Cross-frequency coupling: methods & what do we know?

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Outline

❖ Introduction

➢ What is cross-frequency coupling?
➢ How to measure cross-frequency coupling?
➢ Can we measure time-resolved coupling?
Introduction

- What role, if any, do neuronal oscillations play in shaping computation and communication in large-scale brain networks?

<table>
<thead>
<tr>
<th>MUA</th>
<th>LFP</th>
<th>ECoG</th>
<th>MEG &amp; EEG</th>
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<tbody>
<tr>
<td><img src="signal_images.png" alt="Signal waveforms" /></td>
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</table>

1 - size of neuronal cluster

high - spatial resolution

invasive - non-invasive

>100,000 - low

http://www.neurotechnology.uni-freiburg.de/research/clinic/bmi-overview/box-bmi-scales
Introduction

• What role, if any, do neuronal oscillations play in shaping computation and communication in large-scale brain networks?


What is AVR website: http://www.drmueller-healthpsychology.com/What_is_AVE.html
Introduction

• What role, if any, do neuronal oscillations play in shaping computation and communication in large-scale brain networks?

(Contreras et al., J. Physiology, 1996)
What Is Cross-frequency Coupling?
Cross-frequency Coupling

- Cross frequency coupling (CFC):
  - Interaction between oscillations at different frequency bands

- Several synchronized neuronal assemblies in the brain:
  - Each supports a frequency band of the network rhythm

- Relationship between these frequencies:
  - Interaction between local neural circuits
  - Changing of intrinsic properties in each circuit

- G. Buzsaki. Cerebral Cortex, 1996
Types of CFC

- Phase-phase coupling
- Amplitude-amplitude coupling
- Phase-amplitude coupling

Jirsa et al., Front. Neurosci., 2013
Cross-frequency Phase-amplitude Coupling

- Phase-amplitude coupling

Canolty and Night, Trends Cogn Sci, 2010
Cross-frequency Phase-amplitude Coupling

• Phase-amplitude coupling

✓ Plausible physiological mechanisms
  • Low frequency phase reflects local neuronal excitability
  • High frequency power increases reflect:
    – A general increase in population synaptic activity (broad-band power increase)
    – Selective activation of a connected neuronal subnetwork (narrow-band power increase)

✓ Functional correlations

Canolty and Night, Trends Cogn Sci, 2010
Several studies have been conducted in this field

- Phase of the low-frequency theta (4 to 8 hertz) rhythm modulates power in the high gamma (80 to 150 hertz) band

Functional Correlations

• Several studies have been conducted in this field
  – Multi-item working memory maintenance is accompanied by PAC in human hippocampus

Several studies have been conducted in this field

- Local field potentials recorded from the primary motor cortex (M1) arm area:
  - Three groups of patients undergoing neurosurgery
  - Exaggerated coupling between $\beta$-phase (13–30 Hz) and $\gamma$-amplitude (50–200 Hz) in Parkinson disease

- Coralie de Hemptinne, et al. PNAS, 2013
<table>
<thead>
<tr>
<th>Summary of roles and patterns</th>
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<td><strong>Observed in:</strong></td>
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<td>• Cognitive events</td>
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<td>• Task performance</td>
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<tr>
<td>• Sensory perception</td>
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<tr>
<td><strong>Proposed role in:</strong></td>
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<tr>
<td>• Local computation</td>
</tr>
<tr>
<td>• Learning and memory</td>
</tr>
<tr>
<td>• Inter-areal communication</td>
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<td><strong>Altered pattern in some diseases:</strong></td>
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- Canoltty and Night, Trends Cogn Sci, 2010
- Tort et al., J. Neurophysio., 2010
- Aru et al., Curr. Opin. Neurobiol., 2015
Summary of roles and patterns

Observed in:
- Several species: rats, mice, sheep, monkeys, and human
- Several brain regions: hippocampus, neocortex, basal ganglia

Associated with:
- Cognitive events
- Task performance

“`It is potentially essential for normal brain function and understanding of its patterns can be crucial for diagnosing and eventually treating various disorders”`

Aru et al., 2015

Altered pattern in some diseases:
- Schizophrenia [Allen et al., Front Syst Neurosci, 2011]
- Parkinson Disease [Hemtinne et al., PNAS, 2013]
- Alzheimer Disease [Goutagny et al., Eur J. Neurosci., 2013]

