Structural connections constrain functional dynamics in the brain

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南方科技大学 Southern University of Science and Technology (SUSTech) is a young, public university in Shenzhen, China.

It was founded in 2010, and is working towards becoming a world-class university, ranked 8th in China by Times Higher Education & QS World University Rankings in 2021.

神经计算与控制实验室
NEURAL COMPUTING & CONTROL LAB

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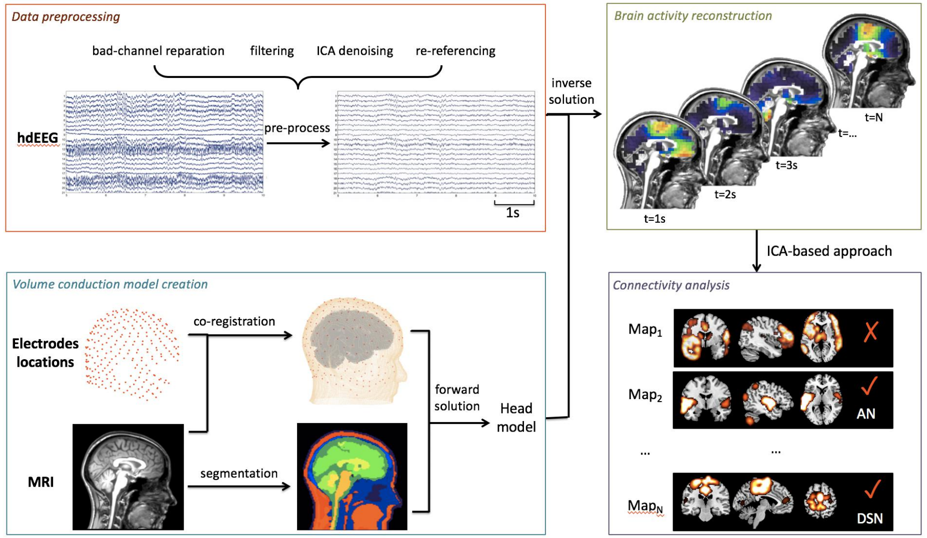
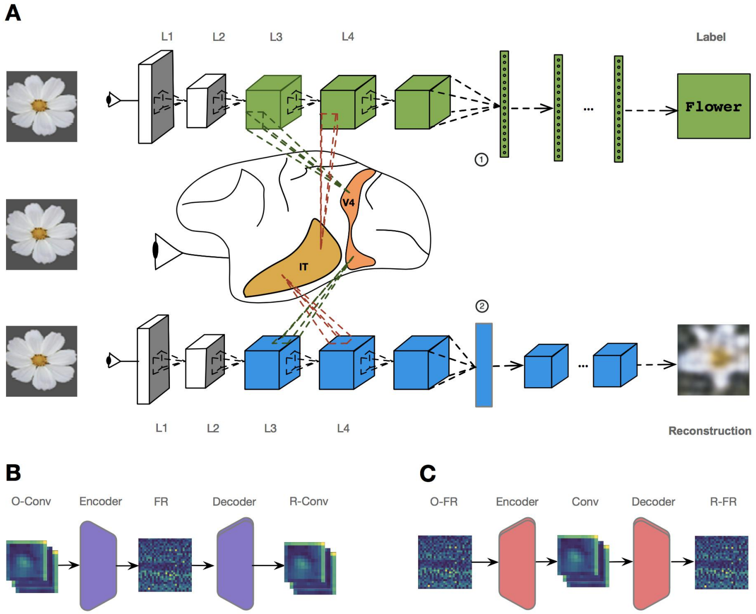
Bachelor/master at Lanzhou University, PhD at ETH Zurich, postdoc at Caltech

Research interests: Multi-modal neural data processing (EEG, iEEG, DTI, fMRI,...), Brain network modelling, AI for neuroscience, Control theory for neurostimulation

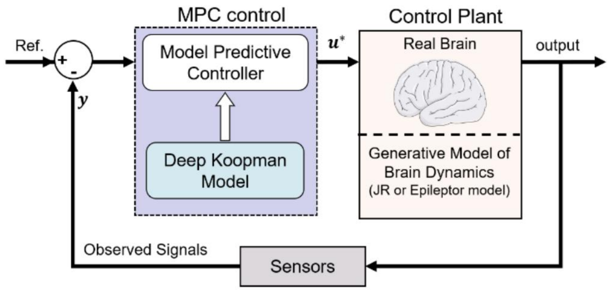
Multi-modal neural data processing

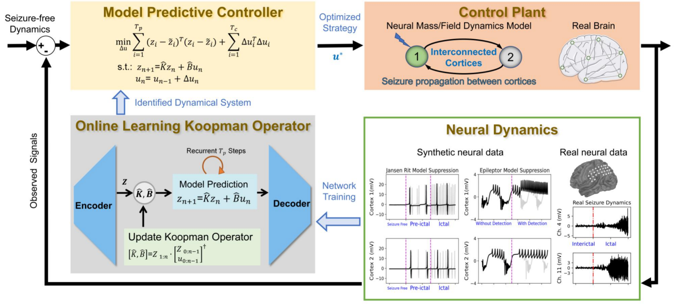


AI for neuroscience



Neurostimulation





Contents

➢ Theory session (Brain network modeling)

- Basic concepts of neuroimages: T1/T2, DTI, fMRI, and their processing pipeline
- Brain network modelling: Structural/functional/effective network
- Structure-function modelling: bridging the brain structure and functional dynamics

➢ Hands-on session (interlacing with theory session)

1. Data analysis pipeline: obtain structural connectome (DTI) and functional series (fMRI)
2. Brain network modelling:
    - Partial Least Square (PLS) Analysis to study Structure-Function relationship
    - Python Implemenation of Structural-Decoupling Index
3. Our fusion optimization method

SUSTech
Southern University of Science and Technology

NEURAL COMPUTING CONTROL

NCC Lab

Neural Computing & Control lab

Achknoledgements

Zhichao Liang (梁智超)

All members in NCC lab

NCC lab的微信公众号

- Youtube课程推荐
- 科普文章
- 学术论文解读

ncclabsustech Update README.md		e1a652f 28 minutes ago 14 commits
article	Add files via upload	44 minutes ago
data	Add files via upload	1 hour ago
script	Add files via upload	42 minutes ago
1. Pipeline_Generating_Structural_...	Add files via upload	1 hour ago
2. Basic_Introduction_of_Nilearn1_...	Add files via upload	1 hour ago
3. Python_implementation_of PLS_...	Add files via upload	1 hour ago
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5. Basic_Optimization_with_PyTorc...	Add files via upload	1 hour ago
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README.md

NM_workshop

Tutorial on Neuroimaging Methods Workshop

We will cover the following tutorials:

1. The steps to generate the structural connectome from mrtrix3. [The script of the whole process is uploaded.]
2. The steps to generate functional time series from nilearn.
3. The python implementation of the partial least square analysis of structural connectome and functional connectivity.

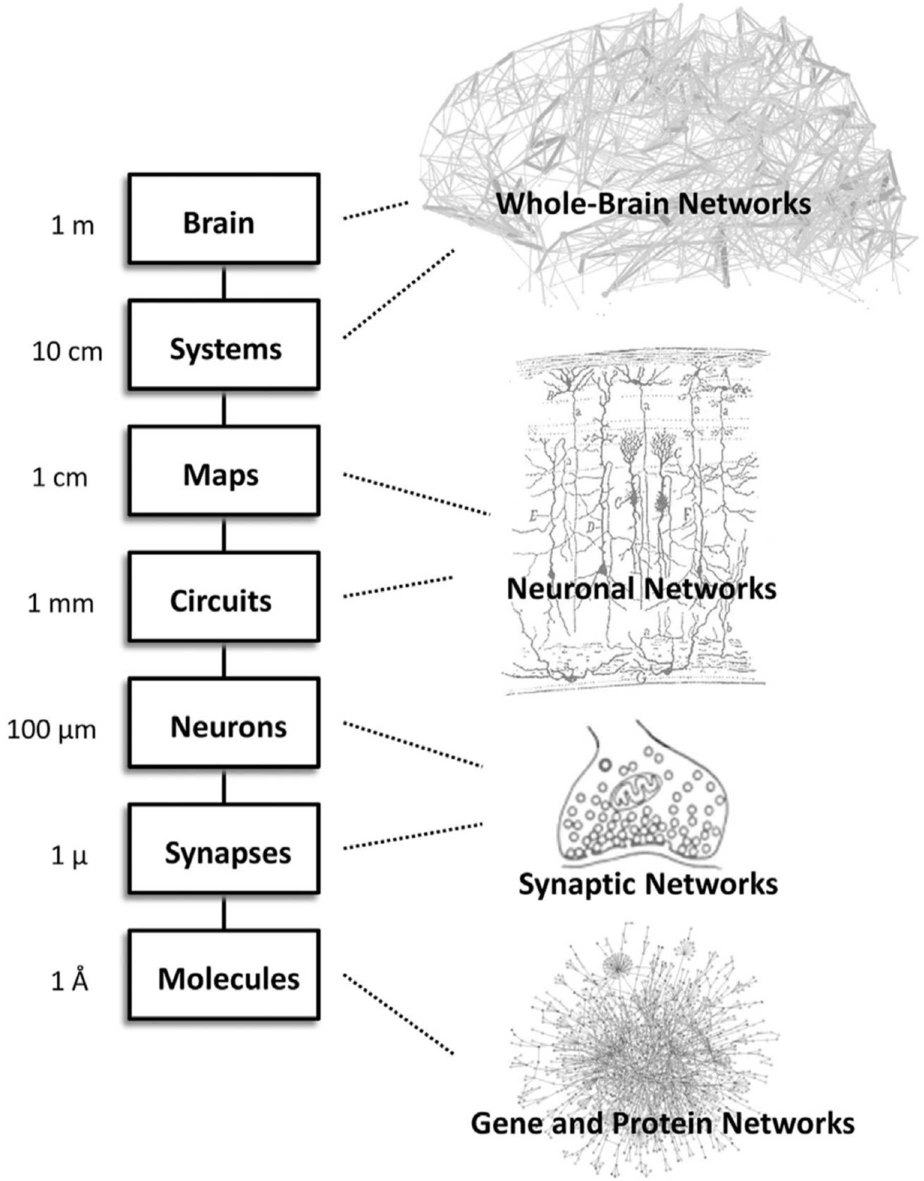
梁智超

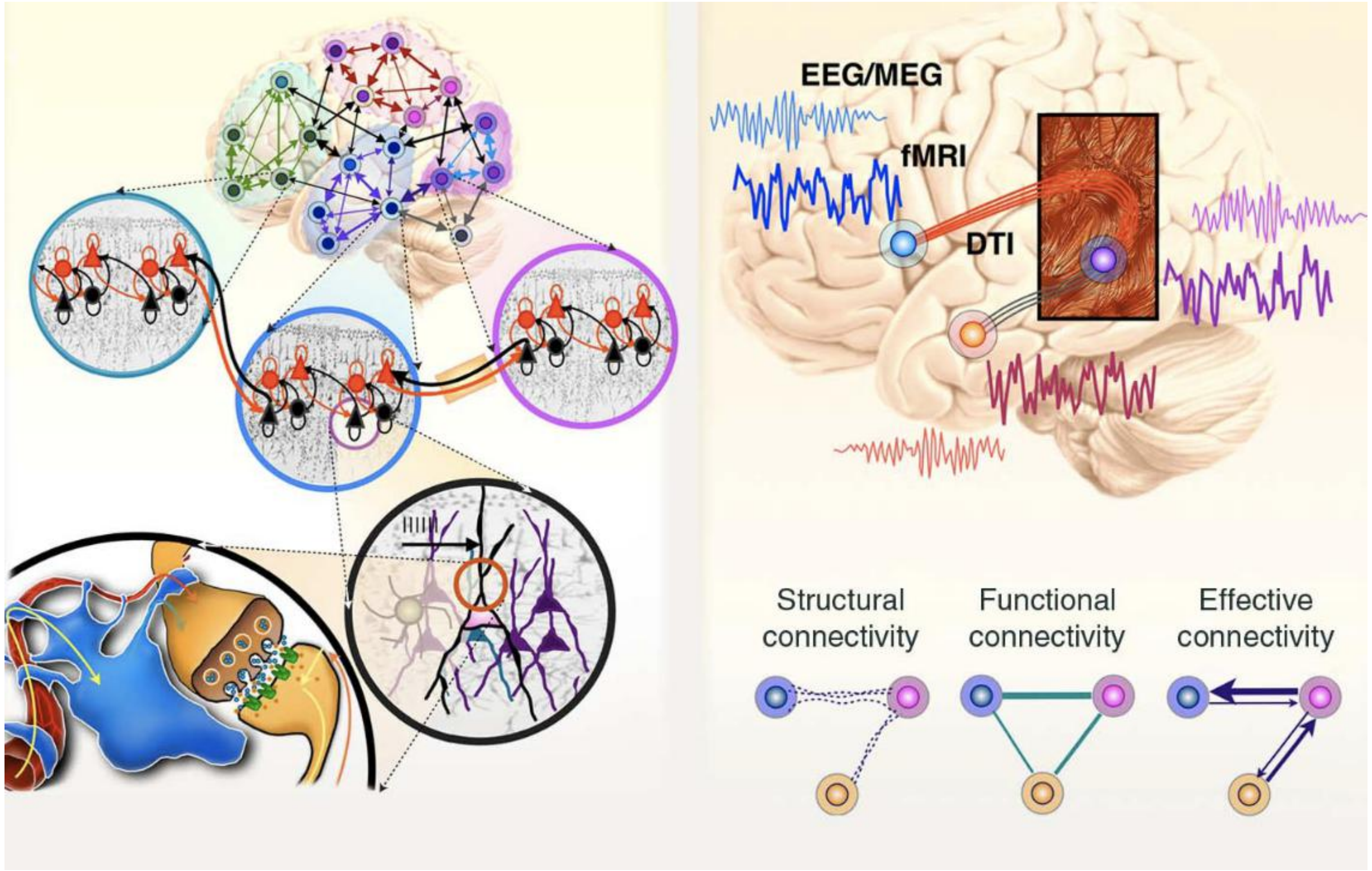
All these code are prepared by Zhichao Liang!

Download the Data & Code:

https://github.com/ncclabsustech/NM_workshop

Brain networks at different scales





Park & Friston (2013) Science

Brain Networks

Structural Connectivity (SC): Anatomical connections

- Synapses, fiber pathways ...

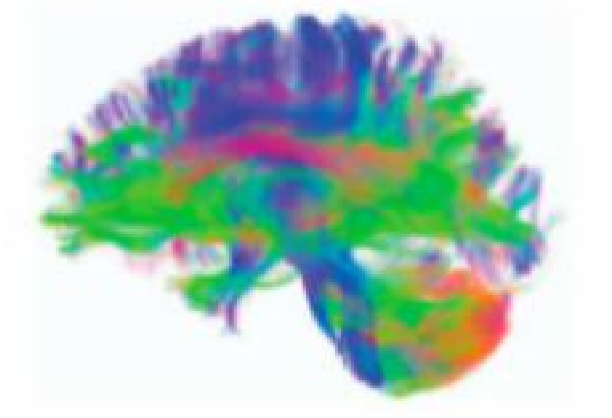
Functional Connectivity (FC): Statistical dependencies

- Correlation, coherence, phase locking index ...

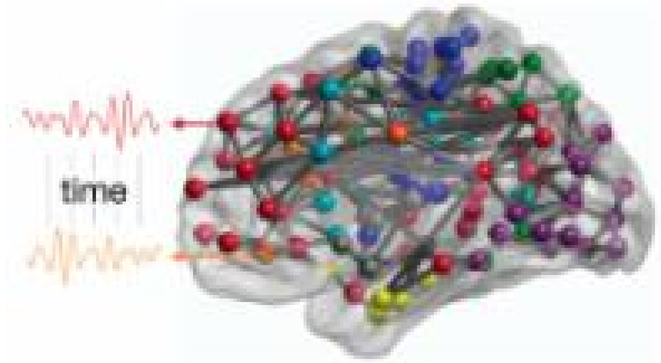
Effective Connectivity (EC): Causal interactions

- Granger causality, dynamical models ...

