WP3 PROGRESS REPORT

DATA PROCESSING, STANDARDIZATION AND DATA-FAIRIFICATION

FZJ
CHARITE , AMU, Fraunhofer, ICM, INRIA, IBEC, UH, UNIGE, UCM, UNIVIE

WP3 SCOPE

- organise all activities that aim at
  - data processing and workflow management
  - integration of a priori knowledge on brain organization, e.g., brain atlases

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- aim for solutions that can be translated into clinical settings rather than being constrained to dedicated research environments

WP3 ROLE IN PROJECT

- bridge platform development and neuroscience research
- critical link between clinical and modelling WPs
- provide software and knowledge infrastructure needed to work with data from WP4 utilizing the HPC infrastructure from WP7

TASKS (1): DATA (PRE-)PROCESSING AND STANDARDIZATION

- **3.1 MRI Data processing, standardization and FAIRification (FZJ)**
  - development of an automated MRI (pre-)processing pipeline (anatomical features, structual/functional connectome)
  - enable response time matching those of clinical tests
  - incorporate data normalization using BIDS community standard
- **3.2 Electrophysiological data processing and analytics (UH)**
  - SEEG preprocessing
    - electrode localization, white-matter referencing
    - co-localization with individual MRI and multiresolution parcellations
  - M/EEG data preprocessing
    - environmental, and physiological artefact removal
    - co-registration with individual MRI
    - inverse modeling to reconstruct cortical source time series

TASKS (2): DATA CURATION AND AGGREGATION

- **3.3 Atlases and harmonized spatial annotations (FZJ)**
  - localization of distinct, biologically meaningful regions for modeling dynamics
  - whole-brain atlas-based data compression (for connectomics and computational efficiency)
  - multimodal atlasing to provide a common reference
  - whole-brain multiresolution parcellations applicable to MRI and MEG/SEEG
- **3.4 Clinical data curation and processing (FRAUNHOFER)**
  - curation of structured clinical data and processing of unstructured clinical information
  - electronic healthcare records, including laboratory tests, clinical rating scales, and physician notes
  - diseases, medications, etc. represented by controlled vocabularies
  - internationalization of terminologies

TASKS (3): METADATA DESIGN AND MANAGEMENT

- **3.5 Unified metadata annotations and data catalogues (UNIGE)**
  - terminologies and ontologies
    - Protein-Ligand-Interaction Ontology (PLIO)
    - Human Physiology Simulation Ontology (HUPSON)
    - Alzheimer Disease Ontology (ADO)
    - Parkinsonism Disease Ontology (PDON)
  - terminology and ontology management system as core annotation service for project data
  - build for metadata evolution (e.g., coherent versioning)
  - open-source tool (CTS2-compliant) to manage metadata catalogue
- **3.6 FAIR implementation on all modalities (FRAUNHOFER)**
  - FAIR data vs. privacy protection, subject identity protection
  - homogeneous annotations based on shared semantics established in Task 3.4
  - harmonized metadata catalogue for use throughout the project

TASKS (4): ENABLE CAUSAL INFERENCE

- **3.7 Deconfounding brain/behaviour/genetics associations (INRIA)**
  - account for statistical confounds to improve validity of discovered causal relationships
  - comparison of two main deconfounding approaches:
    - regression of nuisance variables
    - resampling approach to create test datasets where the main variable of interest is statistically independent from confounders
  - estimation of causal directionality using "Mendelian Randomisation" from genotype, imaging variables (brain volume, amyloid load), cognitive measures, and diagnoses

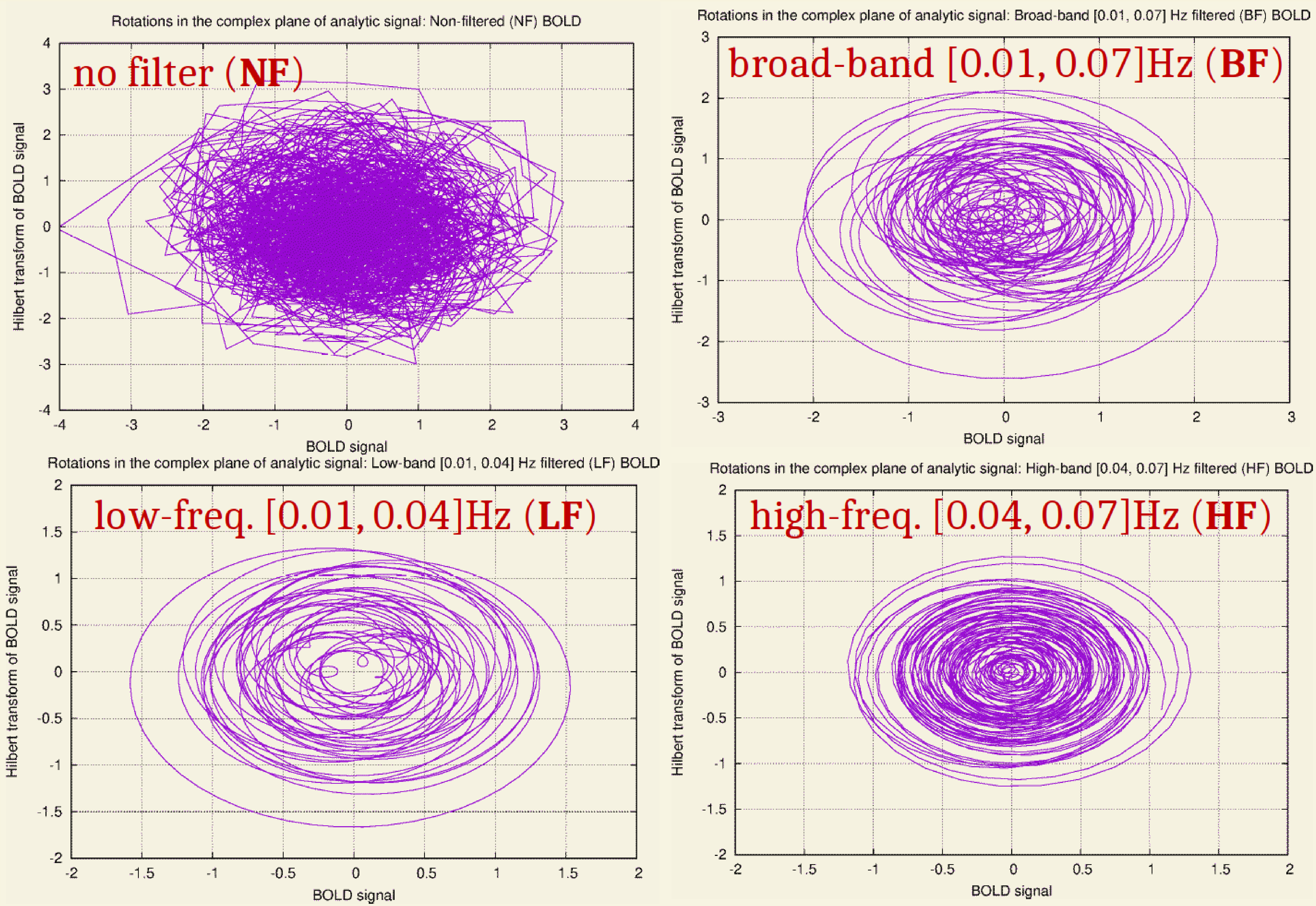
PROGRESS @ FZJ

1. pipeline development and feature evaluation
2. data management and sharing logistics technology

PIPELINE DEVELOPMENT AND FEATURE EVALUATION

- Which features of brain structure and function are most informative and best suitable for computational modeling?
- How can those features be optimally and most efficiently extracted from empirical measurments?
- "closed-loop" evaluation of data processing pipeline design and parameterization in the context of computational modeling
- work by *Oleksandr Popovych*, *Tanos Manos*, *Sandra Diaz-Pier*, *Felix Hoffstaedter*, *Jan Schreiber*, *Alexander Peyser* from INM-7/FZJ, HHU Düsseldorf, SimLab Neuroscience/FZJ, INM-1/FZJ

