Mapping white matter neurodegeneration in the human connectome: a network science study of hereditary diffuse leukoencephalopathy with spheroids

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Network Science Talks

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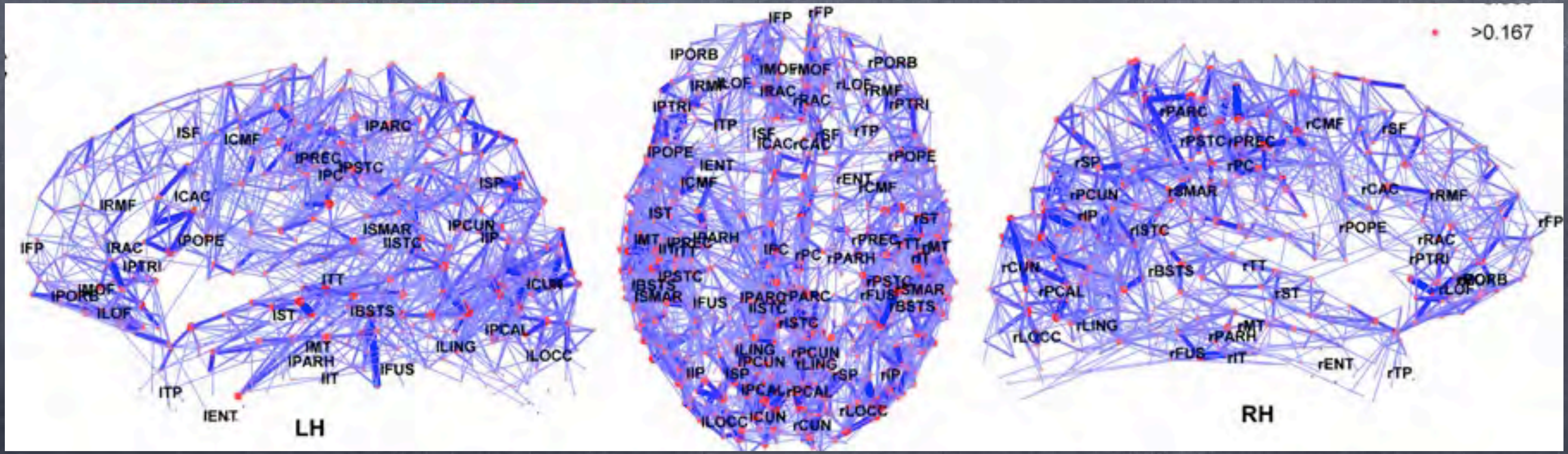
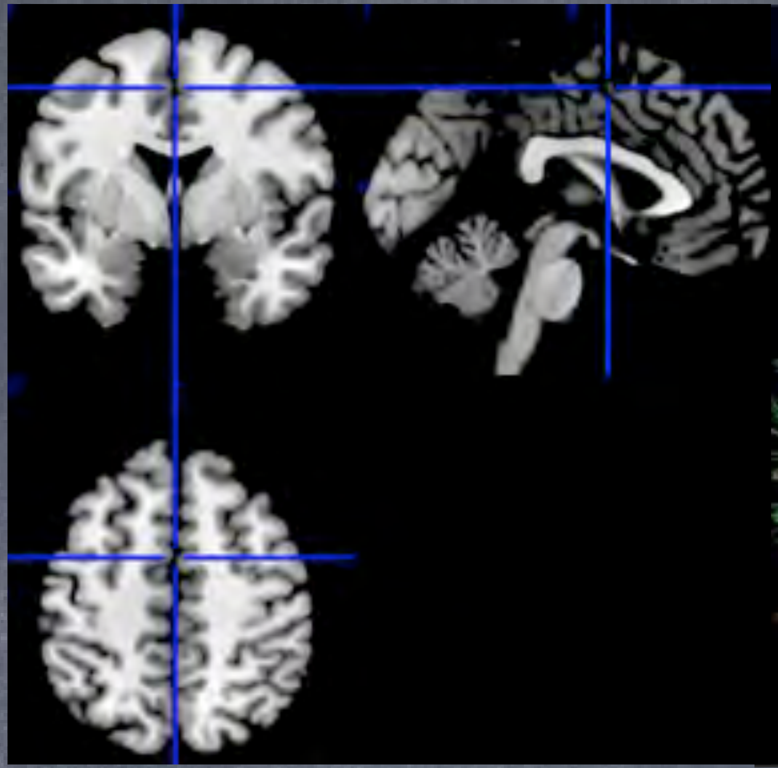
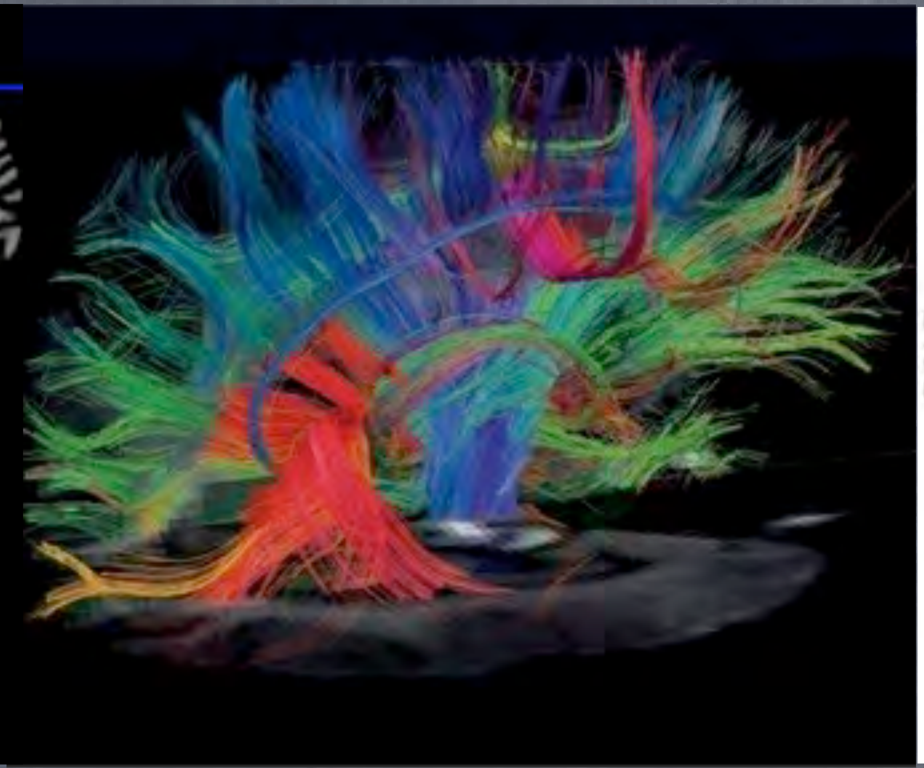
The Human Connectome

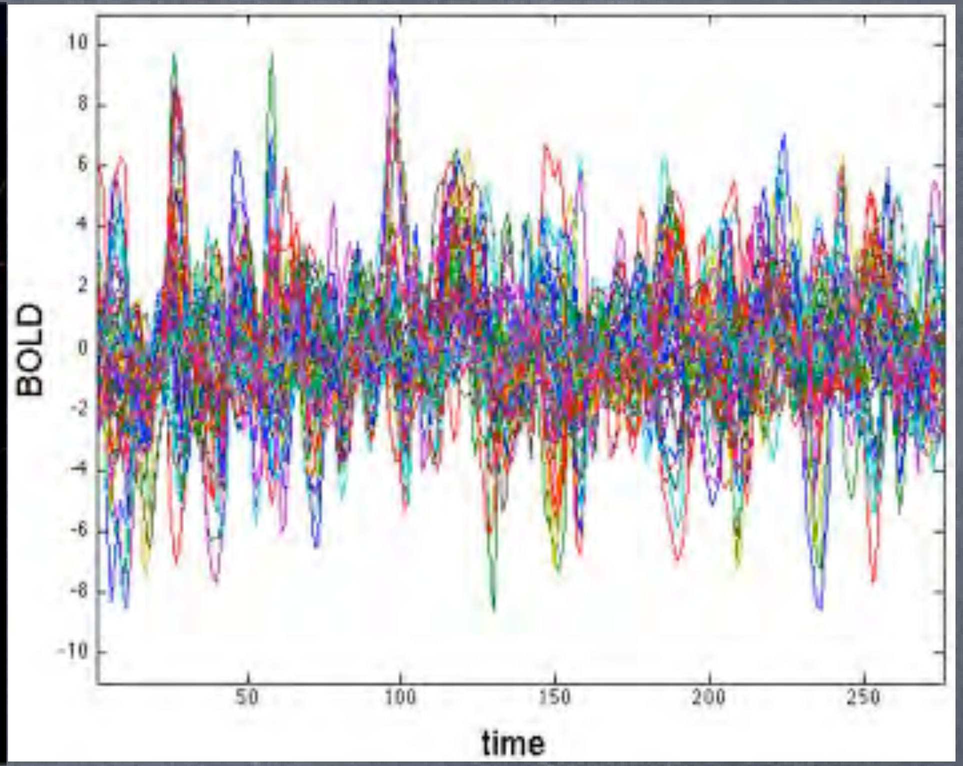
- nodes represent GM regions and edges represent WM fibers connecting those regions
- Integration of information in the brain has been characterized by the length and/or by the efficiency of shortest-paths
- Search-information brings another dimensionality to shortest-paths, i.e. how hidden they are embedded in the rest of the network



Hagmann et al. Plos Biol. 2008







T1 MRI

diffusion weighted imaging, DSI,DTI

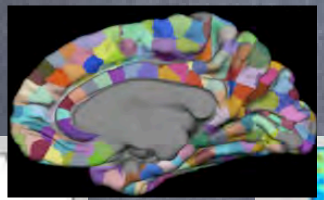
fMRI, resting-state time-series

fibers detection

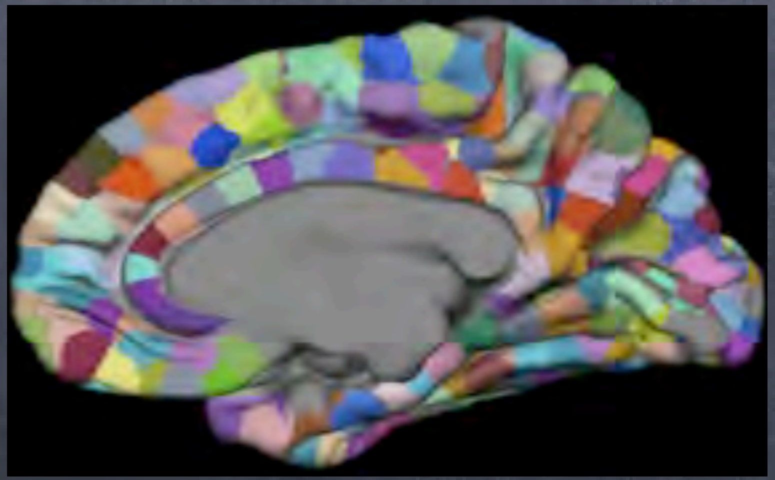
functional coupling

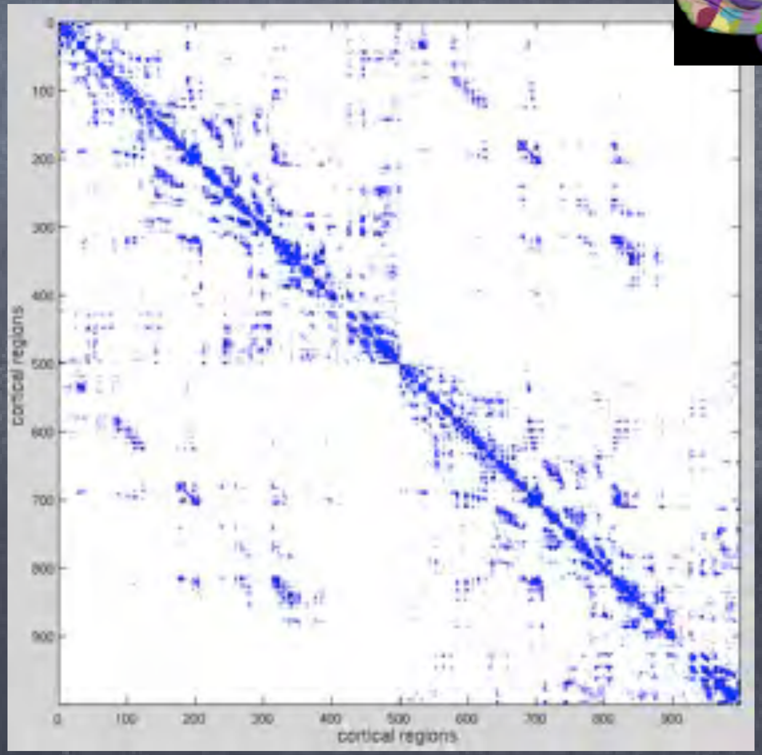
Grey matter segmentation
Cortical partition

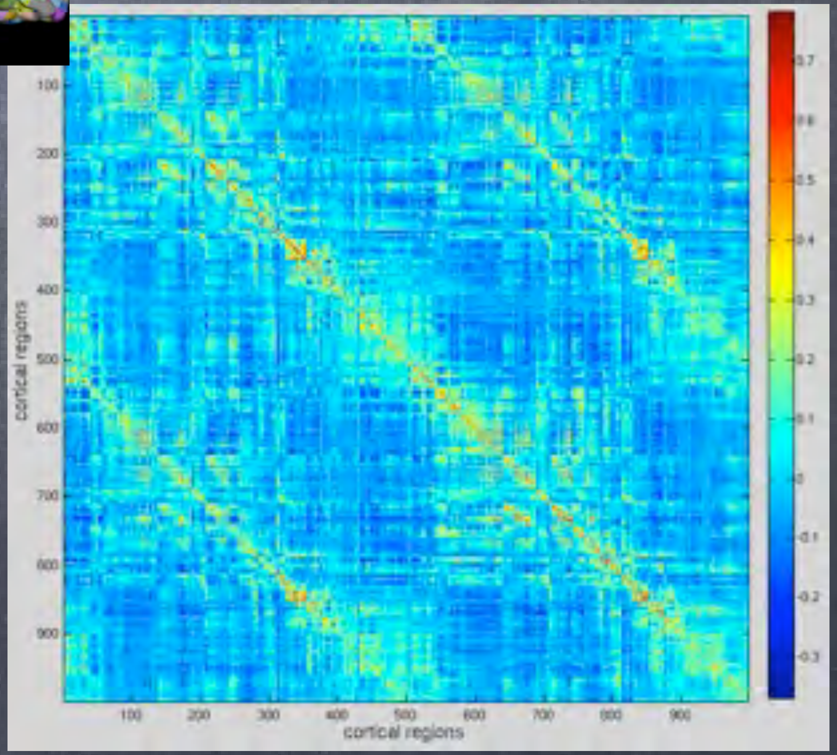
structural connectivity



functional connectivity







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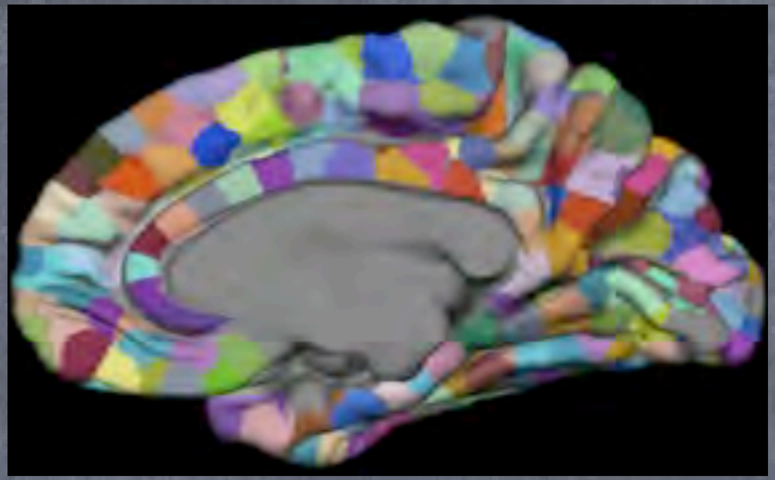
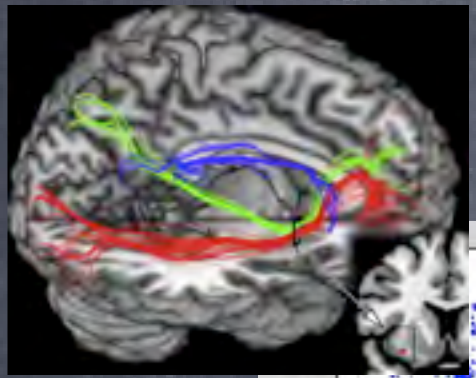
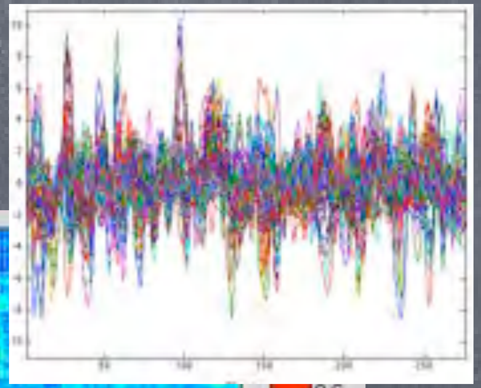
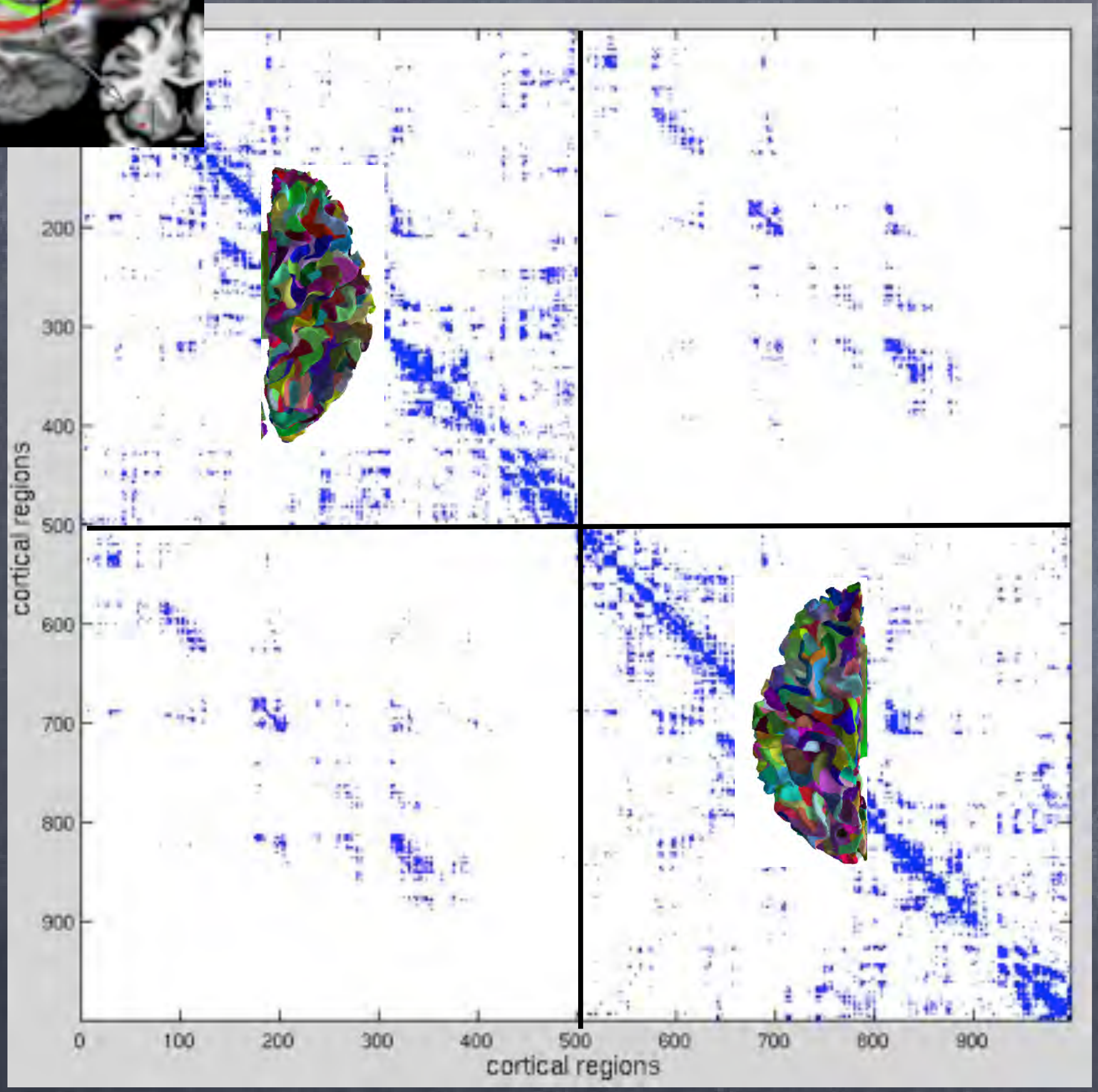


fiber-tracts (model)

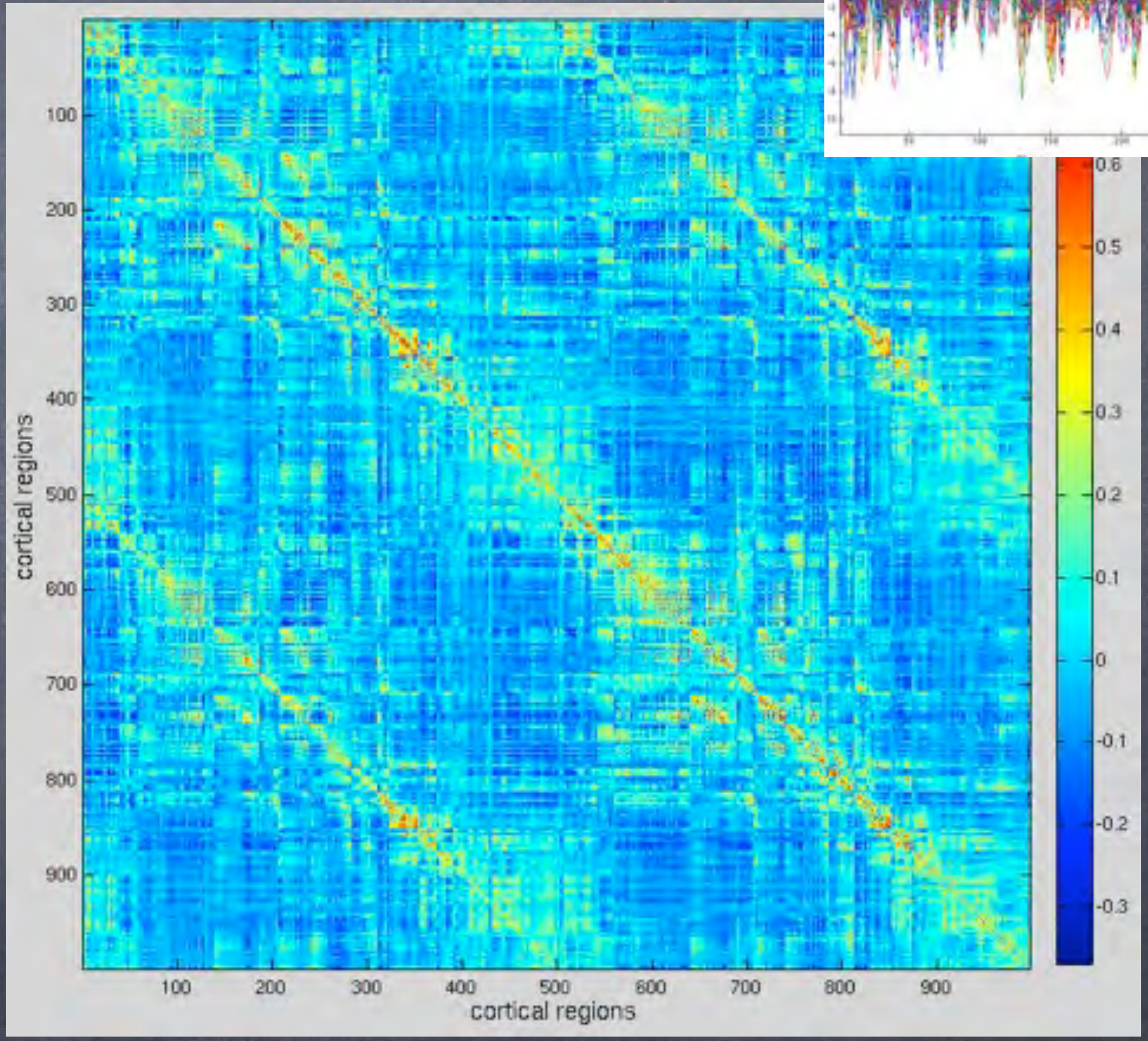


neural activity (model)

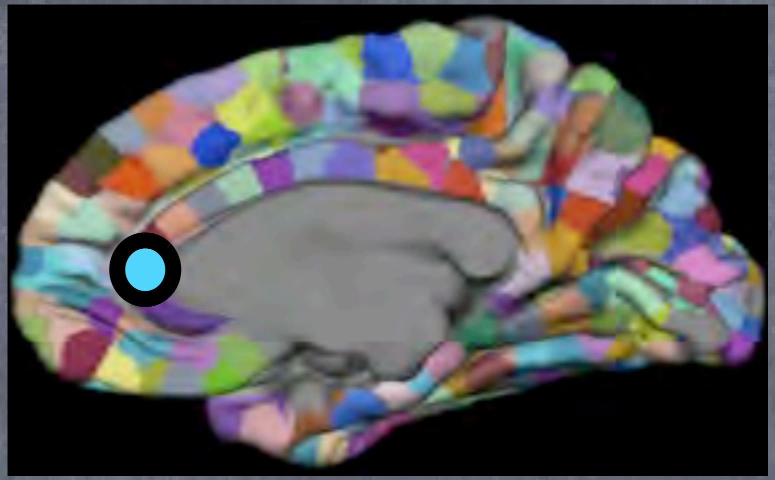




structural connectivity (SC)



functional connectivity (FC)



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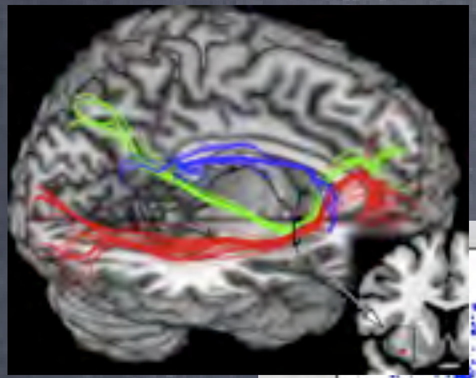

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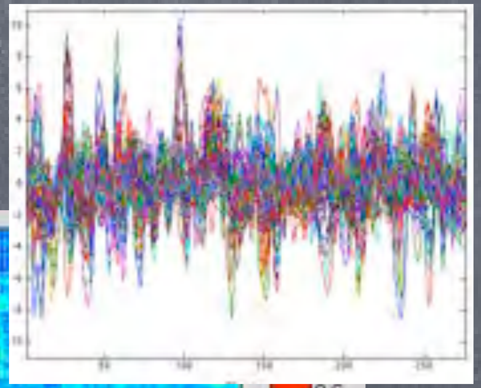

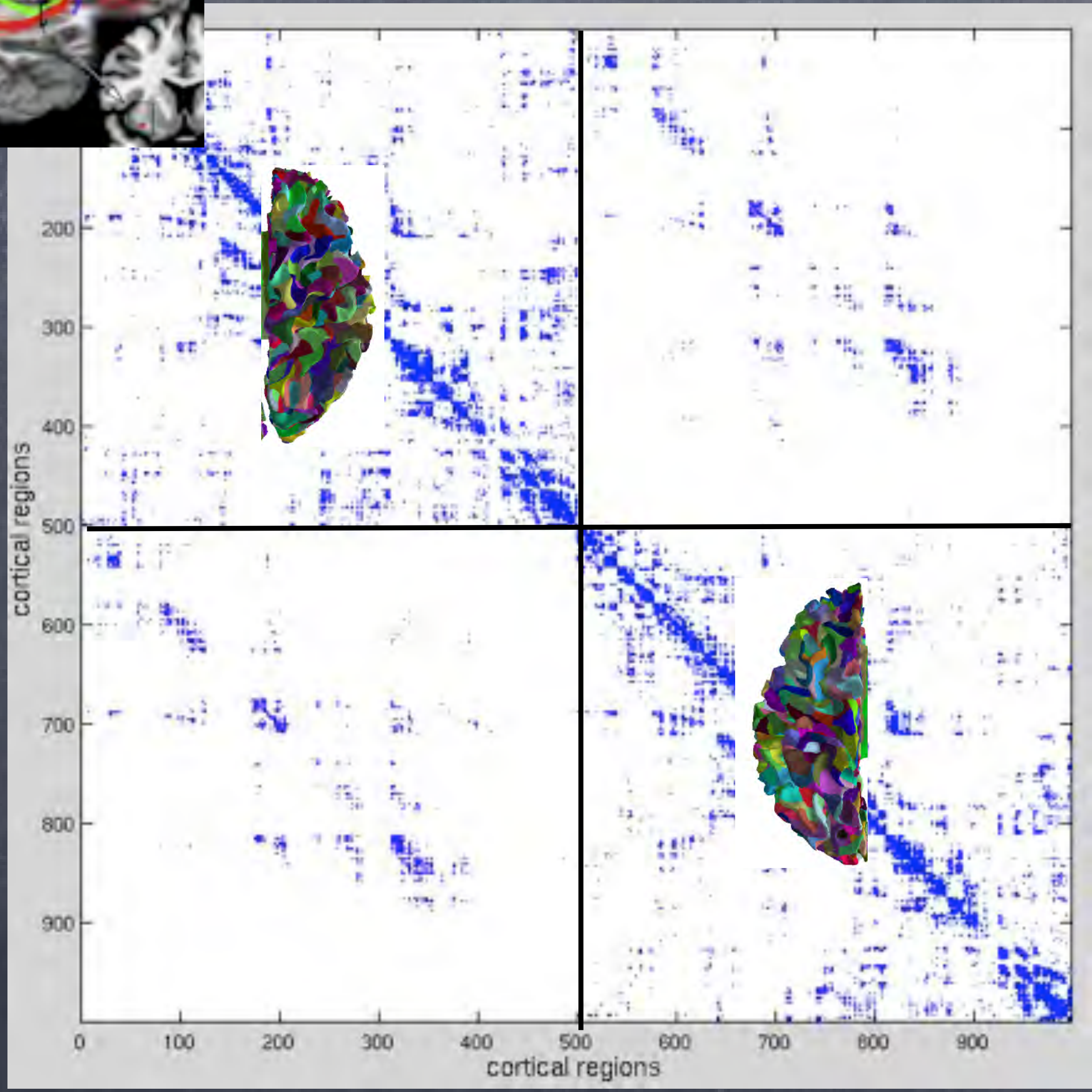

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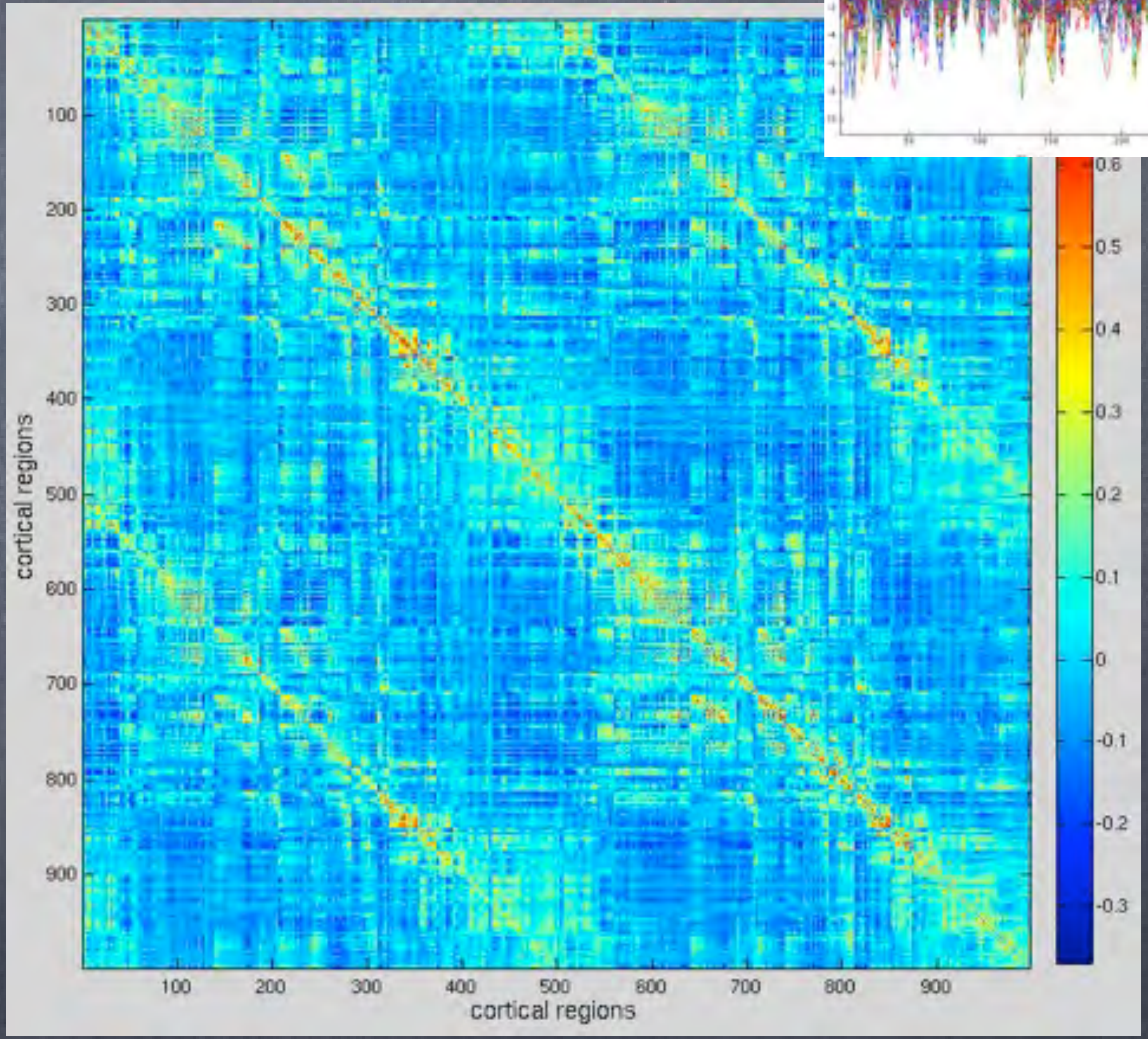

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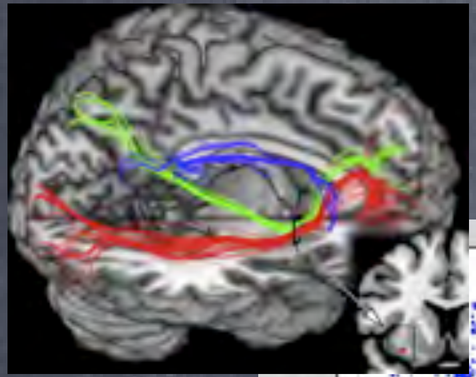

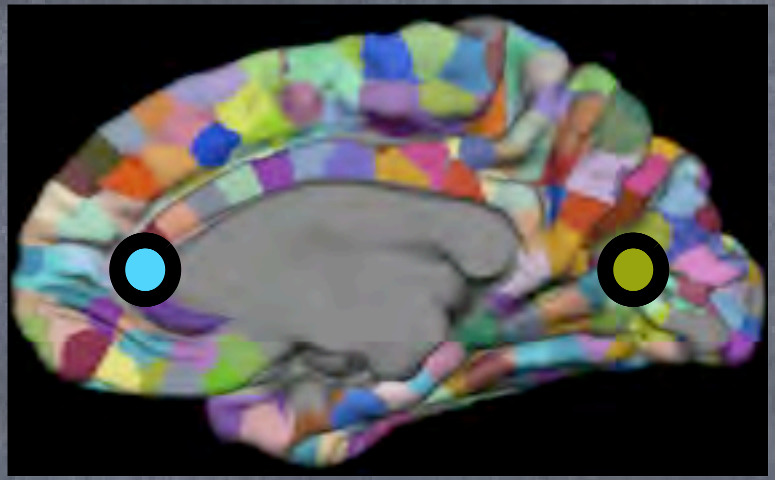

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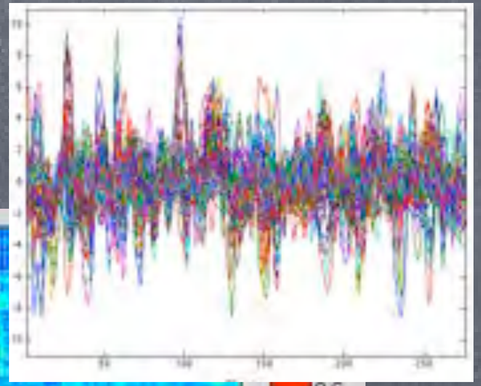

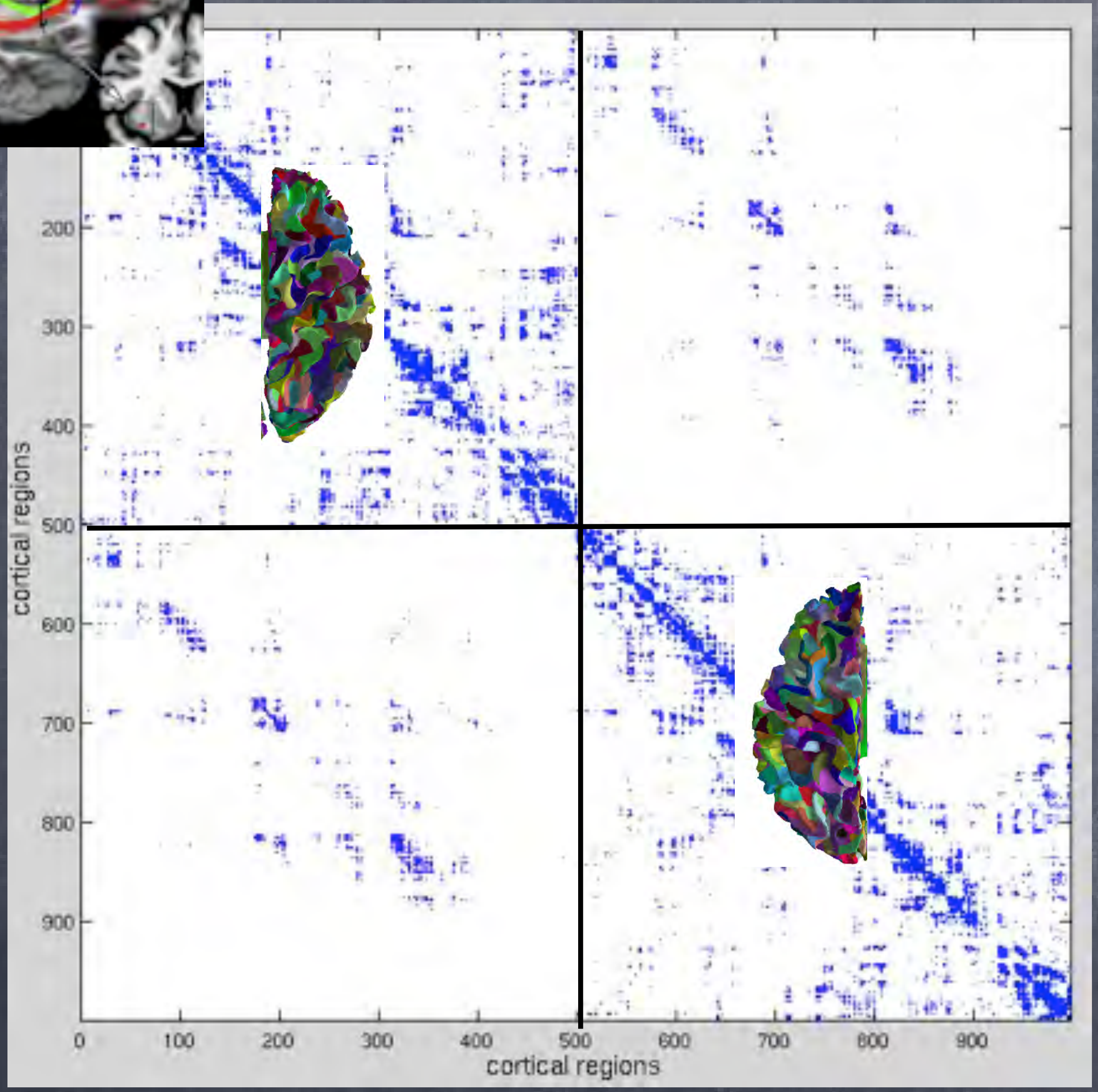

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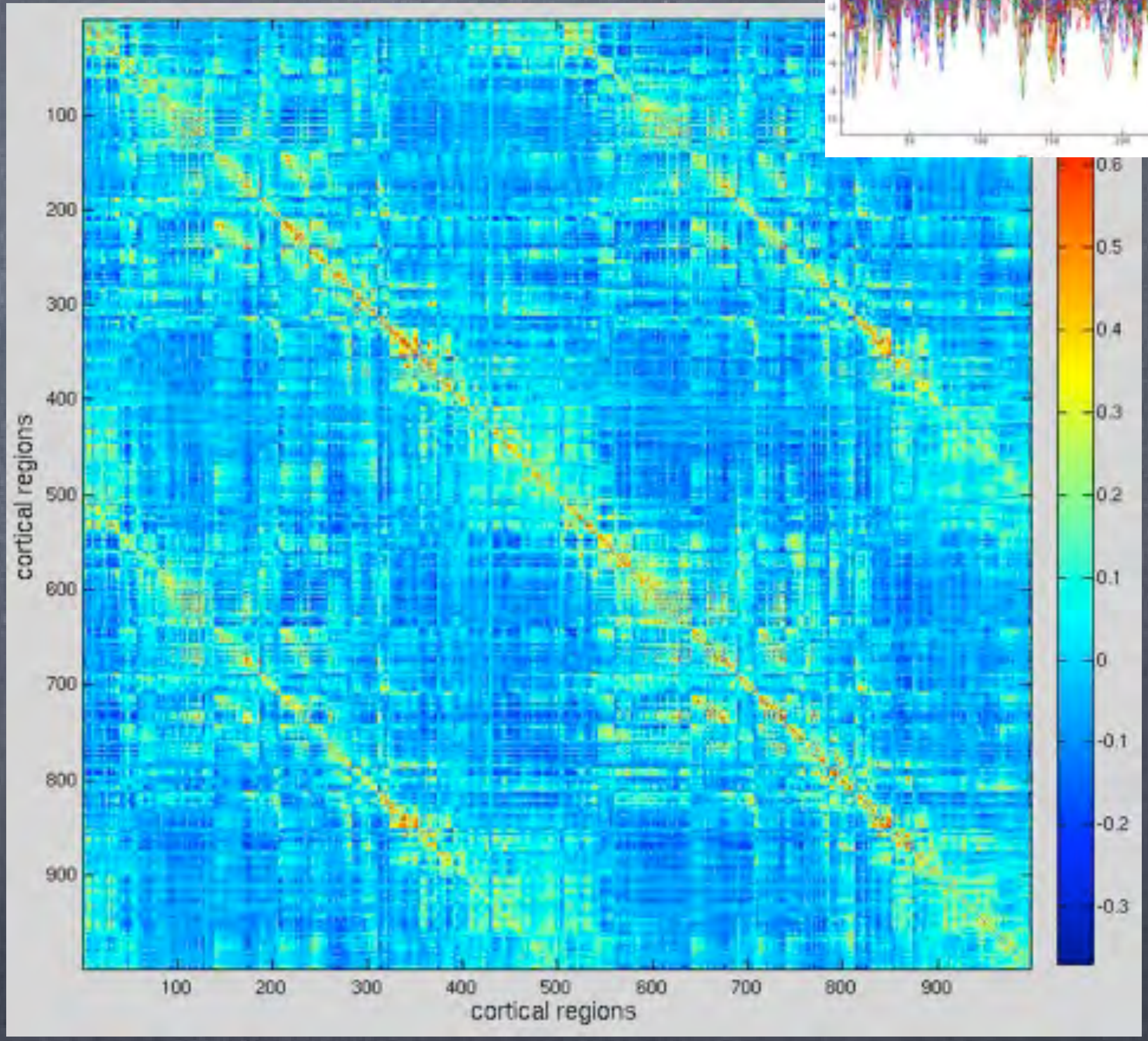