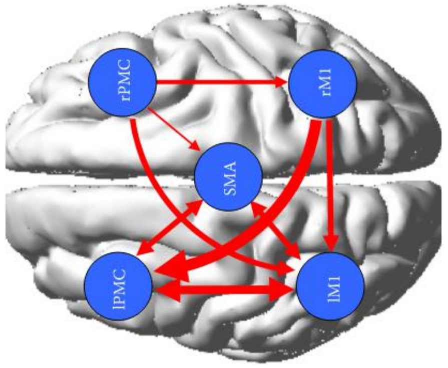
Structural Connectivity



Functional Connectivity

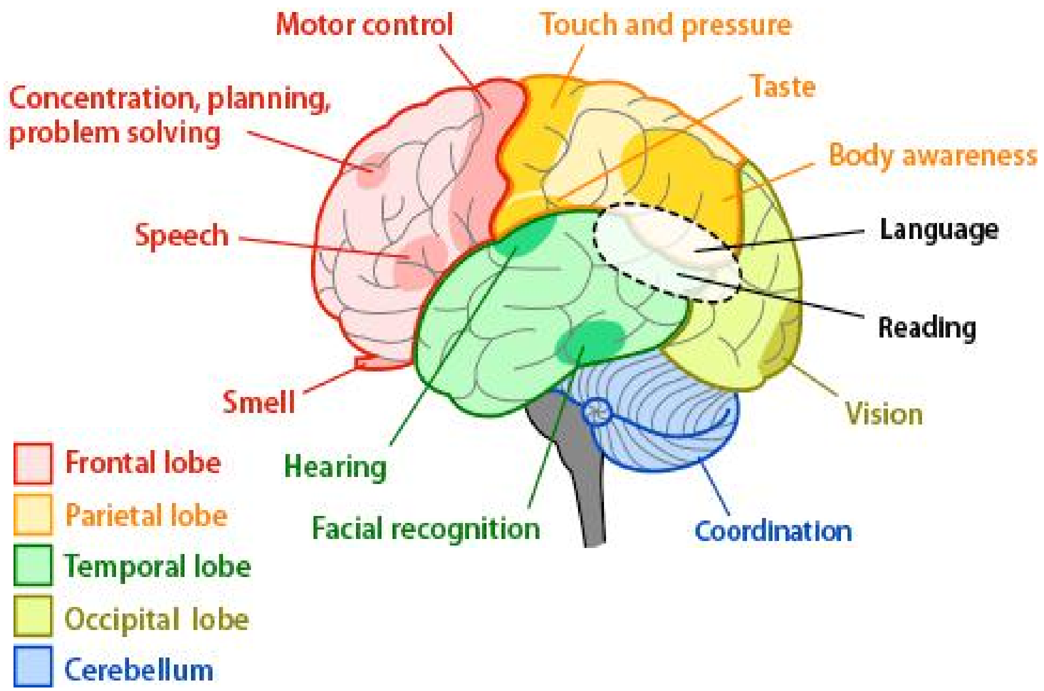


Effective Connectivity



Functionality emerges from connectivity

Brain regions and functions



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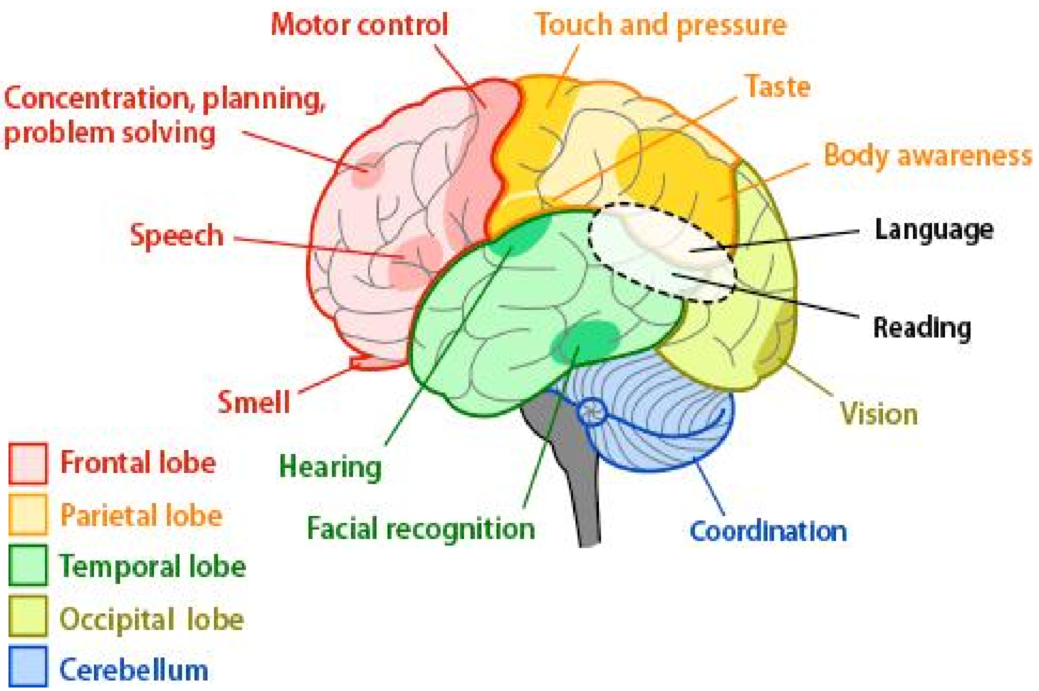
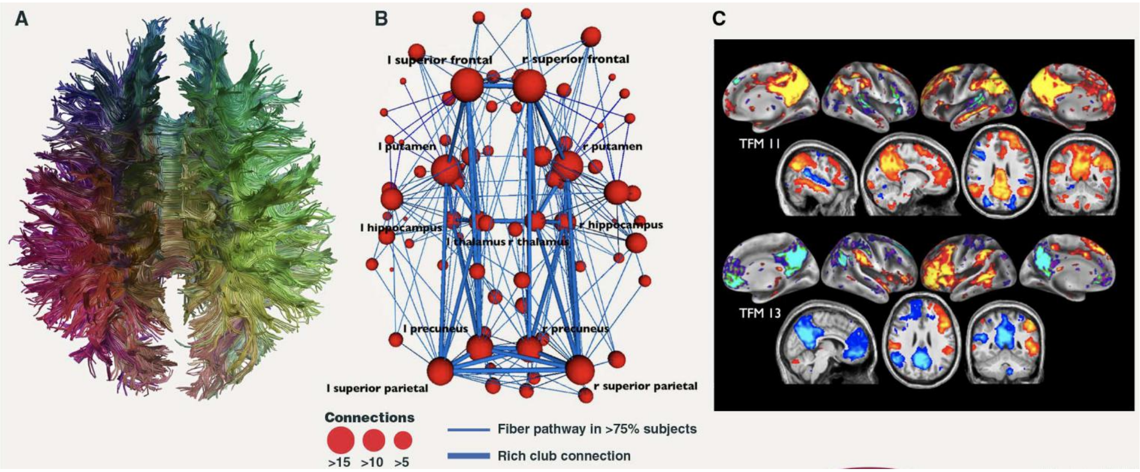


Brain Connectivity



de Schotten and Forkel, 2022, Science
Axer and Amunts, 2022, Science
Leergaard and Bjaalie, 2022, Science
Oh et al., 2014, Nature
Park & Friston, 2013, Sicnece

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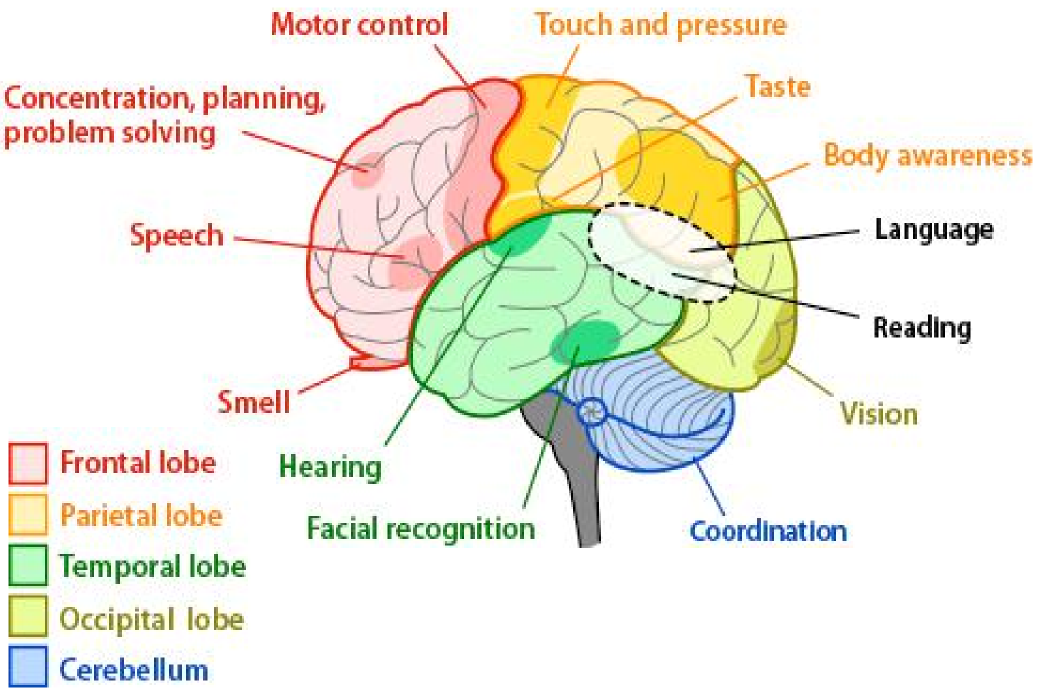
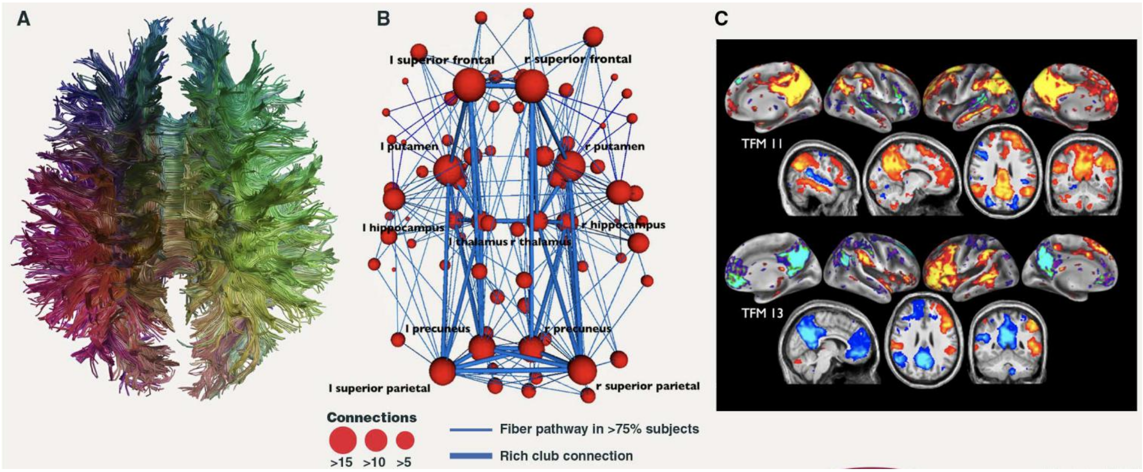


Brain Connectivity



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- ❑ Structure is invariant in a short time.
- ❑ Function is highly dynamical and flexible.

Q: How does the invariant brain structure support instantly-changing brain functions?

Relationship between structure and function

Brain structure
(T1, T2, DTI images)

?

Brain functional dynamics
(~10^{12} neurons, ~10^{2} brain regions)

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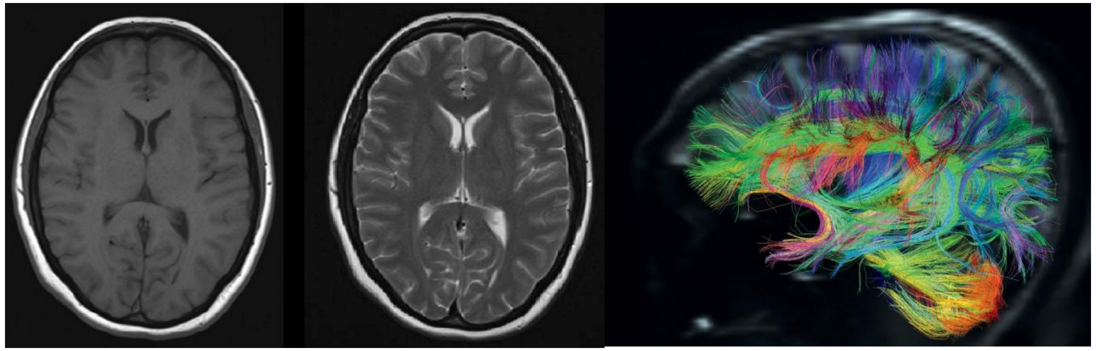


fMRI

Some brain imaging datasets

HCP data (HCP-1000S release, 1000 participants with T1, DTI, resting-state fMRI, 23-task fMRI)
www.humanconnectomeproject.org/data/hcp-project/

PNC: Philadelphia Neurodevelopmental Cohort
https://www.med.upenn.edu/bbl/philadelphianeurodevelopmentalcohort.html

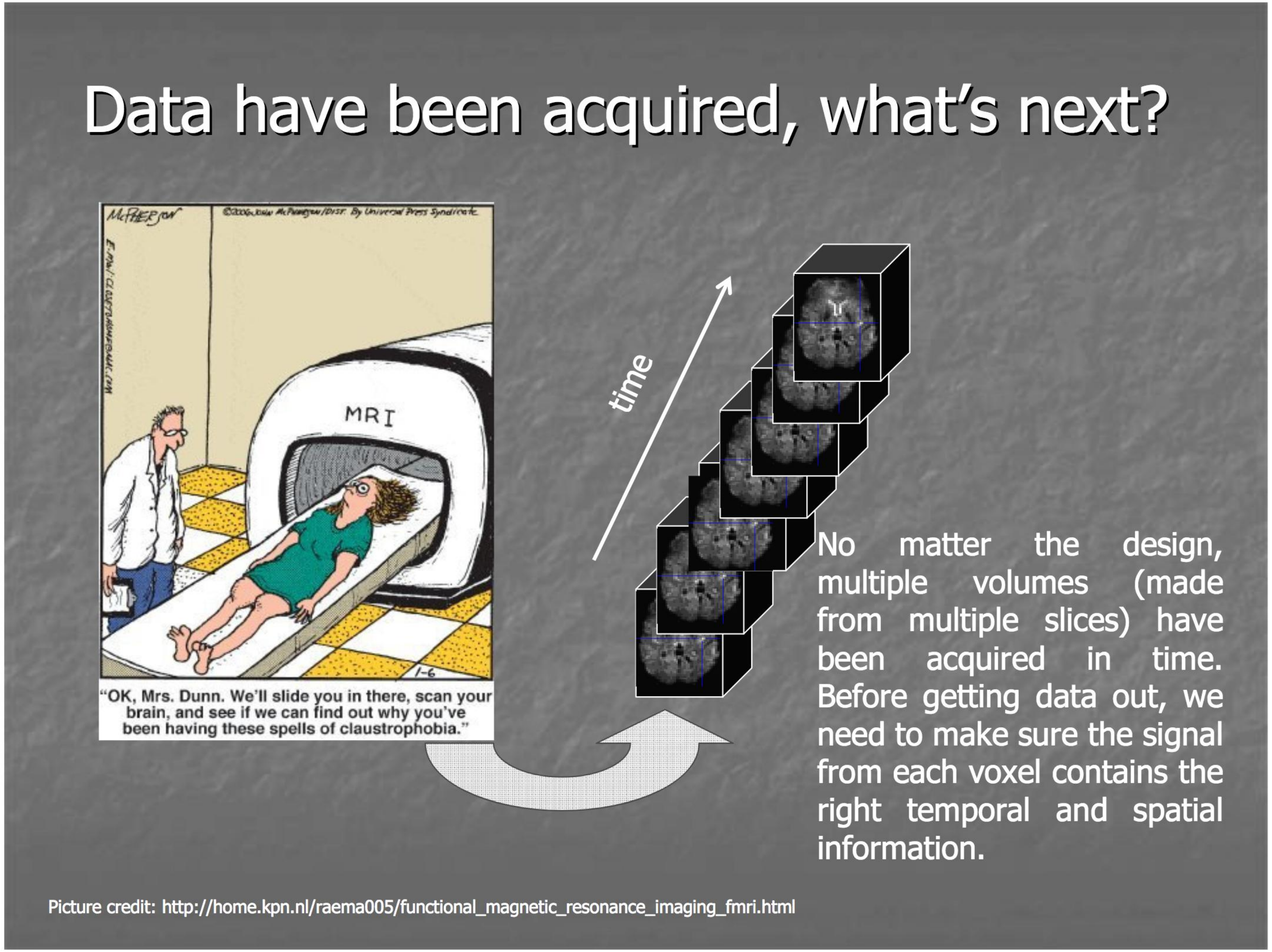
ADNI: Alzheimer's Disease Neuroimaging Initiative
http://adni.loni.usc.edu/

MRI-GENIE: 急性缺血脑卒中数据集
http://www.resilientbrain.org/mrigenie.html

ABIDE: Autism Brain Imaging Data Exchange, around 2000 participants, rsfMRI
https://fcon_1000.projects.nitrc.org/indi/abide/

Scientific Data (a journal where publishes open-source data)

