A physiological connectome of the human brain based on intracranial electrical stimulation in patients with epilepsy

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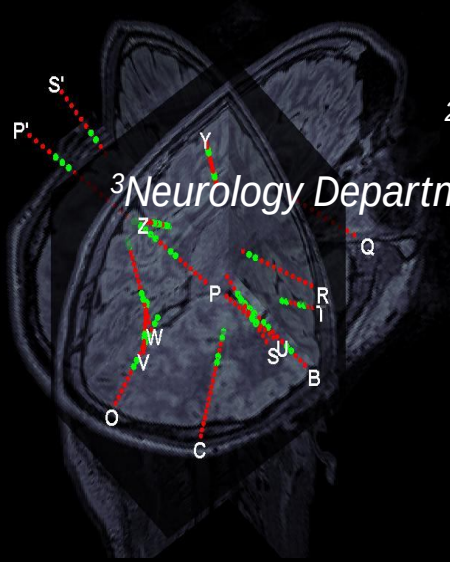

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Therapeutic Options in Drug Resistant Epilepsy
Bucharest, Novotel Hotel, 23-25th of April 2015

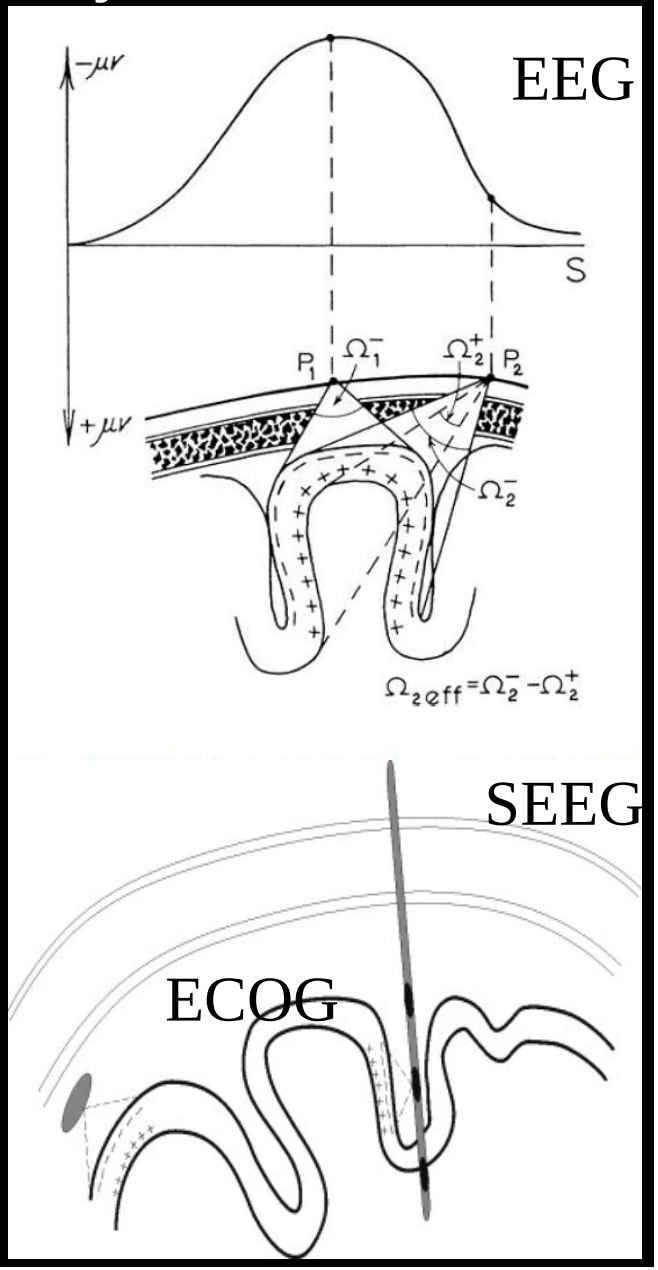
Presentation Outline:

- Presurgical evaluation using Stereoelectroencephalography (SEEG): The challenge of finding the epileptogenic network
- Single Pulse Electrical Stimulation (SPES)
- Physiological Connectome
- Conclusions

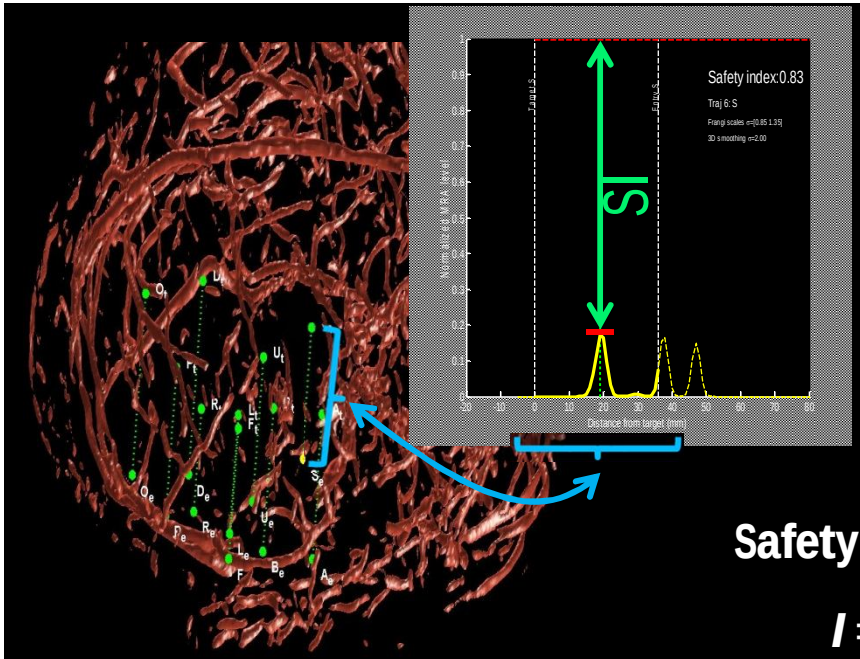
Stereoelectroencephalography (SEEG) is <u>the only</u> recording method that allows to record cerebral activity from the <u>mesial structures</u> !

SEEG

- Provides direct access to electrophysiological recordings in the seizure onset zone, when located in deep brain structures
- Allows delineation of the epileptogenic area in 3D volume
- Provides excellent time & space resolution
- HFOs and spikes are well evidenced



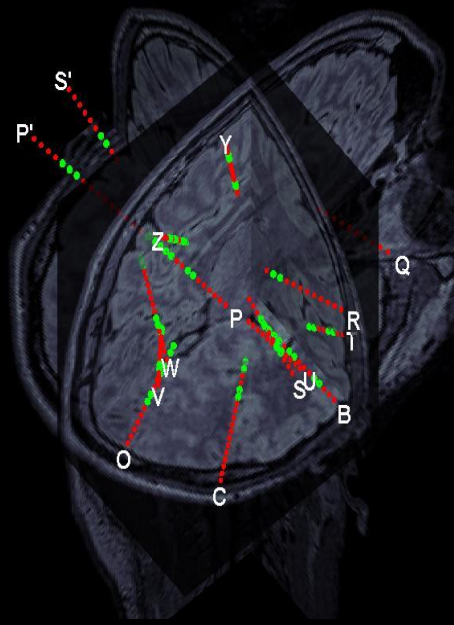
Trajectory Planning: Optimizing placement based on a vascular Safety Index



