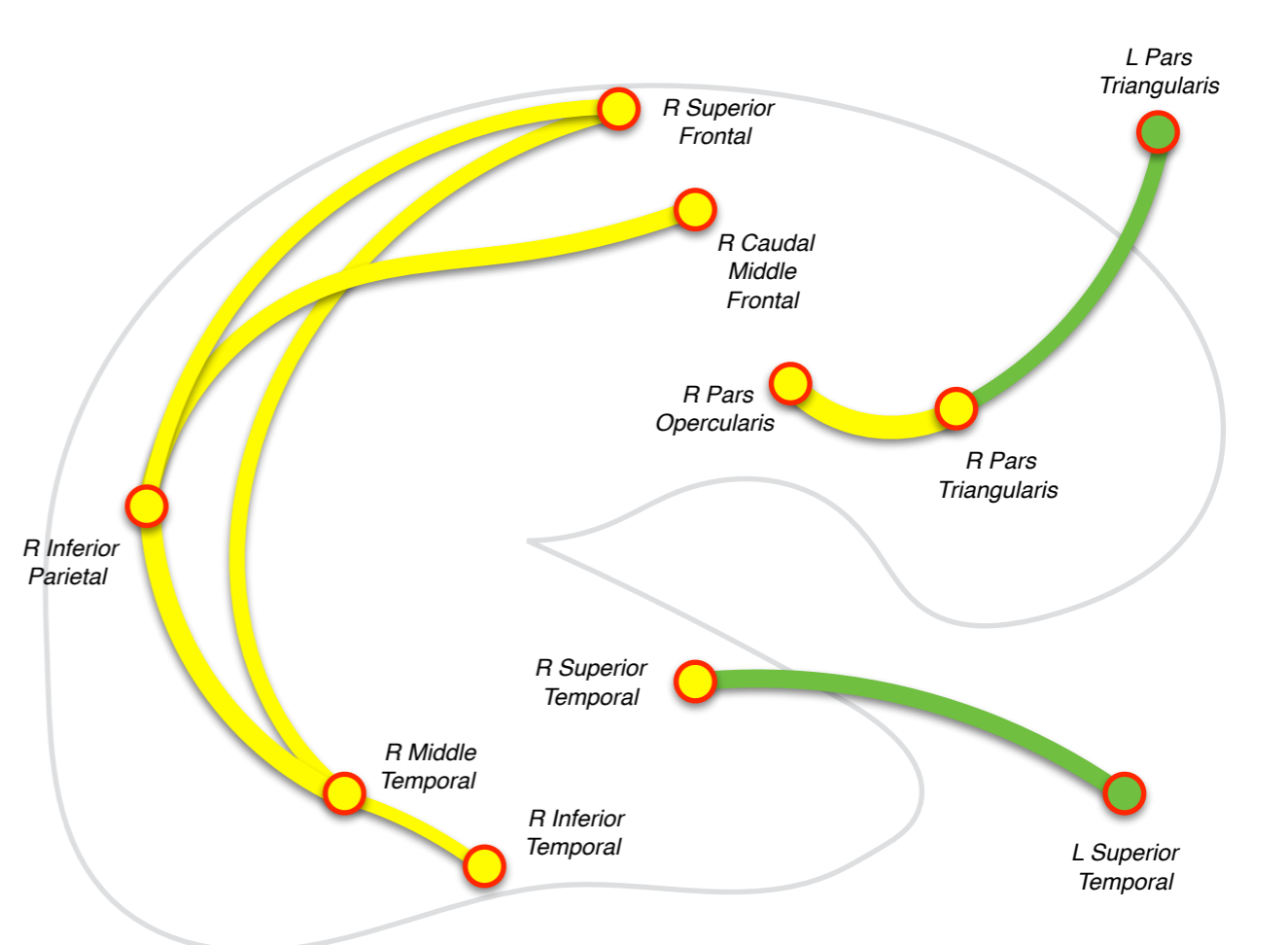
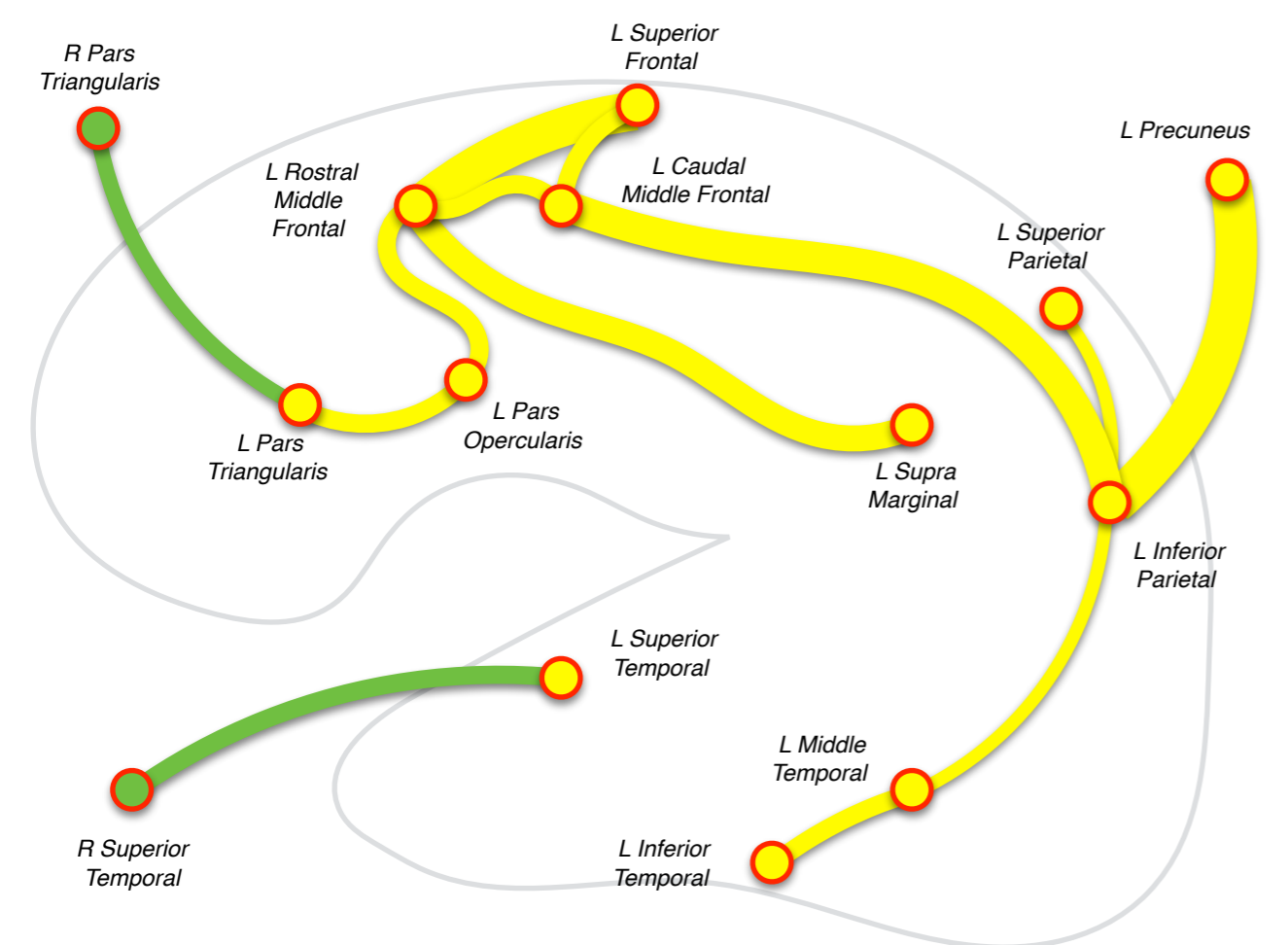
The more cycles (weighed by persistence) pass through an edge, the stronger this edge will be in the scaffold





