Phase synchronisation and cross-frequency coupling

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BENESCO Lecture Series on Signal Analysis

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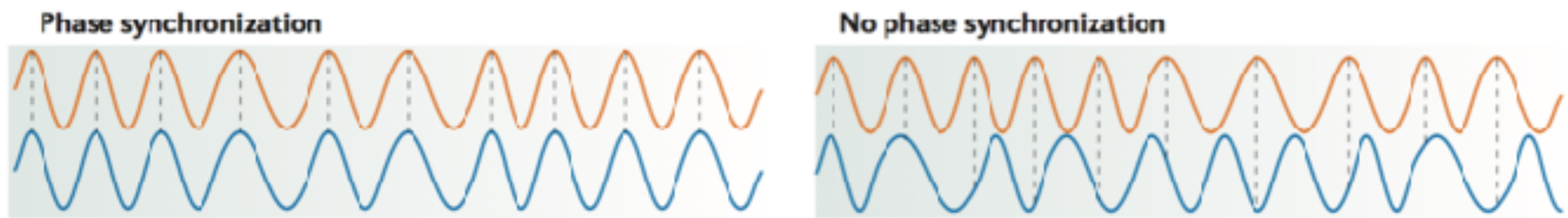
Introduction - Synchronisation and cross-frequency coupling

Phase synchronisation between two time-series



Fell J. and Axmacher N., Nature Review, 2011

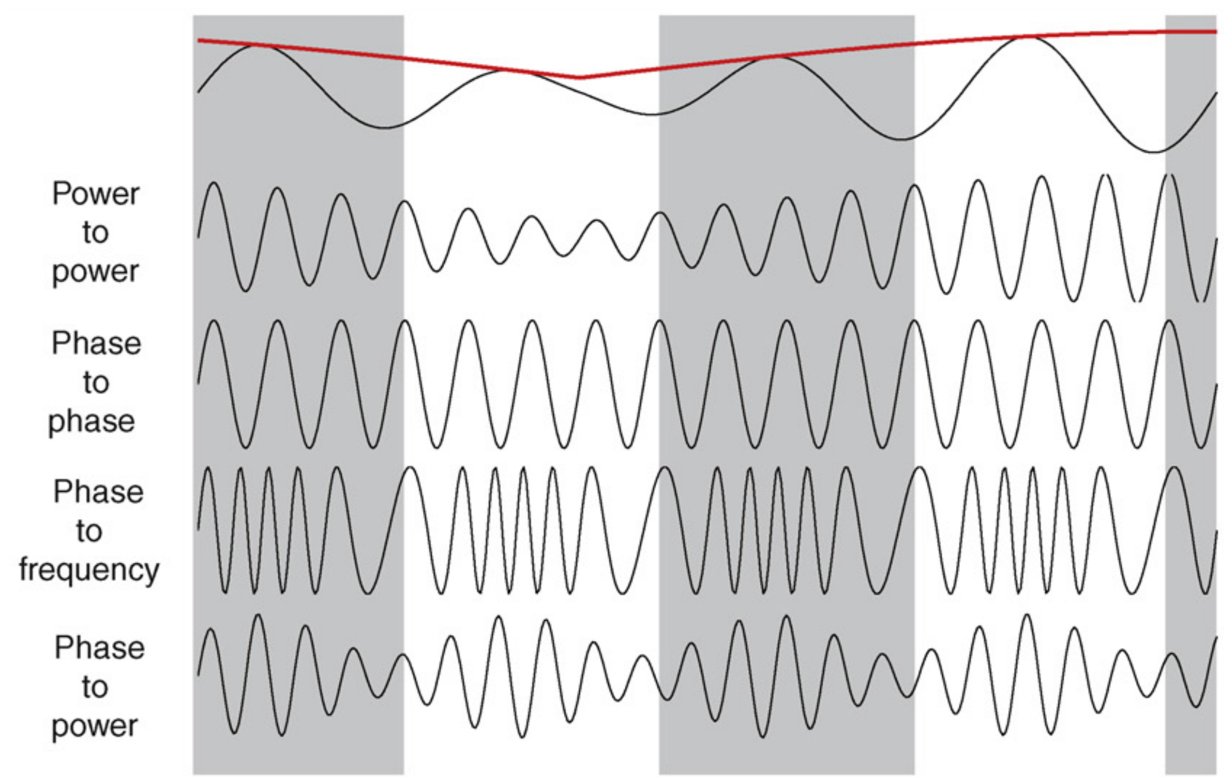
Cross-frequency coupling between different frequency bands

(a) Power of the gamma oscillations are correlated with power in the lower frequency band.

(b) In each slow cycle, there are four faster cycles and their phase relationship remains fixed.

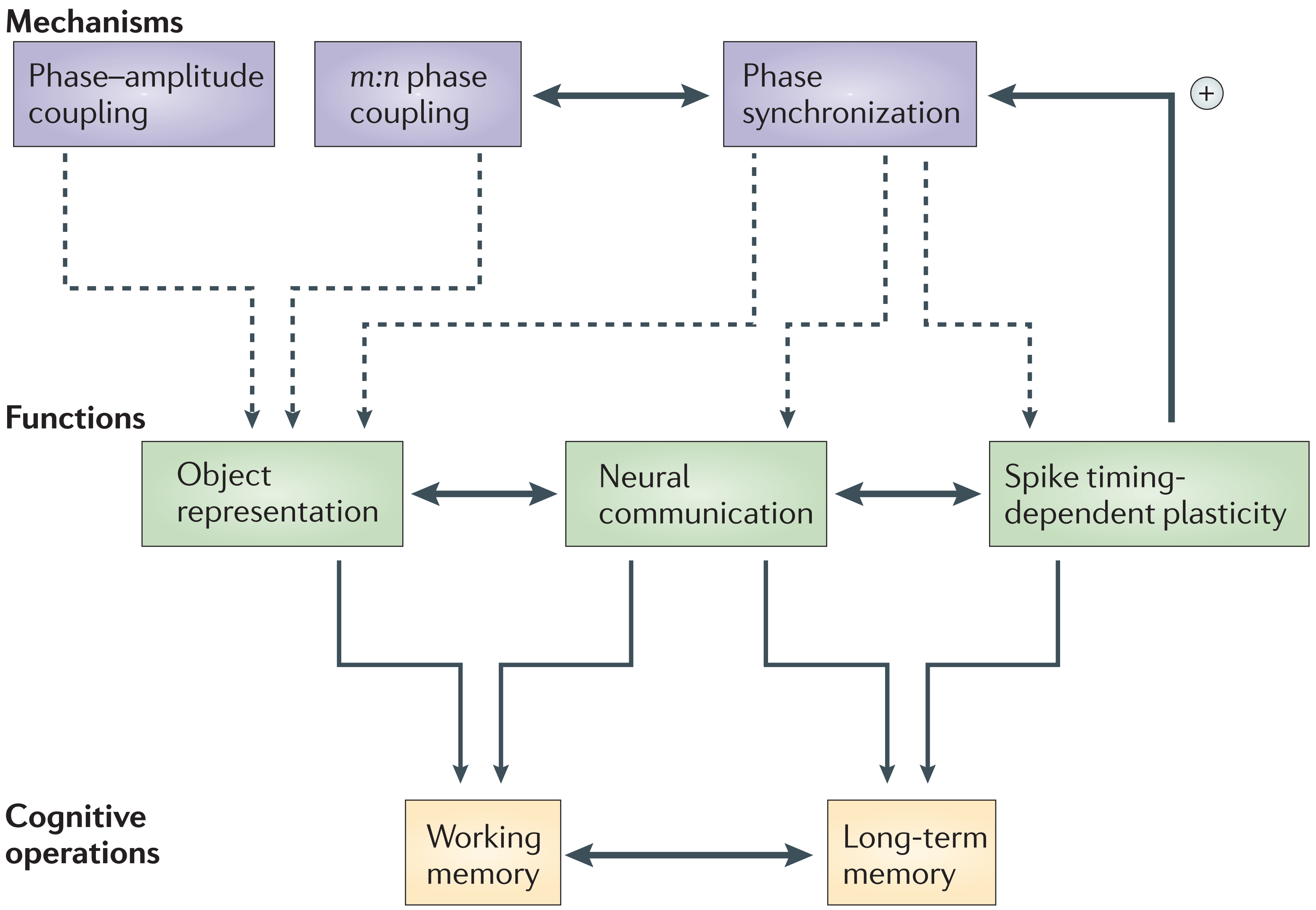
(c) The frequency of the fast oscillations is modulated by the phase of the slower oscillations.

(d) The power of the gamma oscillations is modulated by the phase of the theta oscillations.



Jensen et al., 2007, TRENDS COGN SCI

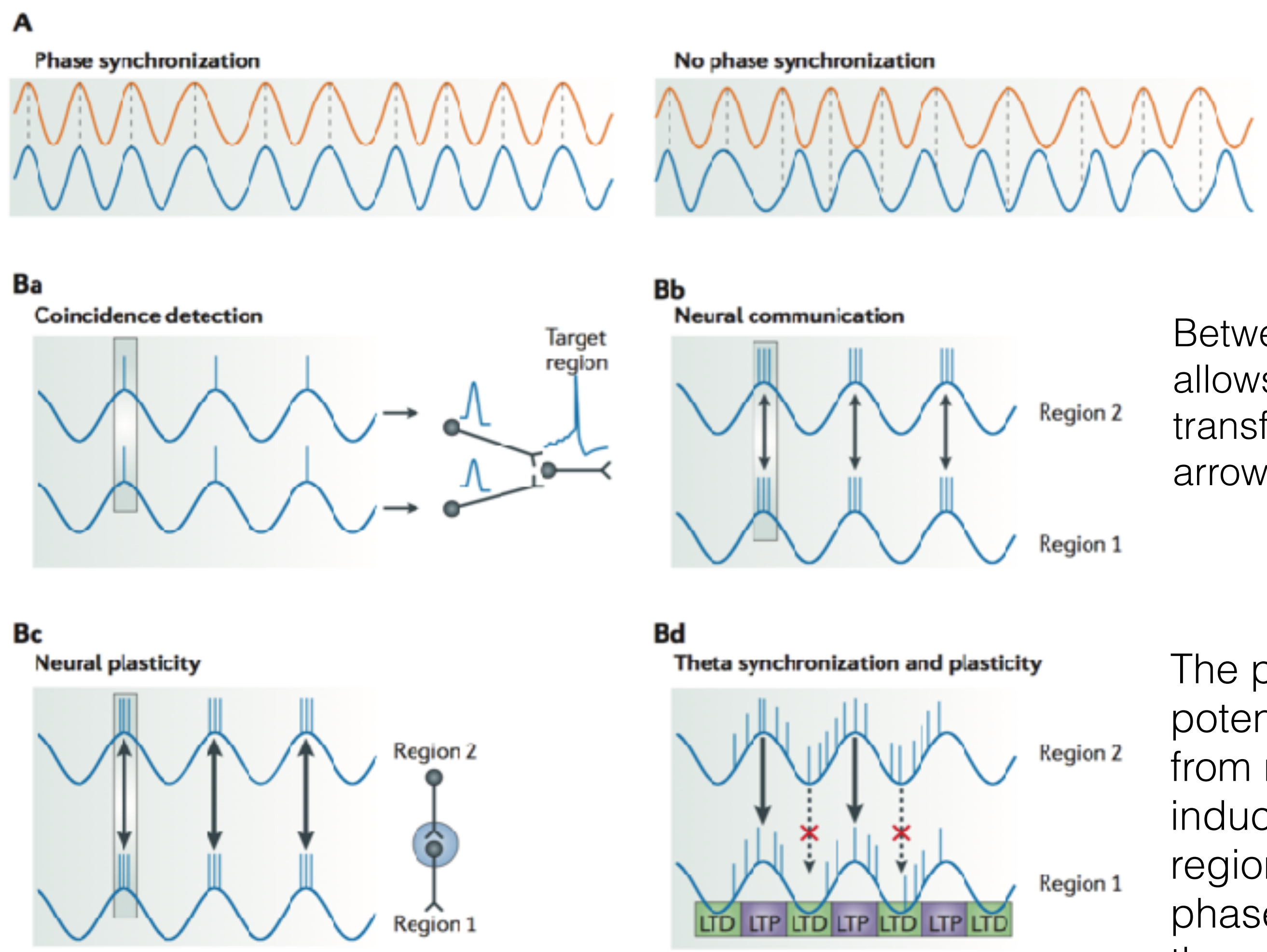
An integrative view of memory-related synchronization mechanisms