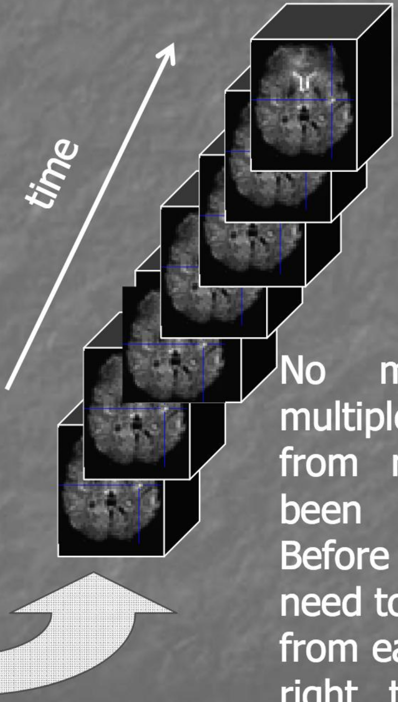
fMRI preprocessing



fMRI preprocessing

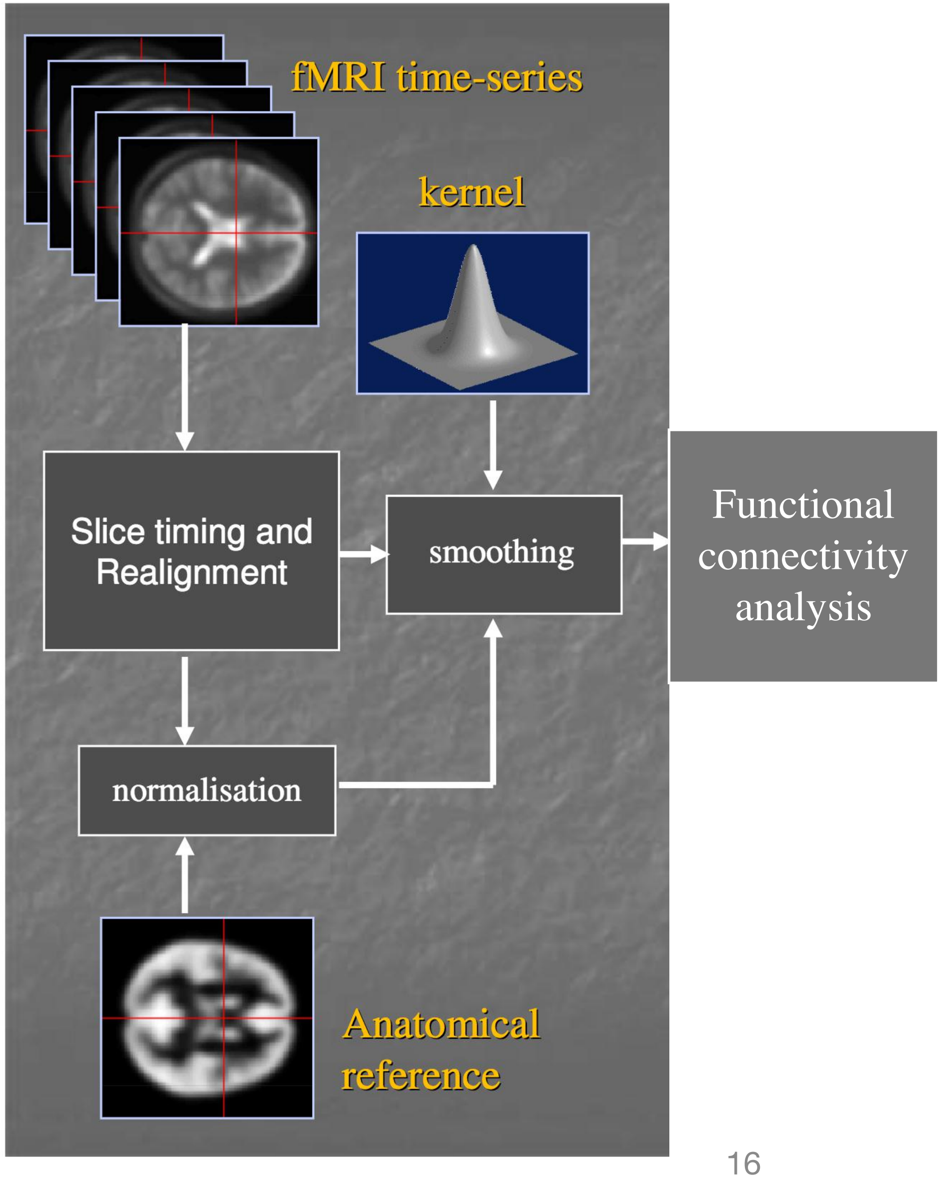
Data have been acquired, what's next?

“OK, Mrs. Dunn. We'll slide you in there, scan your brain, and see if we can find out why you've been having these spells of claustrophobia.”



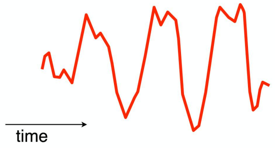
No matter the design, multiple volumes (made from multiple slices) have been acquired in time. Before getting data out, we need to make sure the signal from each voxel contains the right temporal and spatial information.

Picture credit: http://home.kpn.nl/raema005/functional_magnetic_resonance_imaging_fmri.html



fMRI preprocessing

Each voxel contains a time-varying signal
(blood oxygen-level dependent (BOLD) signal).



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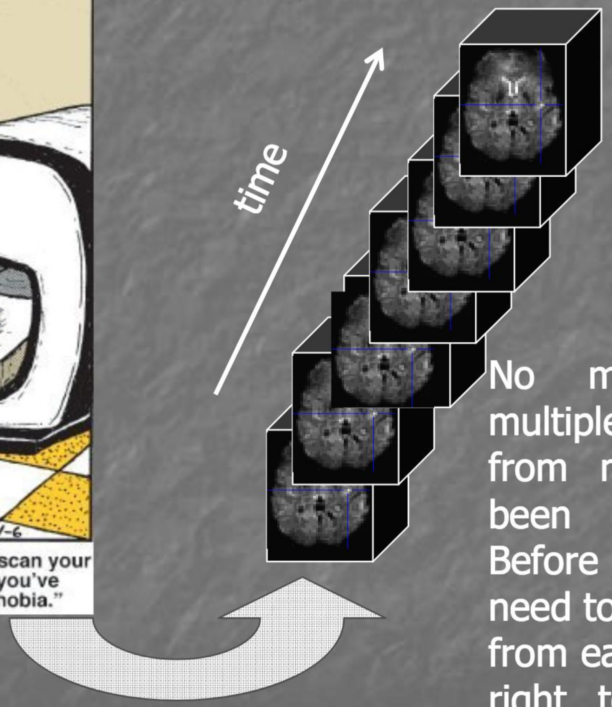

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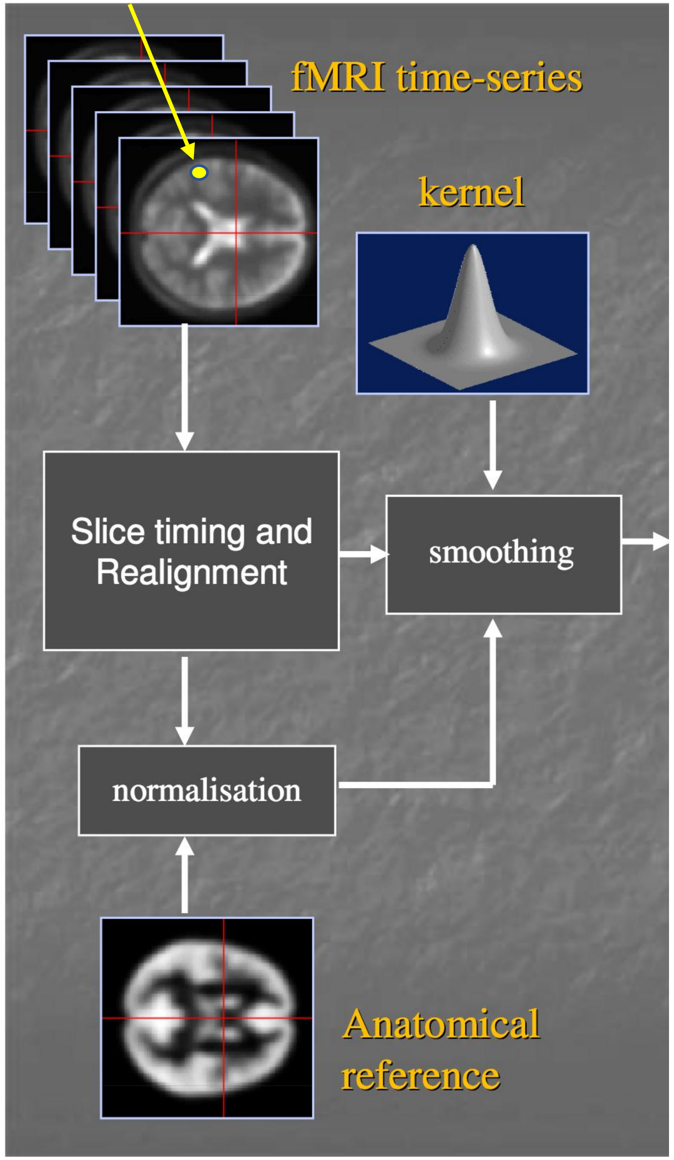
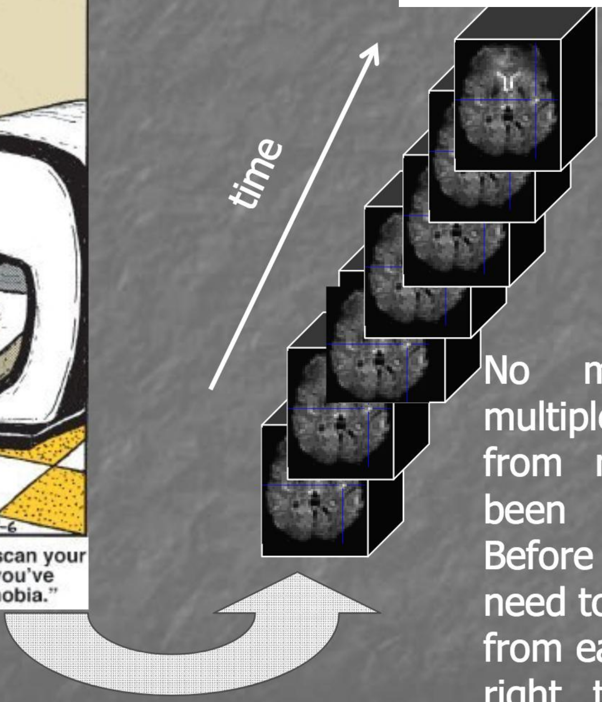


fMRI preprocessing

Data have been acquired, what's next?

MRI scanning takes each slice separately.
Each slice is scanned at a slightly different Time.

"OK, Mrs. Dunn. We'll slide you in there, scan your brain, and see if we can find out why you've been having these spells of claustrophobia."



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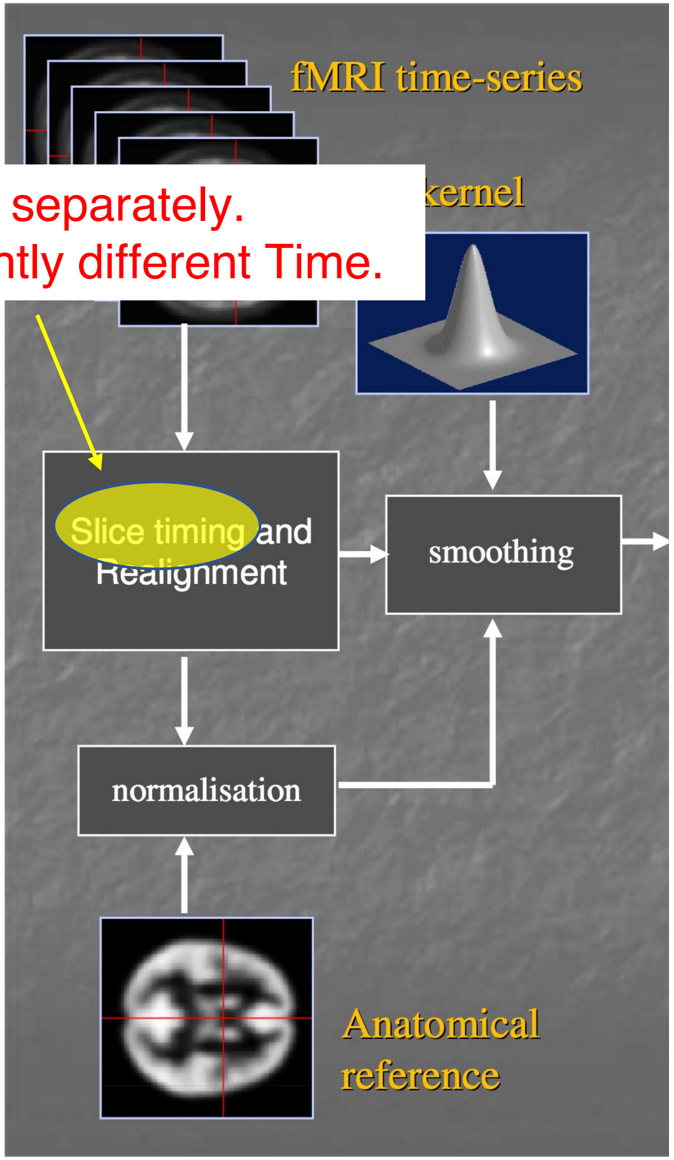
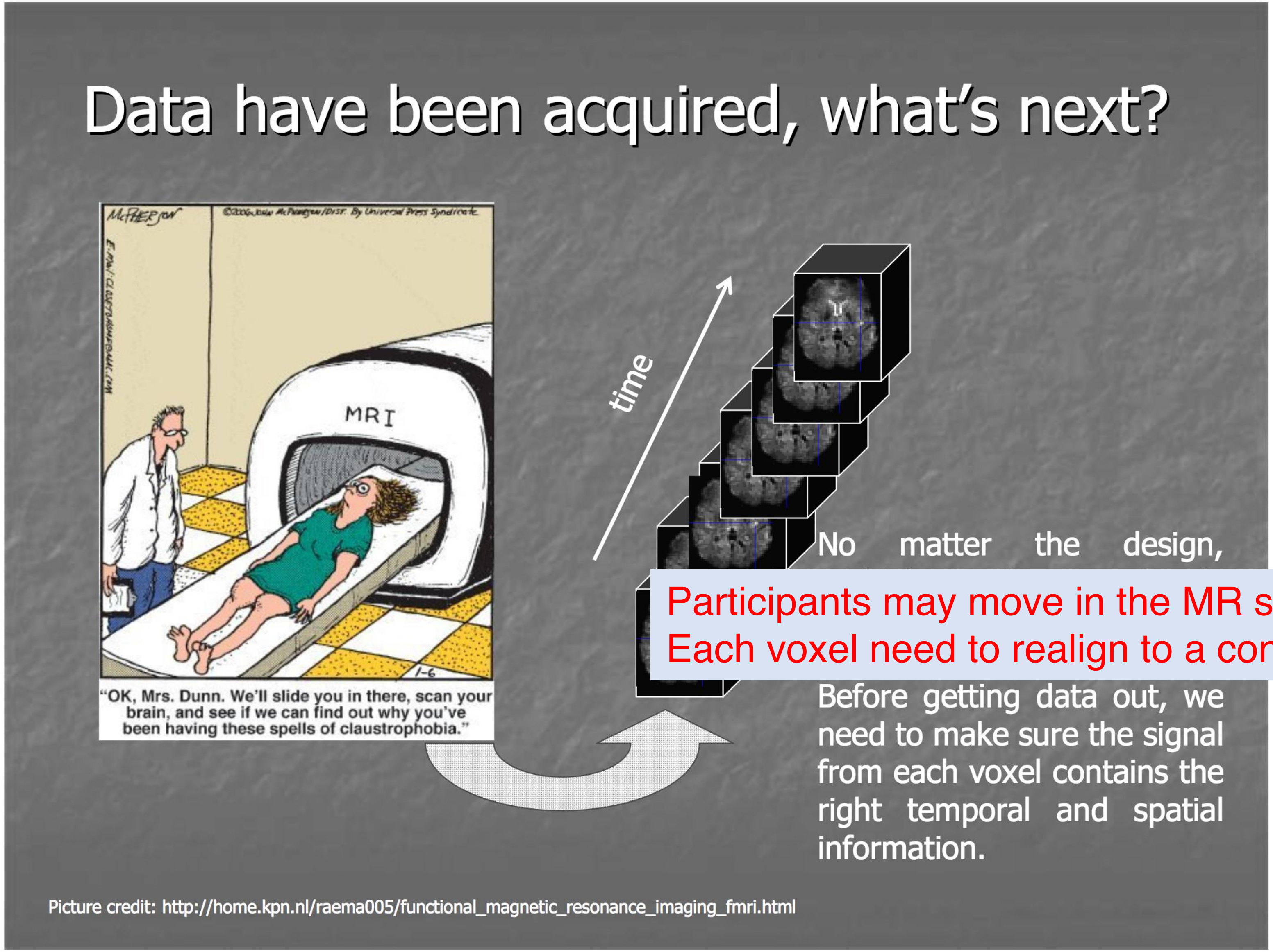
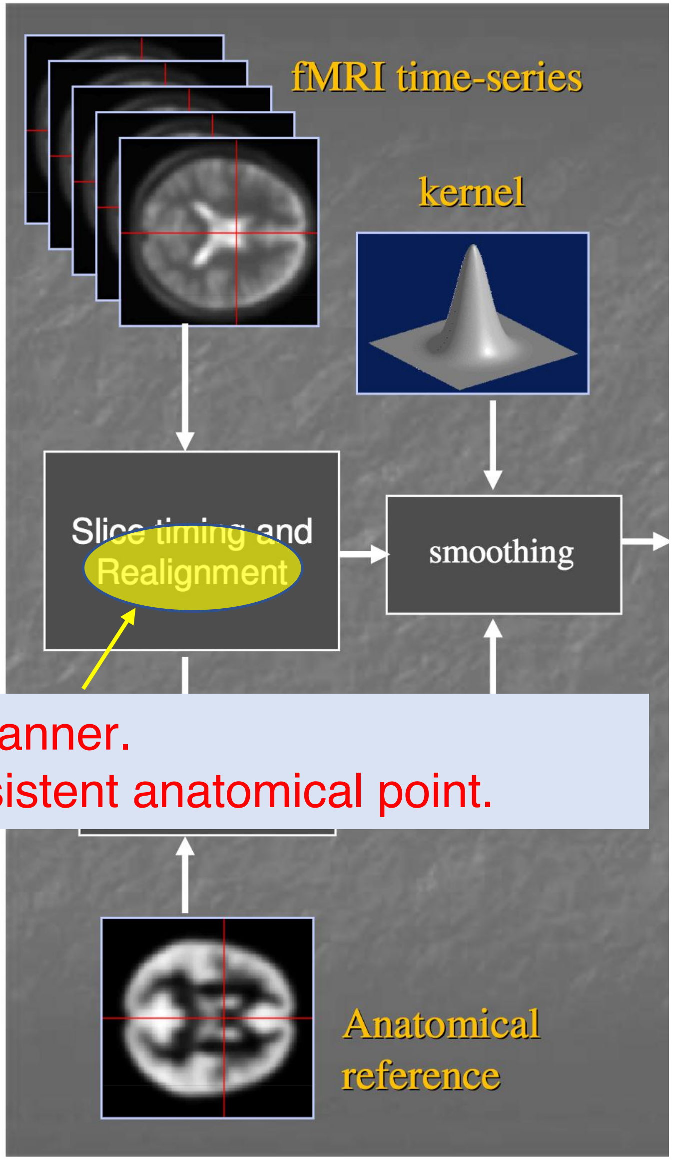