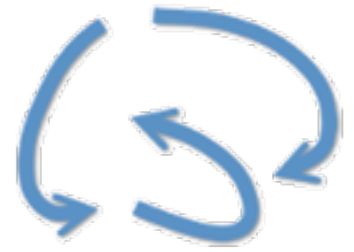
SC scaffold
YOUNG group





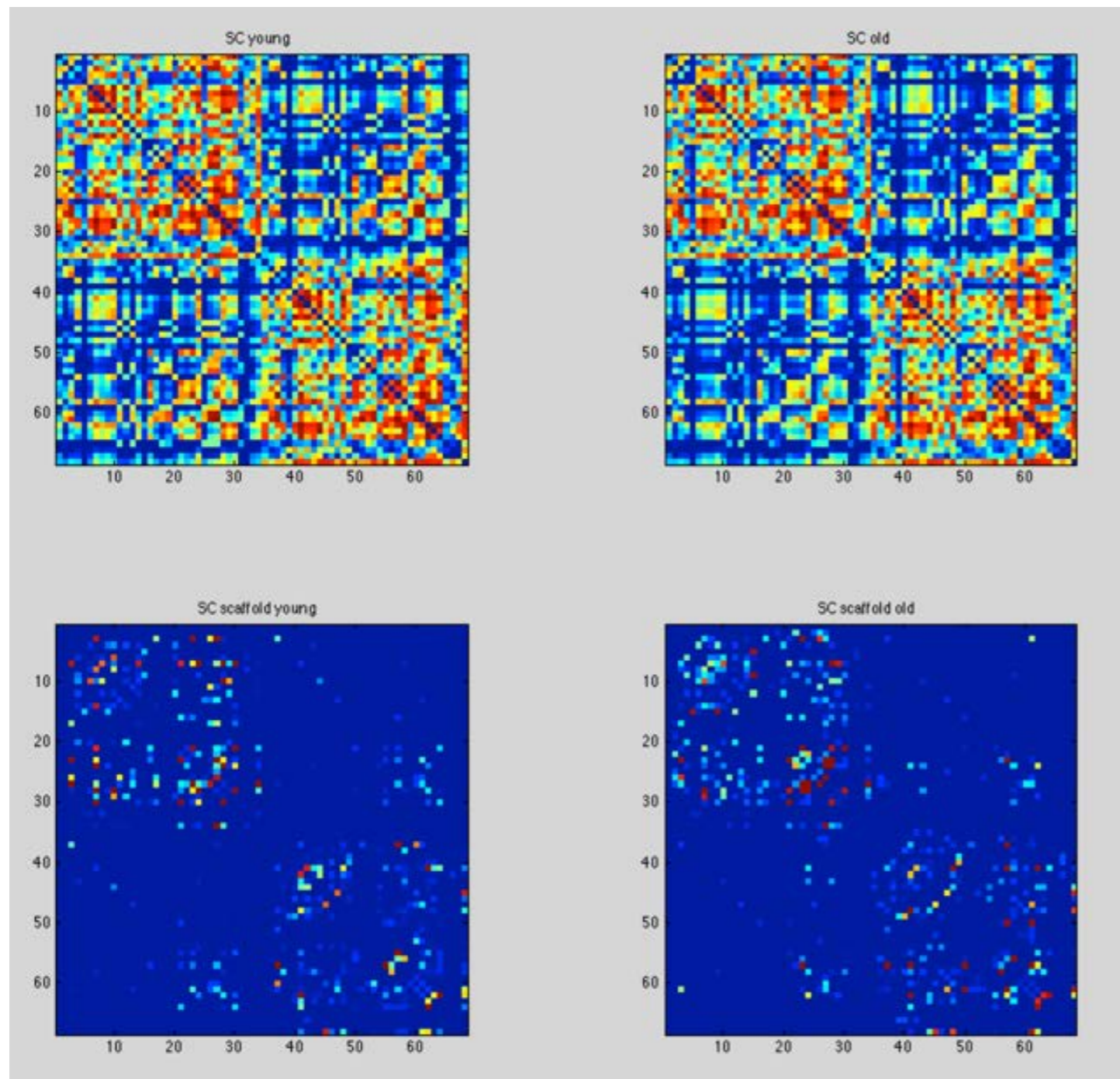
FC scaffold
YOUNG group

Scaffolds are diluted!



YOUNG


OLD



Full SC graph

SC scaffold graph

Some results

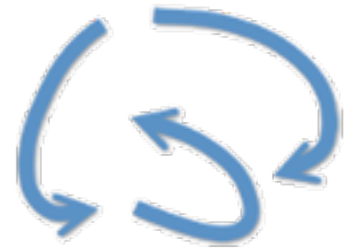
- Structural connectome:
 - *Average persistence maintained*
 - *cycle length increases (“drying sponge”)*
- Functional connectome:
 - *Average persistence and length maintained!*
- In other words: nothing changes too much! 
Homology is conserved through aging