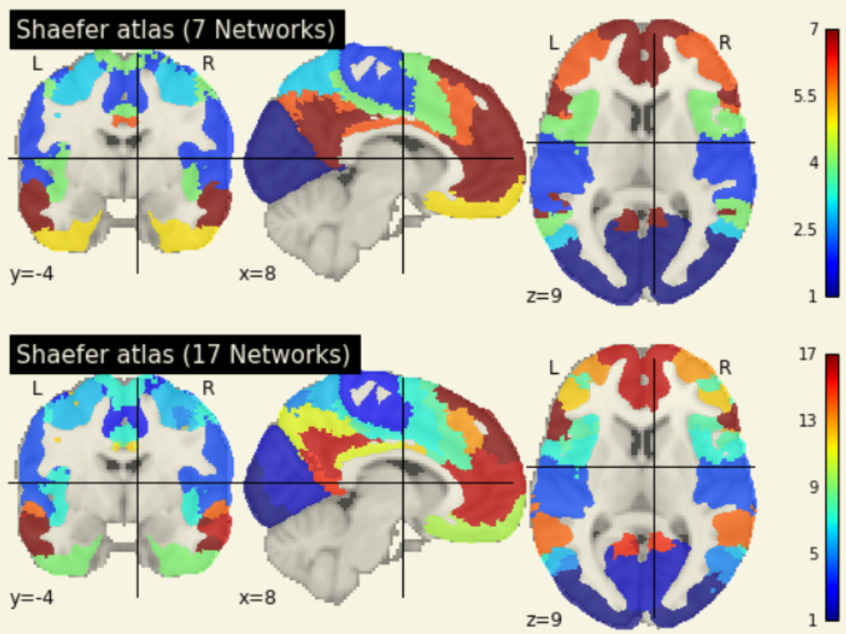
BOLD RFMRI PHASE DYNAMICS FEATURE EXTRACTION



Computation of valid features requires narrow-band spatial filtering

BRAIN ATLAS CHOICE AND GRANULARITY

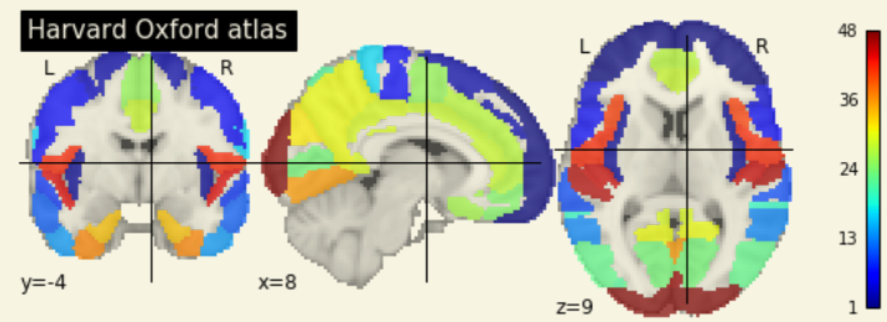
Shaefer functional atlas
(100, 200, 400, 600, 800, 1000 regions)



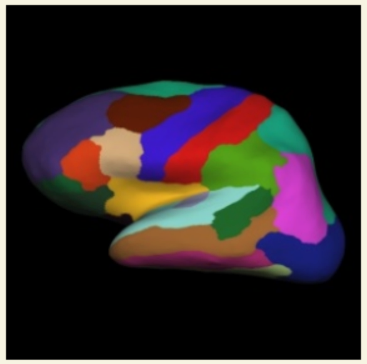
Schaefer *et al.*, Cereb. Cortex 28, 3095–3114 (2018)

Zimmermann *et* al., Subject specificity of the correlation between large-scale structural and functional connectivity Network Neuroscience **3**, 90-106 (2019)

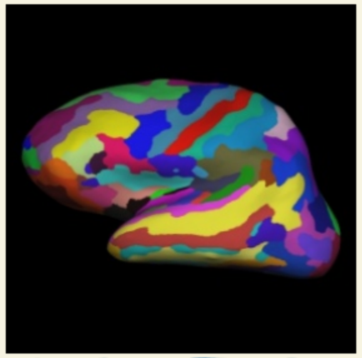
Harvard-Oxford structural
(96 cortical regions)



Desikan-Killiany anatomical
(68 cortical regions)



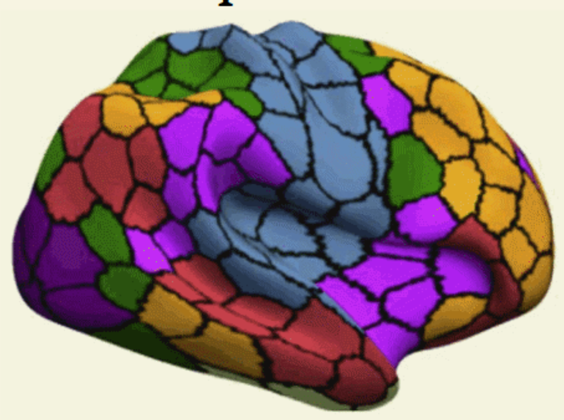
Destrieux anatomical
(148 cortical regions)

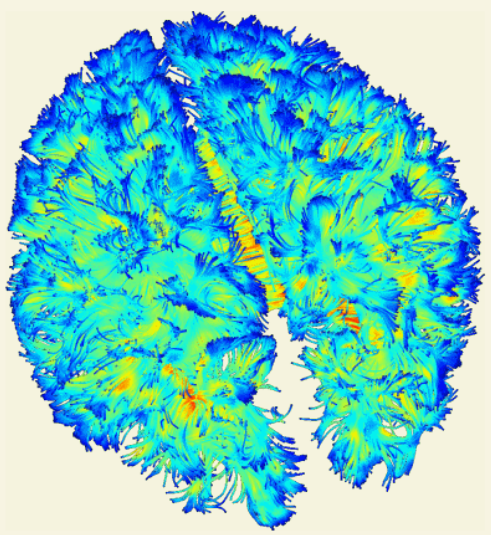


Trade-off between model complexity/richness and computational efficiency

FUNCTIONAL CONNECTIVITY (FC) MODEL TEST CASE

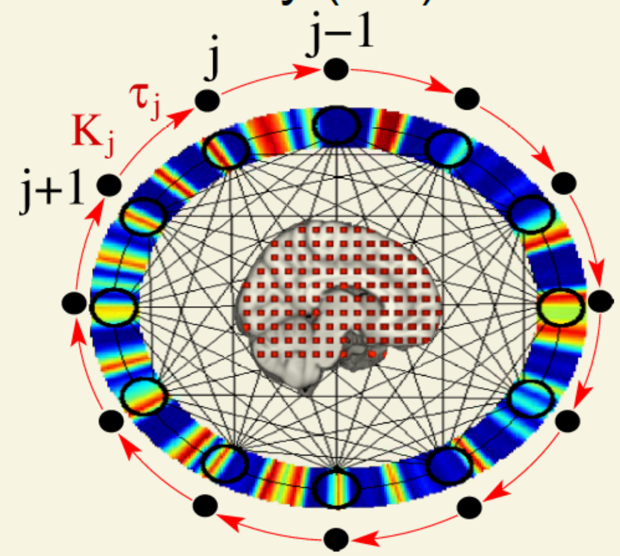
Brain parcellation





Brain tractography

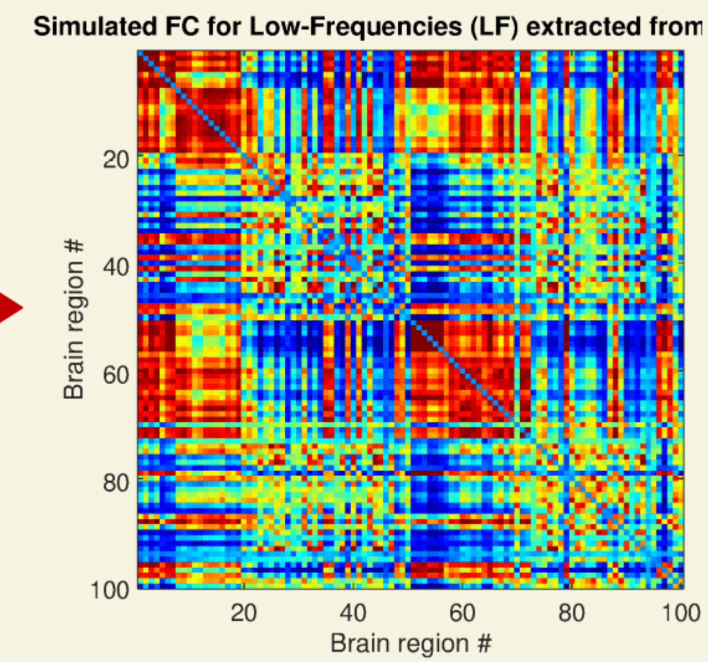
Coupling is based on the empirical structural connectivity (SC)



Mean activity of brain regions is modeled by neuronal (oscillatory) models

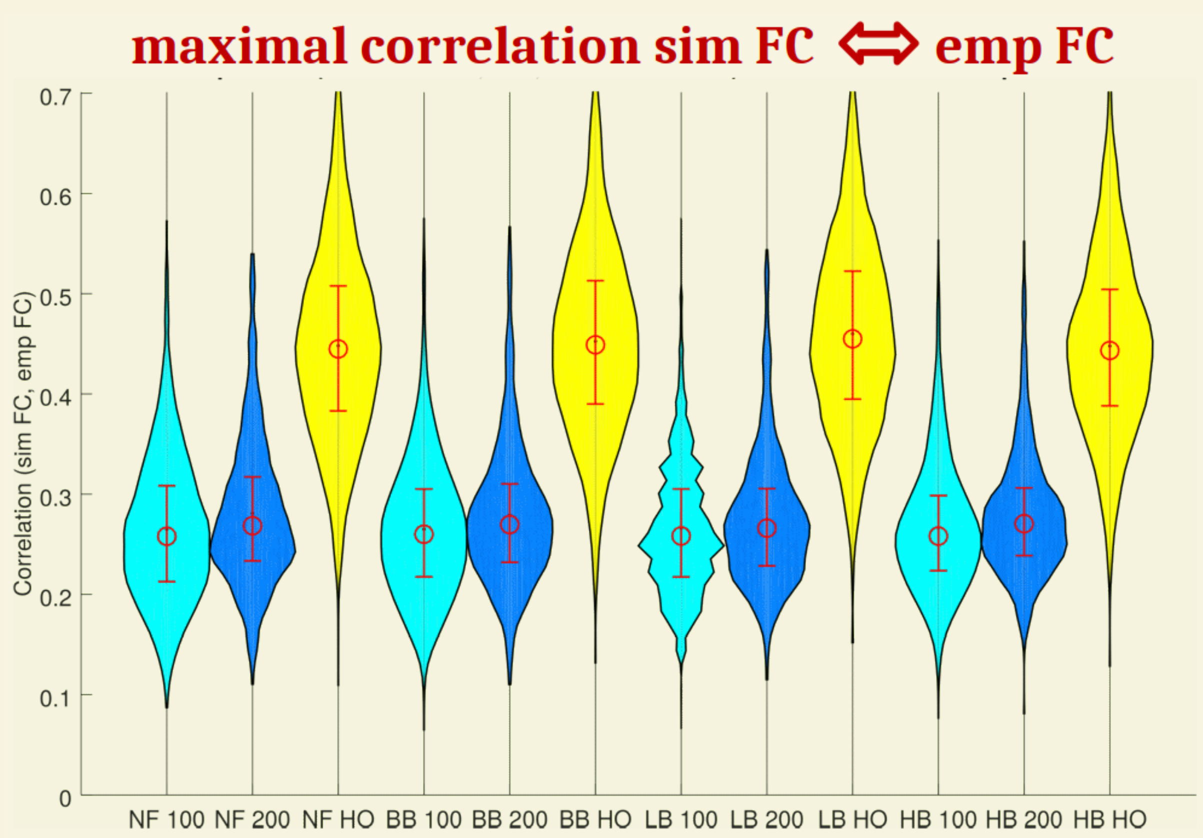
Honey et al., PNAS **106**, 2035-2040 (2009)