$$SI = 1 - \max(I(z))$$

Safety Index (SI) – quantifies proximity to the blood vessels

I = Maximum Intensity Projection on digital angiogram



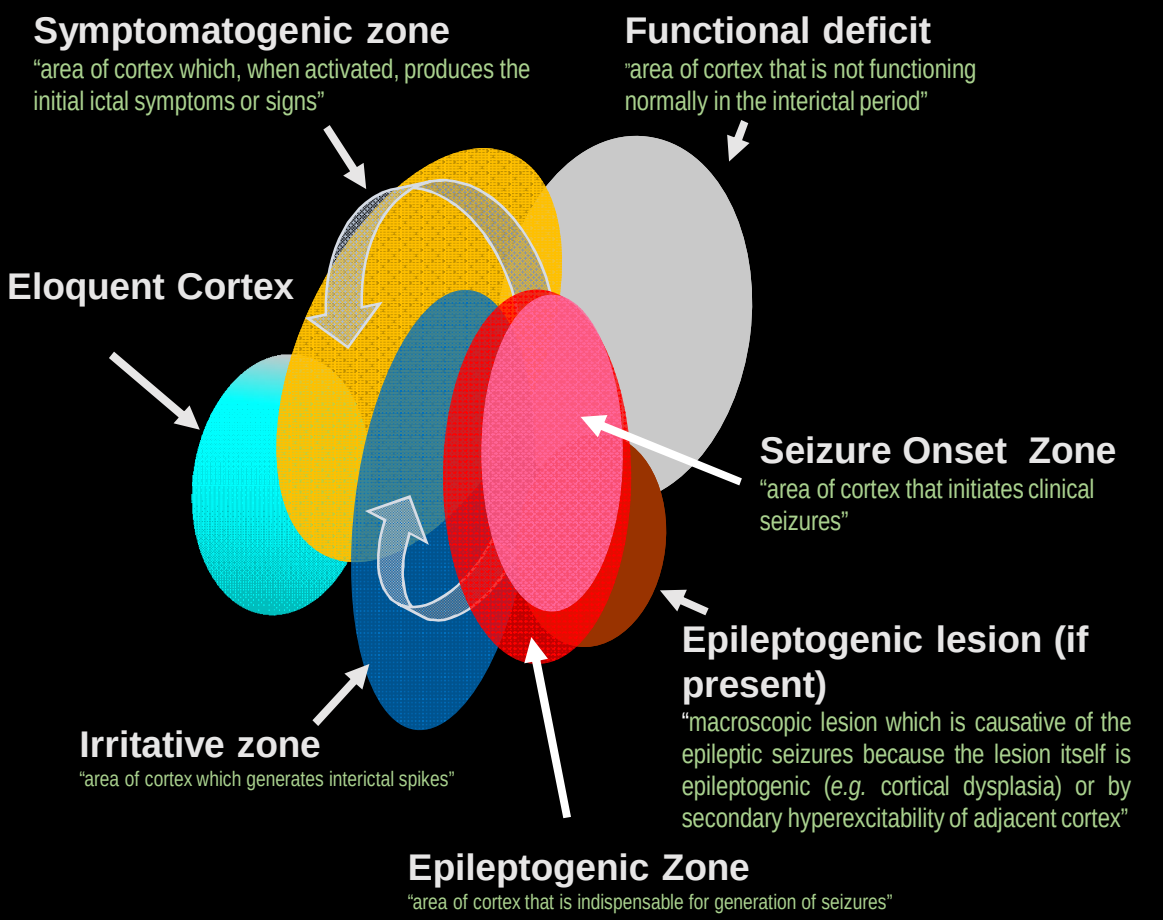
Balanescu et al., Stereotact Funct Neurosurg 2014;92(2):117-25

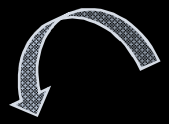
Epileptogenic network

Epileptogenic Zone:

"*the site of the beginning and of the primary organization of the epileptic seizures*" (Munari and Bancaud, 1987)

"*the minimum amount of cortex that must be resected (inactivated or completely disconnected) to produce seizure freedom*" (Luders et al., 2006)





Seizure Propagation

After Luders et al 2006 & Kahane, AES 2012

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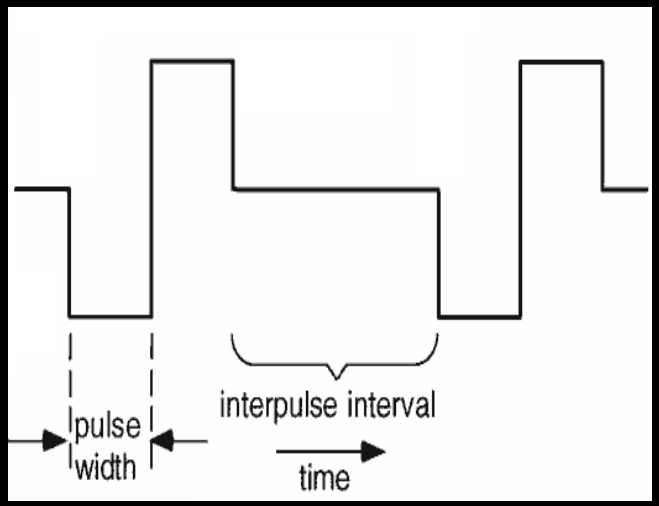
Single Pulse Electrical Stimulation (SPES)

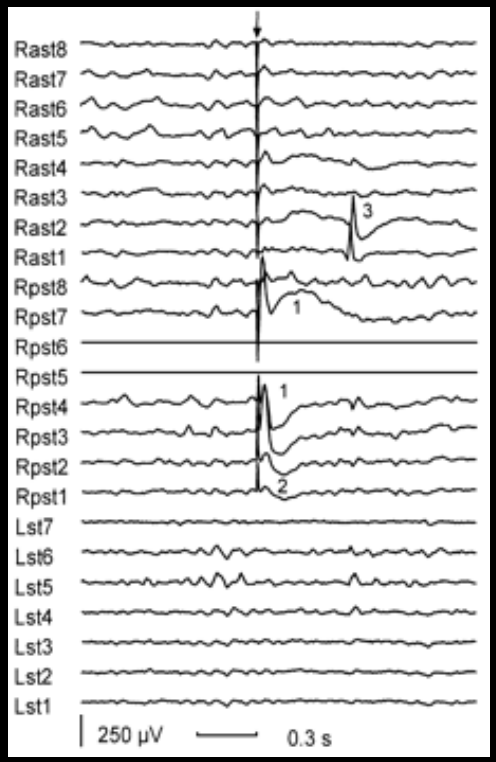
Brain (2002), **125,** 1709–1718

Responses to single pulse electrical stimulation identify epileptogenesis in the human brain *in vivo*

A. Valentín,[1] M. Anderson,[1] G. Alarcón,[1,2] J. J. García Seoane,[2] R. Selway,[1] C. D. Binnie[1] and C. E. Polkey[1]