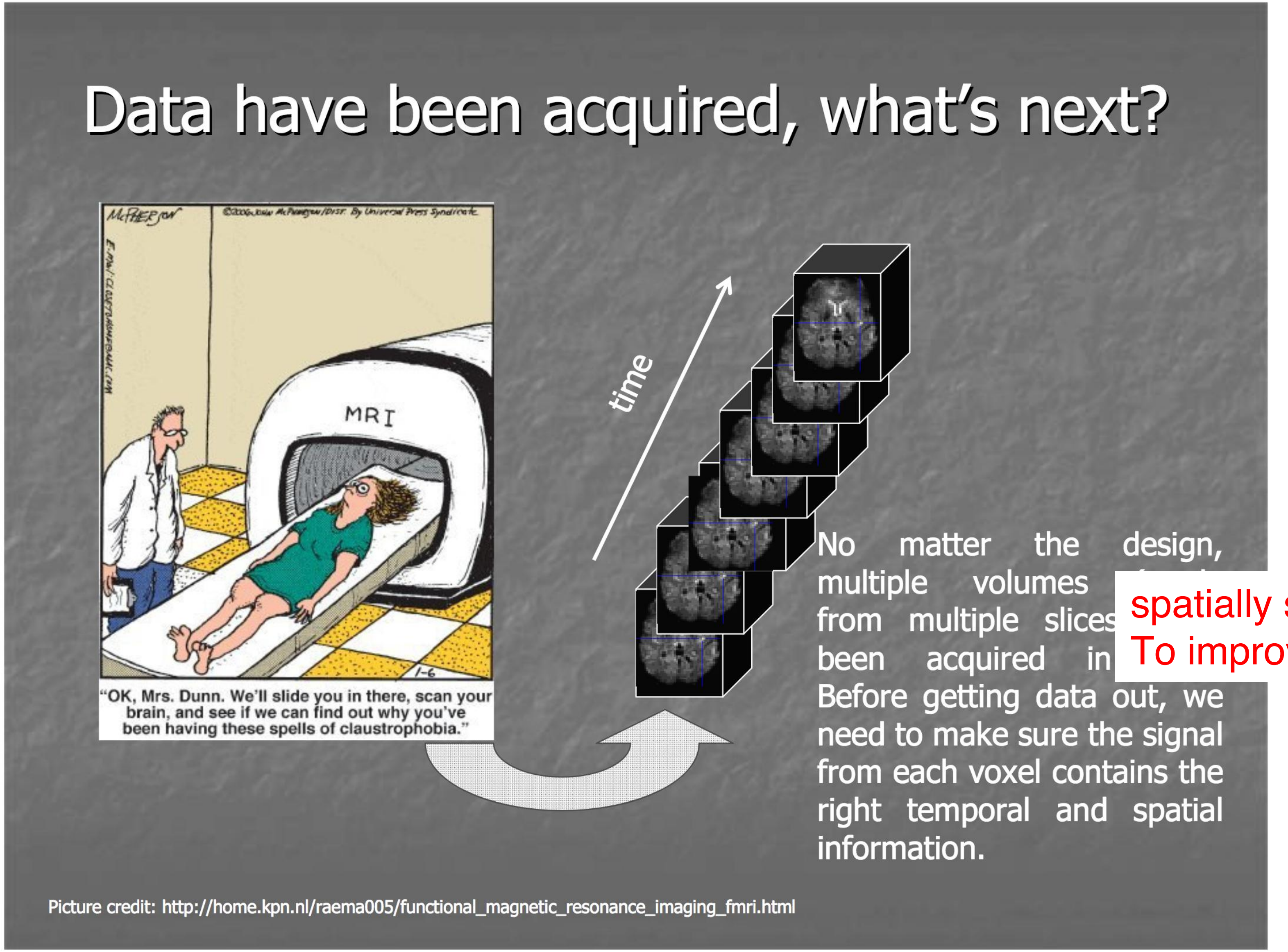
fMRI preprocessing

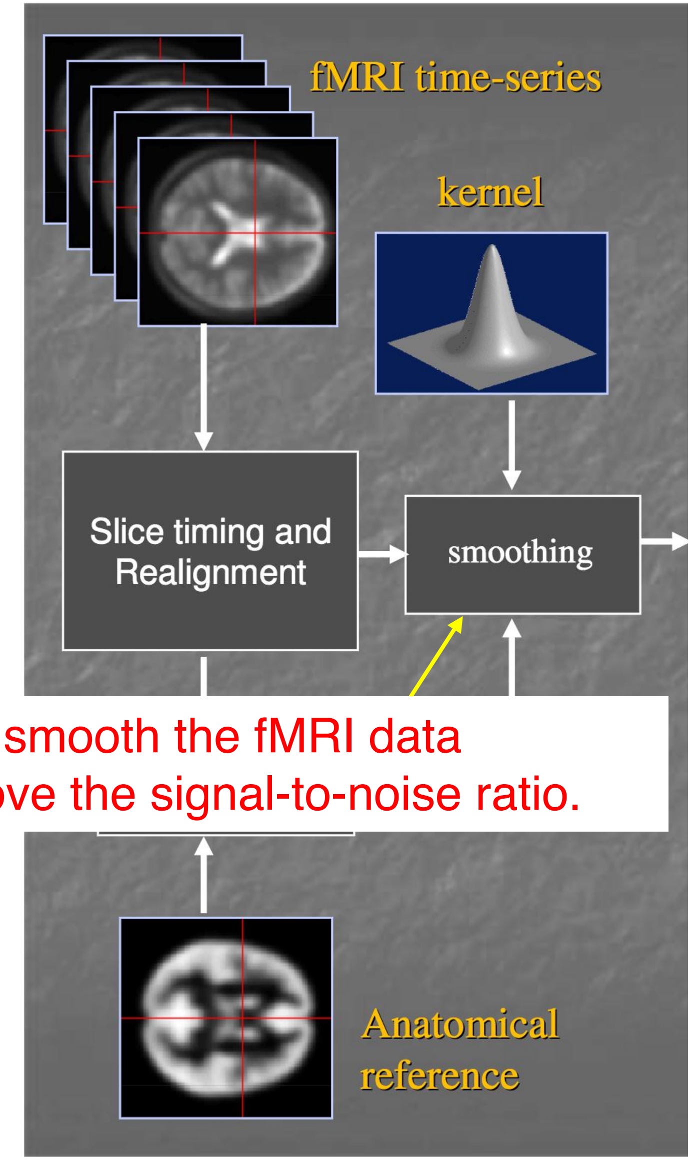




Participants may move in the MR scanner.
Each voxel need to realign to a consistent anatomical point.

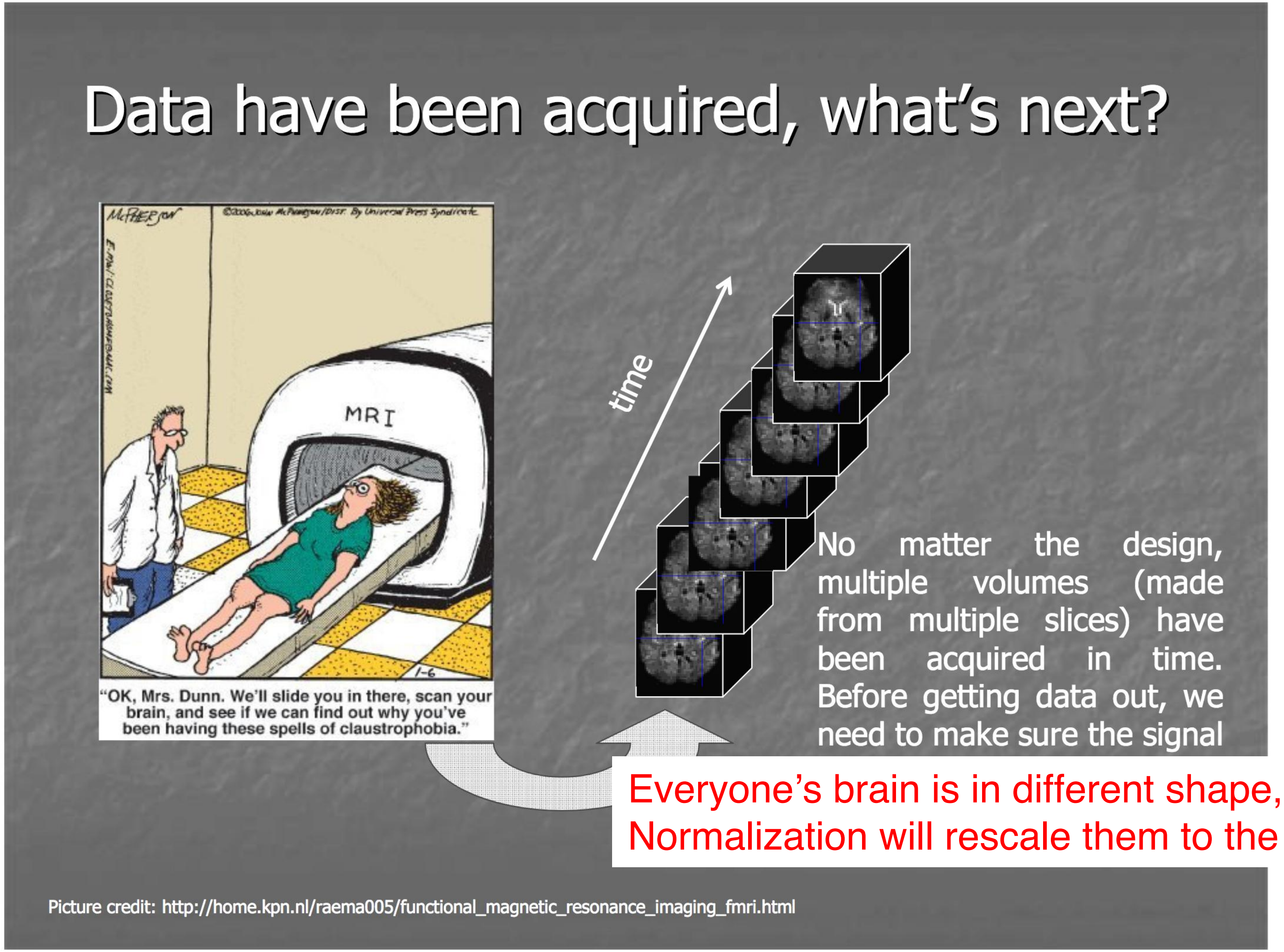
fMRI preprocessing

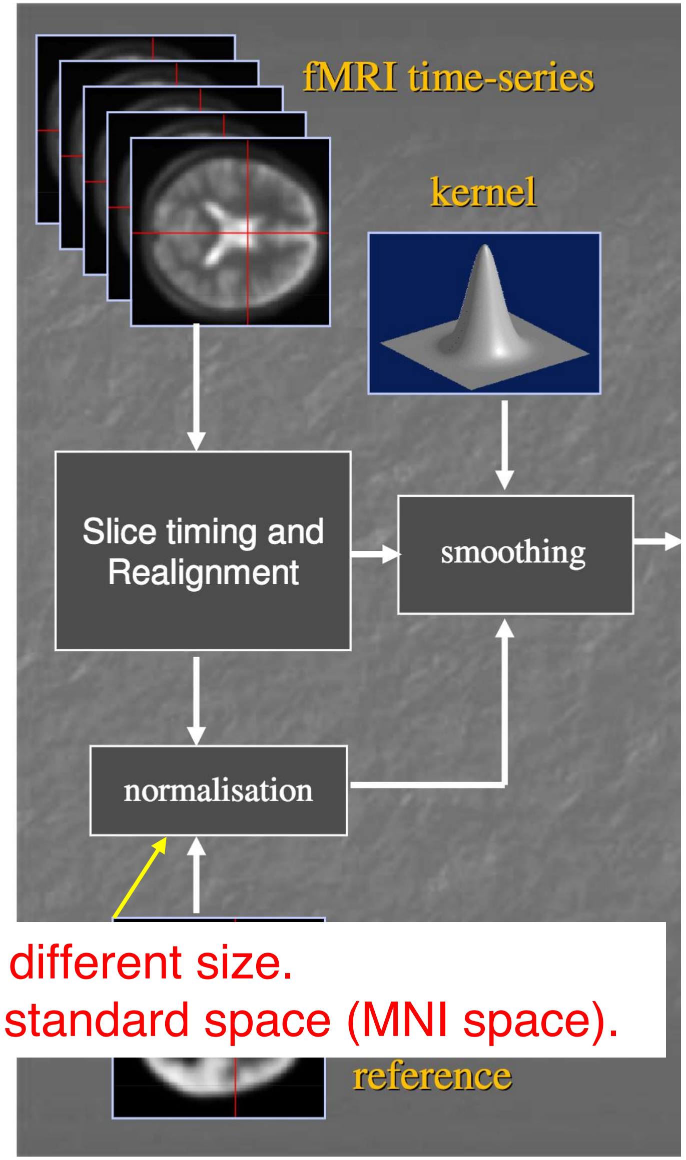




spatially smooth the fMRI data
To improve the signal-to-noise ratio.

fMRI preprocessing

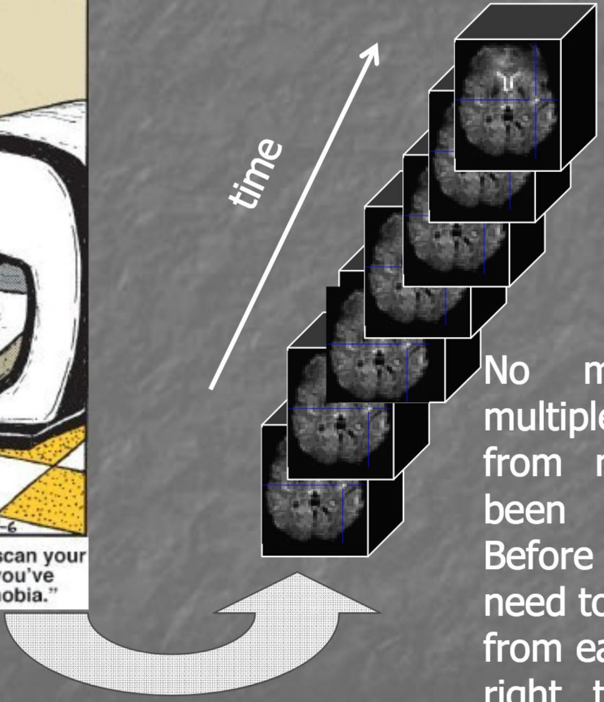




Everyone's brain is in different shape, different size.
Normalization will rescale them to the standard space (MNI space).

fMRI preprocessing

Data have been acquired, what's next?