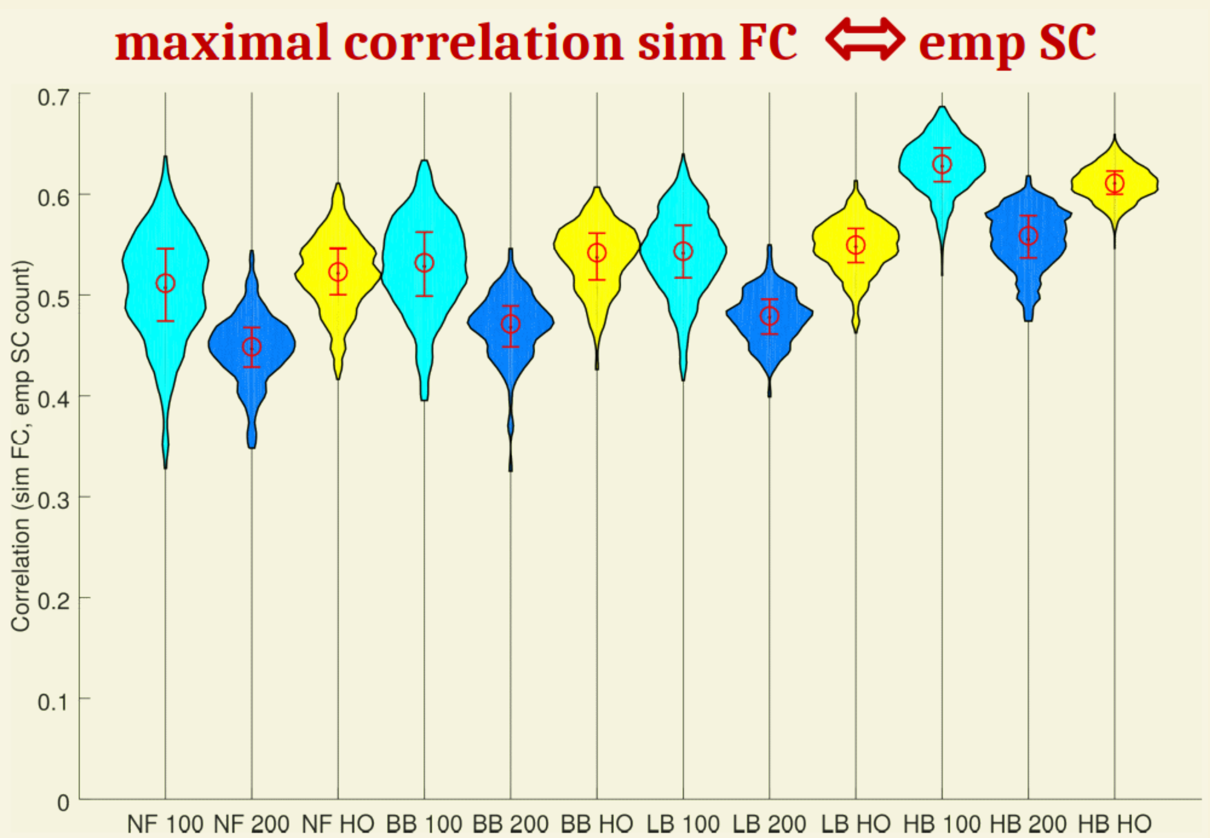
Modeled brain dynamics: simulated functional connectivity (**sim FC**)



Simulated FC is compared with empirical FC (from BOLD signals) and SC.