Some results

- Comparison with null models
 - *We generate surrogate SC and FC by fitting trends with age of the strength of each link...*
 - *... but each link is independently decreasing (or increasing)!*
- Data vs model
 - ***There is matching for structural connectome:** “drying sponge effect” can be simply explained by the individual disconnection rates*
 - ***There is NOT matching for functional connectome:** in the model the Betti number is exploding, the persistence is dropping, the length is reducing... nothing works!*
- **⇒ Homology conservation in FC is a non trivial result!**

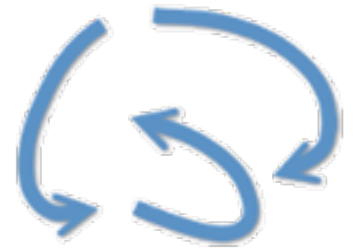
Some results

- The actual scaffolds are changing...
- ... in ways compatible with known hypotheses ("HAROLD", "PASA" ...)
- So holes and cycles relocate... but to build an object with the same homology!
- **⇒ Compensatory effects?**
- **Go to pathological cohorts... *in the future***

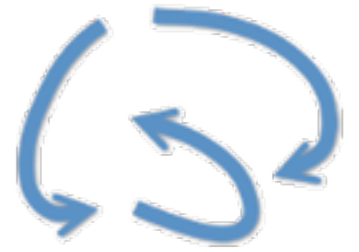


BETTER ?





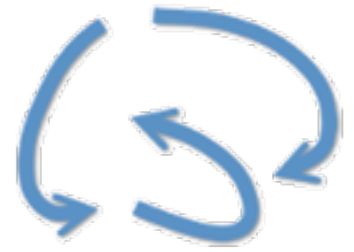
On the meaning of “better”...



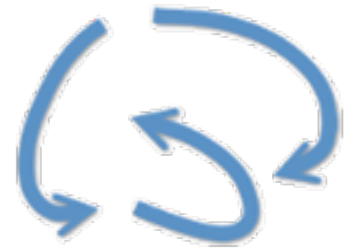
Or better say different!

“Better” we don’t know yet...

Functional Connectivity Dynamics (FCD) as biomarker

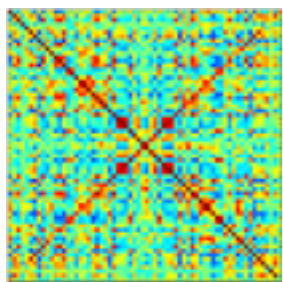


- Closer to the dynamic nature of the brain!
 - *What is altered may be the dynamics, not the networks!*
- Avoids misinterpreting temporal variability as inter-subject variability!



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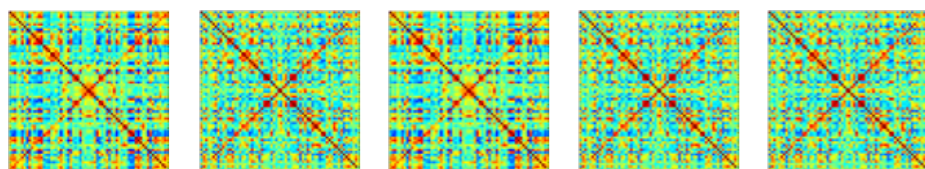
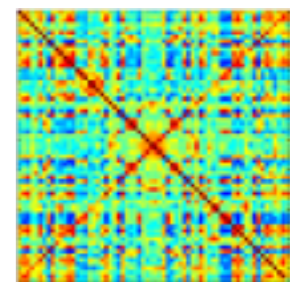
Average FC