Fell J. and Axmacher N., Nature Review, 2011

Phase synchronisation

Functional roles of phase synchronisation



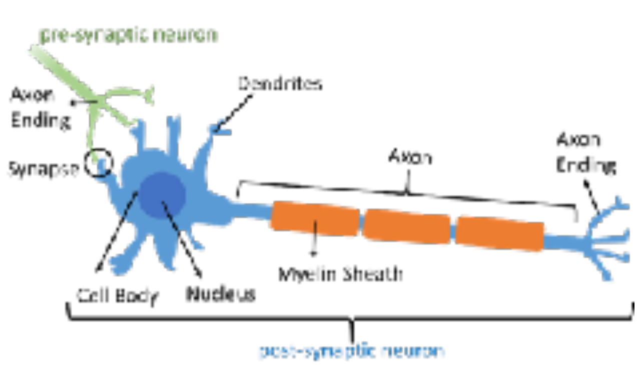
Phase synchronization of neural assemblies coordinates the timing of synaptic inputs to a common target region.

Between multiple brain regions allows for efficient information transfer (indicated by the arrows) during excitable periods.

Precise timing of action potentials resulting from phase synchronization between two regions can induce spike timing-dependent plasticity of the synaptic connections between these regions.

The propensity of action potentials that are propagated from region 2 to region 1 to induce synaptic plasticity in region 1 depends on the theta phase in region 1 during which the action potentials arrive.

Fell J. and Axmacher N., Nature Review, 2011



Measuring phase synchronisation

- Instantaneous phase of each signal is calculated from analytic signal, which is obtained from Hilbert transform.
- The analytic signal: x = xr + i*xi
  - Real part: xr, which is raw data
  - Imaginary part, xi, which is Hilbert transform
- The imaginary part is a version of the original real sequence with a 90° phase shift (sines are transformed to cosines and conversely).
- Mean of differences of instantaneous phases as Mean Phase Coherence (MPC) or Phase-Locking Value (PLV)

$$\tilde{x}(t) = \frac{1}{\pi} p.v. \int_{-\infty}^{+\infty} \frac{x(t')}{(t-t')} dt'$$

Hilbert transform of x(t)

$$Z_x(t) = x(t) + i\tilde{x}(t) = A_x^H e^{i\phi_x^H(t)}$$

Analytic signal of x(t)

$$\phi_x^H(t) = \tan^{-1}\left(\frac{x'(t)}{x(t)}\right)$$

Hilbert phase

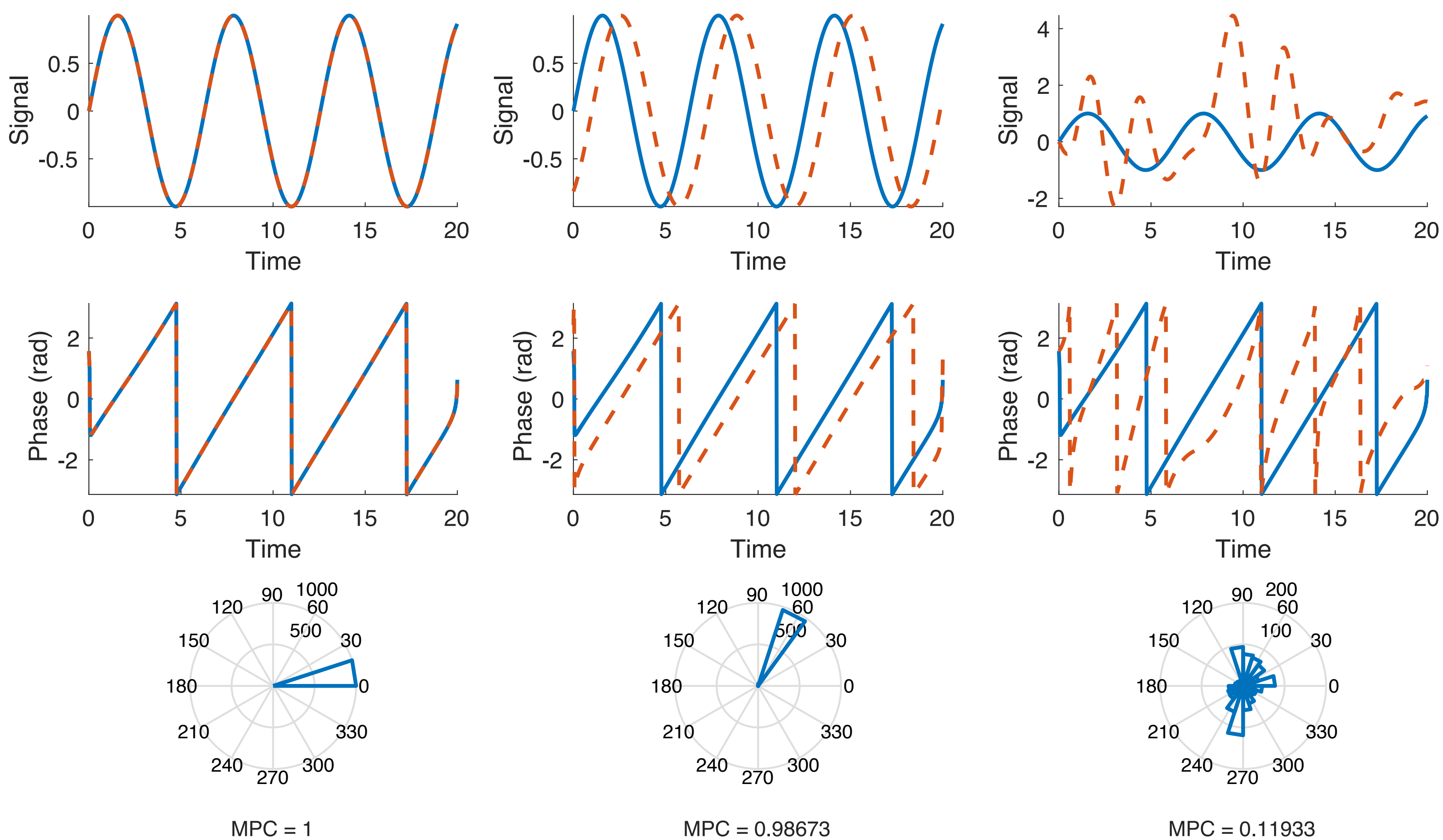
$$R = \left|\frac{1}{N}\sum_{j=1}^{N} e^{j[\phi_x(t_j)-\phi_y(t_j)]}\right|$$

Mean phase coherence

Mean Phase Coherence in MATLAB

- Instantaneous phase of signals are extracted using analytical form of signals (Hilbert phase)
  - phase1 = angle(hilbert(signal1));
  - phase2 = angle(hilbert(signal2));
- MPC is absolute value of the mean phase differences
  - MPC = abs(mean(exp(1i*(phase1-phase2))));

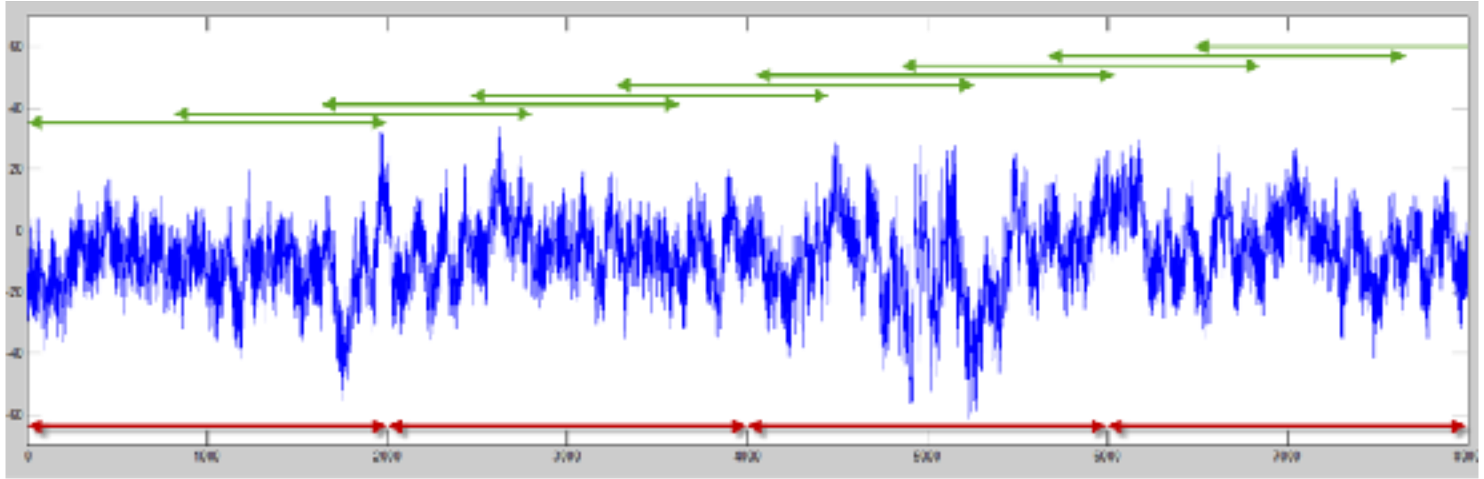
$$R = \left| \frac{1}{N} \sum_{j=1}^{N} e^{i[\phi_x(t_j) - \phi_y(t_j)]} \right|$$



Dynamics of phase synchronisation over time

- Brain is a complex dynamic system and neural signals are non-stationary
- Synchronisation patterns change over time, even in short periods of time
- We need to estimate them for short time windows, e.g. few seconds.
- Segmentation of signals (moving window length and step of moving)