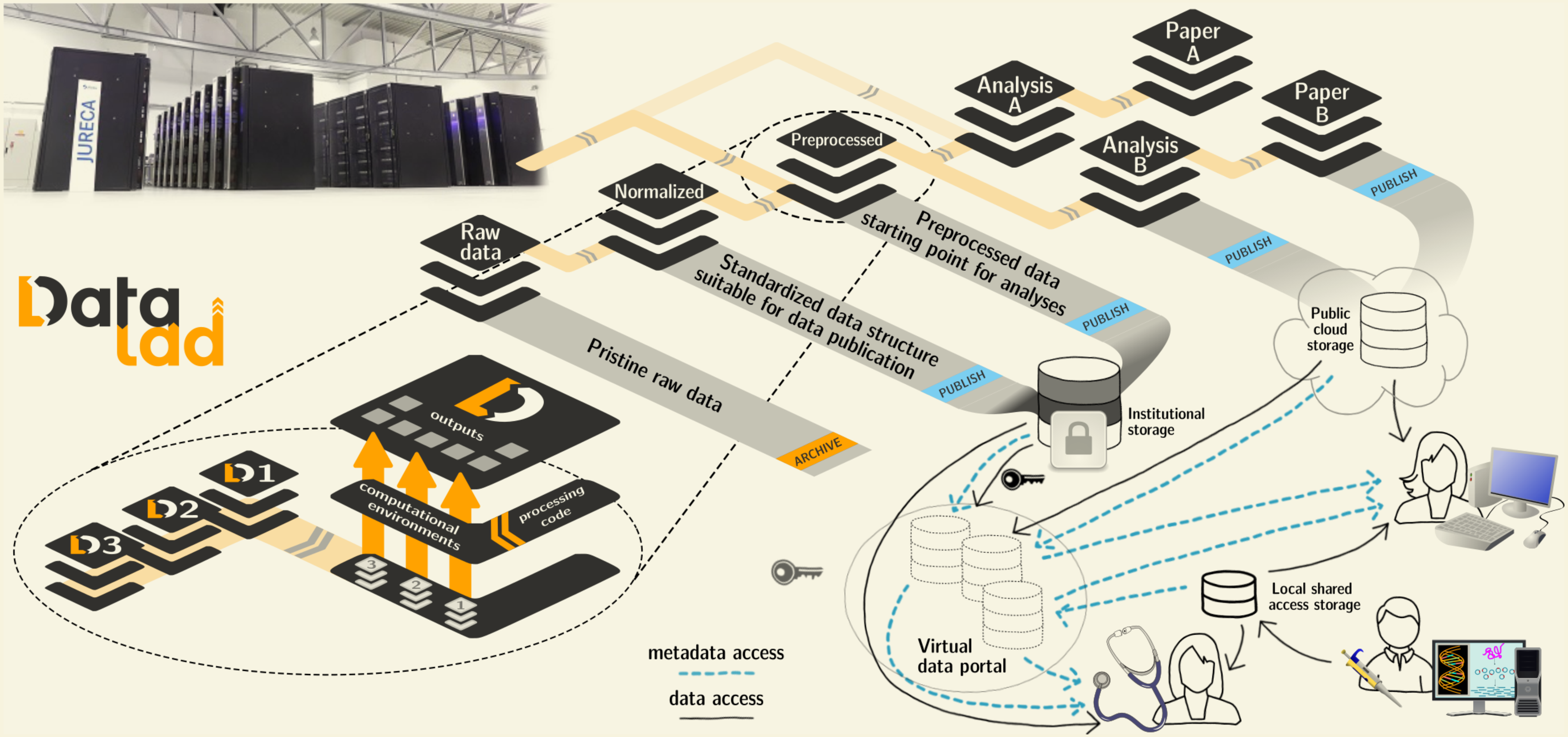
FC MODEL EVALUATION ON DIFFERENT ATLAS CHOICES





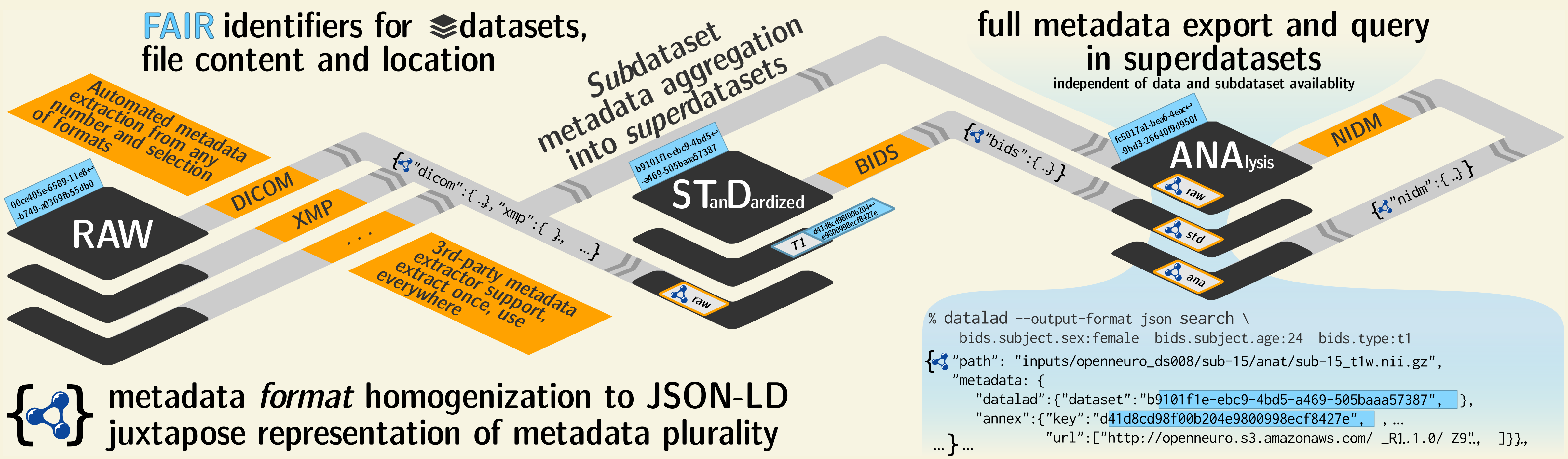
Atlas choice and frequency band impact model performance.

SOLUTION FOR FAIR DECENTRALIZED DATA MANAGEMENT: DATALAD.ORG



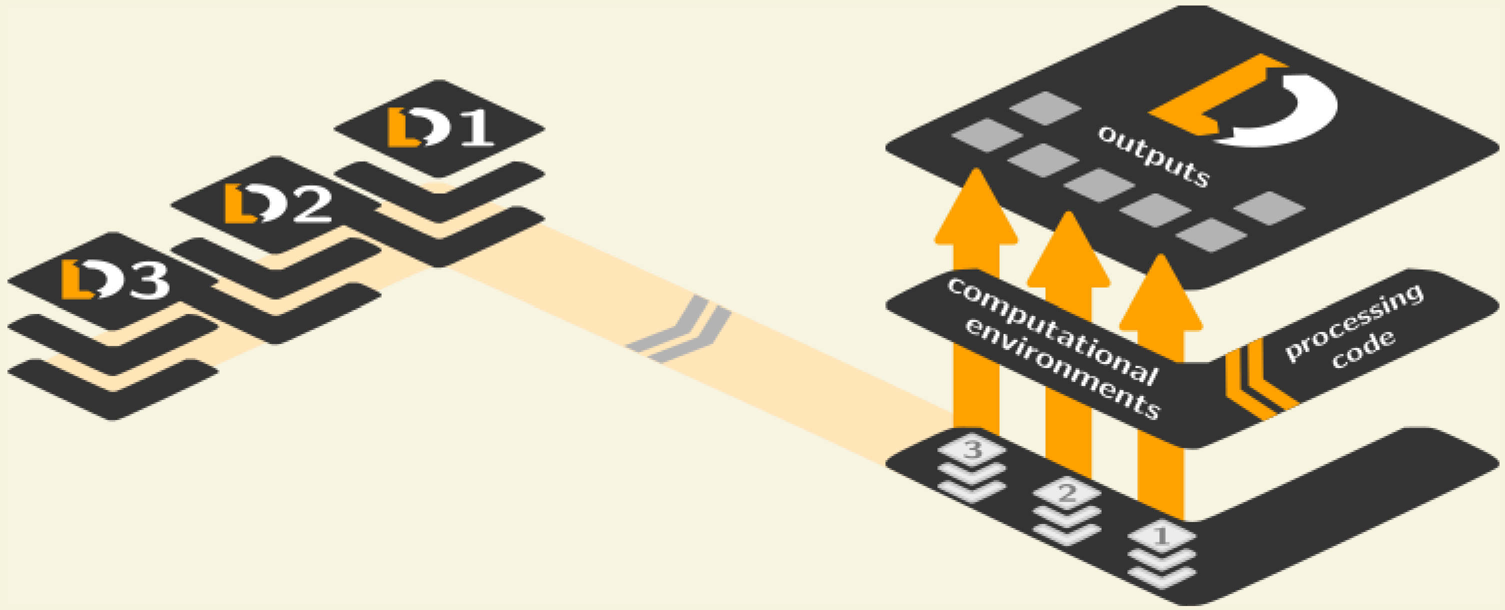
- manage the evolution of digital objects and yield FAIR resources
- Integrations: OpenNeuro management backend, CBRAIN data provider, brainlife.io import
- Funding: CRCNS NSF/BMBF, HBP SGA3, NIH

(AUTOMATED) METALAD LOGISTICS



- transport solution for **arbitrary metadata**
- Metadata **plurality:** no need to decide on a single standard
- **JSON-LD** format (semantic graphs, but low technical threshold for use)
- supports aggregation from individual datasets into collections/catalogues
- independently extensible

"COMPLETE" PROVENANCE CAPTURE



- for any local command

```
$ datalad run -m "Perform eye movement event detection"\
  --input 'inputs/raw_eyegaze/sub-*/beh/sub-*...tsv.gz' \
  --output 'sub-*' \
  bash code/compute_all.sh
```

- for any containerized app (can be tracked in the dataset too)

```
$ datalad containers-run -n nilearn \
  --input 'inputs/mri_aligned/sub-*/in_bold3Tp2/sub-*_task-avmovie_run-*_bold*' \
  --output 'sub-*/LC_timeseries_run-*.csv' \
  "bash -c 'for sub in sub-*; do for run in run-1 ... run-8;
     do python3 code/extract_lc_timeseries.py \$sub \$run; done; done'"
```

Complete capture of any input data, computational environment, code, parameters, and outputs possible — without sacrificing modularity

Enables enigma-style computing — analyze data that you don't have!

WP3 – Task 3
UNIGE

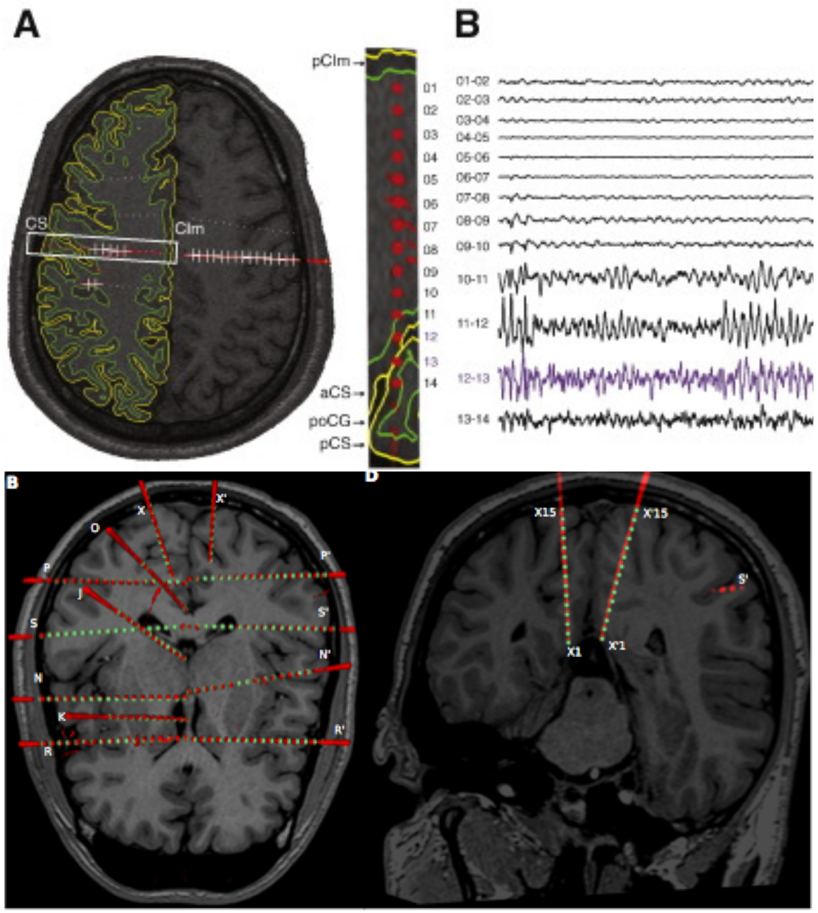
UNIGE – Duties in WP3 - Task 3

1. Pre-process and validation of SEEG dataset
2. Preparation of SEEG cohort in BIDS format (bids-ieeg standard) and validation
3. Studying temporal dynamics in non-demented adults exploiting high-quality intracerebral recordings – i.e. SEEG
   - Contribute to VBC: characterization of complex temporal dynamics in "healthy" adults to inform model parametrization

StereoEEG – a brief introduction

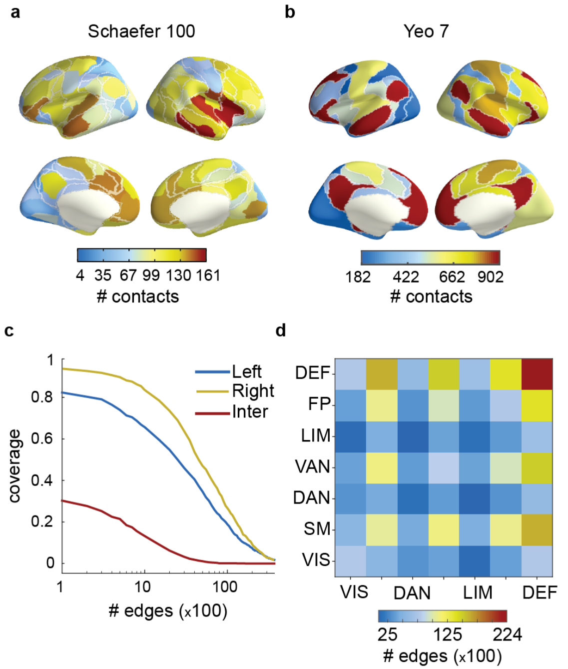
- Deep brain recording technique developed at Saint Anne Hospital, Paris by Bancaud and Talairach 1985.
- It is based on rigorous hypotheses about anatomo-electro-clinical correlations, and requires a comprehensive and multidisciplinary complex approach.
- Alternative to ECoG requires the use of grids electrodes placed directly onto the cortex

… SEEG for research purposes?

