







# Dynamic functional connectivity



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 From stationary to dynamic functional connectivity

- From stationary to dynamic functional connectivity
- Probing the dynamic functional connectivity landscape



- From stationary to dynamic functional connectivity
- Probing the dynamic functional connectivity landscape
  - Traditional sliding window framework



- From stationary to dynamic functional connectivity
- Probing the dynamic functional connectivity landscape
  - Traditional sliding window framework
  - Conceptually innovative directions



- From stationary to dynamic functional connectivity
- Probing the dynamic functional connectivity landscape
  - Traditional sliding window framework
  - Conceptually innovative directions
  - Origins and relevance of dynamic functional connectivity



#### A stationary understanding of brain function

• A bilateral finger tapping experiment started it all...

Finger tapping



(Biswal et al., 1995)

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- A bilateral finger tapping experiment started it all...
  - Probing resting-state voxel-wise synchrony with a seed region
  - Bilateral, symmetric foci with strong seed correlation



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(Biswal et al., 1995)

Functionally relevant resting-state networks co-exist and interact





(Damoiseaux et al. 2006)

#### (Fox et al. 2005)

#### Brain dynamics unraveled

• Within- and cross-network interactions reconfigure over time



(Chang and Glover, 2010)

FC strengt change (+

#### Brain dynamics unraveled

- Within- and cross-network interactions reconfigure over time
- Birth of the dynamic functional connectivity (dFC) field



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#### Sliding window analysis: the simplest dFC tool



(Kucyi et al. 2014)

#### Sliding window analysis: the simplest dFC tool

 More daydreaming = increased FC fluctuations between posterior cingulate cortex and other default mode network regions



(Kucyi et al. 2014)





Optimal window length (W) and window step (S)

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  - W short enough not to miss real dFC fluctuations
  - W long enough to detect only real dFC fluctuations



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 $W > \frac{1}{f_{min}}$  (Leonardi and Van De Ville 2015)



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  - W short enough not to miss real dFC fluctuations
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 Going for more than one window type with a time-frequency analysis



**Cross-magnitude** 

0.75

O 1

**D** 2

× 4 5 🛇  $\nabla 6$ \$ 7

+ 8 ۵۵

p = 0.0013

p = 0.022

0.75

**5**0 Dist

## **Overcoming window limitations**

- Optimal window length (W) and window step (S)
  - W short enough not to miss real dFC fluctuations
  - W long enough to detect only real dFC fluctuations



6 **PECIFICIT** NSITIVIT

- Going for more than one window type with a time-frequency analysis
  - Two facets: cross-magnitude vs cross-phase



#### Playing with the window shape



Playing with the window shape



- Data-driven window definition
  - Detect significant connectivity change points: dynamic connectivity detection (DCD)



(Xu and Lindquist 2015)

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Playing with the window shape



- Data-driven window definition
  - Detect significant connectivity change points: dynamic connectivity detection (DCD)



 Gradually refine pre-built connectivity estimate: dynamic conditional correlation (DCC)

(Xu and Lindquist 2015)











#### Assessing connectivity inside the window

- Using more elaborate measures to assess connectivity
  - Sliding time-window ICA (SlitICA): spatial independence across components



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  - Independent vector analysis (IVA): spatial independence across components + matching between components from different windows



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Casting sparsity on the set of functional connections (Friedman et al. 2008)
# Assessing connectivity inside the window

- Using more elaborate measures to assess connectivity
  - Sliding time-window ICA (SlitICA): spatial independence across components
  - Independent vector analysis (IVA): spatial independence across components + matching between components from different windows



- Casting sparsity on the set of functional connections (Friedman et al. 2008)
- Using window-less assessments of synchrony: multiplication of temporal derivatives (MTD) (Shine et al. 2015)

#### Sliding window analysis: the simplest dFC tool



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Many graph measures enable network-level analysis



Many graph measures enable network-level analysis



(Rubinov and Sporns 2010)

#### Probing dFC landscape

# Dynamic graph analysis

Many graph measures enable network-level analysis



Clustering coefficient (CC)



(Van den Heuvel and Pol 2010)

(Rubinov and Sporns 2010)

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Many graph measures enable network-level analysis



Those measures fluctuate dynamically over time



<sup>(</sup>Tagliazucchi et al. 2012)

 Time points of high modularity and low efficiency vs low modularity and high efficiency



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 Time points of high modularity and low efficiency vs low modularity and high efficiency





 Time points of high modularity and low efficiency vs low modularity and high efficiency





(Zalesky et al. 2014)

- Time points of high modularity and low efficiency vs low modularity and high efficiency
  - Independently active networks vs Interacting modules





#### (Zalesky et al. 2014)

Brain structure constrains strong functional modularity



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R: correlation to brain structure

(Liégeois et al. 2015)

- Brain structure constrains strong functional modularity
- Flexibility in escaping this constraint relates to cognition





(Chen et al. 2016)

- Brain structure constrains strong functional modularity
- Flexibility in escaping this constraint relates to cognition
  - Salience network nodes shift their modular allegiance more in cognitively flexible individuals