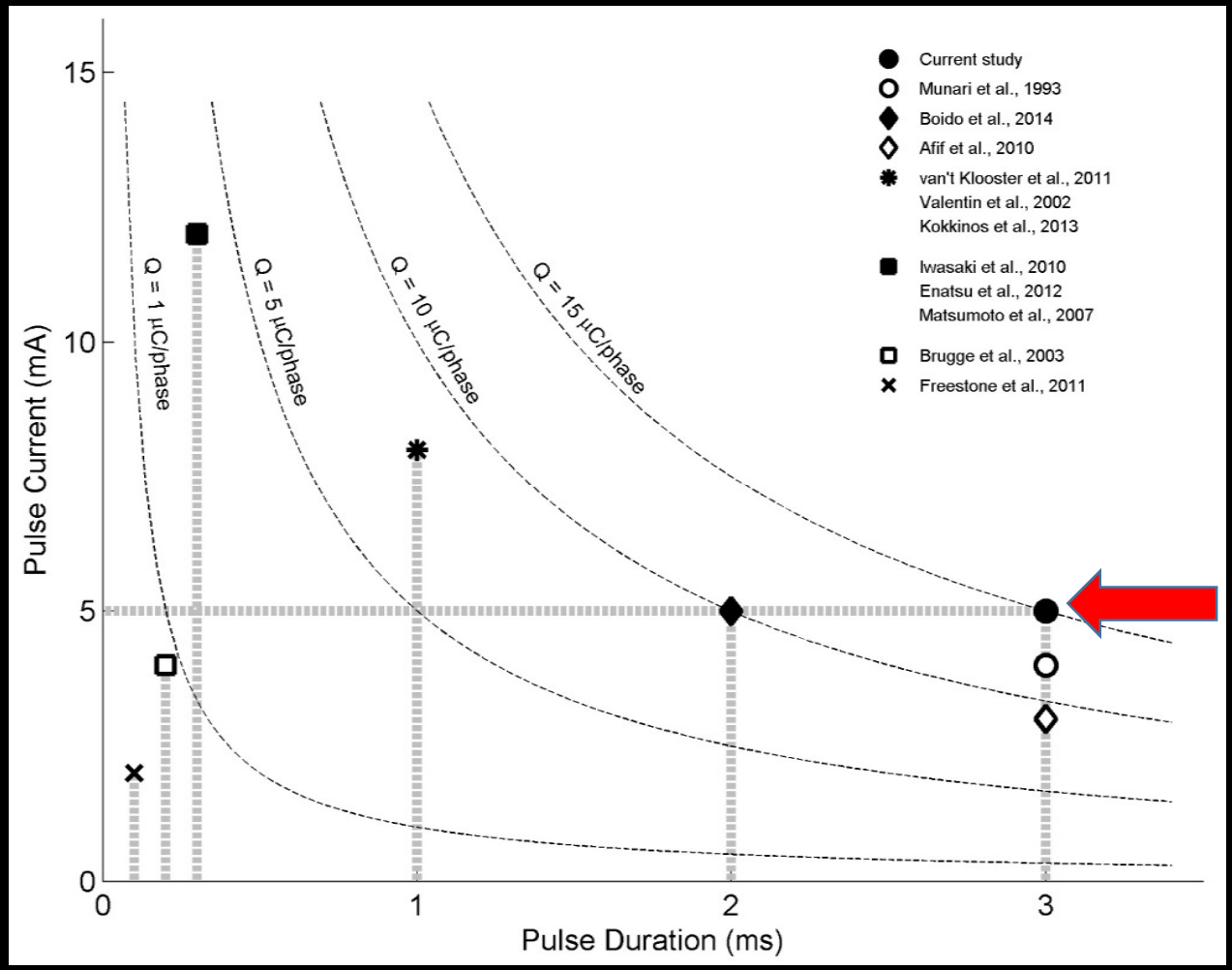
- Current intensity = 1 ÷ 8 mA
- Pulse width = 0.3 ÷ 1 ms
- Interpulse interval = 10 s



1 & 2 : Early Responses < 100 ms

3 : Delayed Responses > 100 ms

SPES Protocol Parameters – what to use?



Charge per phase is the underlying parameter that determines the magnitude of the intra-cranial EEG responses to single pulse electrical stimulation.

Donos et al, Clinical Neurophysiology 2015, doi: http://dx.doi.org/10.1016/j.clinph.2015.02.013

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Physiological Connectome

Connectivity types:

1. Structural connectivity – the neuroanatomical network (DTI, postmortem dissections)
2. Functional connectivity – nonlinear dynamics of neurons and neuronal populations result in patterns of statistical dependencies (fMRI, EEG, etc)
3. Effective connectivity – causal interactions (electrical brain stimulation, Granger causality)

STRUCTURAL + EFFECTIVE → PHYSIOLOGICAL CONNECTOME

Sporns O. Discovering the Human Connectome, MIT Press, 2012

Structural connectivity

NeuroImage 58 (2011) 91–99

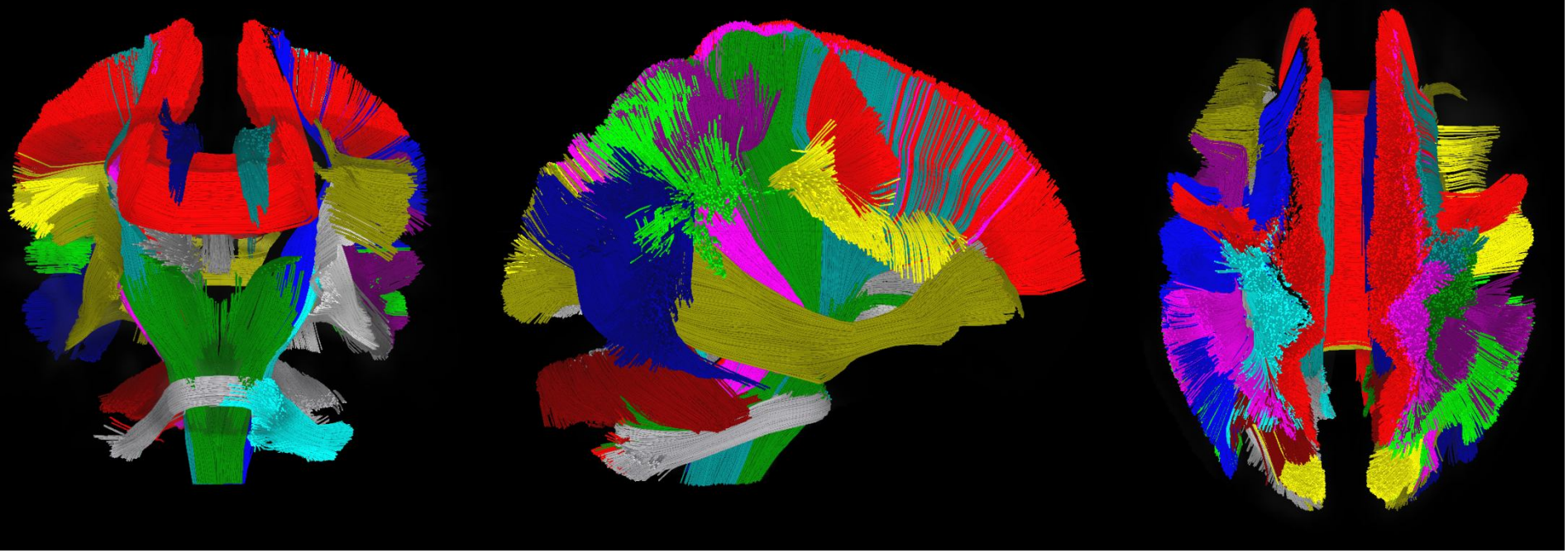
NTU-90: A high angular resolution brain atlas constructed by q-space diffeomorphic reconstruction

