Methods for combining structural and functional connectivity

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Introduction

• MRI powerful tool to study brain connectivity
  - Diffusion MRI → structural connectivity
  - (BOLD, ASL, VASO) fMRI → functional connectivity

• Structural connectivity (SC):
  - Pathways that form the brain’s physical communication network

• Functional connectivity (FC):
  - Synchronisation of neural activity between different neuronal populations

• FC likely facilitated by SC:
  - Degree of correspondence (Honey et al, PNAS 2009)
  - SC plays important role in shaping FC patterns
**SC-FC relationship**

*Predicting human resting-state functional connectivity from structural connectivity*

C. J. Honey, S. Sporns, L. Connors, A. Gigandet, J. P. Thiran, R. Meuli, and P. Hagmann

SC partially predicts FC
(for non-zero SC edges)

FC more reliable if direct SC


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- **FC likely facilitated by SC:**
  - degree of correspondence (Honey et al, PNAS 2009)
  - SC plays important role in shaping FC patterns
  - SC-FC mapping imperfect (e.g. indirect connections, network dynamics, etc)
  - Analogy (Nakagawa et al, NeuroImage 2013): connectome → “road system”

Traffic volume (FC) and street size (SC) are closely related in the long run, but depend much more on the dynamics of the population on shorter time scales
Introduction

• SC & FC: most often considered independently

• Increased interest in combining SC-FC information

• Structural-functional connectivity
  - Superposition of (independent) results → qualitative/quantitative analysis
  - SC-FC correlation of (independent) results
  - FC guides SC: FC results as seed/target for fibre-tracking

Greicius MD et al, Cereb Cortex 19:72-78 (2009)

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  - FC guides SC: FC results as seed/target for fibre-tracking
  - SC guides FC: SC results for seed-based FC
  - FC modelling based on SC

- SC-FC relationship: modelling

  BOLD data correlation
  → Measured FC matrix
  → Simulated FC matrix
  → Modelling (Neural mass model + Balloon-Windkessel model)

• FC modelling: SC partially predicts FC

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• Increased interest in combining SC-FC information
• Structural-functional connectivity
  ➢ Superposition of (independent) results → qualitative/quantitative analysis
  ➢ SC-FC correlation of independent results
  ➢ FC guides SC: FC results as seed/target for fibre-tracking
  ➢ SC guides FC: SC results for seed-based FC
  ➢ FC modelling based on SC
• SC-FC combined at earlier stages
  ➢ Joint analysis
  ➢ Enable better integration

Joint SC-FC analysis: Example 1

• Blind data-driven approaches:
  ➢ e.g. multimodal canonical correlation analysis + joint ICA (mCCA+jICA)

  GLM task-associate network

  Limitation: based on DTI features

Joint SC-FC analysis: Example 2

- Activated Fibres (AF) method:
  - Associate dynamic FC to fibres → GLM analysis → regions of activation


Joint SC-FC analysis: Example 3

- Anatomically-weighted FC (awFC):
  - FC ‘distance’ scaled by (ad-hoc) SC weight

Joint SC-FC analysis: Example 4

- Bayesian-based method:
  - e.g. SC used as prior

Joint SC-FC analysis: Example 5

- Multilayer network approach:
  - Structural layer and functional layer $\rightarrow$ assess interaction between layers
Joint SC-FC analysis: our approach

- **Track-weighted imaging (TWI):** combine tractogram with image/map

  ![Tractogram](image1)
  ![Map A](image2)
  ![TWI Map A](image3)

- Assign ‘weighting’ to each track
- ‘weighting’ → values of map at track coordinates
  - Flexible (user defined) choice: metric, extent, etc.
- TWI intensity: combine ‘weighting’ for all tracks in voxel
  - Flexible (user defined) choice: metric, scalar vs. higher-order, etc.
- Super-resolution properties

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Joint SC-FC analysis: our approach

- **Track-weighted imaging (TWI):** combine tractogram with image/map

  ![Tractogram](image1)
  ![Map A](image2)
  ![TWI Map A](image3)