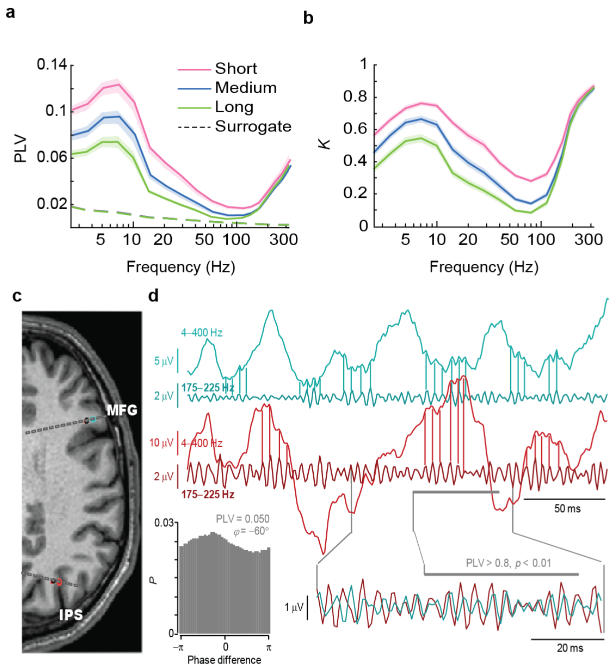


Phase synchrony in the human brain

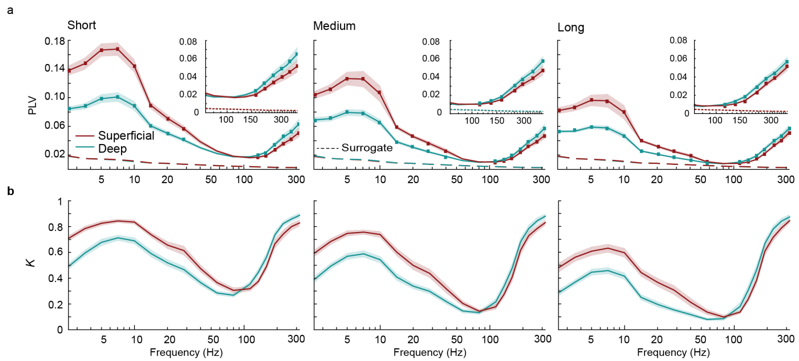
1. Appropriate coverage of edges in Schaefer and Yeo7 atlases



2. Spectral profiles of phase synch show significant coupling at large distances (> 10 cm) and up to high-gamma (> 200 Hz)



3. Phase-synchronization profiles are distinct between cortical layers



… But these don't tell us much about dynamics …

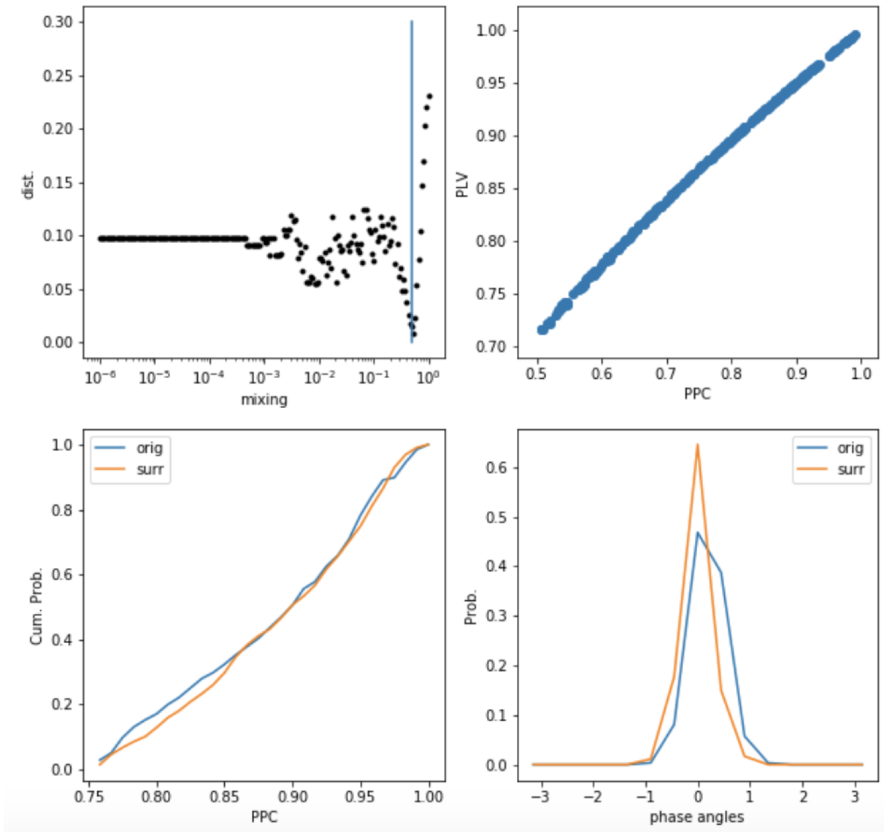
And there are now compelling evidences that functional connectomes are state dependent

3. Temporal dynamics in SEEG

- **Aims:** study temporal dynamics in large-scale brain networks

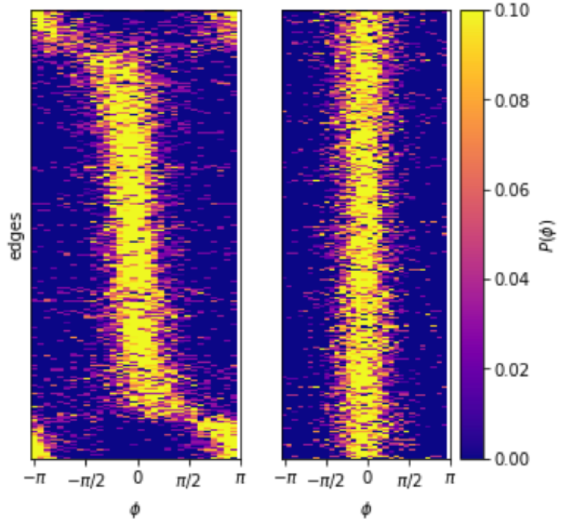
  ... Is there a preferred time-lag for measured static PLV between cortical areas ?

- **Methods:**
  - time-window phase locking value between channel pairs. We used time-window where phase is stable (i.e. flat Instantaneous frequency) for both channels.
  - Compute angles of complex PLV in each time window.
  - Test against surrogates (time-rotated and mixed) that maintained same Pairwise Phase Consistency (as non-biased phase synchrony estimate) to mimic zero-phased “volume-conduction”-like activity

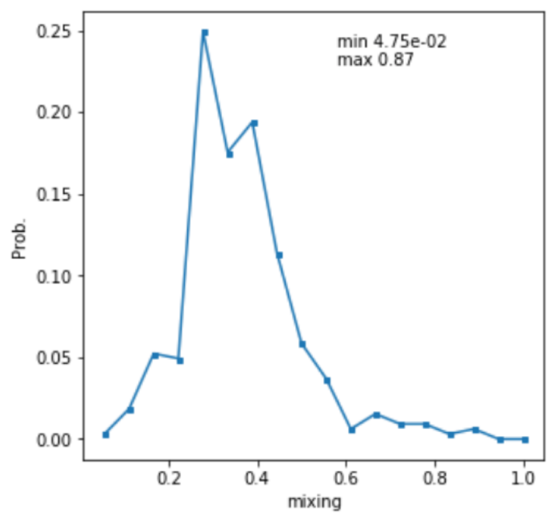


3. Temporal dynamics in SEEG

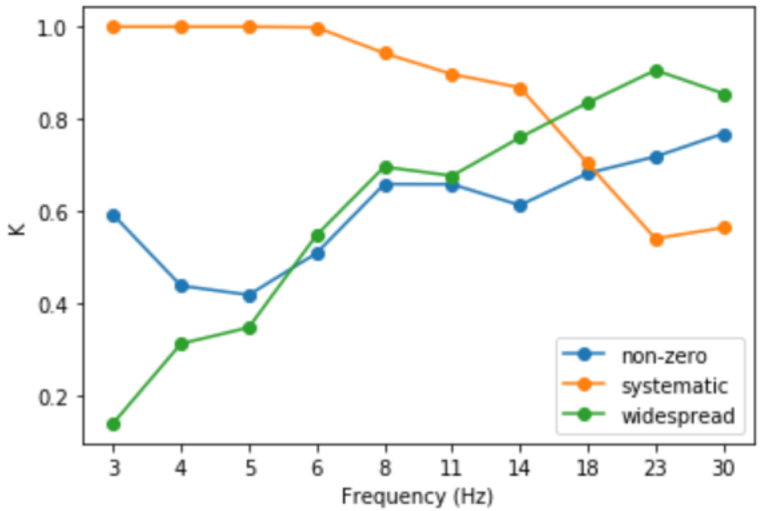
1. Phase difference distributions are



2. skewed mixing coeff. distribution with large values



3. Phase lagged coupling is a wide-spread phenomena => significant zero/near-zero phase coupling that is different from volume conduction



