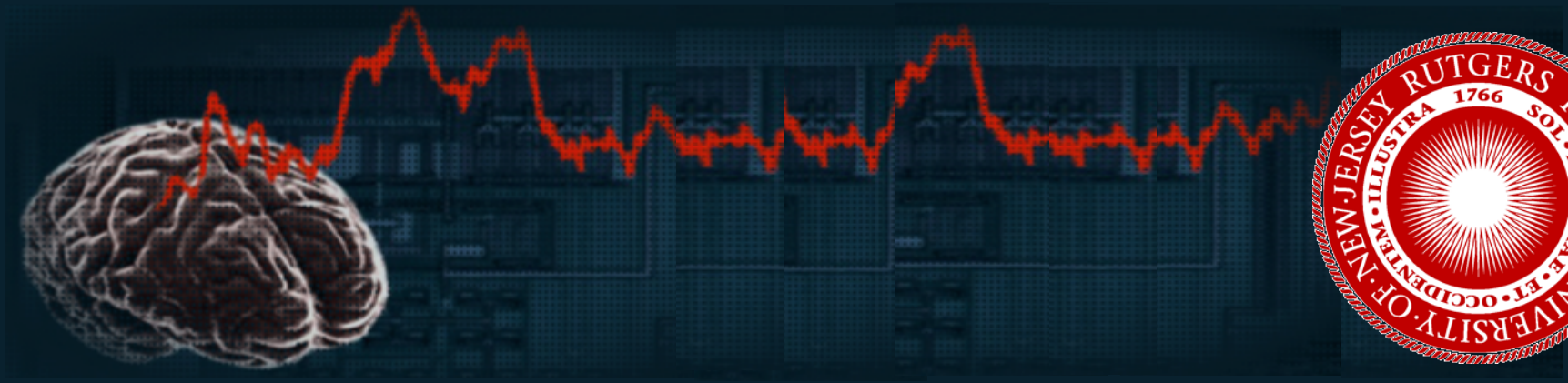


Does Brain Functional Connectivity Alter Across Similar Trials During Imaging Experiments?

Li Zhu, and Laleh Najafizadeh

Integrated Circuits and NeuroImaging Laboratory

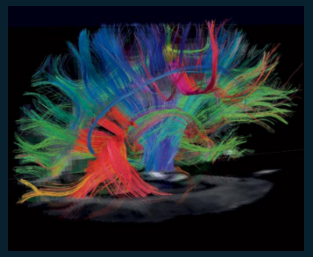
04/29/2015

Outline

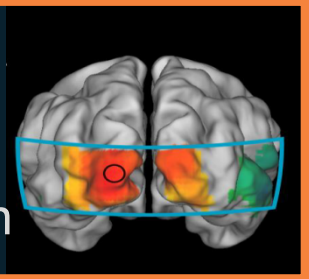
- **Introduction**
  - Brain Connectivity
  - Motivation
  - Problem Definition
- **Experiment Setup**
  - Task Paradigm
  - Imaging Technique
- **Processing**
  - Preprocessing
  - Similarity Analysis
  - Statistical Testing
- **Results**
- **Conclusion**

Brain Connectivity

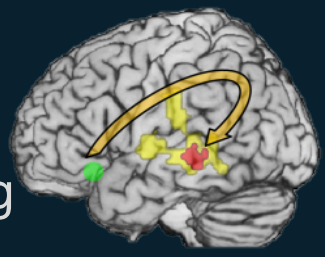
- **Investigates the Networks within the Brain**
- **Anatomical Connectivity**
  - looks for axonal connections
  - diffuse tensor imaging, tracing techniques



- **Functional Connectivity**
  - looks for statistical similarities between regional time series
  - functional neuroimaging techniques, seed-based correlation



- **Effective Connectivity**
  - looks for causal influences between regions of brain
  - functional imaging techniques, causal interactions modeling



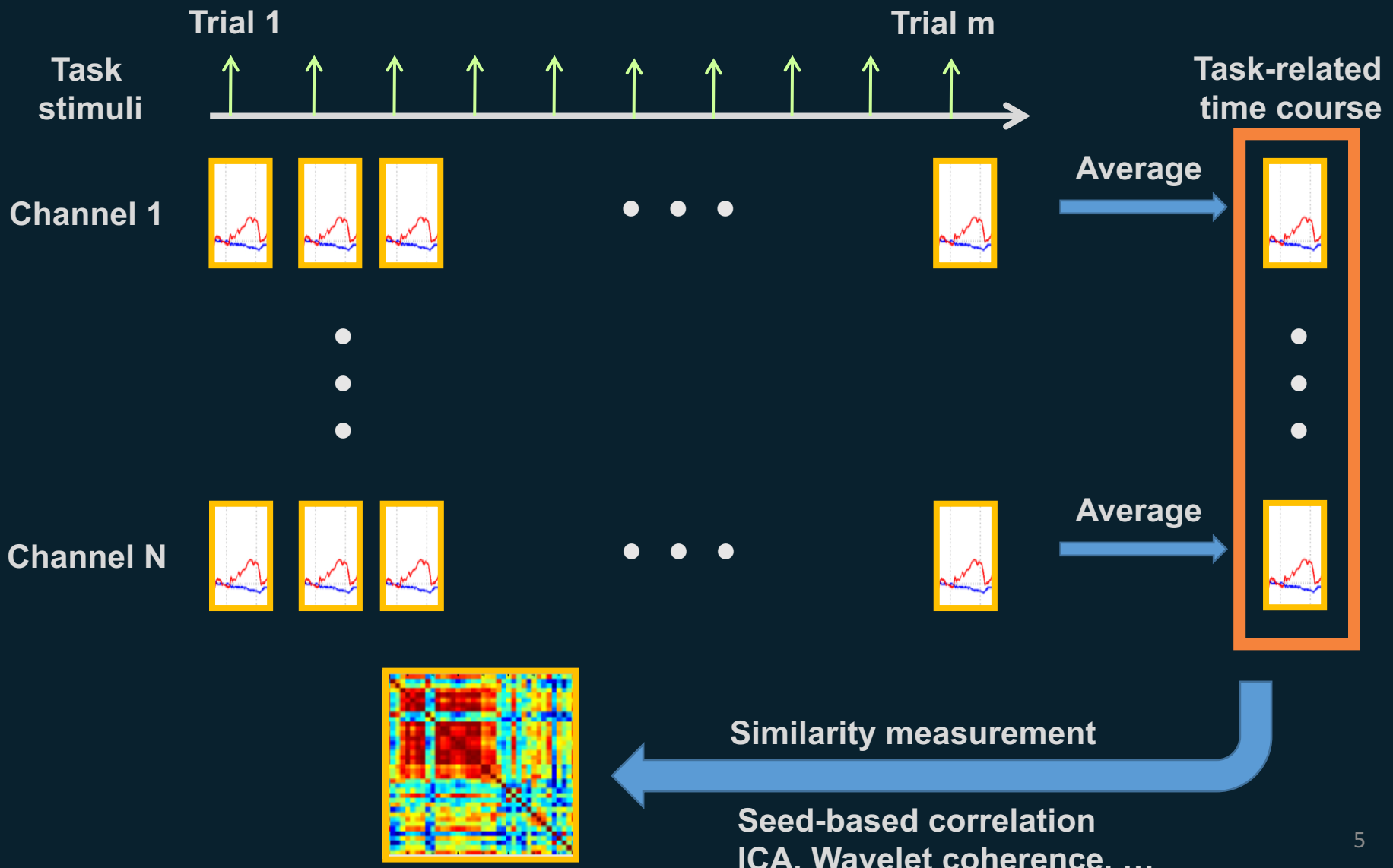
Motivation

- **Understanding the functionality of the brain at the network level**
- **Potential for early diagnosis of brain-related diseases**
  - **Autistic Spectrum Disorders**
    - 1 in 1000 children are diagnosed with Autism
    - Specific cause not known (biological, neurological, environmental…)
    - Early diagnosis could be a key