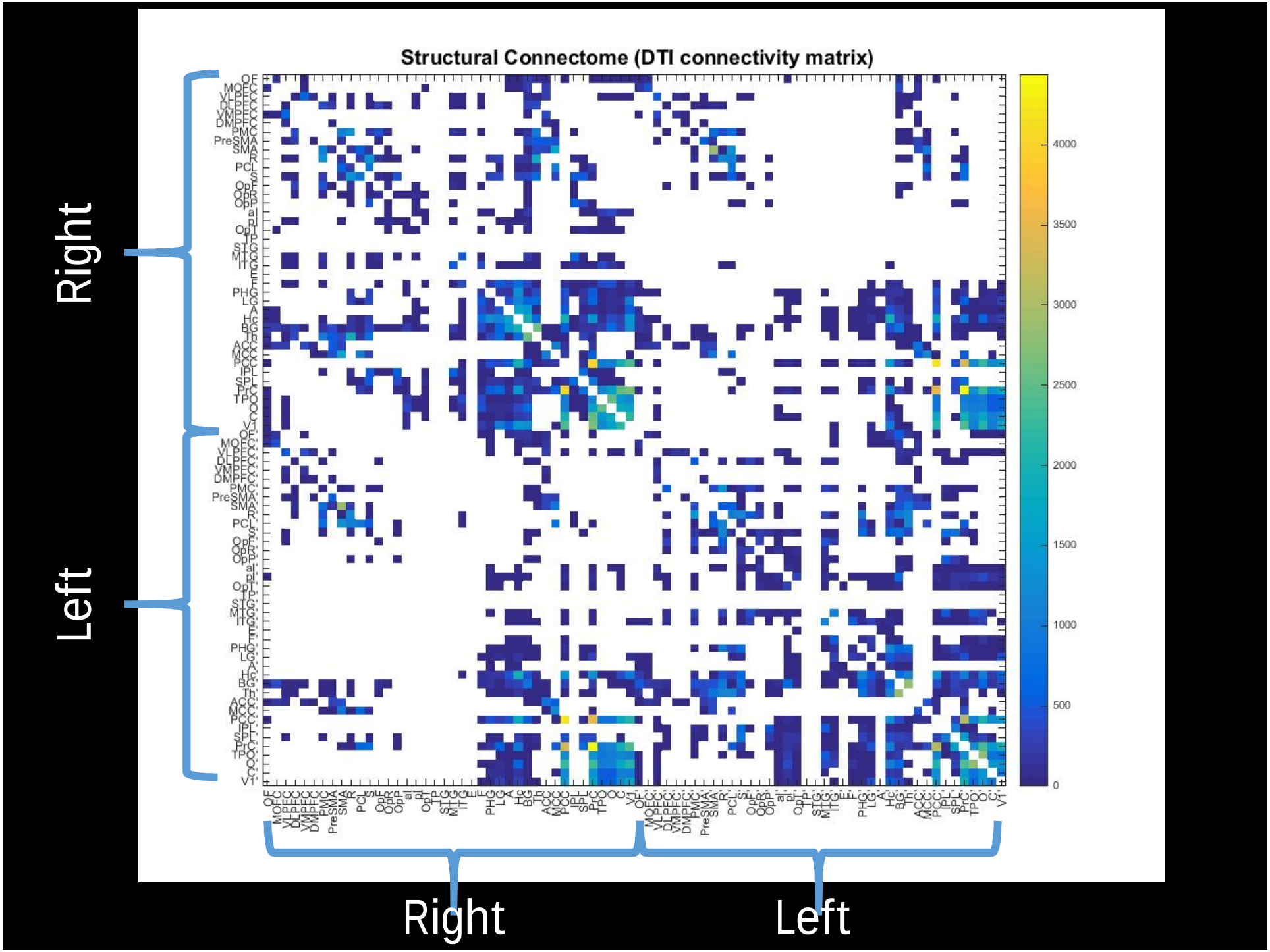
Fang-Cheng Yeh [a], Wen-Yih Isaac Tseng [b,c,*]

[a] Department of Biomedical Engineering, Carnegie Mellon University, Pennsylvania, USA
[b] Department of Medical Imaging, National Taiwan University Hospital, Taipei, Taiwan
[c] Center for Optoelectronic Biomedicine, National Taiwan University College of Medicine, Taipei, Taiwan

90 healthy subjects → 45 males , mean age 32.58±12.96 years
→ 45 females, mean age 33.58±12.26 years

Fibers extracted using DSIStudio (http://dsi-studio.labsolver.org).