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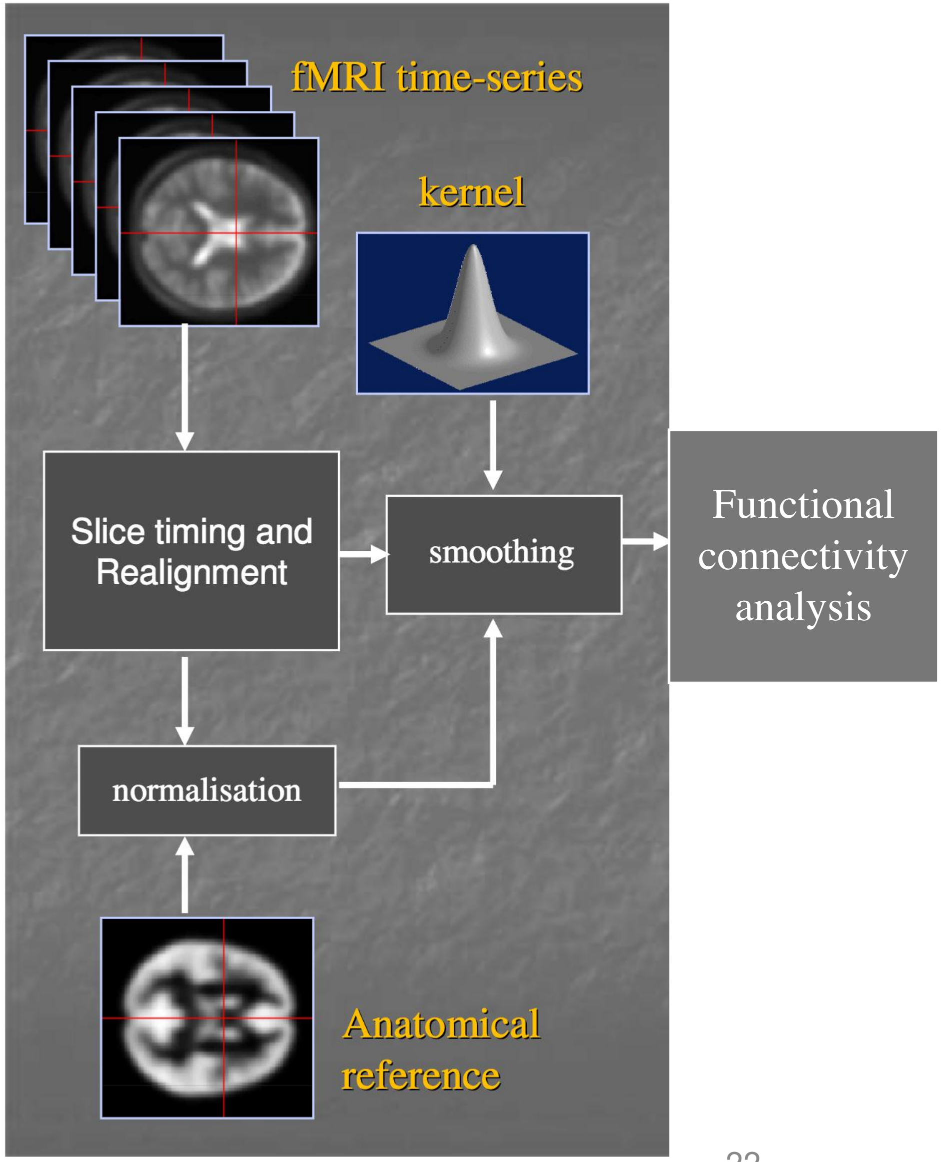

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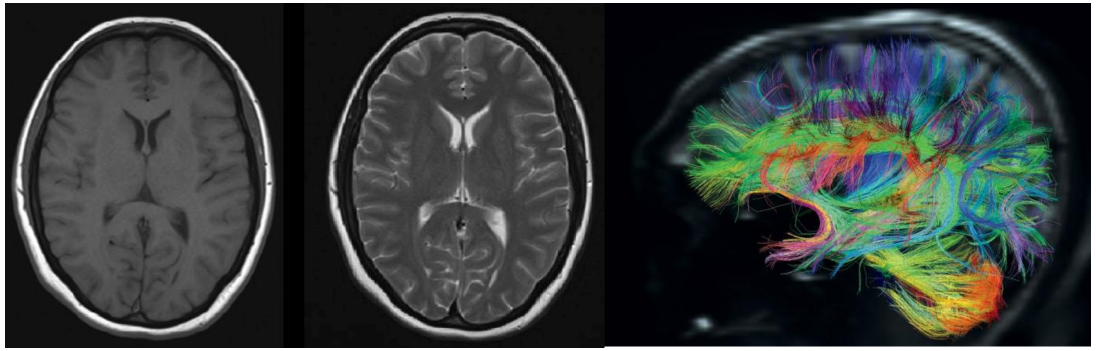
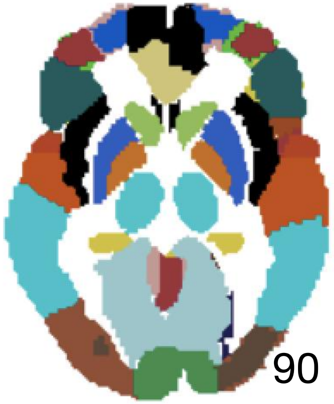


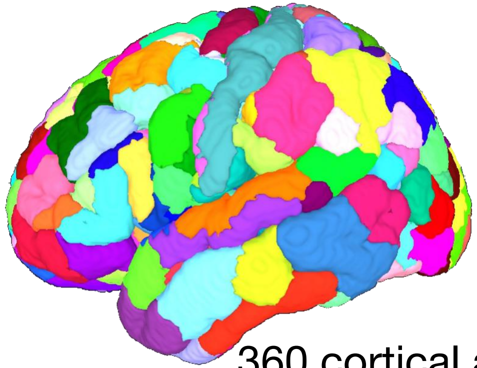
fMRI

AAL atlas



90 regions

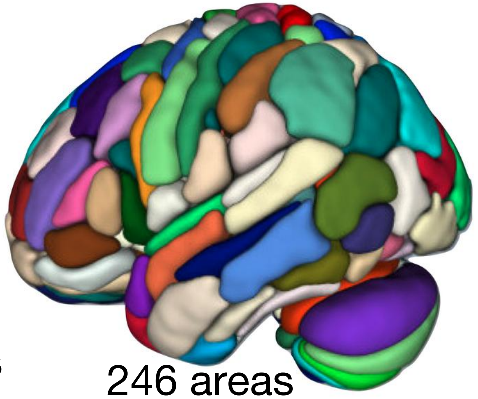
HCP-MMP atlas



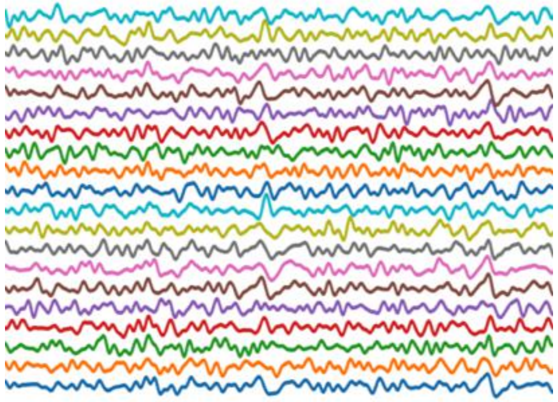
360 cortical areas

Glasser et al., Nature (2016)

Brainnectome atlas



246 areas



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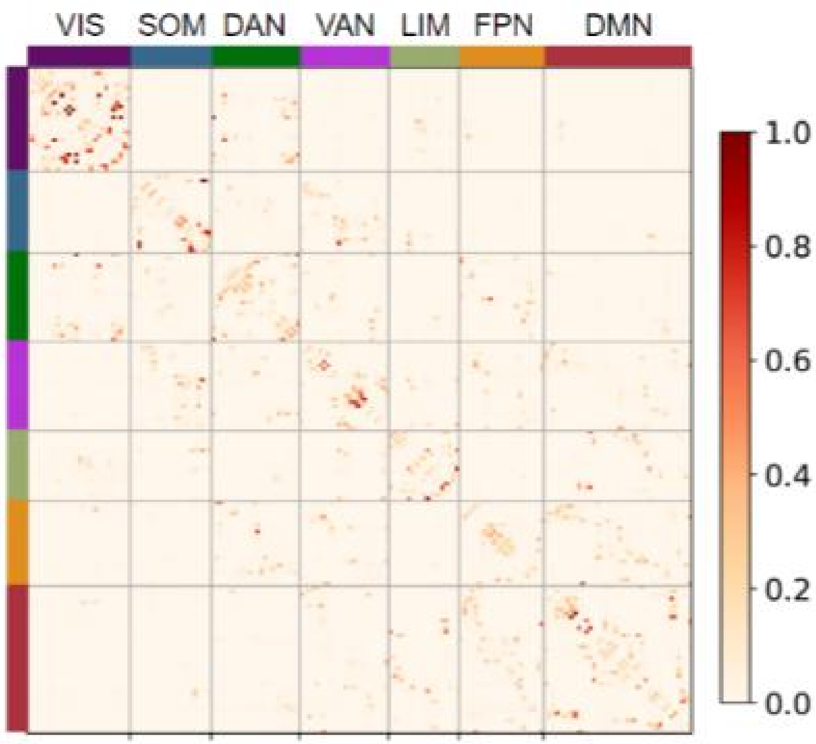
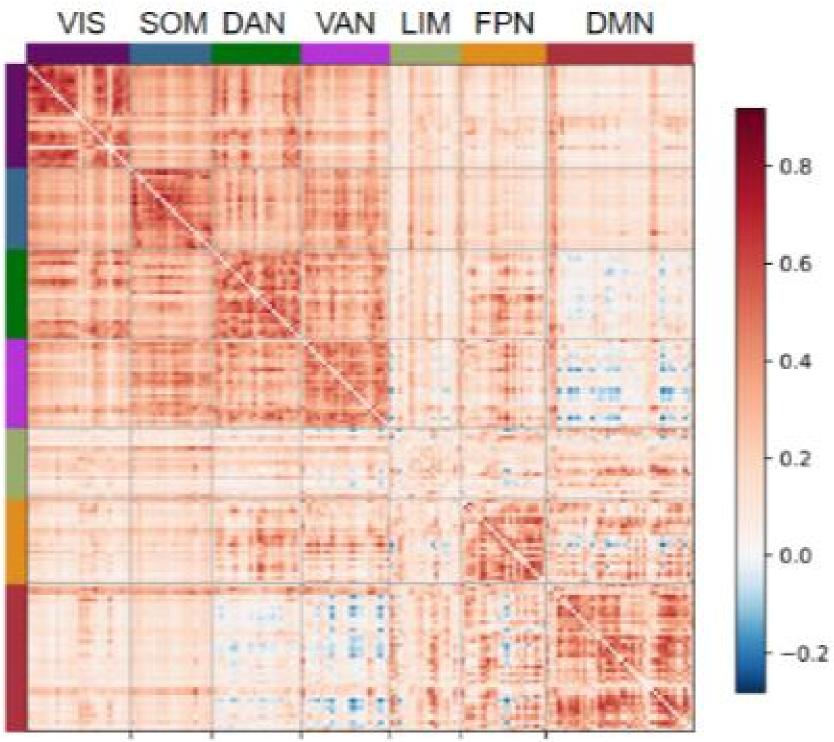


Structural connectivity matrix



Functional connectivity matrix

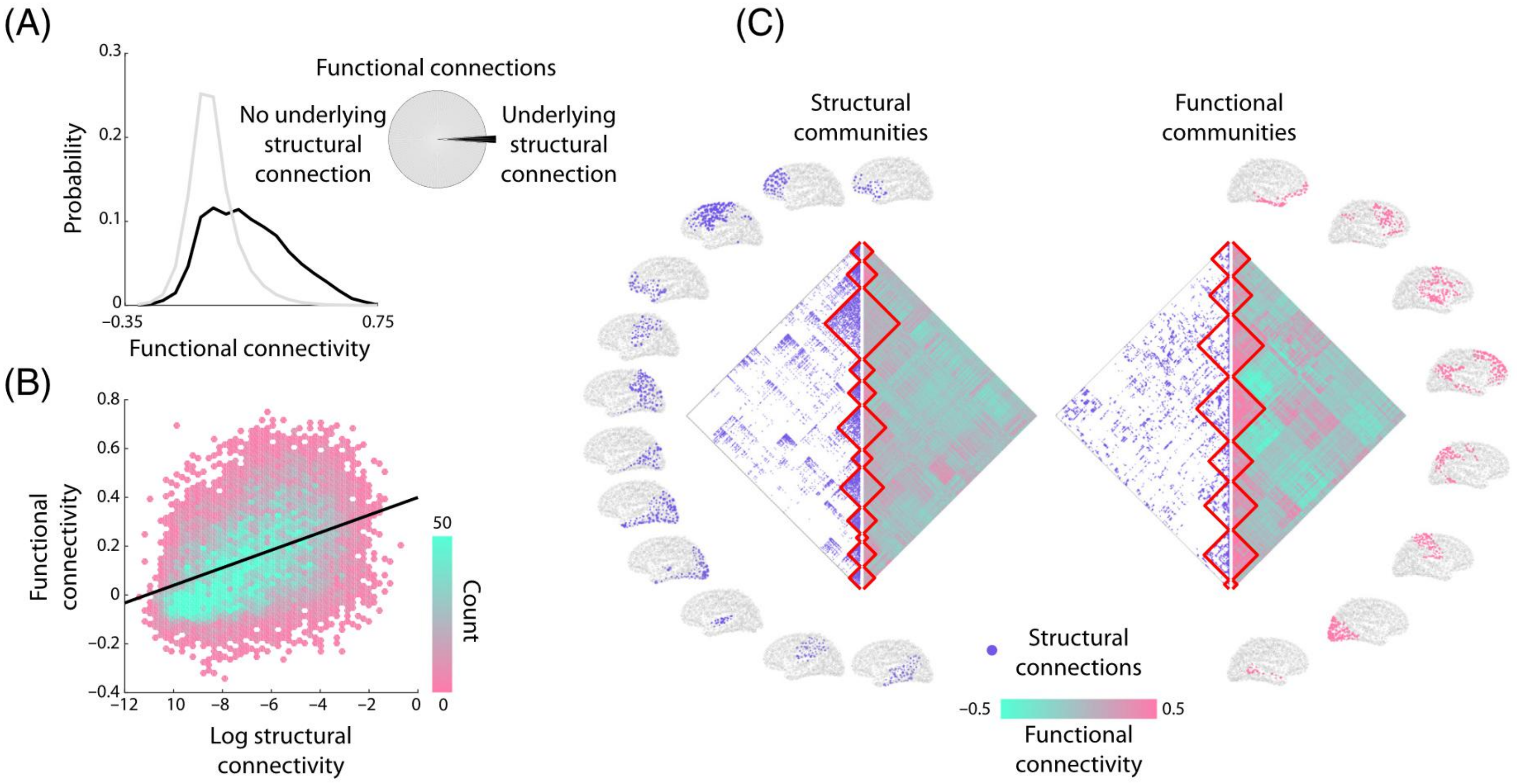
Hands on!

Obtain the Structural Connectome (from DTI)
&
Functional Time Series (from fMRI)

Data & Code: https://github.com/ncclabsustech/NM_workshop

The relationship between brain structure and function

Correspondence between SC and FC



Laura E. Suárez, et al. (2020) Trends in Cognitive Sciences

❑ Functional networks are not a one-to-one reflection of the structural networks. (Tewarie P,et al. NeuroImage, 2020)

How to uncover the higher-order interactions?

How are the higher-order interactions among regions form complex cognitive functions?

- Model-driven methods
- Data-driven methods

Newton's three laws of motion

Newton's first law - If a body is in the state of rest or is moving with a constant speed in a straight line, then the body will remain in the state of rest or keep moving in the straight line, unless and until it is acted upon by an external force.

$$\sum \overrightarrow{F_i} = m\frac{\mathrm{d}\vec{v}}{\mathrm{d}t} = 0$$

Newton's second law - The rate of change of momentum of a body is directly proportional to the force applied on it, and the momentum occurs in the direction of the net applied force.

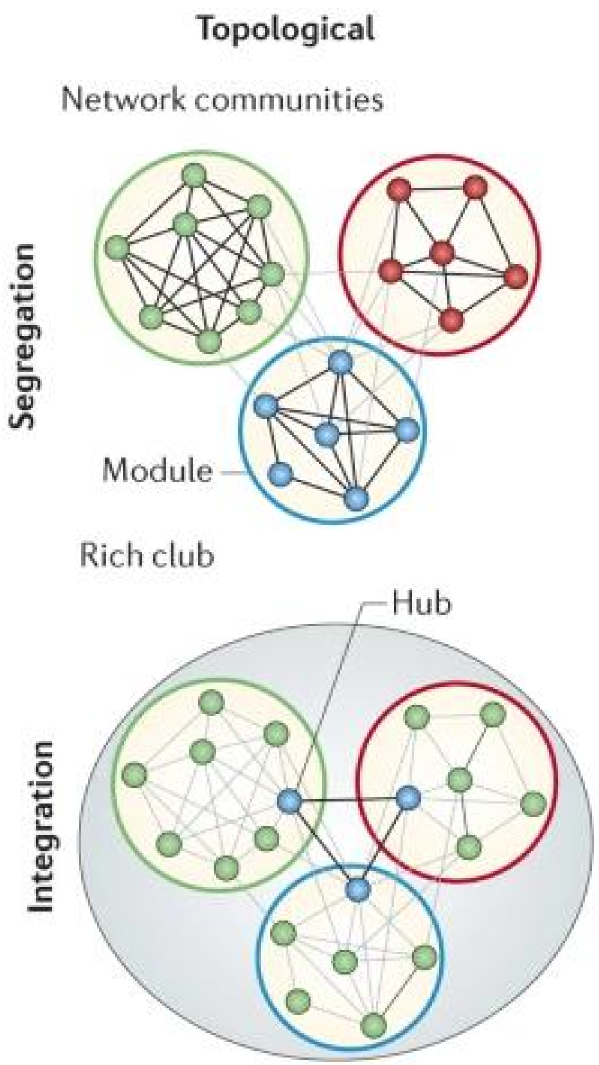
$$\vec{F} = m\vec{a}$$

Newton's third law - To every action, there is always an equal and opposite reaction.

$$\overrightarrow{F_{12}} = -\overrightarrow{F_{21}}$$

Some principles of the brain

- **Structure supports function**: The topology of brain network (network communities and hubs) support functional segregation and integration. (Deco G, et al. Nature Reviews Neuroscience, 2015; Mišić B, et al. Cerebral Cortex, 2016)
- **Anatomical modularity**: each functional module is implemented in a dedicated, relatively small, and fairly circumscribed piece of neural hardware. (Bergeron, Philosophical Psychology, 2007)
- **Optimal wiring:** The layout of neurons in the brain is determined by multiple constraints, including biomorphic and metabolic limitations. (Michael L. Anderson. Behavioral and Brain Sciences, 2010)
- Tradeoffs among efficiency, energy cost, robustness, flexibility...
- Hierachy
- Sparse coding
- ...



