MEG-ROI-nets

- Introduction to MEG functional connectivity

- Typical analysis pipeline

  - Parcellations

  - Leakage correction

- Choosing a connectivity metric

- Analysis example

OHBA
Oxford Centre for Human Brain Activity

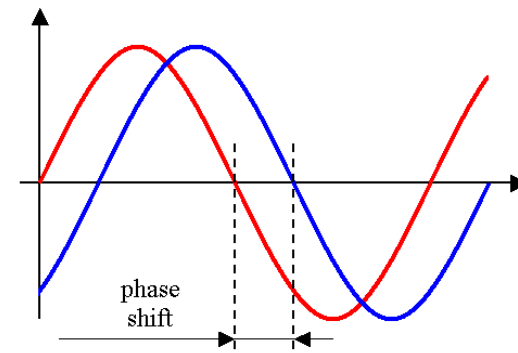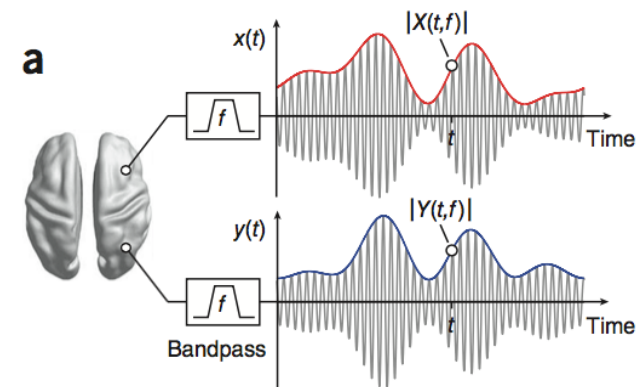UNIVERSITY OF OXFORD

MEG: what FC measure should we use?

- Can NOT use raw zero-lag correlation as we do in fMRI (due to conduction delays)

- Need to use measures that are robust to non-zero lags
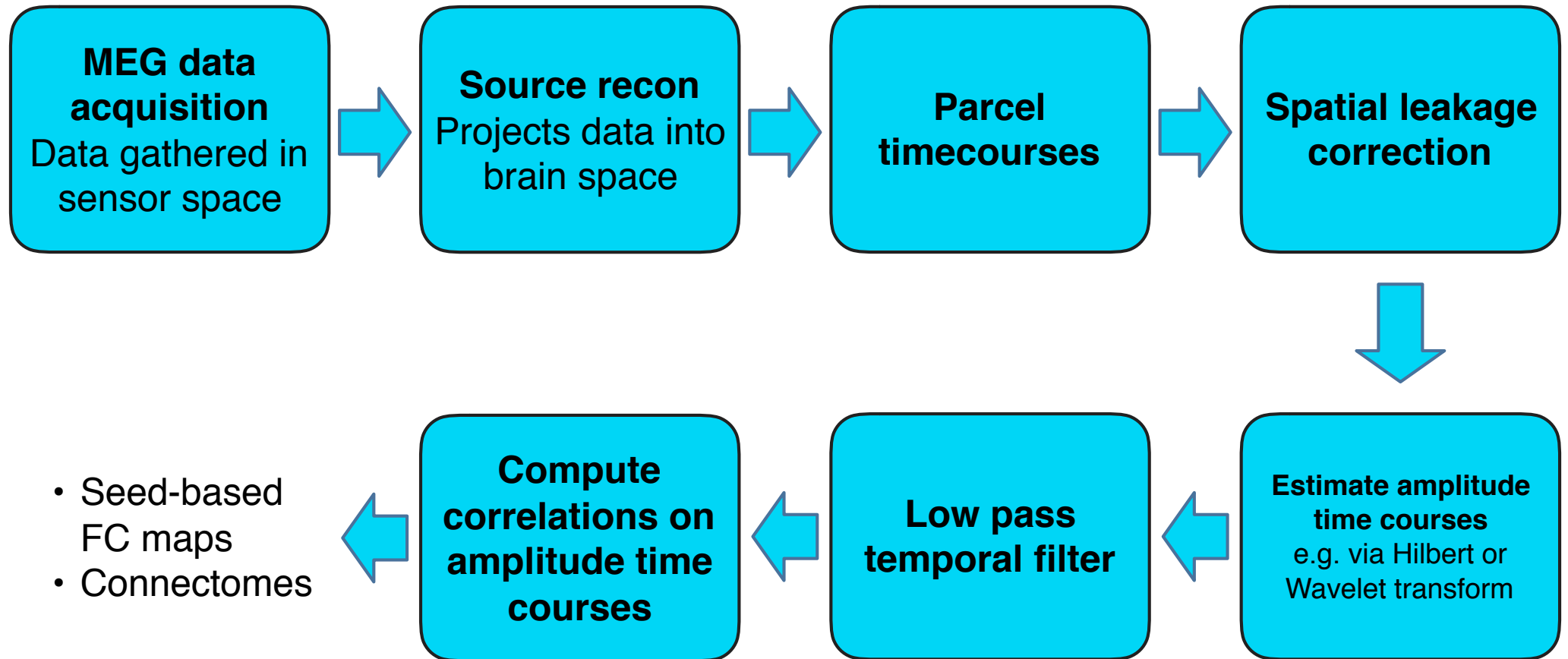
- **Amplitude Coupling**
    - Detects if the amplitude (or power/envelope) time courses in particular frequency bands are correlated
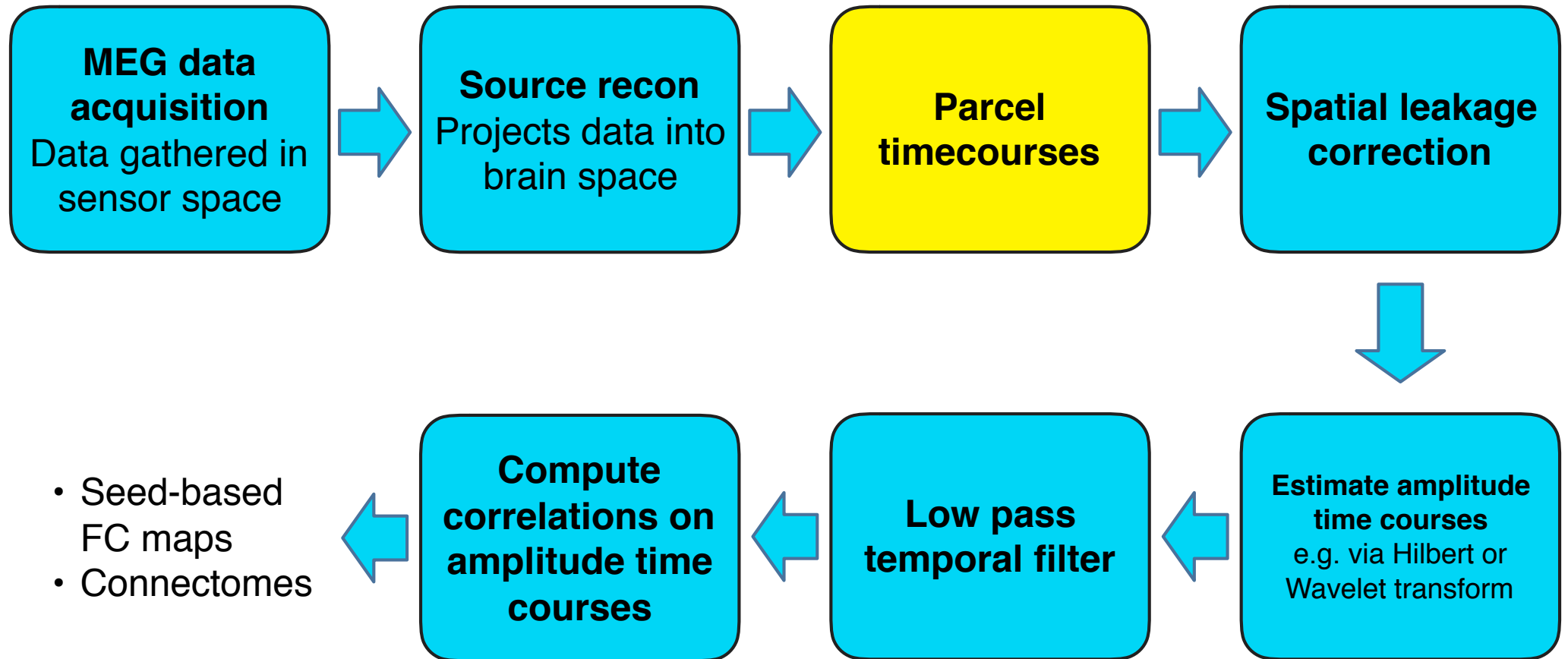
- **Phase coupling**