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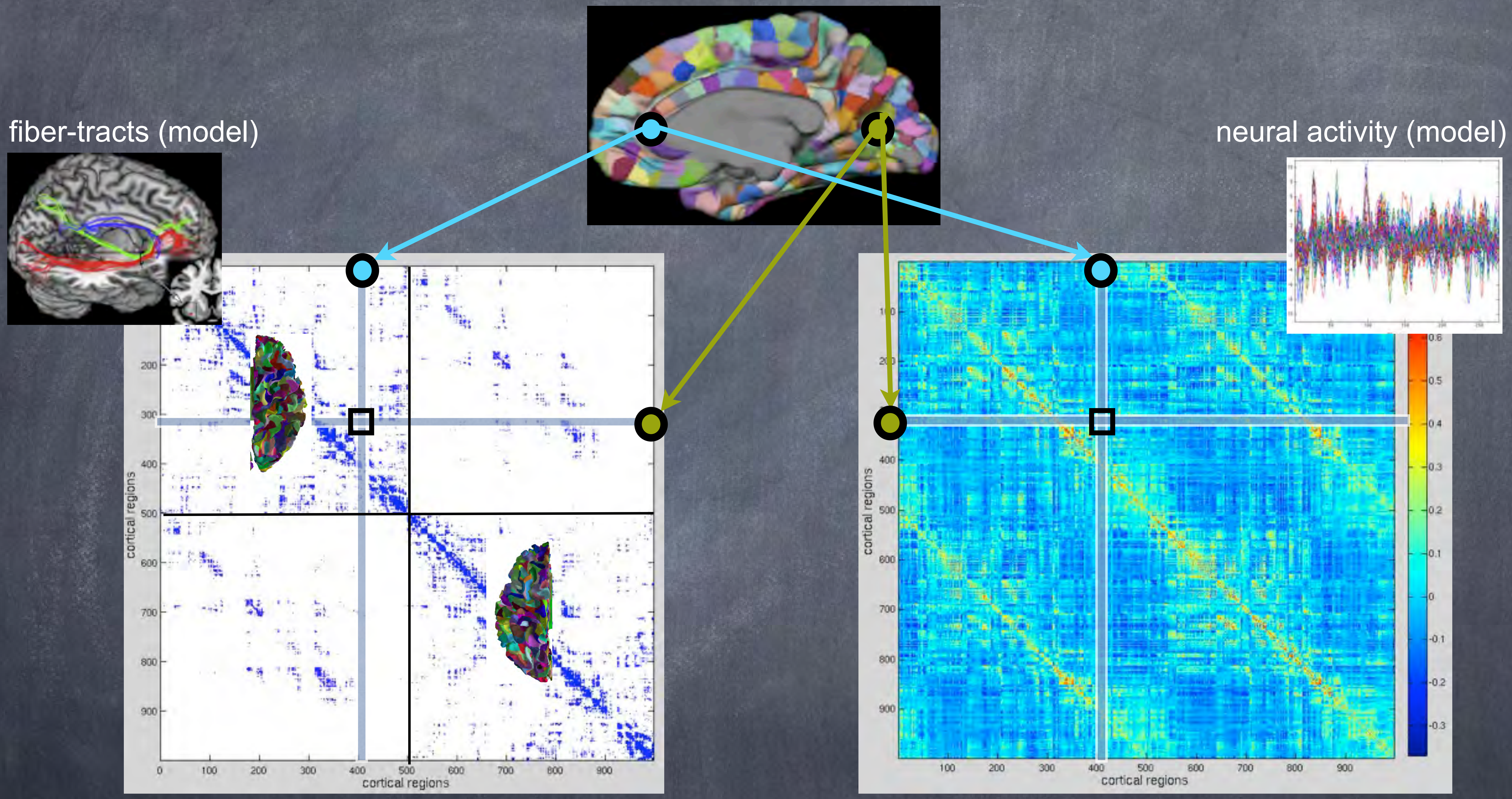

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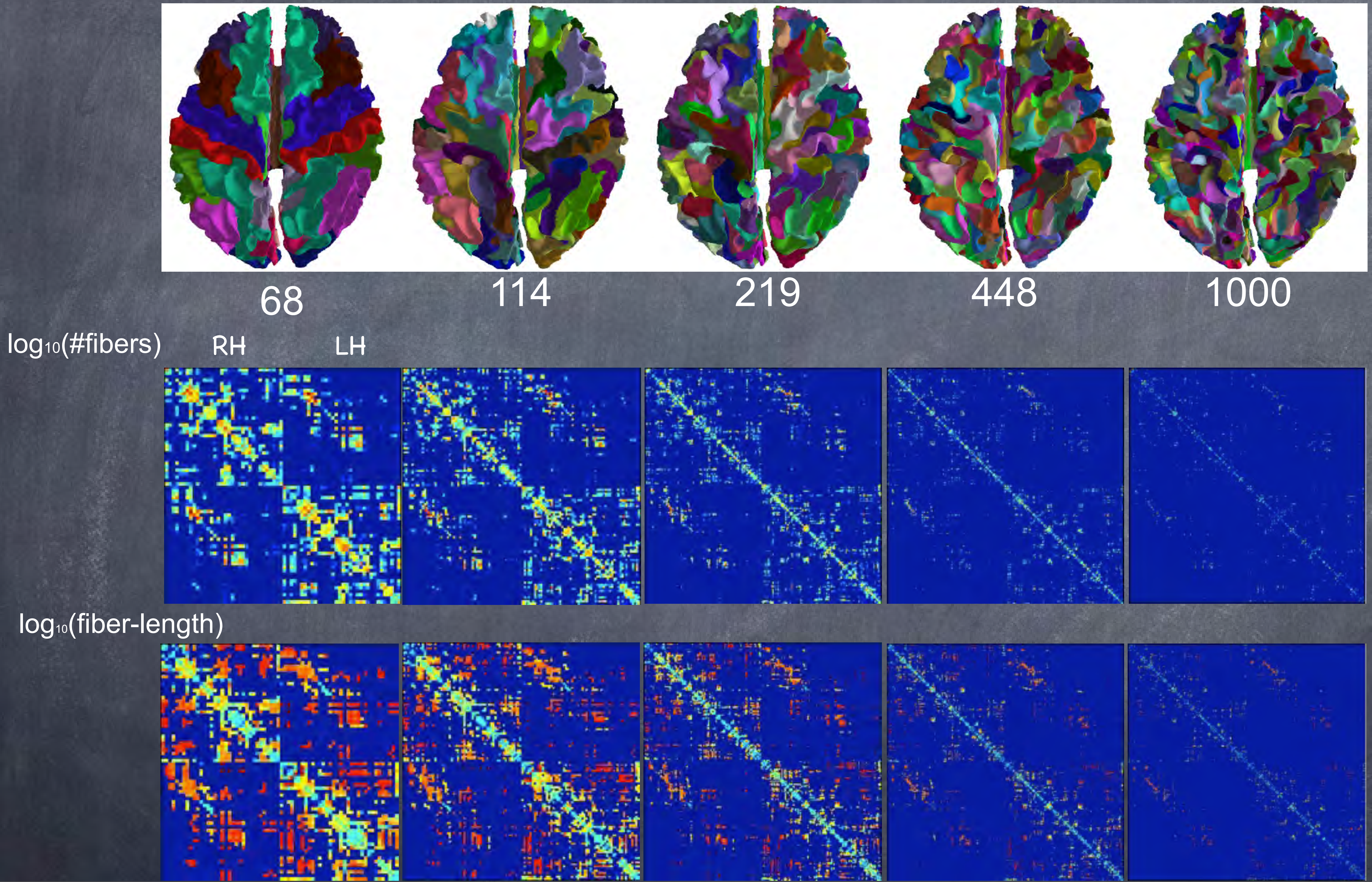
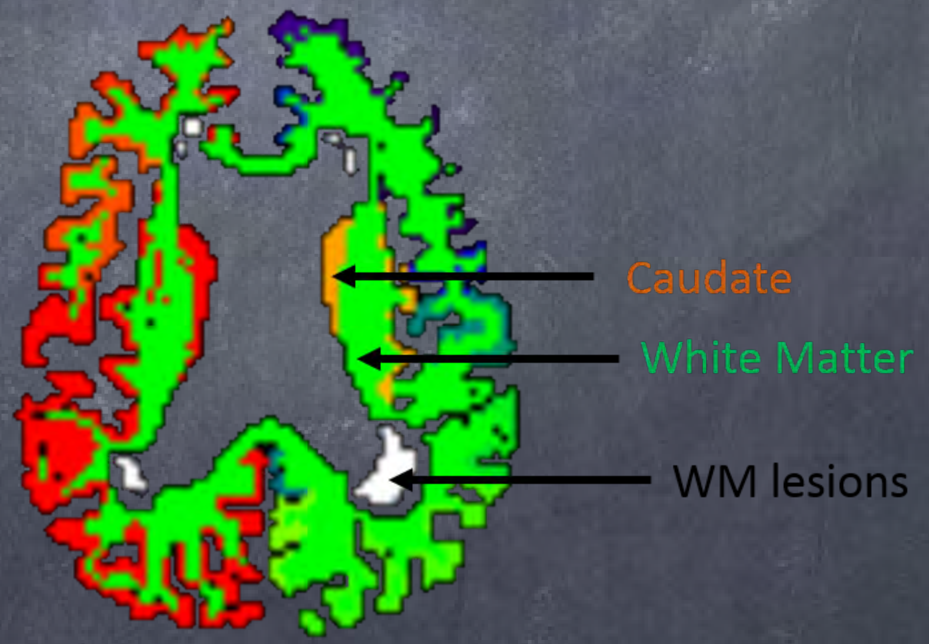
functional connectivity (FC)



68
114
219
448
1000
log10(#fibers)
RH
LH
log10(fiber-length)

A case study of HDLS

- Hereditary diffuse leukoencephalopathy with spheroids, (HDLS), is an autosomal dominant neurodegenerative disorder caused by mutations in the colony stimulating factor 1 receptor (CSF1R) gene.
- It is characterized by white matter damage and axonal swelling (spheroids) leading to subcortical lesions visualized using MRI1.
- Clinical symptoms include progressive motor problems and cognitive decline. Patients with HDLS can often be mistaken for other neurodegenerative diseases.
- two siblings, HC (female, 48) and HDLS (male, 46)
- HDLS mutation: three base deletion (TCT) in CSF1R




reliable
individual
connectomes

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UCL Camino Diffusion MRI Toolkit

Camino is an open-source software toolkit for diffusion MRI processing. The toolkit implements standard techniques, such as diffusion tensor fitting, mapping fractional anisotropy and mean diffusivity, deterministic and probabilistic tractography. It also contains more specialized and cutting-edge techniques, such as Monte-Carlo diffusion simulation, multi-fibre and HARDI reconstruction techniques, multi-fibre PICo, compartment models, and axon density and diameter estimation.

Camino has a modular design to enable construction of processing pipelines that include modules from other software packages. The toolkit is primarily designed for unix platforms and structured to enable simple scripting of processing pipelines for batch processing. Most users use linux, MacOS or a unix emulator like cygwin running under windows. However, the core code is written in Java and thus is simple to call from other platforms and programming environments, such as matlab running under unix or windows.

The microstructure imaging group at UCL lead development and maintenance of the toolkit. The PICSL group at the University of Pennsylvania also contribute heavily, as have Geoff Parker and colleagues at the University of Manchester. Many of the specialist modules arise from the research of the MIG and collaborating groups. However, the toolkit also includes implementations of many other techniques in the literature that we have found useful.

We hope you find Camino useful. We welcome any feedback, contributions or suggestions for additions to the toolkit.

Camino is distributed under the Artistic License 2.0. The full text of the license is here.

If you use Camino in your research, please include the appropriate citations from the citations page.

http://cmic.cs.ucl.ac.uk/camino/index.php

how to model an individual connectome?

Contreras et al. (in prep.)

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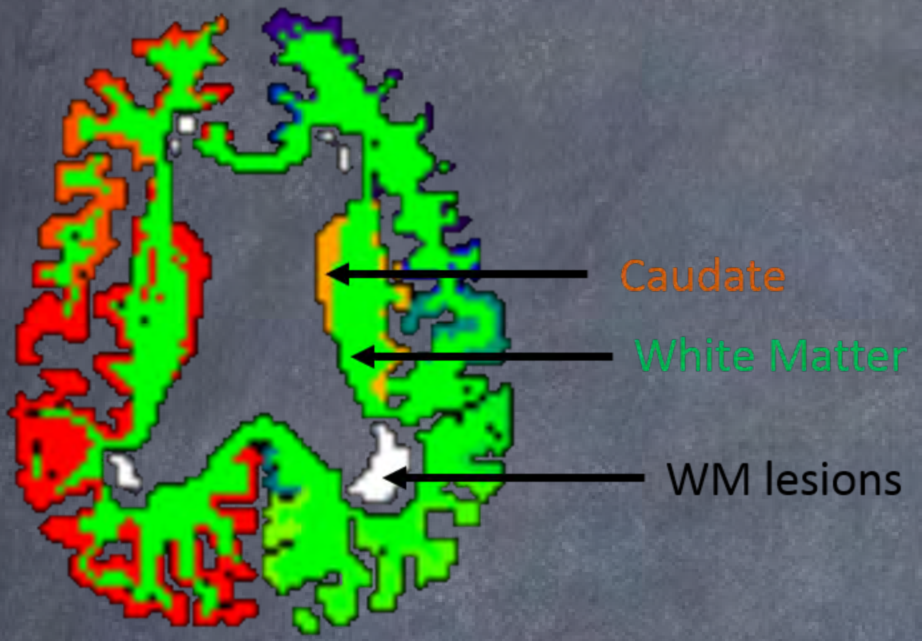

tissue segmentation

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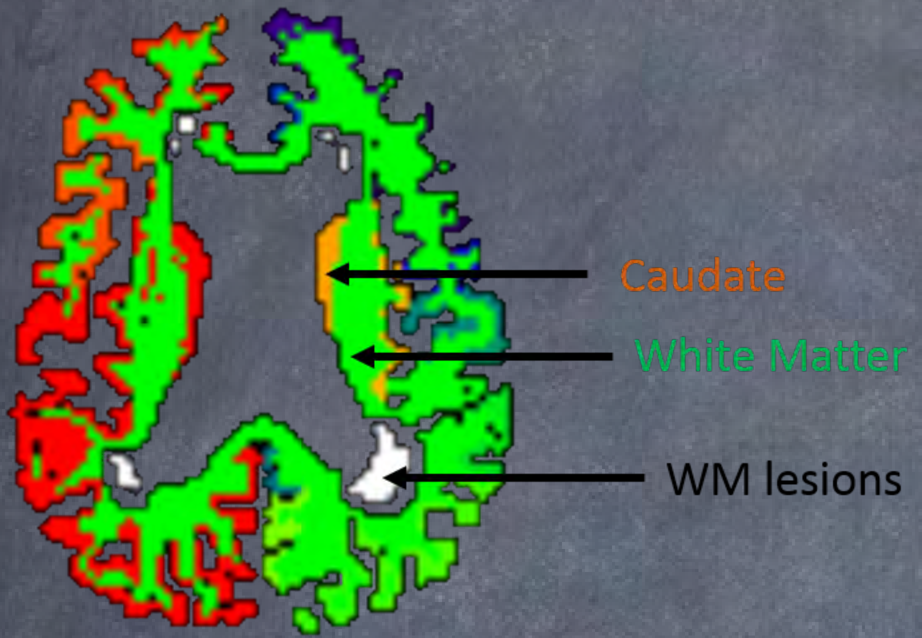

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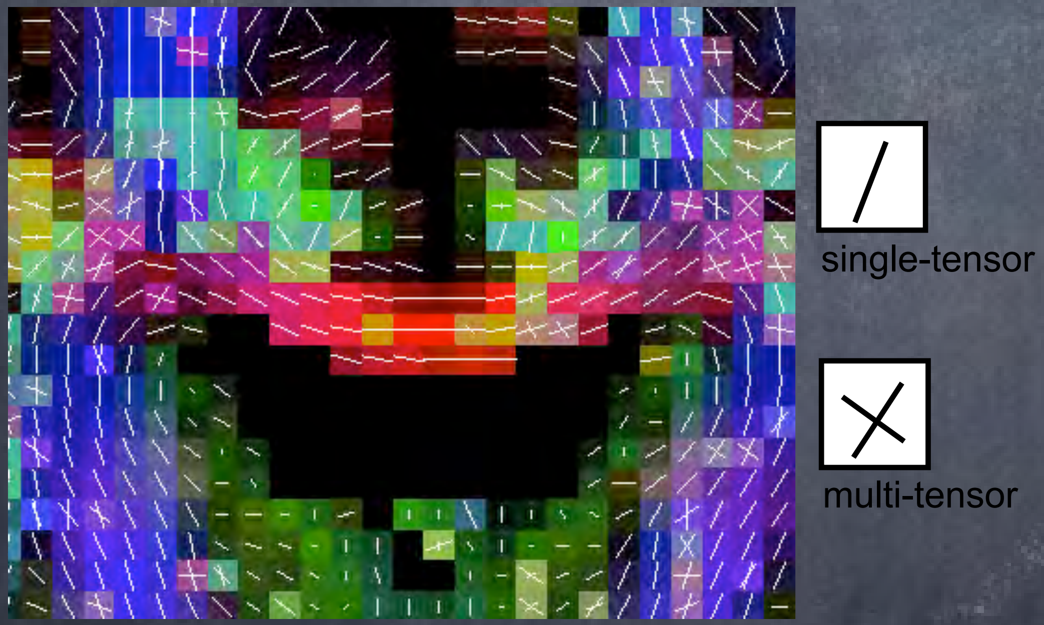

multi-tensor modeling

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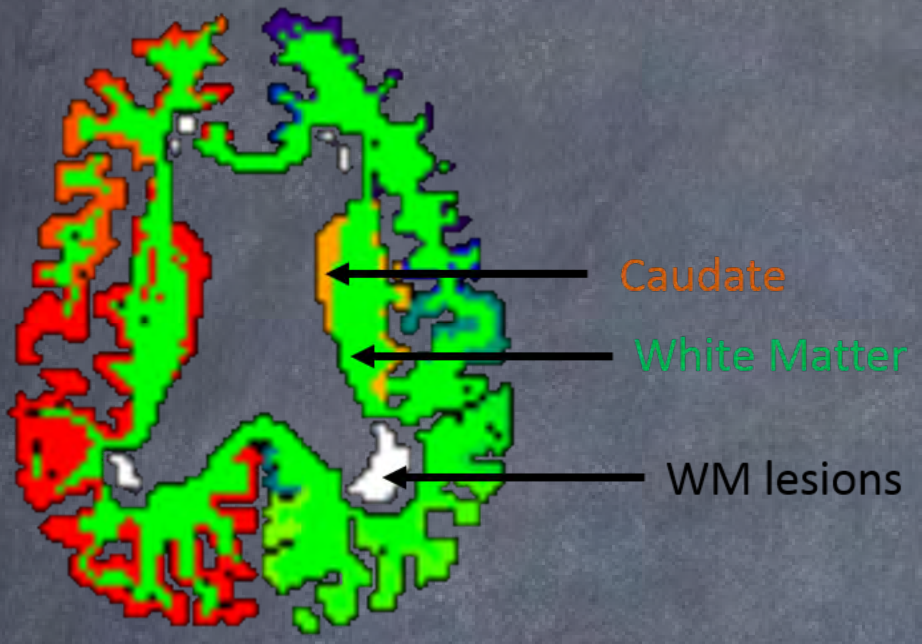

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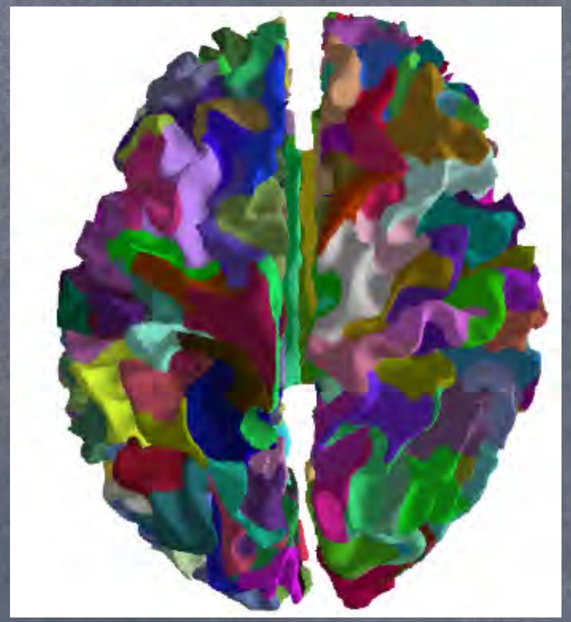
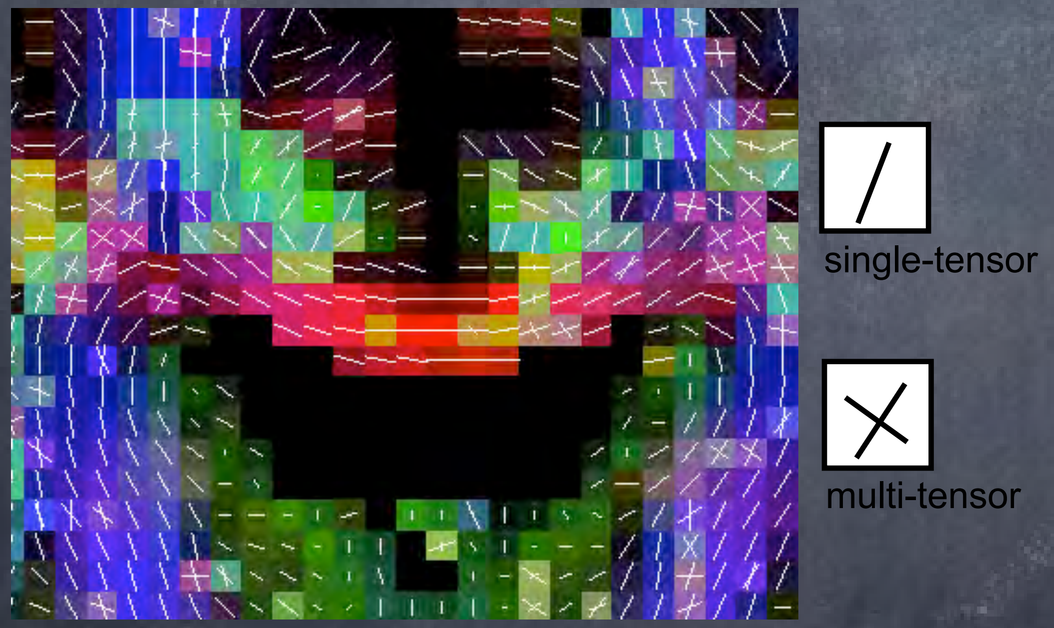


GM parcellation



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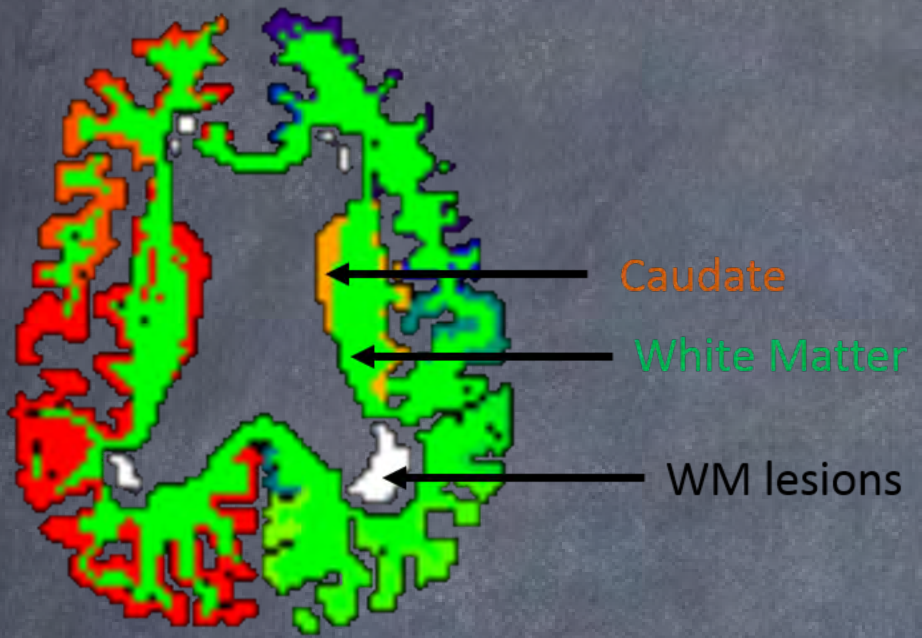

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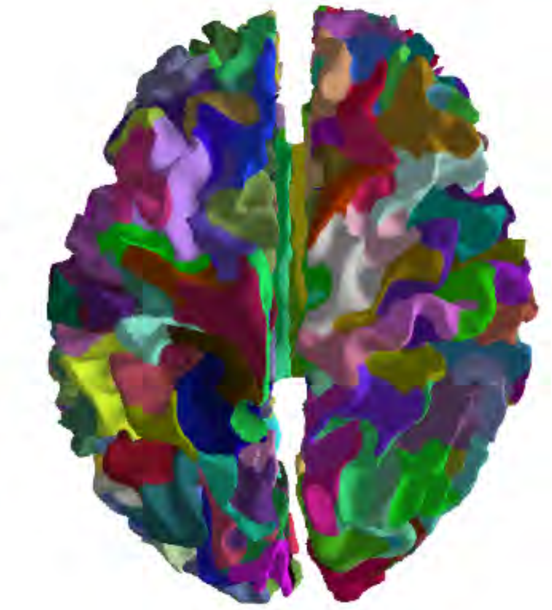

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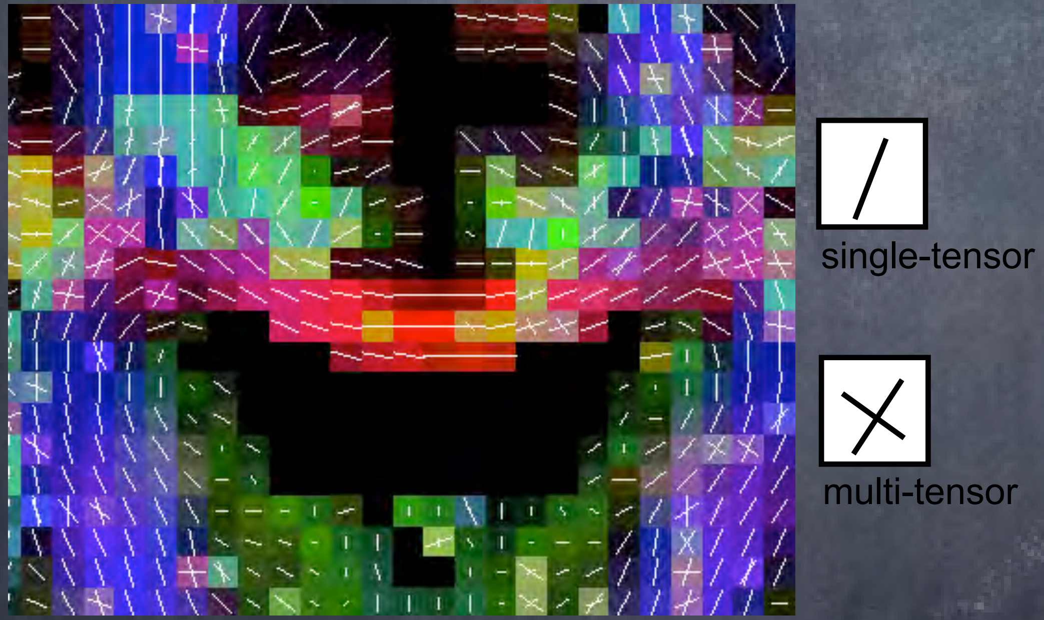

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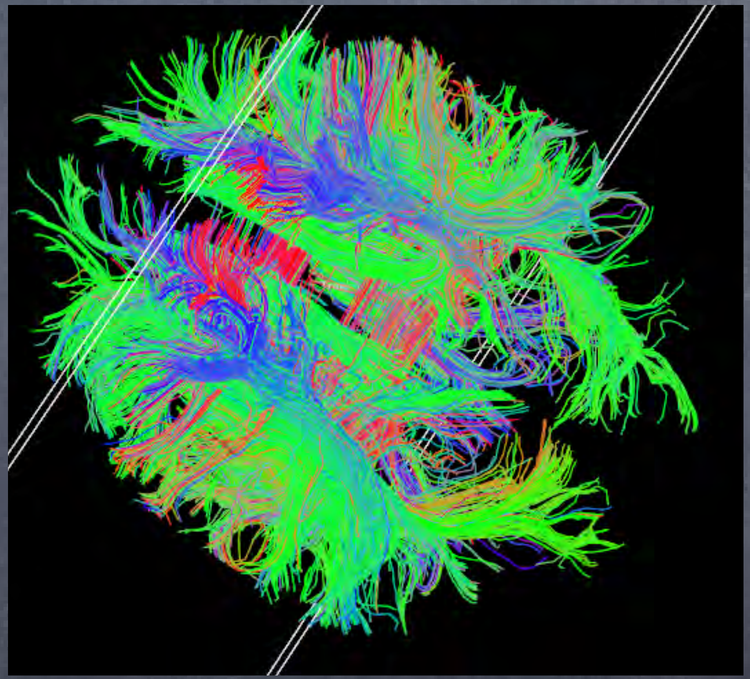

WM fiber-tracts

Contreras et al. (in prep.)

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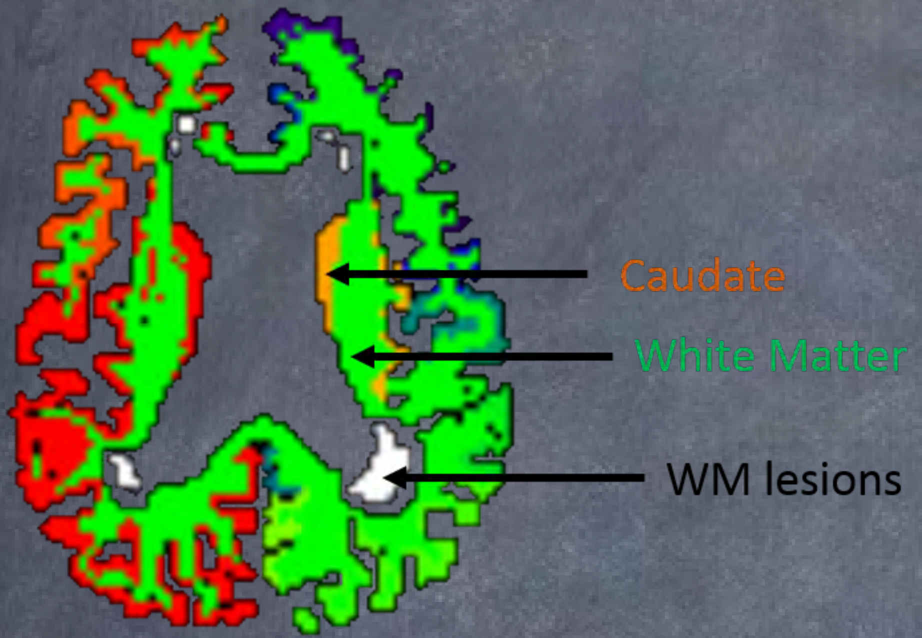

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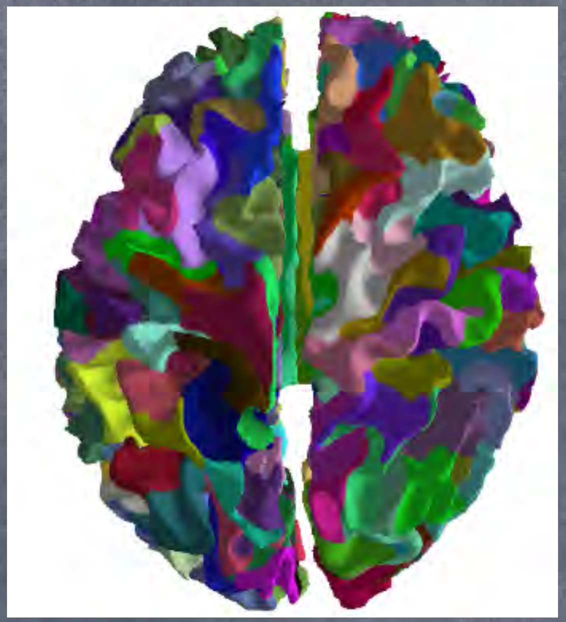

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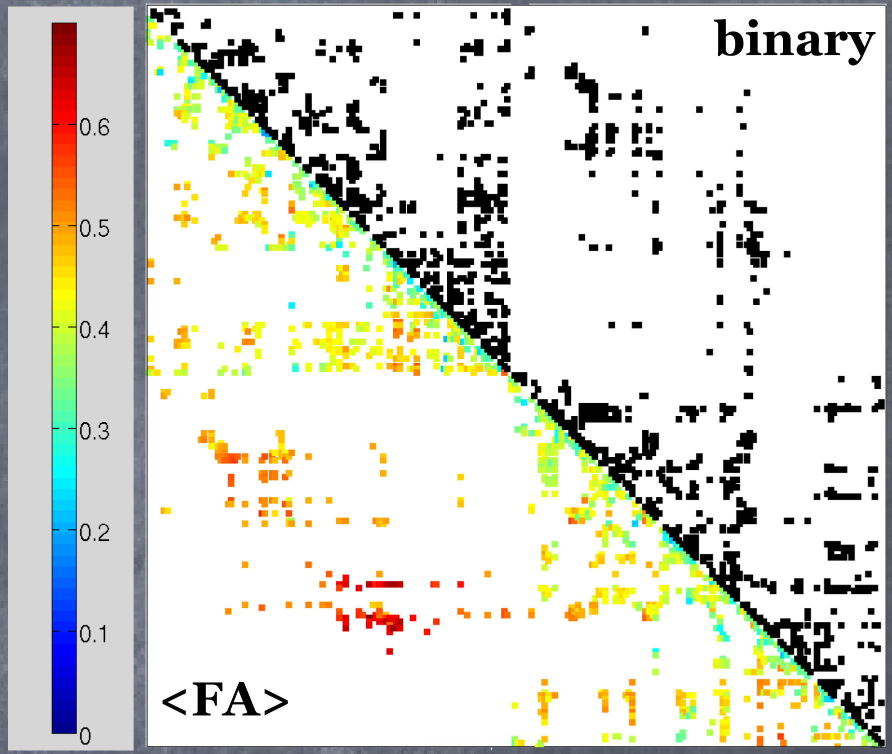

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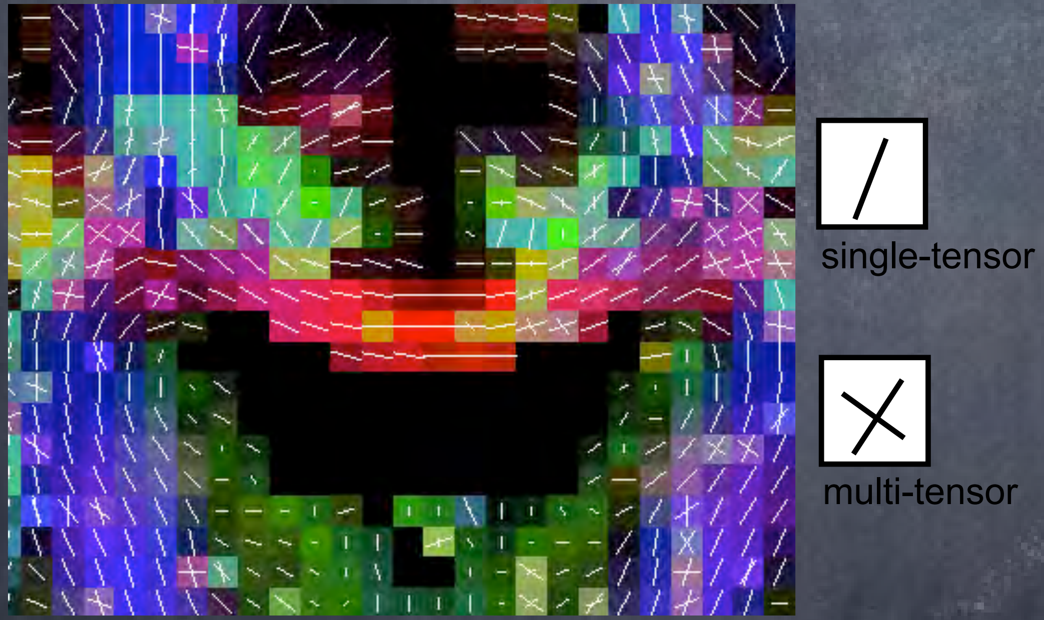

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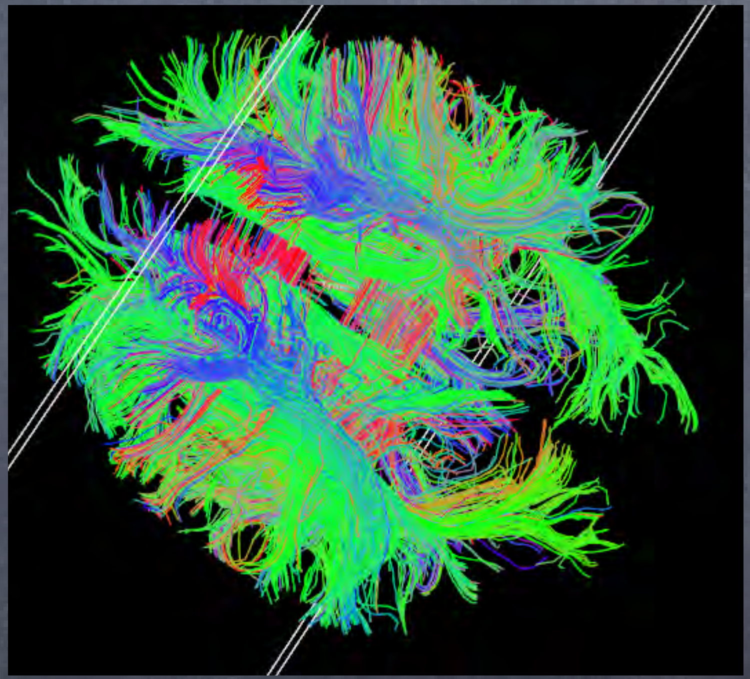

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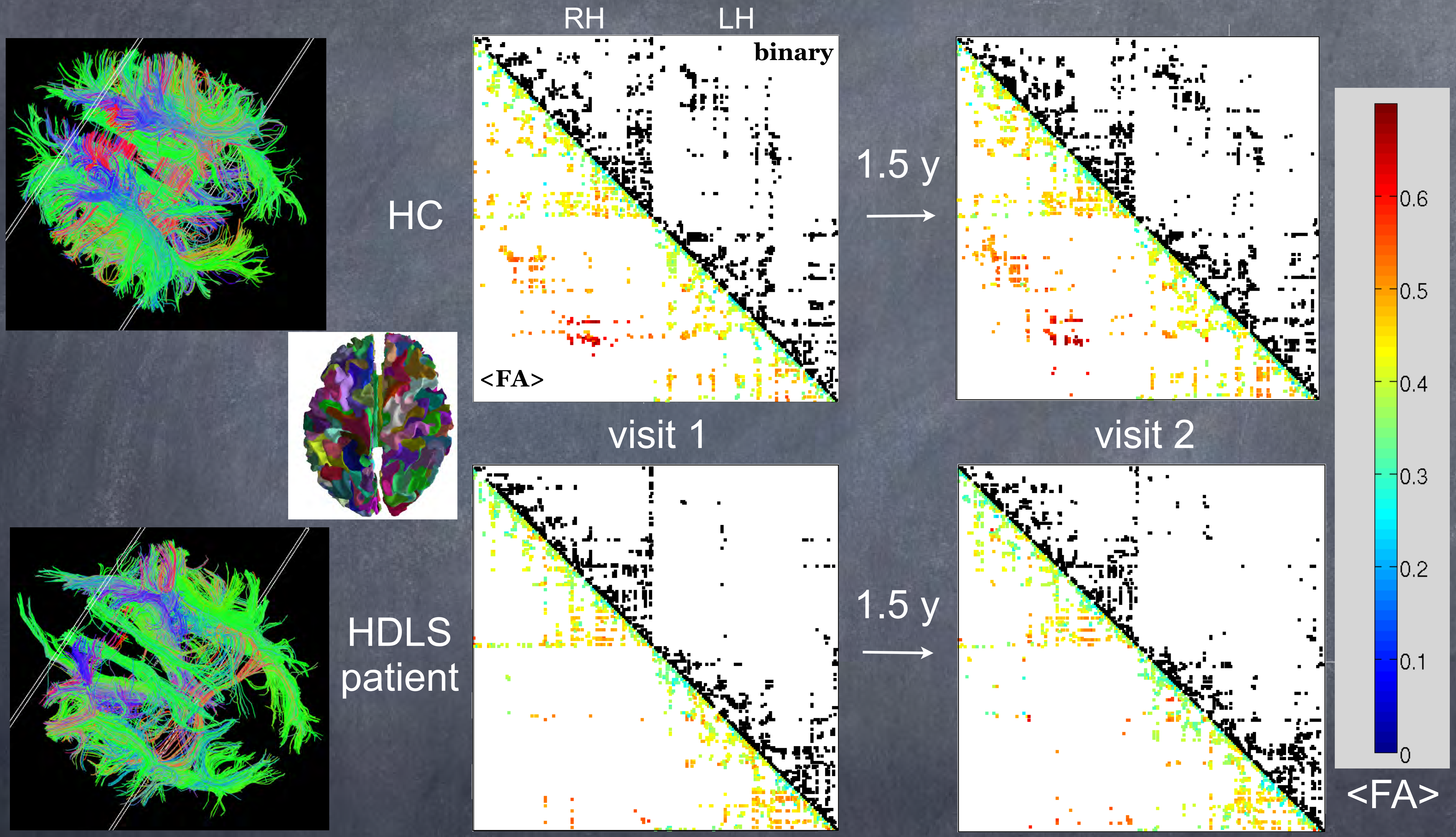
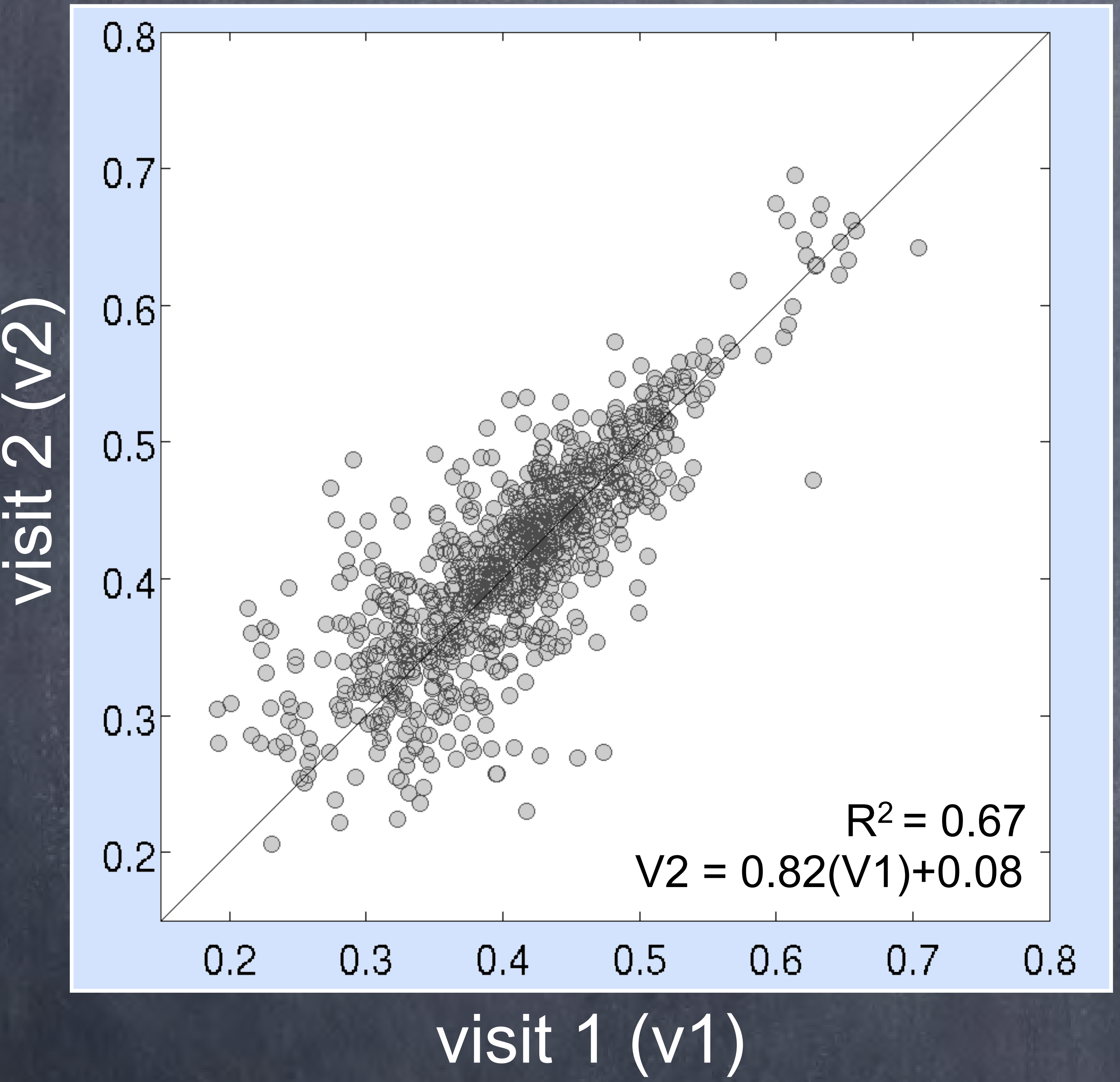