Deco G, et al. (2015) Nature Reviews Neuroscience

Q: How to integrate <u>the principles</u> into <u>brain network modeling</u>?

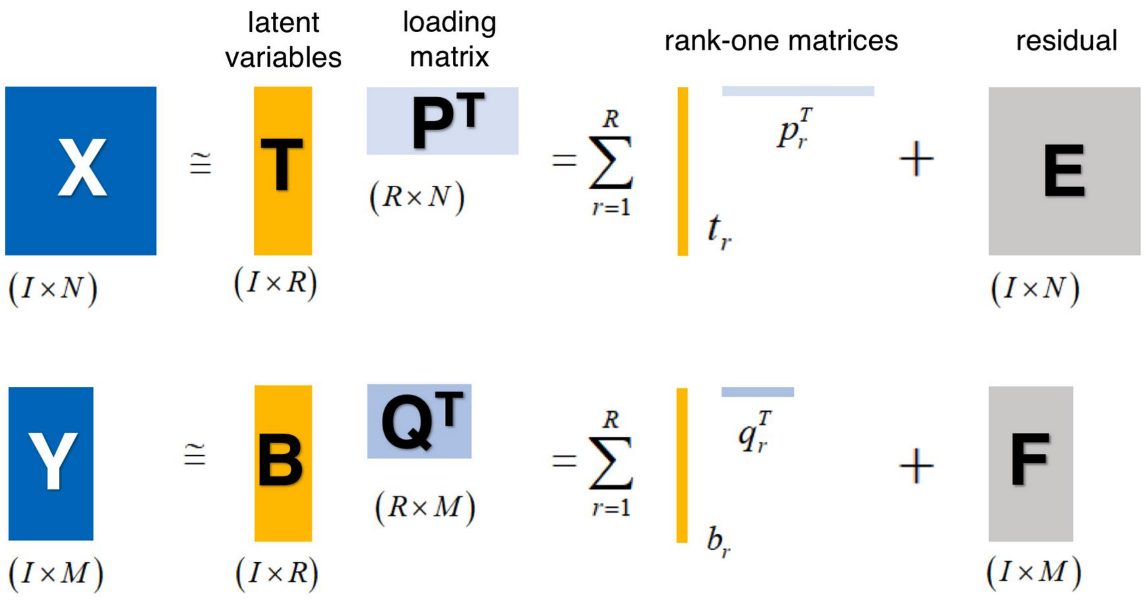
Partial Least Square (PLS) Analysis
to study the relationship of two sets of variables

$$X = TP^T + E = \sum_{r=1}^{R} t_r p_r^T + E$$

$$Y = BQ^T + F = \sum_{r=1}^{R} b_r q_r^T + F$$

$$\max\,[\mathrm{cov}\,(t,b)]^2 = \max_{\{u,v\}}\,[\mathrm{cov}\,(Xu, Yv)]^2 = \max_{\{u,v\}}\,(u^T X^T Y v)^2$$

$$s.t.\ u^T u = 1;\ v^T v = 1$$



PLS is a multivariate statistical method to relate two sets of variables with each other.

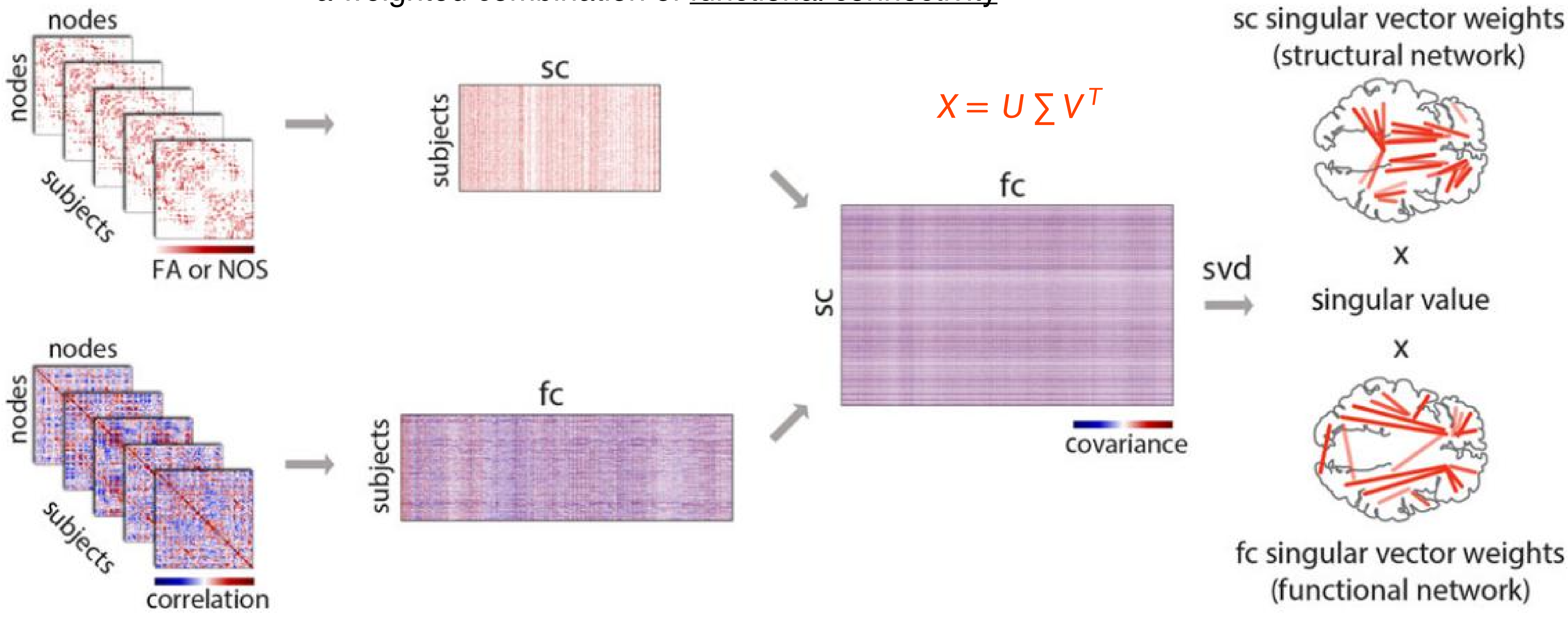
The goal of PLS analysis is to simultaneously find <u>linear combinations</u> of variables in each block that <u>maximally covary with each other</u>.

Yin et al, (2022) arXiv:2208.04324

Partial Least Square (PLS) Analysis to study Structure-Function relationship

A weighted combination of the structural connections and a weighted combination of functional connectivity

$X = U \sum V^T$



Bratislav Mišic et al. Cerebral Cortex, (2016) Network-level structure-function relationships in human neocortex

Some basic backgrounds of linear algebra

Eigendecomposition of a square matrix A: eigenvalues, eigenvectors

For a square matrix $A \in \mathbb{R}^{n \times n}$, its eigenvalue λ and eigenvector $\mathbf{x}$:

$$A\mathbf{x} = \lambda\mathbf{x}$$

For all eigenvalues and eigenvectors, we can derive

$$\begin{aligned} A\left[\mathbf{x}_1\ \mathbf{x}_2\ \ \dots\ \ \mathbf{x}_n\right] &= \left[\lambda_1\mathbf{x}_1\ \lambda_2\mathbf{x}_2\ \ \dots\ \ \lambda_n\mathbf{x}_n\right] \\ &= \left[\mathbf{x}_1\ \mathbf{x}_2\ \ \dots\ \ \mathbf{x}_n\right] \begin{bmatrix} \lambda_1 & 0 & \cdots & 0 \\ 0 & \lambda_2 & \cdots & 0 \\ \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & \cdots & \lambda_n \end{bmatrix} \end{aligned}$$

If the n eigenvalues exist, the eigendecomposition of A is

$$A = S\Lambda S^{-1} \tag{5}$$

Watch Gilbert Strange 22:
https://www.bilibili.com/video/BV1zx411g7gq?p=22

Some basic backgrounds of linear algebra

Singular value decomposition (SVD) of <u>any</u> matrix X (or its demeaned matrx HX)

- **Singular Value Decomposition** (SVD) on the matrix HX

$$HX = U\Sigma V^T \tag{3}$$

$$U^T U = \mathbf{I}_p, \quad V^T V = VV^T = \mathbf{I}_p, \quad \Sigma = diag([\sigma_1, \ldots, \sigma_p])$$

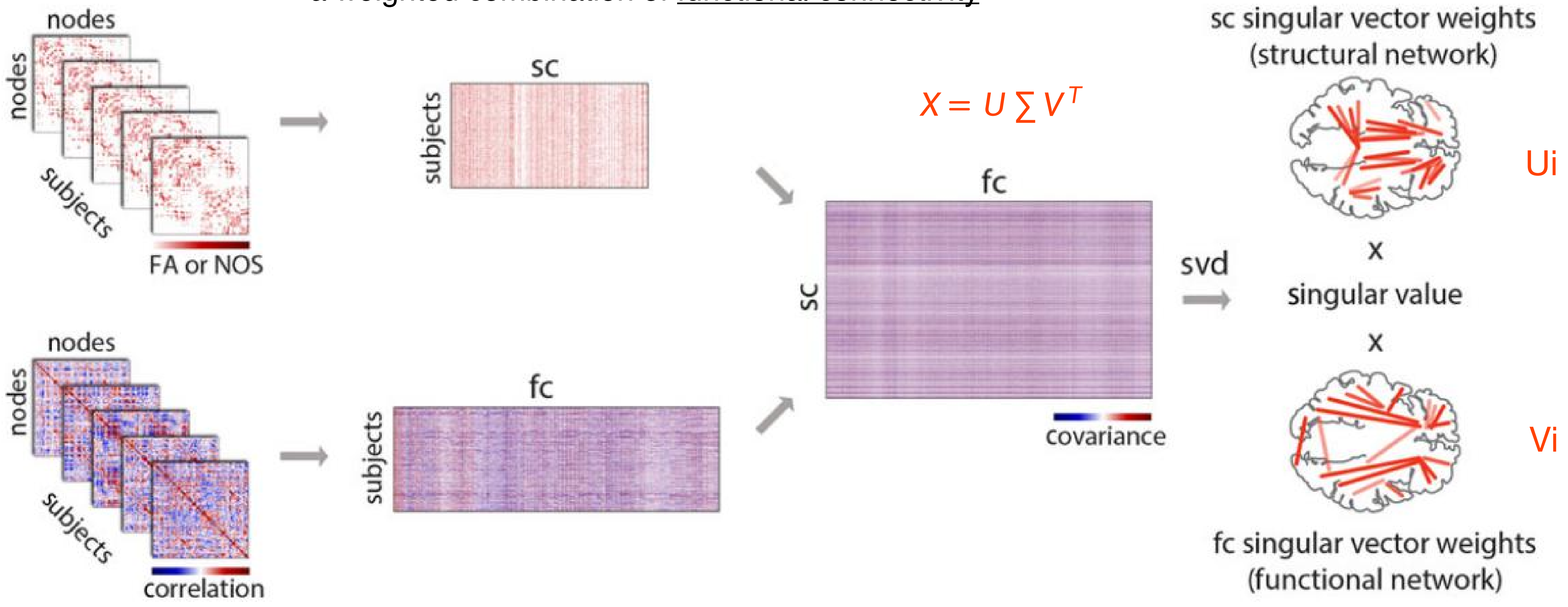
- Substitute Eq. (3) to the covariance matrix S, we derive

$$\begin{aligned} S &= \frac{1}{N}\mathbf{X}^T HH^T \mathbf{X} = \frac{1}{N}(HX)^T(HX) \\ &= \frac{1}{N}(U\Sigma V^T)^T U\Sigma V^T = \frac{1}{N} V\Sigma U^T U\Sigma V^T \\ &= \frac{1}{N} V\Sigma^2 V^T \Longrightarrow \text{Eigendecoposition of } S \end{aligned} \tag{4}$$

Watch Gilbert Strange 30:
https://www.bilibili.com/video/BV1zx411g7gq?p=30

Partial Least Square (PLS) Analysis to study Structure-Function relationship

A weighted combination of the <u>structural connections</u> and
a weighted combination of <u>functional connectivity</u>



Bratislav Mišic et al. Cerebral Cortex, (2016) Network-level structure-function relationships in human neocortex

Hands on!

Partial Least Square (PLS) Analysis
to study Structure-Function relationship

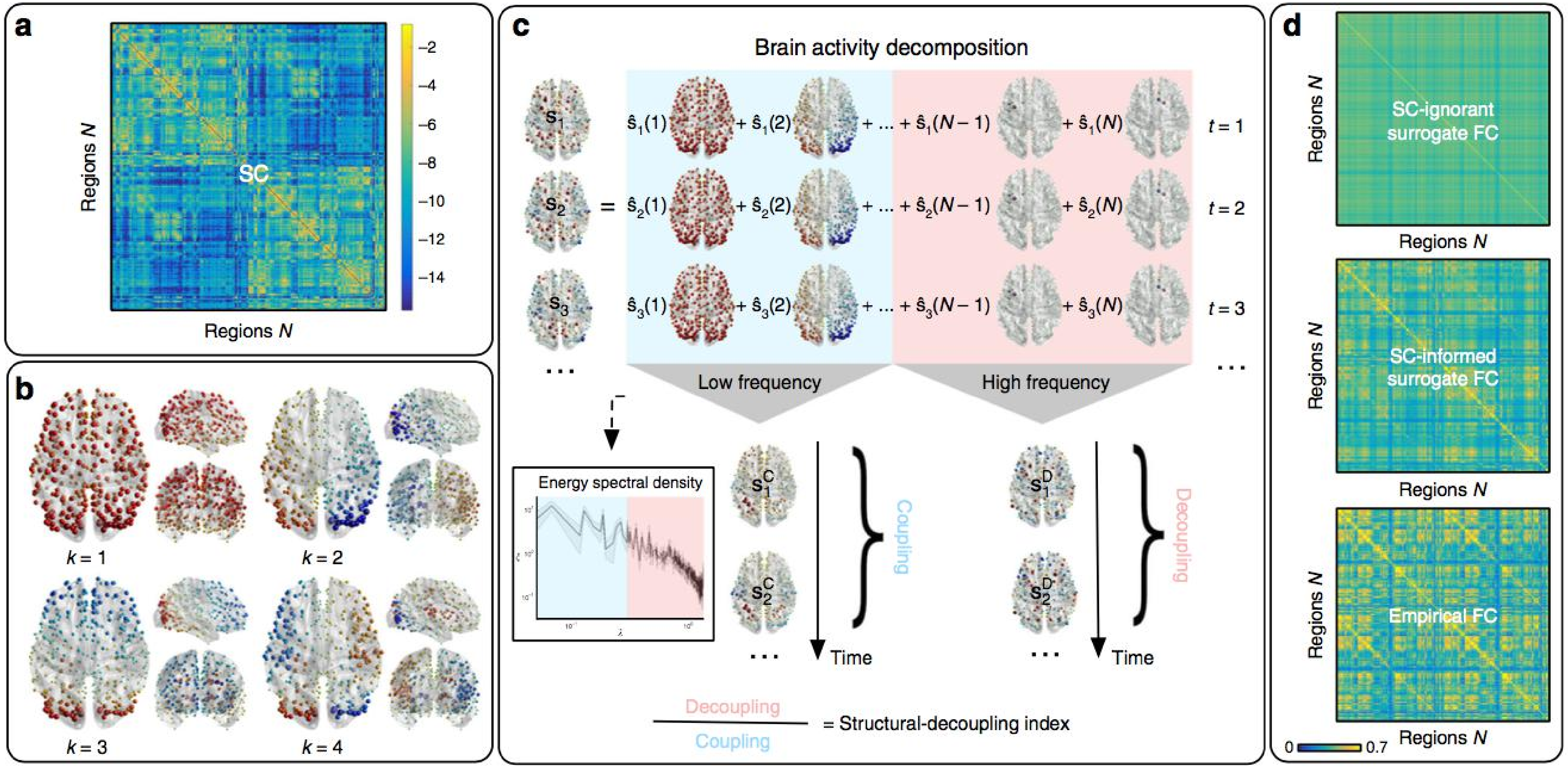
Bratislav Mišic et al. Cerebral Cortex, (2016) Network-level structure-function relationships in human neocortex

Brain activity couples with Structural Connectome

Brain activity at every time point t (s_t) is written as a linear combination of eigenvectors.