2. BIDS-iEEG and code sharing

- **Data:**
  - from 11 subjects have been prepared to comply to bids-ieeg standard and all subsequent analyses (i.e. UNIGE-task3) have been performed according to rules defined in the latest bids-ieeg (planning to add the whole cohort shortly)
  - Phaselag dyamics connectomes have been saved in numpy/cloudpickle format together with analyses parameters metadata (json format)
- **Code:**
  - that produces the temporal dynamics has been completely re-written in python (crosspy) alogn with anatomical co-localisation to Schaefer

Helsinki-team objectives and progress

UNIVERSITY OF HELSINKI

European Commission

- Electrophysiological "validation data" for VBC modelling
- Validation data = numbers to guide model construction and constrain model dynamics
- Initially planned: standard quantifiers of **criticality** (DFA, avalanche exponents) and **connectivity** (phase and amplitude coupling)
- Ongoing developments:
  - Expansion of criticality to include bistable dynamics
  - Expansion of within-frequency connectivity to *true* cross-frequency coupling
  - Novel temporal micro-scale perspective into phase dynamics and coupling

Validation-data in M12 deliverable

Connectome-level:

- Static connectomes of phase coupling (PLV, wPLI)
- Static connectomes of amplitude coupling (CC, oCC)
- Static connectomes of phase and time lags
- Dynamic connectomes of phase coupling (PLV, wPLI in fixed time windows) and/or Burst-based phase-locking-intervals connectomes

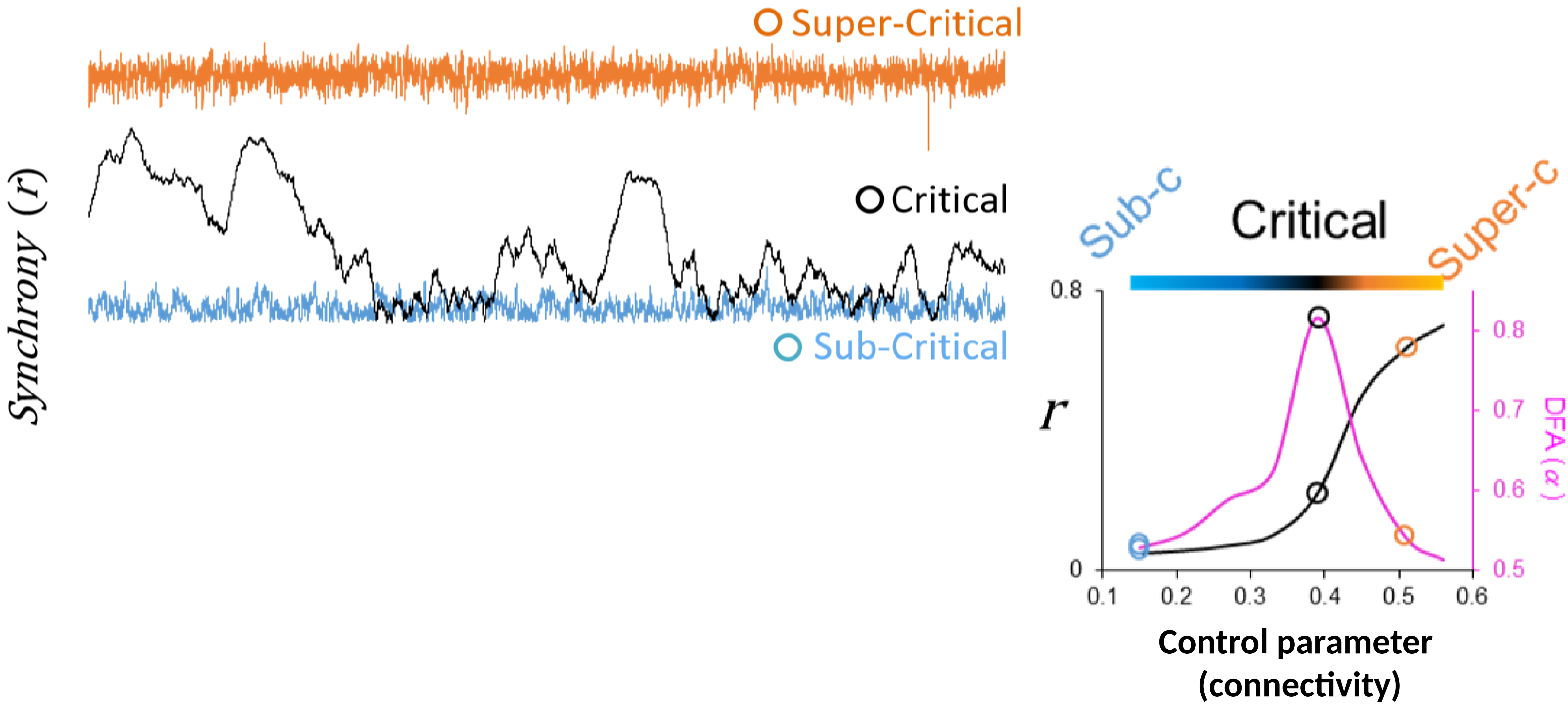
Node-level:

- LRTC estimates with DFA (maybe bistability)
- Phase autocorrelation functions? Burst/Transition statistics

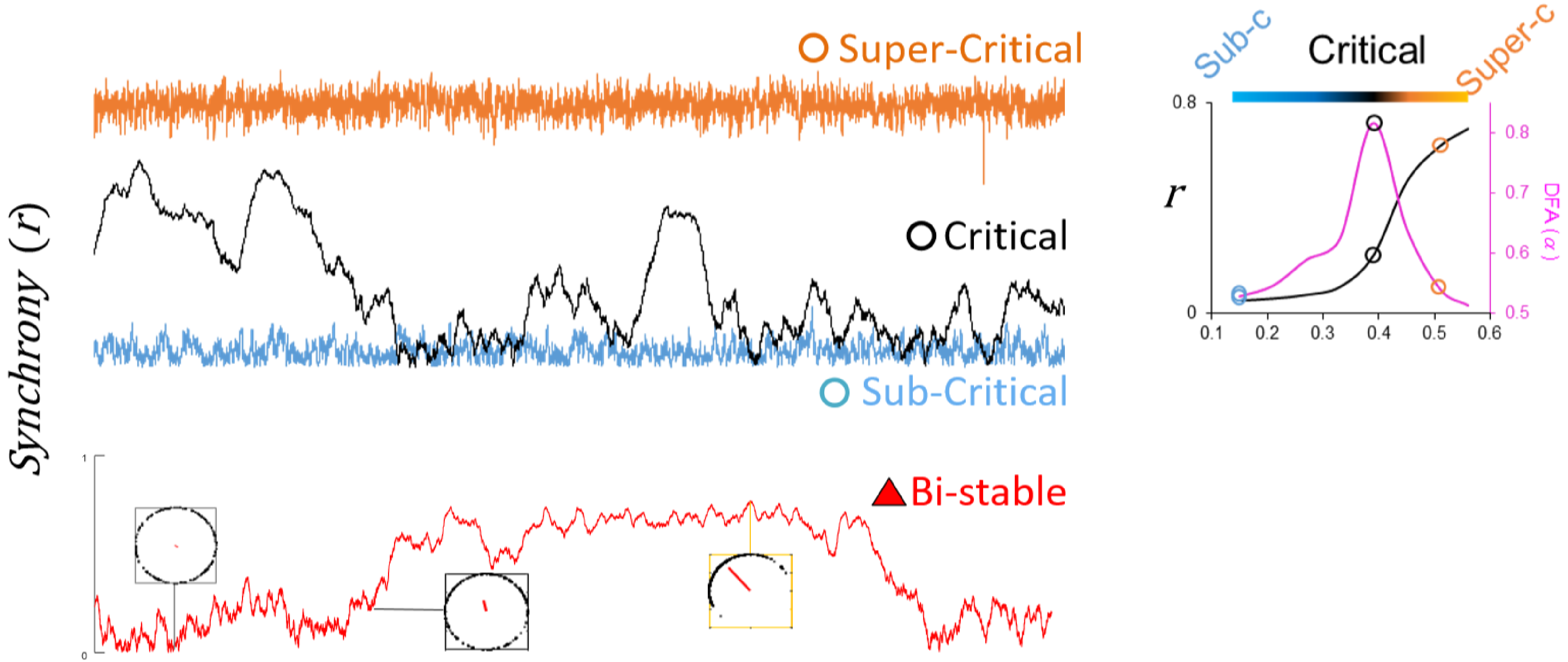
Whole-brain-level:

- Avalanche scaling exponents / distributions
- Avalanche point-process time series
- Graph-strength and module-strength time series

“Classical” critical synchronization dynamics



Expansion to include bistable dynamics



Bistable dynamics: theoretical basis in sub-critical Hopf bifurcation

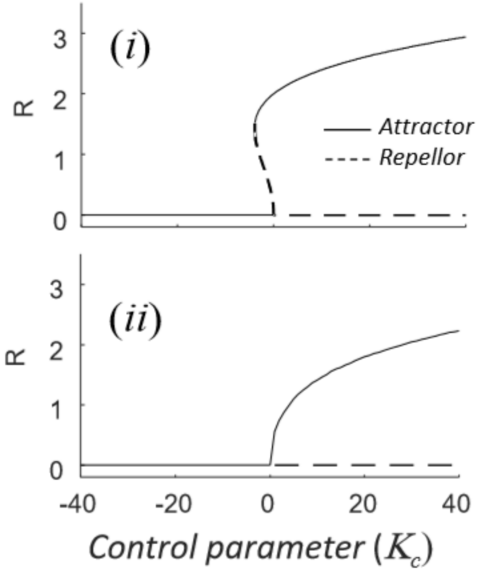
The fGn and BiS critical processes can be explained using the canonical Hopf bifurcation (Freyer et al., 2012):

$$\frac{dr}{dt} = -r^5 + \lambda r^3 + \beta r + \eta[(1-\rho)\xi_a(t) + \rho r \xi_m(t)]$$

Bifurcation parameter: β
Weight of the state-dependent noise: ρ
Shape parameter: λ
noise influence: η
Additive noise: $(1-\rho)\xi_a(t)$
State-dependent noise: $\rho r \xi_m(t)$

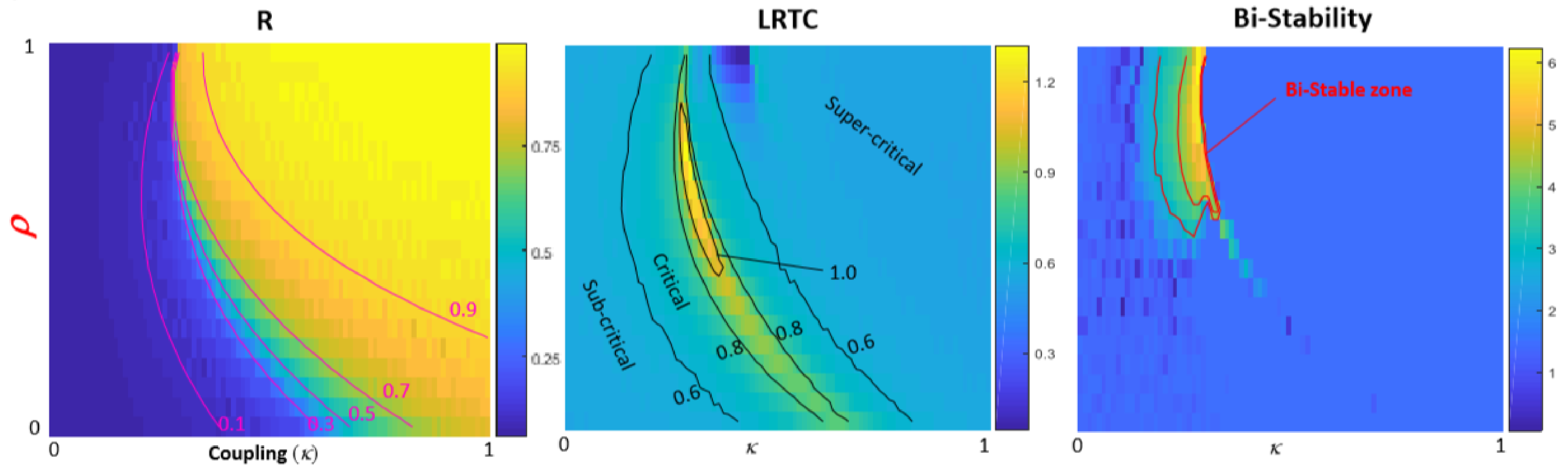
i. Sub-critical bifurcation produces bi-stable dynamics, *i.e.*, two attractors (essence: driven by large state-dependent noise ρ)

ii. Super-critical bifurcation produces gradual, one-attractor dynamics, *i.e.*, fGn fluctations (Palva & Palva, 2018)



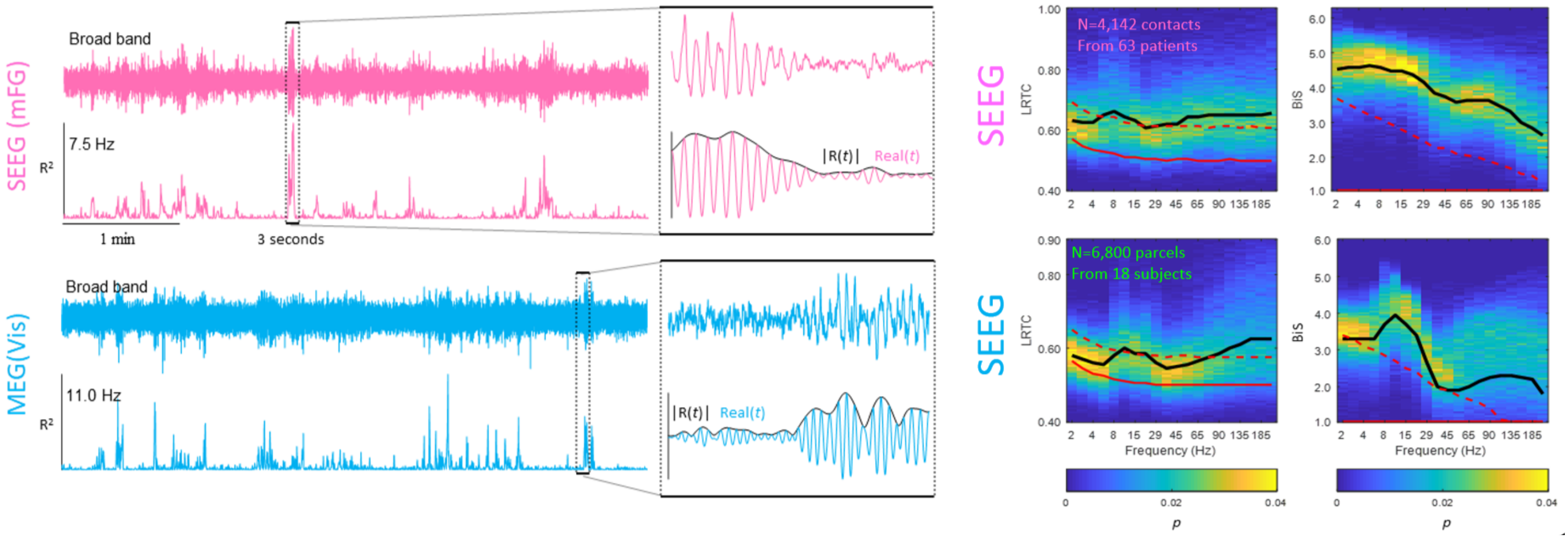
* ***Sub-critical bifurcation***: the limit cycle occurs before the loss of stability of the fix point

① Overlapping of critical regime and BiS – model



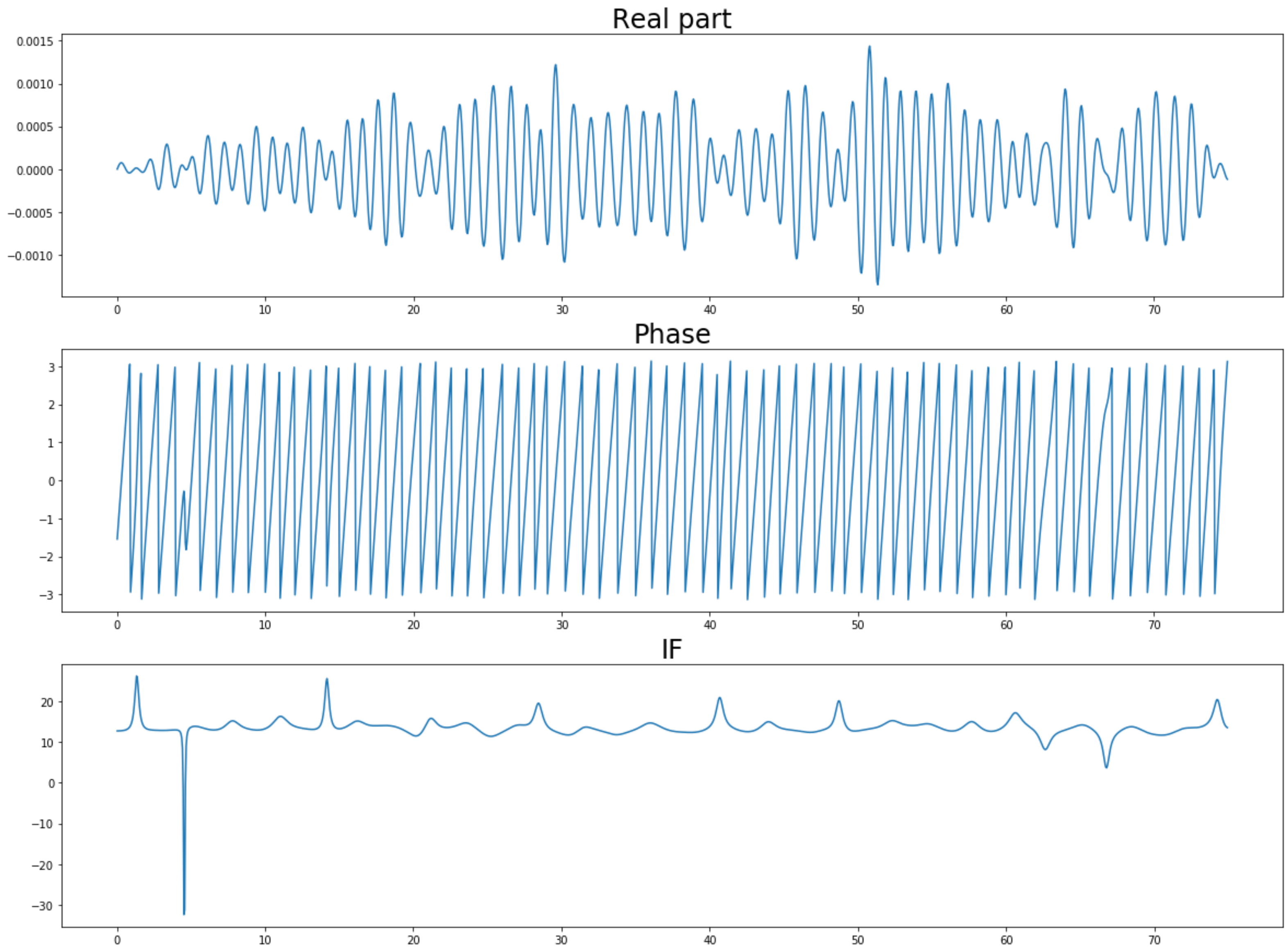
Kuramoto modelling with slow feedback reveals partially overlapping regimes for critical and bistable dynamics