    - Detect consistent phase differences between brain signals

Hipp et al.; Nat Neuro (2012)
Brookes et al.; Neuroimage (2013)

MEG FC: Amplitude Coupling pipeline

MEG FC: Amplitude Coupling pipeline

MEG data acquisition
Data gathered in sensor space

→

Source recon
Projects data into brain space

→

Parcel timecourses

→

Spatial leakage correction

↓

Estimate amplitude time courses
e.g. via Hilbert or Wavelet transform

←

Low pass temporal filter
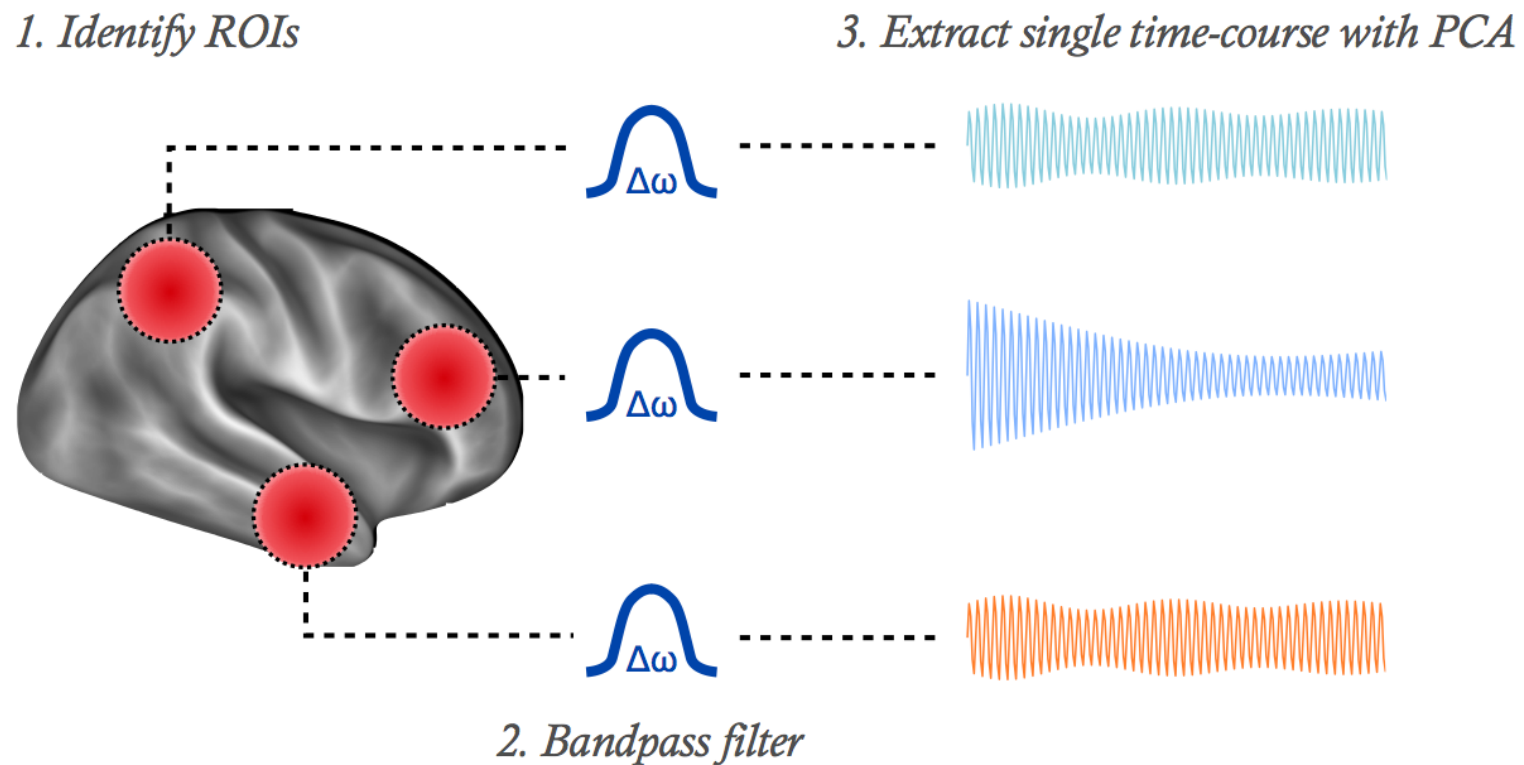
←

Compute correlations on amplitude time courses

←

- Seed-based FC maps
- Connectomes

Compute parcel timecourses

- Reduce from voxels to parcels
- Options available - mean time-course, PCA, single voxel with max power
- We tend to prefer PCA

1. Identify ROIs

3. Extract single time-course with PCA

$\Delta\omega$

2. Bandpass filter

- Functionality provided by **ROInets.get_node_tcs()**
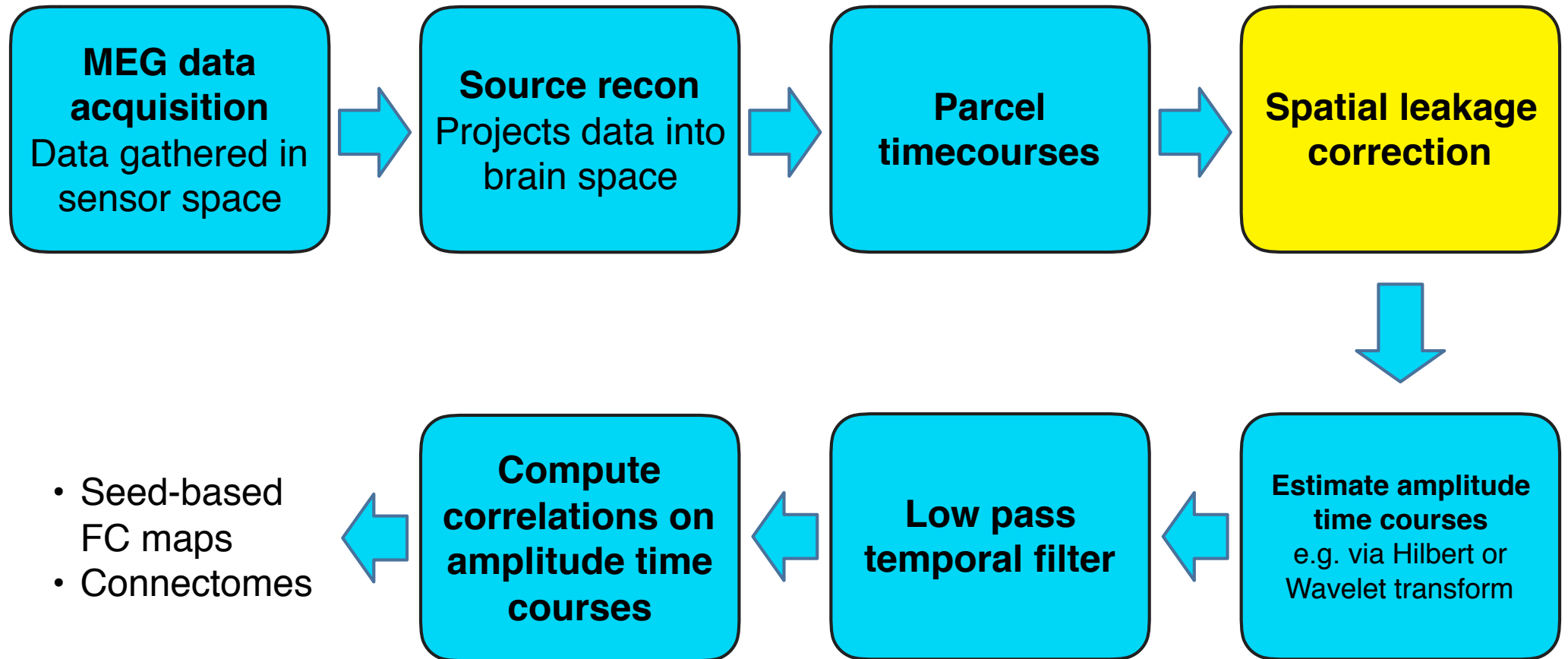
Choosing a parcellation

- Main consideration - do the parcels actually correspond to co-activated voxels?
    - What happens to the PCA if voxels within a parcel are *not* well correlated?
- We tend to use parcellations with around 40-80 regions
    - Important that parcels are small enough to resolve localised activity - especially in task analysis
    - Fewer parcels improves tractability
    - Often helpful to compare several different parcellations