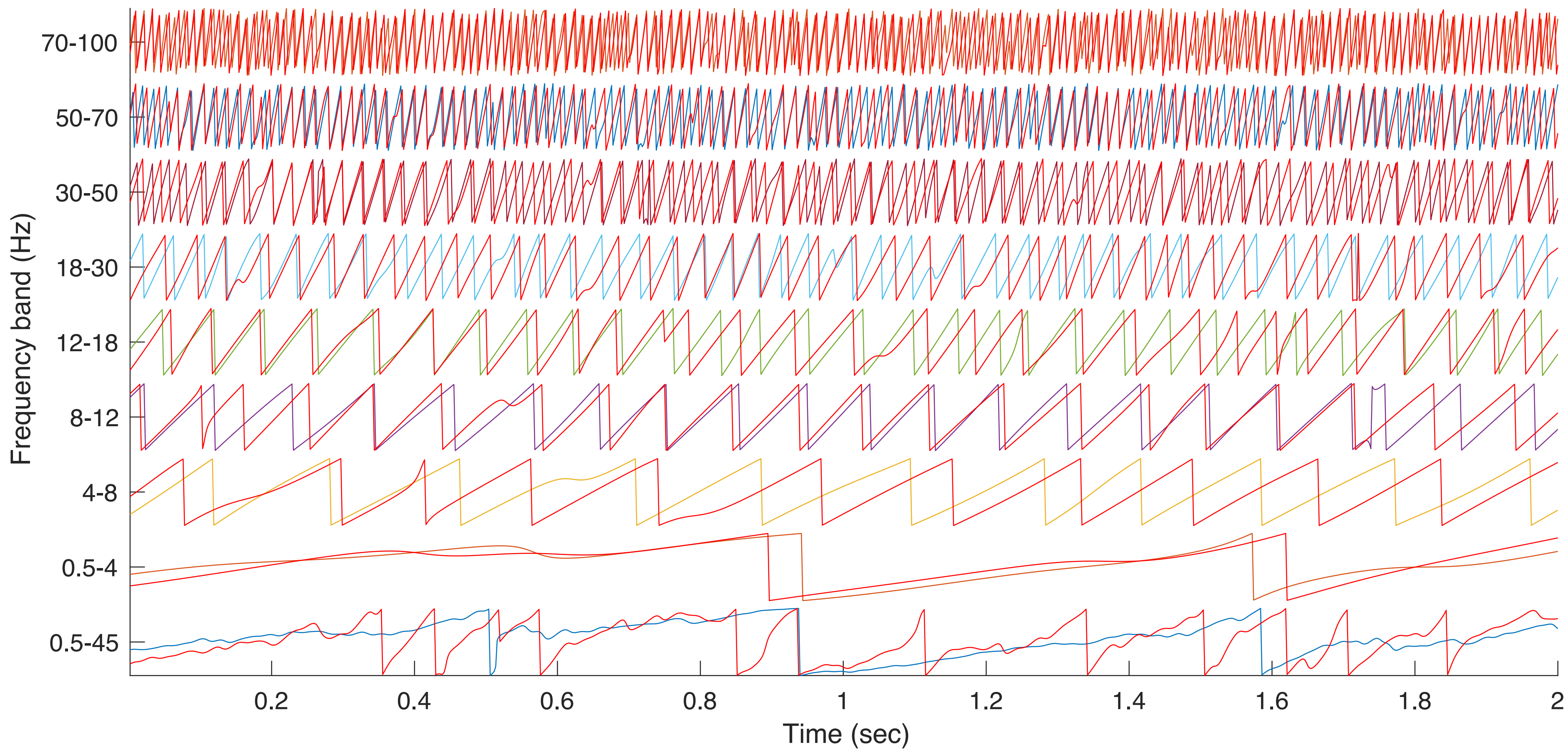
```
winLen = 4;  % length of moving window for segmentation in second
stepLen = 0.5; % step of moving window in second
for i = 1:nSeg % loop for segmentation
    idxSeg = floor((i-1)*stepLen*sampRate+1):...
        floor((i-1)*stepLen*sampRate+winLen*sampRate);
    MPC(i,nf) = abs(mean(exp(1i*(phase1(idxSeg)-phase2(idxSeg)))));
end
```



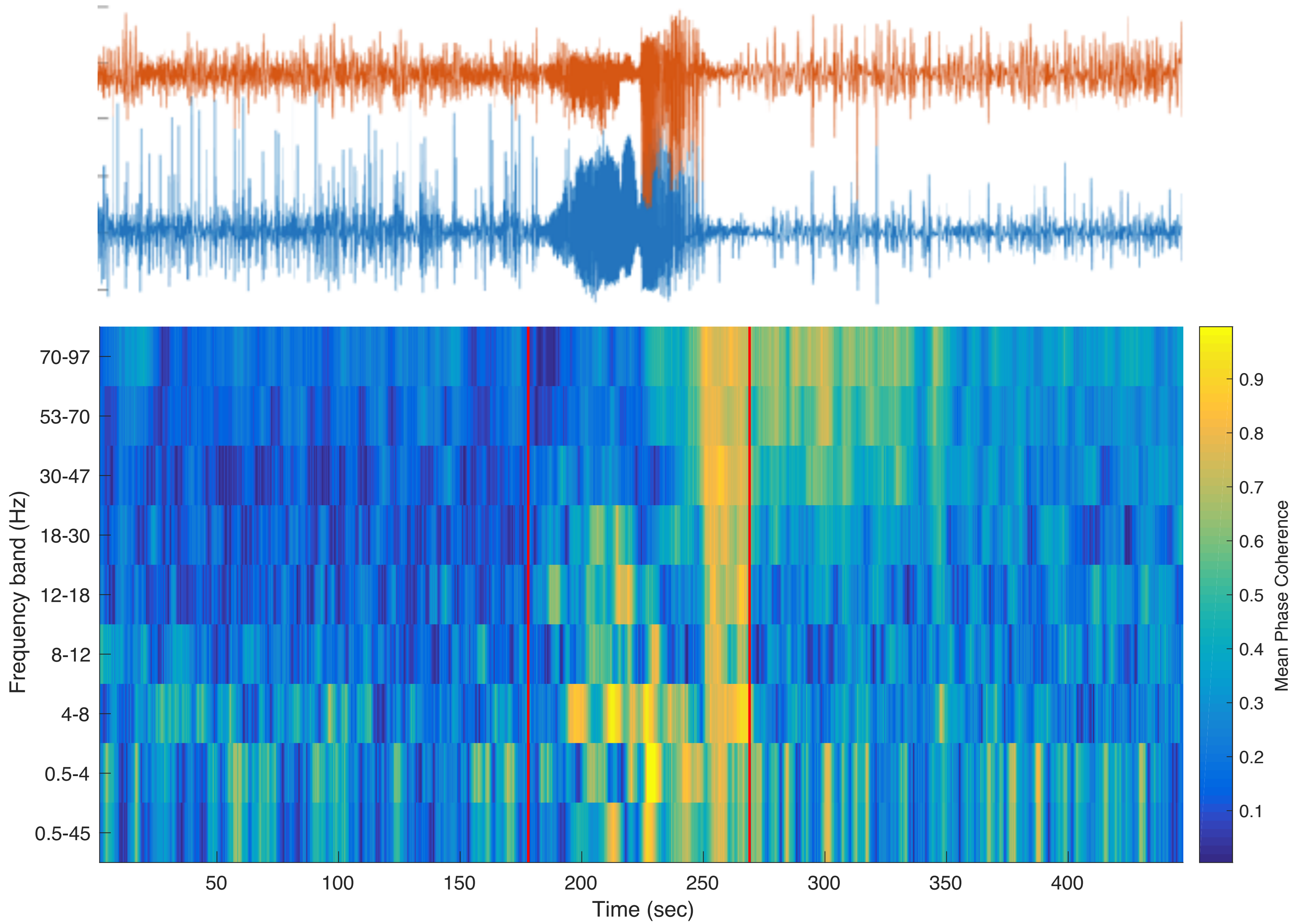
Dynamics of phase synchronisation over time and frequency

- MPC can also be estimated in desired frequency bands

```
% filter signals for frequency bands
order = round(3*(sampRate/freqBands(nf,1)));
fir1Coef = fir1(order,[freqBands(nf,1),freqBands(nf,2)]./(sampRate/2));
filtSignal1 = filtfilt(fir1Coef, 1, signal1);
filtSignal2 = filtfilt(fir1Coef, 1, signal2);

% extract instantaneous phase of signals using hilbert transform
phase1 = angle(hilbert(filtSignal1));
phase2 = angle(hilbert(filtSignal2));
```

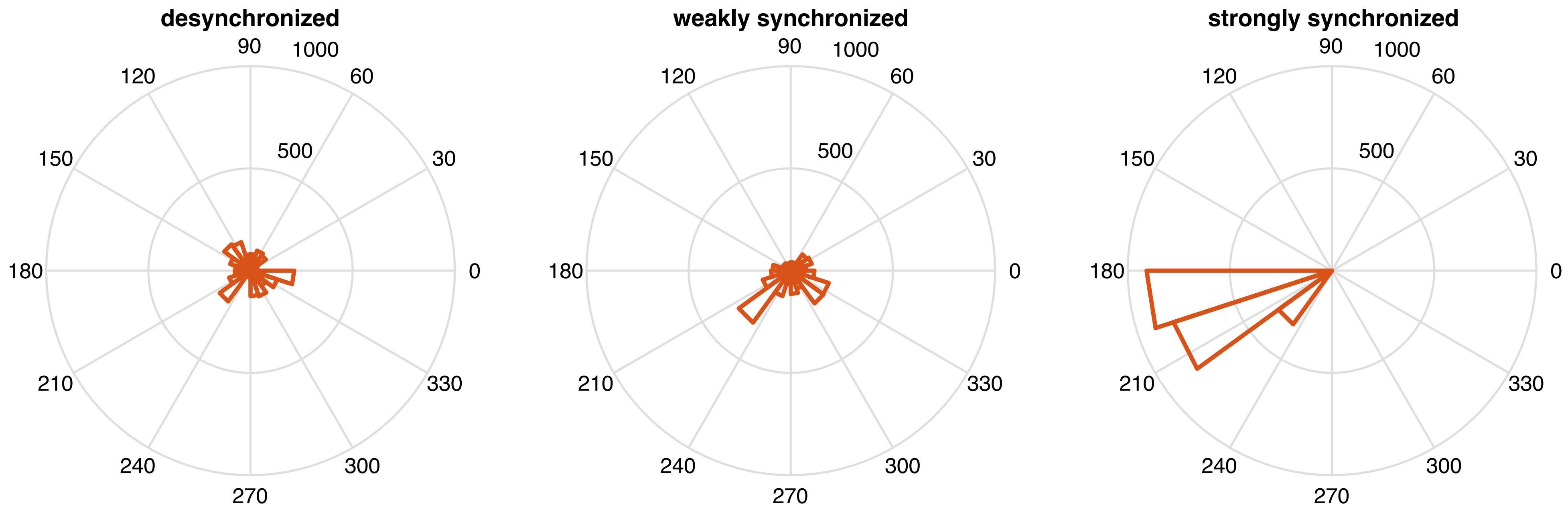


Phase synchronisation during epileptic seizure



Histogram of phase differences in 3 conditions

```
[sortMPC,idxSort] = sort(MPC(:,idxFreq),'ascend');
idx(1) = idxSort(1); % lowest MPC
idx(2) = idxSort(floor(length(idxSort)/2)); % middle MPC
idx(3) = idxSort(end); % highest MPC
```