- Canolty and Night, Trends Cogn Sci, 2010
- Tort et al., J. Neurophysio., 2010
- Aru et al., Curr. Opin. Neurobiol., 2015
How to Measure Cross-frequency Coupling?
Measuring Cross-frequency Coupling

• Several algorithms available
  – Each proper for a particular case
  – No single method has been elected as a preferred standard so far
# Measuring Cross-frequency Coupling

**Available measures:**

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<th>Measure</th>
<th>Description</th>
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<tr>
<td>1</td>
<td>ESC</td>
<td>The envelope to signal correlation</td>
<td>[Bruns and Eckhorn, 2004]</td>
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<td>2</td>
<td>PLVMI</td>
<td>Phase-locking based measure</td>
<td>[Vanhatalo et al., 2004]</td>
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<td>3</td>
<td>MVL</td>
<td>Mean vector length</td>
<td>[Canolty et al., 2006]</td>
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<td>4</td>
<td>GLM</td>
<td>The general linear model measure</td>
<td>[Penny et al., 2008]</td>
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<td>APSD</td>
<td>Amplitude power spectral density</td>
<td>[Cohen, 2008]</td>
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<td>6</td>
<td>CV</td>
<td>Coherence Value</td>
<td>[Colgin et al., 2009]</td>
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<td>7</td>
<td>KL-MI</td>
<td>Kullback-Leibler based modulation index</td>
<td>[Tort et al., 2010]</td>
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<td>8</td>
<td>ERPAC</td>
<td>Event related phase amplitude coupling</td>
<td>[Voytek et al., 2013]</td>
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### Measuring Cross-frequency Coupling

- **Available measures:**

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- ★★ Sensitive to coupling phase (Negative feature)
- ★★★ Need long data length
- ★✔ Only works on event-related datasets
- ★★★ Potentially not capable of calculating coupling intensity
Can We Measure Time-Resolved CFC?
Measuring Time-resolved PAC

- Most of available methods
  - Investigating PAC in frequency domain

- PAC: marks the cycles of relative excitability in neural ensembles
  - Biomarker for ongoing brain activity

- Limitations of available algorithms:
  - Requirement of a relatively long segment of data
  - Not capable of estimating intensity of the coupling

- Brain activity: nonstationary
- Dynamic fluctuation of coupling intensity
- Transient couplings in response to sensory, motor and cognitive events

Proposing a new method: Dynamic phase amplitude coupling

- Samiee & Baillet, in Prep.
Measuring Time-resolved PAC

- Sample Synthesized data
  - Generated with the model introduced by [Tort et al., J. Neurophysiol., 2010]

\[ F_P = 4 \text{ Hz}, \quad F_A = 121.5 \text{ Hz}, \]
\[ F_P = 5 \text{ Hz}, \quad F_A = 91 \text{ Hz}, \]
\[ F_P = 6.8 \text{ Hz}, \quad F_A = 64.5 \text{ Hz}, \]
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Measuring Time-resolved PAC

- Sample Synthesized data

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\[ + \]

\[ F_p = 5 \text{ Hz}, \ F_A = 91 \text{ Hz} \]
Measuring Time-resolved PAC: Applications

• Two applications:
  
  – Continuous data
    • Deep recording of freely moving rat
  
  – Block-designed experiments
    • MEG - Median nerve stimulation
I) Continuous data

- Local Field Potential of rat’s hippocampal area

**DPAC:**
Theta ([5-10]Hz) phase to gamma ([35, 350] Hz) amplitude

- Kenji et al., Neuron, 2009
- Samiee & Baillet, Under Prep.
I) Continuous data

Dynamic phase amplitude coupling in third layer of Entorhinal cortex

- Kenji et al., Neuron, 2009
- Samiee & Baillet, Under Prep.
II) Block-designed experiments

- Median Nerve Stimulation

DPAC:
Alpha ([8 - 12]Hz) phase to gamma ([35, 200] Hz) amplitude

- Samiee & Baillet, in Prep.
SUMMARY AND CONCLUSION
Summary

- **What is cross-frequency coupling?**
  - Interaction between oscillations at different frequency bands
    - ✓ Plausible physiological mechanism
    - ✓ Functional correlates
  - Capability of modulating different process in multiple brain regions
  - Biomarker of brain activity

- **How to measure cross-frequency coupling?**
  - Several algorithms available
    - ✓ Choosing the best method considering limitations and advantages of each method, knowing the particular purpose of the experiment

- **Can we measure time-resolved coupling?**
  - Yes!
    - ✓ ERPAC
    - ✓ DPAC
Thank You for Your Attention