Other choices
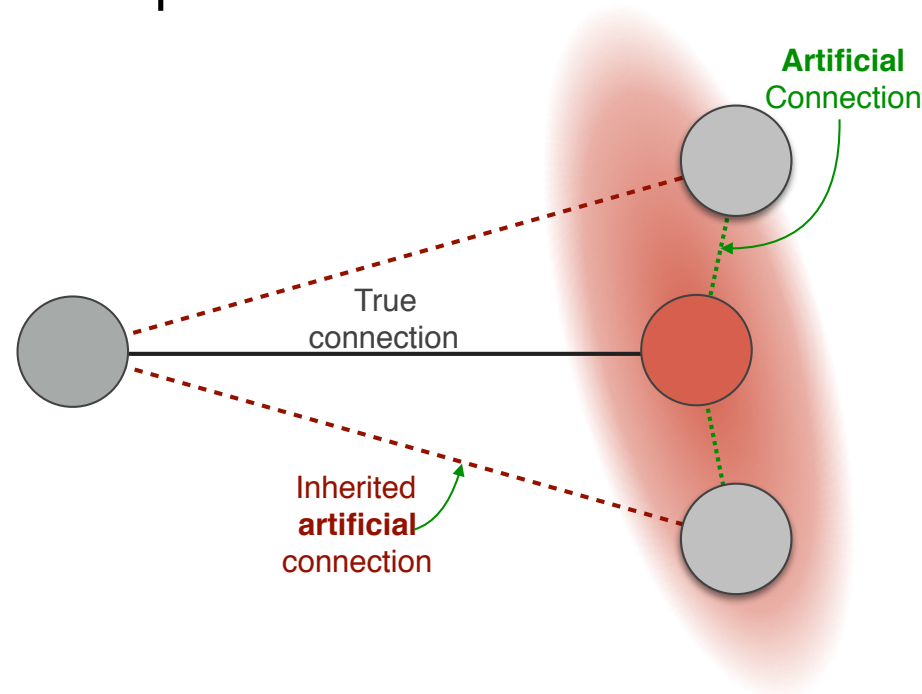- Weighted/unweighted
- Overlapping
- Some steps (e.g. PCA) may require binary, unweighted parcellations

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Compute correlations on amplitude time courses

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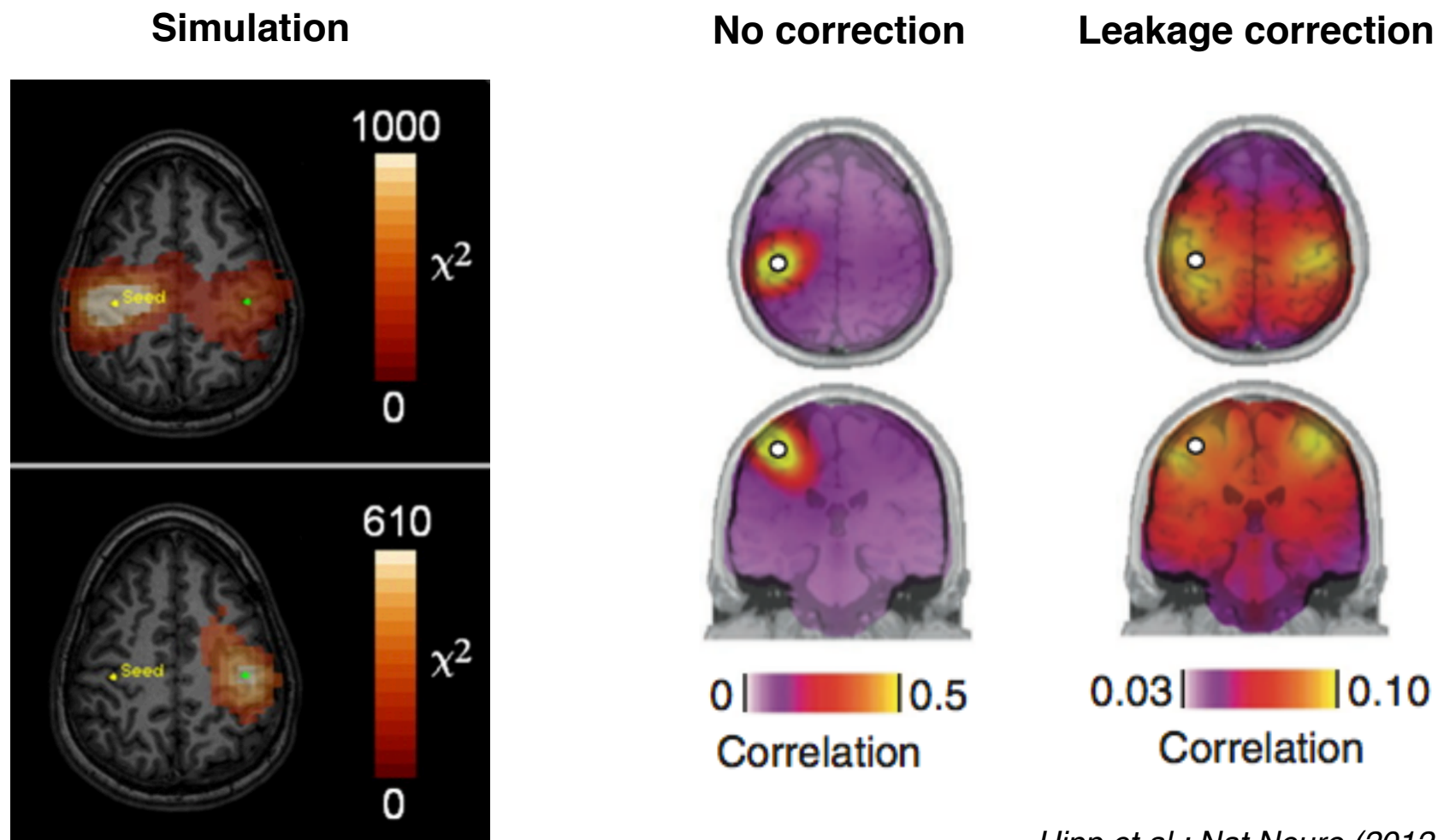- Seed-based FC maps
- Connectomes

Spatial leakage

Uncertainties in the source reconstruction induce **zero-lag** spatial correlations in source space

- Leakage pattern is non-trivial and depends on beamformer inverse solution
  - Depends on the data
  - Not identical for each voxel
- **SOLUTION**: remove all zero-lag correlations
- Still permits lagged interactions, which are genuine

Hipp et al.; Nat Neuro (2012)
Brookes et al.; Neuroimage (2013)

Without leakage correction, connectivity is dominated by signal leakage

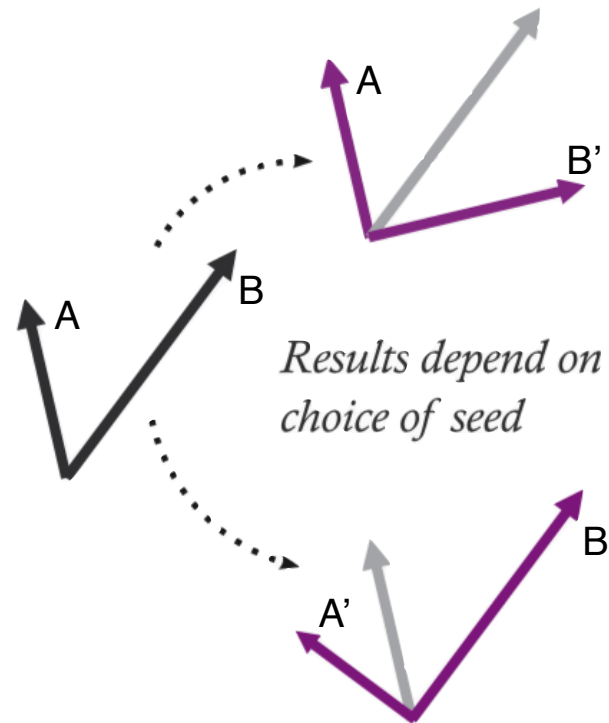**Simulation**

No correction

Leakage correction

Brookes et. al.; NeuroImage (2012)

Hipp et al.; Nat Neuro (2012)

Pairwise leakage correction

Orthogonalise **pairs** of raw time courses (regress one out of the other)
before computing amplitude time courses
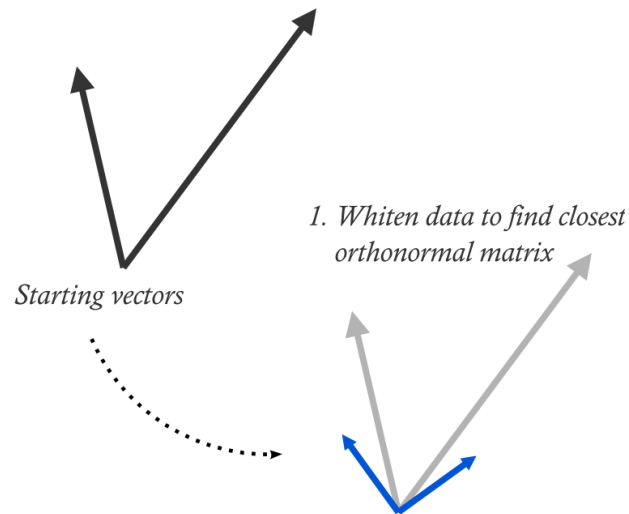