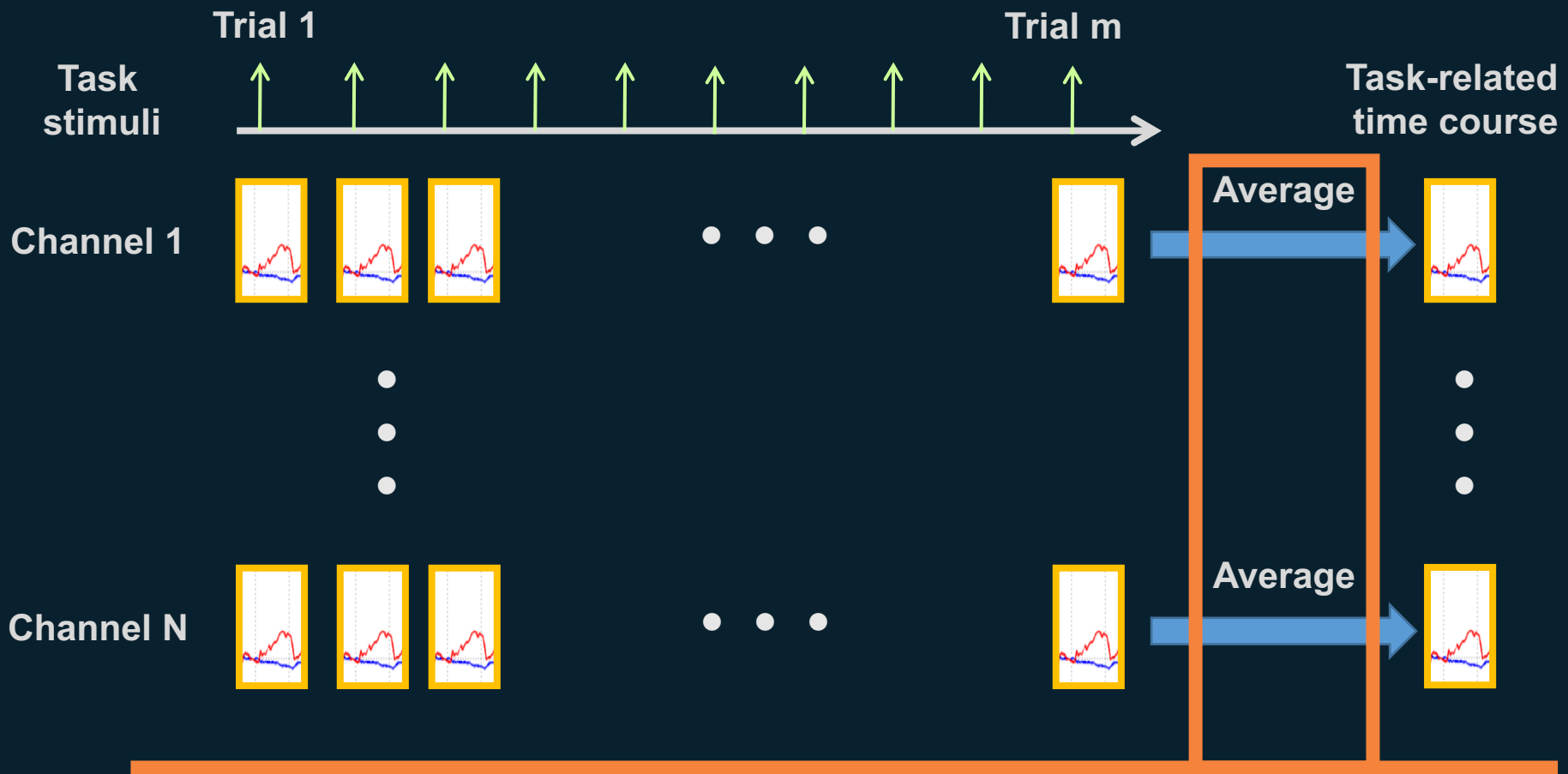
  - **Schizophrenia**
    - 1 in 100 US population are diagnosed with Schizophrenia
    - Abnormal function of neural communication that change the functional connectivity, while the anatomical elements remain intact.

http://www.treatoncemonthly.com/about-schizophrenia

Problem Definition



Problem Definition



Assumption: functional connections do not change across repeated trials

Problem Definition

Variability in the brain activation from trial to trial has been reported in previous studies:

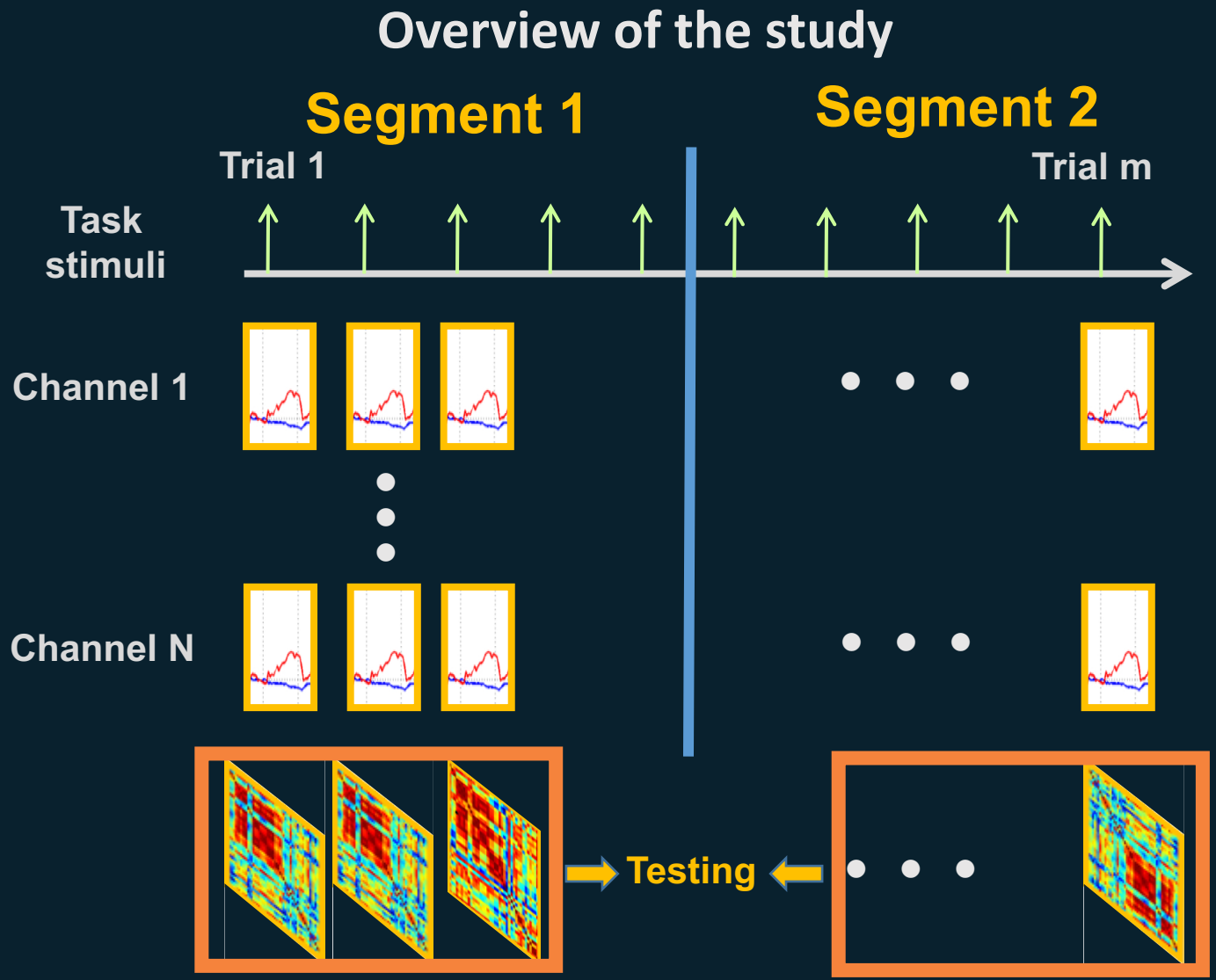
- L. Holper, N. Kobashi, D. Kiper, F. Scholkmann, M. Wolf, and K. Eng, "Trial-to-trial variability differentiates motor imagery during observation between low versus high responders: a functional near-infrared spectroscopy study.," Behavioural brain research, vol. 229, 2012, pp. 29–40.
- XS Hu, KS Hong, and SS Ge, "Reduction of trial-to-trial variability in functional near-infrared spectroscopy signals by accounting for resting-state functional connectivity," Journal of biomedical optics, 2013.
- M. Fox, A. Snyder, J. Zacks, and M. Raichle, "Coherent spontaneous activity accounts for trial-to-trial variability in human evoked brain responses," Nature Neuroscience, vol. 9, 2005, pp. 23–25.

Problem Definition

Functional connections do not change across repeated trials

Is it true?

Problem Definition



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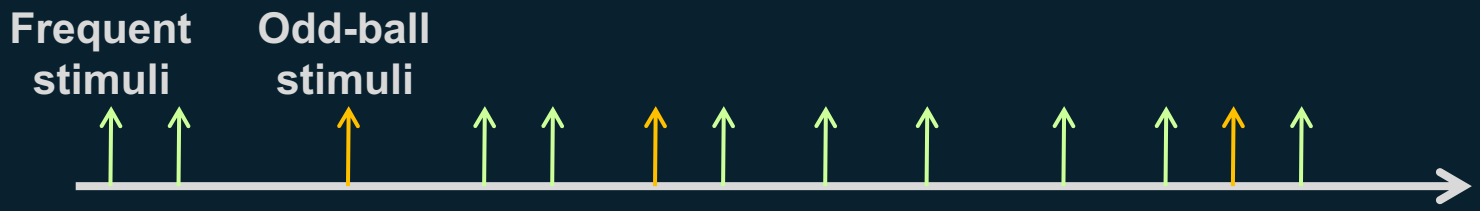
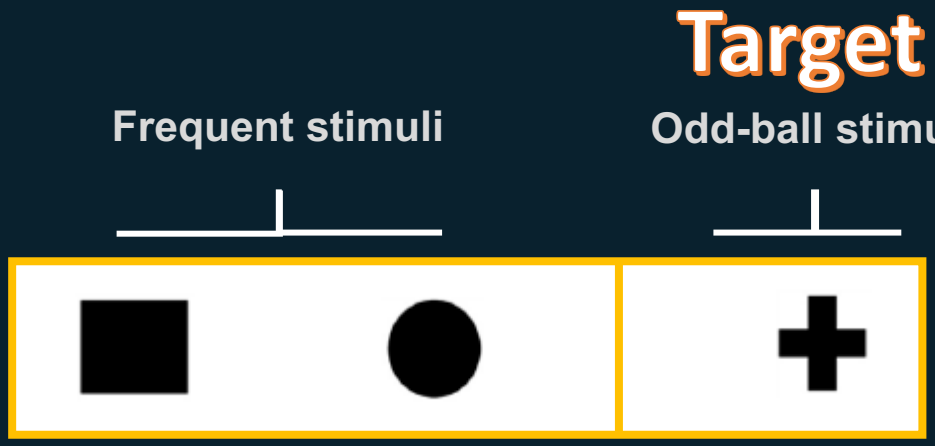
Task Paradigm

- **Modified Visual Odd Ball Task**

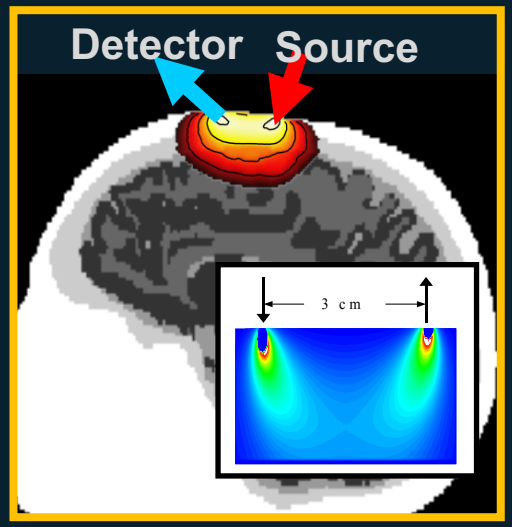


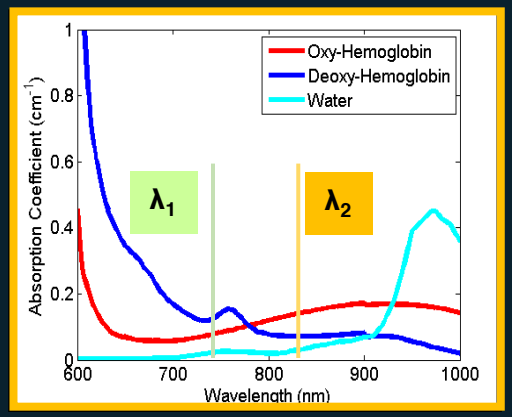


- 30 target trials
- 190 frequent stimuli trials
- Presentation time = 50 ms
- ITI = 10 – 12 s
- Left click if see target
- 5 healthy participants