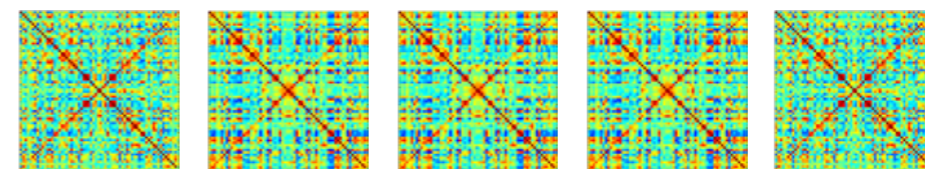
**Big
Mistake!**



Average FC

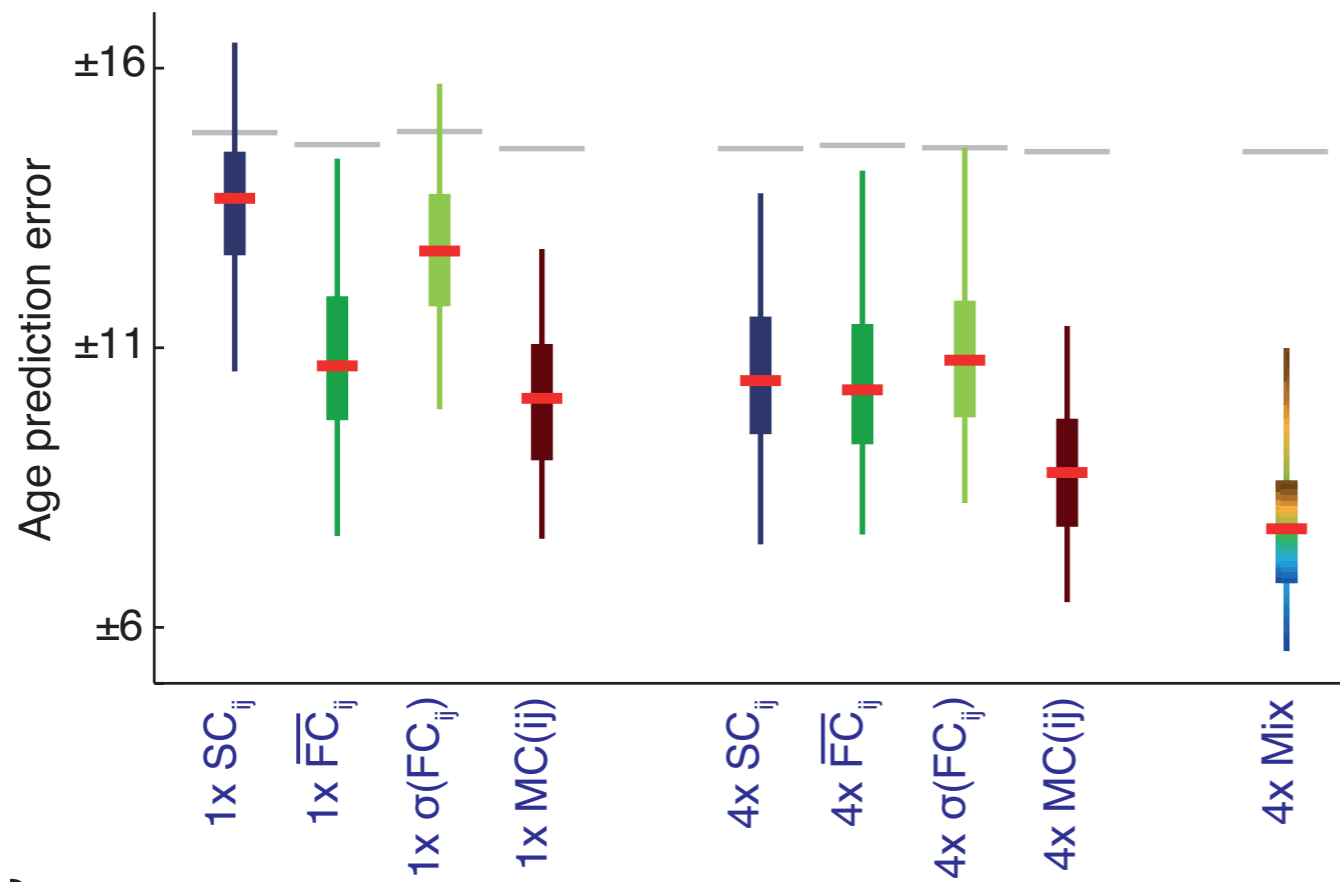
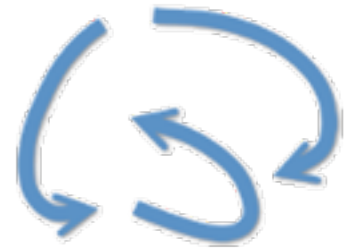