Cross-frequency coupling

Different principles of cross-frequency interactions

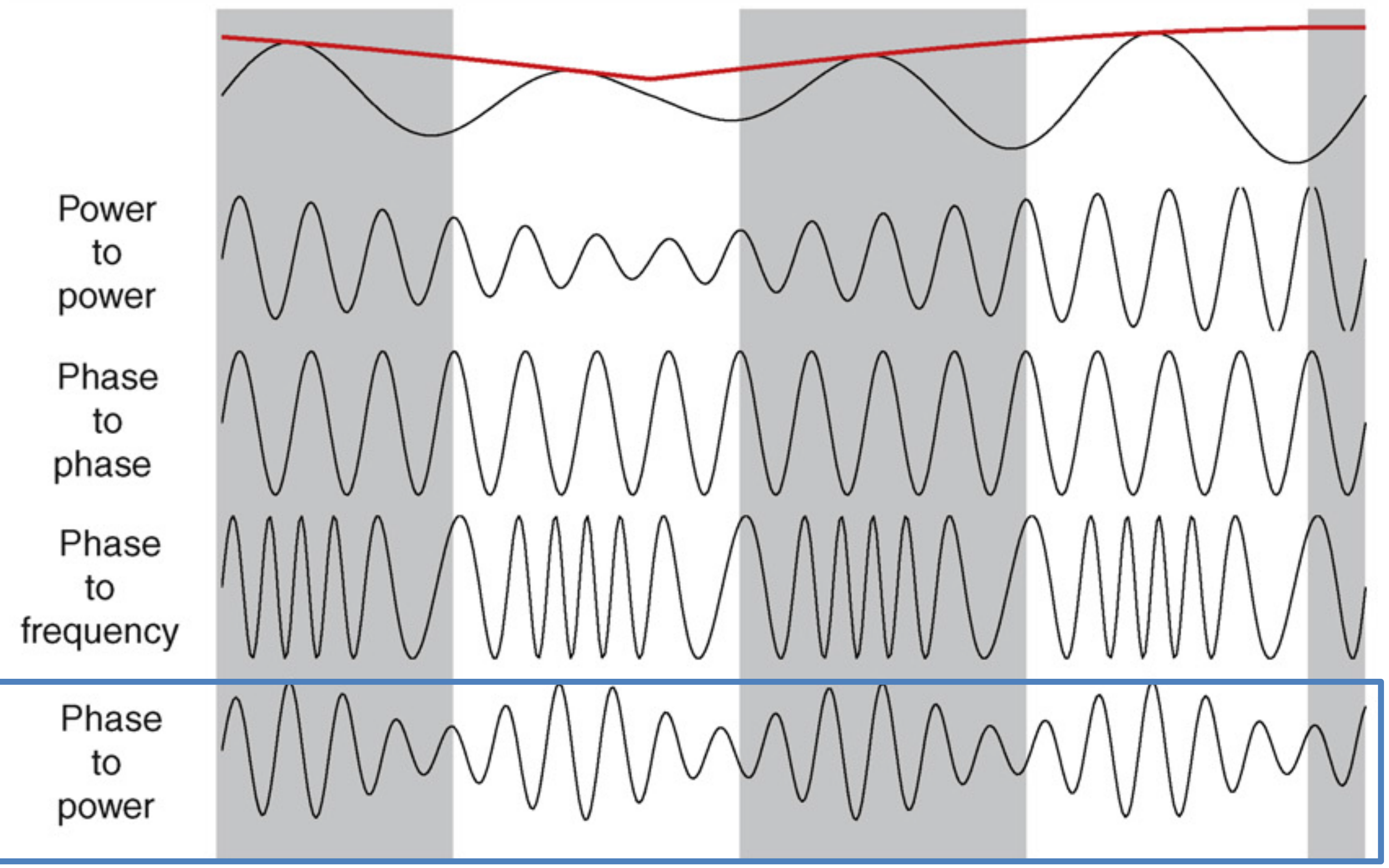
- Quantification of interaction between different frequency bands of a signal is called cross-frequency coupling

(a) Power of the gamma oscillations are correlated with power in the lower frequency band.

(b) In each slow cycle, there are four faster cycles and their phase relationship remains fixed.

(c) The frequency of the fast oscillations is modulated by the phase of the slower oscillations.

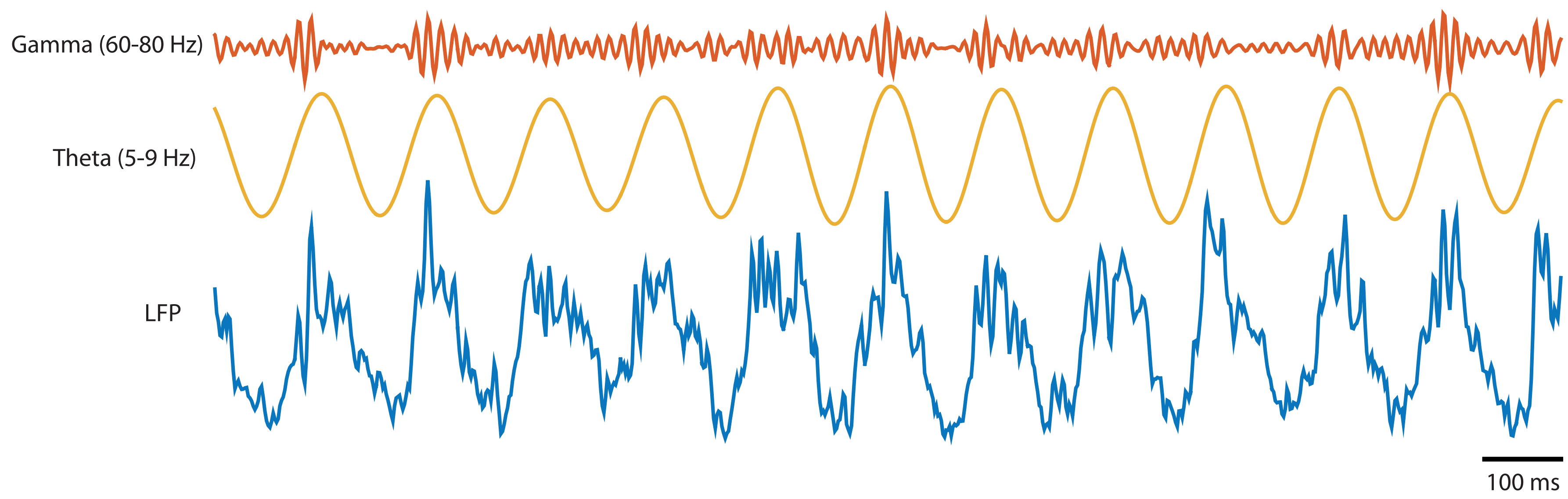
(d) The power of the gamma oscillations is modulated by the phase of the theta oscillations.



Jensen et al., 2007, TRENDS COGN SCI

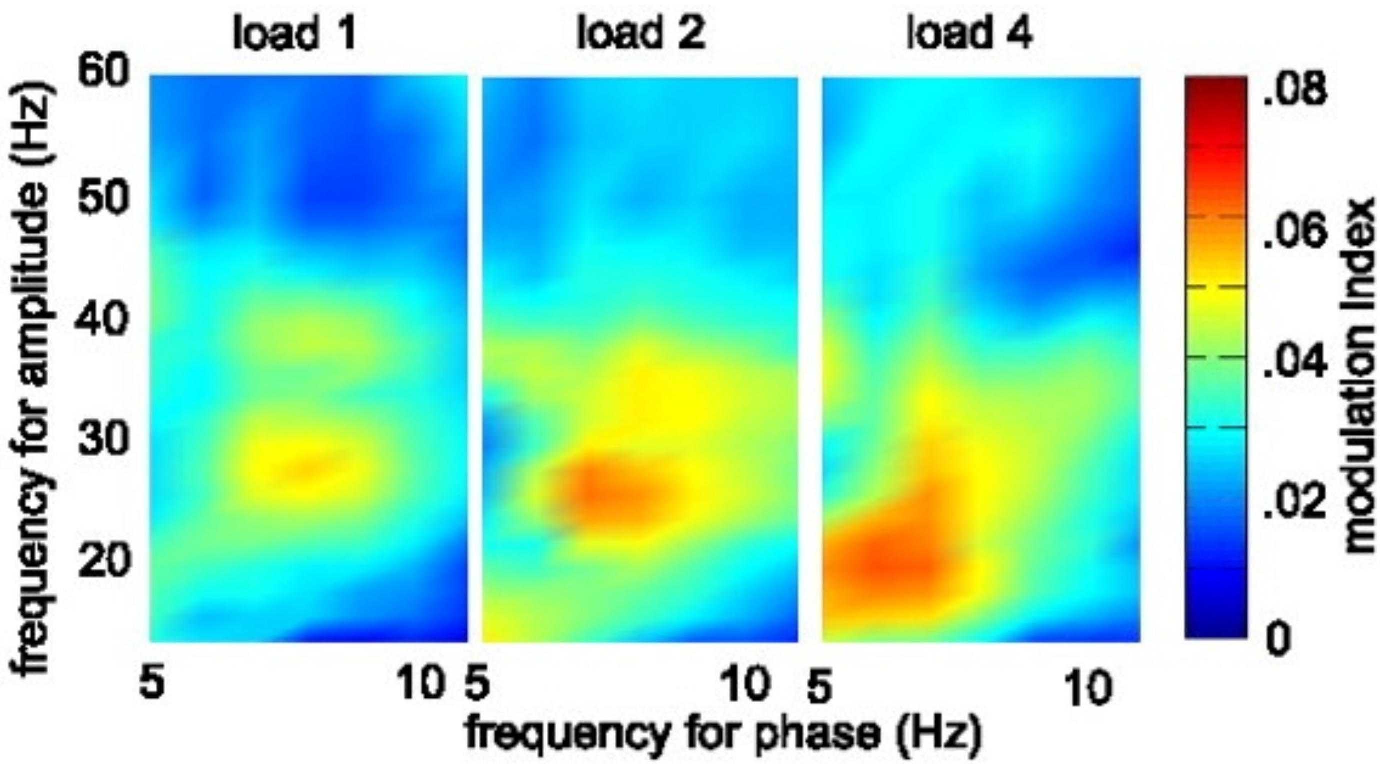
Phase-amplitude theta-gamma CFC

- A good example of phase-amplitude cross-frequency coupling is modulation of gamma activities by phase of theta oscillations in rodent hippocampus



Phase-amplitude CFC and working memory

- Coupling level depends on working memory load in human hippocampus
- Modulation frequency depends on working memory load in human hippocampus
- The frequency of modulating theta oscillations shifts toward lower frequencies with increasing memory load.