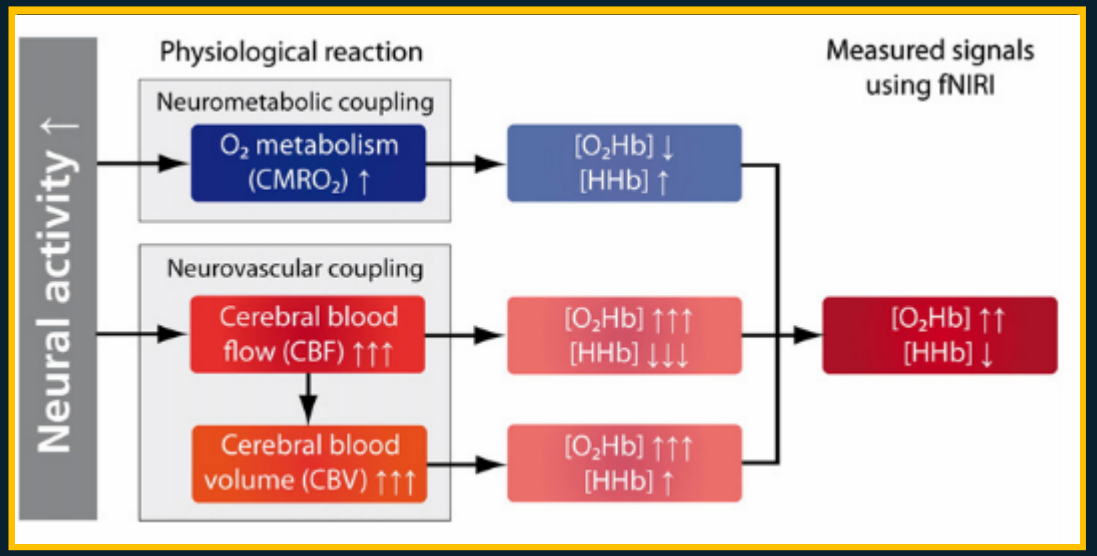
Imaging Technique

- Functional Near-Infrared Spectroscopy





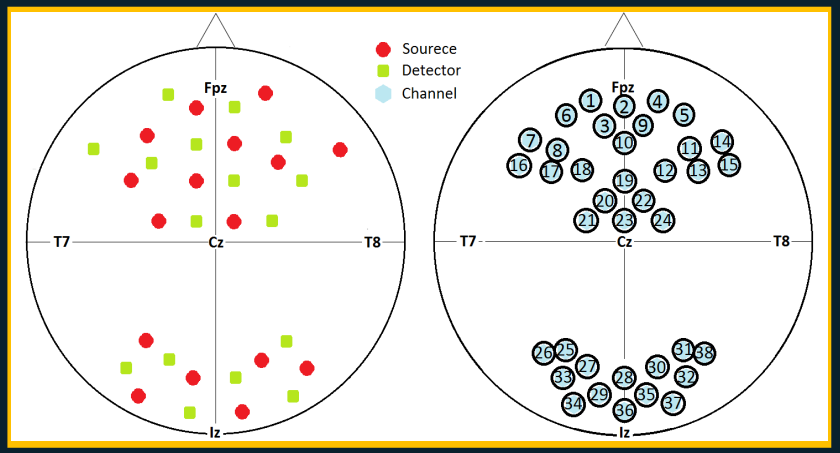
Overview of neurovascular mechanism



F. Scholkmann et. Al., "A review on continuous wave functional near-infrared spectroscopy and imaging instrumentation and methodology.," NeuroImage, vol. 85 Pt 1, Jan. 2014, pp. 6–27.

Imaging Technique

- **Functional Near-Infrared Spectroscopy**



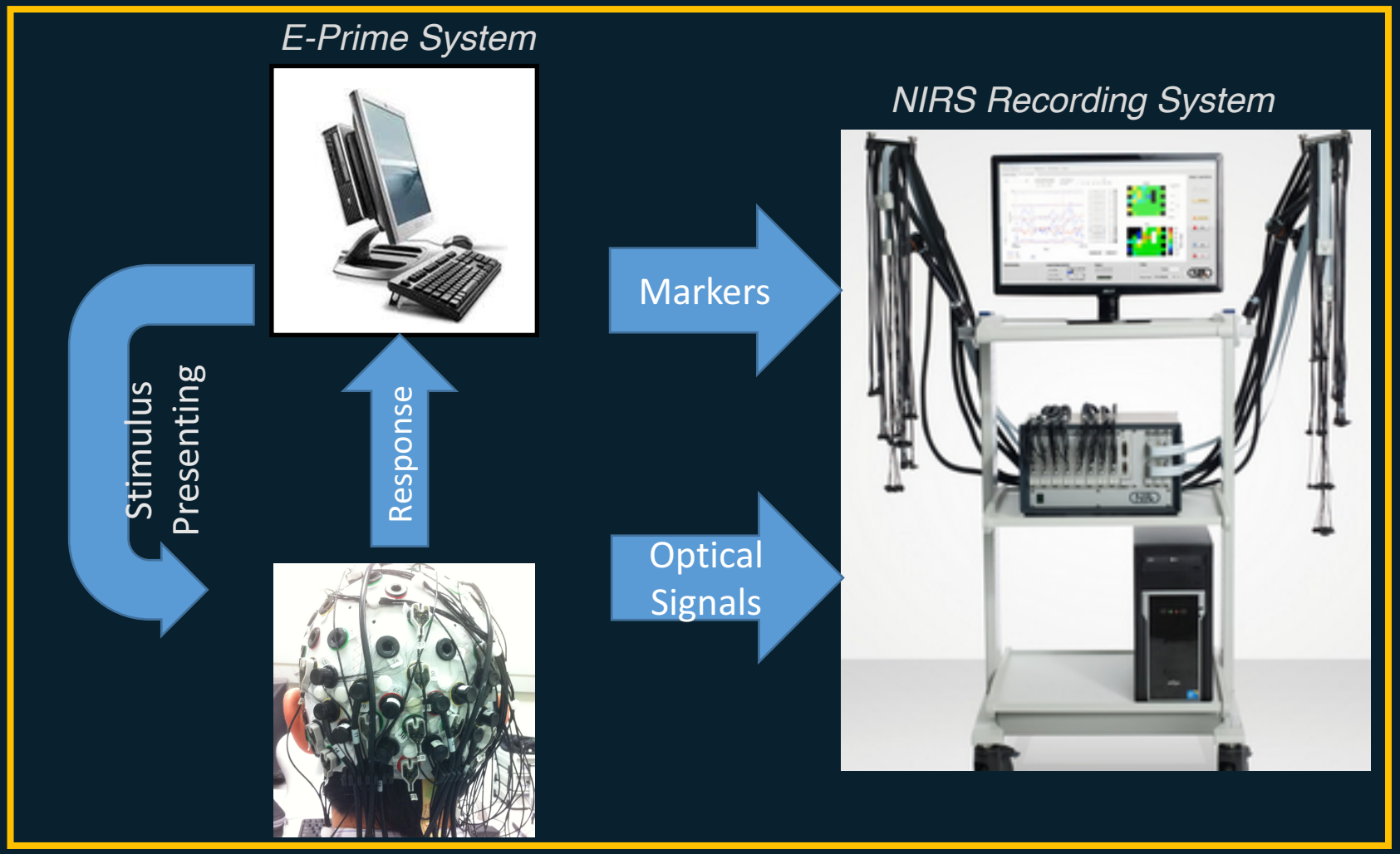
NIRx Medical Technologies
Model: NIRScout