Results depend on choice of seed

But what about **multi-region** analyses?
  e.g. regularised partial correlation (direct vs indirect connections)
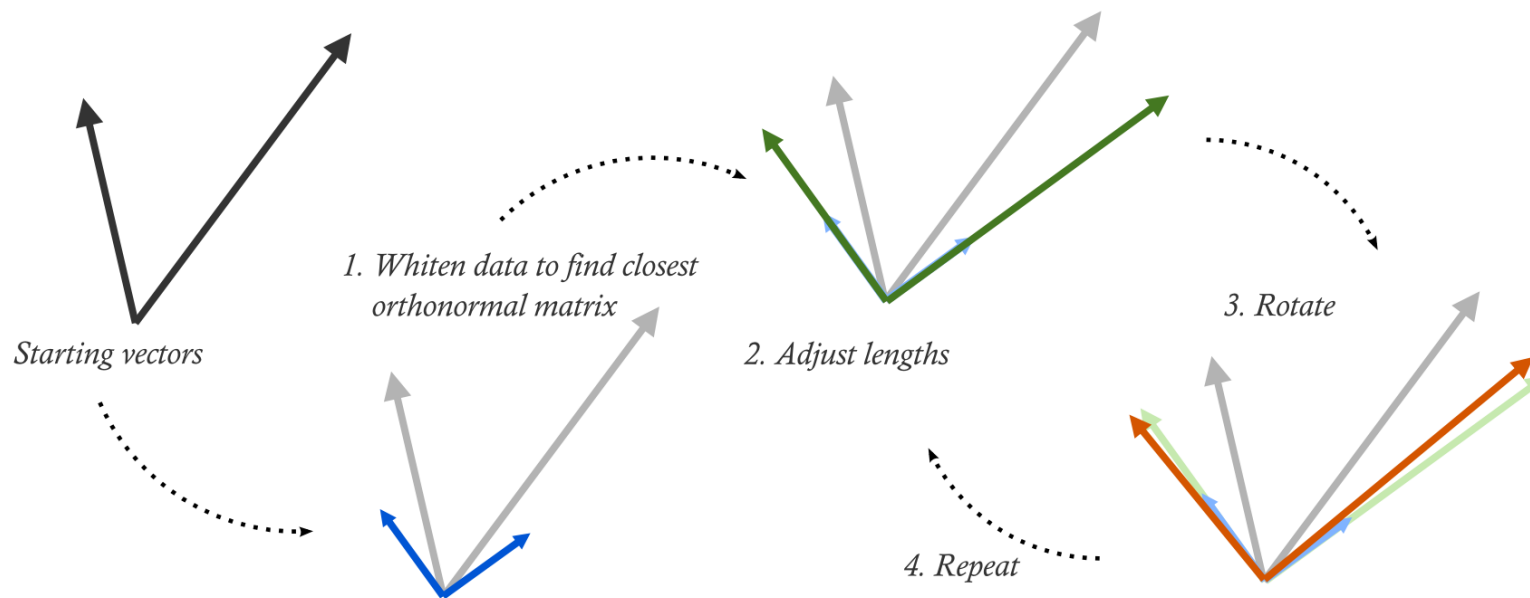
Multi-region leakage correction

Can perform a **multi-region** orthogonalisation in one shot:

Starting vectors

1. Whiten data to find closest orthonormal matrix

- Find the the closest orthonormal basis for the original timecourses
- Any subsequent multi-variate analysis is possible
- **Requires number of parcels < rank of data (affected by Maxfilter)**
- In general, good results up to about 100 parcels
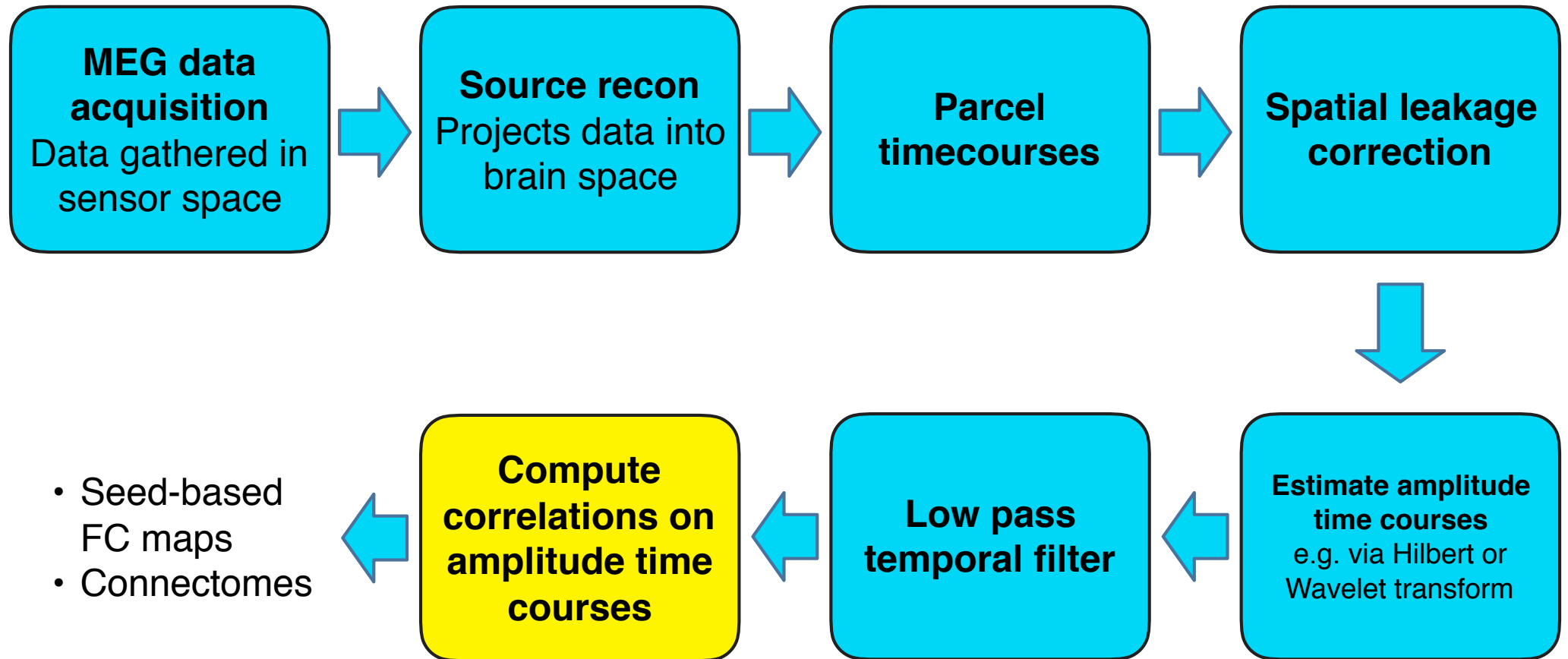
Colclough et. al. Neuroimage 2015

Multi-region leakage correction

- The orthonormal basis still differs from the signals in terms of their amplitudes
- Can iteratively adjust amplitudes and rotate to find orthogonal (but not normal) basis that best matches the original signals
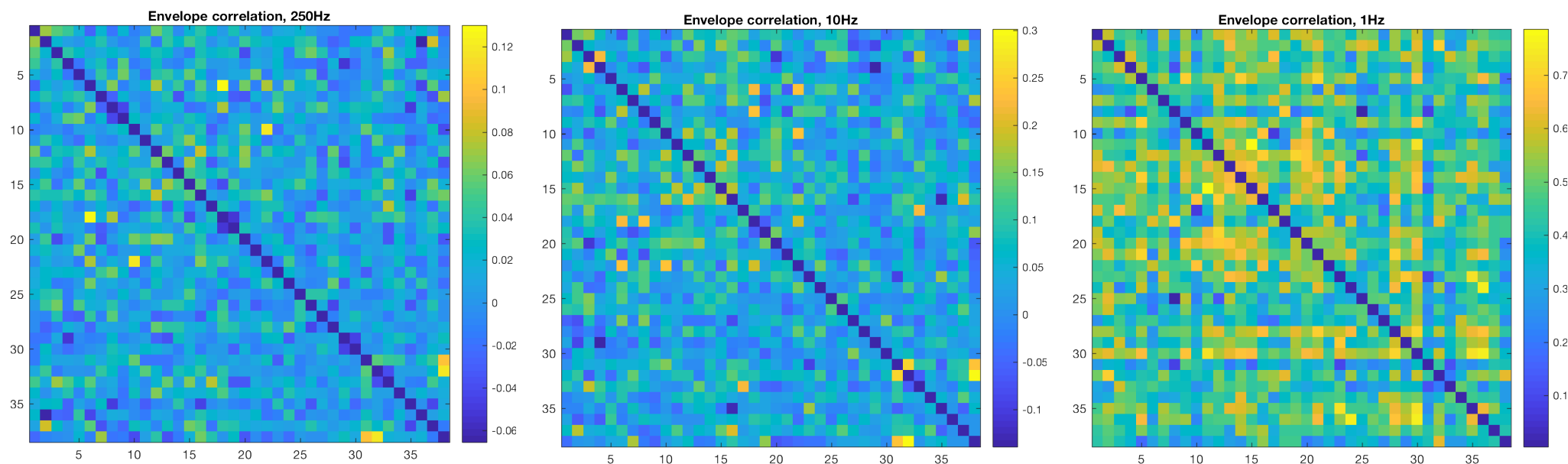