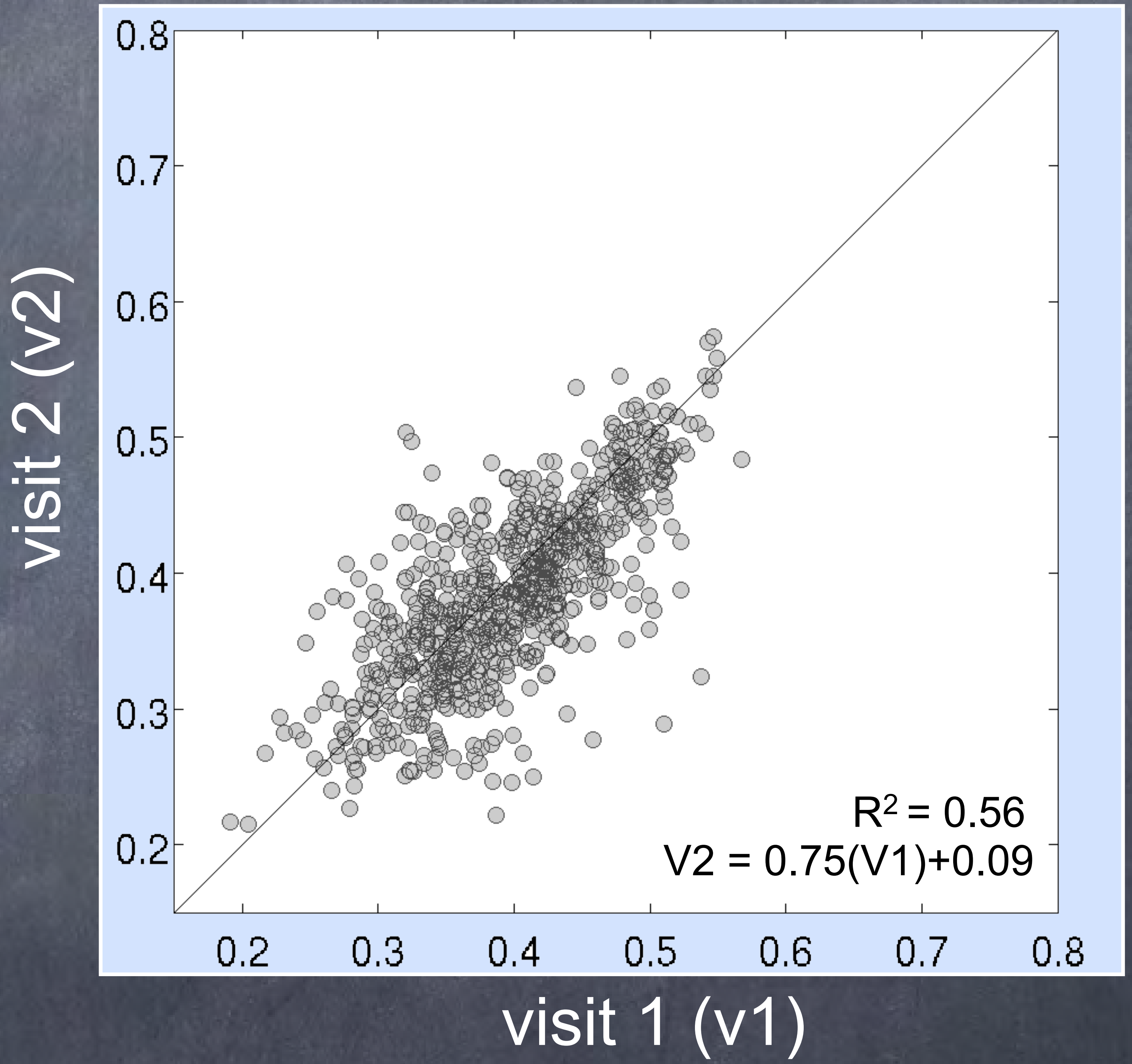
Hereditary diffuse leukoencephalopathy with spheroids

Contreras et al. (in prep.)

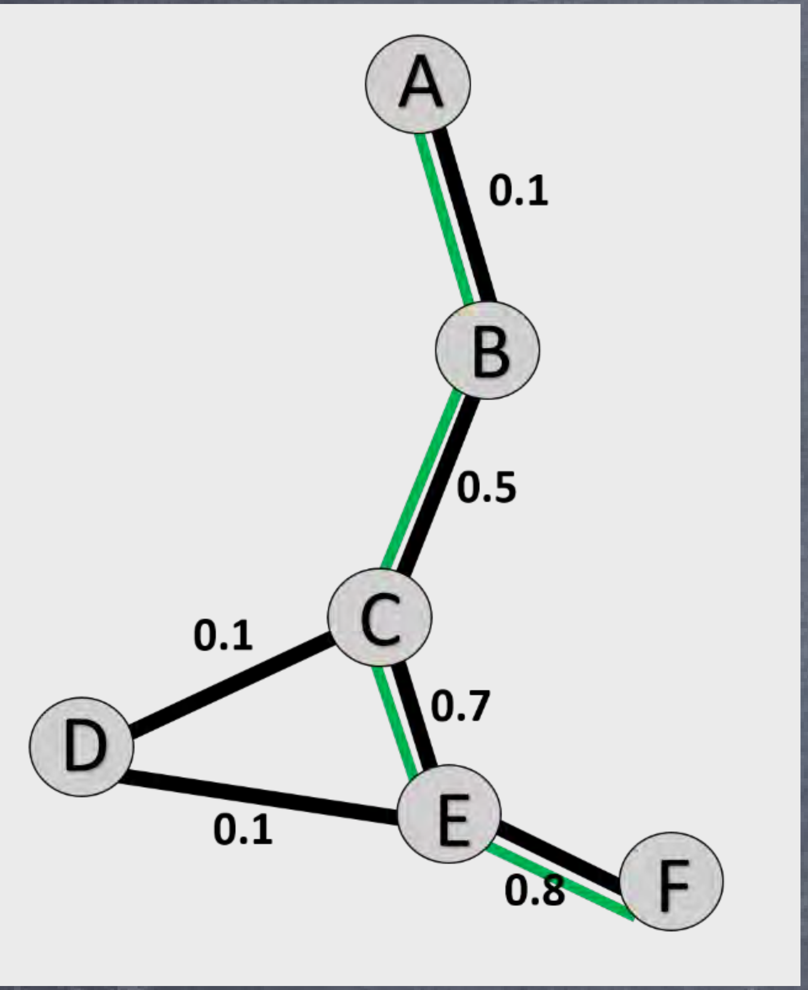
HC (<FA> progression)



HDLS (<FA> progression)



shortest-paths on networks



SP(A,B) = {A,B,C,E,F}

adjacency matrix

	A	B	C	D	E	F
A	0	0.1	0	0	0	0
B	0.1	0	0.5	0	0	0
C	0	0.5	0	0.1	0.7	0
D	0	0	0.1	0	0.1	0
E	0	0	0.7	0.1	0	0.8
F	0	0	0	0	0.8	0

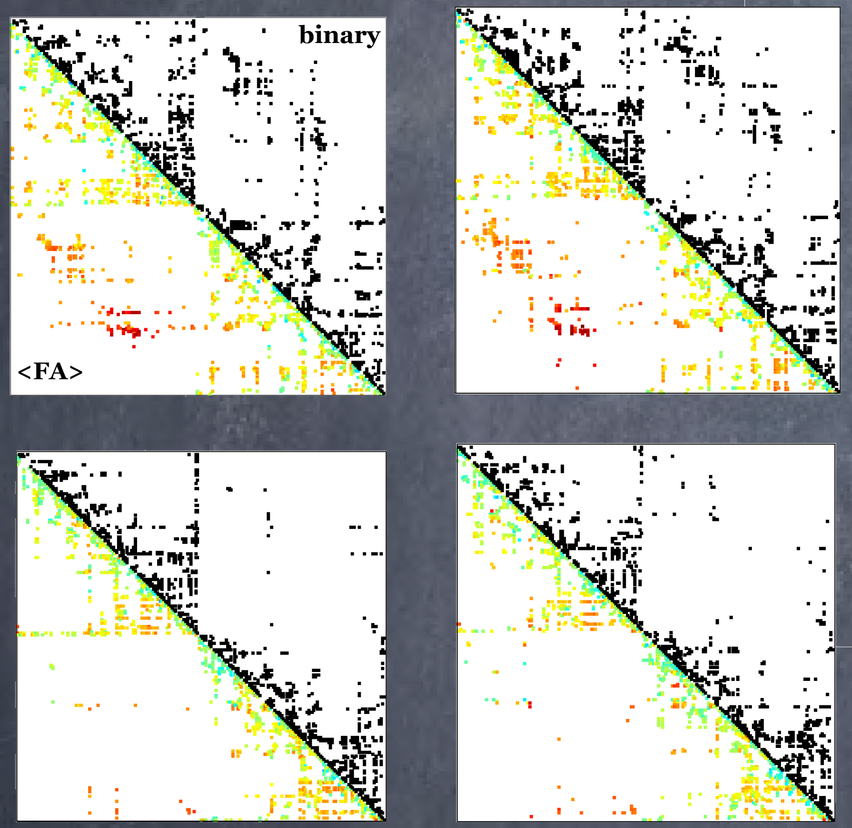
shortest-path distance (SPD)

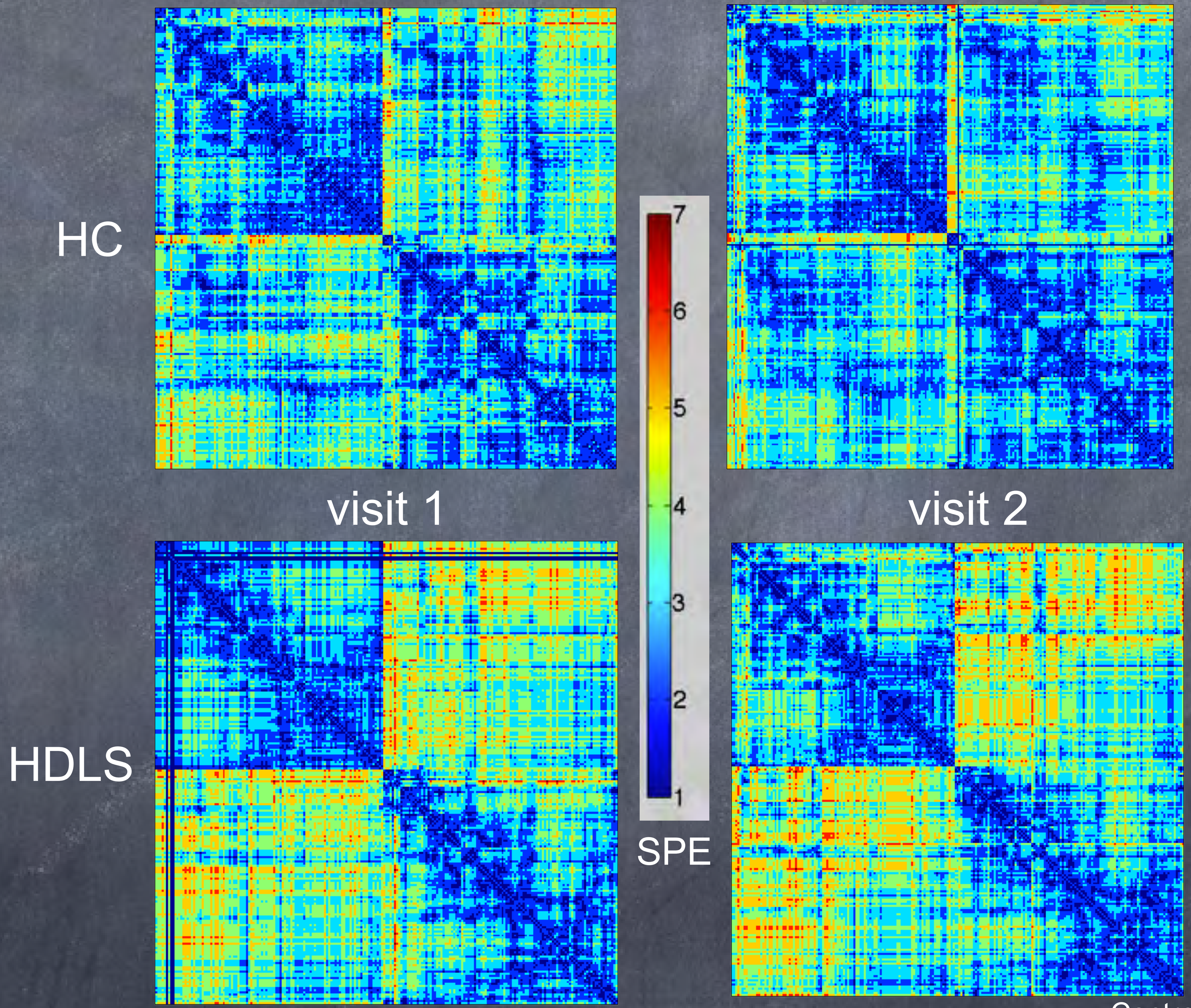
	A	B	C	D	E	F
A	-	10	12	22	13.4	14.7
B	10	-	2	12	3.4	4.7
C	12	2	-	10	1.4	2.7
D	22	12	10	-	10	11.3
E	13.4	3.4	1.4	10	-	1.3
F	14.7	4.7	2.7	11.3	1.3	-

shortest-path #edges (SPE)

	A	B	C	D	E	F
A	-	1	2	3	3	4
B	1	-	1	2	2	3
C	2	1	-	1	1	2
D	3	2	1	-	1	2
E	3	2	1	1	-	1
F	4	3	2	2	1	-

Shortest-path # Edges (SPE)





Contreras et al. (in prep.)

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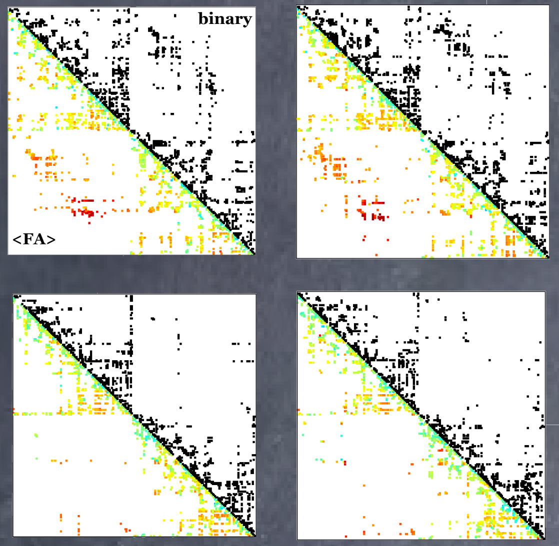
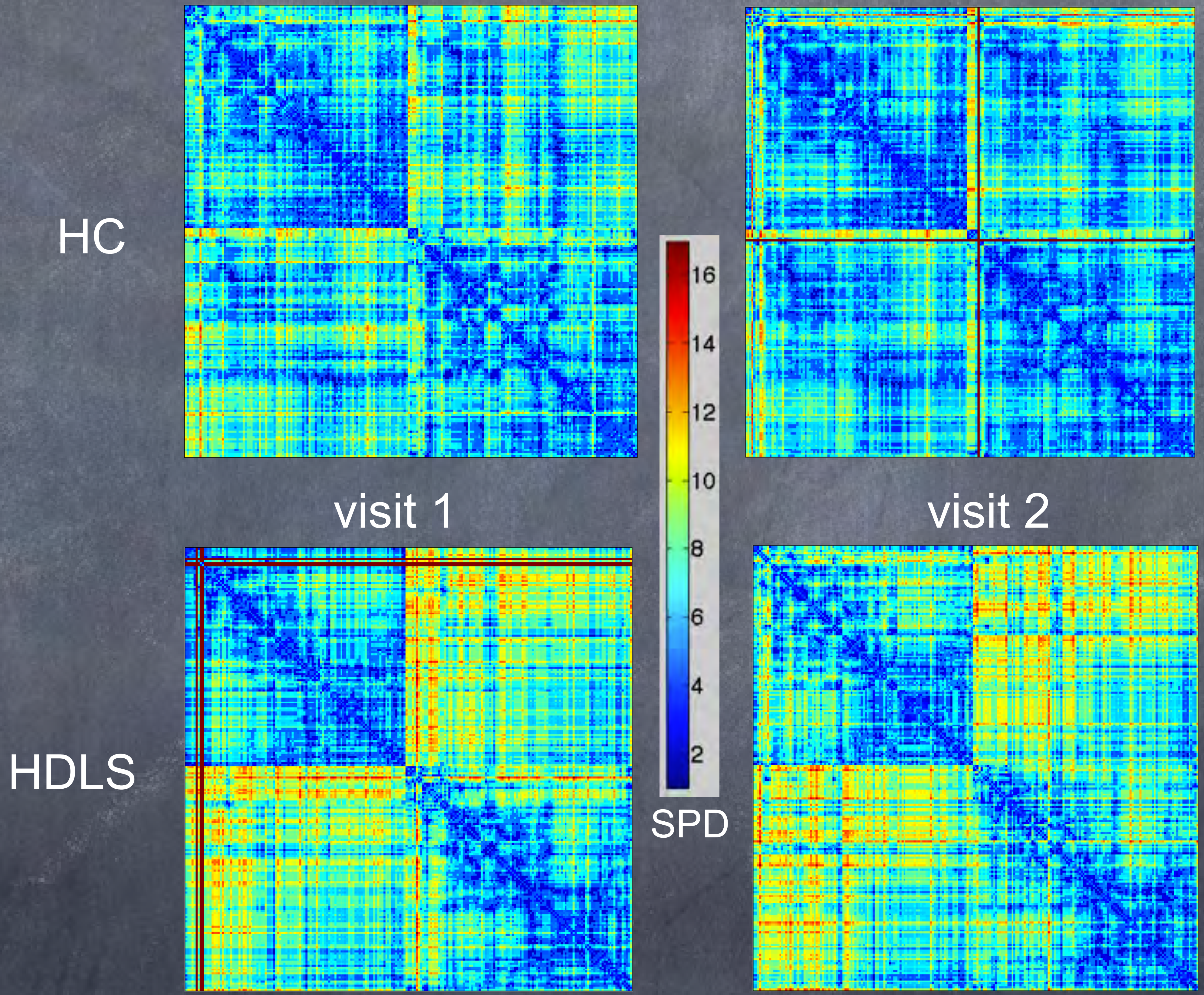


Brain regions ranked by integration impairment



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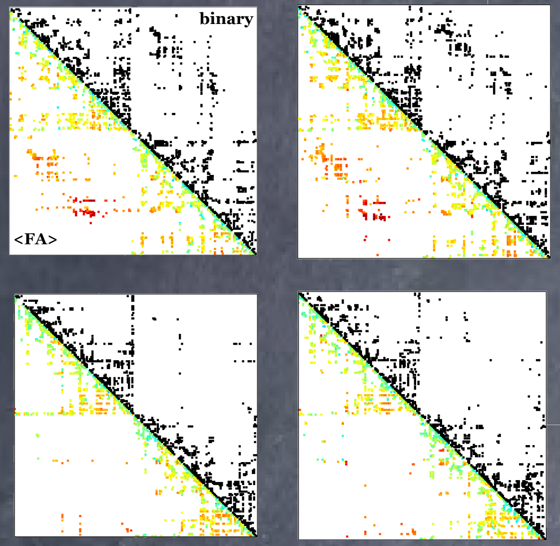
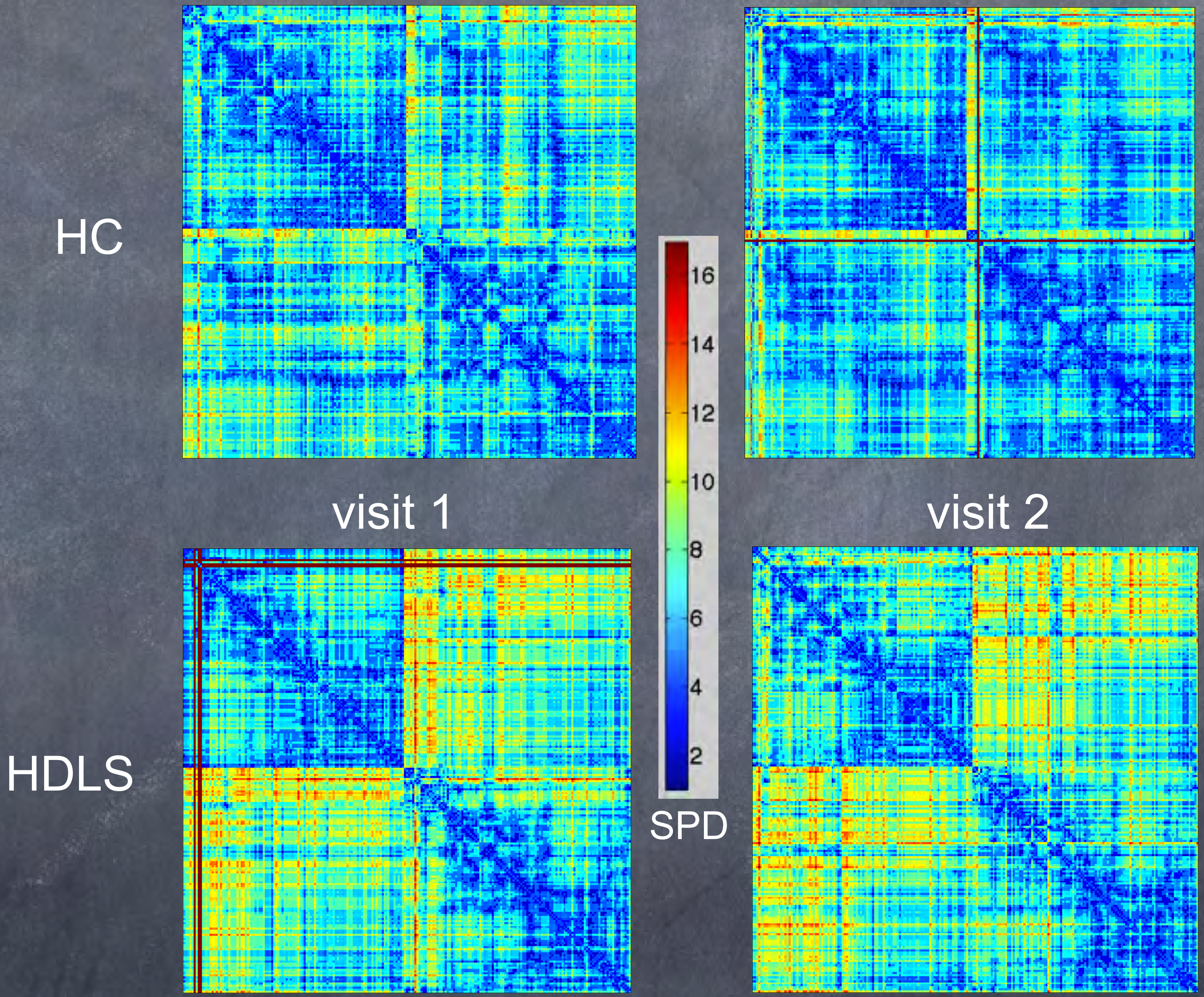


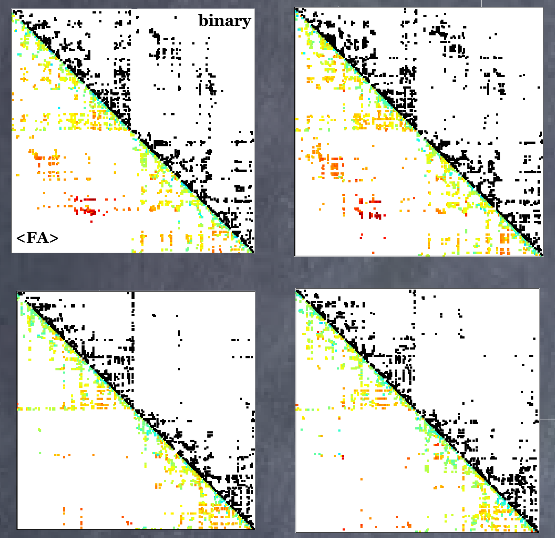
Brain regions ranked by integration impairment

- superior frontal (L,R),
- caudal middle frontal (R)
- precentral (L,R),
- inferior parietal (R),
- insula (R)
- paracentral (L)

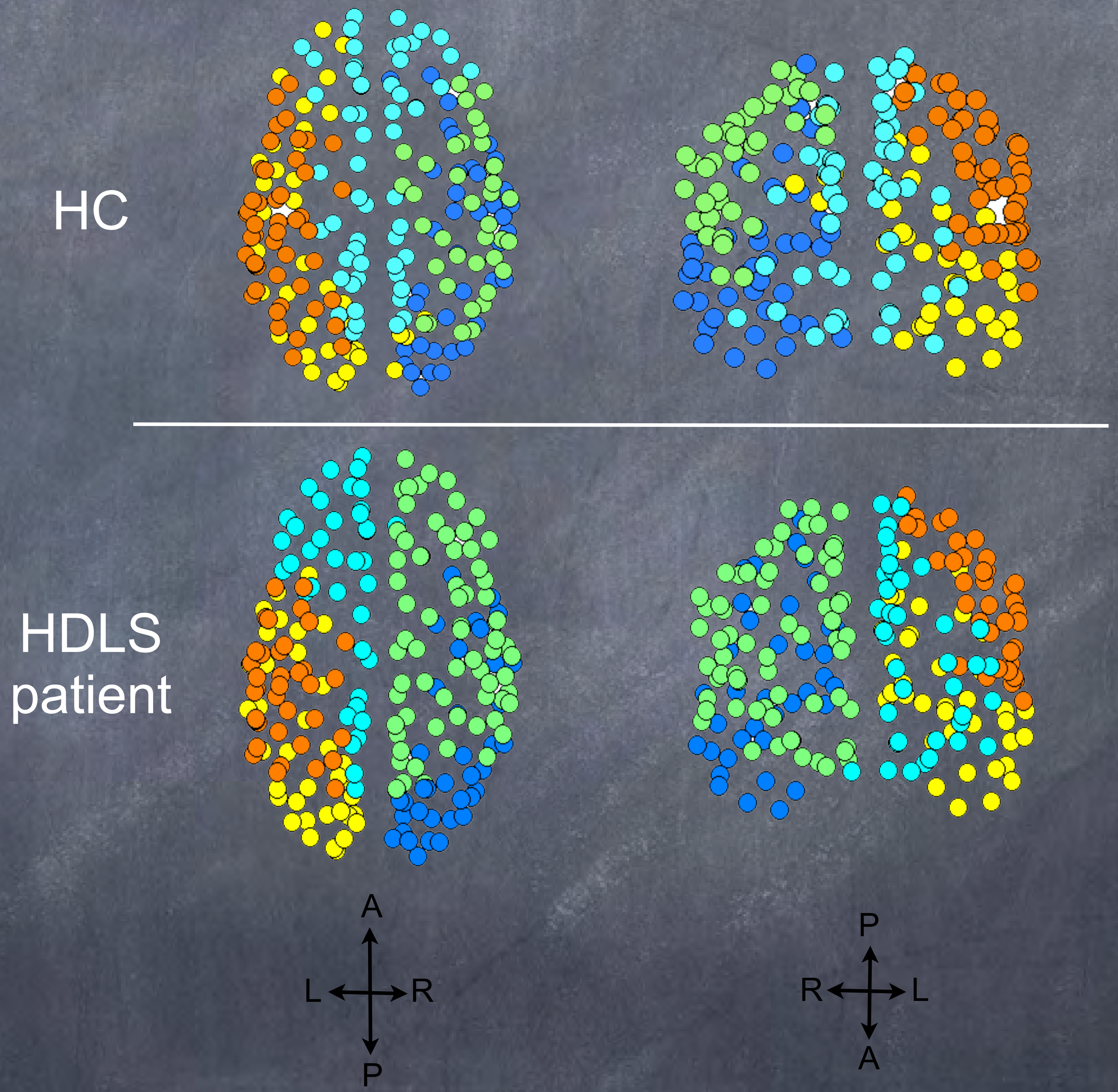


Contreras et al. (in prep.)

Segregation: organization in communities



Main segregation changes



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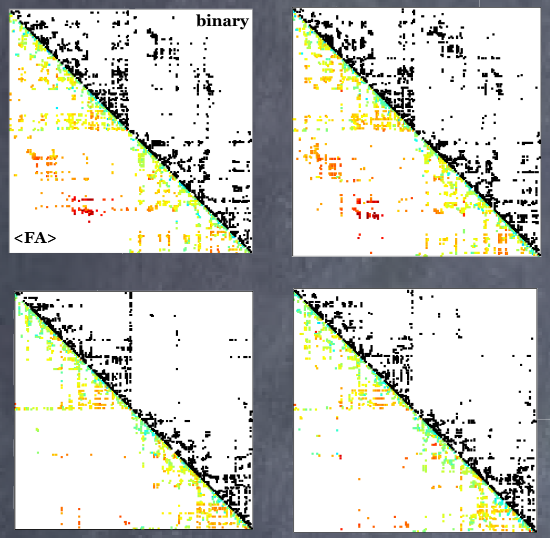
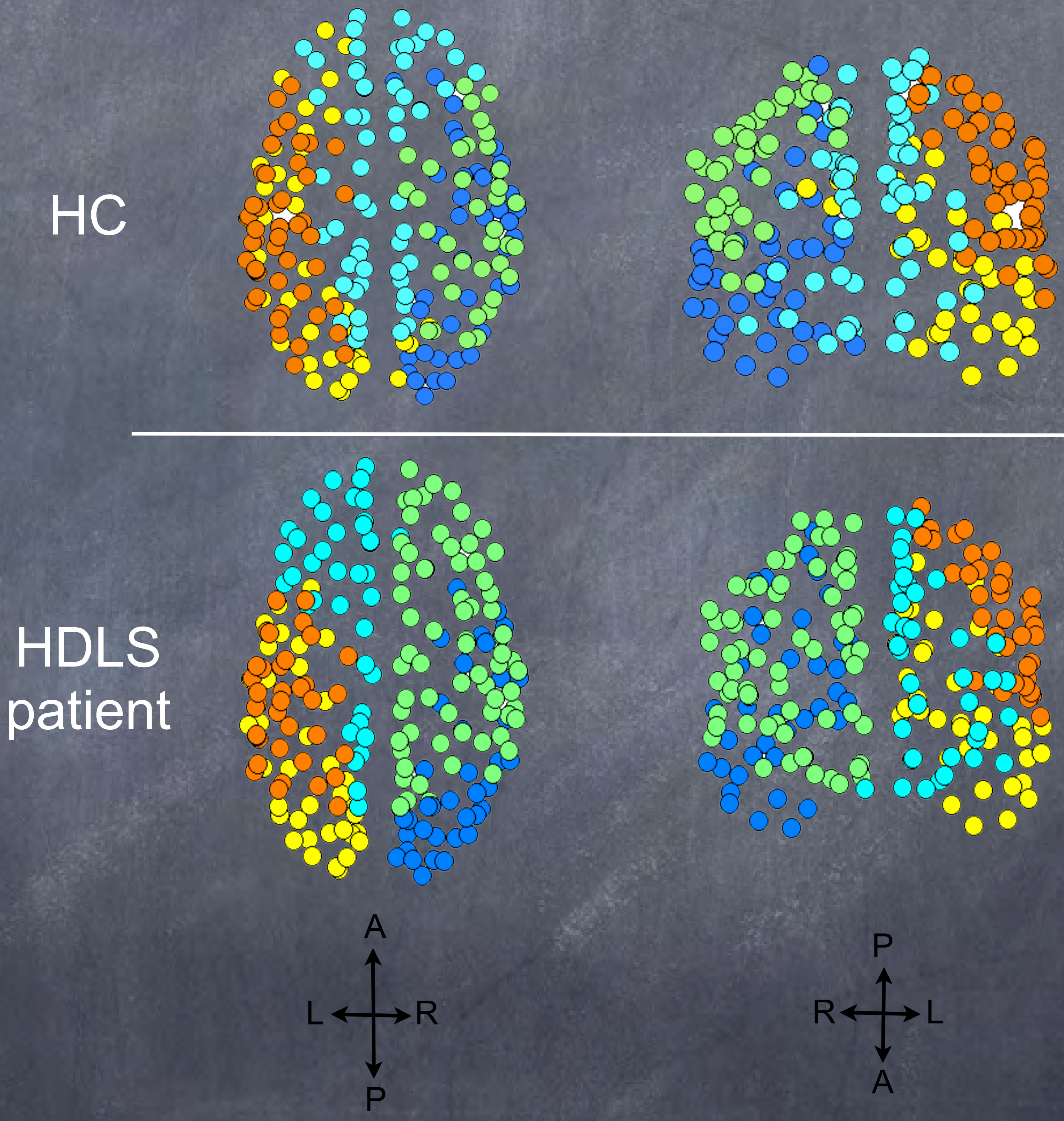


Main segregation changes

- HDLS patient a more segregated structural organization
- Module 2 disruption involves bilateral portions of insula, superior frontal area, caudate and pre/paracentral areas



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Information theoretical approaches to brain connectivity

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(making sense on network measurements, what they represent, and what the assumptions are when using them)

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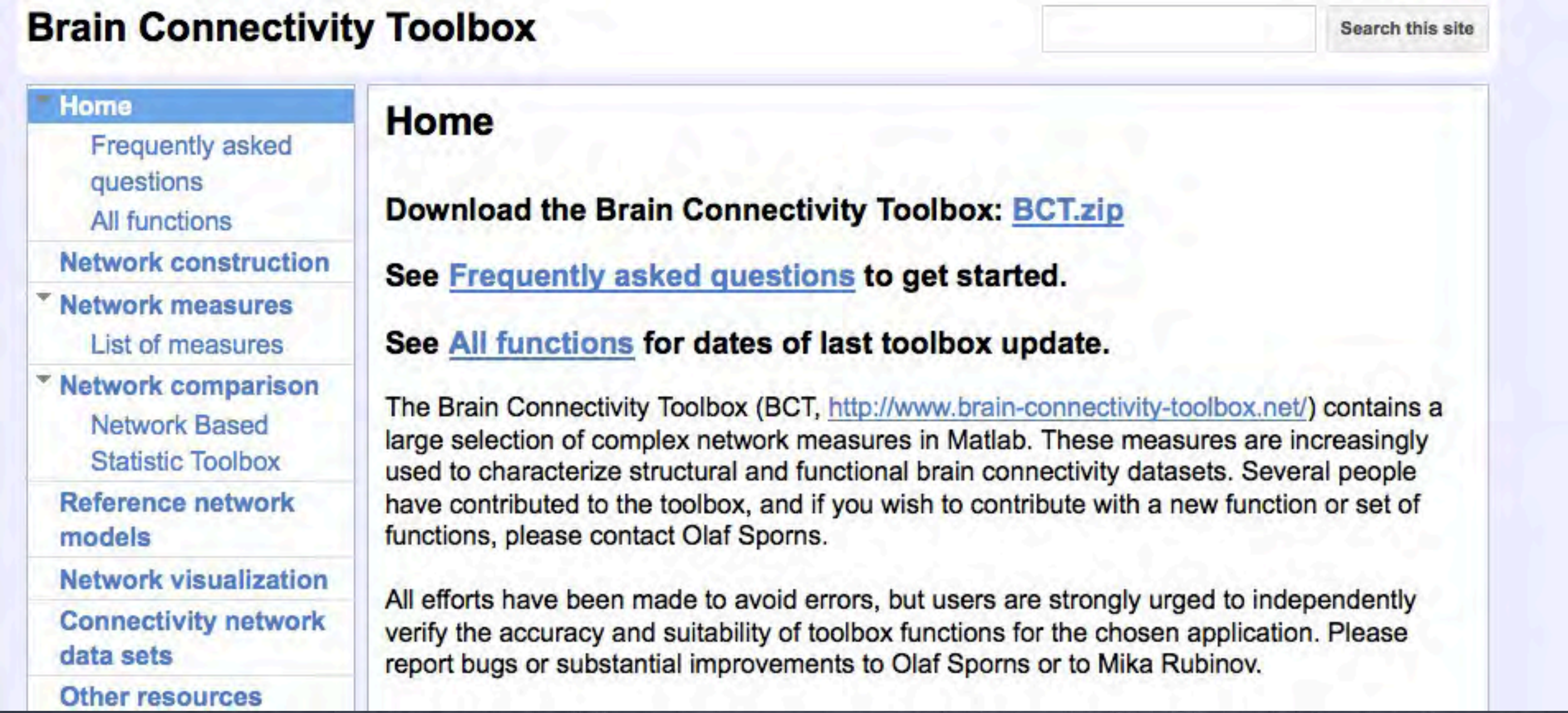
Brain Connectivity Toolbox

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  - List of measures
- Network comparison
  - Network Based Statistic Toolbox
- Reference network models
- Network visualization
- Connectivity network data sets
- Other resources

Home

Download the Brain Connectivity Toolbox: BCT.zip

See Frequently asked questions to get started.

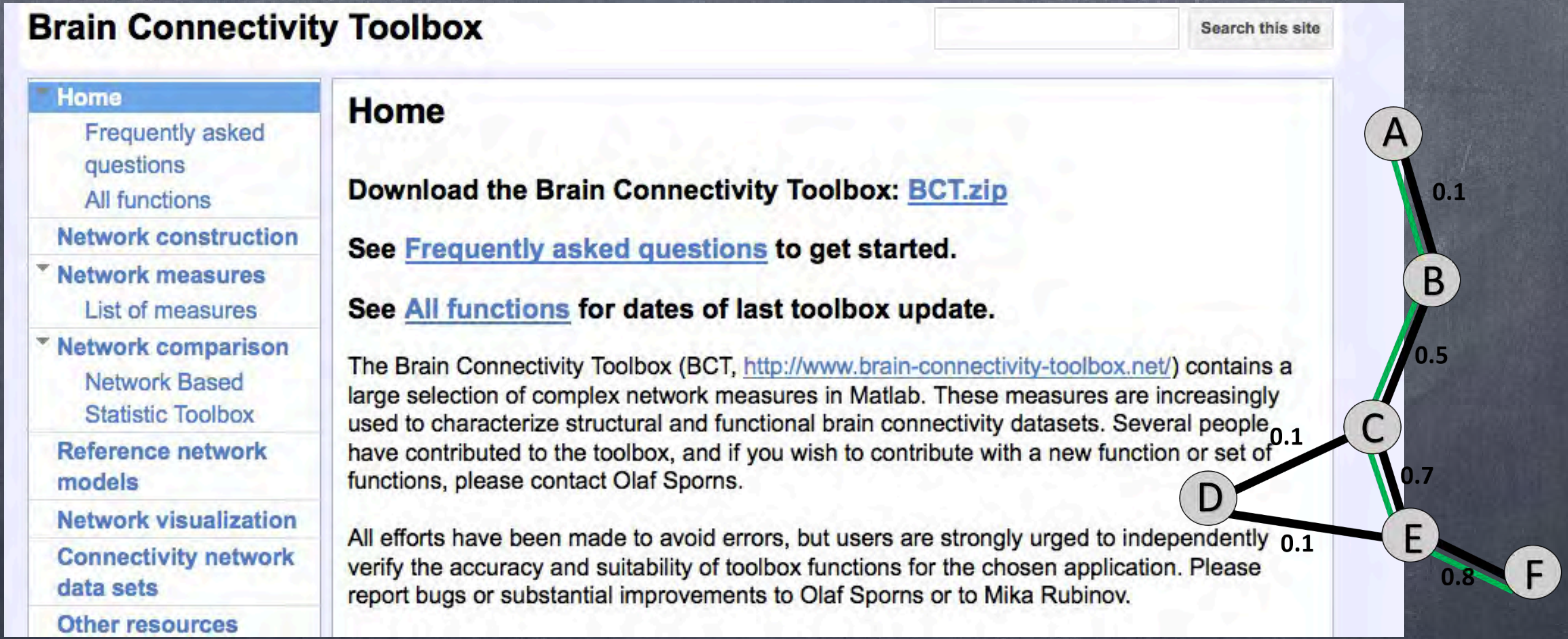
See All functions for dates of last toolbox update.

The Brain Connectivity Toolbox (BCT, http://www.brain-connectivity-toolbox.net/) contains a large selection of complex network measures in Matlab. These measures are increasingly used to characterize structural and functional brain connectivity datasets. Several people have contributed to the toolbox, and if you wish to contribute with a new function or set of functions, please contact Olaf Sporns.

All efforts have been made to avoid errors, but users are strongly urged to independently verify the accuracy and suitability of toolbox functions for the chosen application. Please report bugs or substantial improvements to Olaf Sporns or to Mika Rubinov.

Information theoretical approaches to brain connectivity

(making sense on network measurements, what they represent, and what the assumptions are when using them)



Shortest-paths vs random-walks : routing vs exploration

will be studied further elsewhere [14]. The random walk is also interesting since it could be a mechanism of transport and search on networks [15, 16, 17]. Those processes would be optimal if one follows the shortest path between two nodes under considerations. Among all paths connecting two nodes, the shortest path is given by the one with the smallest number of links [18]. However the shortest path can be found only after global connectivity is known at each node, which is improbable in practice.

J.D Noh and H.D. Rieger. Physical Review Letters 2004

Shortest-paths vs random-walks : routing vs exploration

Routing requires knowledge ...