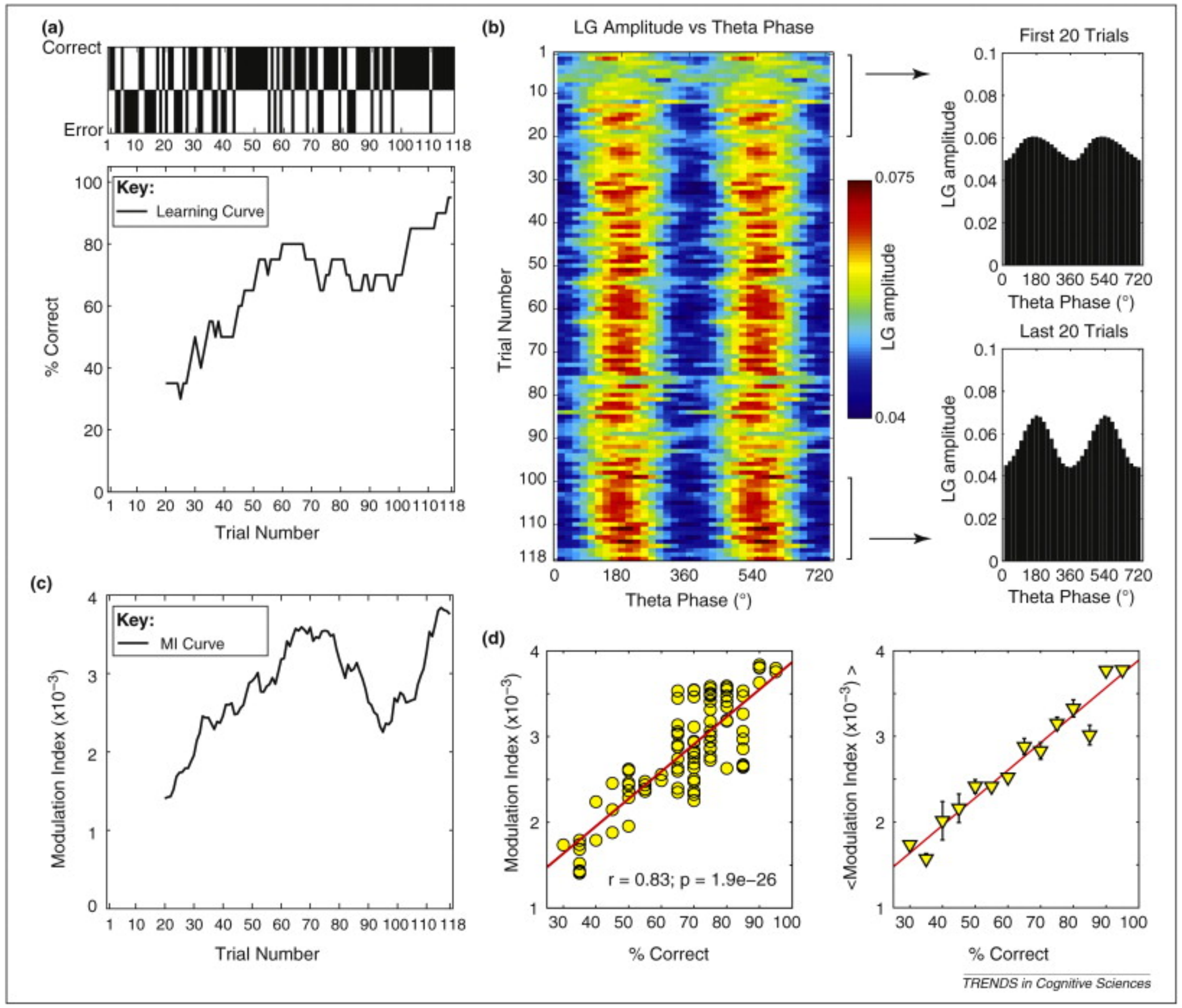


Axmacher et al., 2010, Proc. Natl. Acad. Sci.

Correlation between CFC and learning performance

- Phase-amplitude CFC strength is the most predictive neurophysiological marker of learning yet found.

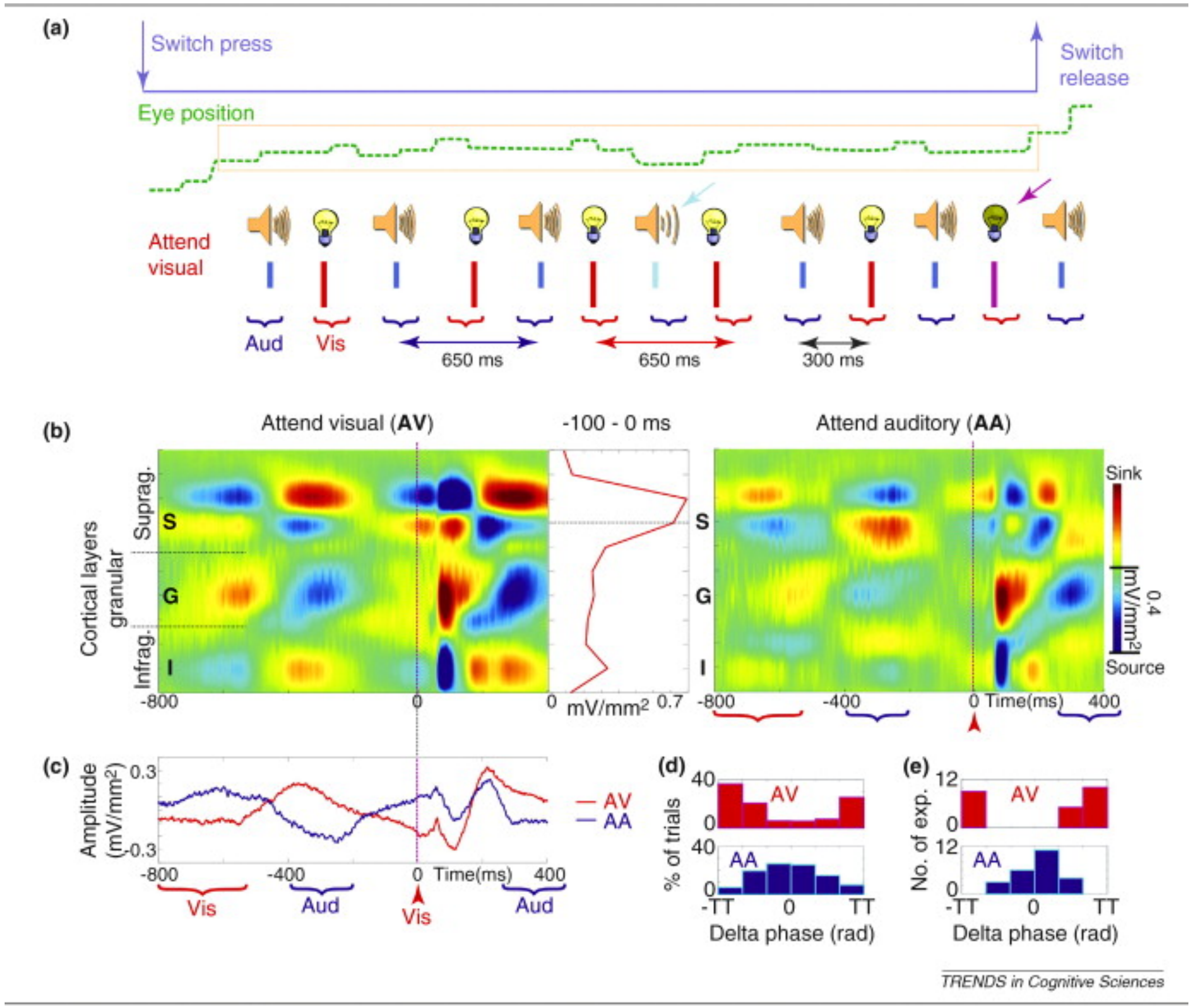
Learning task in rodent - Hippocampal CA3 recordings (118 trials)



Tort et al, Proc Natl Acad Sci, 2009

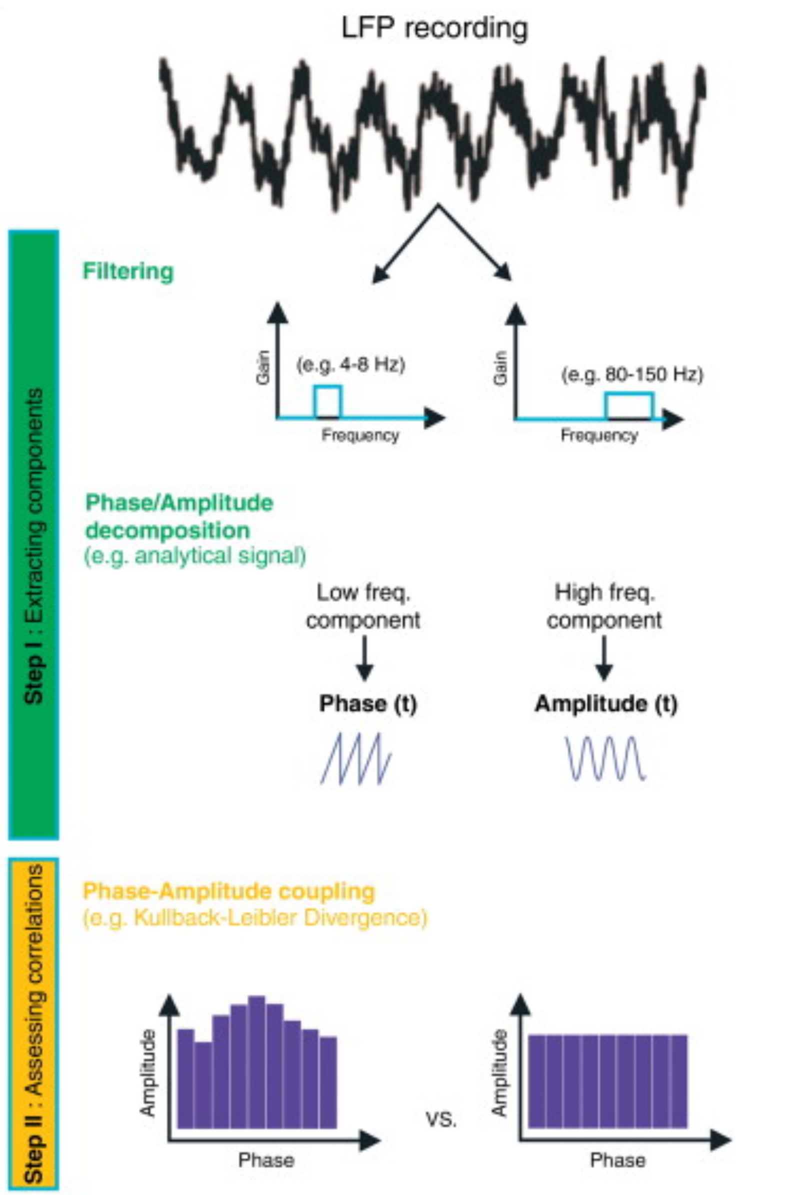
Dynamic entrainment of low-frequency phase

- Phase of low frequency oscillations can be entrained by rhythmic external sensory and motor events, or internal cognitive processes (learning and memory)
- Is it possible that P-A CFC exists but is unrelated to functional activity, computation or communication? **No**! why?
- Low frequency phase entrainment combined with presence of phase-amplitude CFC implies that the modulation of HF power by CFC will be entrained and coordinated with the occurrence of slower, behaviourally relevant internal and external events.