Starting vectors

1. Whiten data to find closest orthonormal matrix

2. Adjust lengths

3. Rotate

4. Repeat

Functionality provided by **ROInets.remove_source_leakage()**

MEG FC: Amplitude Coupling pipeline

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Spatial leakage correction

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Estimate amplitude time courses
e.g. via Hilbert or Wavelet transform

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Low pass temporal filter

←

Compute correlations on amplitude time courses

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- Seed-based FC maps
- Connectomes
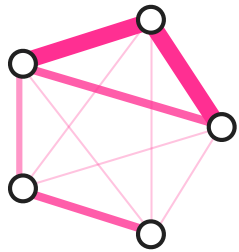
Correlation options: Downsampling

- Enhances functional connectivity measures between regions that are known to be connected
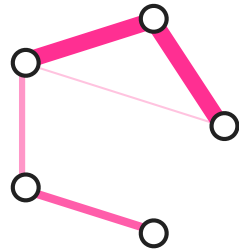- Tradeoff because downsampling also increases correlation between genuinely uncorrelated regions

- Optimal sampling rate depends on the amount of data you have
- **Don't forget to low-pass filter!**

Luckhoo et. al. Neuroimage 2012

Correlation options: Partial correlation

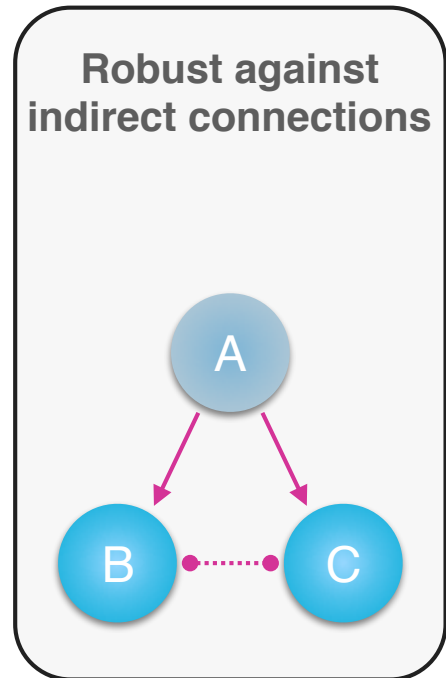*Problems*

Solutions

Robust against indirect connections

Correlation
(indirect connections)

Partial Correlation
(direct connections only)

- Partial Variance

- Partial Correlation
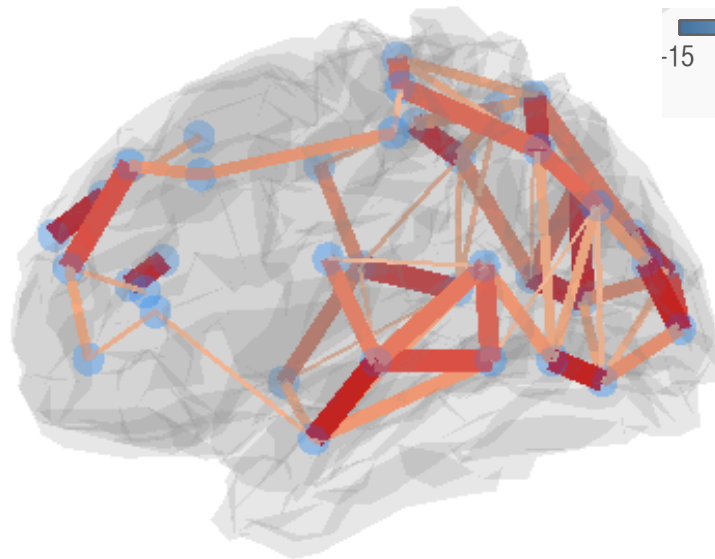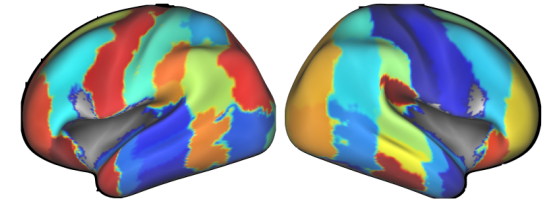
- Partial Directed Coherence

- Partial correlations are included in ROInets
- Work by Colclough et. al. (2015) advocates general use of partial methods
- *But regularization is almost essential (will examine in tutorial) and this can be computationally expensive*
- Both full and partial correlations are acceptable in literature

Colclough, Smith … Woolrich; Neuroimage (2015)

Connectome in resting-state MEG
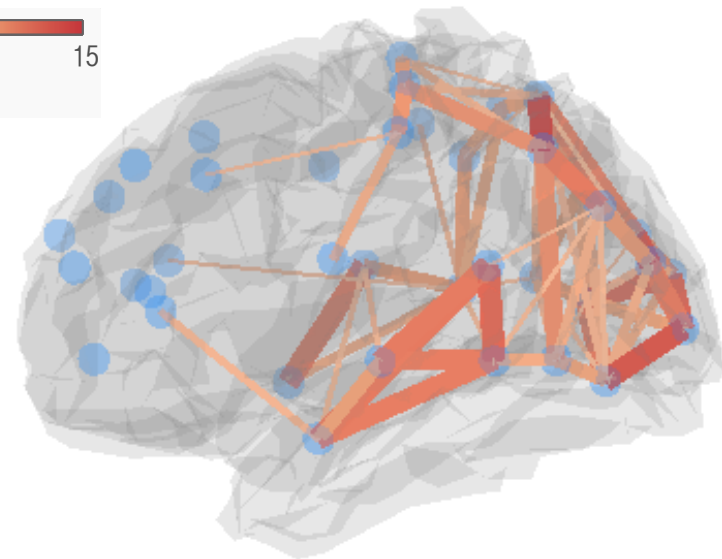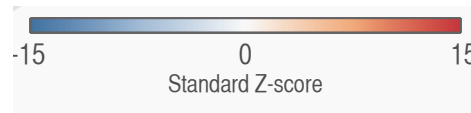
38 cortical regions