- Joint SC-FC analysis → **specific case of TWI**
  - Map A → functional data

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TWI: structure meets function

- TWI: tool to study structure-functional connectivity
  - Combines structural/functional information

- Two (main) variants:
  1. With specific functional network

- TWI: structure meets function

- TWI: tool to study structure-functional connectivity
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- Two (main) variants:
  1. With specific functional network
  2. Without specific functional networks
Case (1): TW-FC with specific network

- For TW-FC:
  - assign ‘FC weighting’ to each track (sum of DMN values)
  - intensity: mean ‘FC weighting’ of tracks traversing voxel
  - it ‘propagates’ FC information along tracks

TW-fMRI: with specific network

- Any functional network can be used
TWI: scalar vs. fibre-specific

- For any TWI map \(\rightarrow\) with/without orientation averaging in voxel

- Benefits of fibre-specific version
  - Increased specificity
  - Statistics \(\rightarrow\) connectivity-based enhancement (Raffelt et al, NeuroImage 2015)

TWI: structure meets function

Case (2): without specific functional network
TW-FC: without specific network

- Assign to each track a ‘FC weighting’ (cross-correlation)
- Consider also dynamic FC:
  - FC(t) → cross-correlation using sliding window
- TW dynamic FC (TW-dFC):
  - average ‘weighting’ from all tracks in voxel
- For comparison (static) → TW-sFC
  - using full BOLD data (i.e. no sliding window)


TW-dFC: Example

<table>
<thead>
<tr>
<th>Anatomical</th>
<th>TW static FC (no sliding window) 3D image</th>
<th>TW dynamic FC (1 min sliding window) 3D+time image</th>
<th>TW-dFC(_{\text{variation}}) (temporal 95% conf. interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><img src="image1" alt="TW static FC image" /></td>
<td><img src="image2" alt="TW dynamic FC image" /></td>
<td><img src="image3" alt="TW-dFC(_{\text{variation}}) image" /></td>
</tr>
</tbody>
</table>

Seven illustrative time-points of the TW-dFC data-set

TW-dFC: single subject results

- Independent component analysis of the (3D+time) TW-dFC
  - FSL MELODIC

  Example components

- ICA results → parcellation application


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TW-dFC: WM parcellation

- Parcellation example: corpus callosum (CC)
  - Mid-sagittal corpus callosum ROI
  - Identify IC: z>3 and cluster>160 mm²

  Single healthy subject

  Group analysis (n=8)

- It does not rely on cortical parcellation
  - Consistent with previous studies with parcellation specified

TW-dFC: cortical segregation

- WM parcellation $\rightarrow$ track-editing $\rightarrow$ cortical segregation
- ROI-based track-editing
  - isolate tracks that traverse an ROI


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TW-dFC: cortical segregation

- WM parcellation $\rightarrow$ track-editing $\rightarrow$ cortical segregation
- ROI-based track-editing
  - isolate tracks that traverse an ROI

- cortical segregation in data-driven way

Discussion: general

• Structural – functional
  - Many methods
  - Analysed independently
  - One informs/drives the other
  - Joint analysis
  - Advantages/disadvantages

Discussion: TWI

• TW-FC & TW-dFC: methods for SC-FC synergy
  - Fuse structural/functional information into single (3D or 3D+time) quantitative image
  - Super-resolution properties

• TW-FC:
  - Highlights white matter connections of FC network
  - Methodology can be applied to fMRI activation maps (or any other functional network)
**Discussion: TWI**

- **TW-dFC:**
  - more general than TW-FC
    - it does not rely on pre-specifying a network
  - tool to study dynamic FC
  - operates in white matter
    - dynamic FC of GM regions that WM pathways connect
  - constrains the (very large) data
    - only end-to-end track correlation (direct connections)
  - Possible application: tool for parcellation
    - exploits SC + dynamic FC information
    - no assumption of prior cortical segregation