www.nirx.net/imagers/nirscout

- 16 sources, 16 detectors
- 38 channels
- cover prefrontal/visual cortices
- 760 and 830 nm
- Sampling rate: 10.42 Hz
- Spatial Resolution: 3 cm
- Stimuli Sent by E-prime

Imaging Technique

- **Experimental Setup**



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Preprocessing

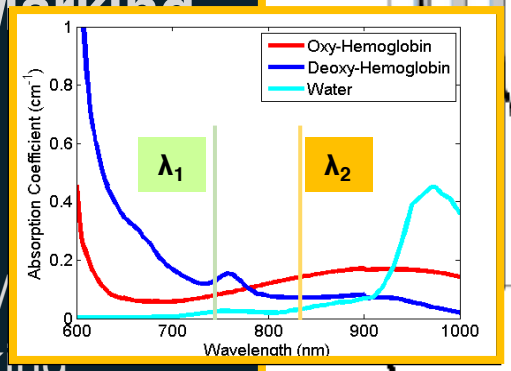
Preprocessing → **Wavelet transform coherence** → **Data organization & testing**

- **Extracting Brain Activities**
  - both ΔHbO_2 and ΔHbR were extracted using Modified Beer Lambert Law:

Wavelength 1 (760 nm): $$ln\left(\frac{I_{\text{task},\lambda_1}}{I_{\text{baseline},\lambda_1}}\right) = -\left(\epsilon_{HbO_2,\lambda_1}\Delta C_{HbO_2} + \epsilon_{HbR,\lambda_1}\Delta C_{HbR}\right)\cdot \mathrm{L}_{\lambda_1}$$

Wavelength 2 (830 nm): $$ln\left(\frac{I_{\text{task},\lambda_2}}{I_{\text{baseline},\lambda_2}}\right) = -\left(\epsilon_{HbO_2,\lambda_2}\Delta C_{HbO_2} + \epsilon_{HbR,\lambda_2}\Delta C_{HbR}\right)\cdot \mathrm{L}_{\lambda_2}$$

- **Artifacts Detection/Marking**
  - Detrending
  - Segmentation
  - Baseline Correction
  - Rapid slope Detection/
  - Outlier Detection/Marking



Wavelet Transform Coherence

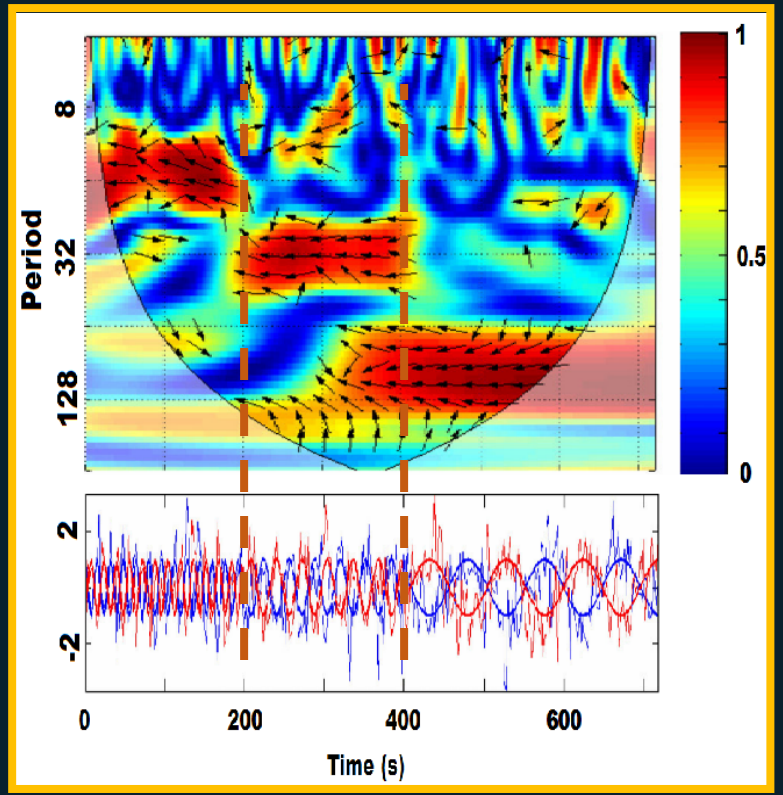
Preprocessing → **Wavelet transform coherence** → Data organization & testing

- Wavelet transform used for investigating the time-frequency features of the non-stationary signals:

$$W_{x_n}(n,s) = \sqrt{\frac{\Delta t}{s}} \sum_{m=1}^{N} x_m \Psi_0^*[(m-n)\frac{\Delta t}{s}]$$

- Wavelet transform coherence measures the cross-correlation between two time series in both time and frequency domain:

$$R^2_{x_n,y_n}(n,s) = \frac{|Smooth(s^{-1}W_{x_n,y_n}(n,s))|^2}{Smooth(s^{-1}|W_{x_n}(n,s)|^2)\cdot Smooth(s^{-1}|W_{y_n}(n,s)|^2)}$$



Simulated signals

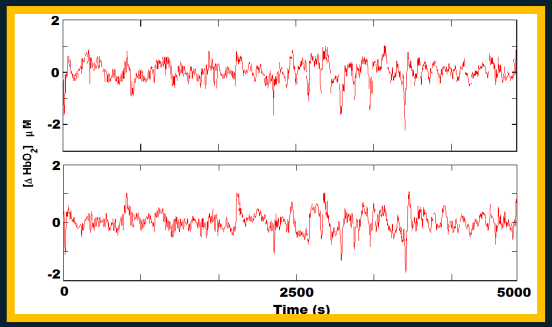
Chang et al., "Time–frequency dynamics of resting-state brain connectivity measured with fmri," *Neuroimage*