Bistable human brain dynamics in MEG and SEEG



“Micro-scale” oscillation phase dynamics

~7.5 Hz oscillations in SEEG



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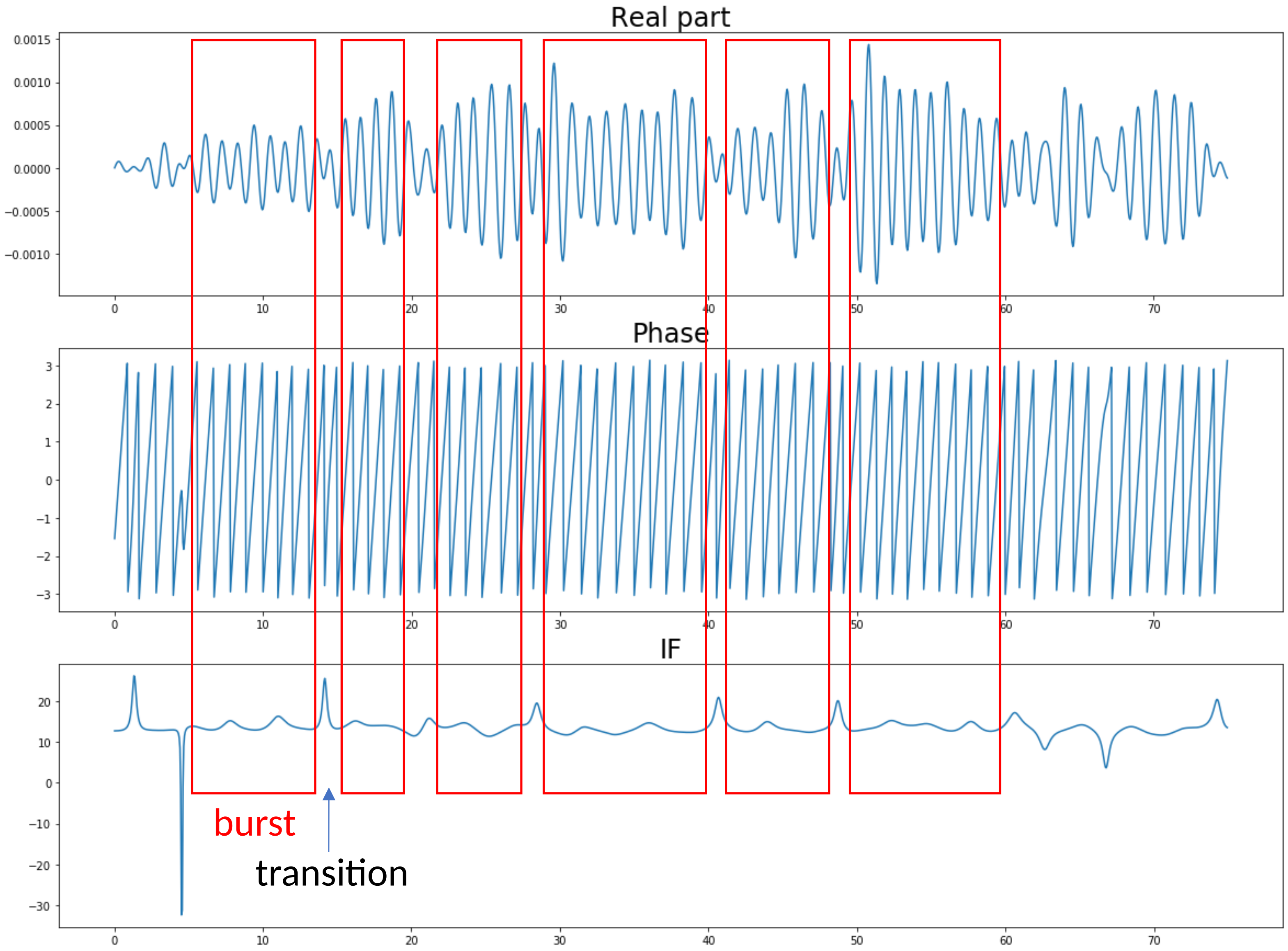
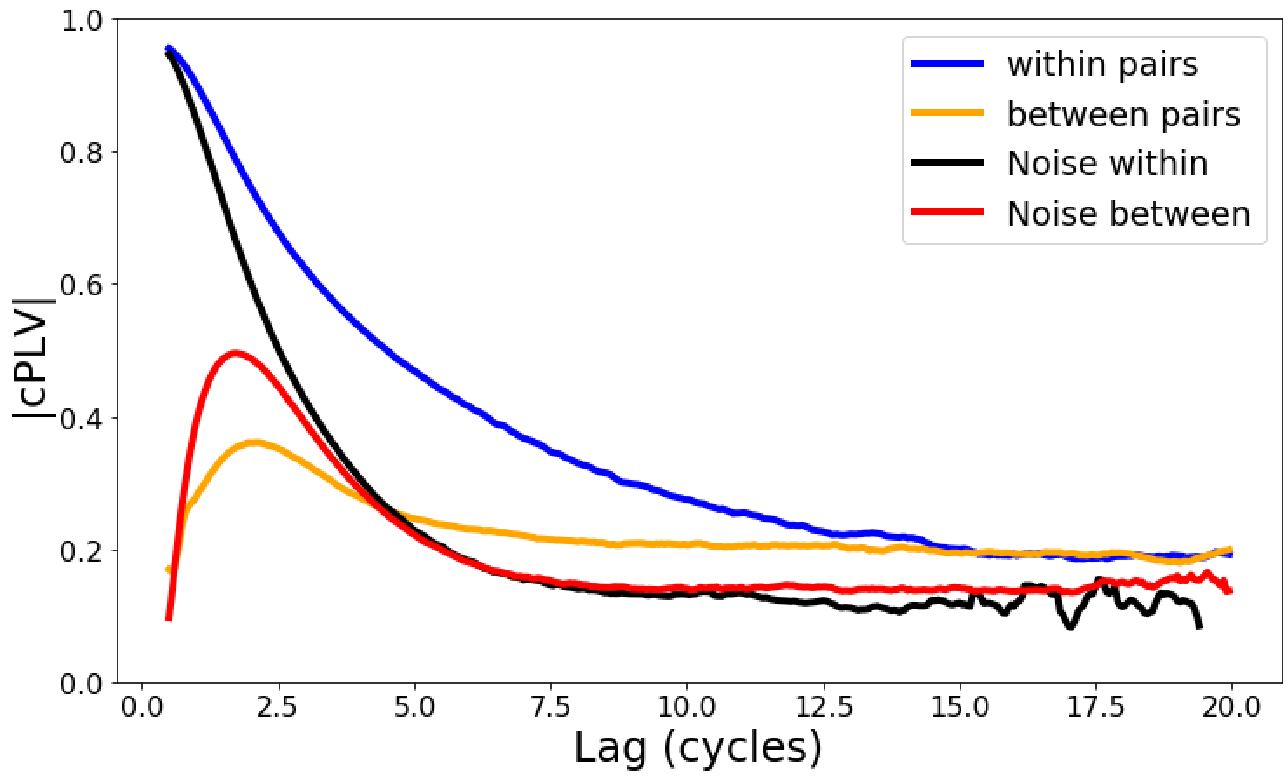


Phase autocorrelations within and between bursts



=> Phase continuity within bursts

=> Phases uncorrelated between bursts

Thank you!

- Helsinki team

Satu & Matias Palva

Sheng Wang *(criticality and bistability)*

Felix Siebenhühner *(connectivity and cross-frequency coupling)*

Vladislav Myrov *(local and network synchronization dynamics)*

Ehtasham Raja *(starting 16.9.)*