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J.D Noh and H.D. Rieger. Physical Review Letters 2004

... but topologies may favor communication without such knowledge

Navigability of complex networks

Marián Boguñá[1]*, Dmitri Krioukov[2] and K. C. Claffy[2]

Routing information through networks is a universal phenomenon in both natural and man-made complex systems. When each node has full knowledge of the global network connectivity, finding short communication paths is merely a matter of distributed computation. However, in many real networks, nodes communicate efficiently even without such global intelligence. Here, we show that the peculiar structural characteristics of many complex networks support efficient communication without global knowledge. We also describe a general mechanism that explains this connection between network structure and function.

M. Boguñá et al. Nature Physics 2009

Get directions | My places

355 W 16th St
Indianapolis, IN 46202

1. Head **west** on **W 16th St** toward **Senate Blvd**

318 ft

2. Take the 1st right onto **Senate Blvd**

0.5 mi

3. Turn left onto **W 21st St**

0.1 mi

4. Take the ramp onto **I-65 S**

4.3 mi

5. Keep left to stay on **I-65 S**

4.2 mi

6. Take exit **106** for **I-465 E/I-74 E/I-465 W/ I-74 W**

0.1 mi

7. Keep right at the fork, follow signs for **Interstate 465 W/Interstate 74 W** and merge onto **I-465 W/I-74**

4.1 mi

8. Take exit **4** for **Indiana 37 S/Harding St**

0.2 mi

9. Turn left onto **IN-37 S/S Harding St**
Continue to follow IN-37 S

39.0 mi

10. Take the **Walnut St N** exit toward **College Ave**

0.5 mi

11. Merge onto **N State Road 37 Business/N Walnut St**
Continue to follow N Walnut St

3.2 mi

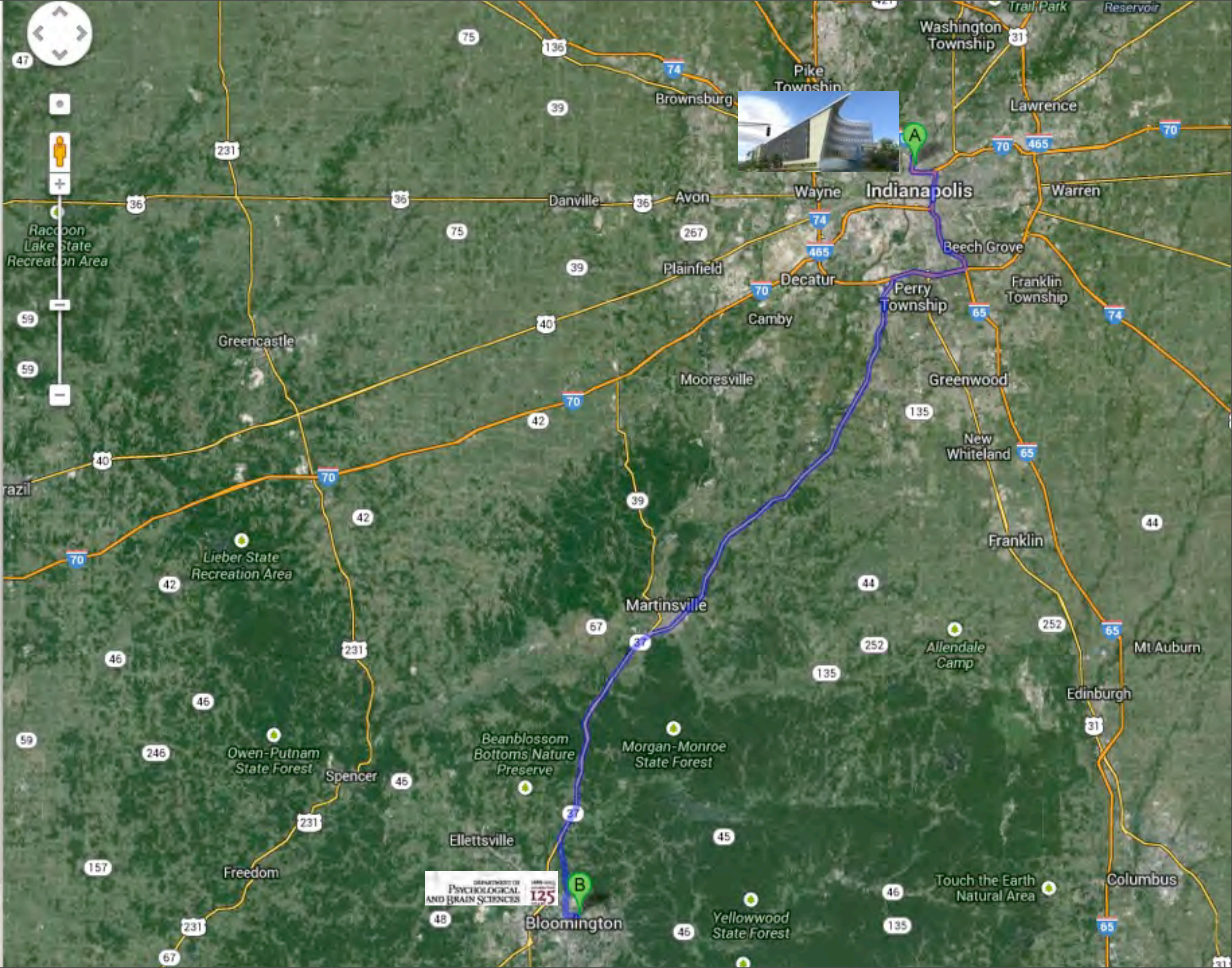
12. Continue onto **N College Ave**

1.0 mi

13. Turn left onto **W 10th St**
Destination will be on the left

0.8 mi

1101 E 10th St



Get directions My places

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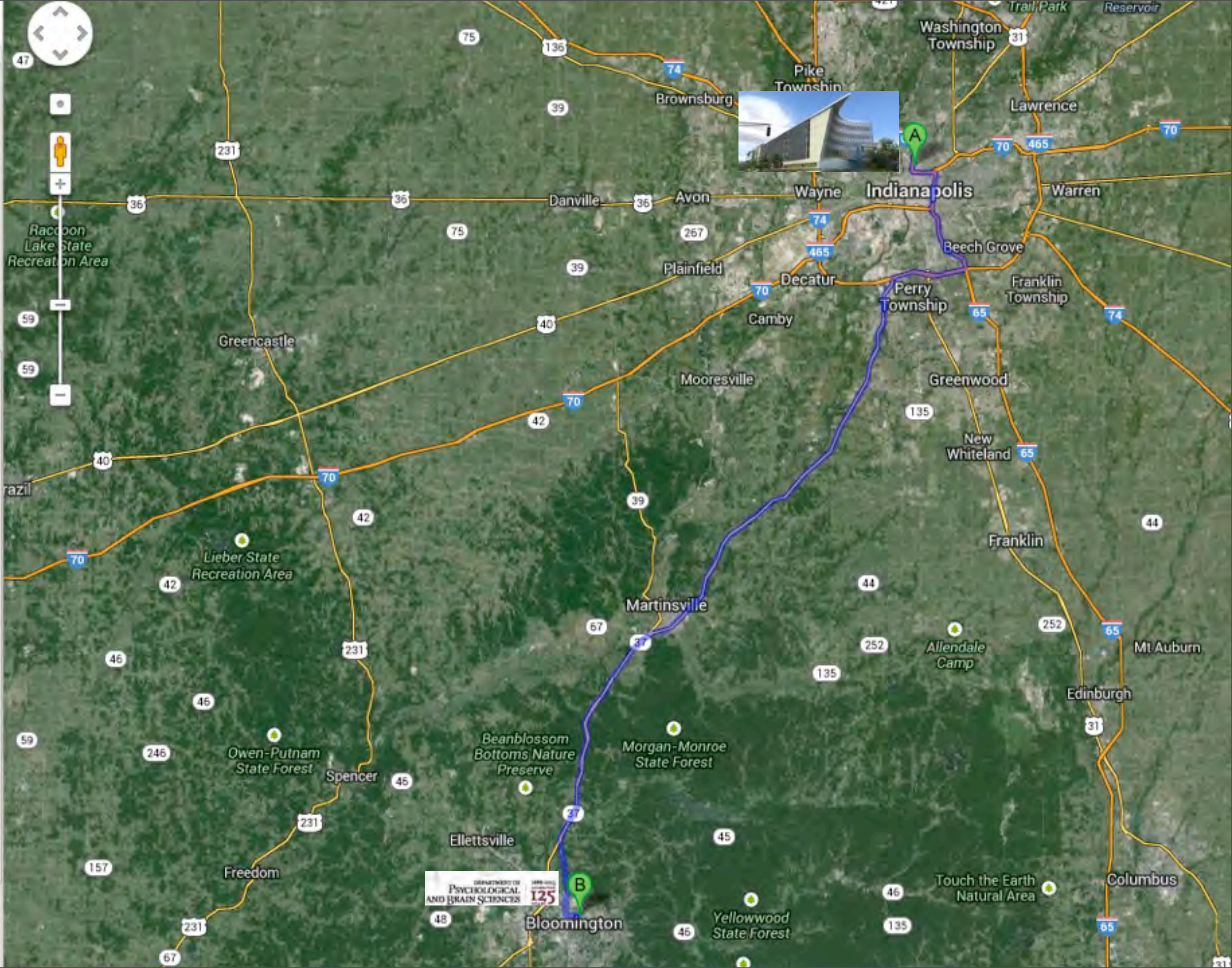
Continue to follow N Walnut St
3.2 mi

12. Continue onto **N College Ave**

58 mi, 13 decisions

0.8 mi

1101 E 10th St



Get directions | My places

A

355 W 16th St
Indianapolis, IN 46202

1. Head **west** on **W 16th St** toward **Senate Blvd**

318 ft

2. Take the 1st right onto **Senate Blvd**

0.5 mi

3. Turn left onto **W 21st St**

0.1 mi

4. Take the ramp onto **I-65 S**

4.3 mi

5. Keep left to stay on **I-65 S**

42.0 mi

6. Take exit **68** for **IN-46** toward **Columbus/ Nashville/Bloomington**

0.3 mi

7. Turn right onto **IN-46 W/Jonathan Moore Pike**
Continue to follow IN-46 W

15.9 mi

8. Turn left onto **IN-46 W/Van Buren St**
Continue to follow IN-46 W

16.6 mi

9. Turn right to stay on **IN-46 W**

0.5 mi

10. Turn left onto **E 10th St**
Destination will be on the right

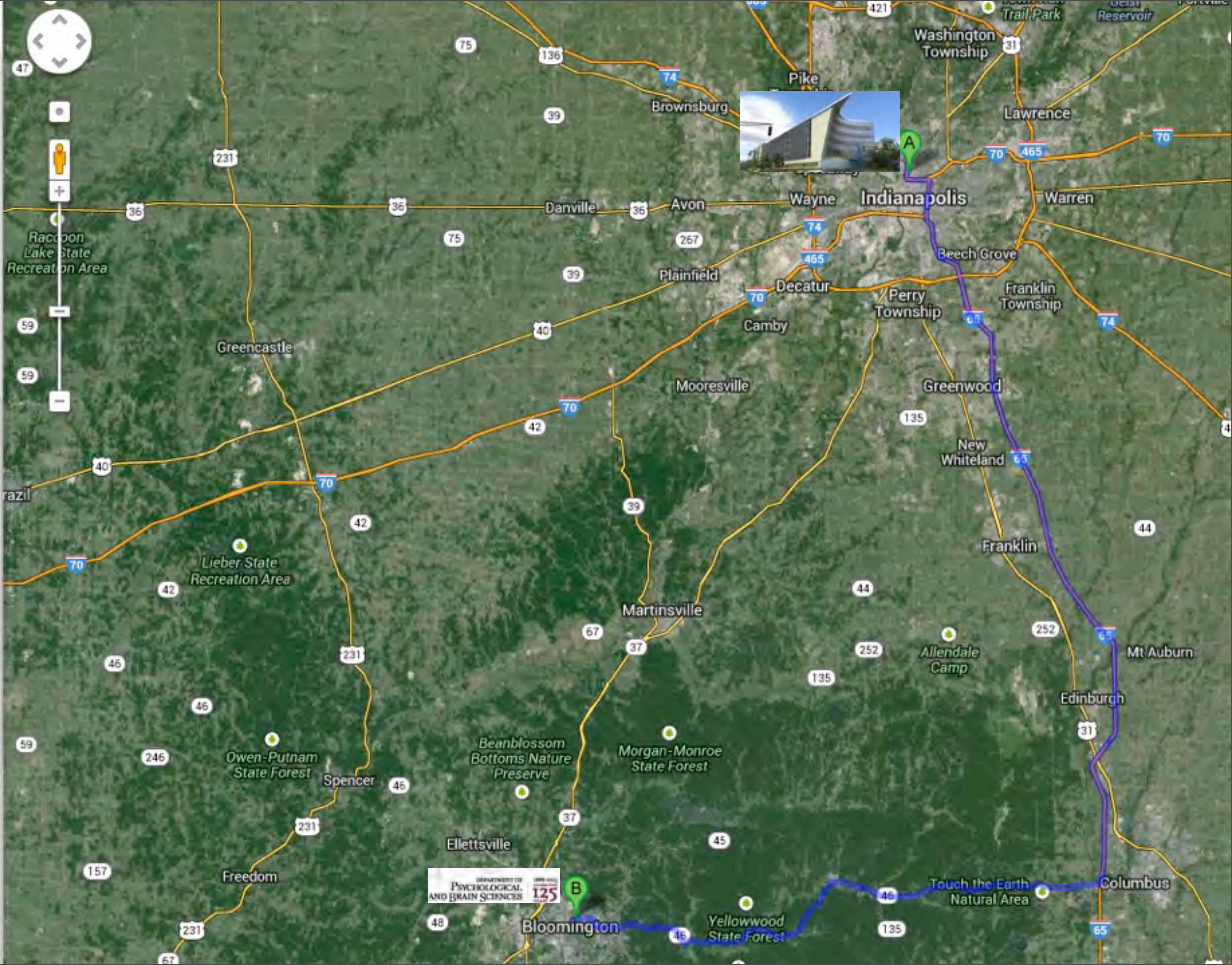
1.0 mi

B

1101 E 10th St
Bloomington, IN 47405

Save to My Maps

These directions are for planning purposes only. You may find that construction projects, traffic, weather, or other events may cause conditions to differ from the map results, and you should plan your route accordingly. You must obey all signs or notices regarding your route.



Get directions | My places

355 W 16th St
Indianapolis, IN 46202

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318 ft

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0.5 mi

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Destination will be on the right

1.0 mi

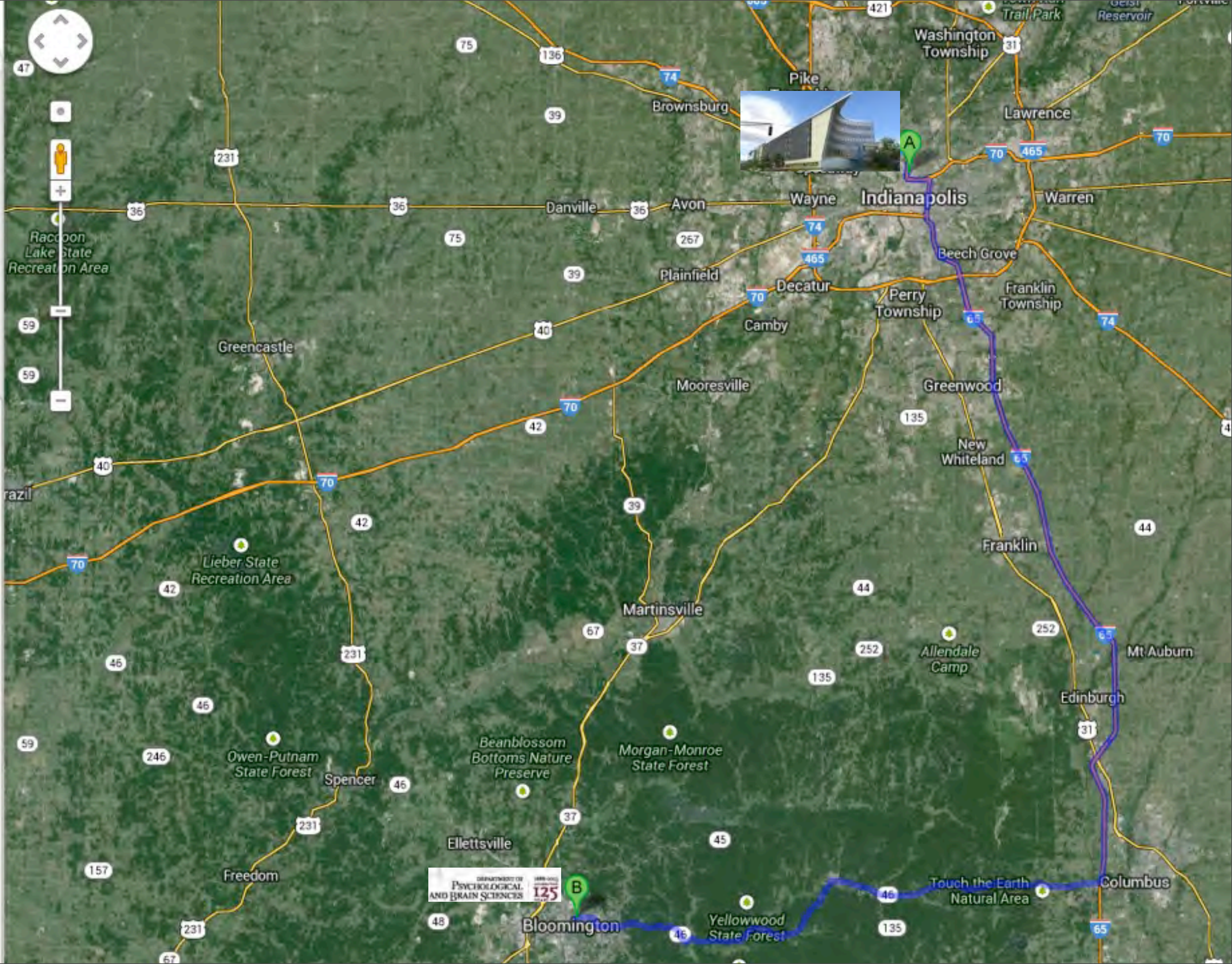
1101 E 10th St
Bloomington, IN 47405

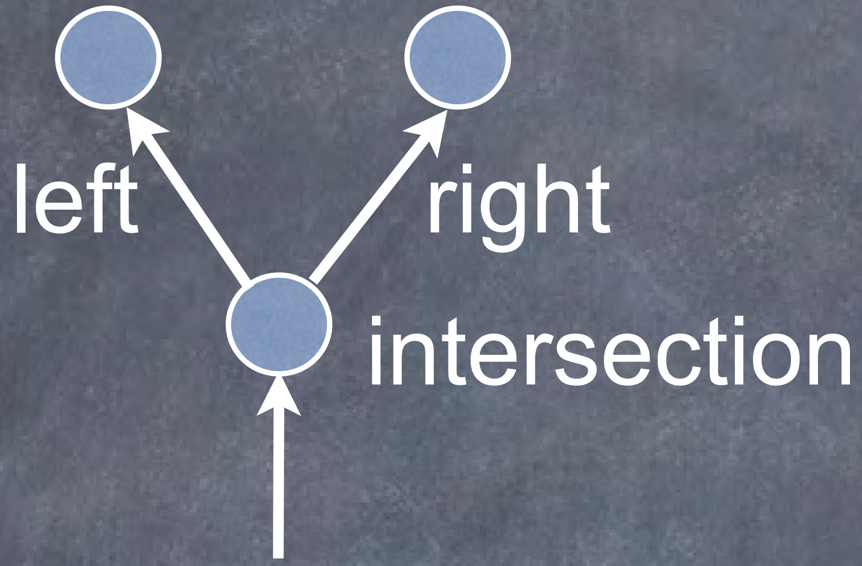
Save to My Maps

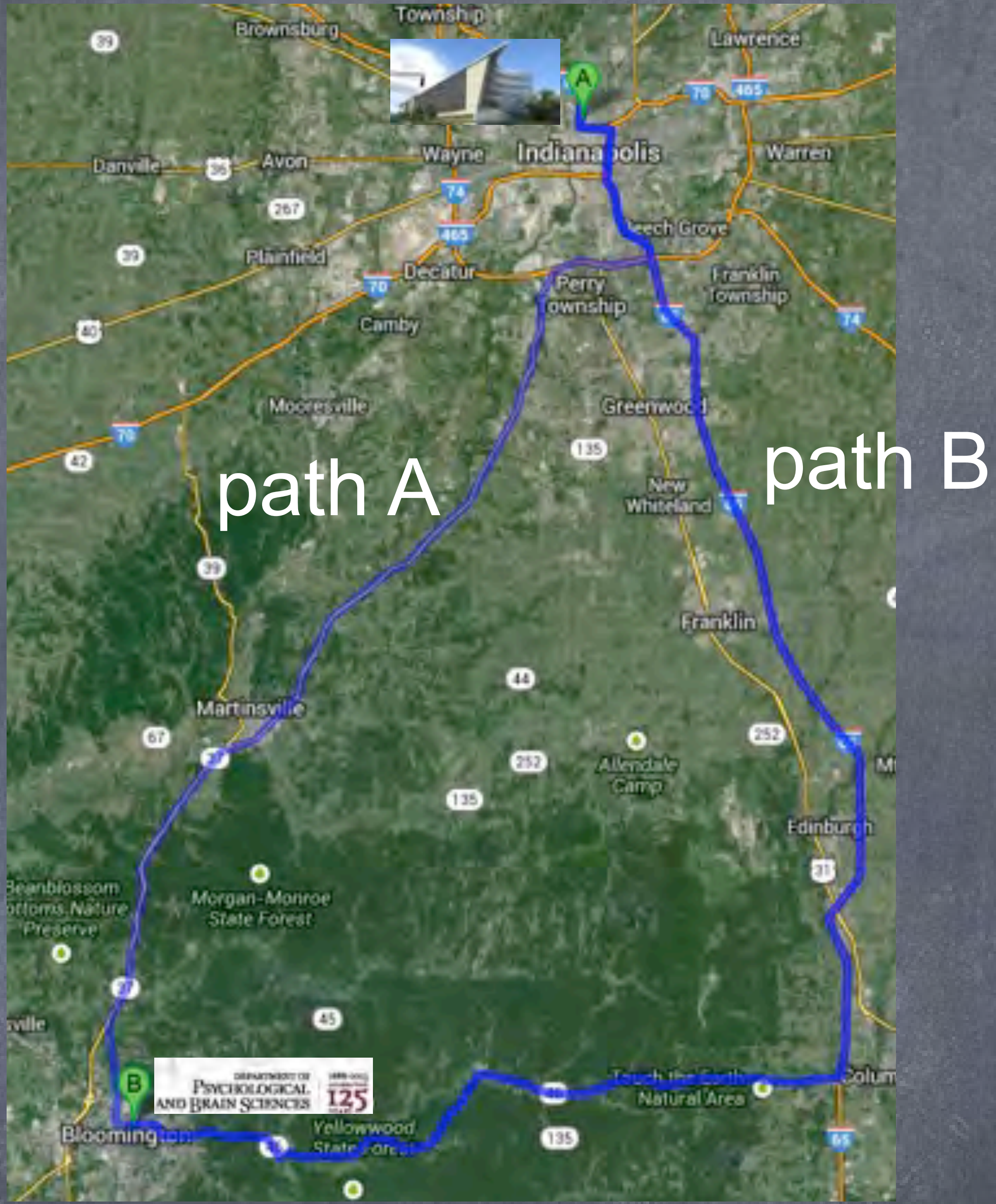
81mi,10 decisions

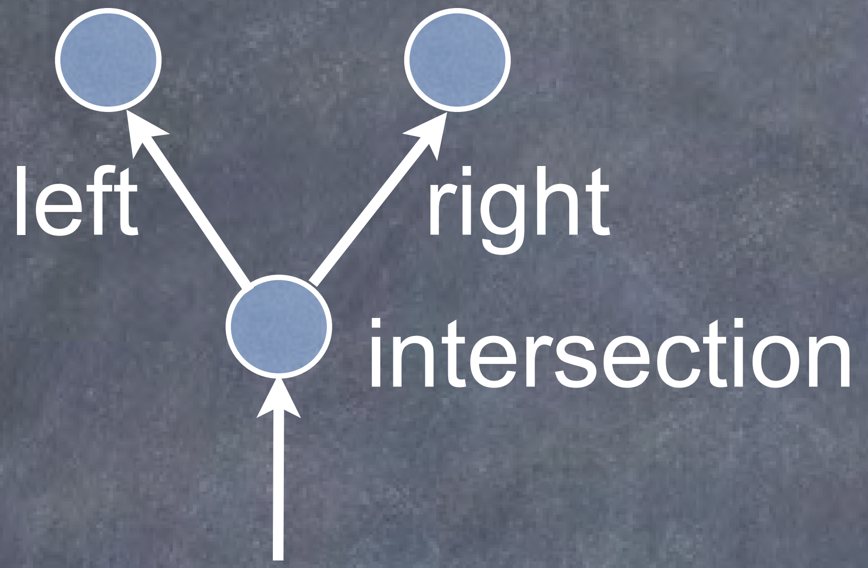
regarding your route.

Map data ©2013 Google

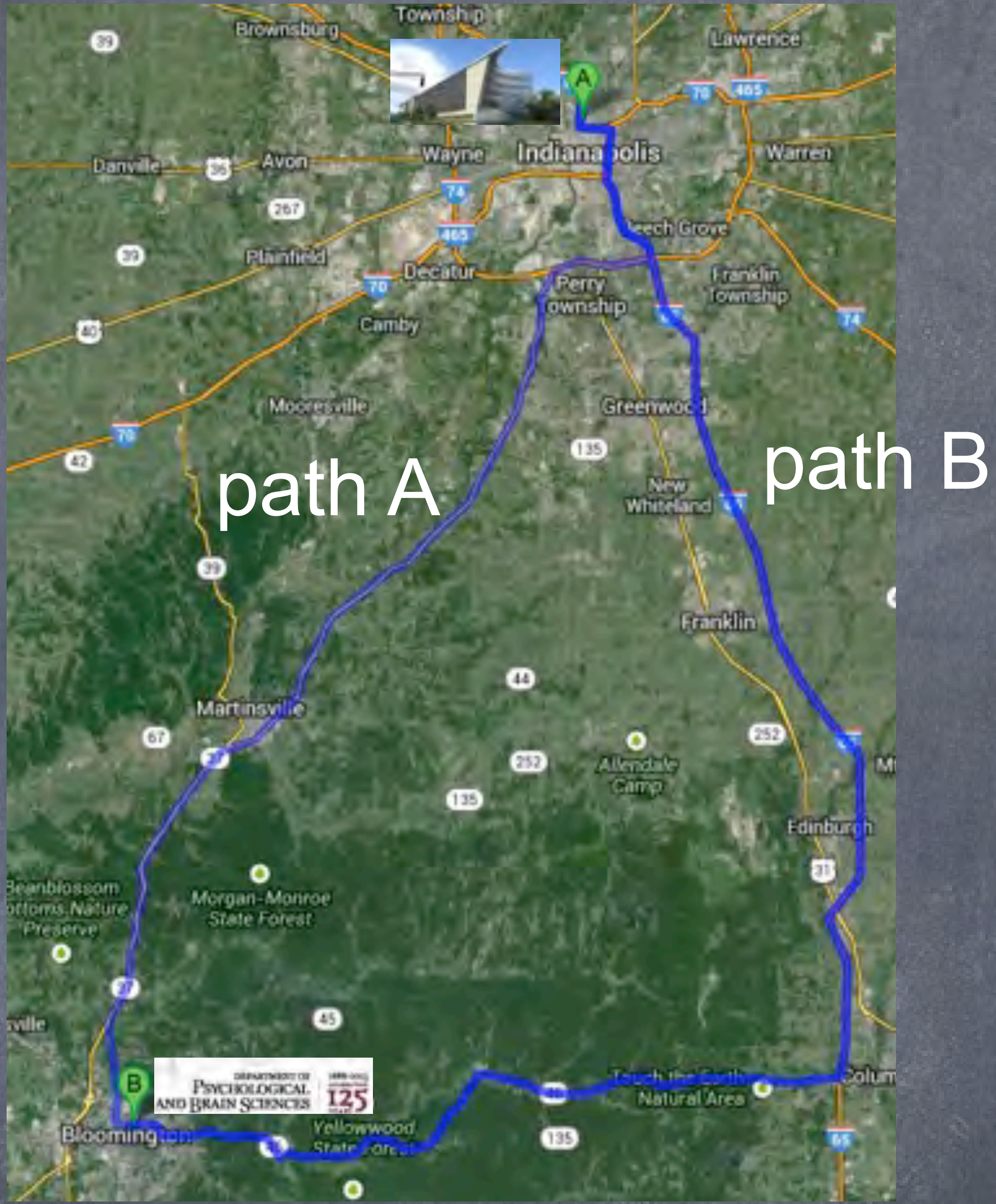


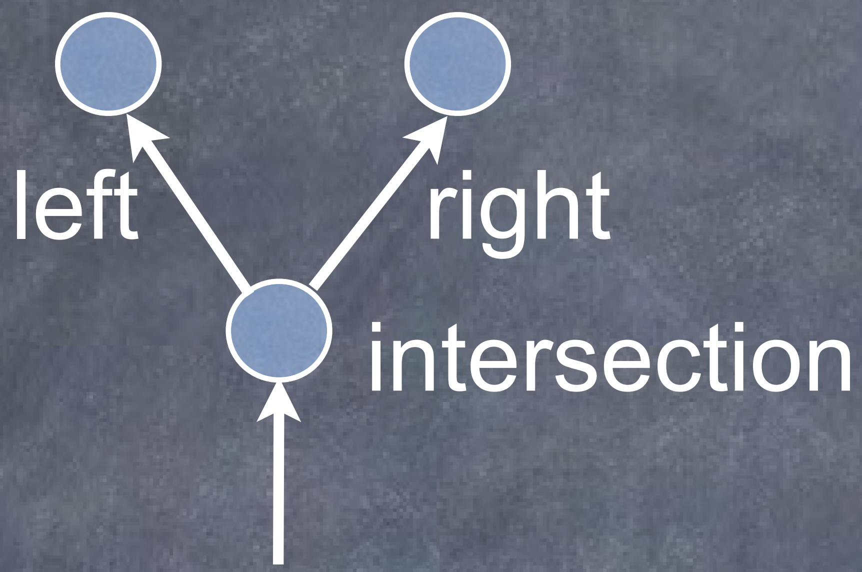

left
right
intersection


path A
path B
Brownsburg
Township
Lawrence
Danville
Avon
Wayne
Indianapolis
Warren
Plainfield
Decatur
Perry Township
Franklin Township
Camby
Mooresville
Greenwood
New Whiteland
Franklin
Martinsville
Allendale Camp
Edinburgh
Morgan-Monroe State Forest
Natural Area
Yellowwood State Forest
Bloomington
Psychological and Brain Sciences
125


left
right
intersection

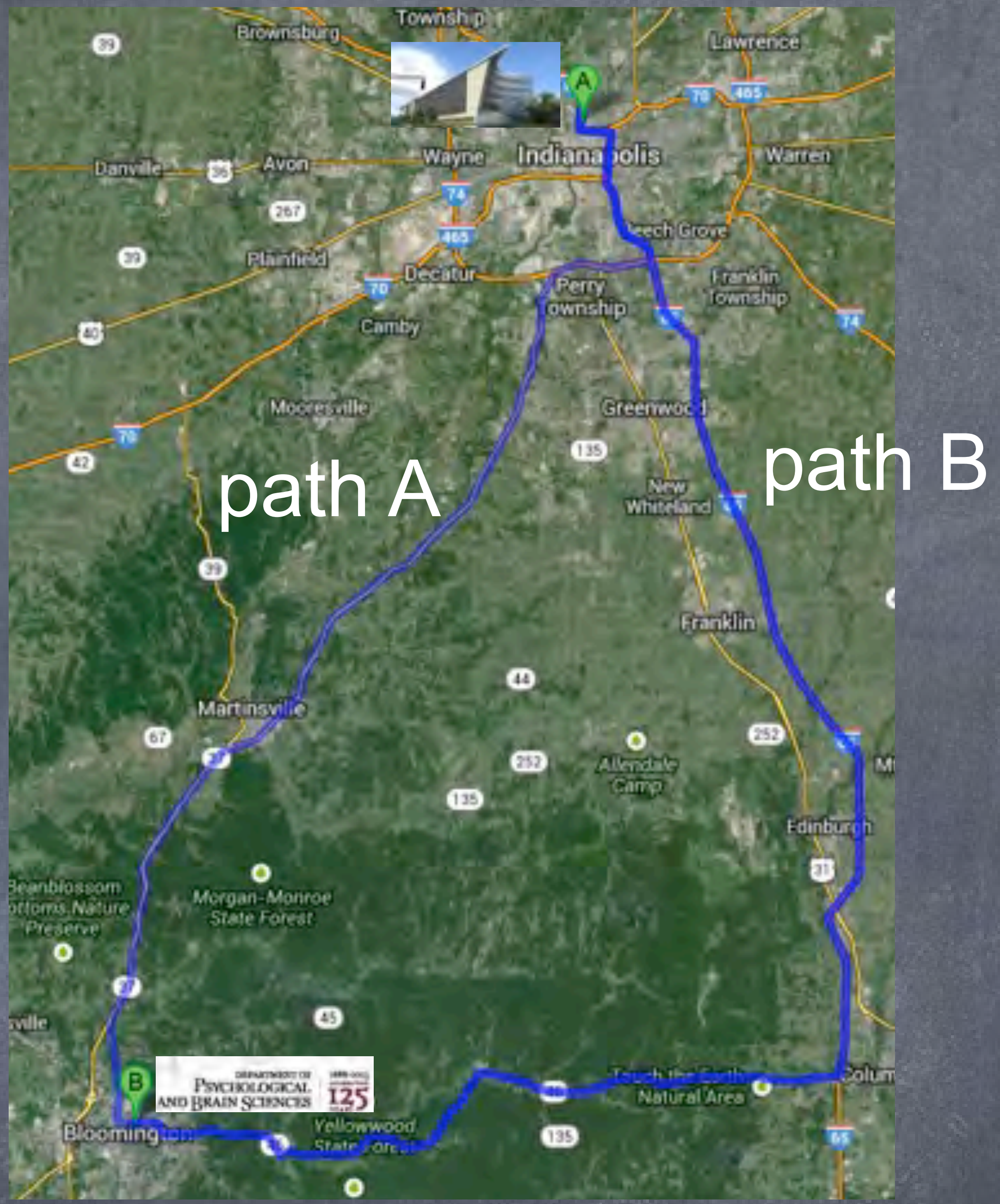
p(choice)=.5

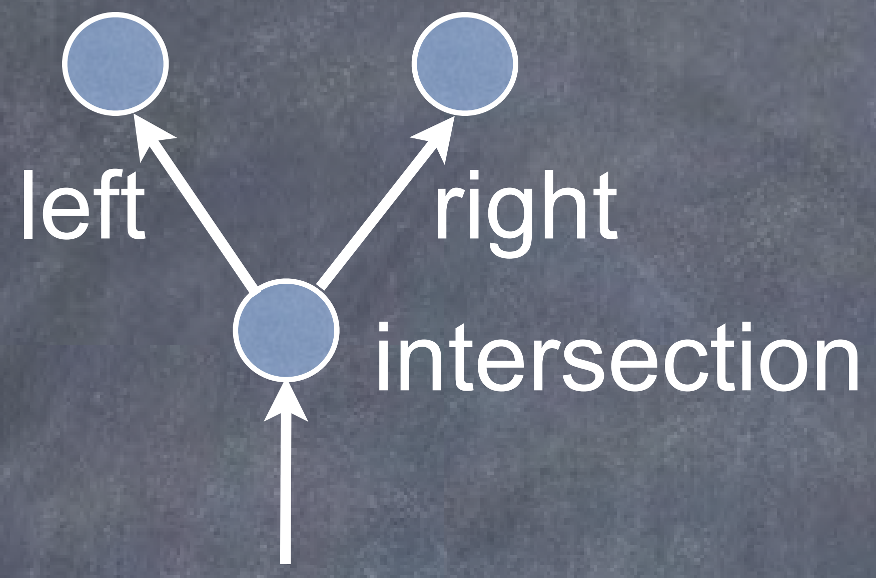

path A
path B
Brownsburg
Township
Lawrence
Danville
Avon
Wayne
Indianapolis
Warren
Plainfield
Decatur
Franklin Township
Camby
Mooresville
Greenwood
New Whiteland
Franklin
Martinsville
Allendale Camp
Edinburgh
Morgan-Monroe State Forest
Psychological and Brain Sciences
125
Natural Area