Wavelet Transform Coherence

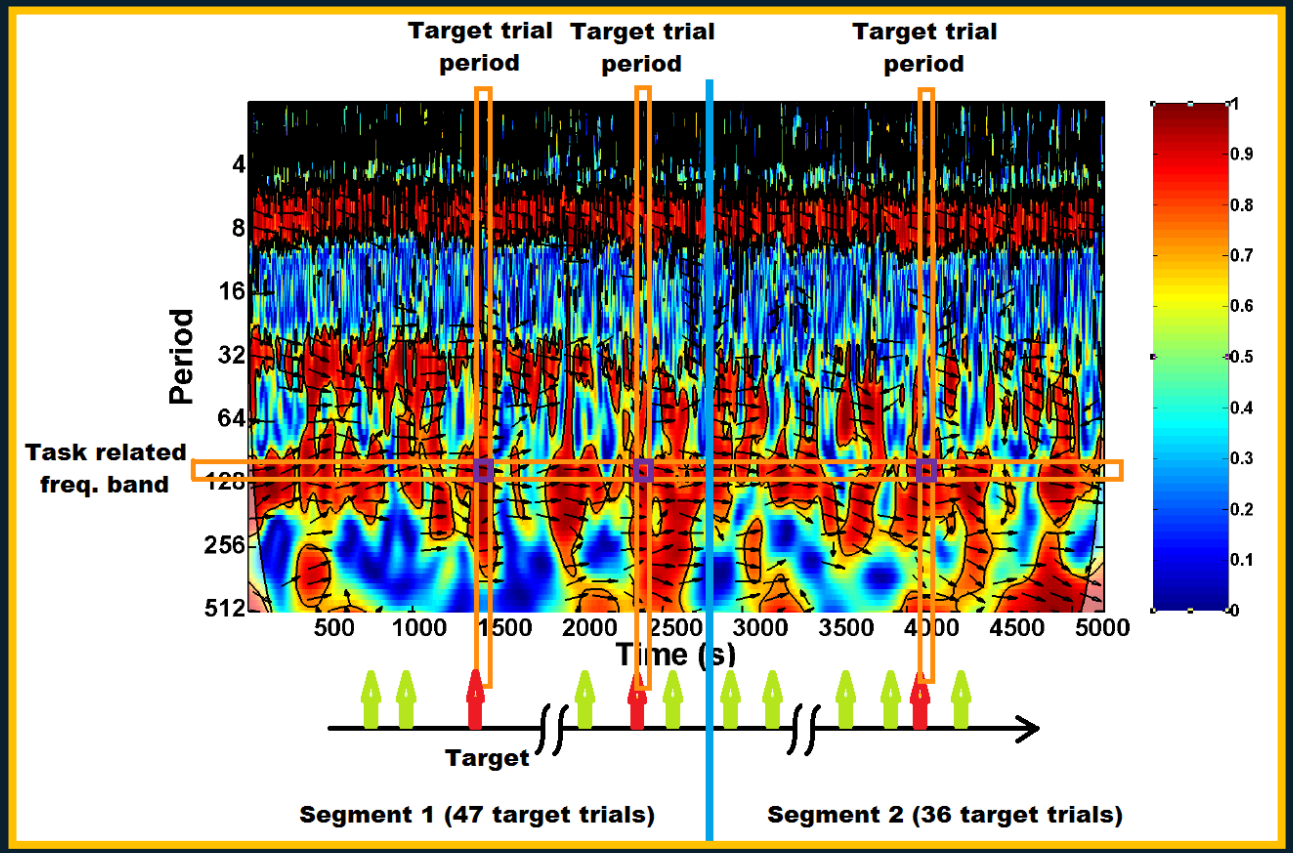
Preprocessing → Wavelet transform coherence → Data organization & testing

- WTC was computed for each channel-pair.