Eyes open CTF resting-state data - 8 subjects
- Alpha band (8-12 Hz) amplitude time-courses
- **Regularised partial correlation** connectome
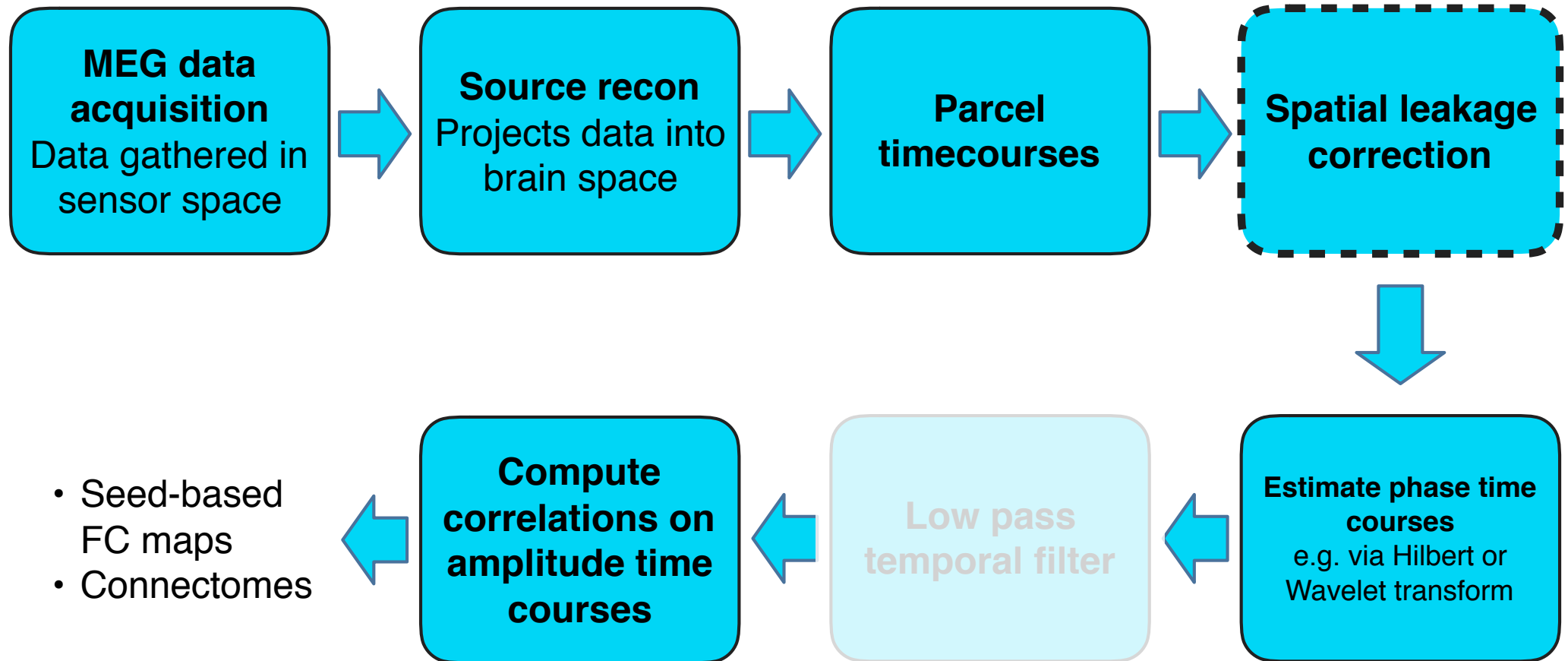- Thresholded at 5% FDR (multiple comparison correction)

-15   0   15
Standard Z-score

No Spatial Leakage Correction

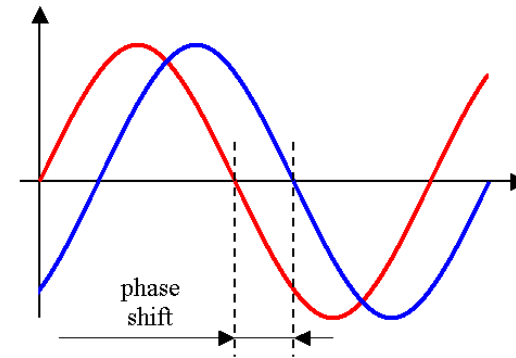*Multivariate Spatial Leakage Correction*

