Estimating transient phase-amplitude coupling using local mutual information

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Outline

Intro to theory

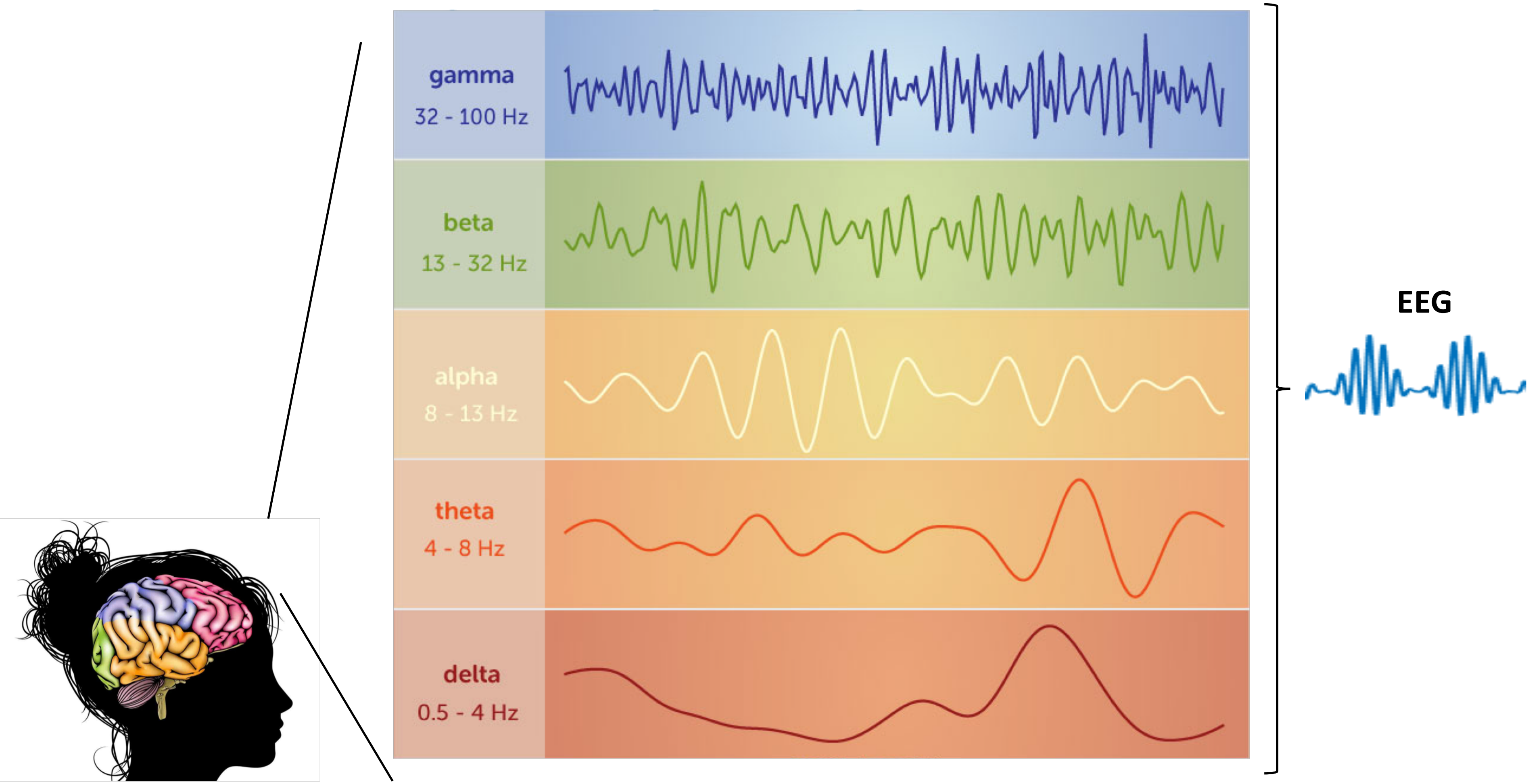
- Intro to Phase-Amplitude Coupling (PAC)
- Local (pointwise) Information Theory Measures
- Estimating PAC with Local Mutual Information