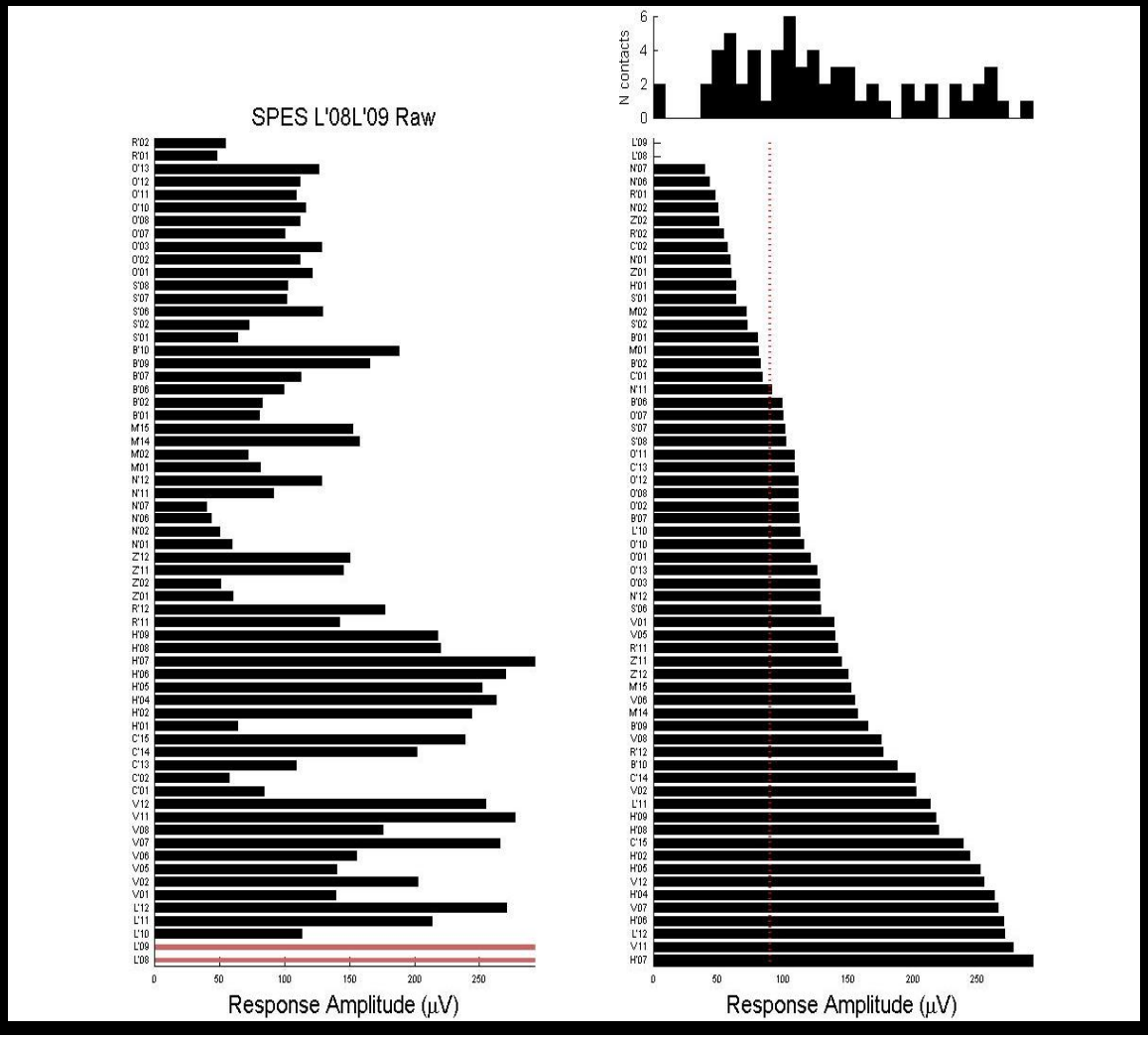


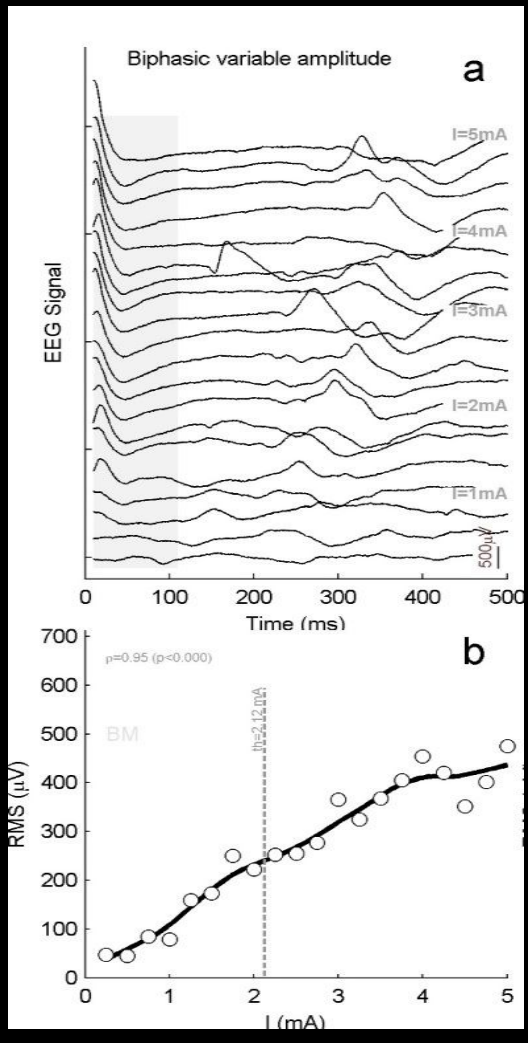

Structural Connectome (DTI connectivity matrix)
Right
Left
Right
Left
4000
3500
3000
2500
2000
1500
1000
500
0

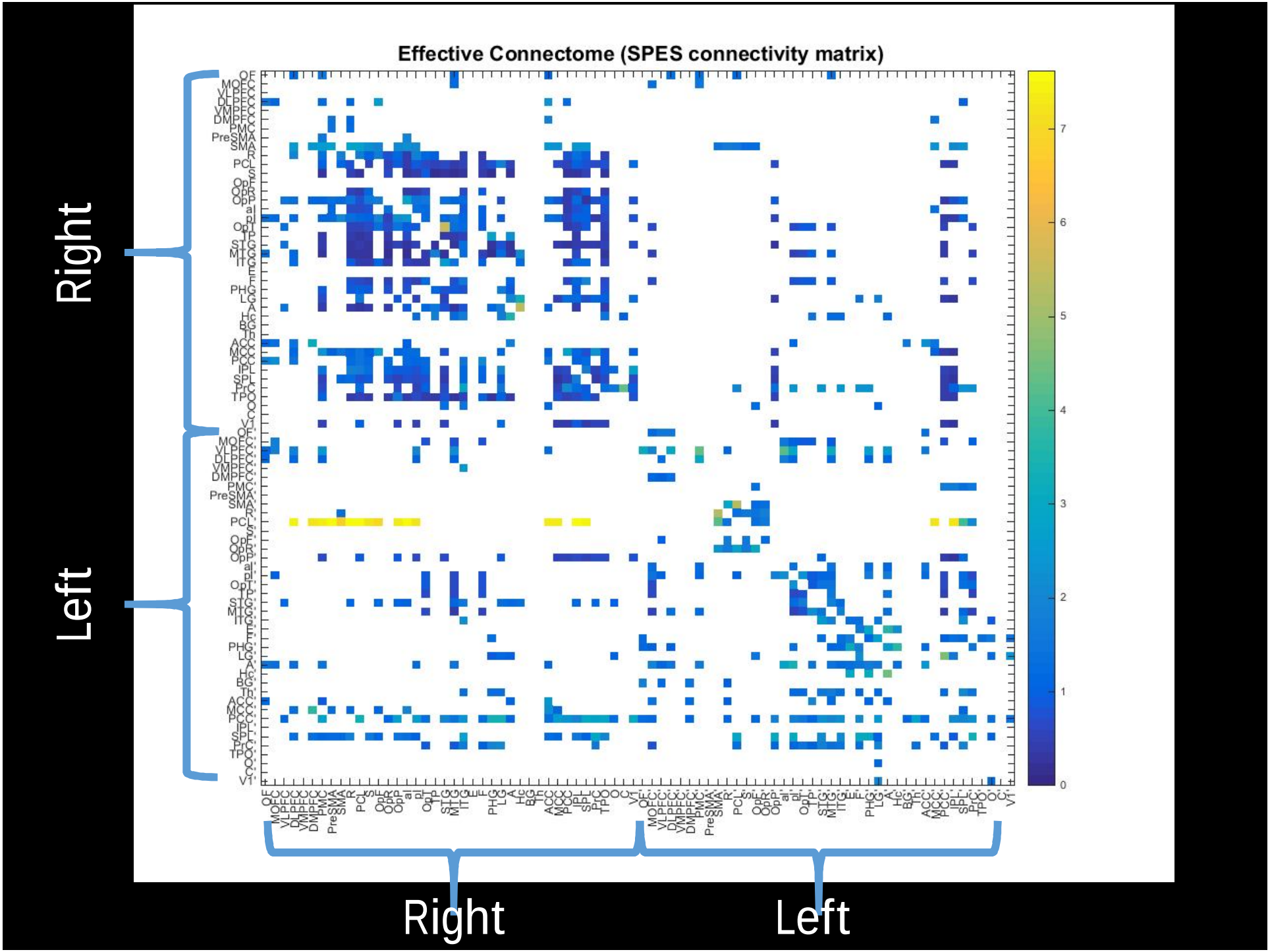
Effective connectivity

Contact selection criteria:

- Outside the epileptogenic network
- SPES responses are over the 3rd quartile (RMS Q3)
- SPES responses with Spearman's correlation coefficient ρ>0.5 and p<0.05