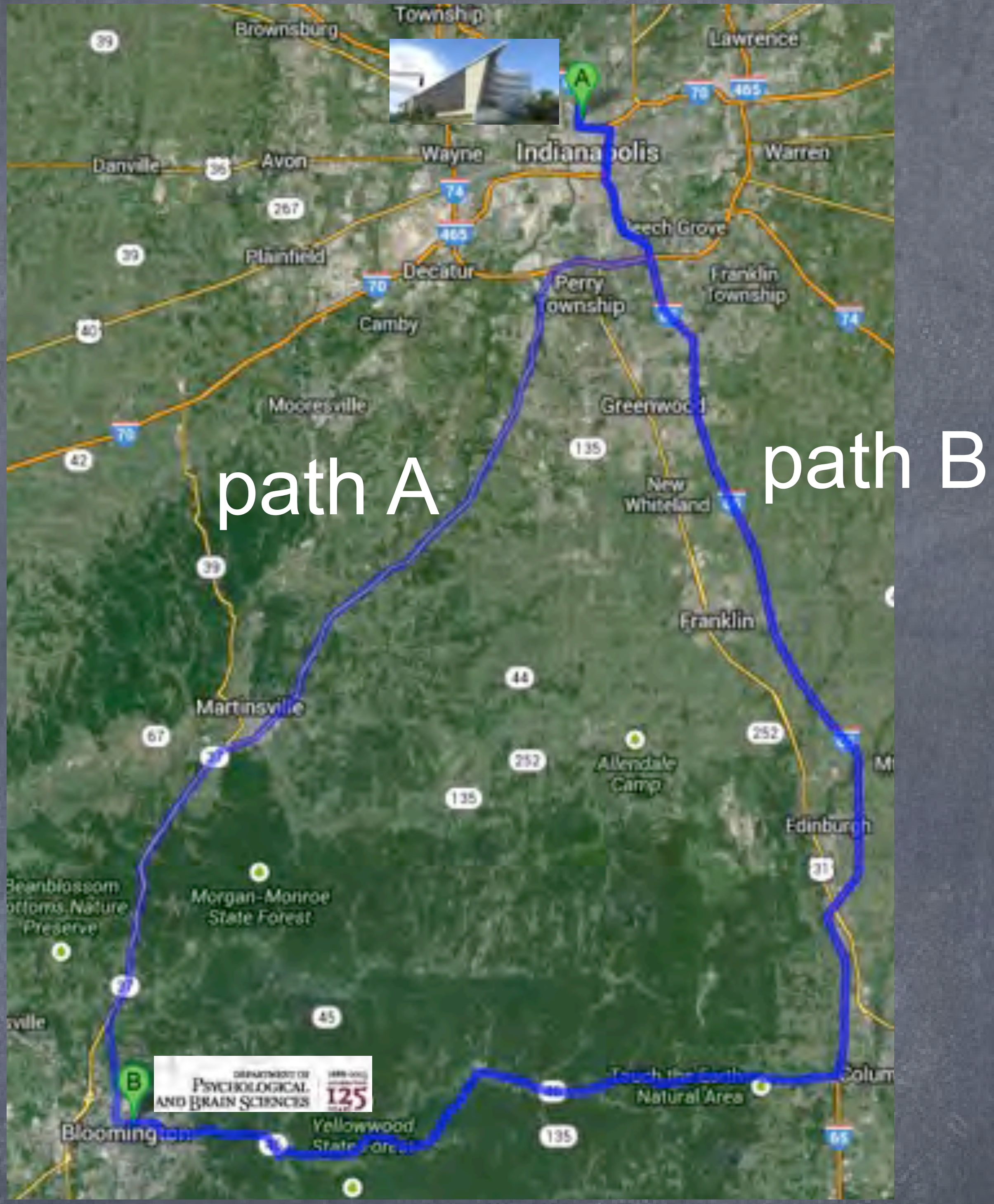


$p(\text{choice})=.5$

$p(\text{path})= (.5)^{\#d}$



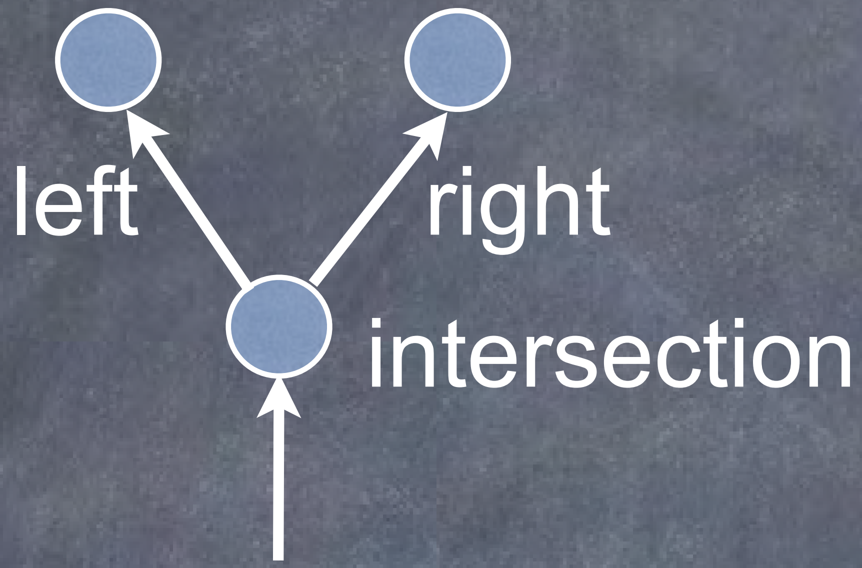




p(choice)=.5

p(path)= $(.5)^{\#d}$

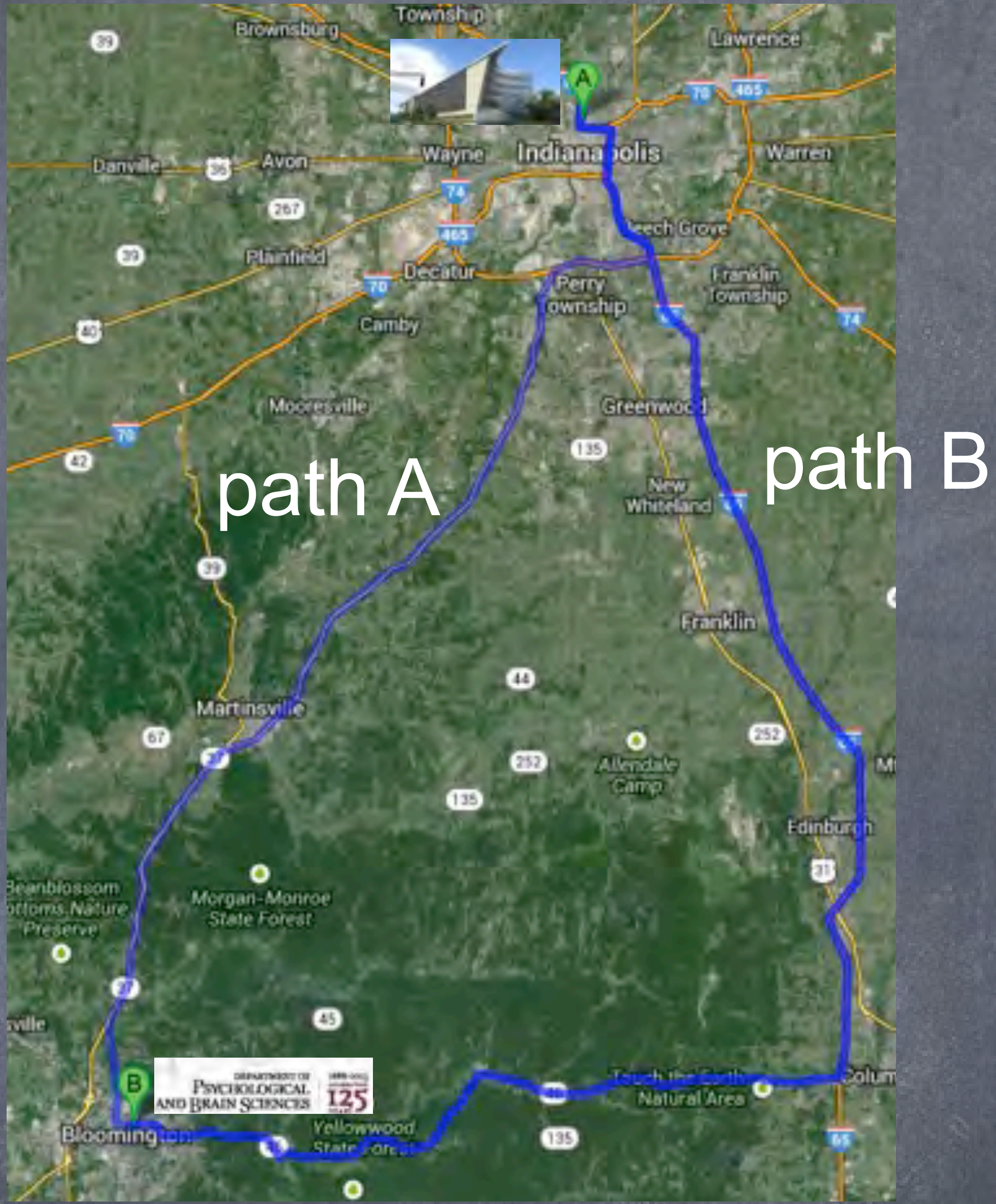
search information: $-\log(.5^{\#d})$



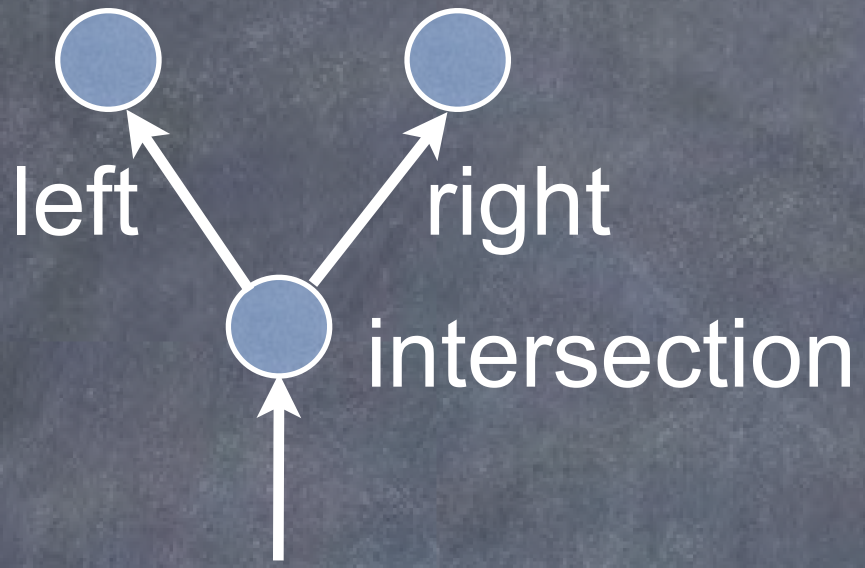
$p(\text{choice})=.5$

$p(\text{path})= (.5)^{\#d}$

search information: $-\log(.5^{\#d})$



	length	#d	S
path A	58 mi	13	9.01 bits
path B	81 mi	10	6.93 bits



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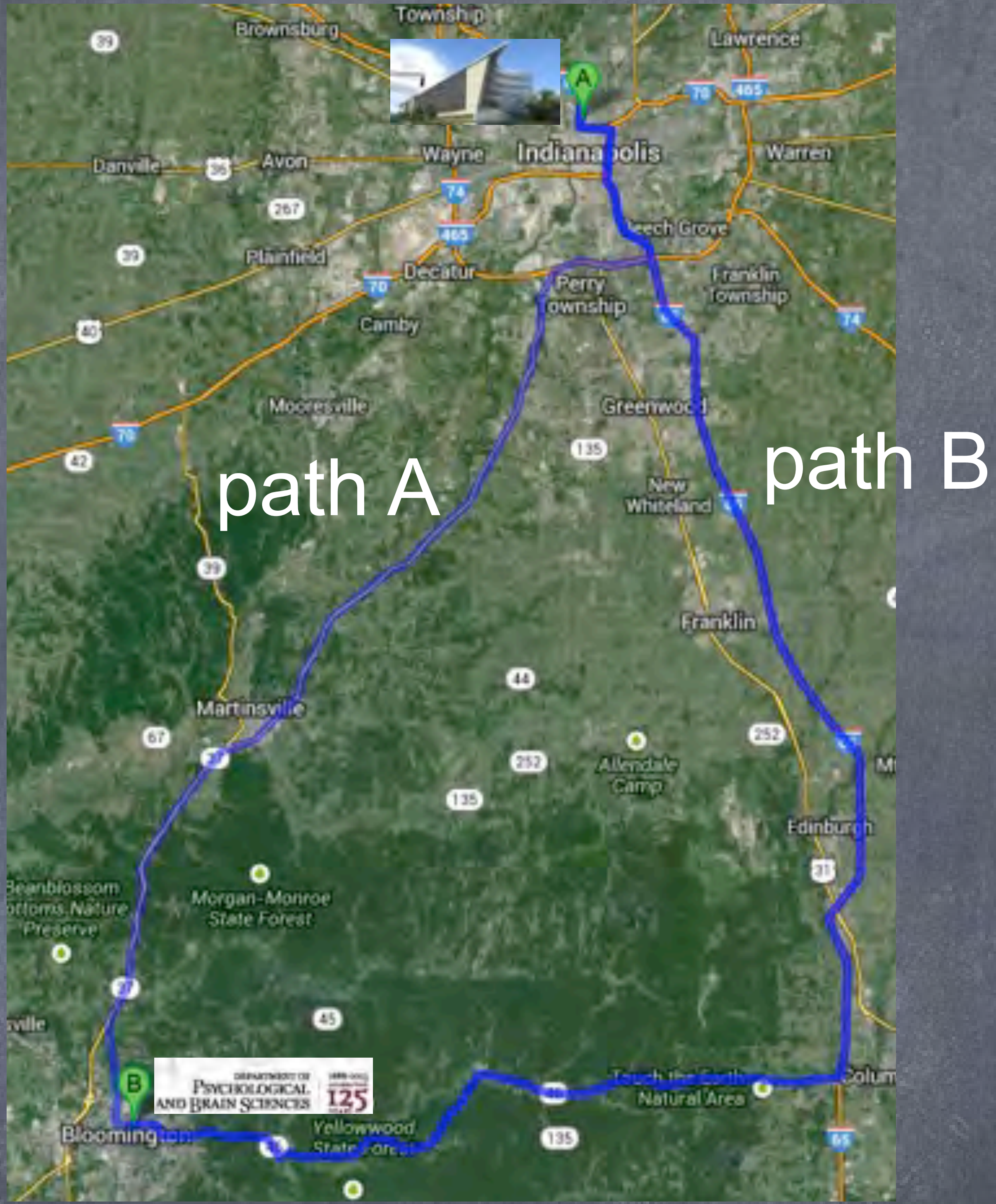
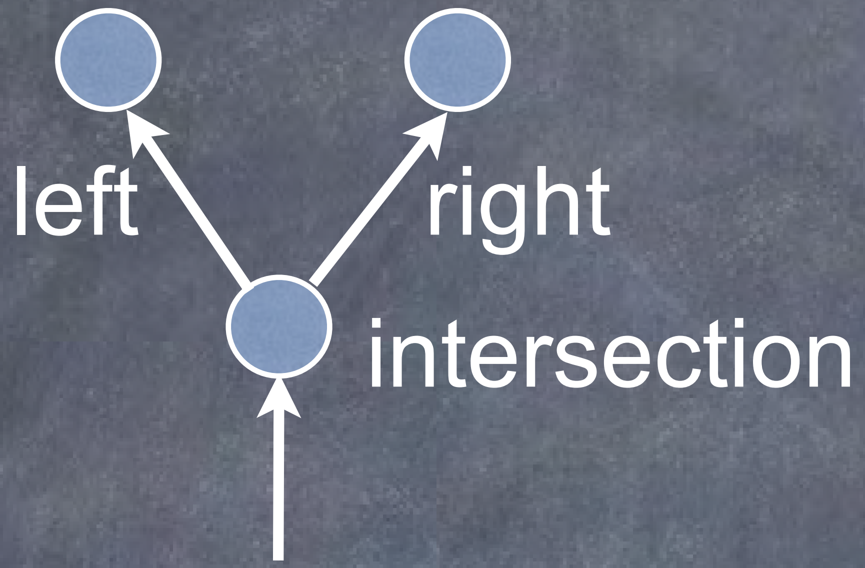


path A is **shorter** than path B



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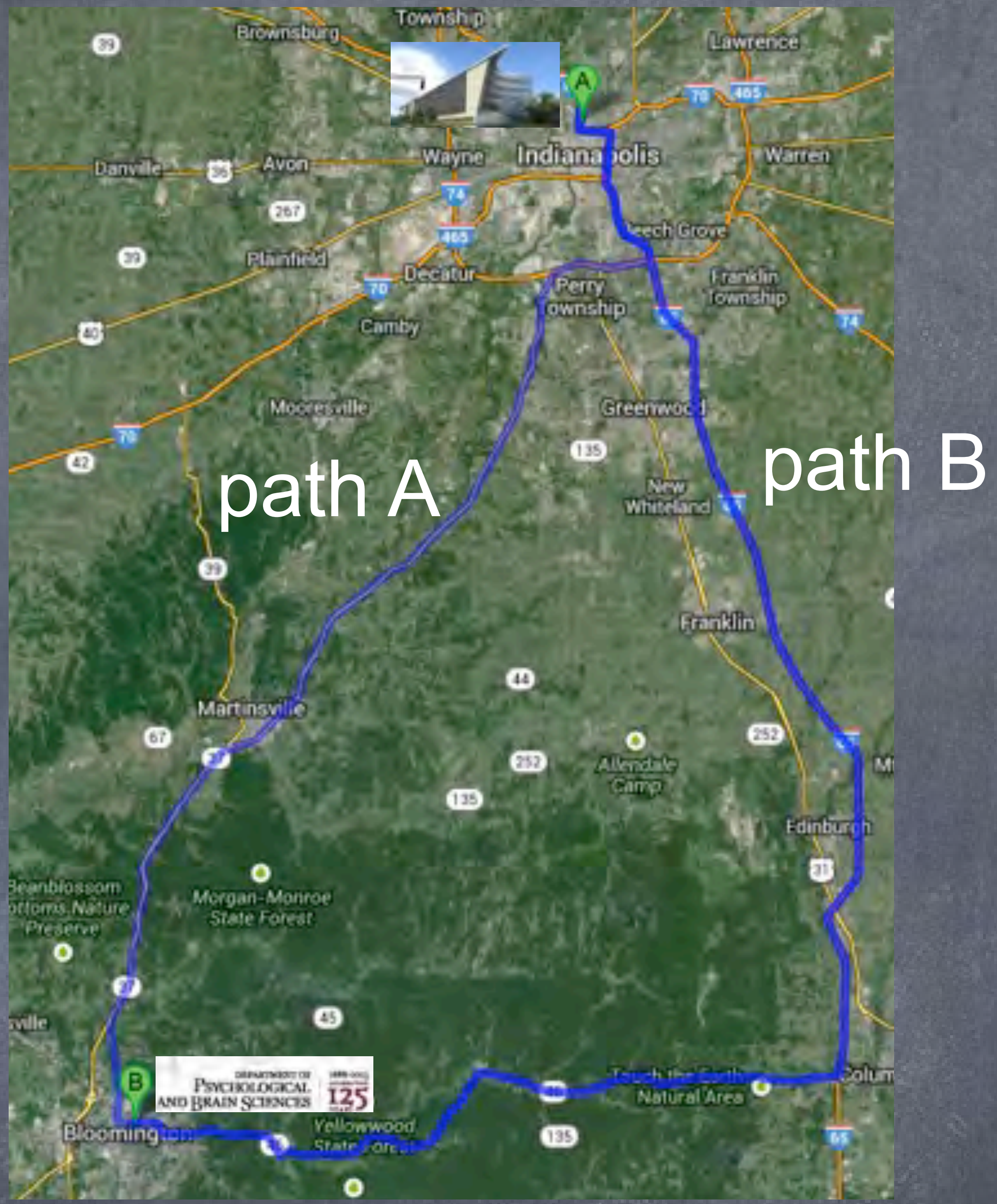
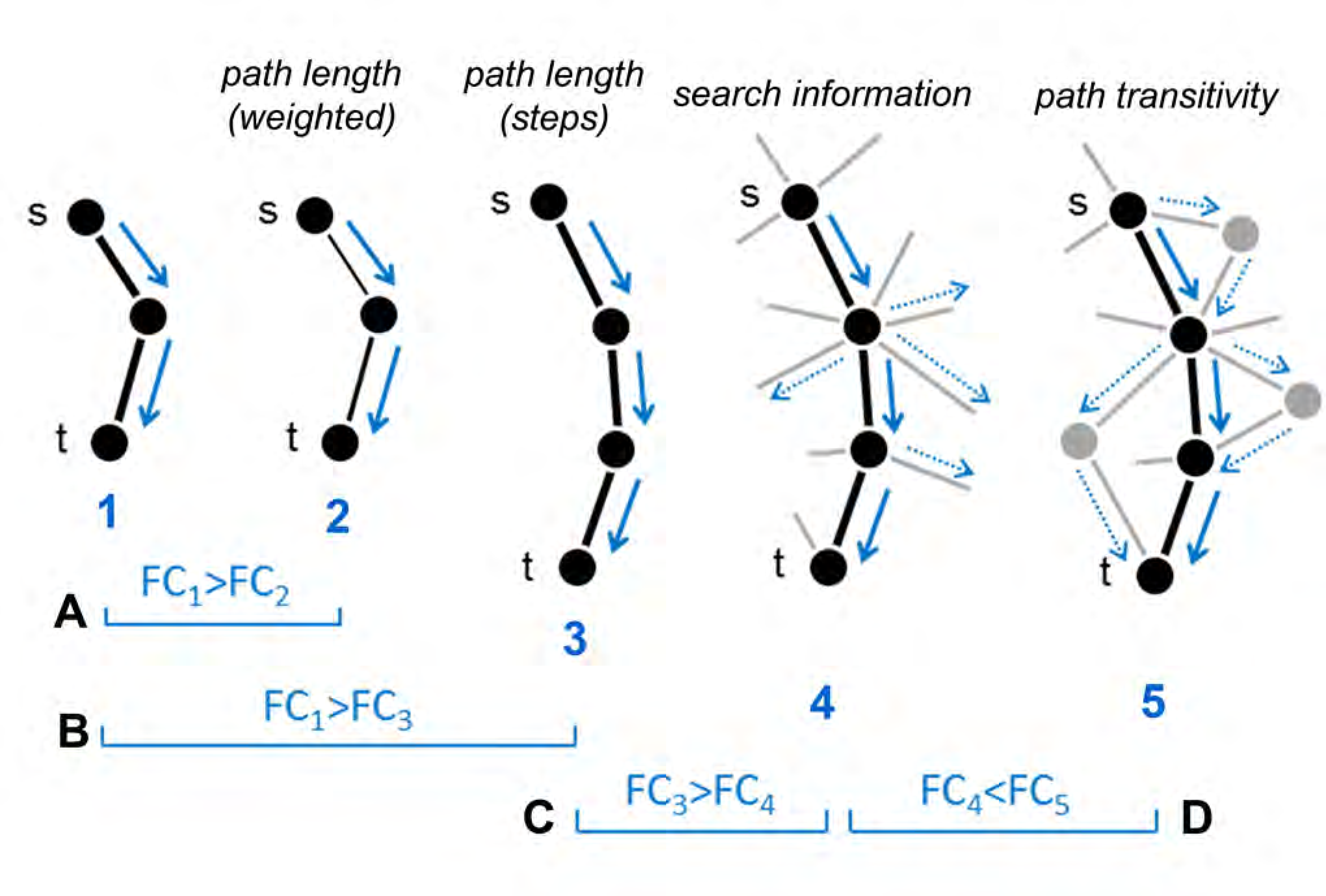


path A is **shorter** than path B

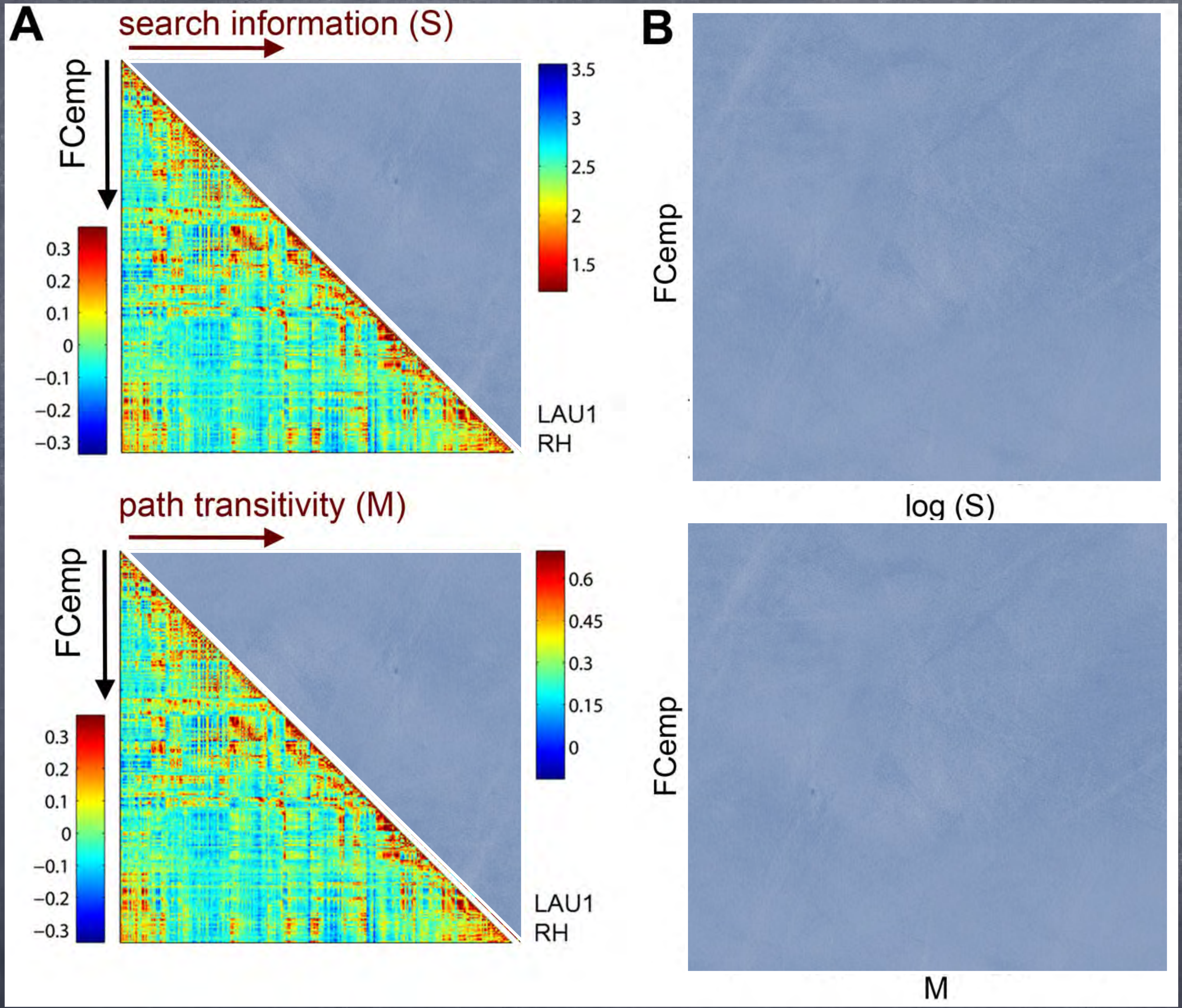
path A is more **hidden** than path B

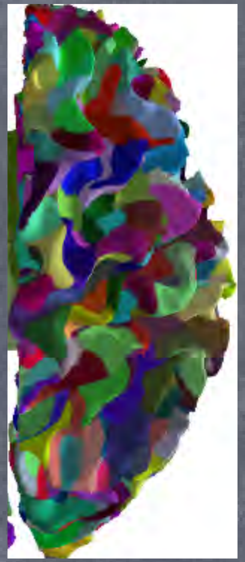
Which hypotheses are we aiming to test?

shortest-path communication measures



Goñi et al. PNAS 2014





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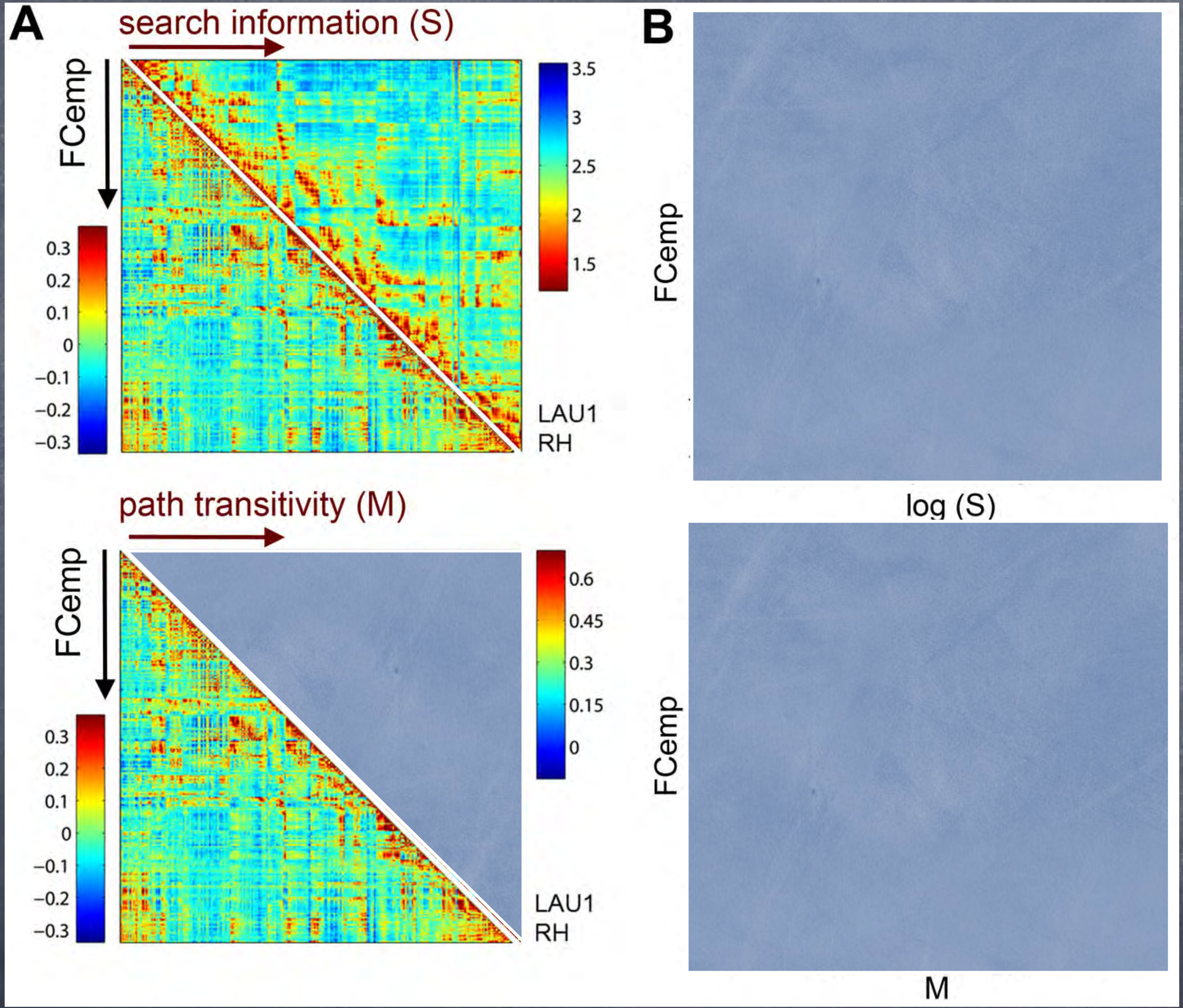
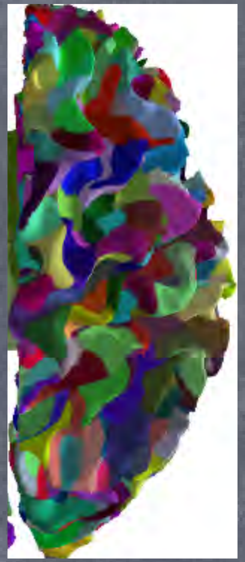
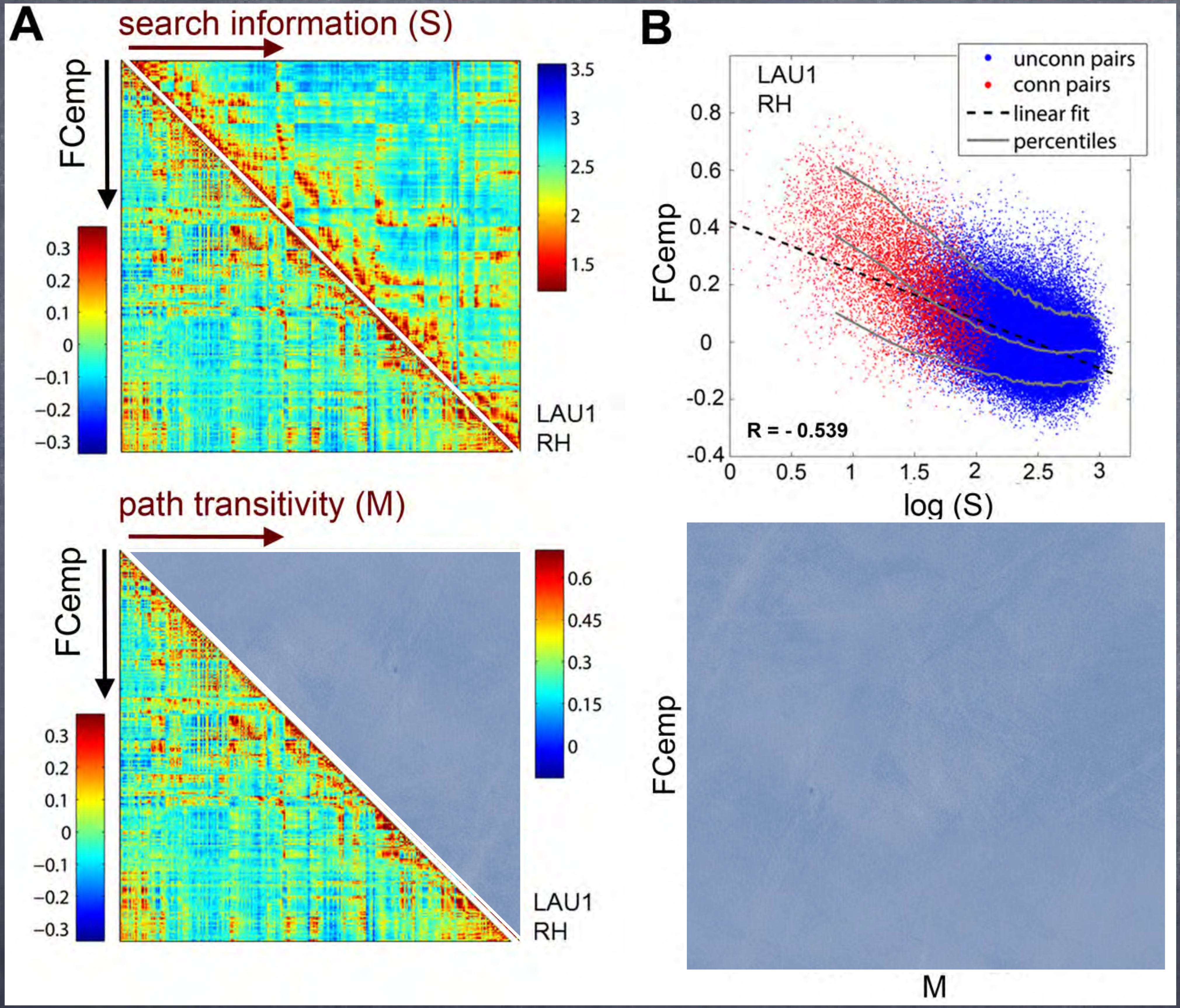
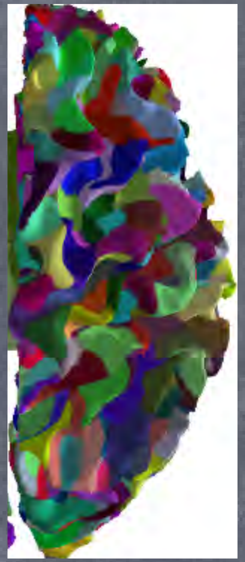


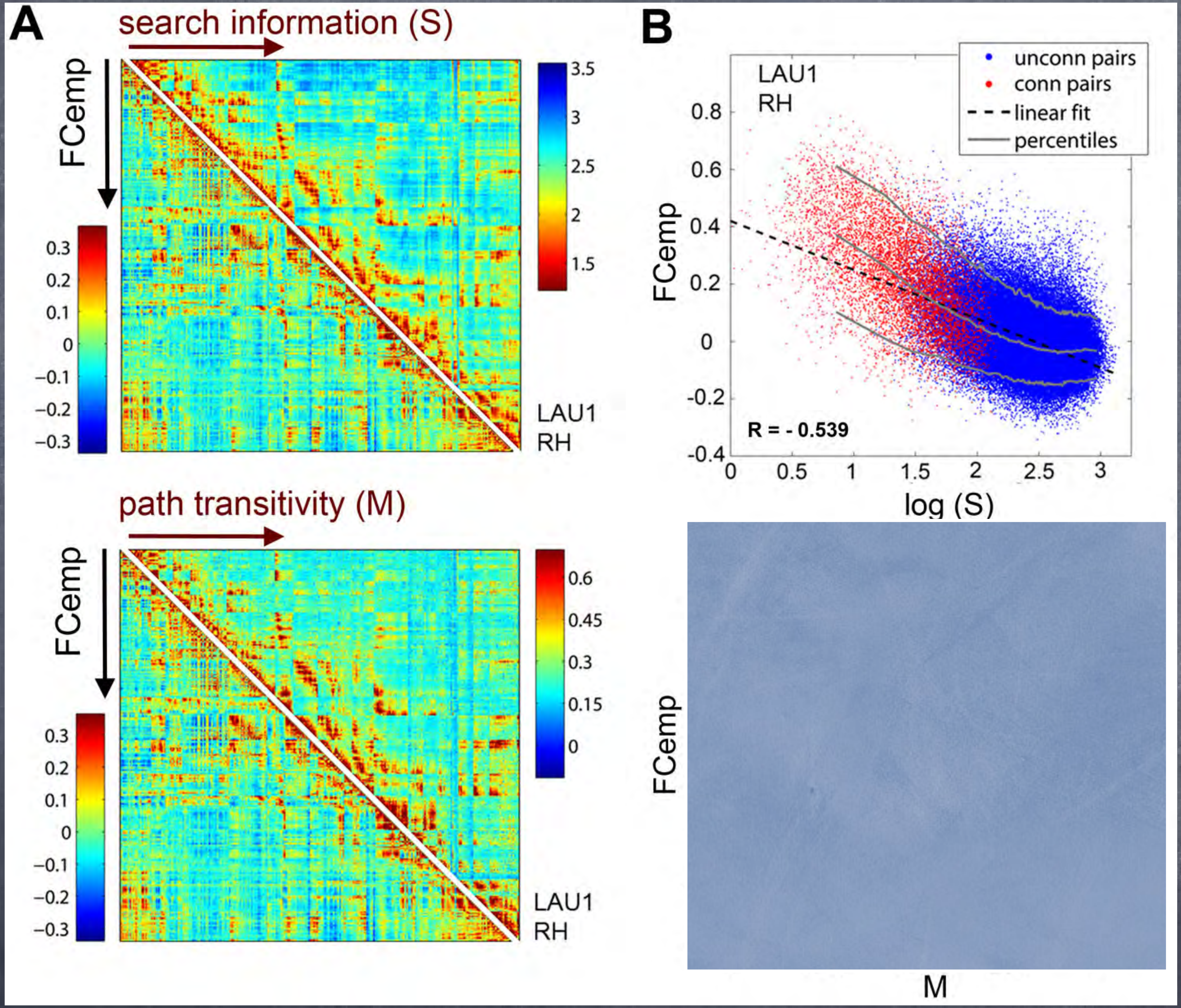


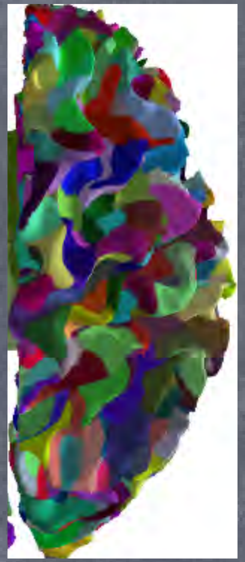
Goñi et al. PNAS 2014





Goñi et al. PNAS 2014





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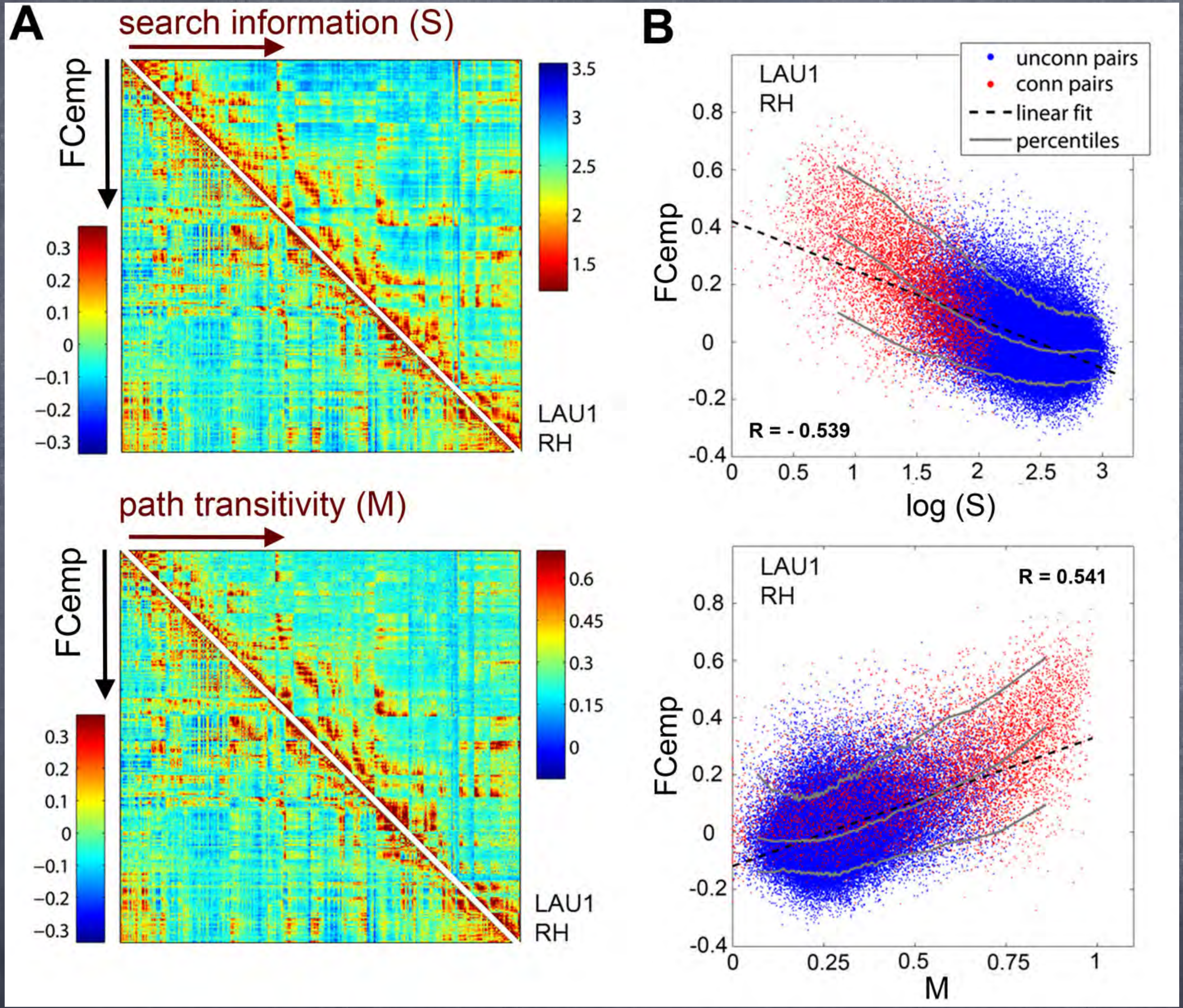
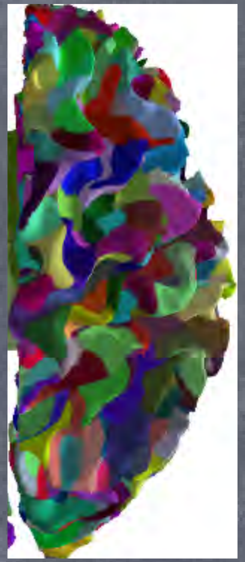
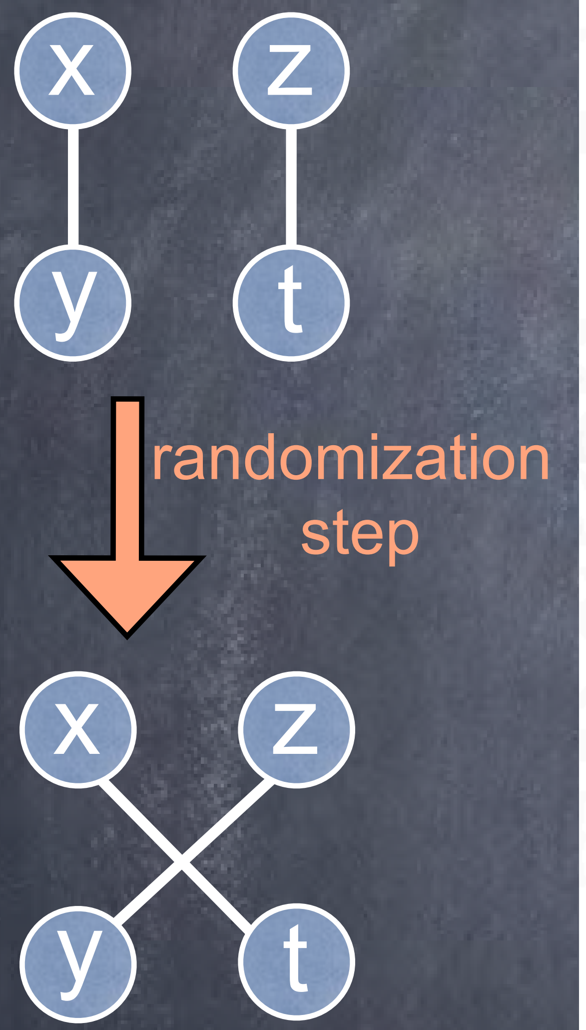