FC_A FC_B FC_A FC_B FC_B



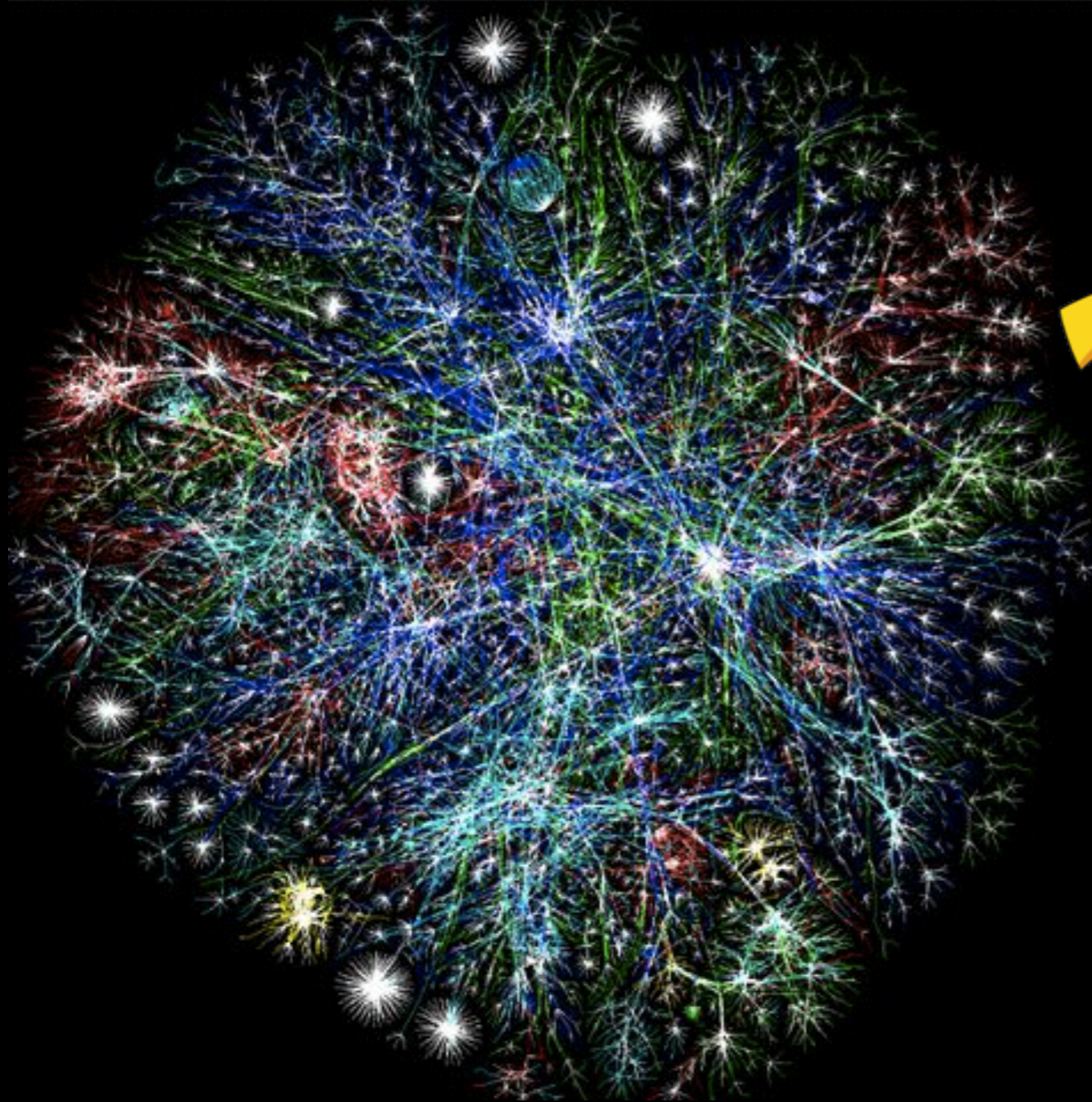
FC_B FC_A FC_A FC_A FC_B

Predicting age

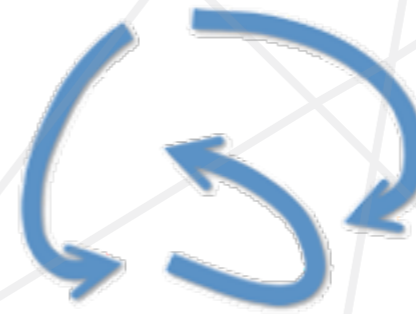


SYNERGY!

Crappy linear prediction



**Let's go
beyond graphs!**



Institut de
Neurosciences des
Systèmes

Thanks!