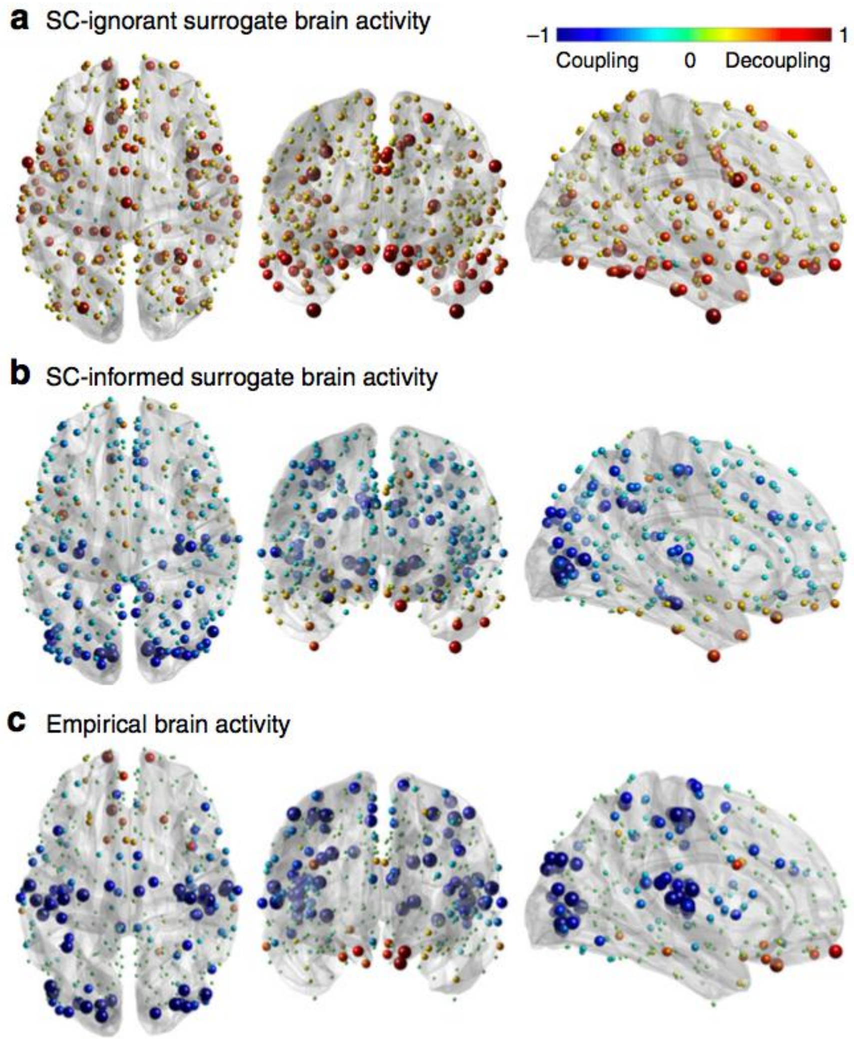
Structural connectome (SC)

SC eigen decomposition



Maria Giulia Preti et al. Nature Communications, (2019) Decoupling of brain function from structure reveals regional behavioral specialization in humans

Brain activity couples/detaches with Structural Connectome



Two different patterns emerge:

- Functional activity significantly couples with the structural connectome

  (Primary sensory and motor networks)

- Functional signals detach from the structure, identifying a high-level cognitive network

  (orbitofrontal, temporal, parietal areas)

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Bridging the series expansion and eigenmode approaches

The existing theory supports that:

(1) Functional networks can be explained by a Taylor series expansion of the structural network, which we refer to as the series expansion approach.

(2) Functional networks can be explained by a weighted combination of the eigenmodes of the structural network, which is the so-called eigenmode approach.

Bridging the series expansion and eigenmode approaches

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(1) Series expansion approach

W : functional connectivity matrix

A : structural connection matrix

$$W \approx \sum_{m=1}^{d} \frac{c_m}{\|A^m\|_2} A^m$$

$$\Big\Downarrow \quad A^m = VD^mV^T$$

$$W \approx \sum_{m=1}^{d} \frac{c_m}{\|A^m\|_2} VD^mV^T$$

(2) Eigenmode approach

$$W \approx VSV^T$$

Combining (1) and (2) $\quad S \approx \sum_{m=1}^{d} \frac{c_m}{\|A^m\|_2} D^m$

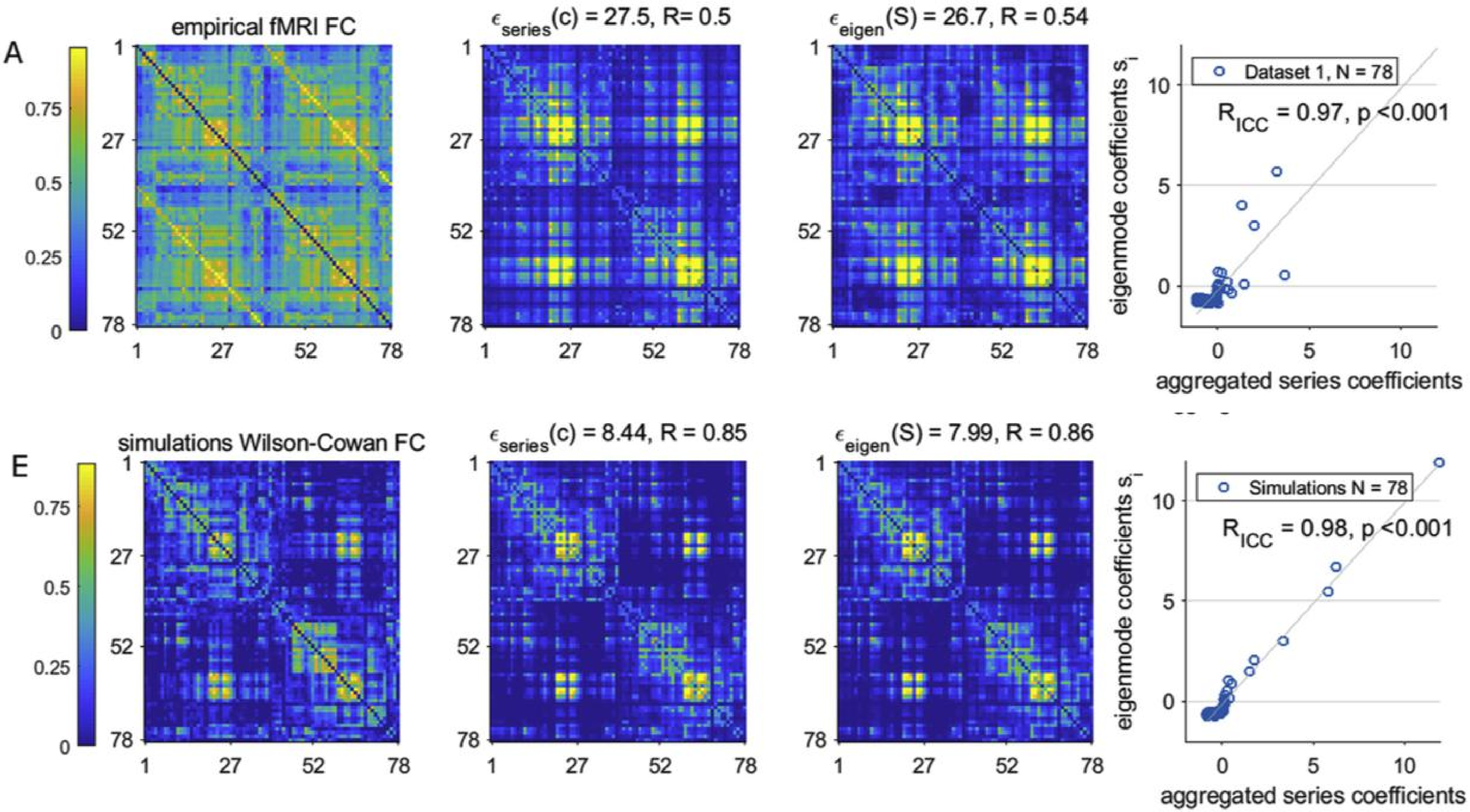
It becomes an optimization problem to learn the coefficient vector c.

$$\varepsilon_{series}(c) = \left\| W - \sum_{m=1}^{d} \frac{c_m}{\|A^m\|_F} VD^mV^T \right\|_F$$

$$\varepsilon_{eigen}(S) = \left\| W - VSV^T \right\|_F$$

(Prejaas Tewarie et al. NeuroImage, 2020)

Bridging the series expansion and eigenmode approaches



$$S \approx \sum_{m=1}^{d} \frac{c_m}{\|A^m\|_2} D^m$$

(Prejaas Tewarie et al. NeuroImage, 2020)

Hands on!

Python Implemenation of Structural-Decoupling Index

Maria Giulia Preti et al. Nature Communications, (2019) Decoupling of brain function from structure reveals regional behavioral specialization in humans

A fusion model to bridge brain structure and function

Some principles from neuroscience

1. There is psychological and physiological evidence for parts-based representation in the human brain (E. Wachsmuth et al. Cerebral Cortex,1994; Deng Cai et al. TPAMI, 2011)

   (Nonnegative Matrix Factorization) Nonnegative constraints lead to a parts-based representation because they allow only additive (not subtractive) combinations.

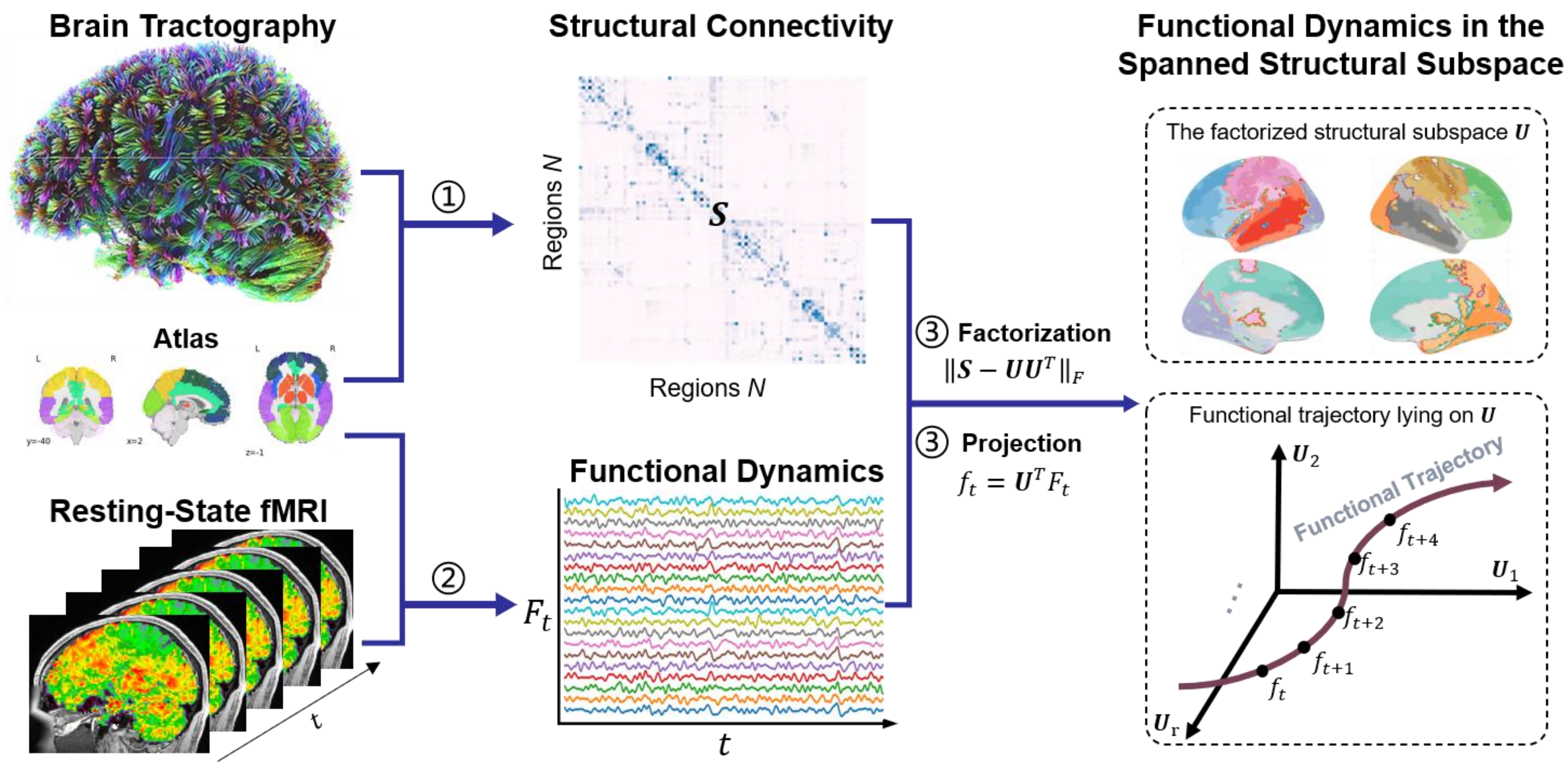
2. Segregation and integration in the brain. Human brain is a small-world network that is structured around spatially distributed communities with local computations, and the integration of the segregated information with network hubs ensure efficient information integration.

   (Orthogonality) (Deco et al. 2015).

3. Brain functional networks are shaped and constrained by the underlying structural network (George C O'Neill et al. Neuroimage,2018; Prejaas Tewarie et al. NeuroImage, 2020)

   (Matrix Projection) Brain functional dynamics are embedded in underlying structural spaces.

A fusion model to bridge brain structure and function



Some variables in model:

U: structure space

F_t: functional state dynamics
f_t: projected functional state

A_i: transitioin matrix to capture information flow

We define a joint optimization problem.

Constrain the functional dynamics into the structure basis space *U*.

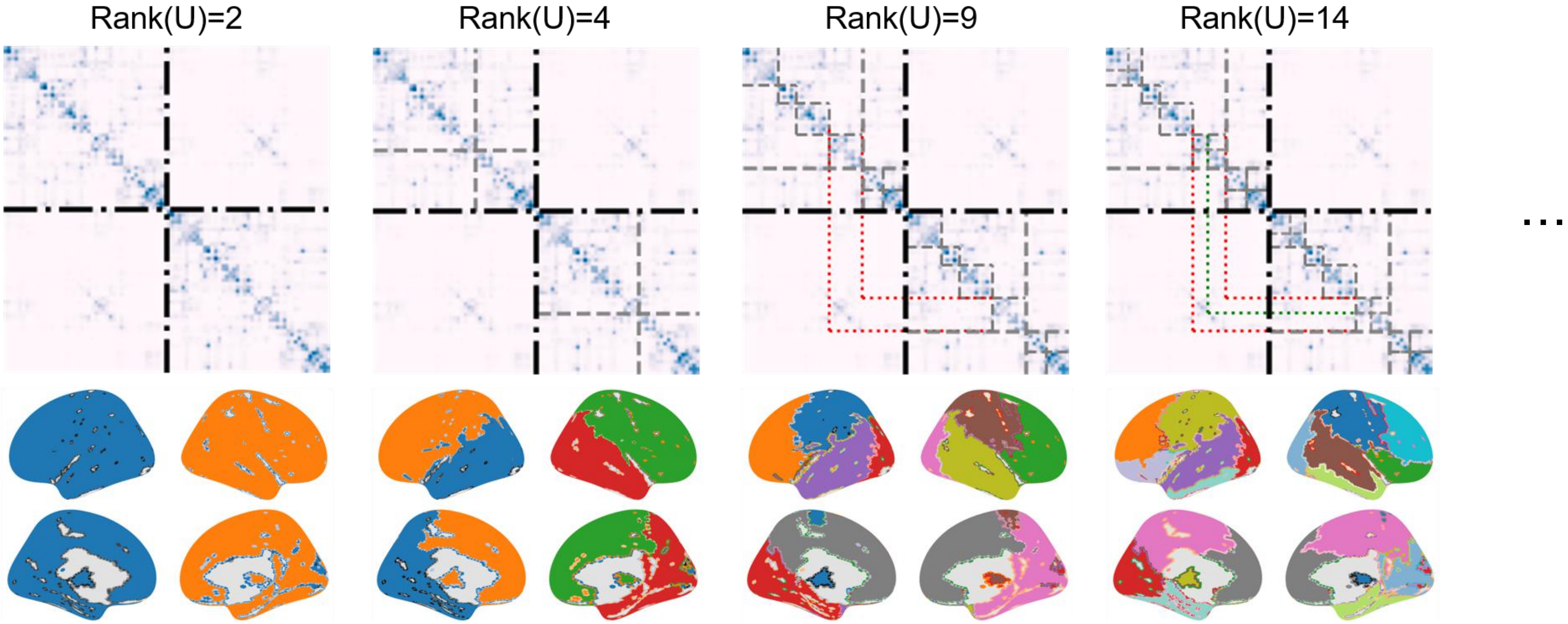
$$\min_{U,A} \sum_{t=1}^{T_{len}} \left\| U^T F_t - \sum_{i=1}^{n} A_i U^T F_{t-i} \right\|_F^2 + \lambda \left\| UU^T - S \right\|_F^2$$

$$\text{s.t. } U^T U = I_r, \qquad rank(U) = r$$

$$U_{i,j} \geq 0 \quad i \in [1, N] \text{ and } j \in [1, r].$$

(Liang et al. in prep)