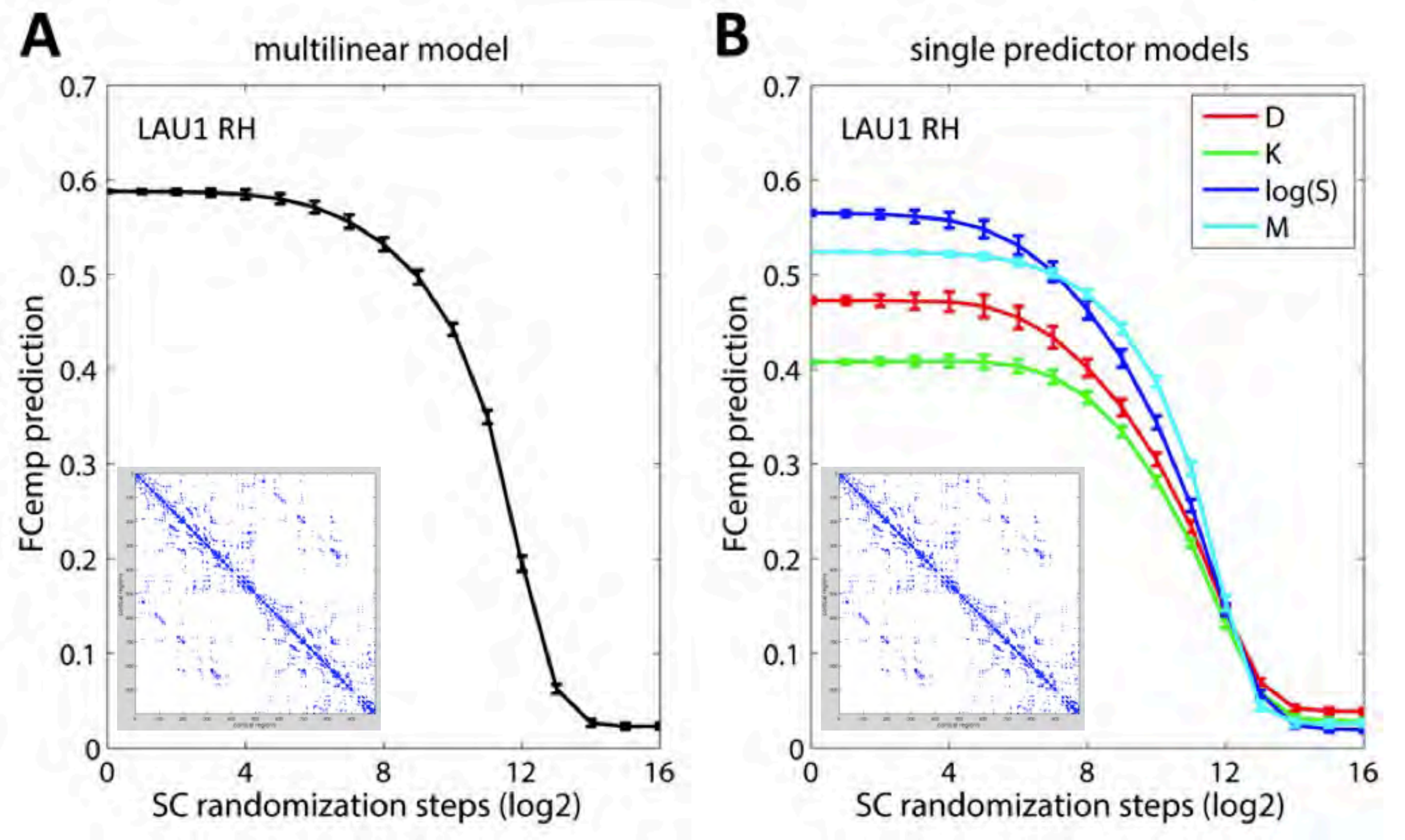


Goñi et al. PNAS 2014

Network randomization test

Goñi et al. PNAS 2014

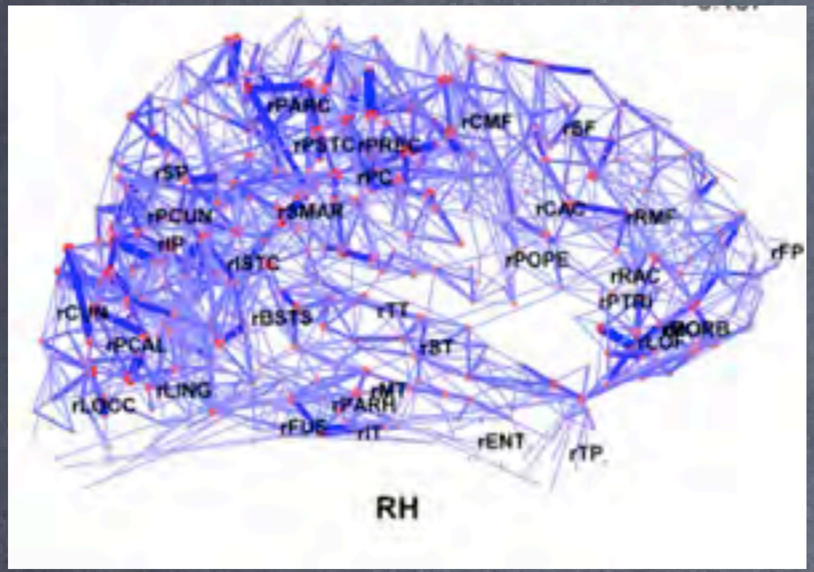




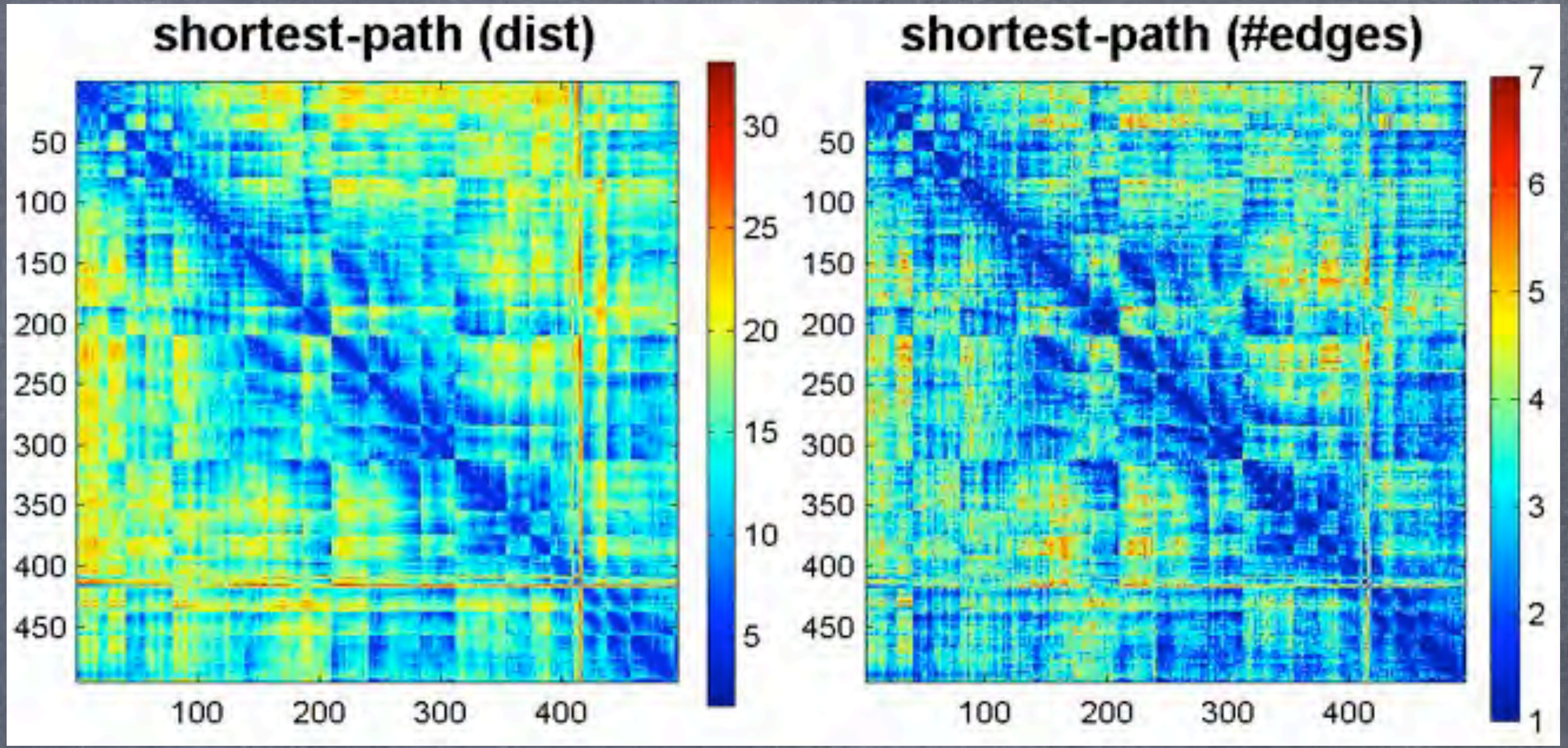
Summary

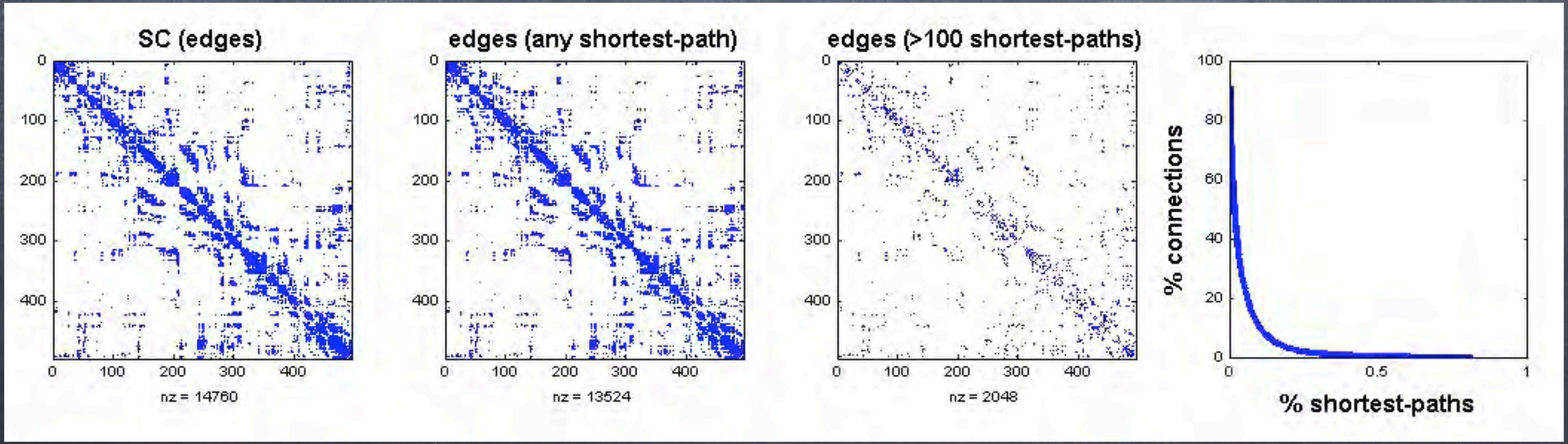
- network theory is a useful framework to better understand the human brain and how its connectivity gets affected by diseases
- communication model(s) based on SC can predict resting-state FC
- the way shortest-paths are embedded (hidden) in the network is a strong predictor of resting-state FC.
- evidence of SC driving / shaping collective dynamics and fluctuations of neural activity during resting-state
- analytical, almost immediate computation.

the shortest-path 'paradox'

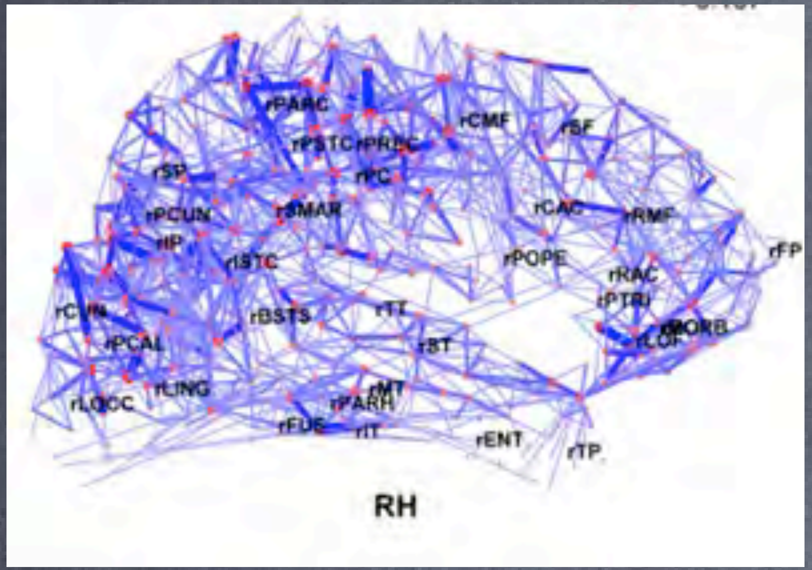


Hagmann et al. Plos Biol. 2008





the shortest-path (the only one?)



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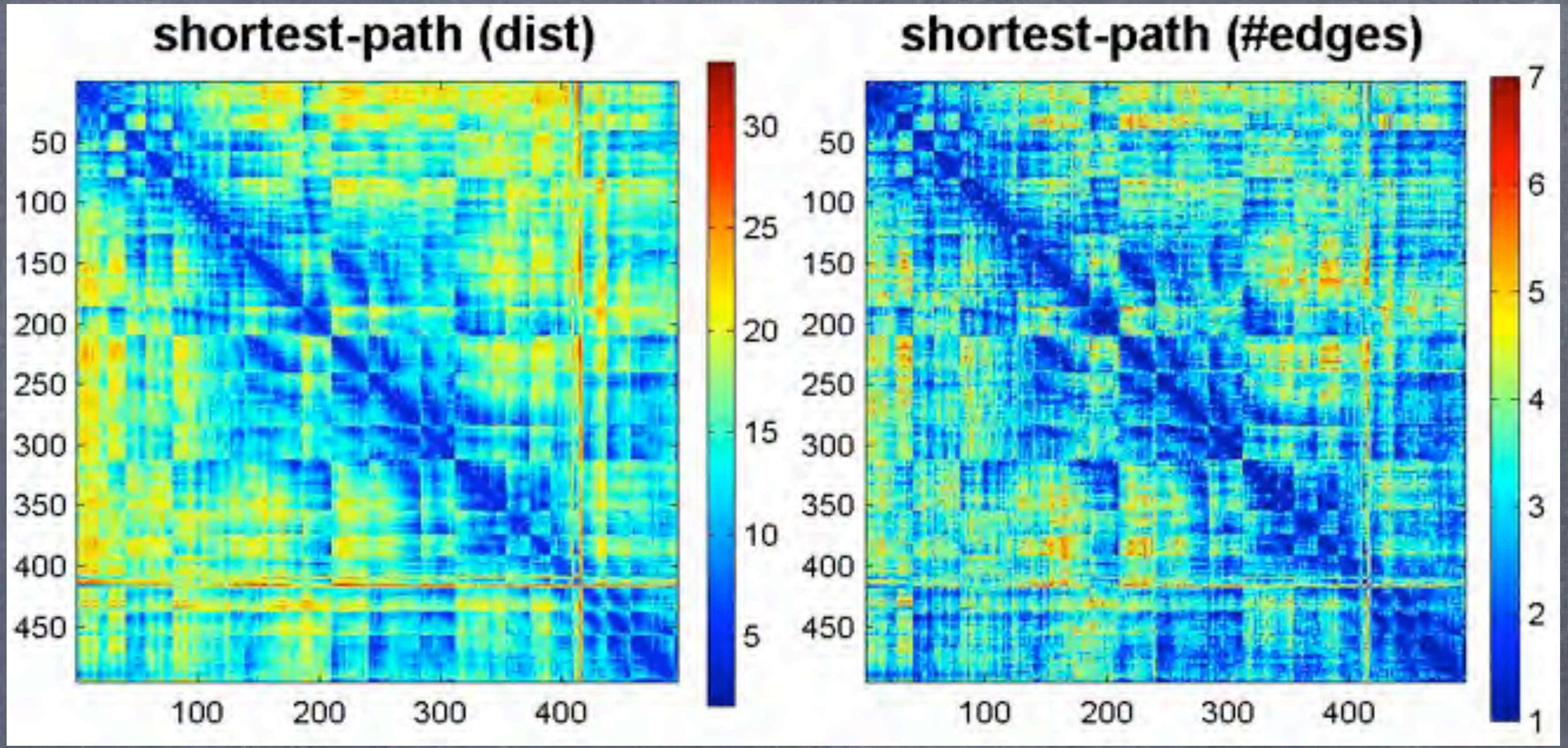
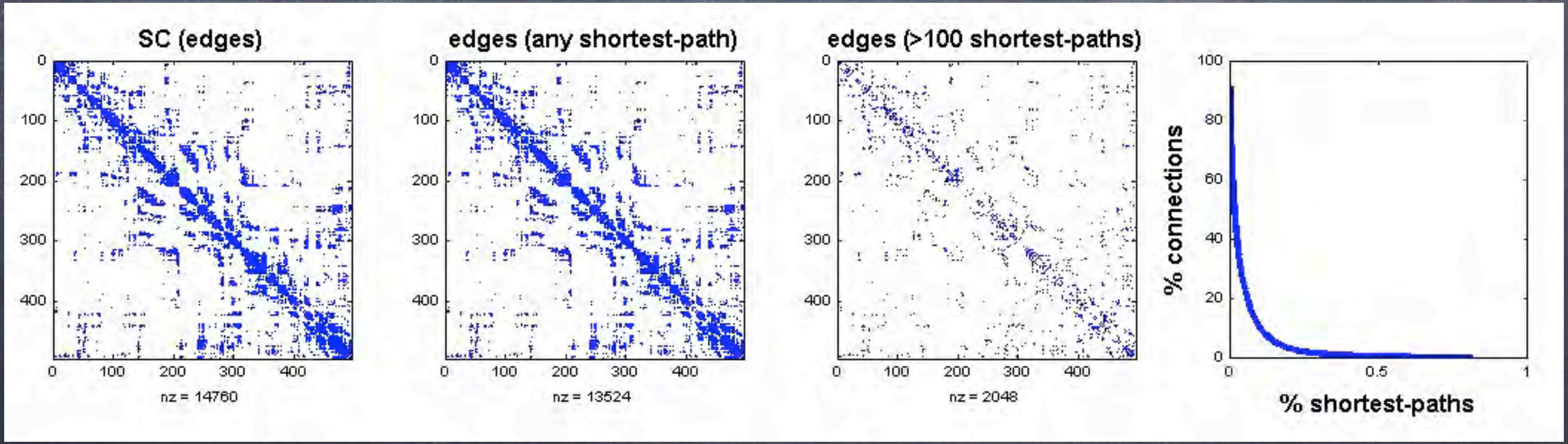


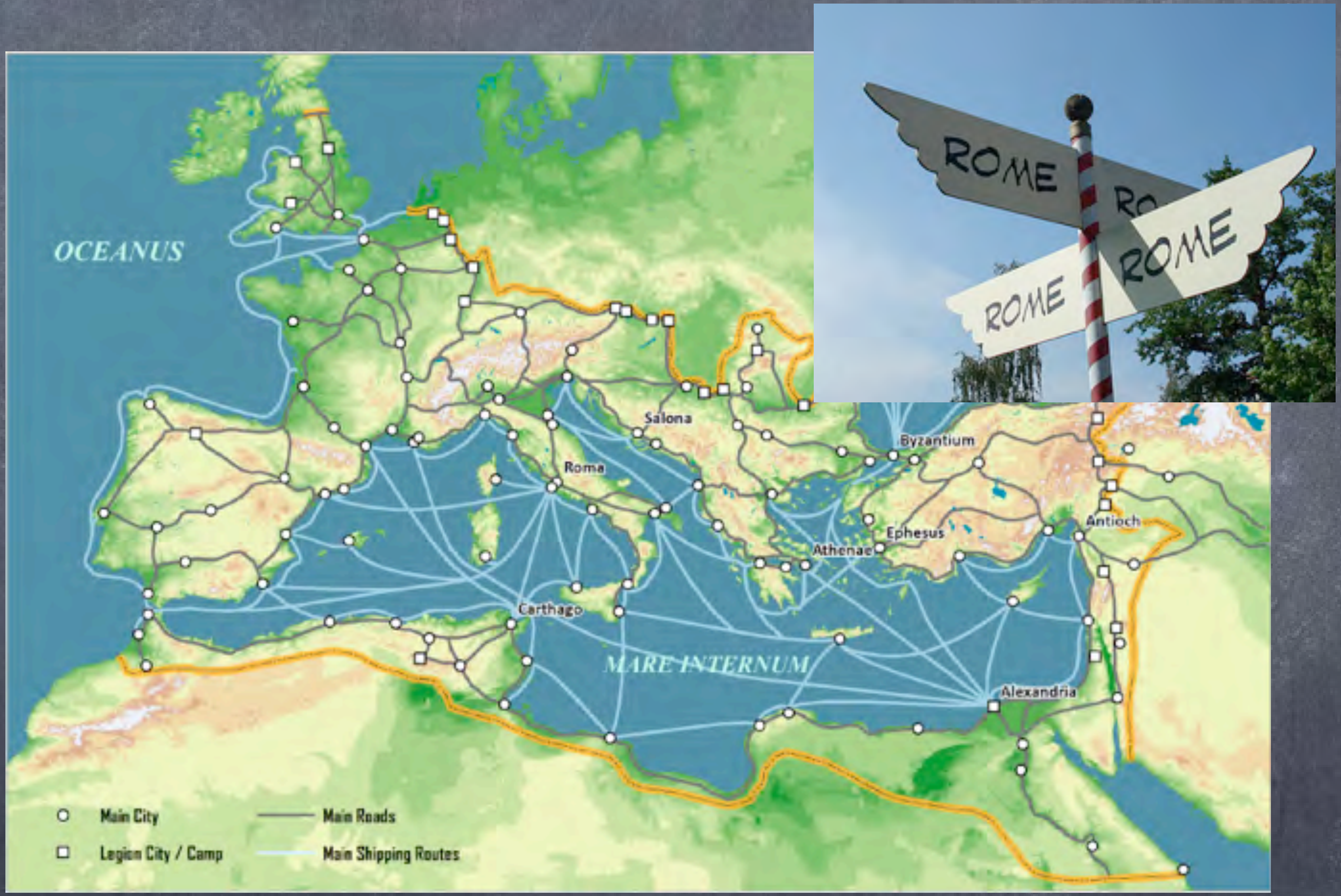


"all roads lead to Rome"

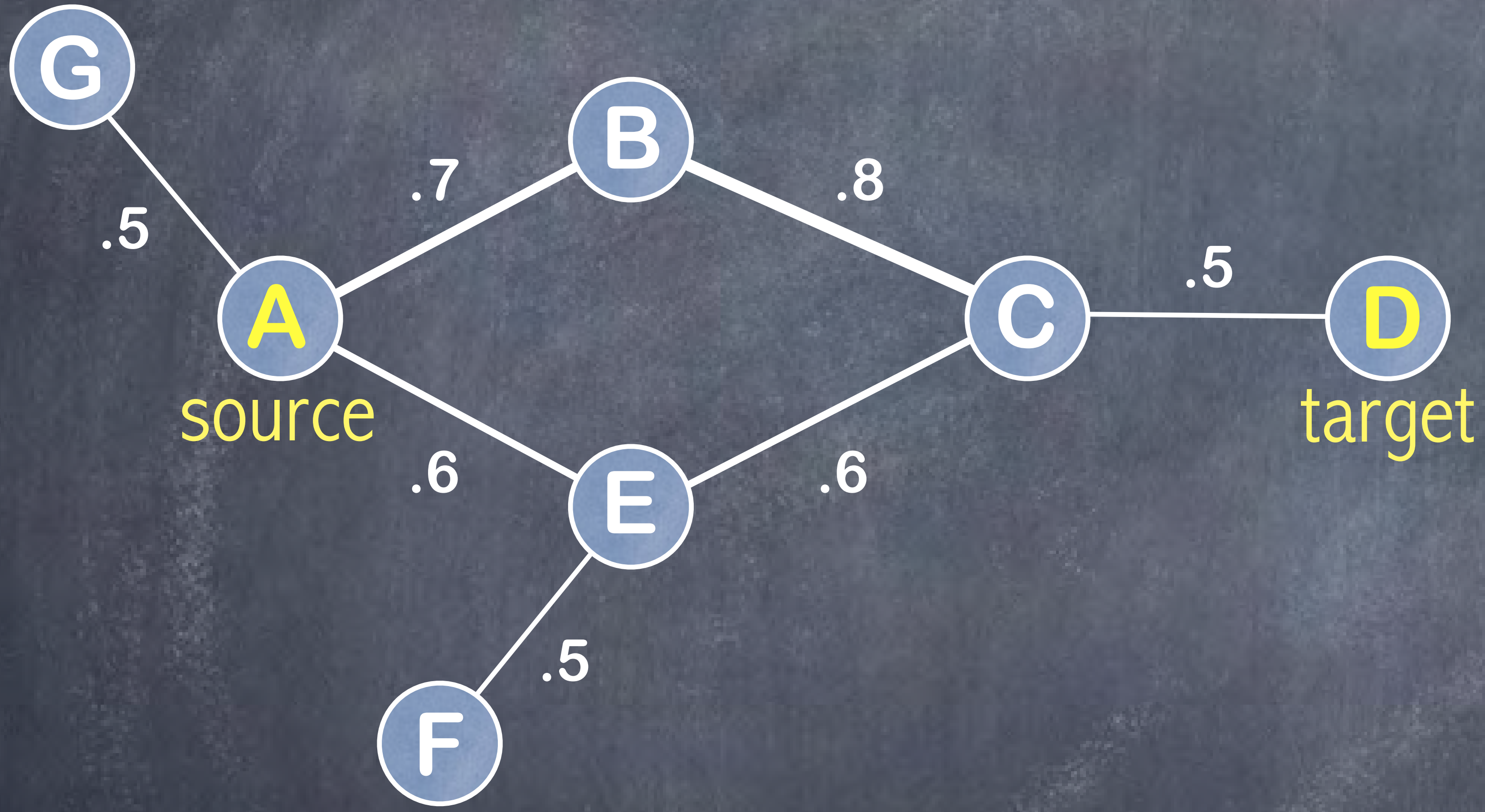
“all roads lead to Rome”

understanding the human connectome from an information theoretical perspective

"I promise you I'll reach the destination. But I cannot really tell you which path I will take. Hopefully a good one among a set of possible ones."

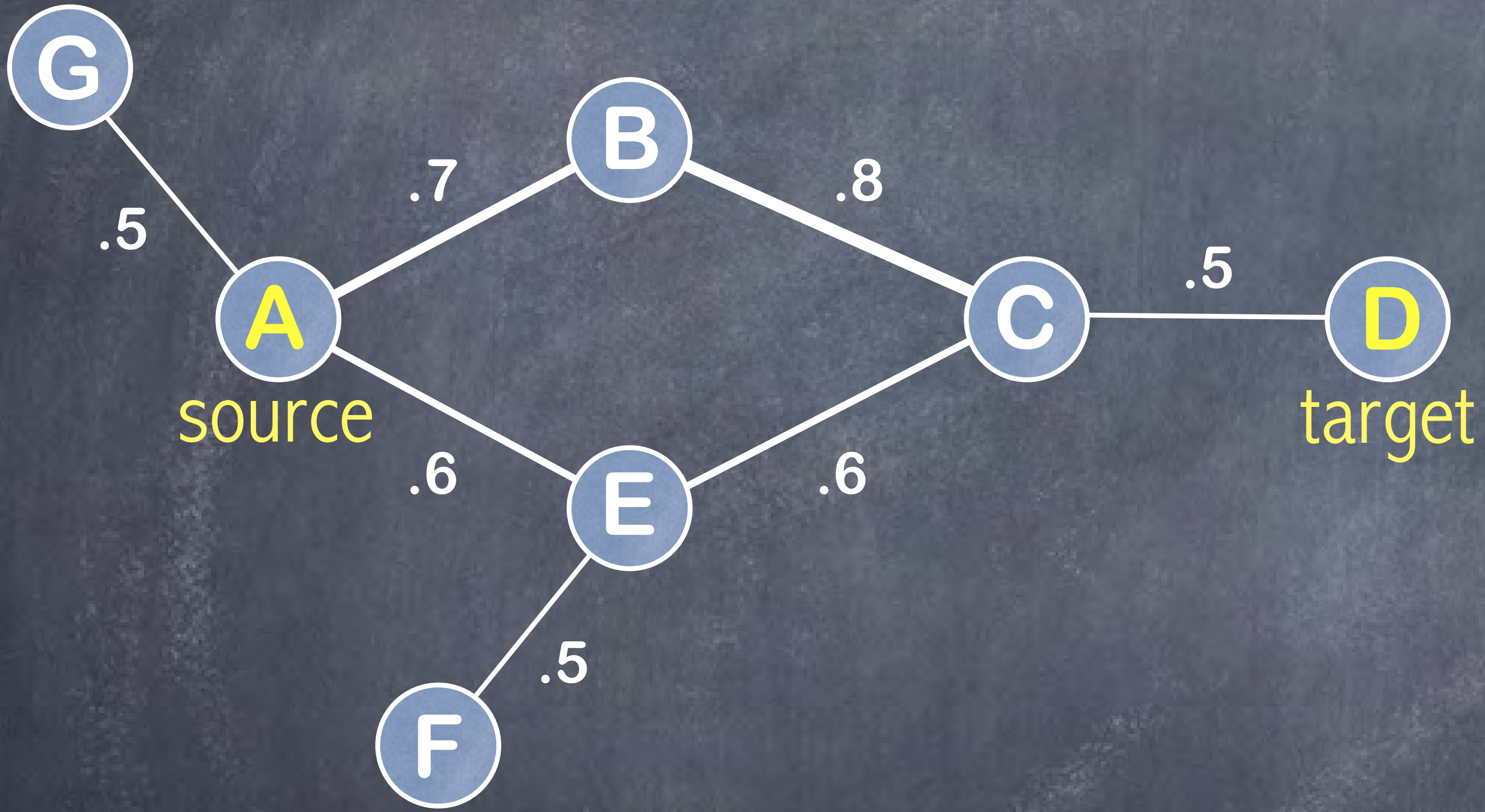


generalized k-search-information. Example A



generalized k-search-information. Example A

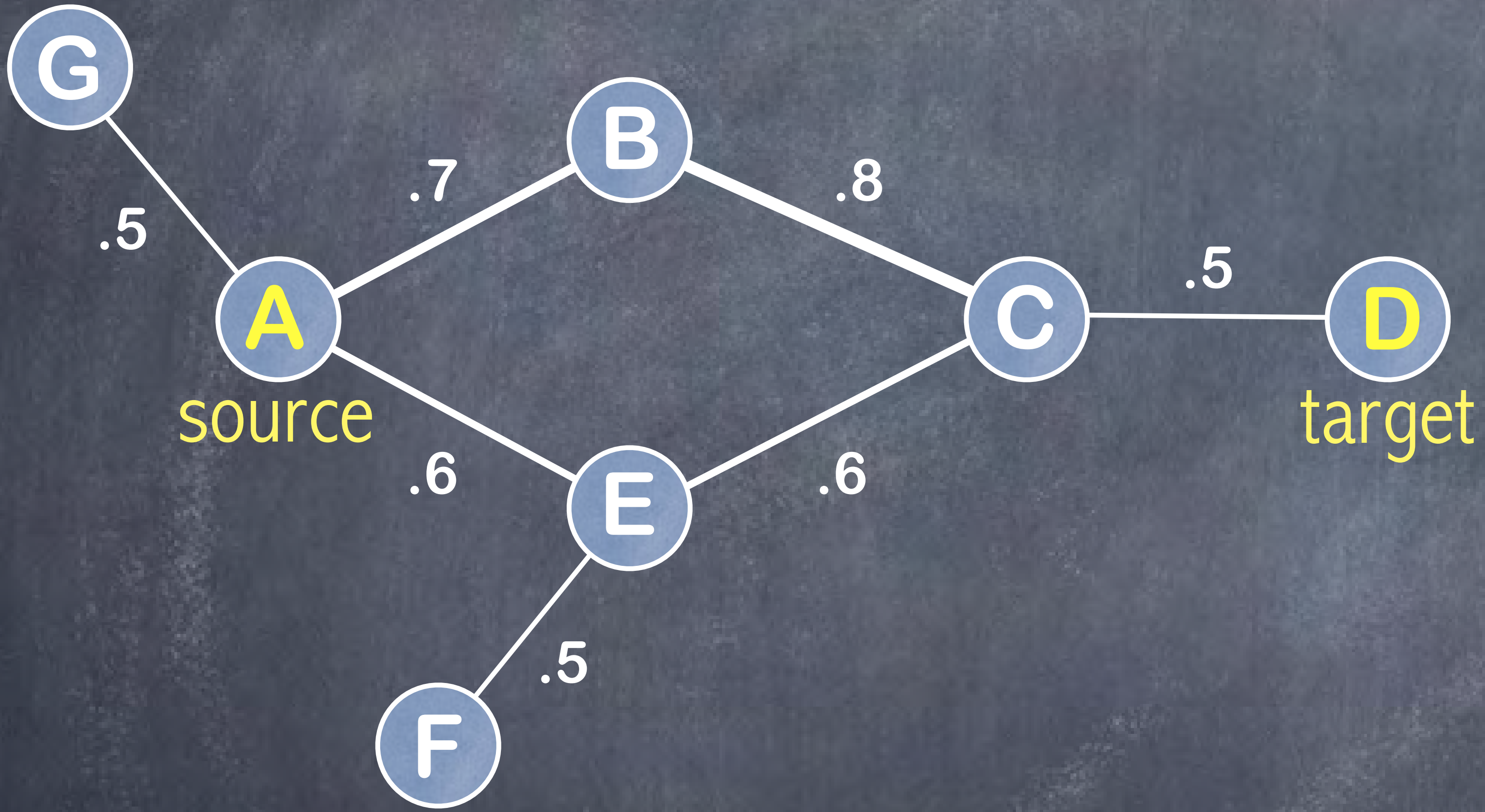
$\prod_1=\{A,B,C,D\}$



generalized k-search-information. Example A

$\prod_1=\{A,B,C,D\}$

$SI(\prod_1) = -\log(.7/1.8 \cdot 1 \cdot .5/1.1) = 1.73$ bits

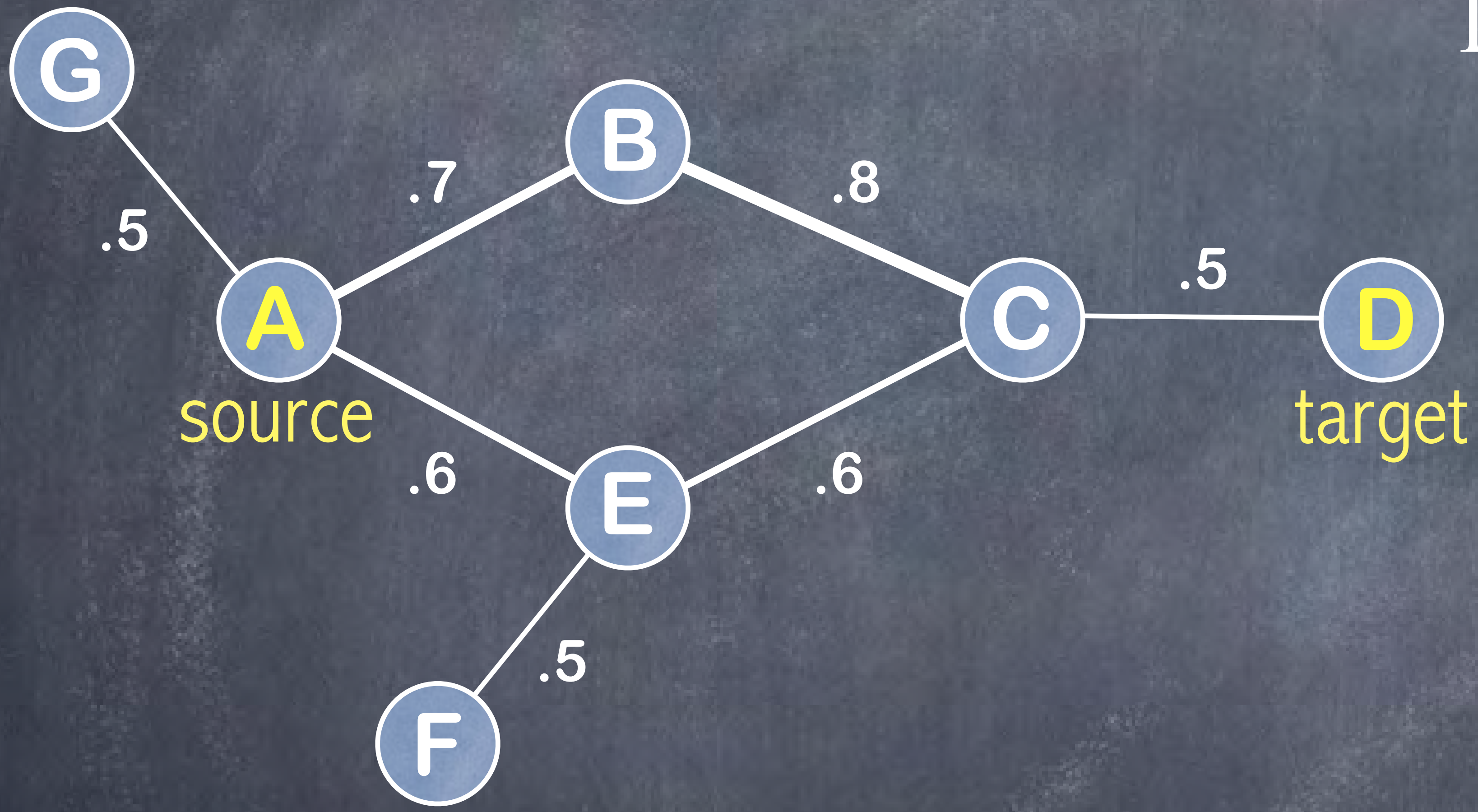


generalized k-search-information. Example A

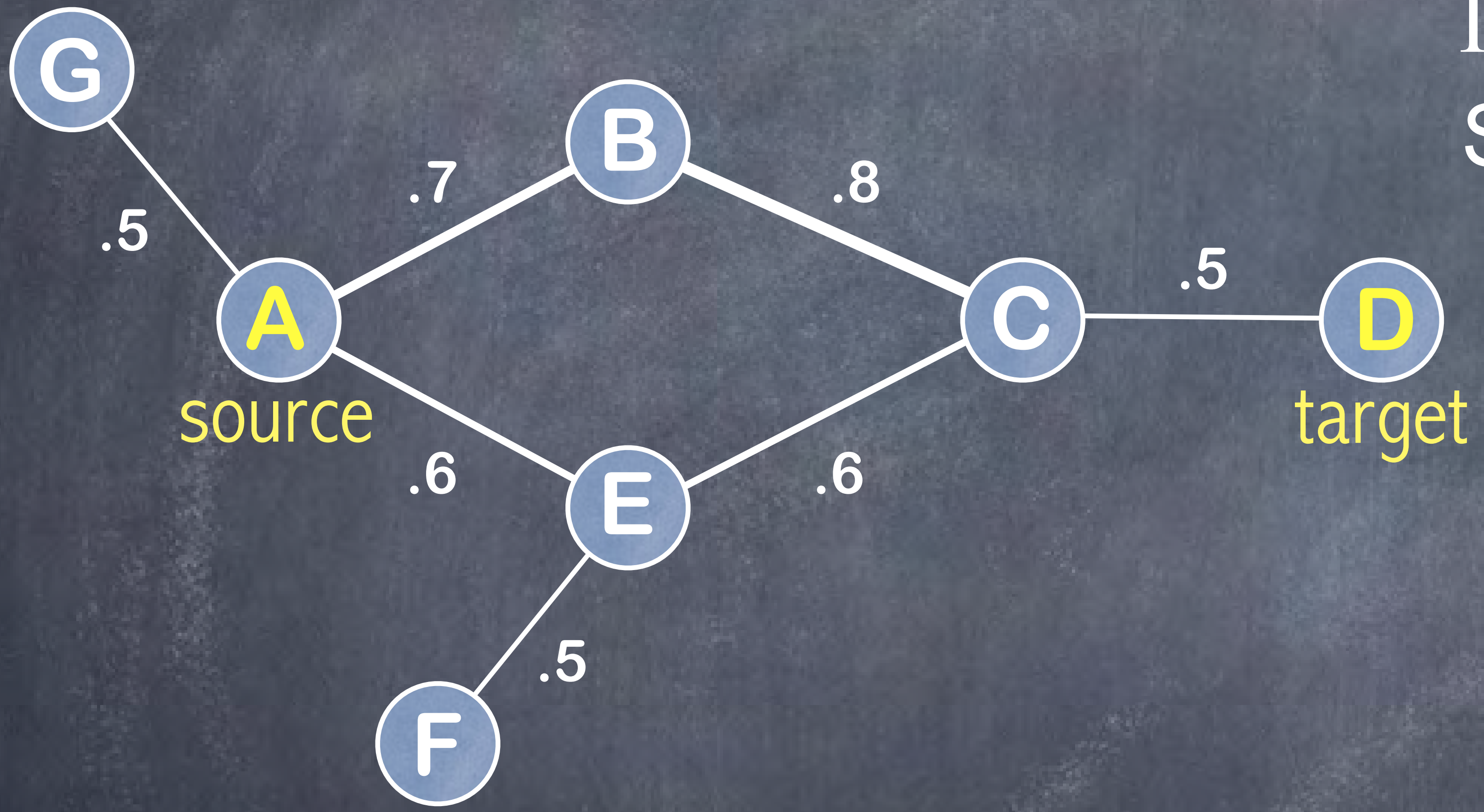
$\prod_1$={A,B,C,D}

SI($\prod_1$) = -log(.7/1.8 • 1 •.5/1.1) = 1.73 bits

$\prod_2$={A,E,C,D}



generalized k-search-information. Example A



$\prod_1$={A,B,C,D}

SI($\prod_1$) = -log(.7/1.8 • 1 •.5/1.1) = 1.73 bits

$\prod_2$={A,E,C,D}

SI($\prod_2$) = -log(.6/1.8 • .6/1.1 •.5/1.3) = 2.66 bits

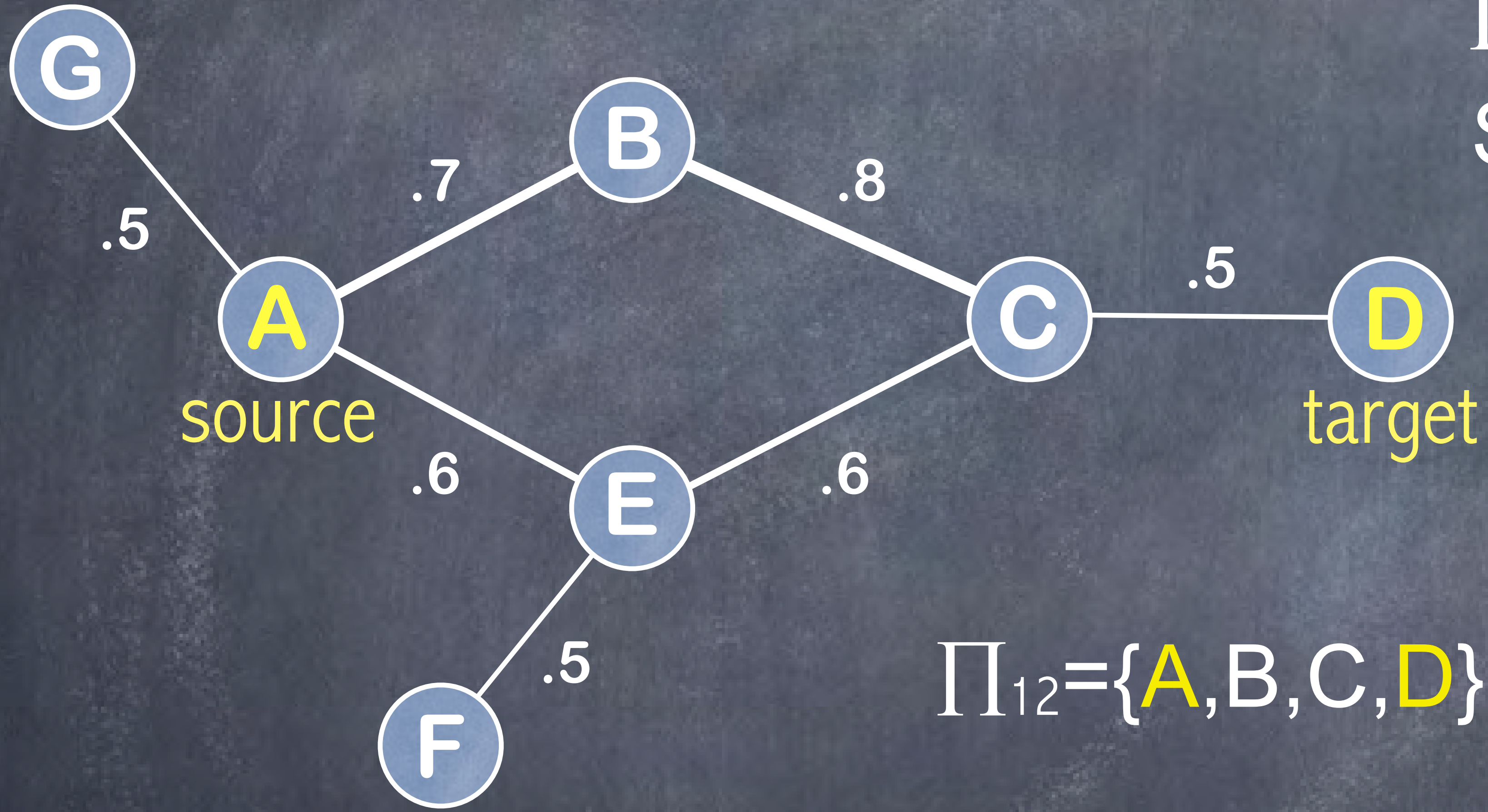
generalized k-search-information. Example A