MEG FC: Amplitude Coupling pipeline

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┌─────────────────┐     ┌─────────────────┐     ┌─────────────────┐     ┌─────────────────┐
│  MEG data       │     │  Source recon   │     │  Parcel         │     │  Spatial leakage│
│  acquisition    │ ──▶ │  Projects data  │ ──▶ │  timecourses    │ ──▶ │  correction     │
│  Data gathered  │     │  into brain     │     │                 │     │                 │
│  in sensor space│     │  space          │     │                 │     │                 │
└─────────────────┘     └─────────────────┘     └─────────────────┘     └─────────────────┘
```

- Seed-based FC maps
- Connectomes

Compute correlations on amplitude time courses

Low pass temporal filter

Estimate phase time courses
e.g. via Hilbert or Wavelet transform

- Very similar workflow to amplitude envelopes
- Some phase connectivity measures not affected by spatial leakage
- Typically don't low pass filter - open question whether this is beneficial

Phase Coupling Measures

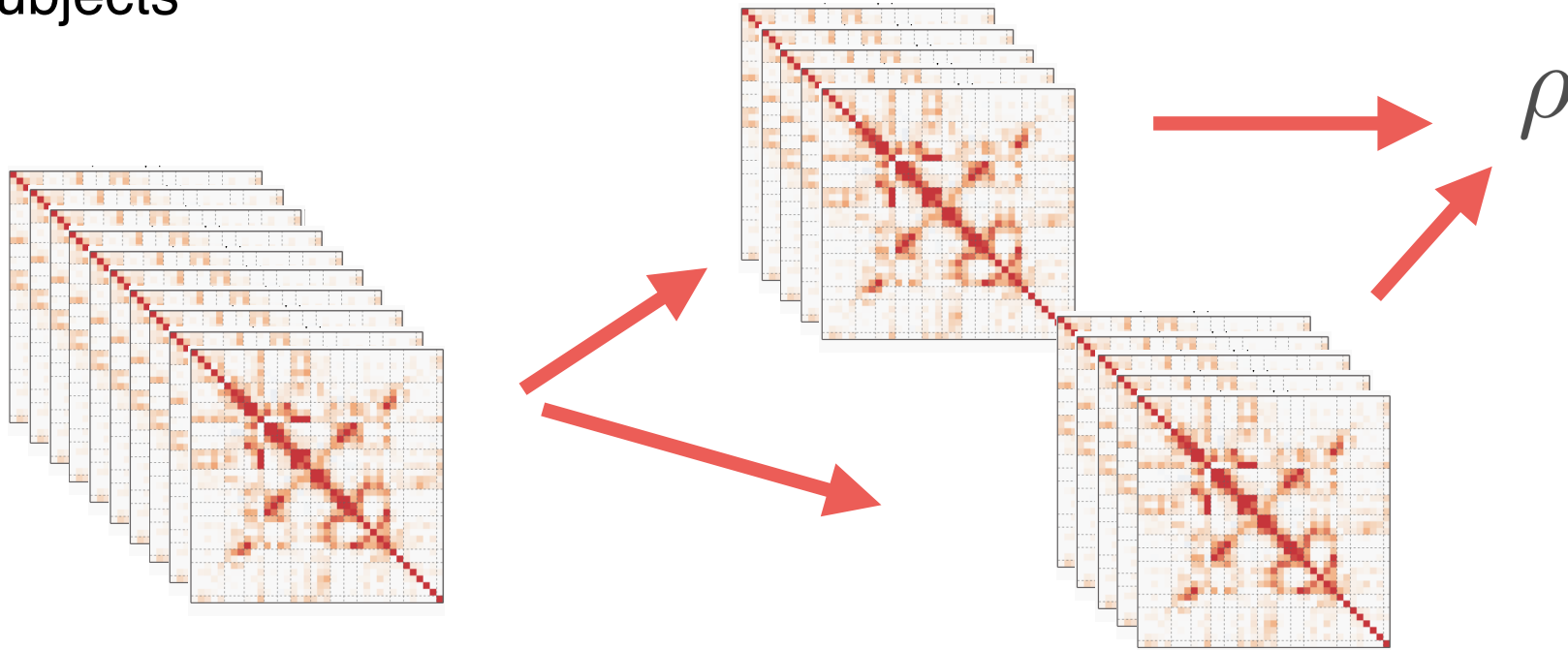- Detect consistent phase differences between brain signals

- Spectral methods
  - Estimated via multi-tapers, wavelets or MAR models
  - Need to choose parameters e.g. taper size or model order

- Phase estimation methods
  - Phase estimated on band-pass filtered data
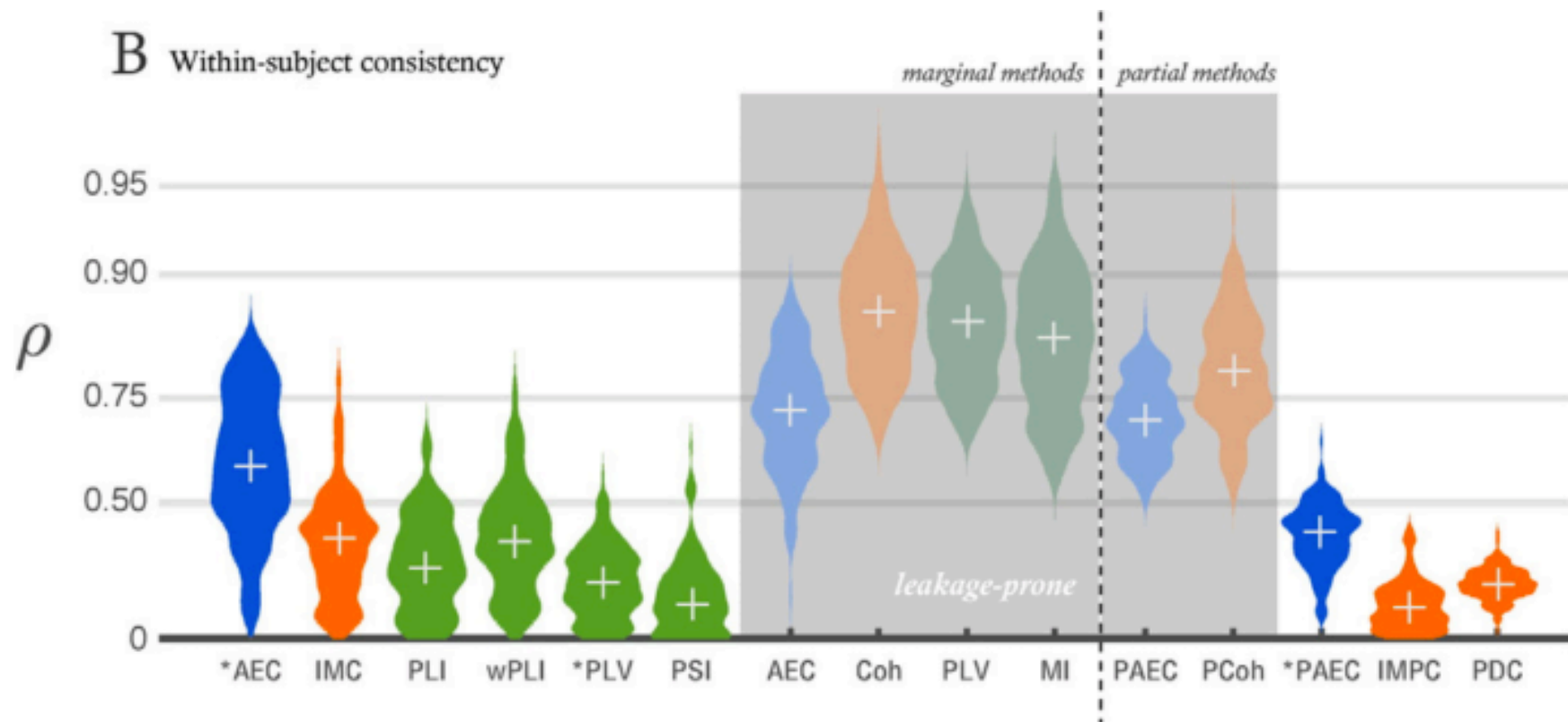 - Need to choose sensible frequency bands

	Robust to spatial leakage	Partial?
Coherence	No	No
Imaginary coherence	Yes	No
Partial coherence	No	Yes
Phase Locking Value (PLV)	No	No
Phase Lag Index (PLI)	Yes	No

Colclough et al., How reliable are MEG resting-state connectivity metrics? Neuroimage, 2016
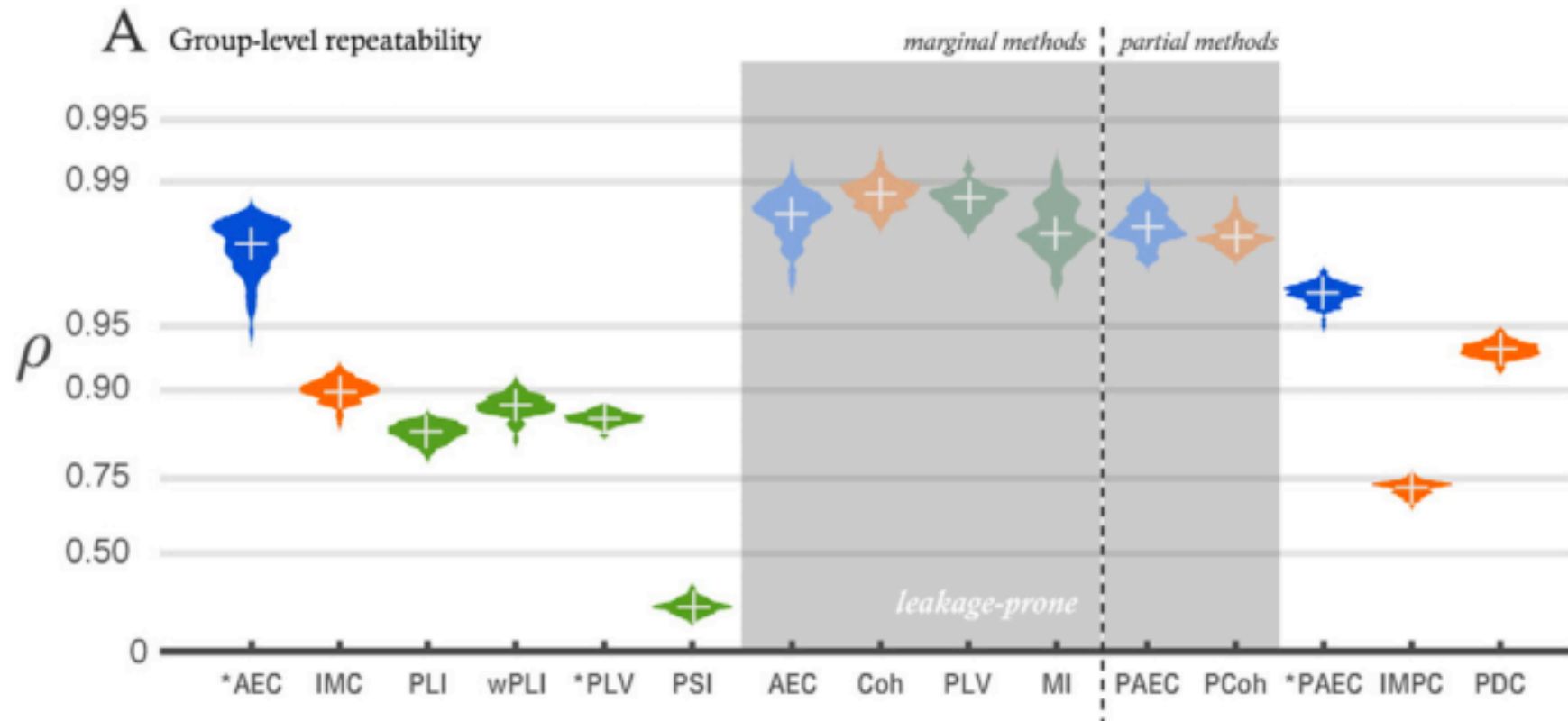
Choosing a metric - consistency

- Tested metrics using **Resting-state** data from Human Connectome Project, 61 subjects with 3 (6 min) sessions each
- Within-subject consistency - similarity between the 3 sessions
- Group-level consistency - similarity between different partitions of the 61 subjects