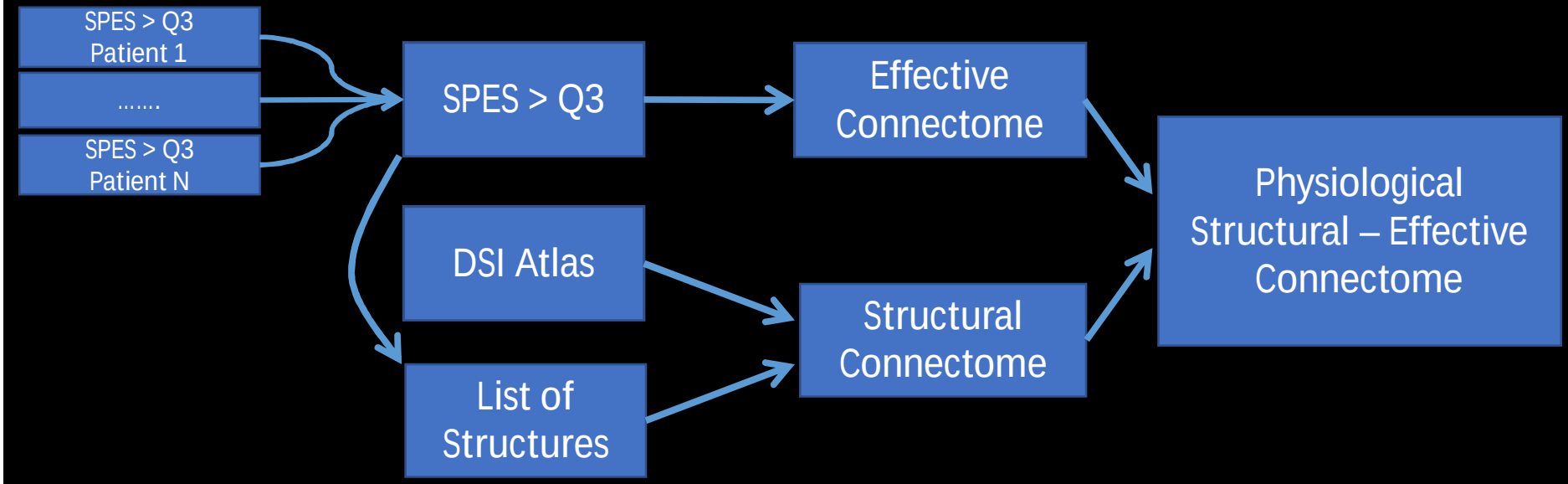




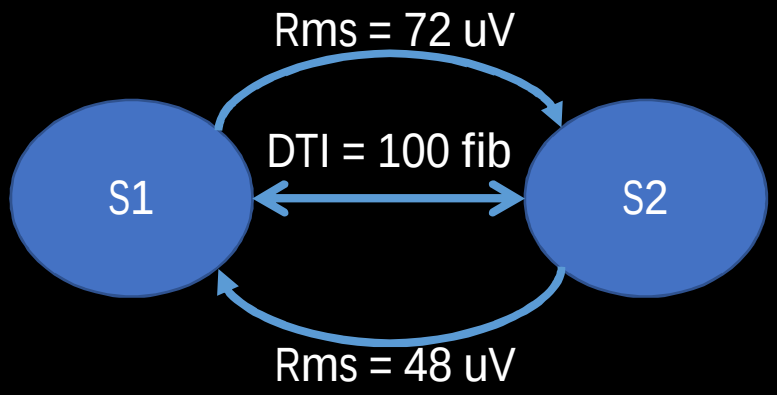

Effective Connectome (SPES connectivity matrix)
Right
Left
Right
Left

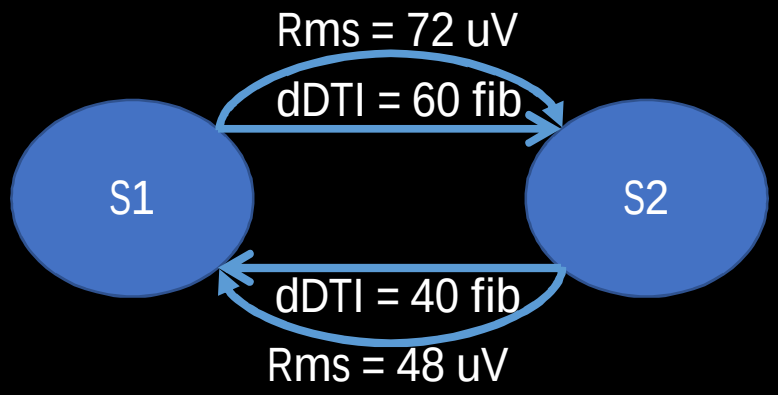
Physiological Connectome

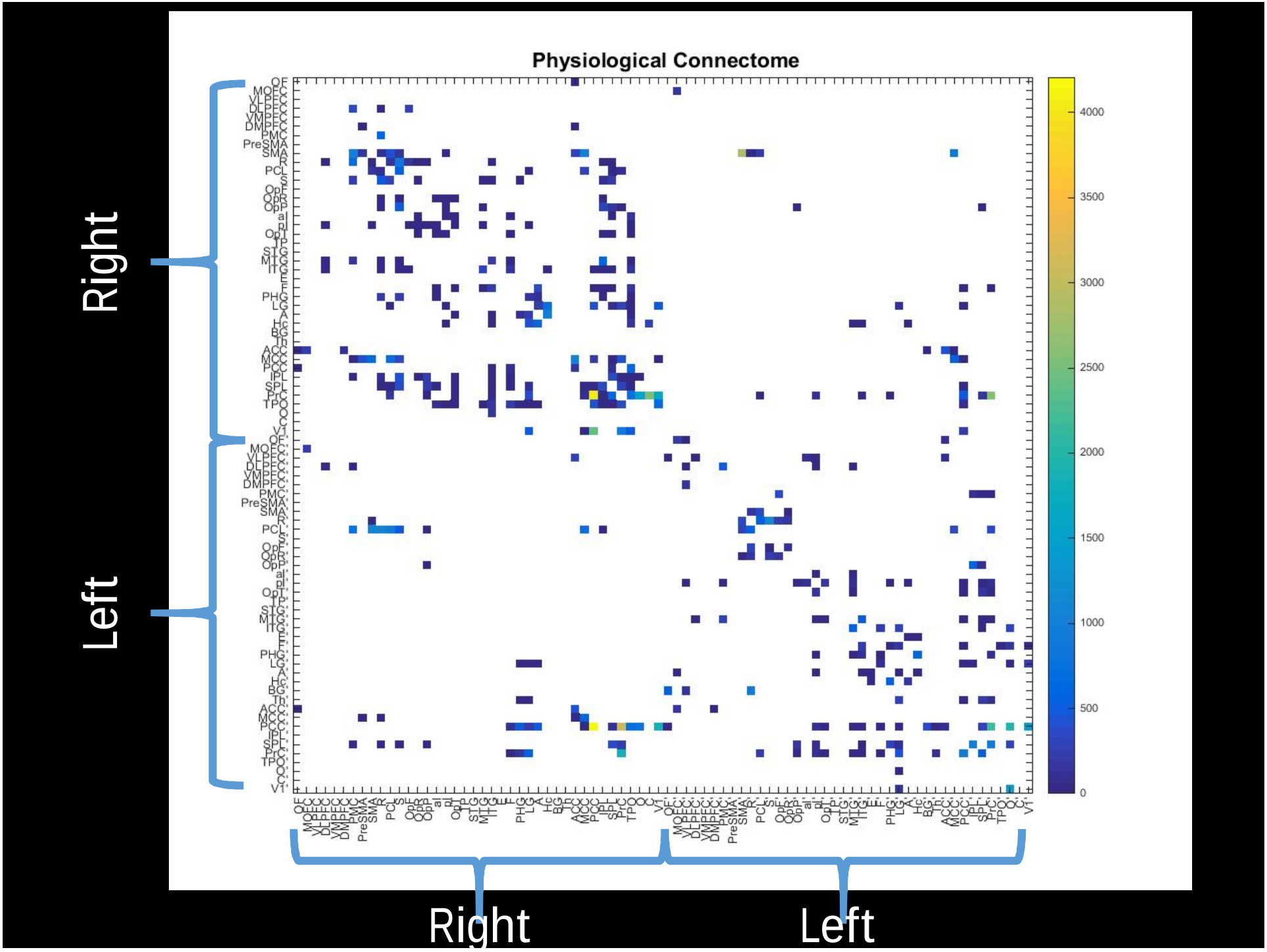
Workflow:



Fiber directionality:






Physiological Connectome
Right
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4000
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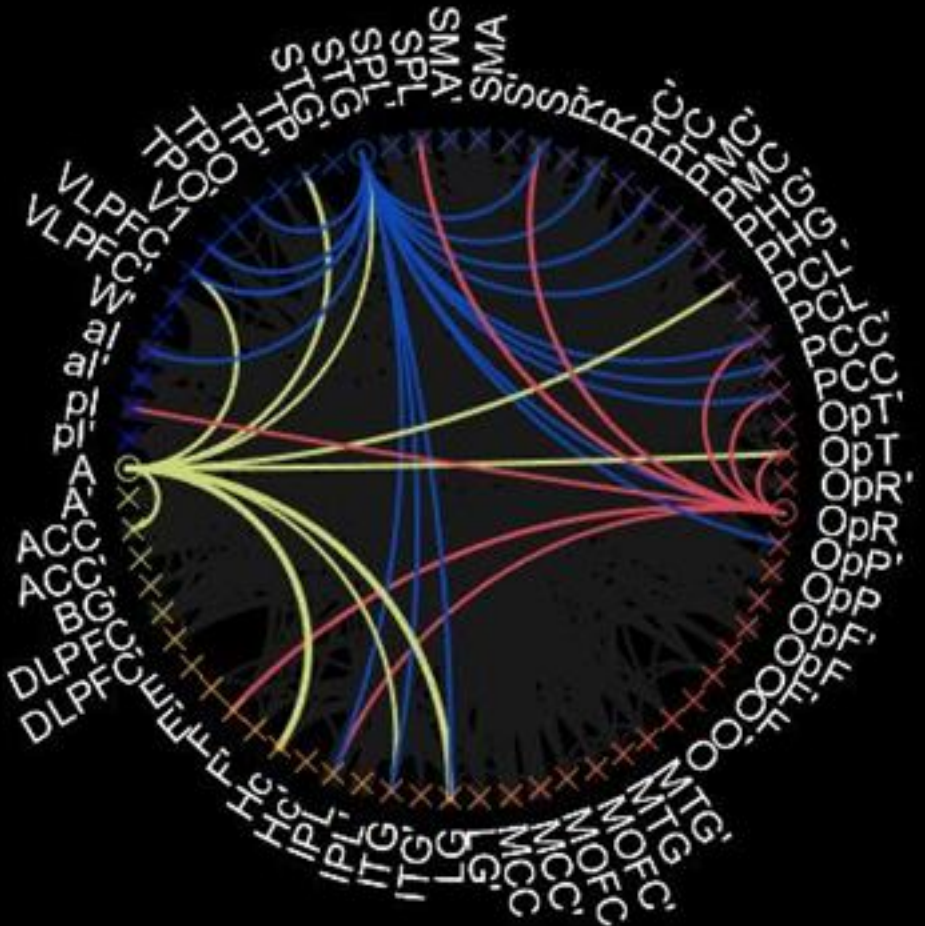
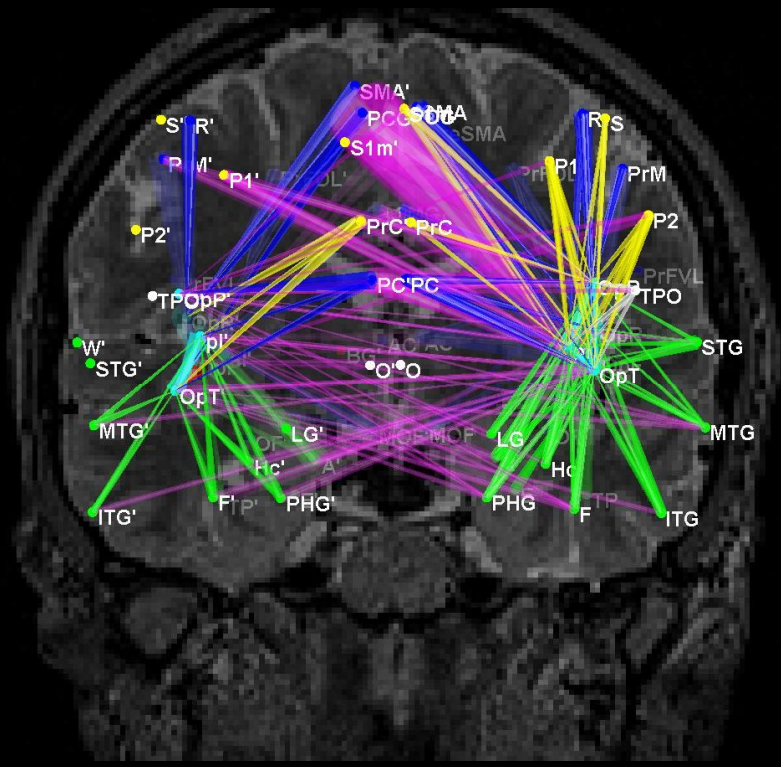
Physiological Connectome





Applications:

- Epileptogenic network identification by comparing patient's specific connectome with the physiological connectome.
- Identification of stimulus (seizure?) propagation pathways.

Propagation pathways

Given two structures A and B, the pathfinding algorithm performs a multi-level search in the physiological connectome.

The search priorities (at each level) are:

1. Direct connections between A and B
2. The largest number of fibers connecting A to another structure X which is an intermediate structure along the path from A to B

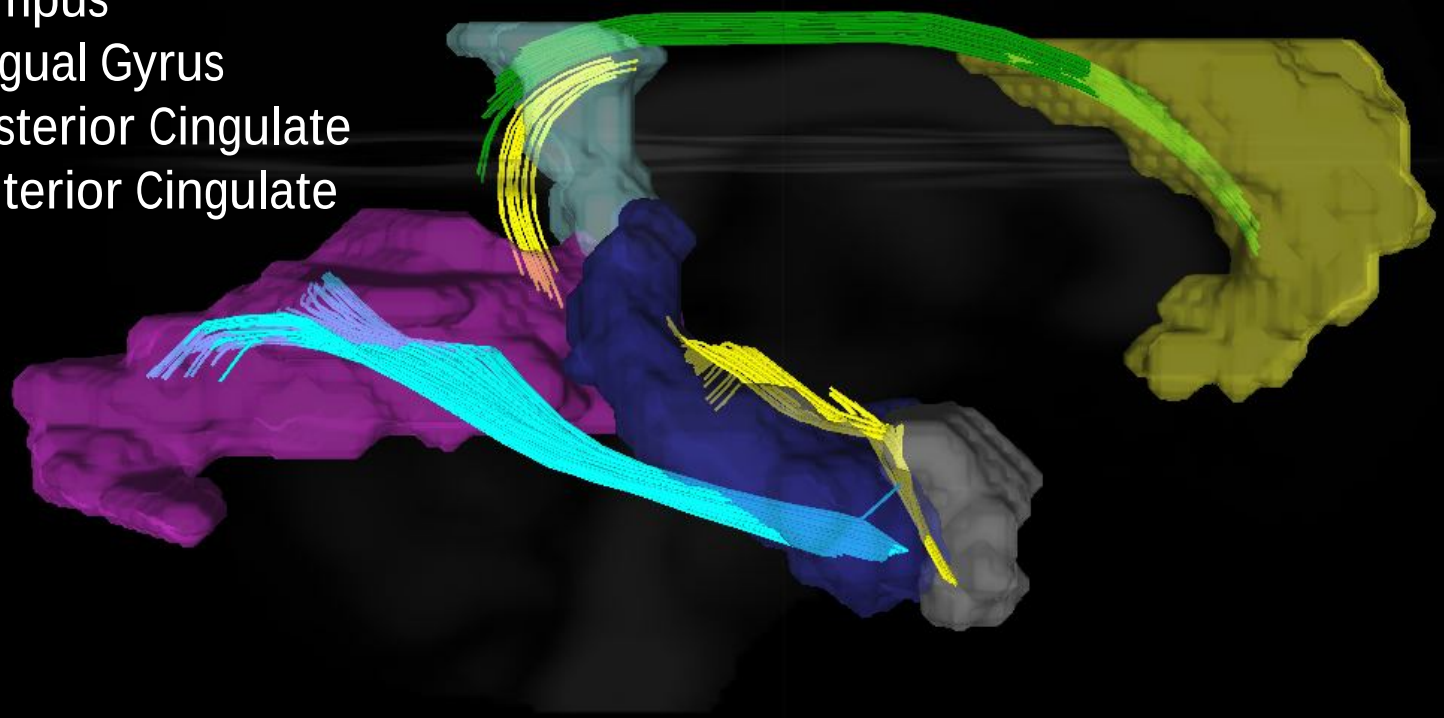
If pathway not found, the search continues with Y, an intermediate structure with the second largest number of fibers connecting A to Y.