$\prod_1=\{A,B,C,D\}$

$SI(\prod_1) = -\log(.7/1.8 \cdot 1 \cdot .5/1.1) = 1.73$ bits

$\prod_2=\{A,E,C,D\}$

$SI(\prod_2) = -\log(.6/1.8 \cdot .6/1.1 \cdot .5/1.3) = 2.66$ bits



$\prod_{12}=\{A,B,C,D\} \,||\, \{A,E,C,D\}$

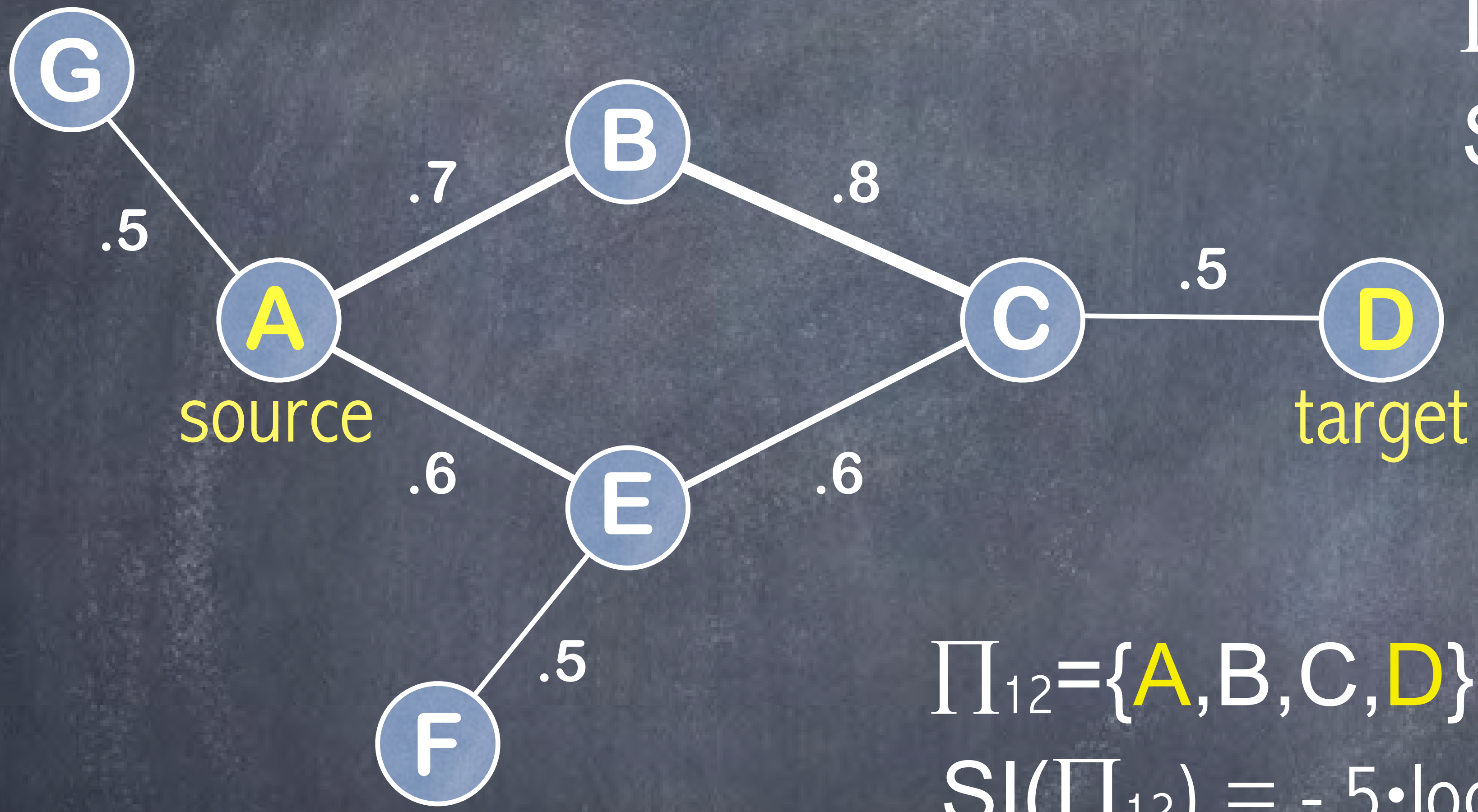
generalized k-search-information. Example A

$\prod_1=\{A,B,C,D\}$

$SI(\prod_1) = -\log(.7/1.8 \cdot 1 \cdot .5/1.1) = 1.73$ bits

$\prod_2=\{A,E,C,D\}$

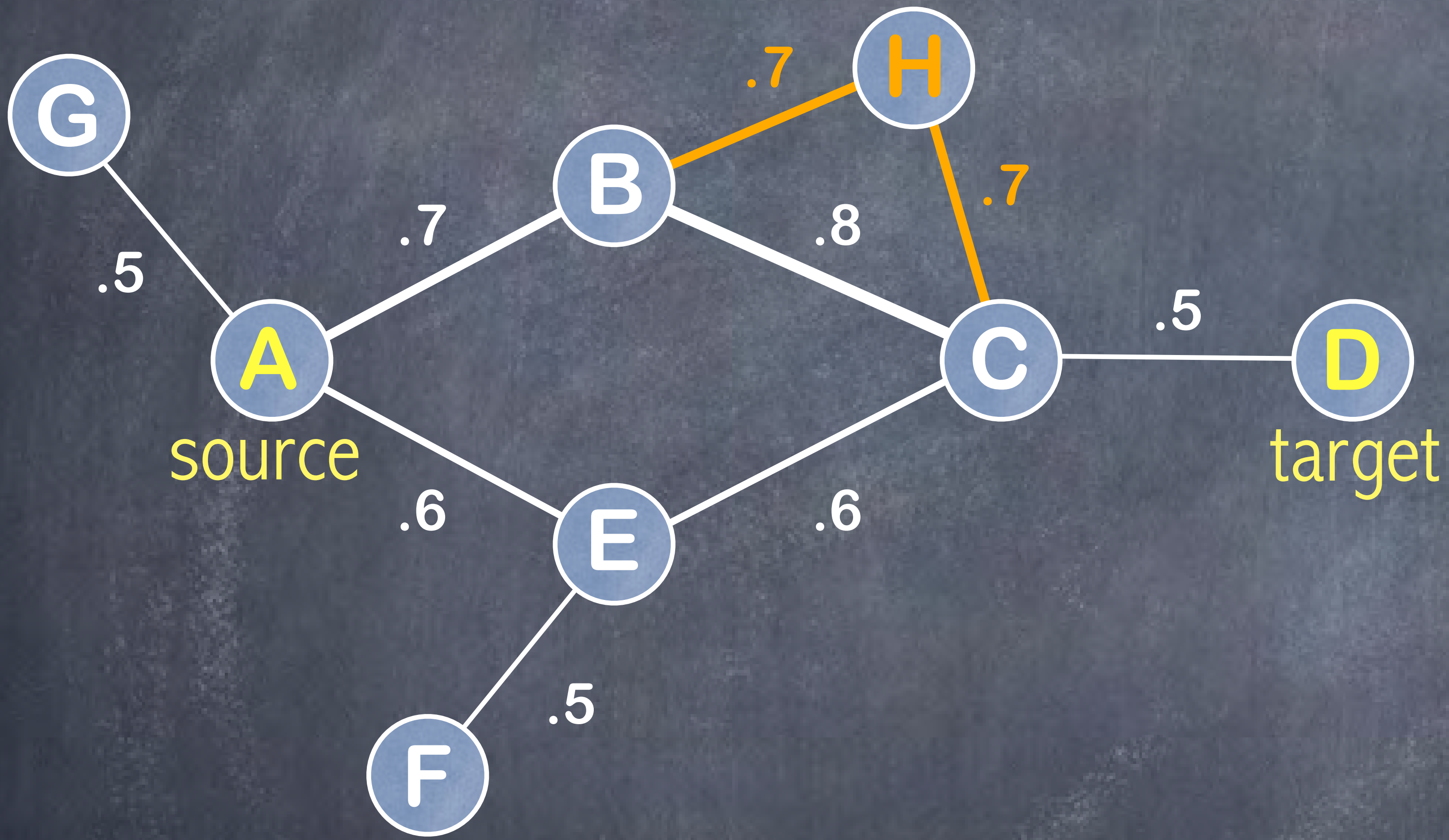
$SI(\prod_2) = -\log(.6/1.8 \cdot .6/1.1 \cdot .5/1.3) = 2.66$ bits



$\prod_{12}=\{A,B,C,D\} \mid\mid \{A,E,C,D\}$

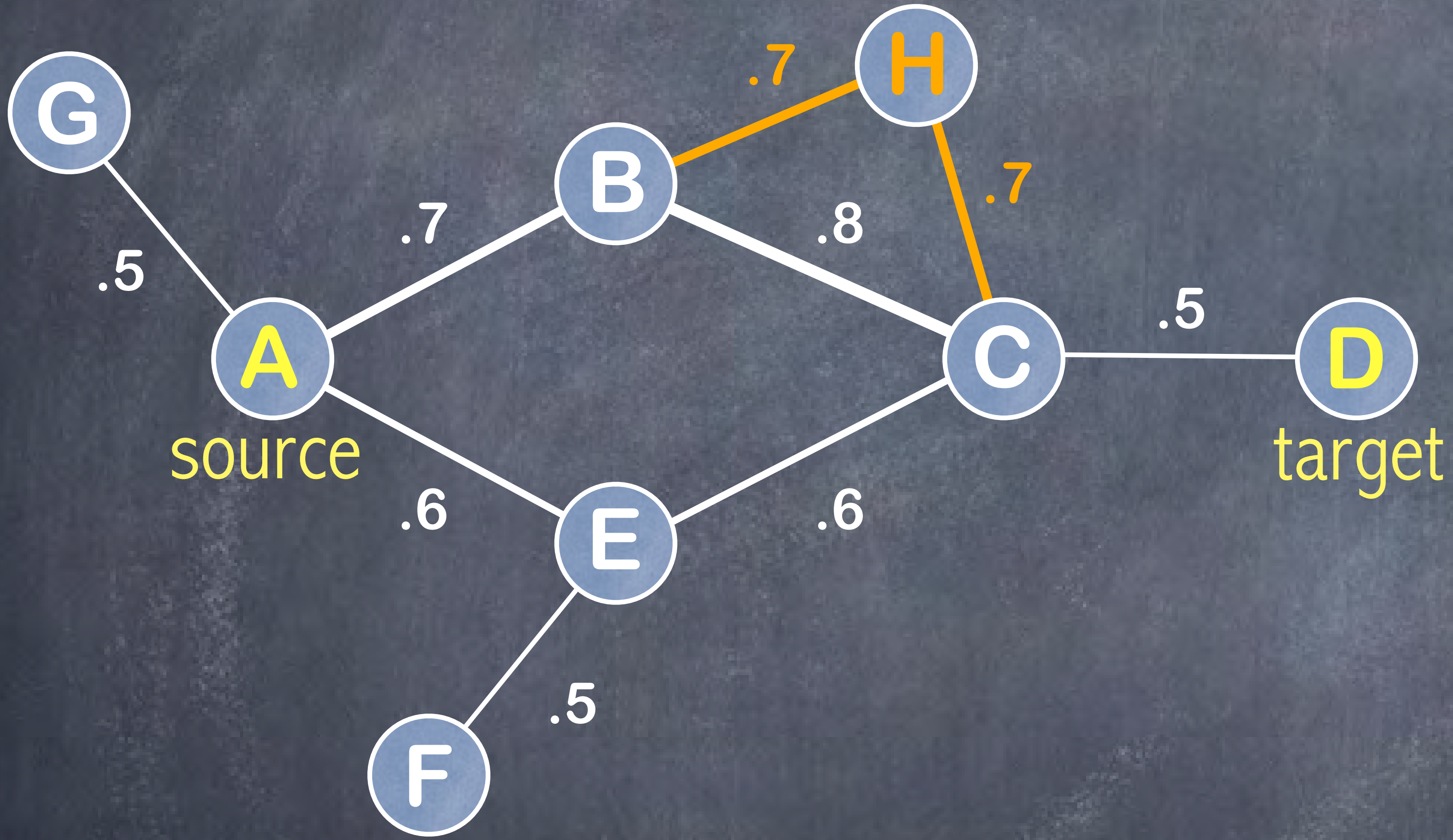
$$SI(\prod_{12}) = -.5 \cdot \log(1.3/1.8) - \log(1 \cdot .5/1.1)$$
$$-.5 \cdot \log(1.3/1.8) - \log(.6/1.1 \cdot .5/1.3)$$
$$= 1.5 \text{ bits}$$

generalized k-search-information. Example B



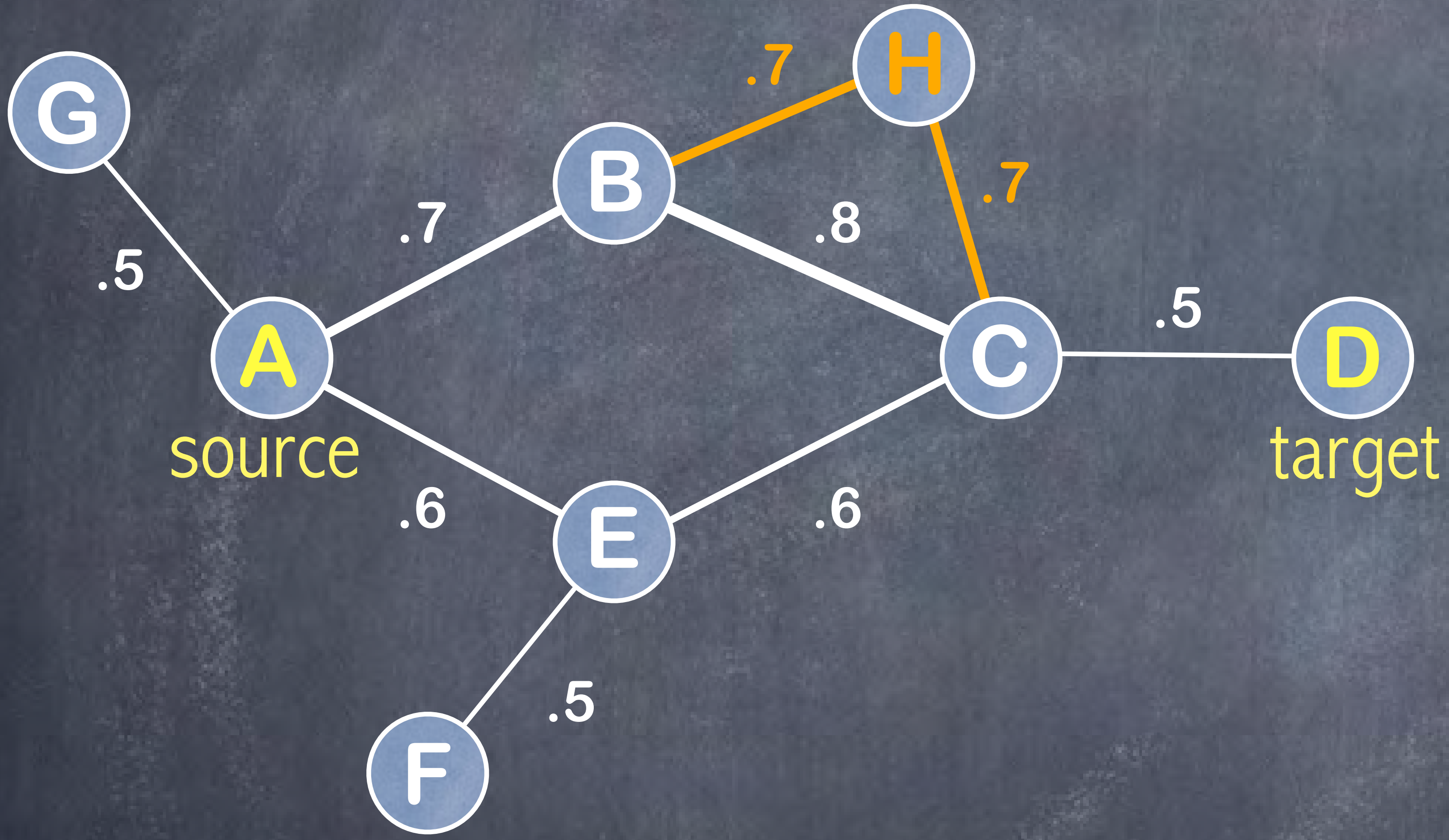
generalized k-search-information. Example B

$\prod_1$={A,B,C,D}



generalized k-search-information. Example B

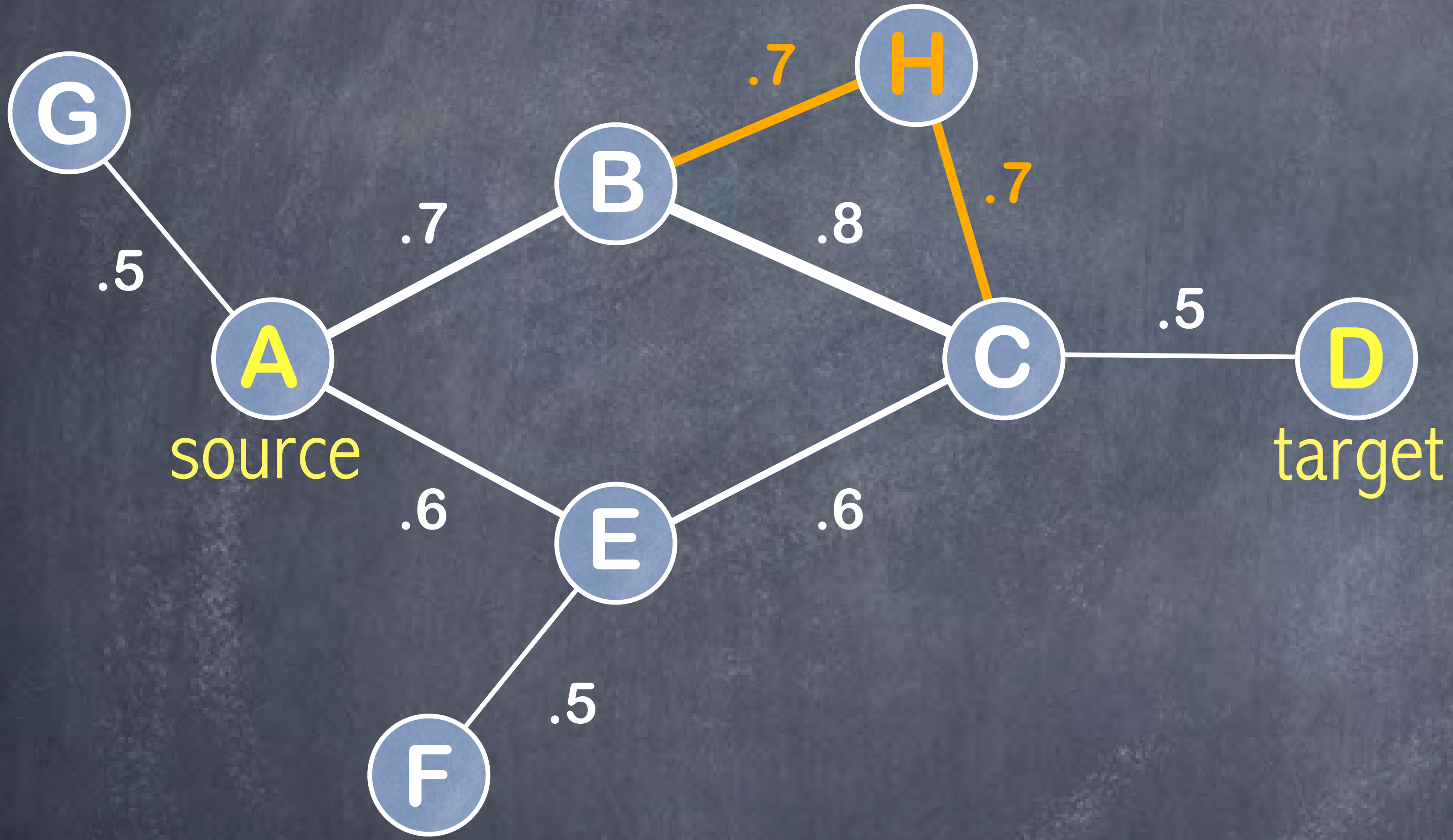
$\prod_1$={A,B,C,D} SI($\prod_1$) = 2.85 bits



generalized k-search-information. Example B

$\prod_1$={A,B,C,D} SI($\prod_1$) = 2.85 bits

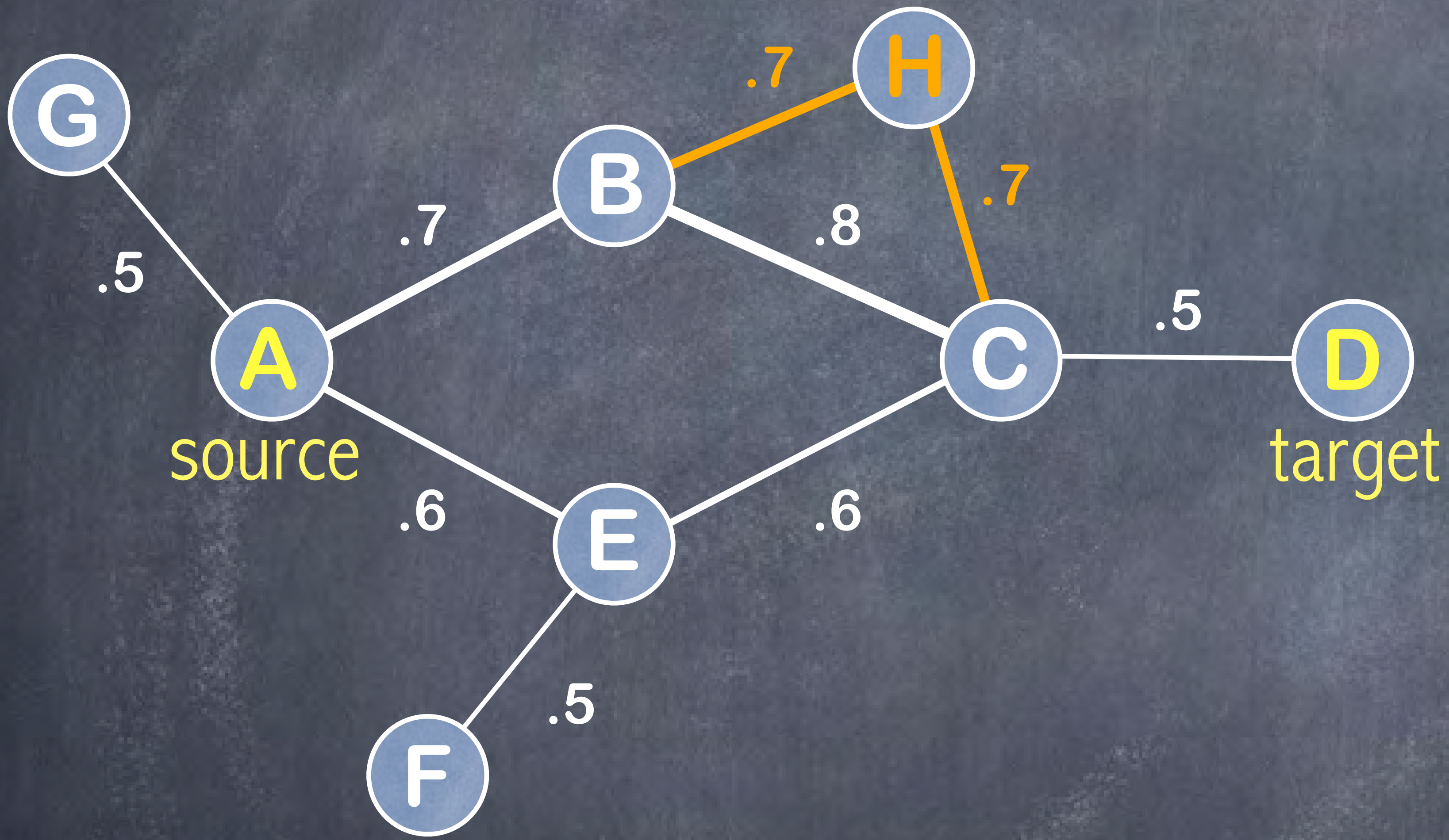
$\prod_2$={A,E,C,D}



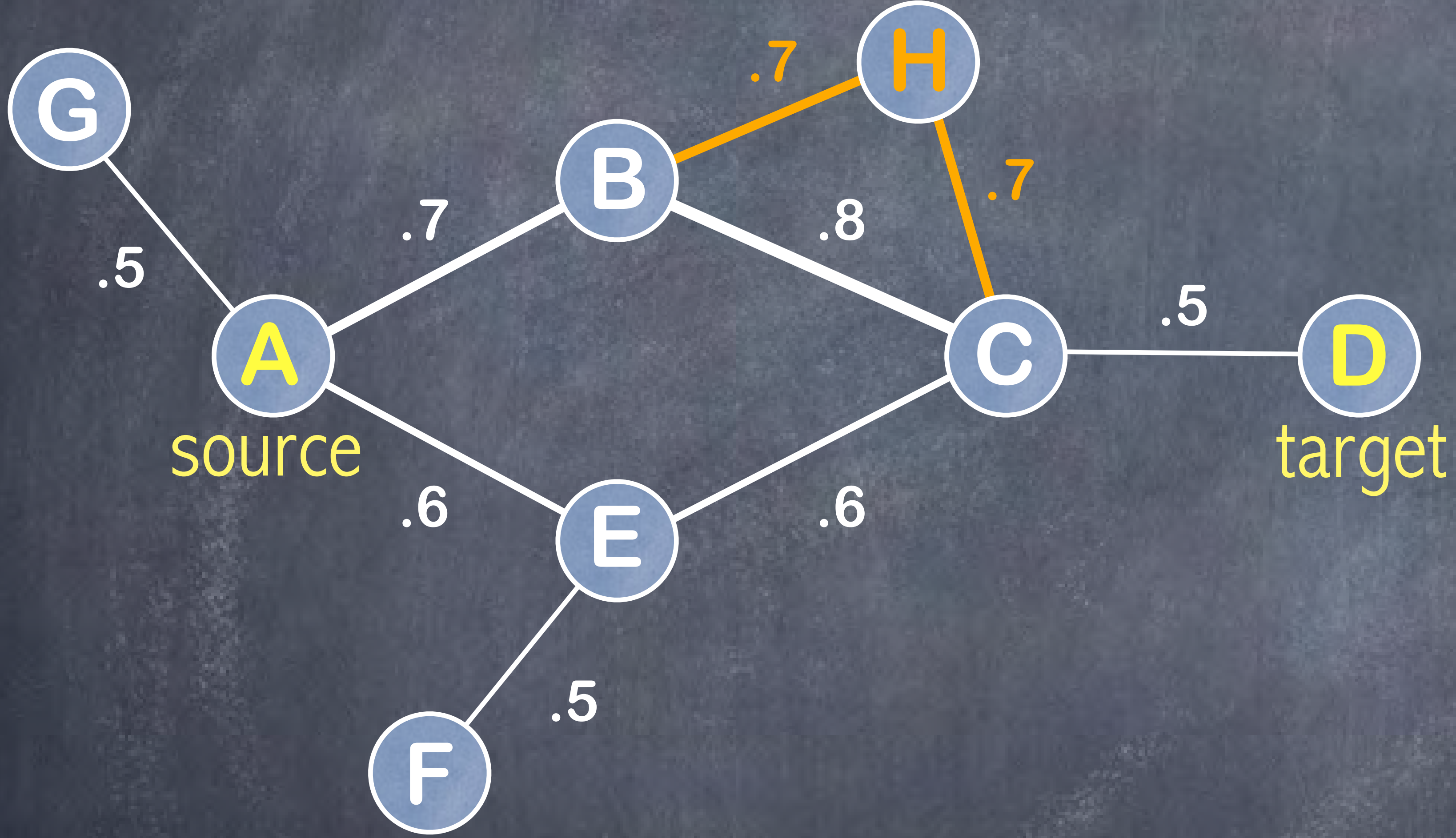
generalized k-search-information. Example B

$\Pi_1=\{A,B,C,D\}$ $SI(\Pi_1) =$ 2.85 bits

$\Pi_2=\{A,E,C,D\}$ $SI(\Pi_2) =$ 3.09 bits



generalized k-search-information. Example B

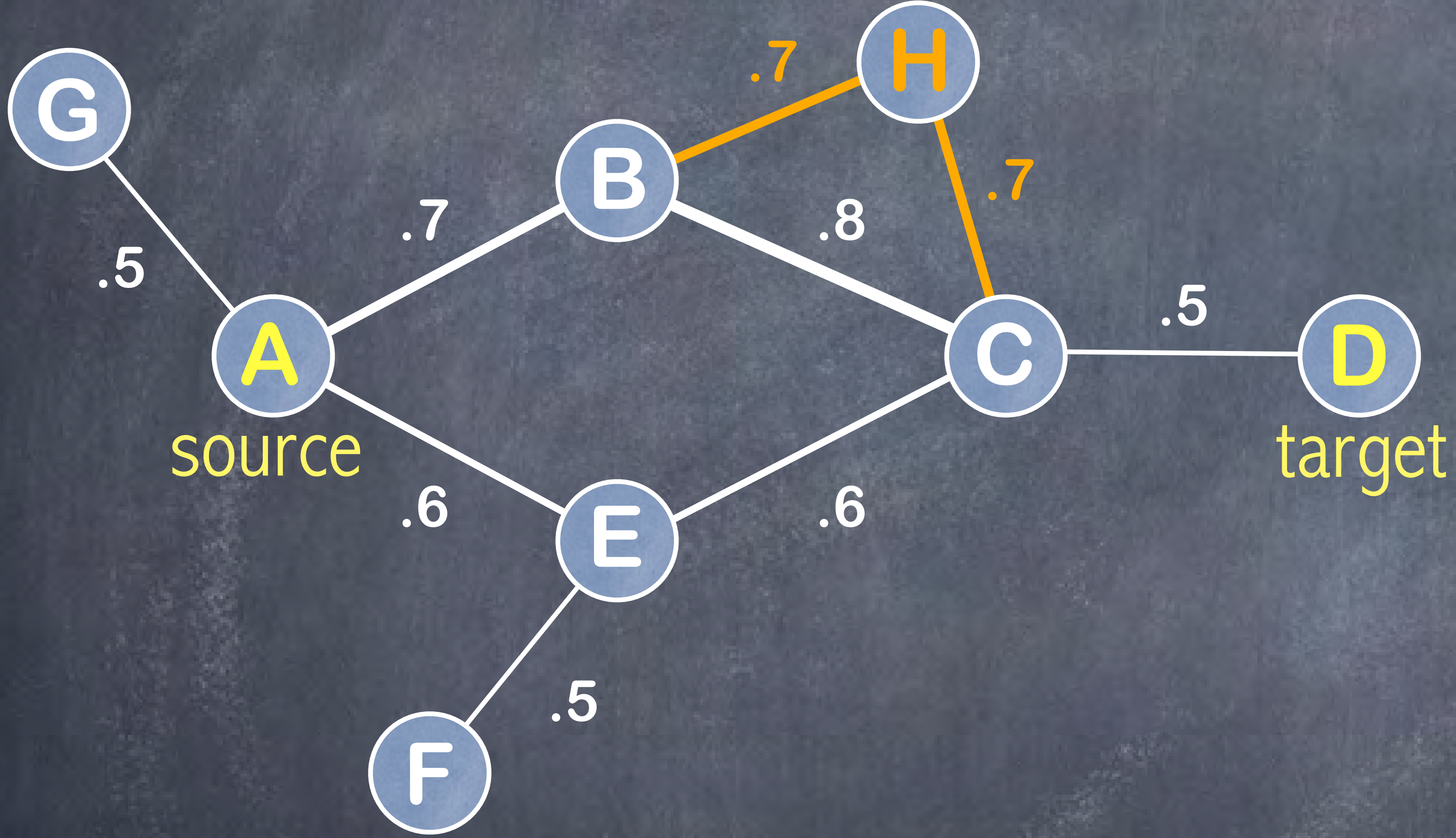


$\Pi_1=\{A,B,C,D\}$ $SI(\Pi_1) = 2.85$ bits

$\Pi_2=\{A,E,C,D\}$ $SI(\Pi_2) = 3.09$ bits

$\Pi_3=\{A,B,H,C,D\}$

generalized k-search-information. Example B

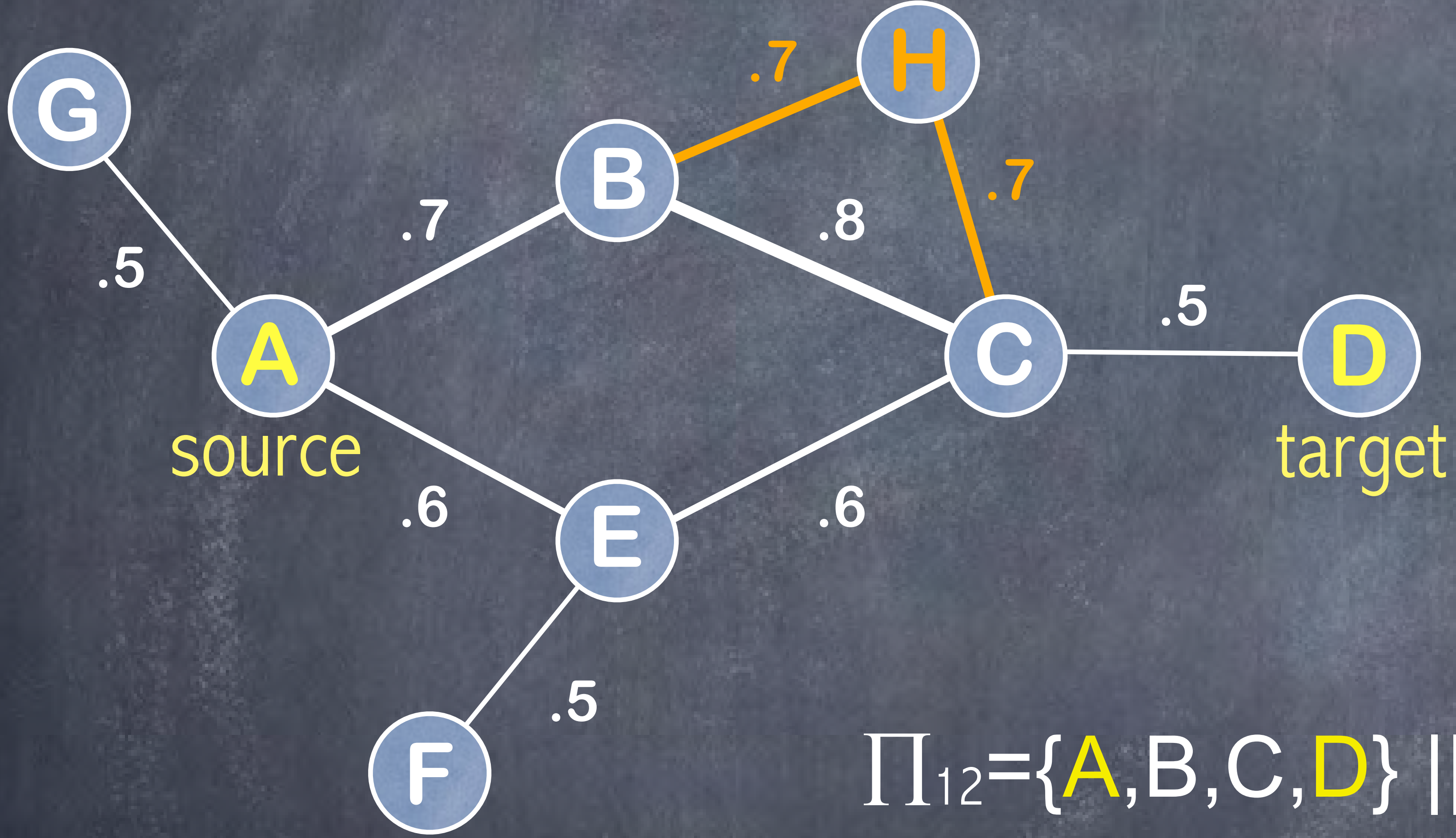


$\prod_1=\{A,B,C,D\}$ $SI(\prod_1) = 2.85$ bits

$\prod_2=\{A,E,C,D\}$ $SI(\prod_2) = 3.09$ bits

$\prod_3=\{A,B,H,C,D\}$ $SI(\prod_3) = 3.04$ bits

generalized k-search-information. Example B



$\prod_1$={A,B,C,D}   SI($\prod_1$) = 2.85 bits

$\prod_2$={A,E,C,D}   SI($\prod_2$) = 3.09 bits

$\prod_3$={A,B,H,C,D}   SI($\prod_3$) = 3.04 bits

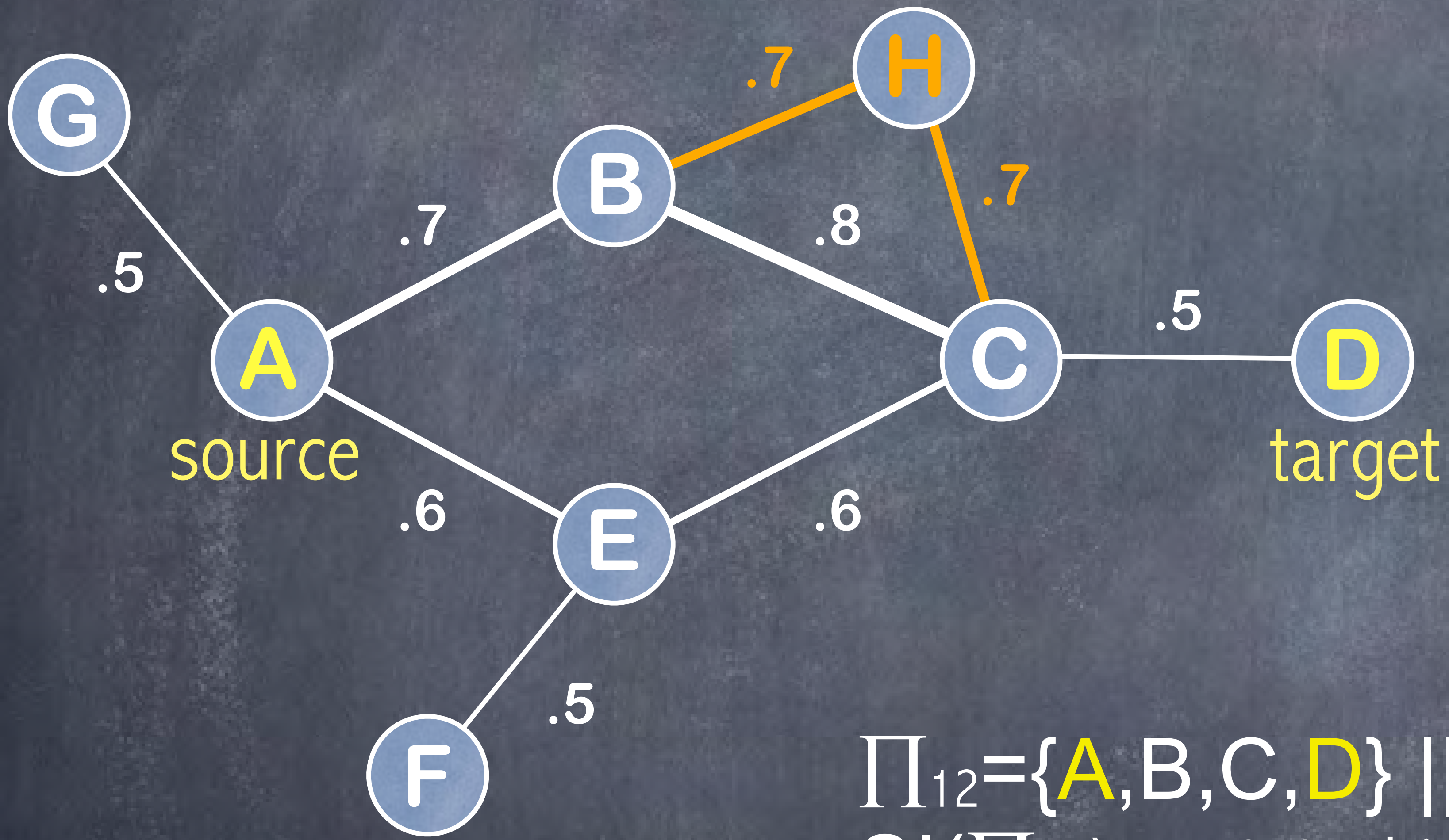
$\prod_{12}$={A,B,C,D} || {A,E,C,D}

generalized k-search-information. Example B

$\prod_1=\{A,B,C,D\}$ $SI(\prod_1) = 2.85$ bits

$\prod_2=\{A,E,C,D\}$ $SI(\prod_2) = 3.09$ bits

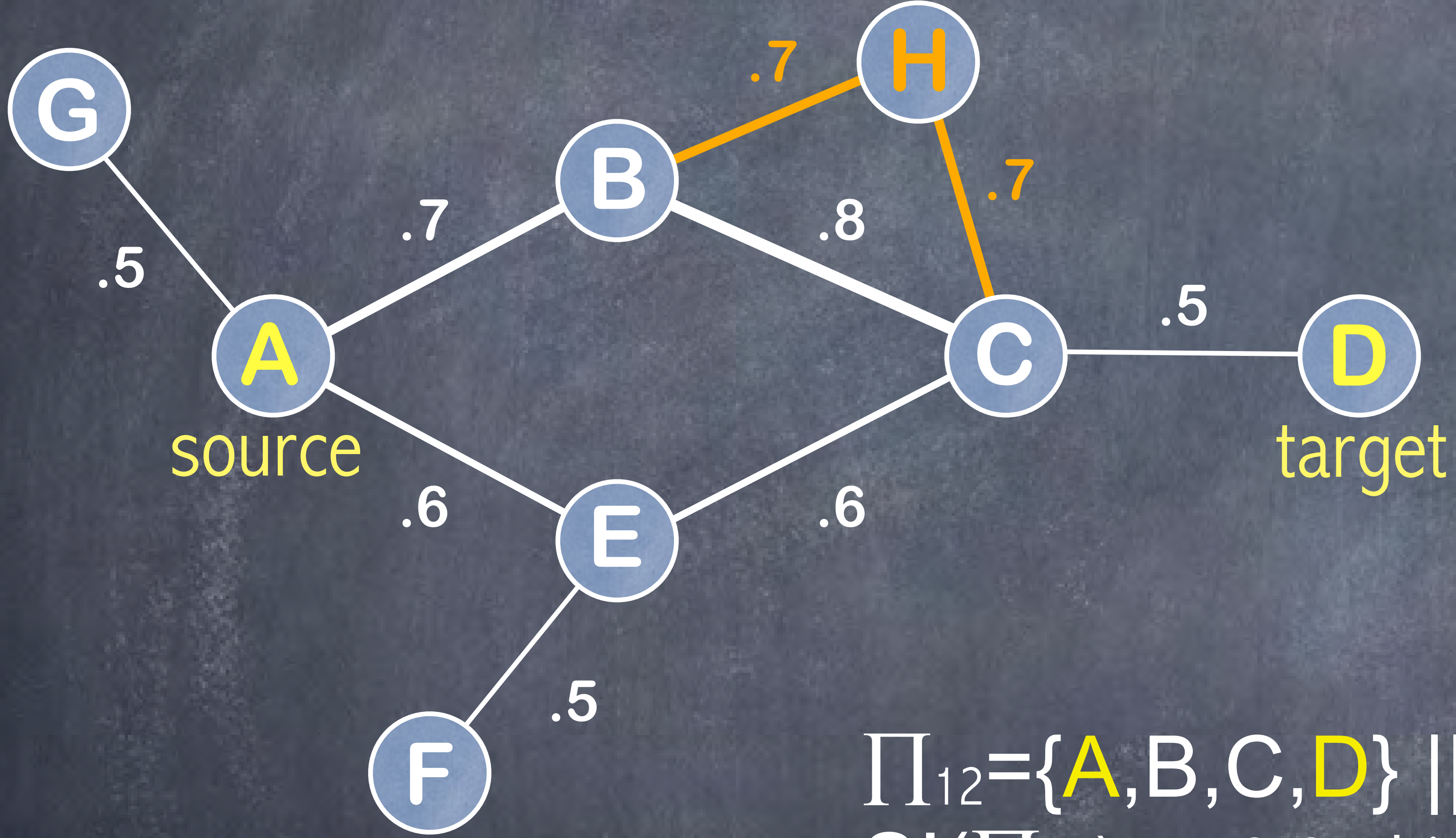
$\prod_3=\{A,B,H,C,D\}$ $SI(\prod_3) = 3.04$ bits