Probing dFC landscape

## Sliding window analysis: the simplest dFC tool



Probing dFC landscape

## Sliding window analysis: the simplest dFC tool



Concatenated data yield building blocks for the whole population



(Leonardi et al. 2013)

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  - Resting-state view: mutually exclusive states



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(Leonardi et al. 2013)

(Allen et al. 2014)

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  - Interpretation: state reflective of connectivity value vs change from mean
  - Informative metrics: counts, dwell time vs weights, meta-states



(Leonardi et al. 2013)

#### Towards novel dFC analytical tools



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#### From sliding window to single frames

- Point process analysis (PPA)
  - From second-order (connectivity) to first-order (activation) information



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- Point process analysis (PPA)
  - From second-order (connectivity) to first-order (activation) information
  - Less data needed in computations, but arbitrary threshold to select
- Co-activation pattern (CAP) analysis
  - Disentanglement of separate networks co-(de)activating with a seed





(Liu and Duyn 2013)

Hemodynamic effect undone by paradigm-free mapping (PFM)

(Karahanoglu et al. 2013)



measured fMRI signal

Hemodynamic effect undone by paradigm-free mapping (PFM) 

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activity-related signal

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(Caballero Gaudes et al. 2013)

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SPFM: sparse paradigm free mapping GLM: general linear model

(Caballero Gaudes et al. 2013)





**BOLD** signal (PCC)

# From sliding window to single frames





- Generation of *innovation-driven co-activation patterns* 
  - Selection and clustering of whole-brain significant innovations



**BOLD signal (PCC)** 

# From sliding window to single frames



- Generation of innovation-driven co-activation patterns
  - Selection and clustering of whole-brain significant innovations
  - Spatially and temporally overlapping network maps



#### Towards novel dFC analytical tools



Frame-wise analysis





Extracting dFC states



#### Towards novel dFC analytical tools



Frame-wise analysis



Brain activity can be seen as a *spatiotemporal sequence* 



(Majeed et al. 2011)

- Brain activity can be seen as a *spatiotemporal sequence*
- Smoothening up activity or connectivity estimates (Monti et al. 2014)
  - Cannot capture abrupt changes of the system



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  - Cannot capture abrupt changes of the system
- Assuming temporally independent systems (Smith et al. 2012)
  - Physiologically implausible
- Explicitly model the spatiotemporal sequence of brain states
  - Requires a lot of data and good hypotheses, but generative and flexible





(Majeed et al. 2011)

(Eavani et al. 2013, Chiang et al. 2016)

- part of dFC fluctuations survive rigorous statistical testing
  - Cross-session shuffling, (amplitude-adjusted) phase randomisation...

(Betzel et al. 2016, Zalesky et al. 2014, Keilholz et al. 2013)



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dFC correlates with brain electrical activity

(Thompson et al. 2013, Tagliazucchi et al. 2012, Chang et al. 2013)



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dFC varies along demographic variables

• Age, gender... (Hutchison and Morton 2015, Yaesoubi et al. 2015)



(Betzel et al. 2016)

(Hutchison and Morton 2015)

- dFC is modulated by changes in arousal level
  - Caffeine, anesthesia...

(Rack-Gomer and Liu 2012, Barttfeld et al. 2015, Tagliazucchi et al. 2014)

	САР	WAKEFULNESS	UNCONSCIOUSNESS
	1		
	2		
	3		
	4		
	5		
-VALUE	6		
20 40	7		
0 10 2	8		
PCC-SEED VOXEL MAP			

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- dFC correlates with cognition
  - Daydreaming, cognitive flexibility, attentional ressources...

(Kucyi and Davis 2013, Yang et al. 2014, Chen et al. 2016, )

	САР	WAKEFULNESS	UNCONSCIOUSNESS	Au
	1			Cingulo-ope
	2			Fronto-pa Dorsal atte
	3			
	4			Default
	5			A
Z-VALUE	6			Si Fronto-p
0 10 20 40	7			Dorsal att Default
	8			Somet
PCC-S VOXEL	EED MAP			Ventral at: N Subo Cere



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				Pre-Hits > Pre-Misses	
	CAP	WAKEFULNESS	UNCONSCIOUSNESS	Auditory	0.25 p=0.033 n.s p=0.027
	1			Cingulo-opercular	0.2-
	2			Fronto-parietal	Хіь-
- Z-VALUE	3			Dorsal attention	Wodul
	4			Default mode	Graph ing Stat
	5			Pre-Hits > Pre-Misses t	Rest
	6			Salience Fronto-parietal	pre-Hits Modularity: 0.33 pre-Misses Modularity
20 40	7			Dorsal attention Default mode	
0 10	8			Visual	
PCC-S VOXE	SEED L MAP			Somatomotor Ventral attention Memory Subcortical Cerebellum	

(Amico et al. 2014)

(Sadaghiani et al. 2015)

- dFC is altered in many brain disorders
  - Schizophrenia, autism, major depressive disorder...



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#### Frame-wise analysis





Extracting dFC states





#### Frame-wise analysis

![](_page_106_Figure_3.jpeg)

#### **Temporal modeling**

![](_page_106_Picture_5.jpeg)

![](_page_106_Picture_6.jpeg)

![](_page_106_Picture_7.jpeg)

![](_page_106_Figure_8.jpeg)