Lakatos et al., Science, 2008

Measuring phase-amplitude coupling using Modulation Index (MI)



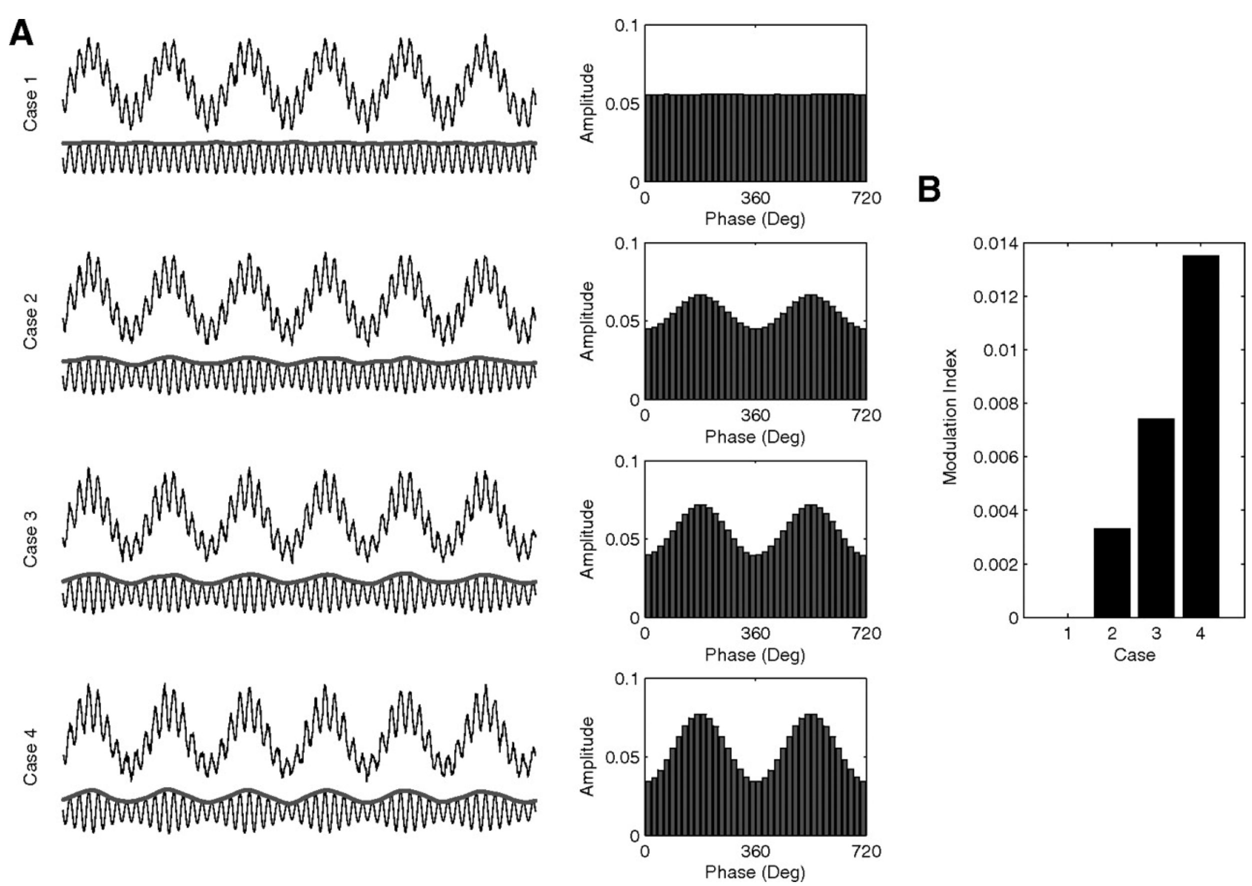
Aru et al., 2015, Curr Opin Neurobiol

Kullback-Leibler (KL) distan

$$D_{KL}(P,\ Q) = \sum_{j=1}^{N} P(j) \log \left[\frac{P(j)}{Q(j)} \right]$$

Modulation Index (MI)

$$MI = \frac{D_{KL}(P,\ U)}{\log\ (N)}$$

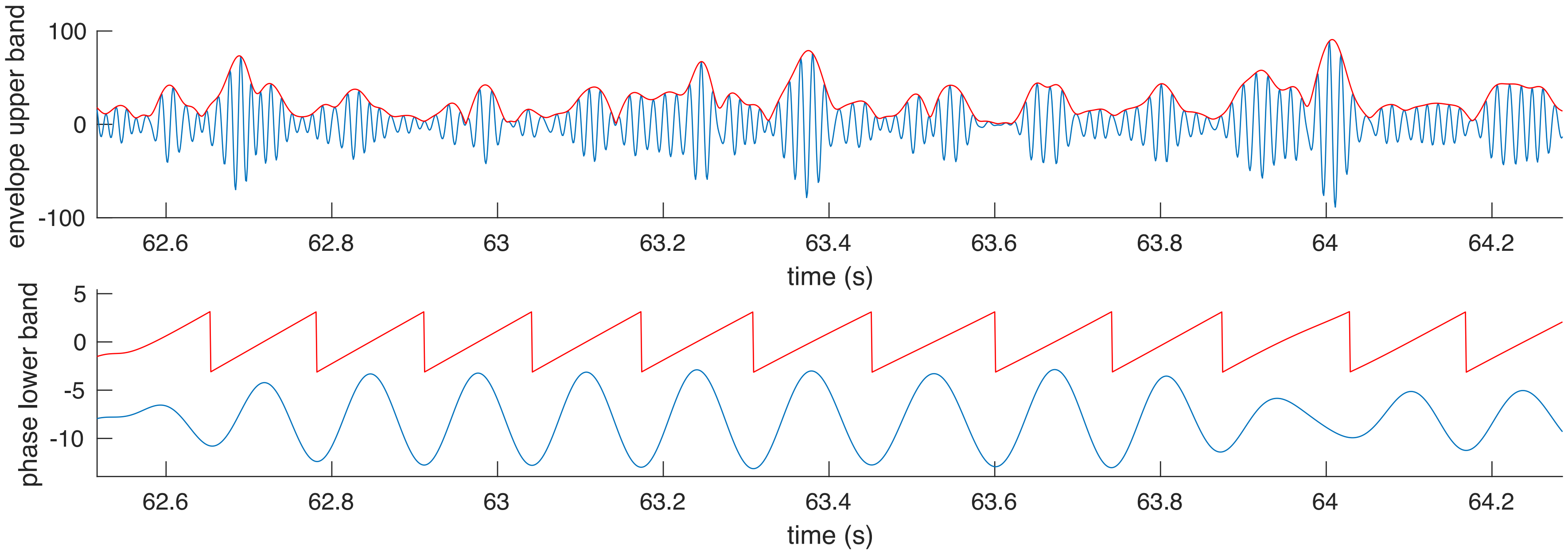


Tort et al., 2010, J Neurophysiol

Steps to calculate Modulation Index

- Filtering signal for slow (modulating) and fast (modulated) frequency bands
- Extracting envelope of fast oscillations and phase of slow oscillations

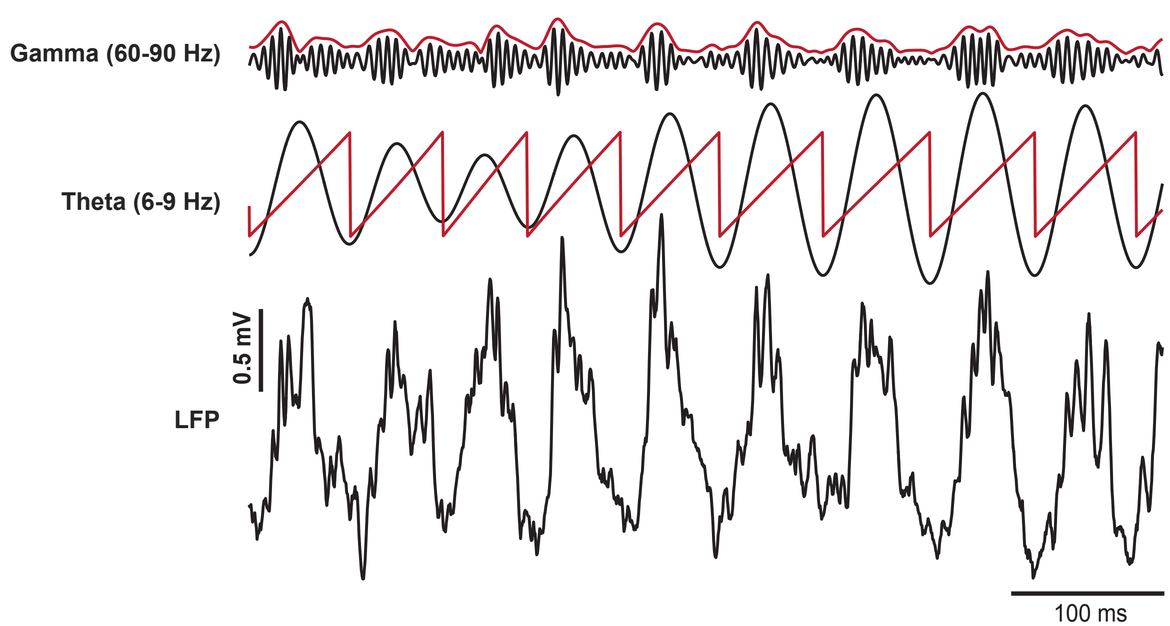
```
%% Define phase/amplitude frequency bands of interest
phaseFreq = [6 9]; % frequency band for phase (Hz)
ampFreq = [55 95]; % frequency band for amplitude (Hz)

%% Extract envelope for amplitude frequency band using Hilbert transform
order = round(3*(sampRate/ampFreq(1)));
fir1Coef = fir1(order,[ampFreq(1),ampFreq(2)]./(sampRate/2));
ampSignal = filtfilt(fir1Coef, 1, signal);
Amp = abs(hilbert(ampSignal));

%% Extract phase for phase frequency band using Hilbert transform
order = round(3*(sampRate/phaseFreq(1)));
fir1Coef = fir1(order,[phaseFreq(1),phaseFreq(2)]./(sampRate/2));
phaseSignal = filtfilt(fir1Coef, 1, signal);
Phase = angle(hilbert(phaseSignal));
```