Channel 1 vs Channel 26

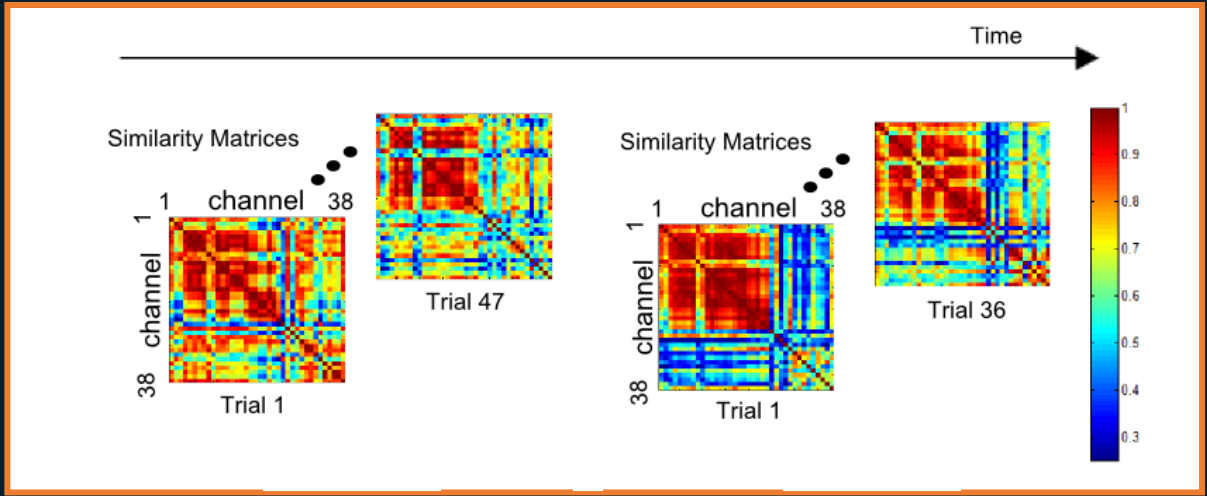


WTC Computing



Data organization & testing

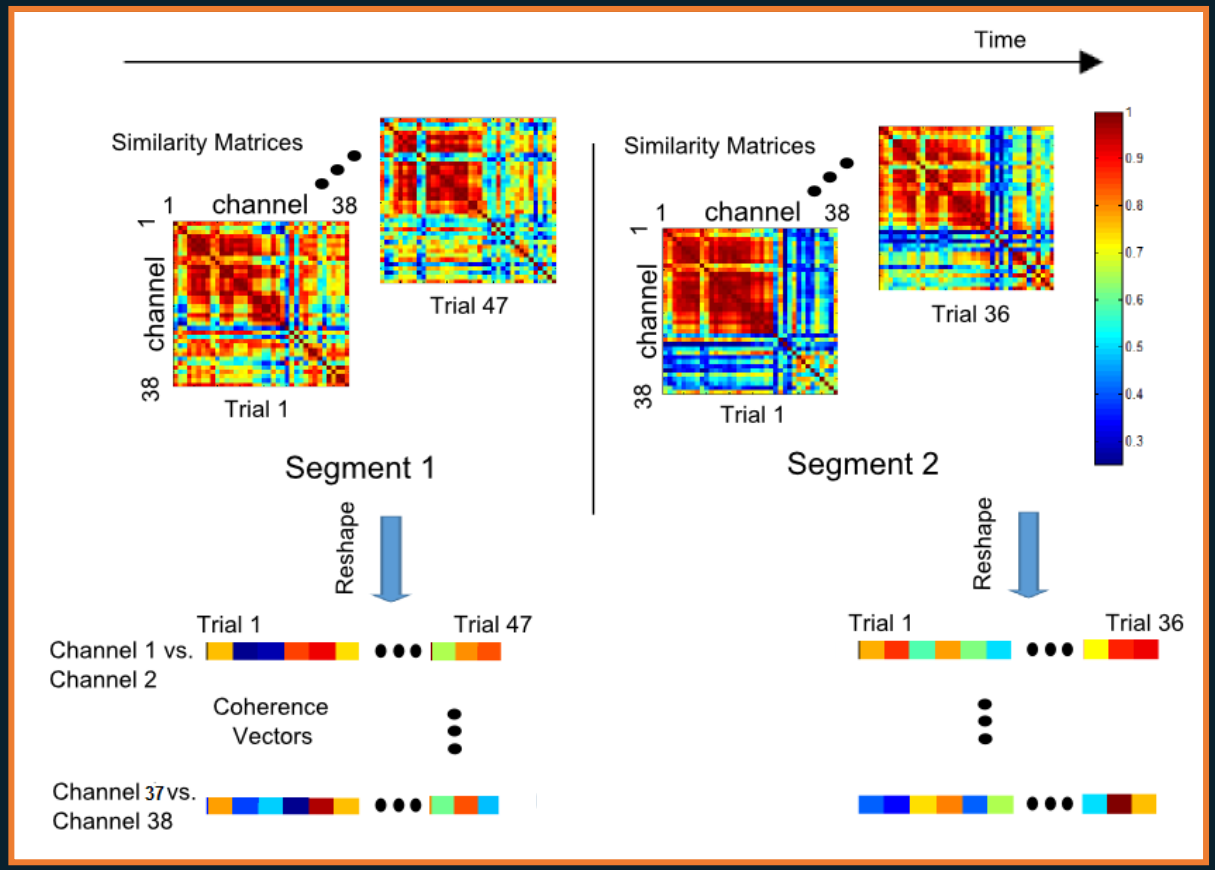
Preprocessing → Wavelet transform coherence → Data organization & testing



- The similarity measurements were organized into a series of matrices.

Data organization & testing

Preprocessing → Wavelet transform coherence → **Data organization & testing**



Data organization & testing

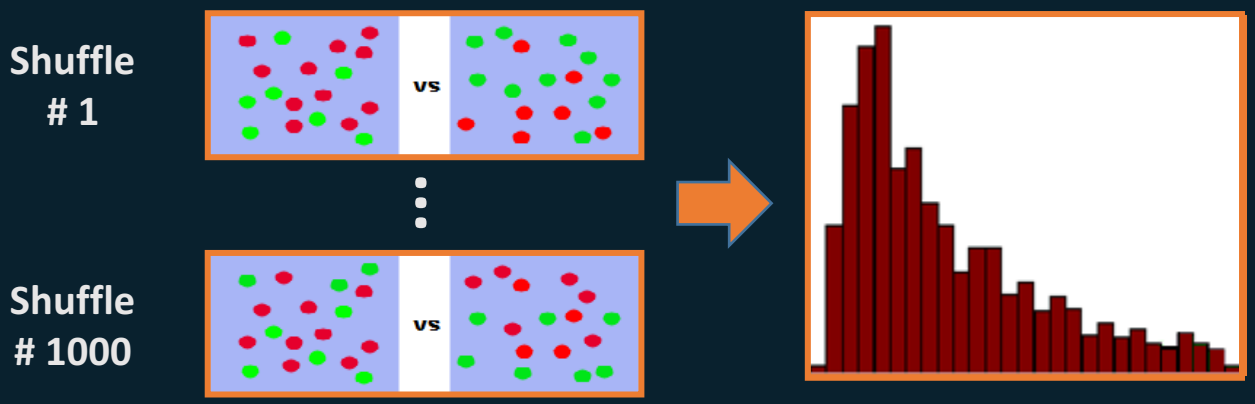
Preprocessing → Wavelet transform coherence → Data organization & testing

- **Statistical Testing**
  - Statistical testing was implemented for each channel-pair.
  - Null hypothesis H_0: The measure of functional connectivity from two segments are equivalent.
  - Non-parametric permutation testing: complete freedom with respect to the distribution of the data or their parameters, which could increase the sensitivity of the statistical test.

Data organization & testing

Preprocessing → Wavelet transform coherence → Data organization & testing

- **Permutation testing**
  - No need distributional assumptions
  - If H_0 is true, shuffling the data won't affect the test statistics
  - Algorithm
    - Shuffle data across segments, compute t-value
    - Repeat 1000 times, obtain null distribution
    - Compute t-value t_0 from the observed datasets
    - Compute p-value using t_0 with the null distribution



Data organization & testing

Preprocessing → Wavelet transform coherence → Data organization & testing

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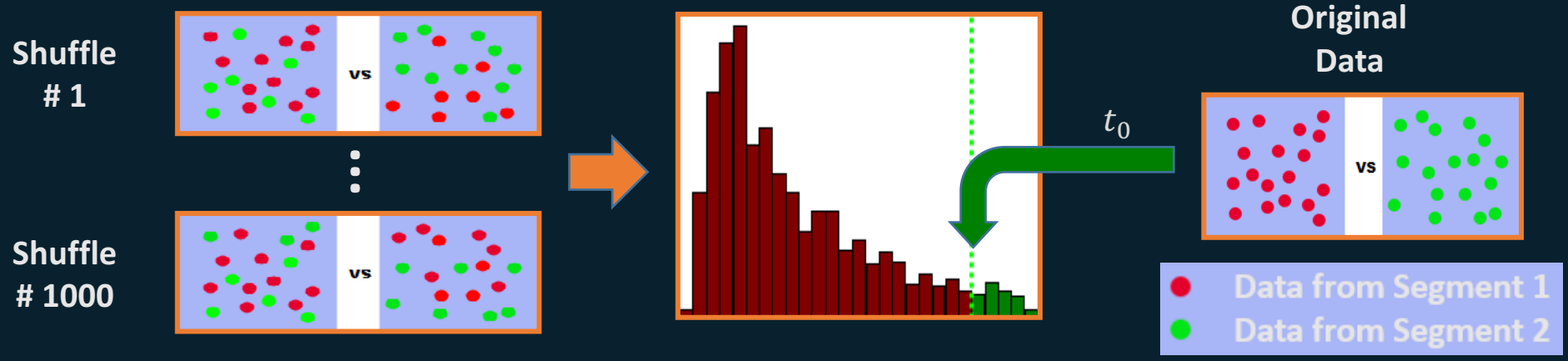