Results: Hierarchical structural subspace representation



Left & right hemisphere

Anterior & Posterior

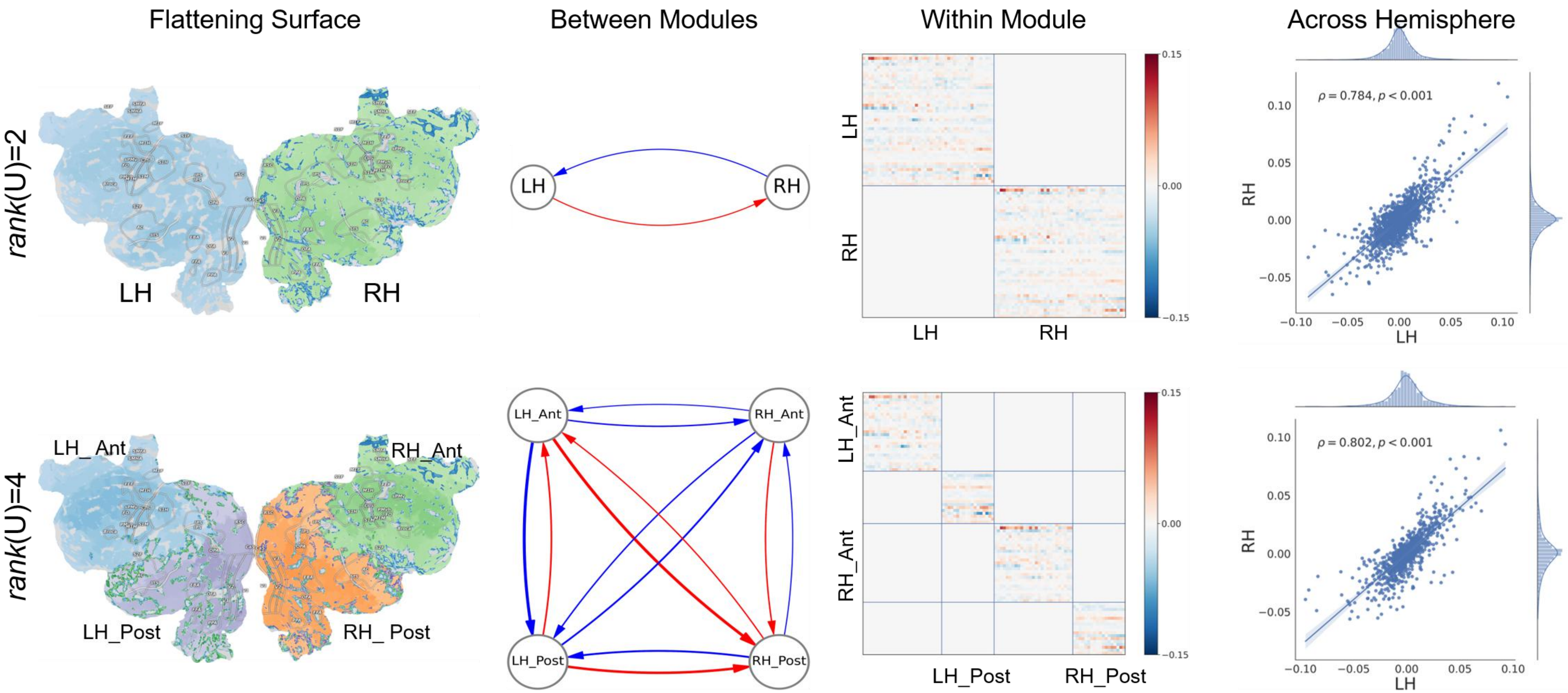
Frontal, Parietal, Temporal, Occipital and Medial side

More complex hierarchical structure

- Increasing rank(U), the representation of structural subspace shows the complex hierarchical structural arrangement.

(Liang et al. in prep)

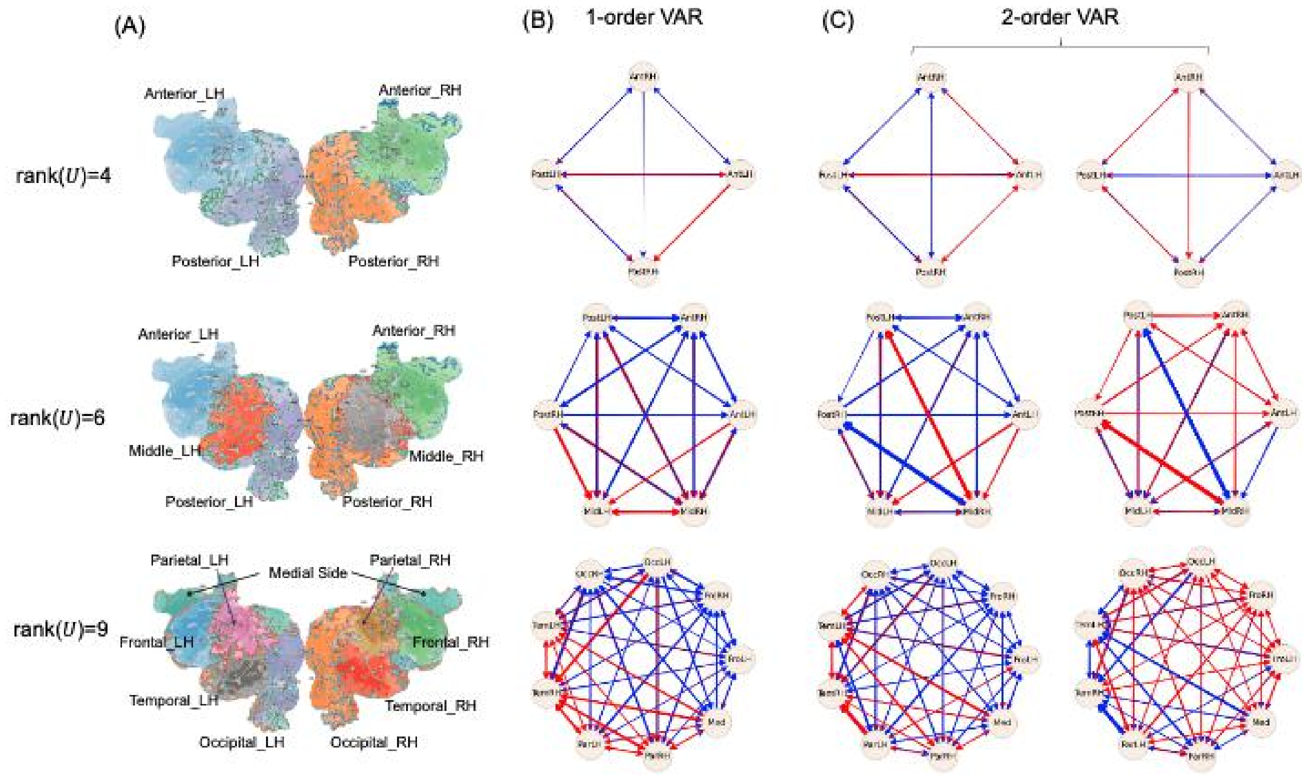
Results: Functional integration within & cross segregated modules



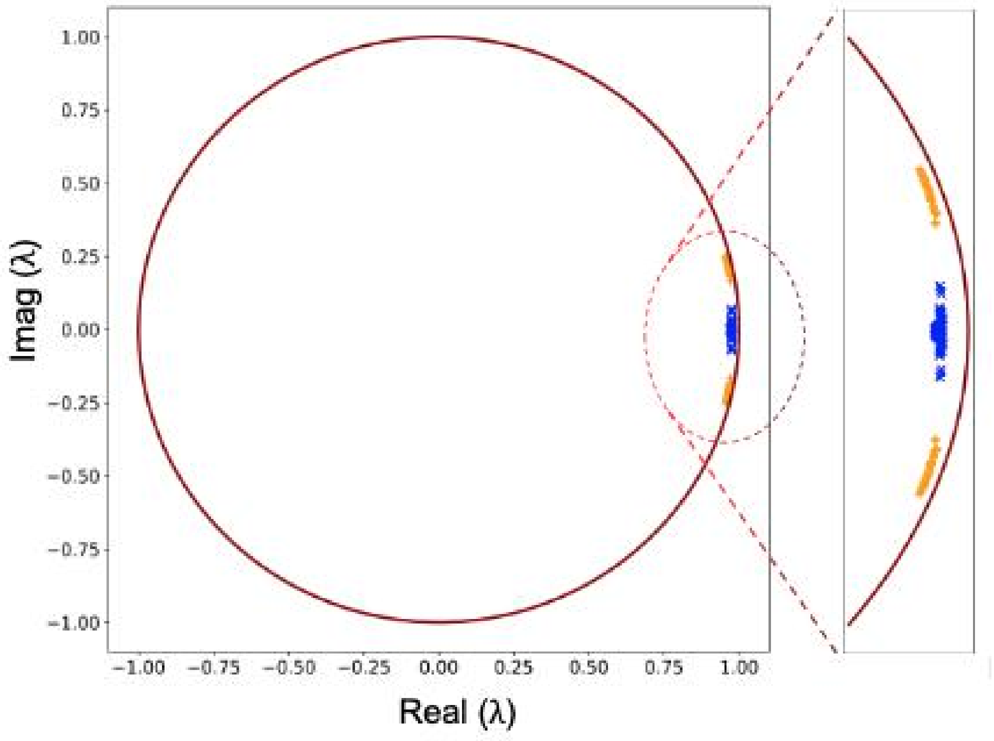
- Functional integration at the different hierarchical layers of structural subspace have both excitatory and inhibitory connections.
- Functional integration shows similarity across hemispheres.

(Liang et al. in prep)

Results: State transition A and its eigenvalue distribution



LH: Left Hemisphere RH: Right Hemisphere
Ant: Anterior Post: Posterior Mid: Middle Med: Medial Side Cortex
Fro: Frontal Cortex Occ: Occipital Cortex Par: Parietal Cortex Tem: Temporal Cortex



- The state transition is characterized by the matrix A.
- The distribution of eigenvalue of A suggests that the human brain is stable, critical.

(Liang et al. in prep)

Model-driven approach

fusion models

Brain structure (T1, T2, DTI images) ⟷ **Brain functional dynamics** (~10^{12} neurons, ~10^{2} brain regions)

- Series expansion of SC: Functional networks can be explained by a Taylor series expansion of the structural network.
- Eigenmode decomposition of SC: Functional networks can be explained by a weighted combination of the eigenmodes of the structural network.
- Nonnegative Matrix Factorization of SC: Nonnegative constraints lead to a parts-based representation for they allow only additive combinations.
- Matrix Projection: Embedding brain functional dynamics into the underlying structural space.
- Structural subspace: The factorization results show the hierarchical topological arrangement with rank(U) increasing.

Hands on!

1. Pytorch tutorial of Numerical Optimization
2. Pytorch implementation of our methods

$$\mathcal{L}(\beta) = \frac{1}{n}\sum_{i=1}^{n}\left(y^{(i)} - \beta x^{(i)}\right)^2$$

$$\min_{U,A} \sum_{t=1}^{T_{len}} \left\| U^T F_t - \sum_{i=1}^{n} A_i U^T F_{t-i} \right\|_F^2 + \lambda \left\| UU^T - S \right\|_F^2$$

$$\text{s.t. } U^T U = I_r,$$

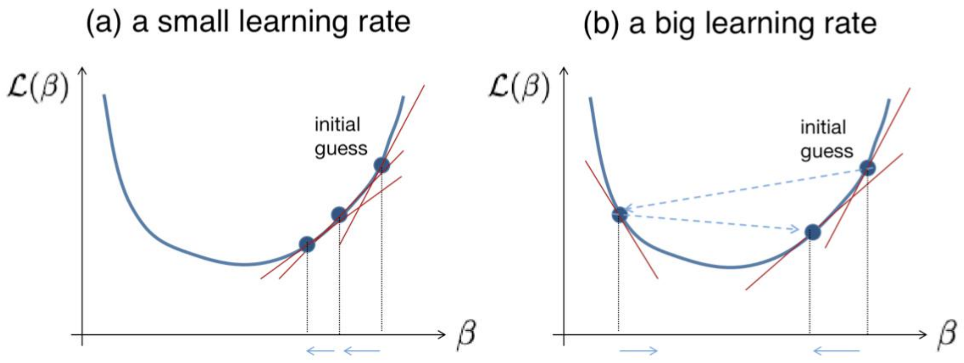
$$U_{i,j} \geq 0 \quad i \in [1, N] \text{ and } j \in [1, r].$$

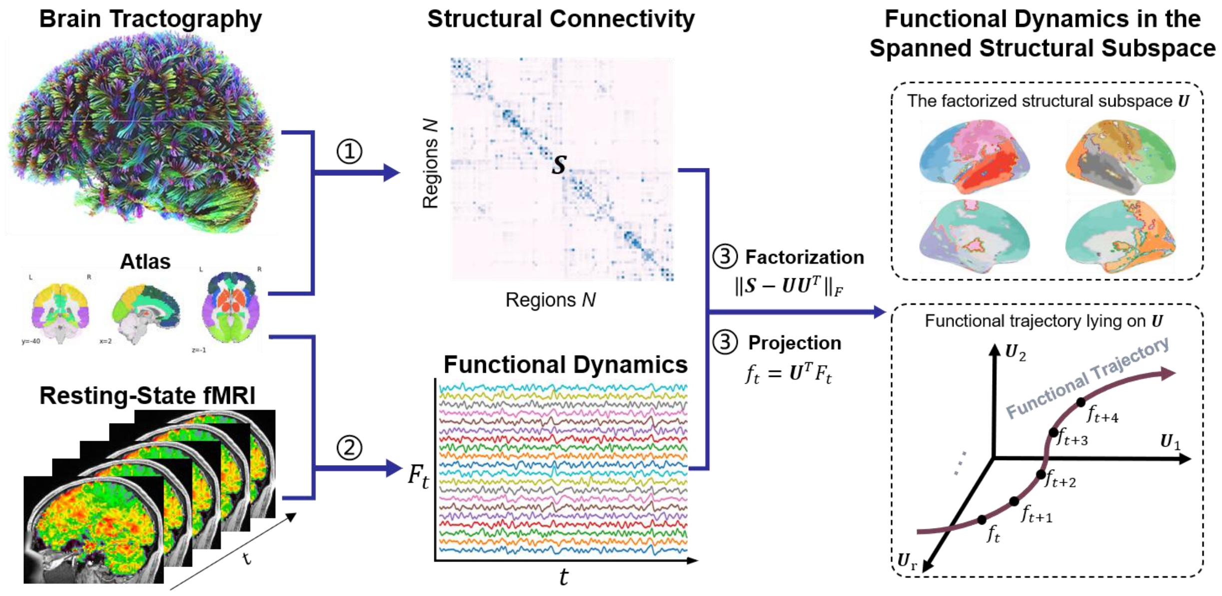
- Analytical solution
- Numerical solution with gradient descent

Update rule:

$$\beta^{(j+1)} \longleftarrow \beta^{(j)} - \eta \frac{d\mathcal{L}(\beta)}{d\beta}. \tag{5}$$

Here η is the *learning rate*.
Choosing a good η is important: (i) too small – slow convergence; (ii) too large – divergence.





Hands on!

1. Pytorch tutorial of Numerical Optimization
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Summary

➢ Theory session (Brain network modeling)

- Basic concepts of neuroimages: T1/T2, DTI, fMRI, and their processing pipeline
- Brain network modelling: Structural/functional/effective network
- Structure-function modelling: bridging the brain structure and functional dynamics

➢ Hands-on session (interlacing with theory session)

1. Data analysis pipeline: obtain structural connectome (DTI) and functional series (fMRI)
2. Brain network modelling:
   - Partial Least Square (PLS) Analysis to study Structure-Function relationship
   - Python Implemenation of Structural-Decoupling Index
3. Our fusion optimization method

Download the Data & Code: https://github.com/ncclabsustech/NM_workshop

Model-driven methods: Pros vs Cons

"All models are wrong, but some are useful."

——By George E. P. Box

Pros

1. White-box: model-driven methods are designed with consideration of the optimization objectives, neural mechanism and neuroscience priors.
2. Integration of neuroscience knowldge and statistical priors in model-driven methods supports interpretability of results.

Cons:

1. Limited by the weak expressive power of simple models, performance of model-driven methods is usually not as good as deep learning.
2. The results and findings from the inaccurate models could be wrong.

Ads: BI&AI course on bilibili (for free)

https://space.bilibili.com/544658986/channel/collectiondetail?sid=699874

1: Introduction
2: Visual system
3: CNN (GD, BP, hands-on)
4: What do neurons learn?
5: Auditory system
6: Somatosensory system
7: EEG analysis
8: EEG analysis hands-on
9: Motor system 1
10: Motor syste, 2
11: Data for deep learning
12: Emotion in brain & Ai
13: language processing
14: sleep & dreaming
15: RNN
16: fMRI hands-on
17: Brain structure, function & behavior
18: Neuromodulation

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Southern University of Science and Technology

NEURAL COMPUTING CONTROL
NCC Lab
Neural Computing & Control lab

Achknoledgements

Zhichao Liang (梁智超)

All members in NCC lab

Thank you for your listening.

Thank Prof. Jixing Li for hosting the workshop.

NCC lab的微信公众号

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