$\prod_{12}=\{A,B,C,D\} \,||\, \{A,E,C,D\}$

$SI(\prod_{12}) = 2.27$ bits

generalized k-search-information. Example B



$\prod_1$={A,B,C,D} $SI(\prod_1)$ = 2.85 bits

$\prod_2$={A,E,C,D} $SI(\prod_2)$ = 3.09 bits

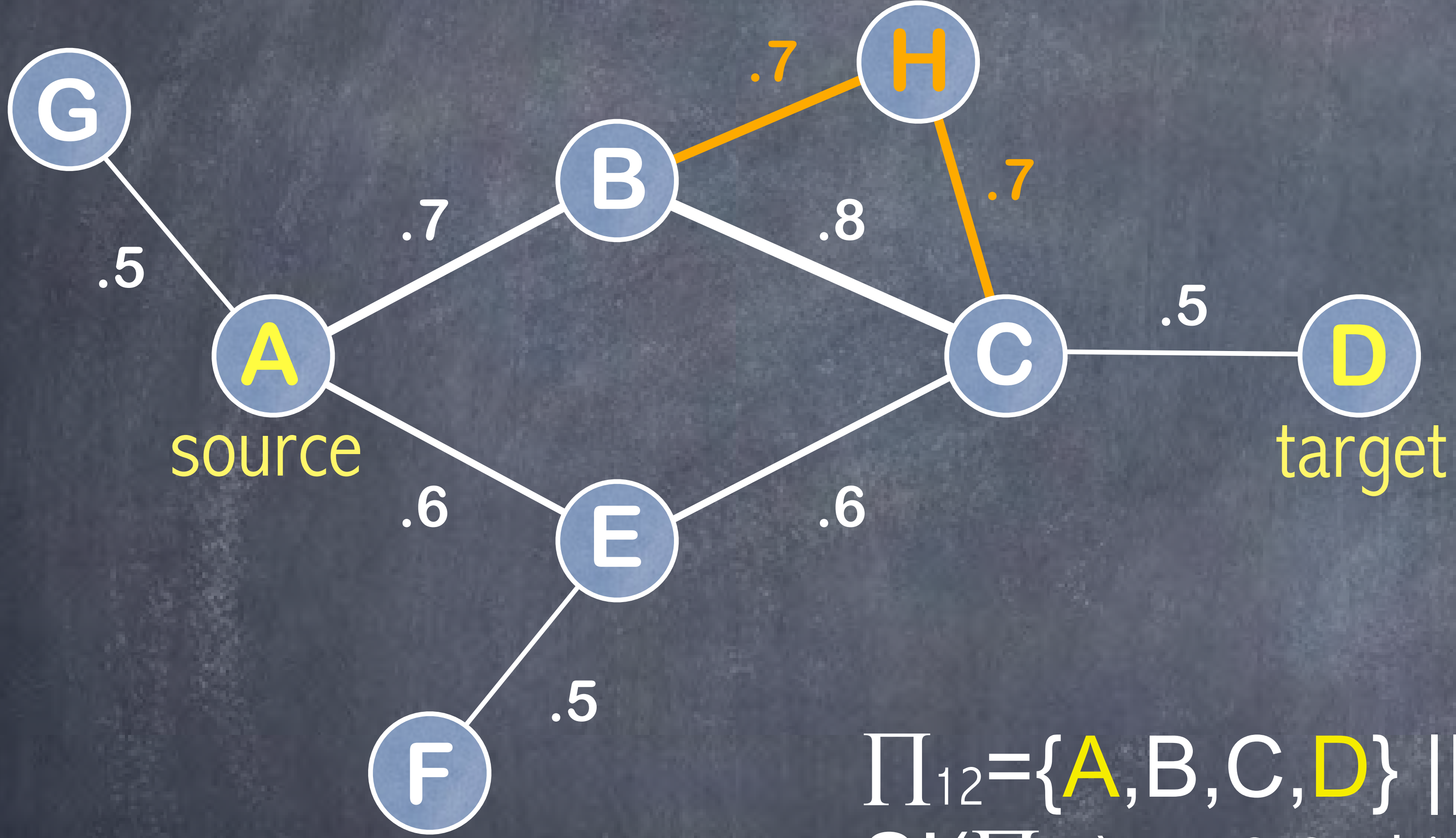
$\prod_3$={A,B,H,C,D} $SI(\prod_3)$ = 3.04 bits

$\prod_{12}$={A,B,C,D} || {A,E,C,D}

$SI(\prod_{12})$ = 2.27 bits

$\prod_{123}$={A,B,C,D} || {A,E,C,D} || {A,B,H,C,D}

generalized k-search-information. Example B



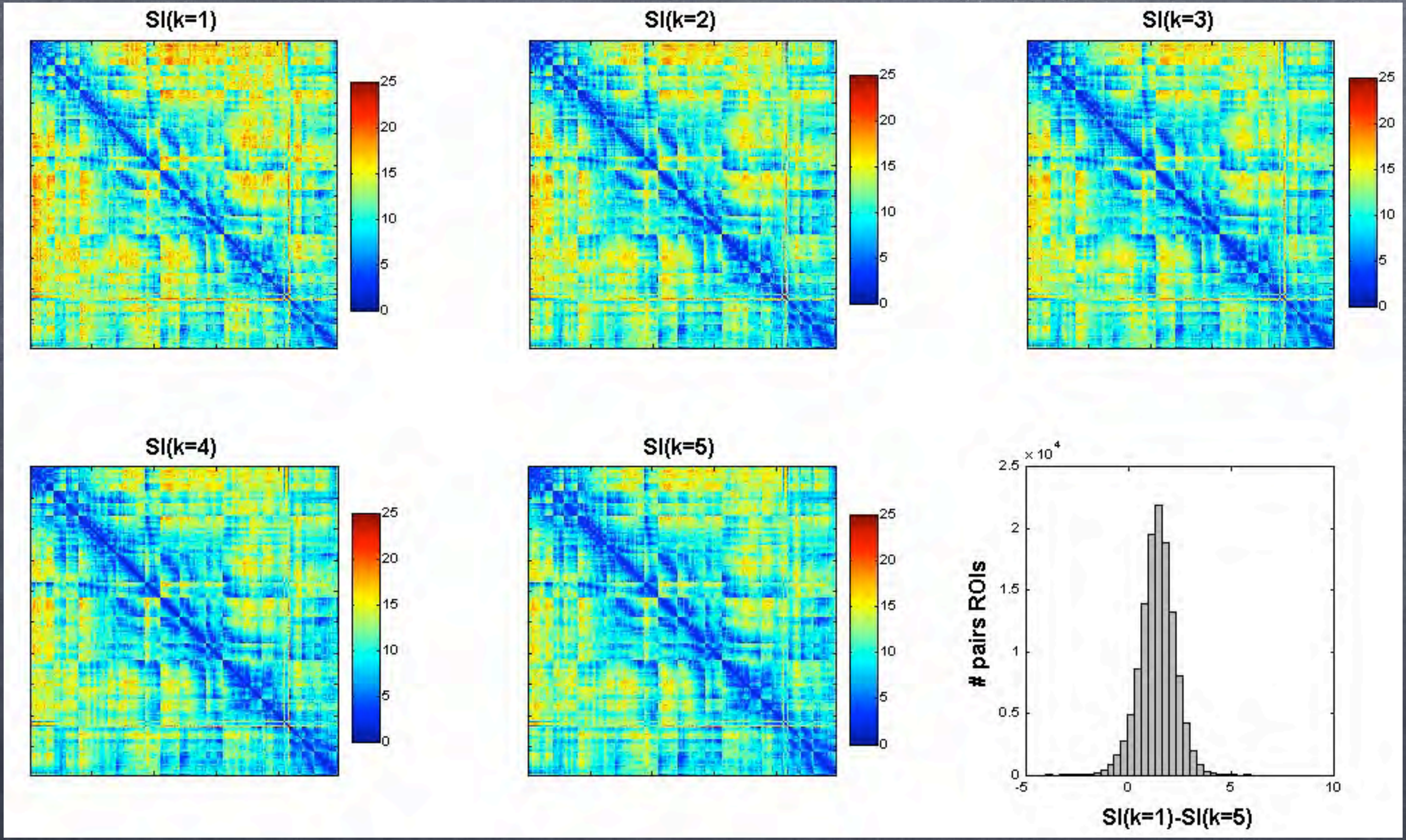
$\prod_1=\{A,B,C,D\}$ $SI(\prod_1) = 2.85$ bits

$\prod_2=\{A,E,C,D\}$ $SI(\prod_2) = 3.09$ bits

$\prod_3=\{A,B,H,C,D\}$ $SI(\prod_3) = 3.04$ bits

$\prod_{12}=\{A,B,C,D\} \,||\, \{A,E,C,D\}$
$SI(\prod_{12}) = 2.27$ bits

$\prod_{123}=\{A,B,C,D\} \,||\, \{A,E,C,D\} \,||\, \{A,B,H,C,D\}$
$SI(\prod_{123}) = 1.97$ bits

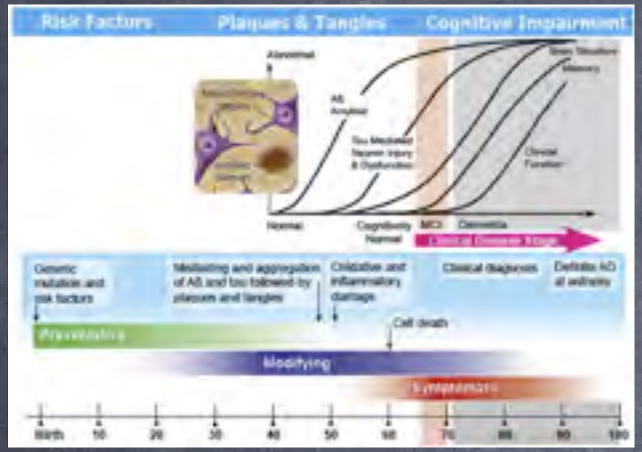


unpublished

generalized k-search-information

- Framework that permits to introduce the concept of information along the first k-shortest-paths within a system
- It represents a generalization on integration of information (by allowing local segregation).
- It permits to evaluate how a system may operate under different amounts of information.
- Challenging questions:
    - Is resting-state ‘parsimonious’ with respect to k-search-information?
    - Are task-specific FCs related to particular k-shortest-paths?
    - Are there k-values for which SI is particularly affected in neurodegeneration?

Brain network disruption in neurodegeneration



- What are the network features and parcellation resolution that better characterize WM disruption in neurodegeneration?
- Mapping episodic memory into connectome neurodegeneration
- Impaired relationship between SC and FC in neurodegeneration
- Approaches based on multiplex networks

neurodegeneration: a disconnection syndrome in “**the**” human connectome?

literature summary

resolution of GM parcellation

definition of weights

article	diagnostics	# subjects	#regions	parcellation	subcortical	connectome
Daianu et al. 2013	HC,eMCI,lMCI,AD	111	68	Freesurfer	no	relative #fibers
Reijmer et al. 2013	HC,eAD	30	90	AAL	yes	relative #fibers
Bai et al. 2012	HC,aMCI,RGD	103	90	AAL	yes	#fibers
Lo et al. 2010	HC,AD	55	78	AAL	no	#fibers * FA

Evidence of white matter disruption in MCI

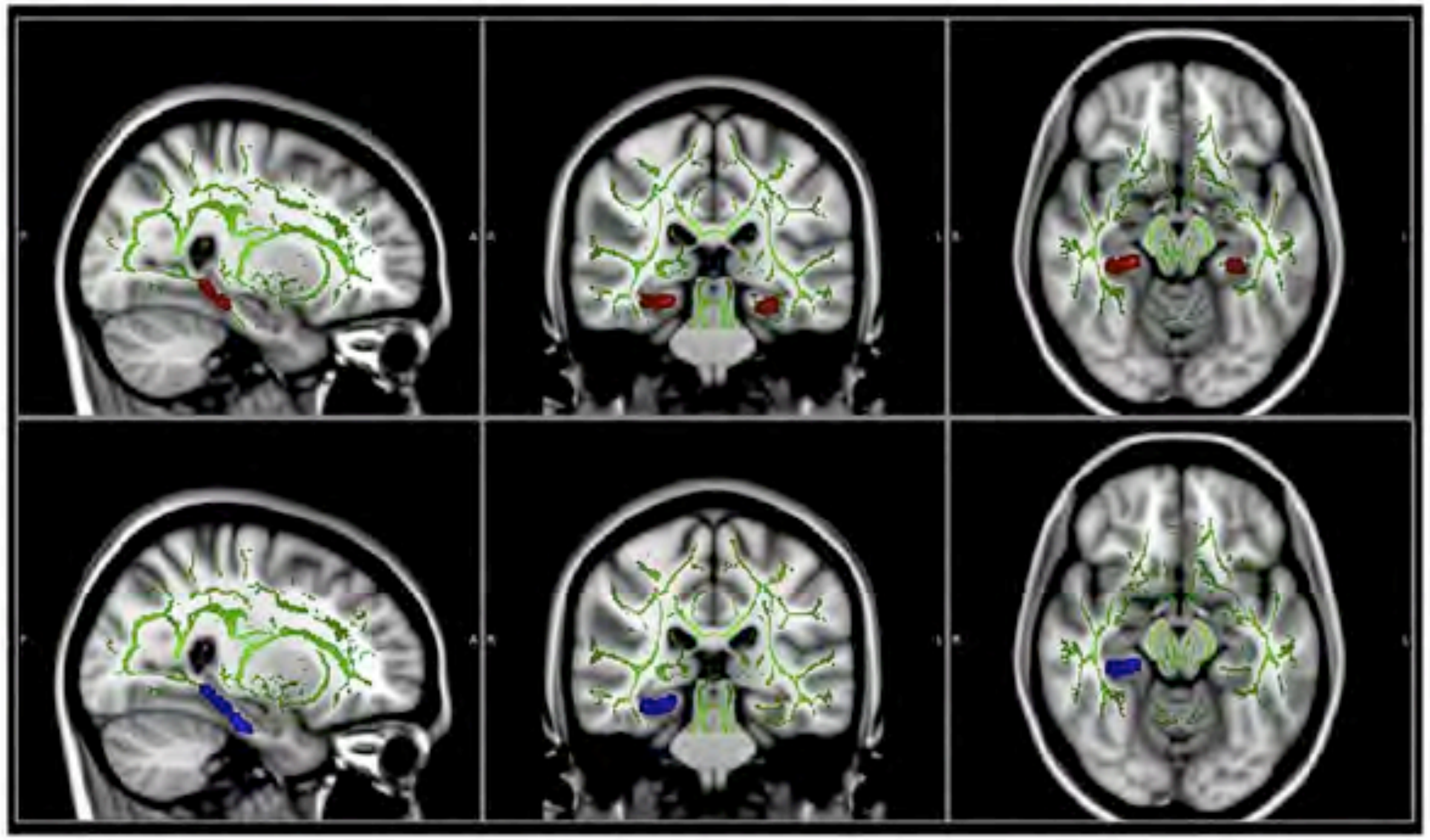
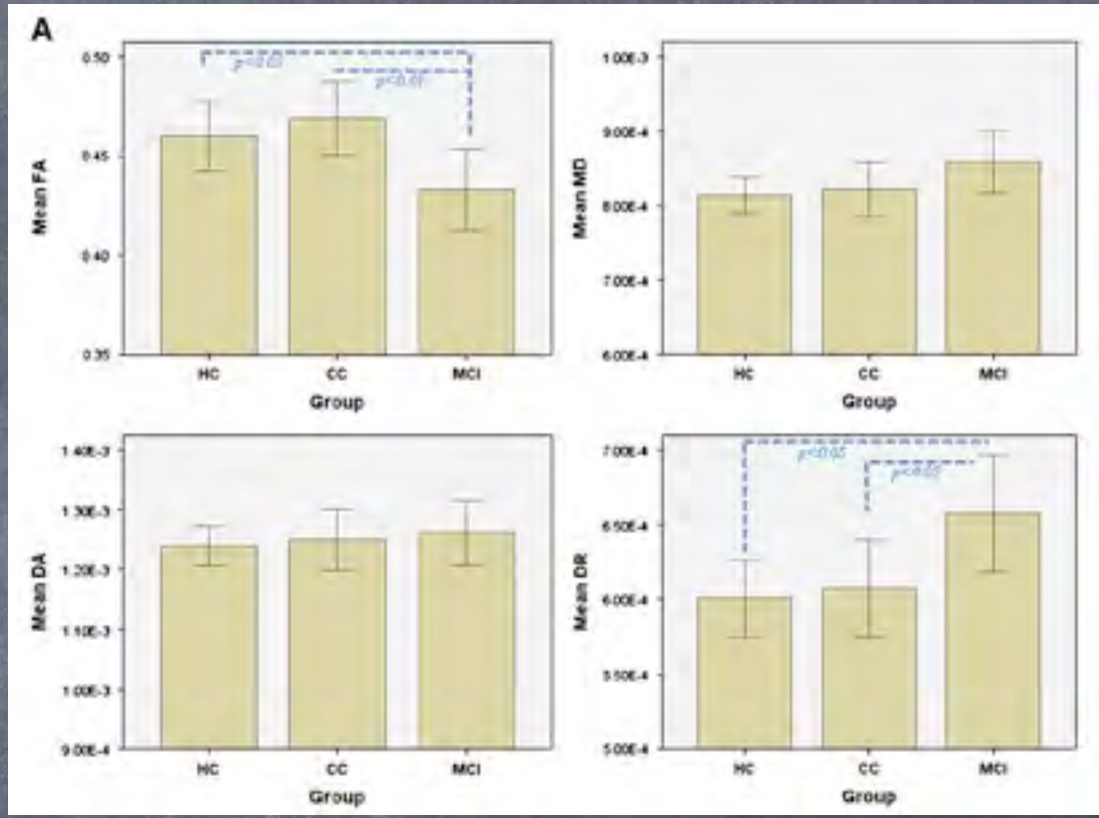


Fig. 1. Voxel-wise DTI comparison using tract-based spatial statistics analysis. The brain images showing underlying standard Montreal Neurological Institute (MNI) atlas MNI152 1-mm brain template and white matter skeleton derived from tract-based spatial statistics (TBSS) analysis (shown in green). Red color indicates tracts with reduced fractional anisotropy (FA) in bilateral parahippocampal white matter in patients with MCI vs. controls; Blue color indicates region with increased radial diffusivity (DR) in right parahippocampal white matter in MCI vs. controls. Only clusters surviving correction for multiple comparisons of voxel-wise whole brain analysis are shown on brain images ($p<0.01$). Statistical maps were dilated from the TBSS skeleton for visualization purposes.

Wang et al. (2012)

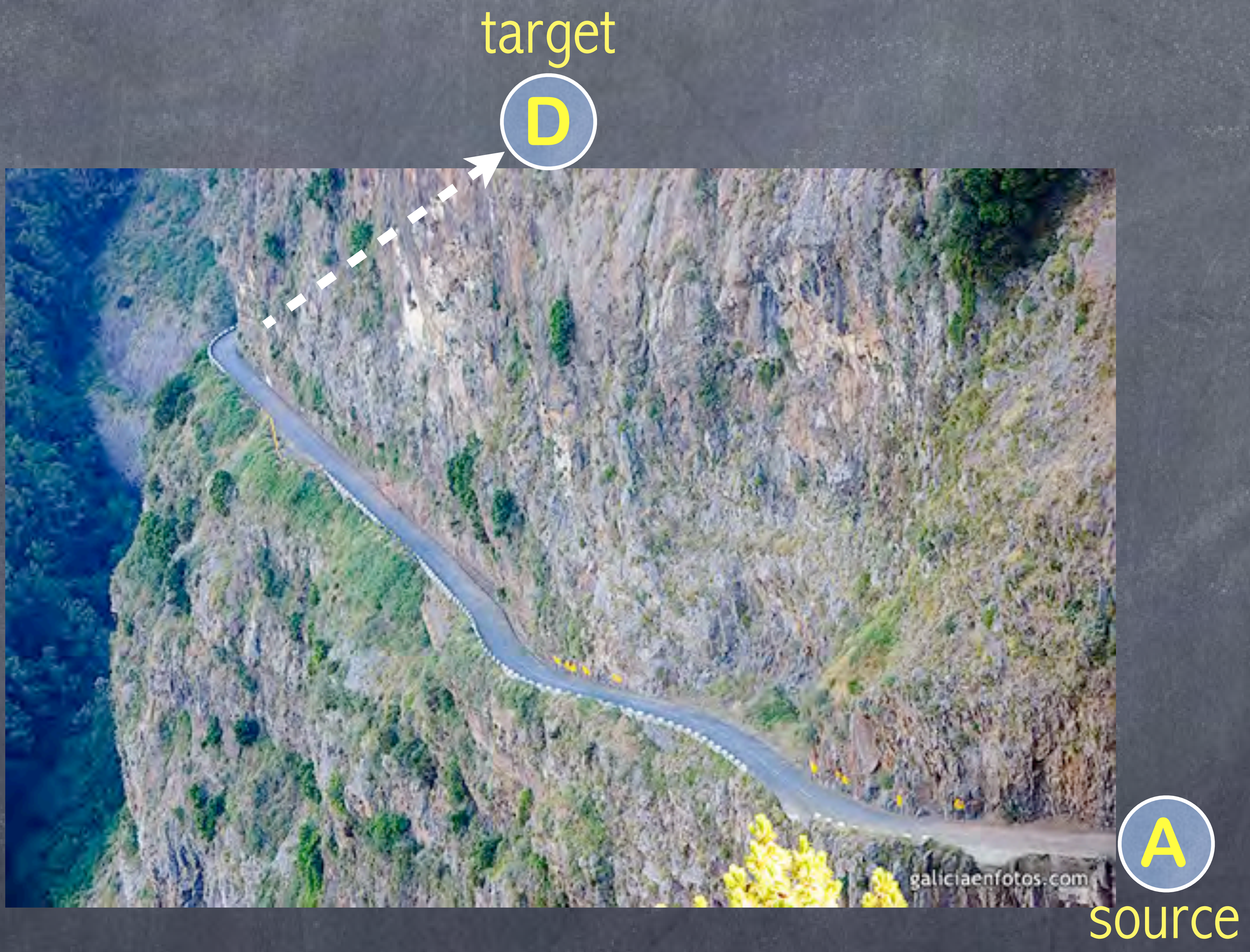


Wang et al. (2012)

Reduced FA in parahippocampal WM (bilateral)

Increased RD in parahippocampal WM (right hemisphere)

interpretations on fractional anisotropy along fibers



interpretations on fractional anisotropy along fibers

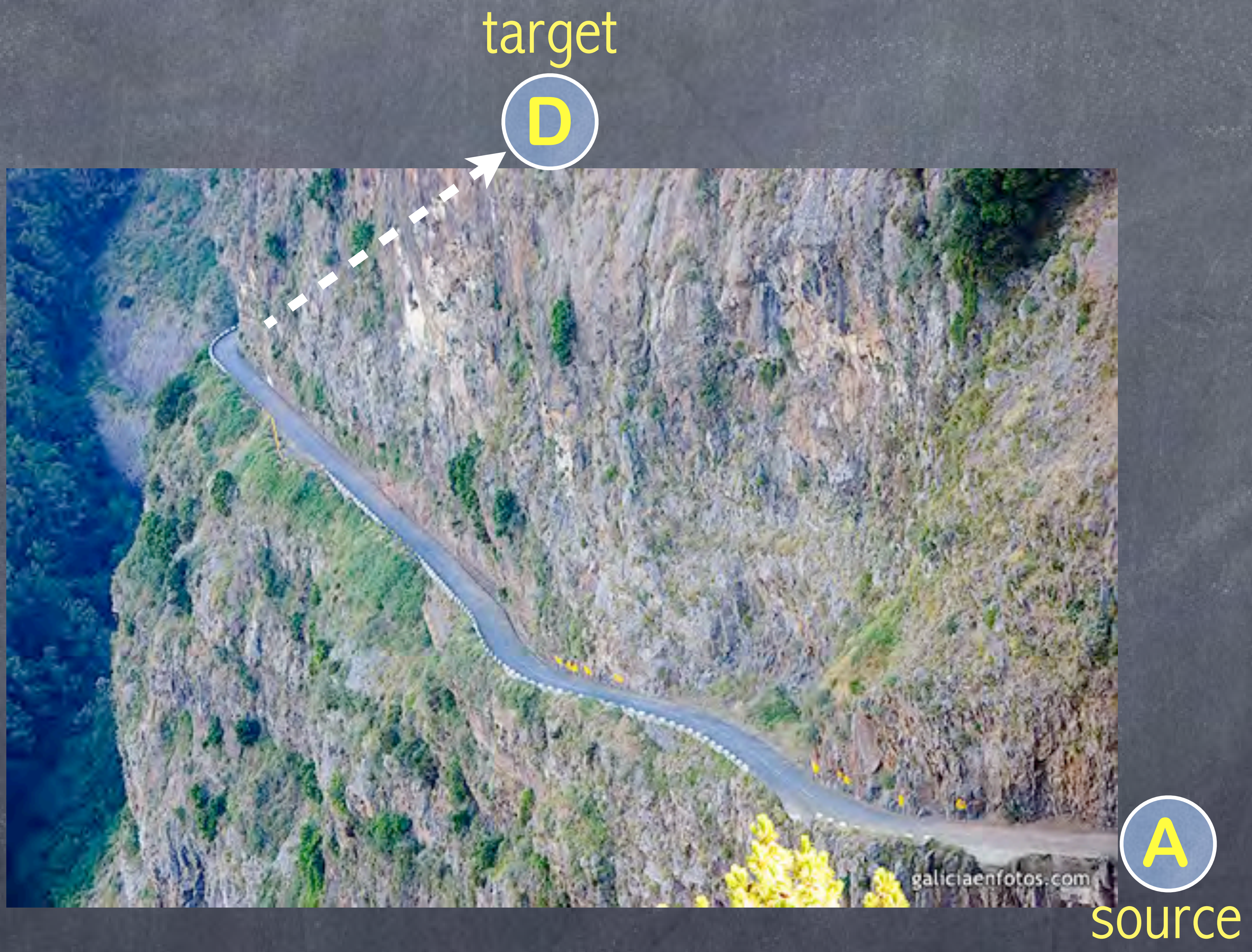
target

D

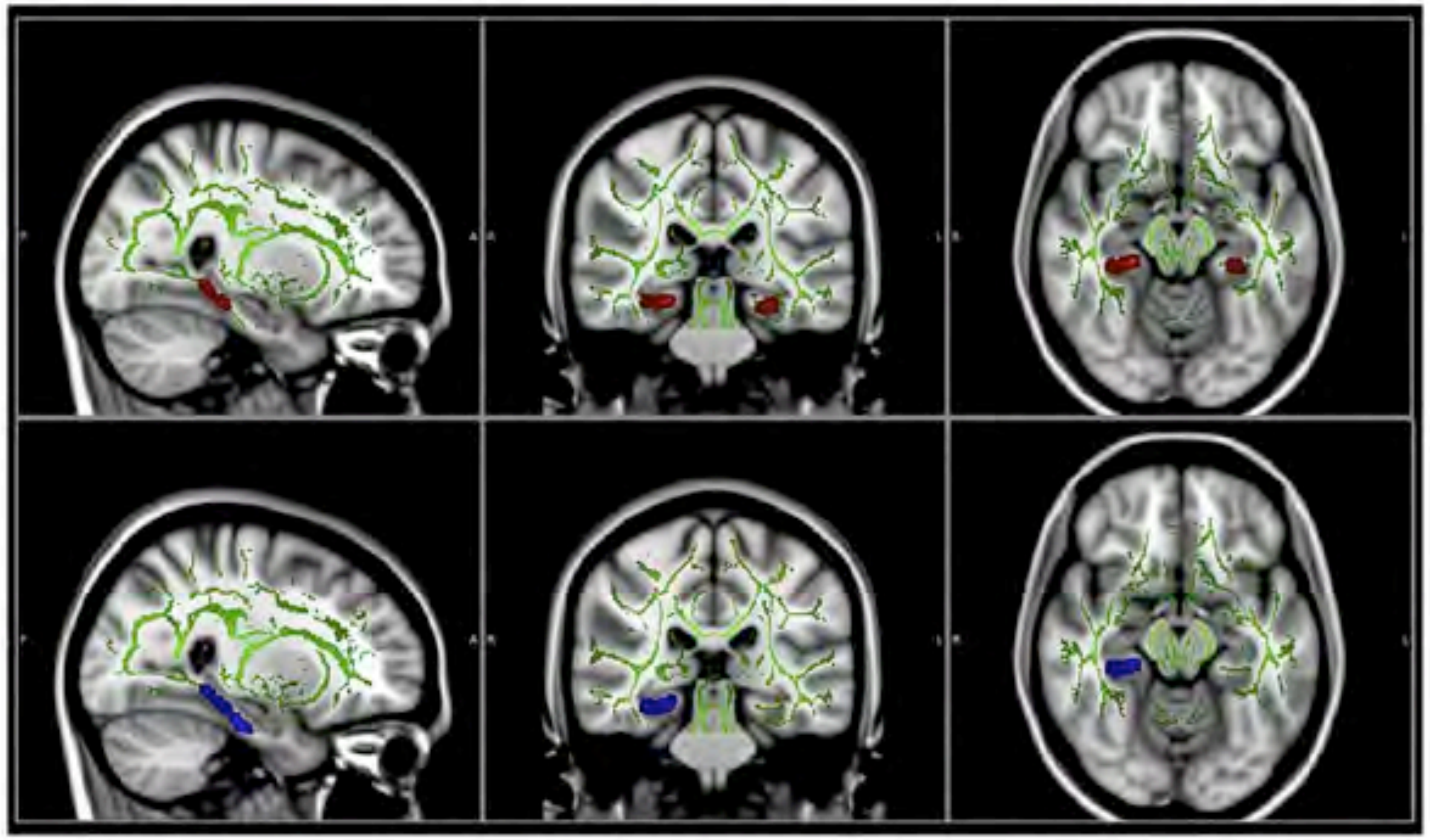
A

source

interpretations on fractional anisotropy along fibers



Evidence of white matter disruption in MCI



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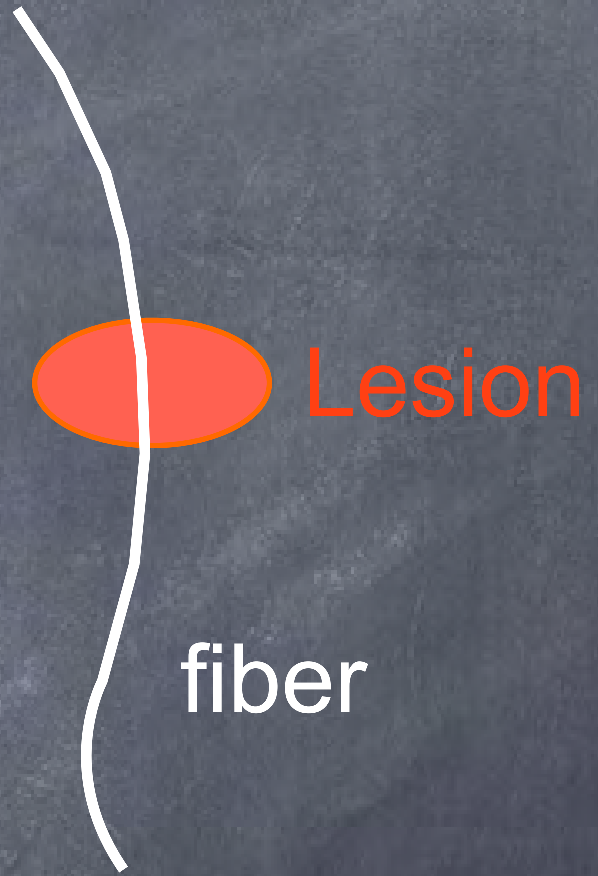
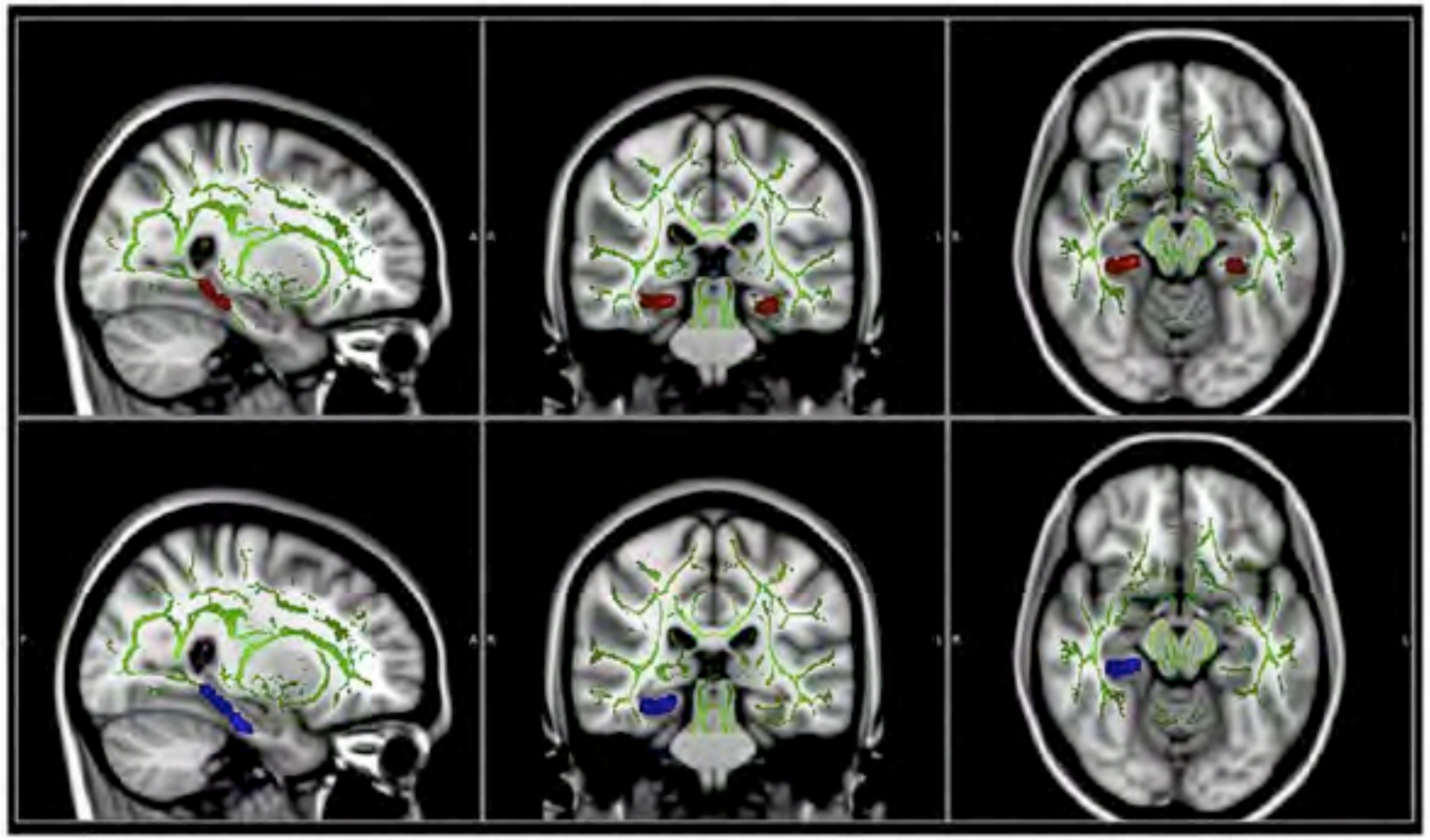


Reduced FA in parahippocampal WM (bilateral)

Increased RD in parahippocampal WM (right hemisphere)

Evidence of white matter disruption in MCI



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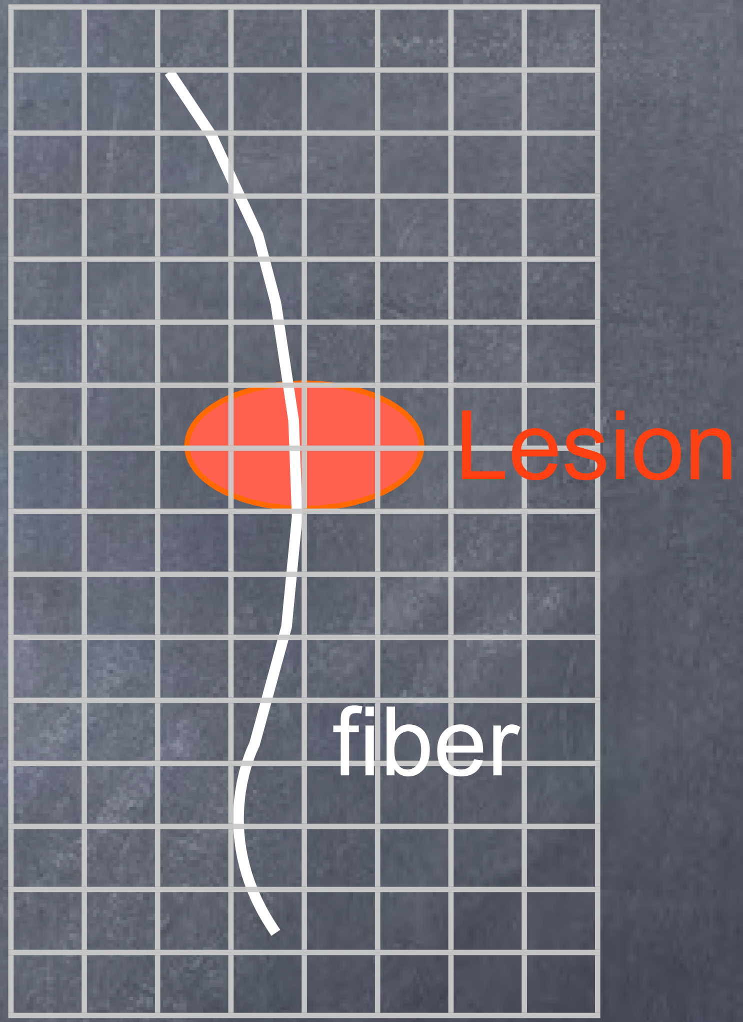
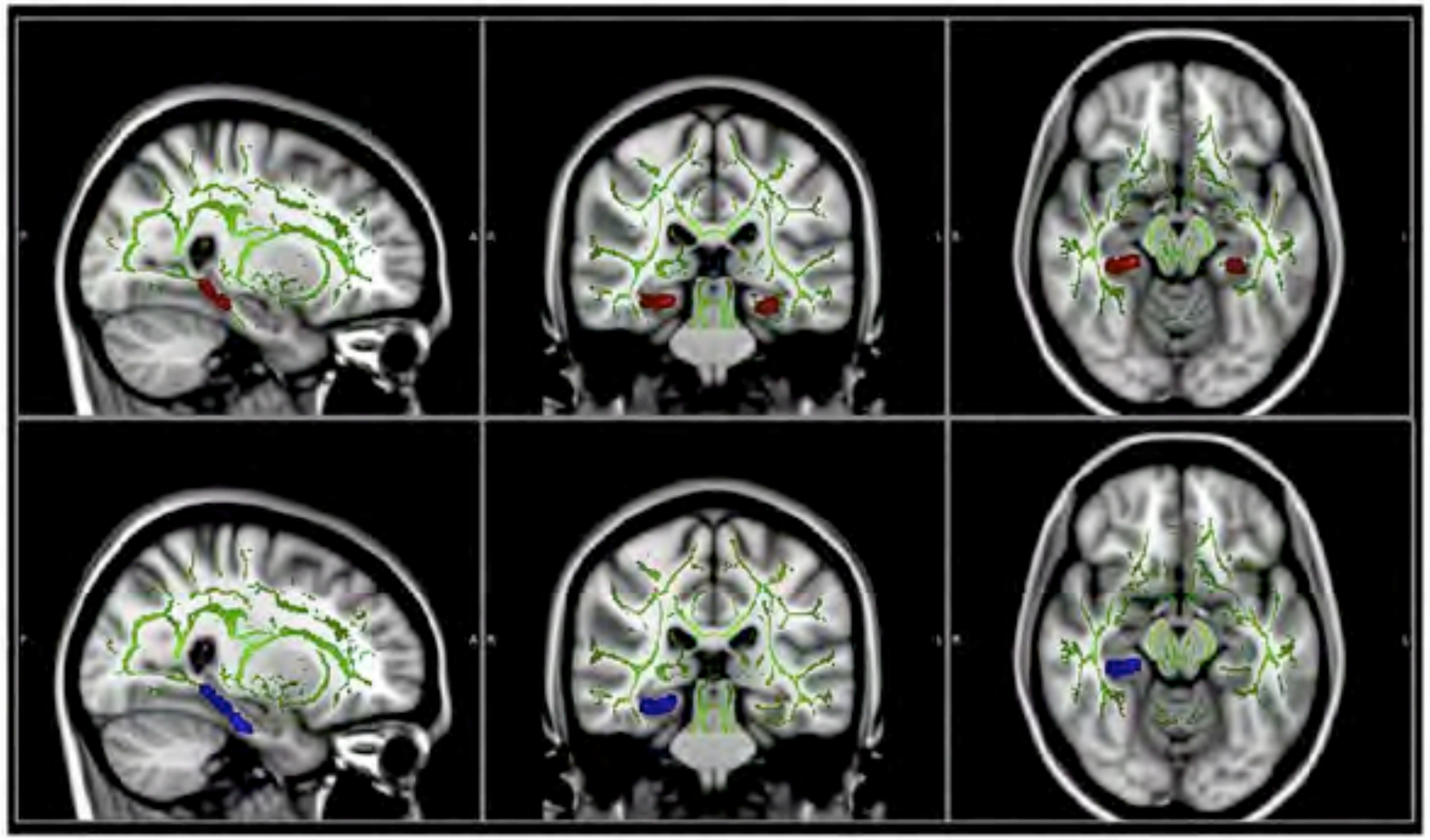


Wang et al. (2012)

Reduced FA in parahippocampal WM (bilateral)

Increased RD in parahippocampal WM (right hemisphere)

Evidence of white matter disruption in MCI



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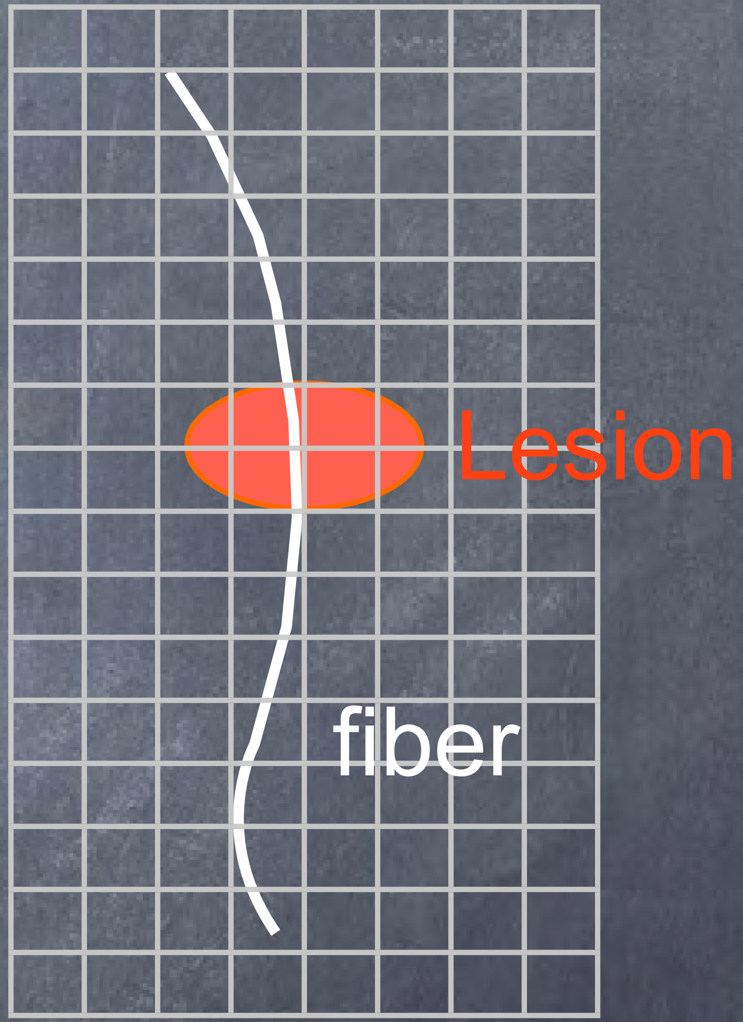

2 out of 15 voxels go through the lesion

Reduced FA in parahippocampal WM (bilateral)

Increased RD in parahippocampal WM (right hemisphere)

thank you for your attention

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