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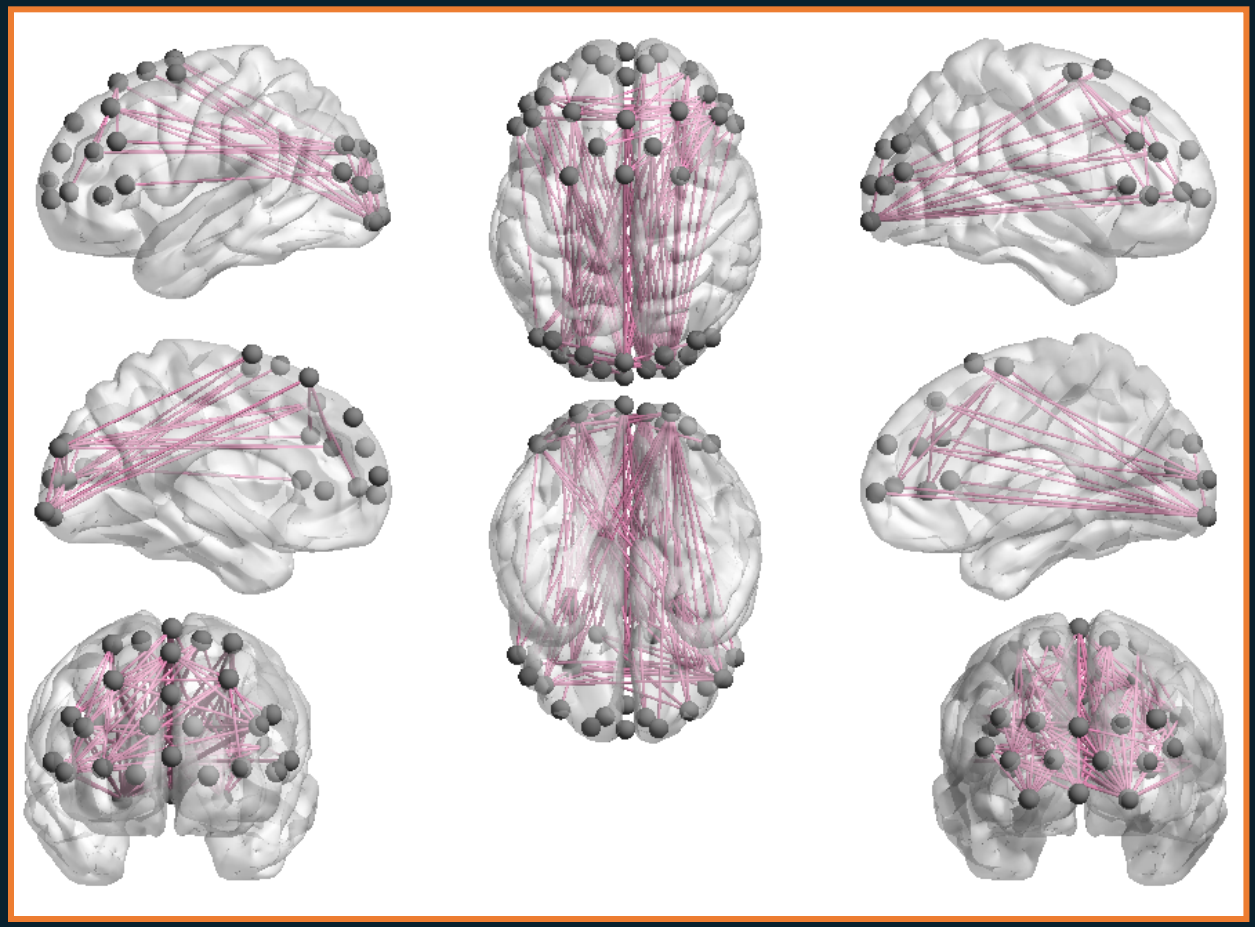
Results

- **Channel-pairs with Significant variation ($p<0.01$)**

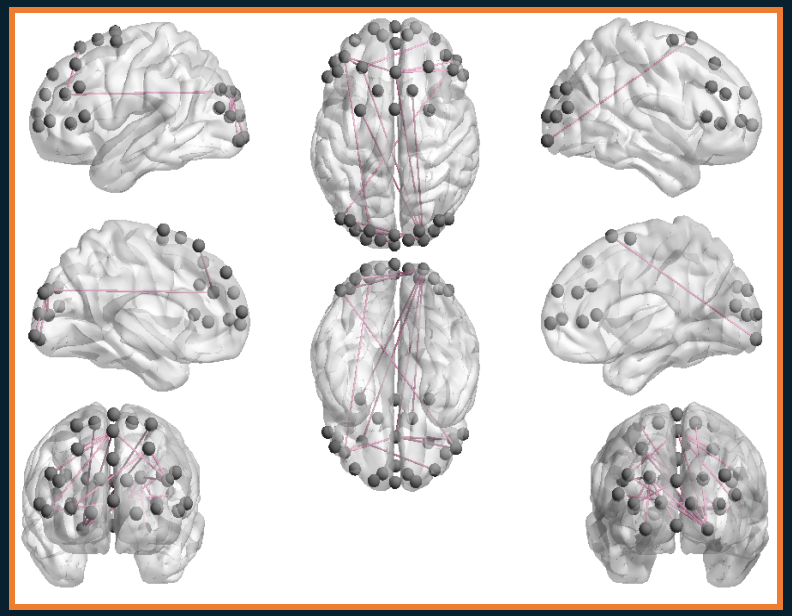
Segment 1 vs Segment 2



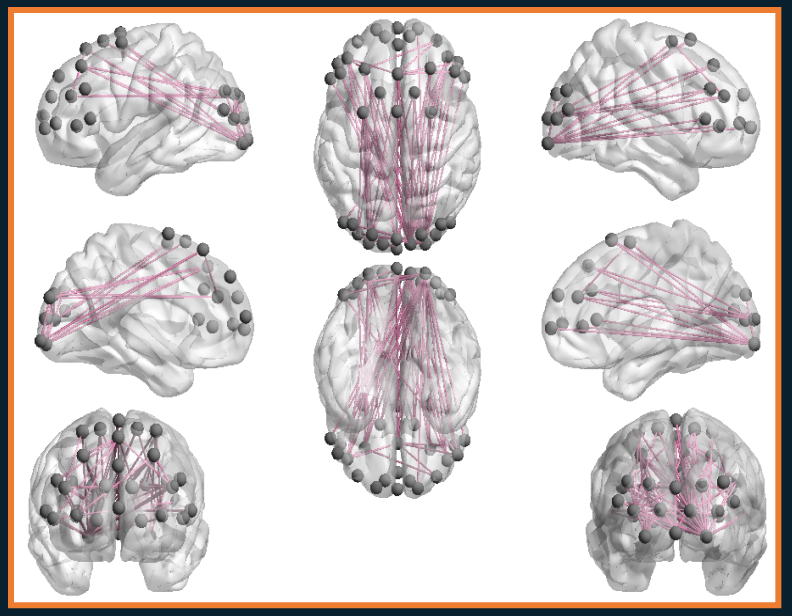
Results

- Channel-pairs with Significant variation ($p<0.05$)

Segment 1 vs
whole number of trials



Segment 2 vs
whole number of trials



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Conclusion and Future Work

- There exists channel-pairs that revealed significant variation between the two temporal segments in their functional connections
- Extracting the characteristics of the brain networks from all similar trials in a long-lasting experiment might introduce bias in the result
- The analysis procedure in this study might be extended to be used for determining the maximum number of similar trials in an experiment for which functional connections between brain networks do not vary significantly

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Thank you!