And so on...

Propagation pathways

Path finding: stimulus propagation in spite of 0 direct fibers between A - ACC

A - Right Amygdala
Hc - Hippocampus
LG - Right Lingual Gyrus
PCC - Right Posterior Cingulate
ACC - Right Anterior Cingulate



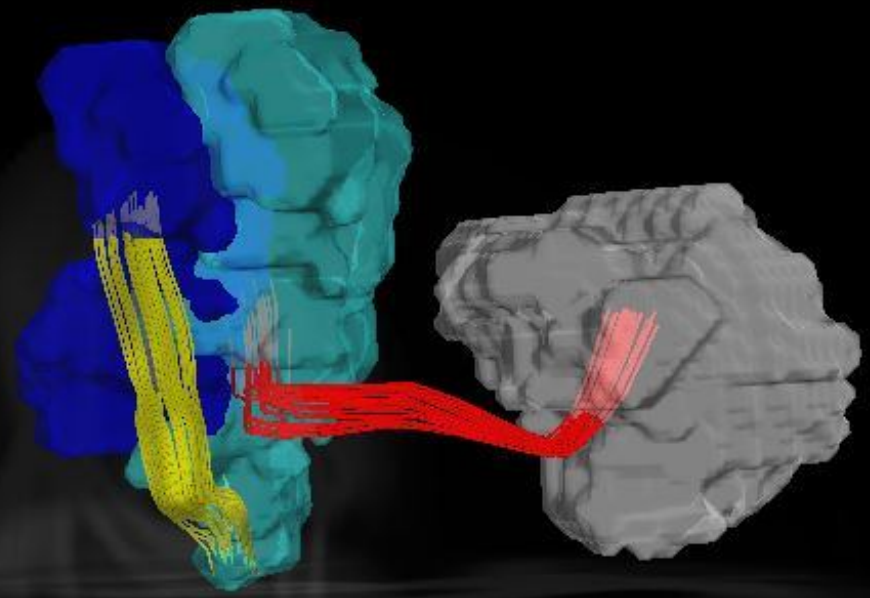
Answer: A-> Hc -> LG-> PCC-> ACC
Cingulum Bundle – role in emotion processing (Doucet et al. Hum Brain Mapp 2013)

Propagation pathways

Horizontal part of Longitudinal Superior Fascicle

Role: language articulation, verbal memory [disartria and anartria obtained during intraoperative stimulations] (Duffau et al 2003)

PMC – Pre Motor Cortex
R – Rolandic
IPL – Inferior Parietal Lobule



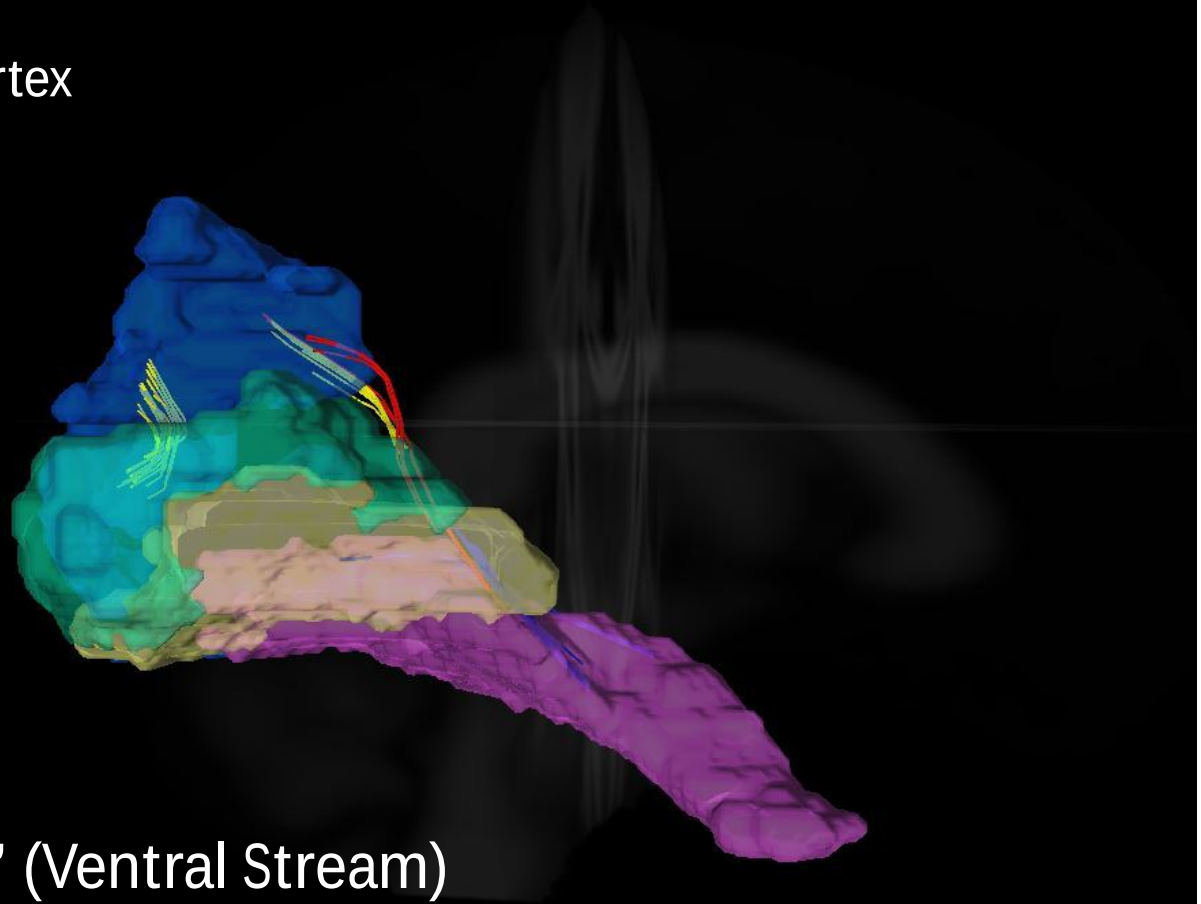
Path: PMC-> R -> IPL (hLSF)

Propagation pathways

Ventral Stream

Role: object identification and recognition

V1’ – Left Primary Visual Cortex
O’ – Left Lateral Occipital
LG’ – Left Lingual Gyrus
F’ – Left Fusiform Gyrus



Path: V1’-> O’ -> LG’ -> F’ (Ventral Stream)

Conclusions

Advantages:

- ✓ Based on DTI Atlases and subclinical stimulations (SPES)
- ✓ Can be updated by adding more patients
- ✓ Interactive plots for easy visualization of connections

Limitations:

- × Spatial sampling of SPES
- × Subjectivity in choosing the fiber extraction parameters

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