ρ

Colclough et al., How reliable are MEG resting-state connectivity metrics? Neuroimage, 2016

Choosing a metric - consistency

B Within-subject consistency

marginal methods | partial methods

leakage-prone

ρ

*AEC   IMC   PLI   wPLI   *PLV   PSI   AEC   Coh   PLV   MI   PAEC   PCoh   *PAEC   IMPC   PDC

Colclough et al., How reliable are MEG resting-state connectivity metrics? Neuroimage, 2016
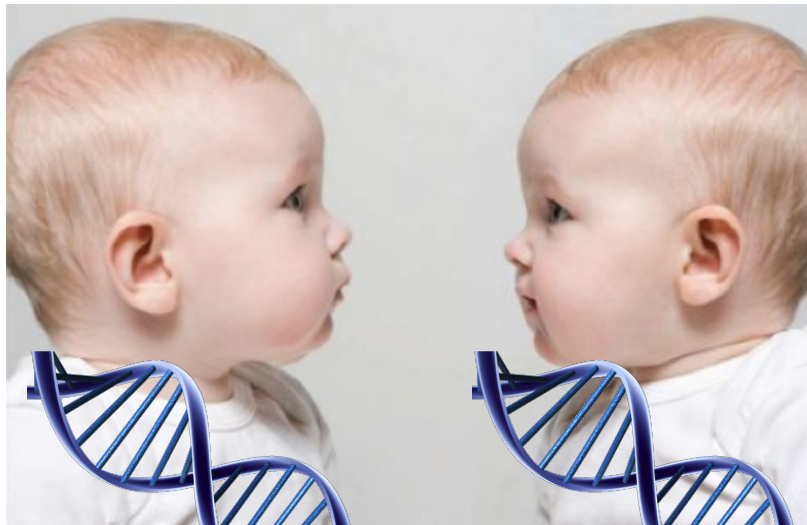
Testing the consistency of connectome estimation

- **Overall** - most consistent is amplitude coupling with spatial leakage correction (***AEC**)

Colclough et al., How reliable are MEG resting-state connectivity metrics? Neuroimage, 2016

Group-level analysis application - heritability of MEG connectomes
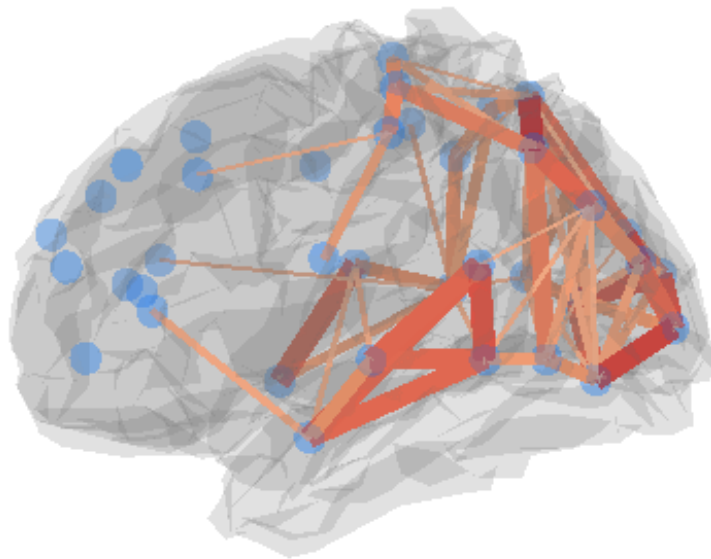
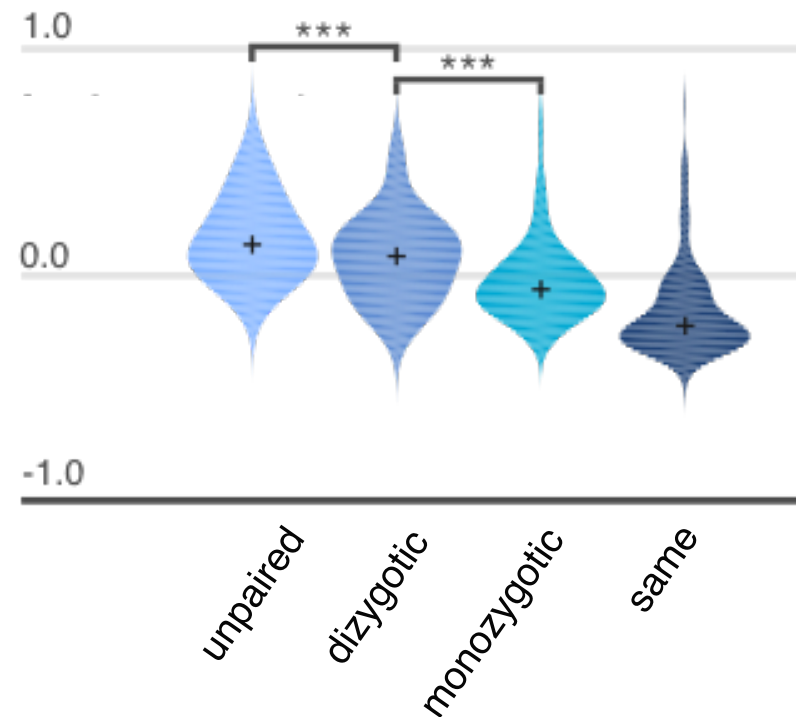## Human Connectome Project twin rest data

MZ

DZ

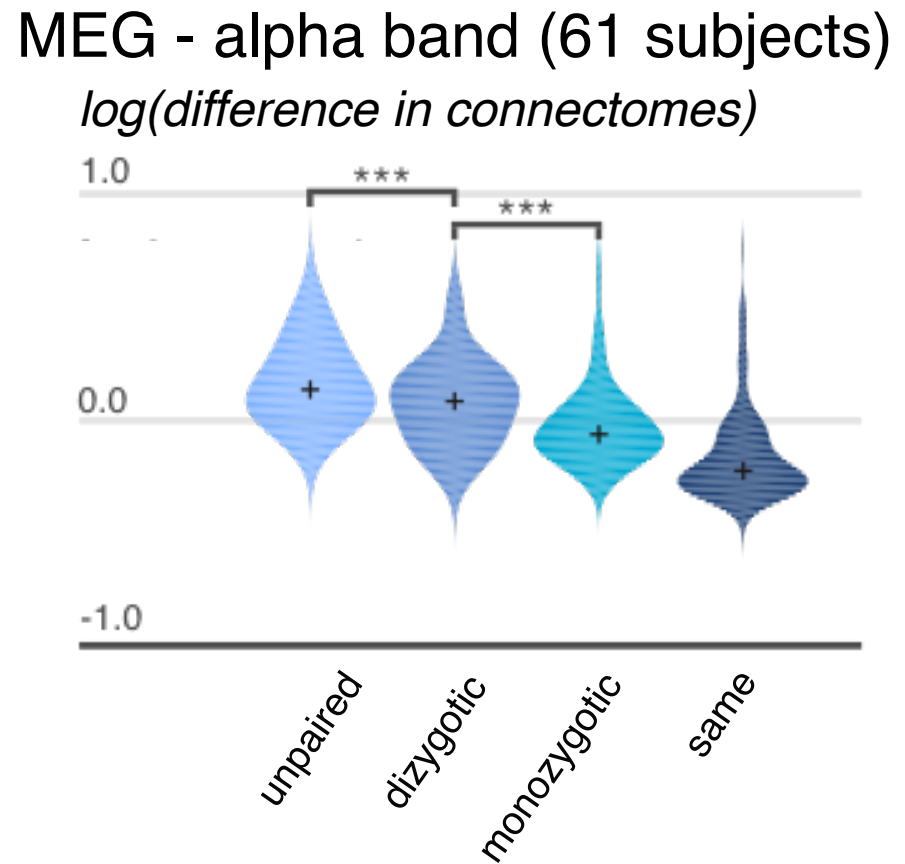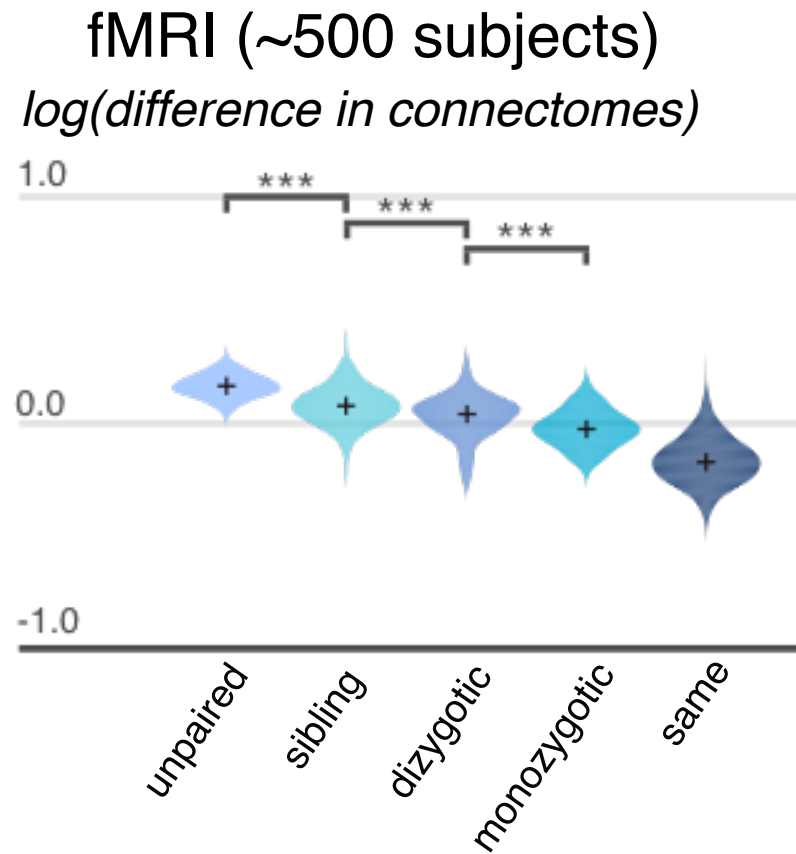# Group-level analysis application - heritability of MEG connectomes

MEG - alpha band (61 subjects)

log(difference in connectomes)

- Mean edge heritability: 33% (p = 0.01)
- Shared genetics outweigh shared environment (p = 0.02)

Colclough, Smith … Woolrich; In submission

Group-level analysis application - heritability of MEG connectomes

fMRI (~500 subjects)
log(difference in connectomes)

MEG - alpha band (61 subjects)
log(difference in connectomes)

- Mean edge heritability: 33% (p = 0.01)
- Shared genetics outweigh shared environment (p = 0.02)

Colclough, Smith ... Woolrich; In submission

Software implementation

- **MEG-ROI-nets** (Region of Interest Network Analysis for MEG)

- Basic functions operate on matrices

- Included as part of OSL, can work with SPM MEEG objects directly

- Also contains scripts to perform analysis of entire datasets

Tutorials

1. Introduction to orthogonalization

2. Using ROInets with a single subject

3. Using ROInets on a group of subjects