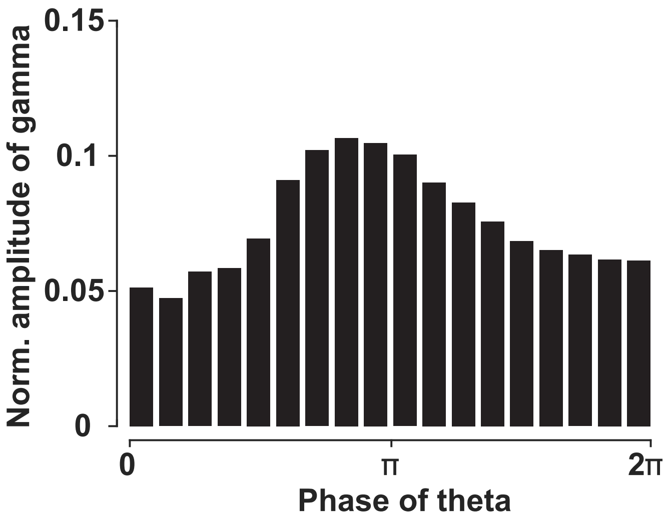


Steps to calculate Modulation Index

- Divide phase of slow oscillations into several bins

```
%% Dividing phase [0 2*pi] into several equal bins
nBin = 18; % 18 bins, each bin covers 20 degrees
binStart = zeros(1, nBin);
binSize = 2*pi/nBin;
for i = 1:nBin
    binStart(i) = (i-1)*binSize-pi; % start of each bin
end
```





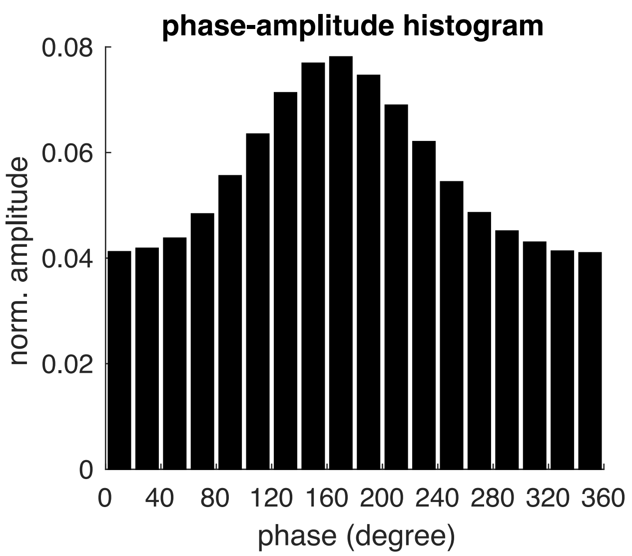
Steps to calculate Modulation Index

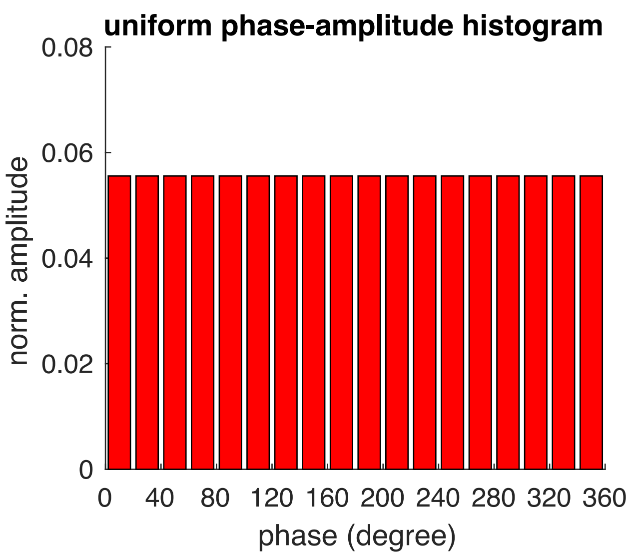
- Calculate average power of fast oscillations within each bin to construct phase-power histogram
- Compare it with a uniform distribution using Kullback-Leibler distance

```
%% Compute Modulation Index
meanAmp = zeros(1,nBin); % Mean power in each phase-bin
for k = 1:nBin
    meanAmp(k) = nanmean(Amp(Phase>=binStart(k) & Phase<(binStart(k)+binSize)));
end
meanAmp = meanAmp./sum(meanAmp); % normalize phase-amplitude histogram
KLdist = meanAmp.*log(nBin.*meanAmp); % Kullback-Leibler distance
KLdist(isnan(KLdist)) = 0;
MI = sum(KLdist)./log(nBin); % Normalize KL distance by log(nBin)
```

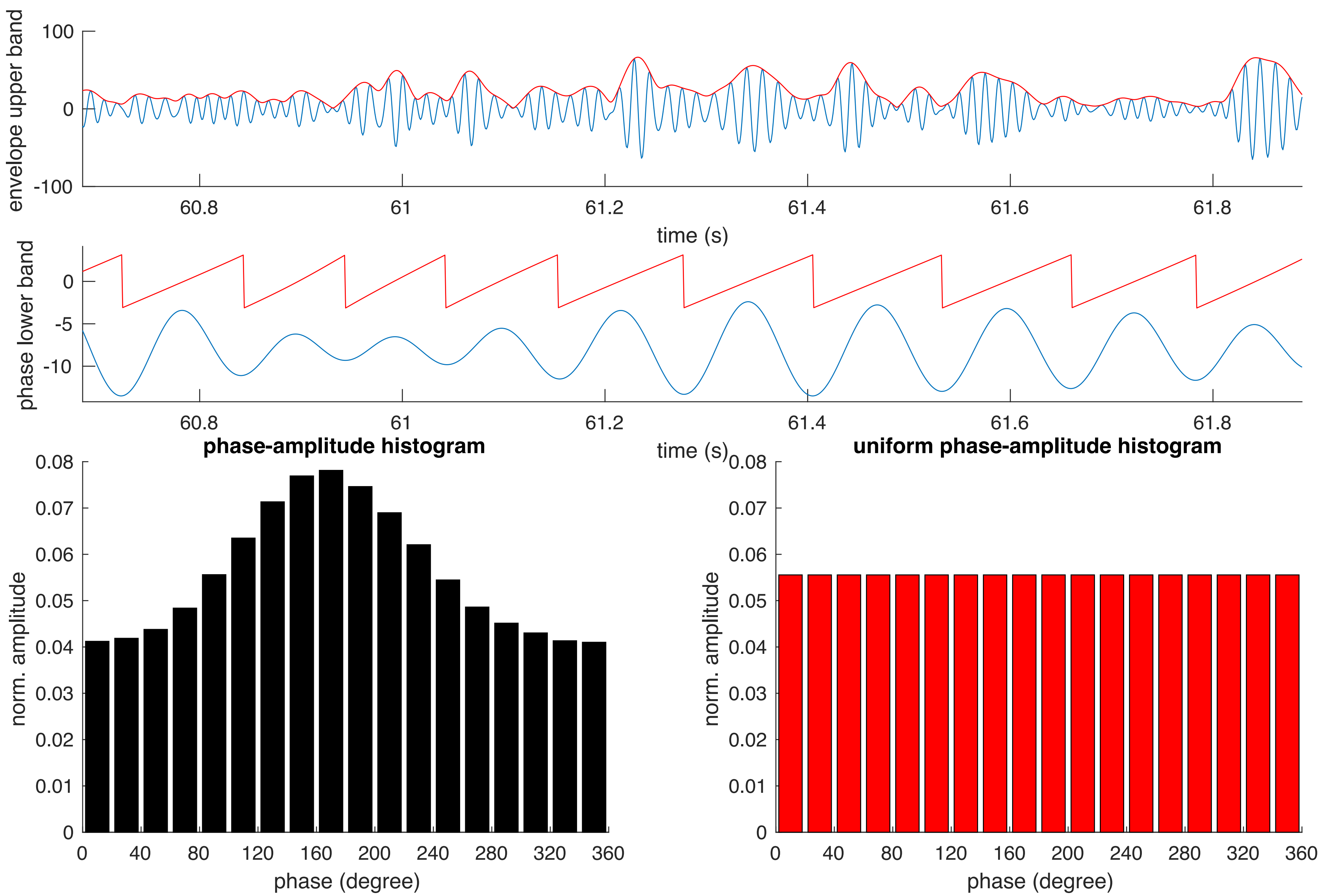
$$D_{KL}(P,\ Q) = \sum_{j=1}^{N} P(j) \log \left[\frac{P(j)}{Q(j)} \right]$$

$$MI = \frac{D_{KL}(P,\ U)}{\log\ (N)}$$



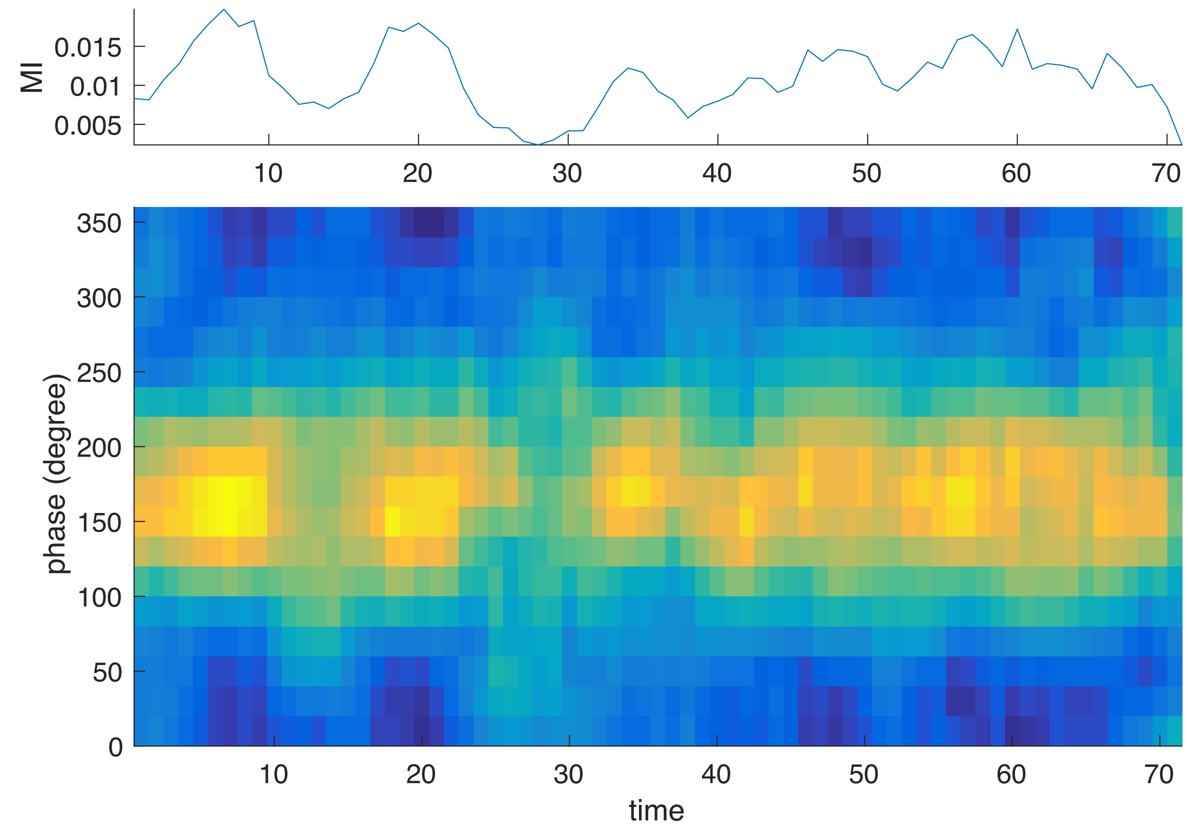


Phase-amplitude CFC



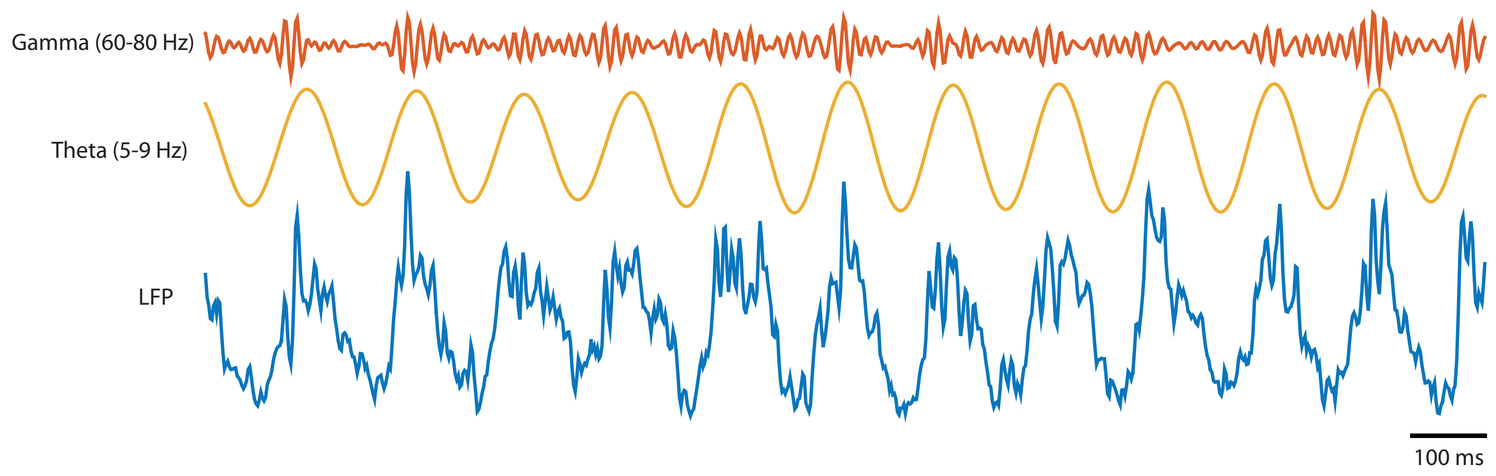
Phase-amplitude CFC over time

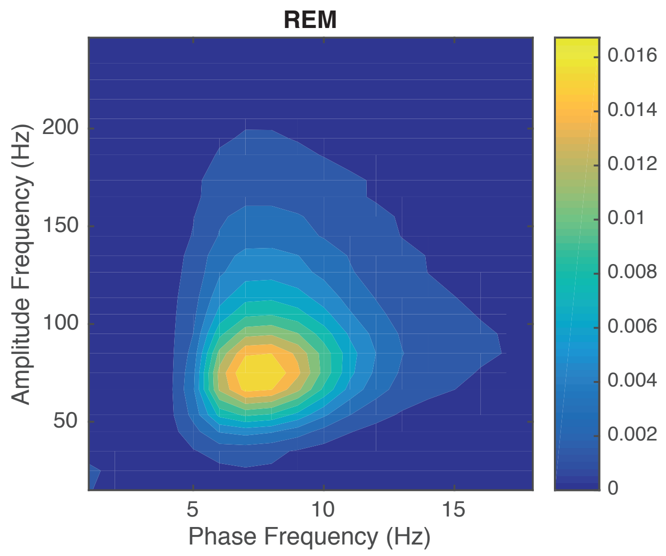
```
winLen = 5;  % length of moving window for segmentation in second
stepLen = 1; % step of moving window in second

%% Compute Modulation Index for each segment
nSeg = floor(length(Phase)/(stepLen*sampRate))-ceil((winLen-stepLen)/stepLen); % number of segments
MI = zeros(1, nSeg);
meanAmp = zeros(nSeg, nBin);
for j = 1:nSeg
    idx = (j-1)*stepLen*sampRate+1:((j-1)*stepLen+winLen)*sampRate; % index of segment
    AmpT = Amp(1,idx);
    PhaseT = Phase(1,idx);
    meanAmpT = zeros(1,nBin); % Mean power in each phase-bin
    for k = 1:nBin
        meanAmpT(k) = nanmean(AmpT(PhaseT>=binStart(k) & PhaseT<(binStart(k)+binSize)));
    end
    meanAmpT = meanAmpT./sum(meanAmpT);
    KLdist = meanAmpT.*log(nBin.*meanAmpT);
    KLdist(isnan(KLdist)) = 0;
    MI(1,j) = sum(KLdist)./log(nBin);
    meanAmp(j,:) = meanAmpT;
end
```



Comodulogram analysis

- Comodulogram analysis is a data-driven approach to explore coupling across different pairs of frequency bands.
- Modulation Index is calculated for frequency pairs of interest to obtain comodulogram graph.

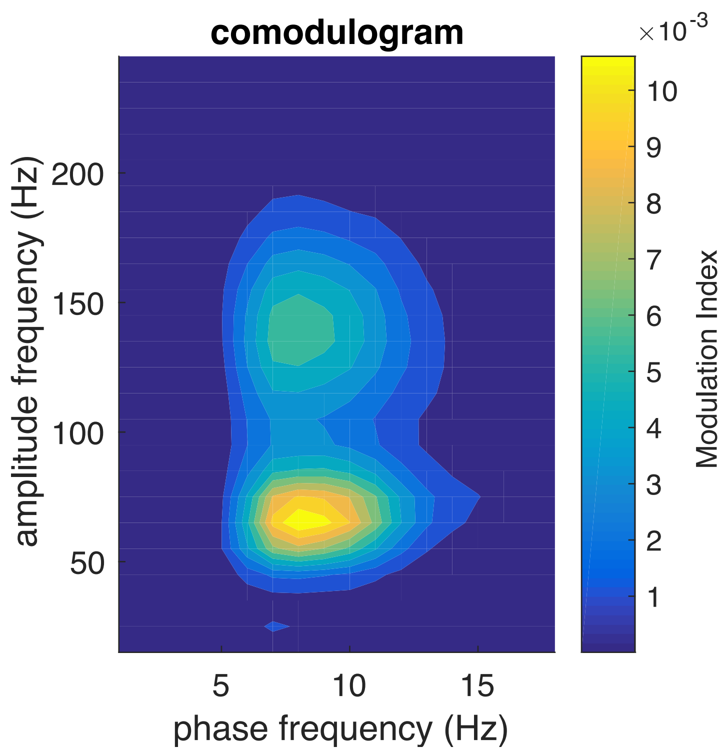


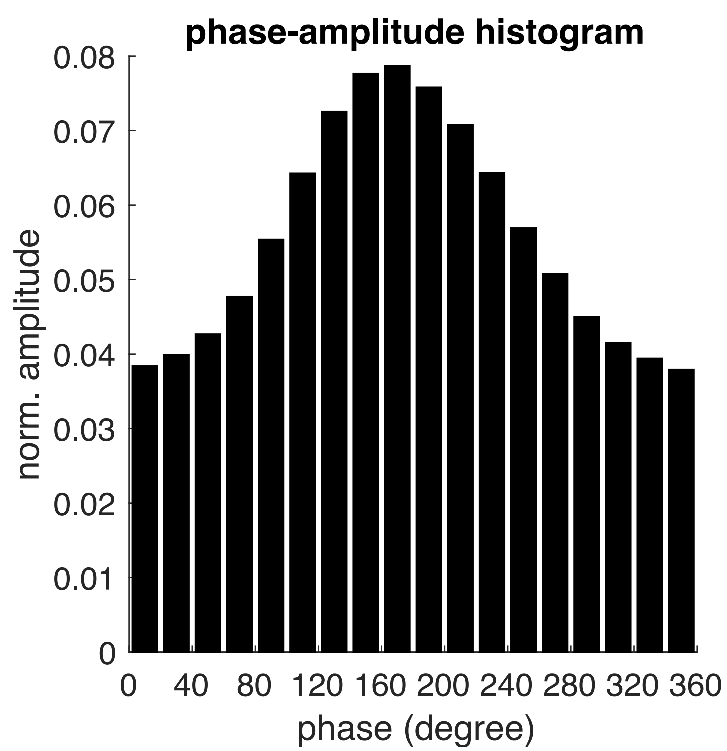


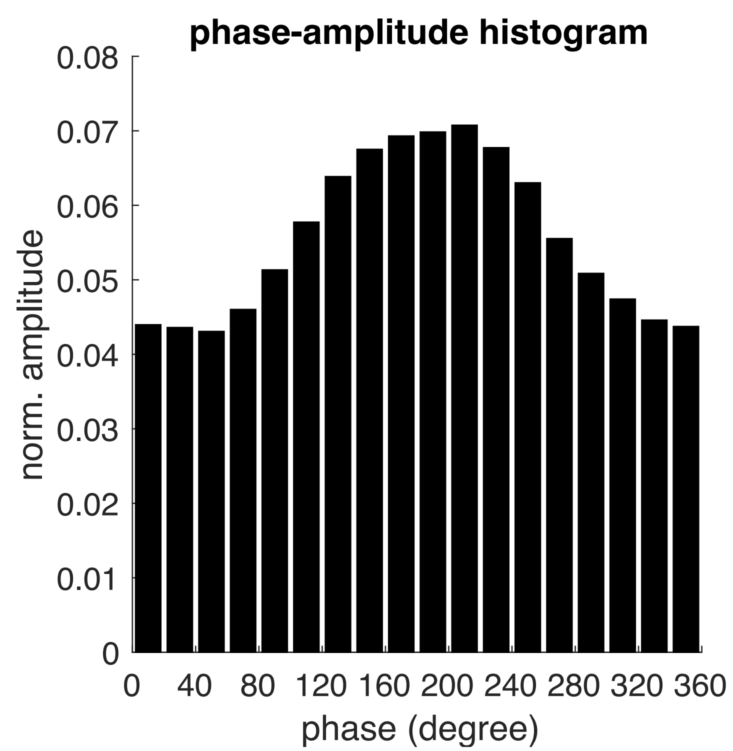
Comodulogram analysis - MATLAB

- Modulation Index is calculated for each pair of low and high frequency oscillations

```
%% Comodulogram analysis
stPh = 0.5:17.5;
edPh = stPh+1;
phaseFreq = [stPh' edPh'];

stA = 10:10:240;
edA = stA+10;
ampFreq = [stA' edA'];

[comod, meanAmp] = f_comodulogram(signal, sampRate, phaseFreq, ampFreq);
```







References for further studies

- Fell J., The role of phase synchronization in memory processes, Nature Review, 2011.

- Canolty & Knight, The functional role of cross-frequency coupling, Trends in Cognitive Sciences, 2010.

- Tort et al., Measuring Phase-Amplitude Coupling Between Neuronal Oscillations of Different Frequencies, J Neurophysiol. 2010.

Thank you