Results

- Simulations
- ECoG data analysis

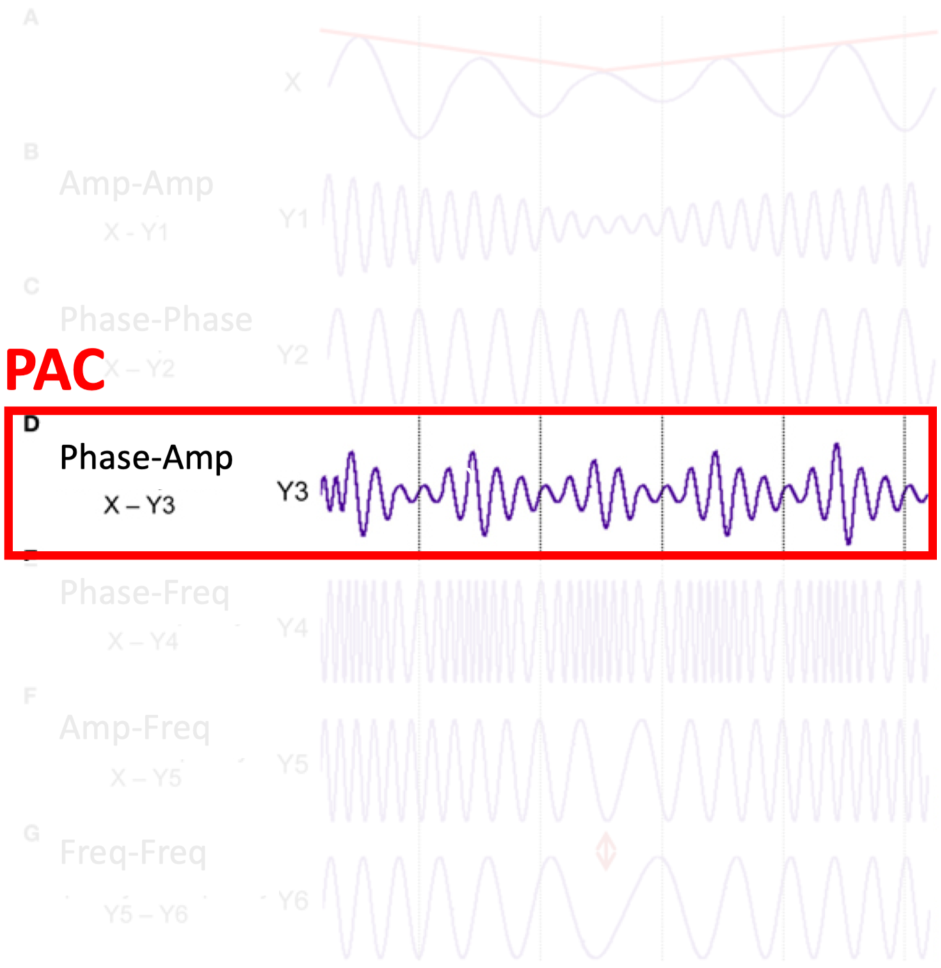
Demo

Brain oscillations



Copyright: artellia

Cross-Frequency Coupling



Jirsa and Muller, 2013

Found both in **animals** and **humans**

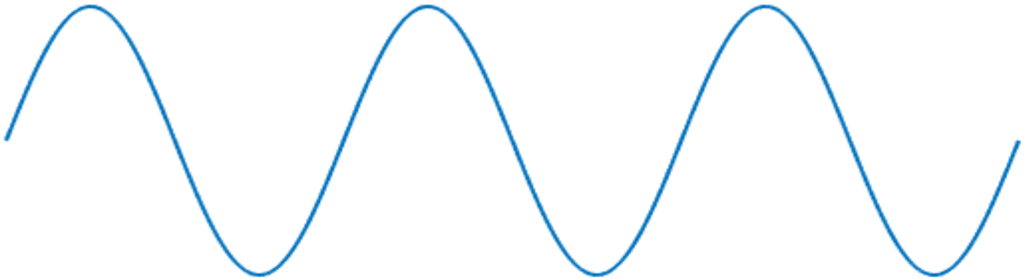
Associated to epilepsy, Parkinson’s disease, Alzheimer’s disease, schizophrenia, obsessive-compulsive disorder and mild cognitive impairment.

(Mormann et al., 2005; Cohen, 2008; Osipova et al., 2008; Tort et al., 2008, 2009, 2010; Cohen et al., 2009a,b; Colgin et al., 2009; Axmacher et al., 2010a,b; Voytek et al., 2010)

Amplitude Modulation Fundamentals

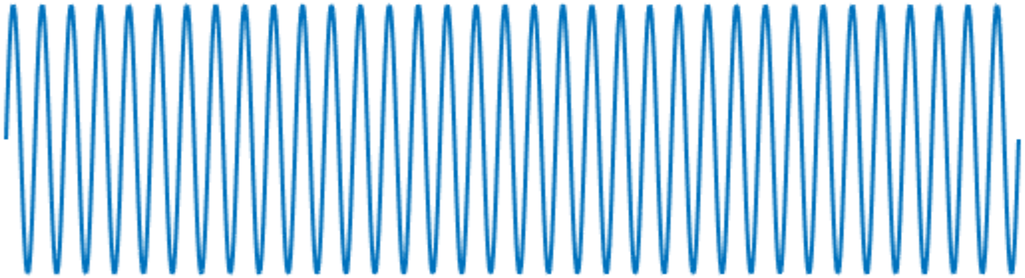
Modulator

$$v_{\mathrm{mod}} = V_{\mathrm{mod}} \sin\left(2\pi f_{\mathrm{mod}} t\right)$$



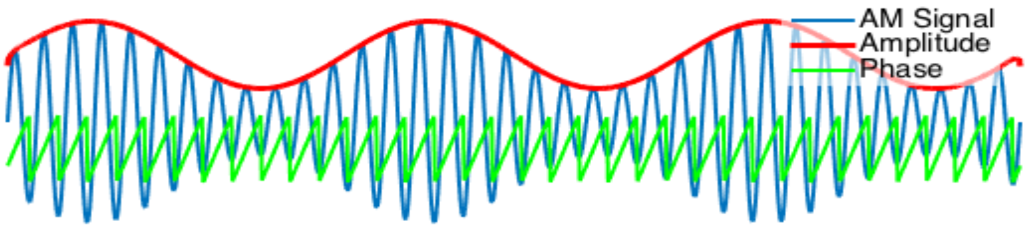
Carrier

$$v_{carr} = V_{carr} \sin\left(2\pi f_{carr} t\right)$$



AM Signal

$$v_{AM} = V_{carr} \sin\left(2\pi f_{carr} t\right) + \left[V_{\mathrm{mod}} \sin\left(2\pi f_{\mathrm{mod}} t\right)\right] \sin\left(2\pi f_{carr} t\right)$$



Instantaneous Phase and Amplitude

$$S_t = s_{m_t} e^{i\phi_t}$$

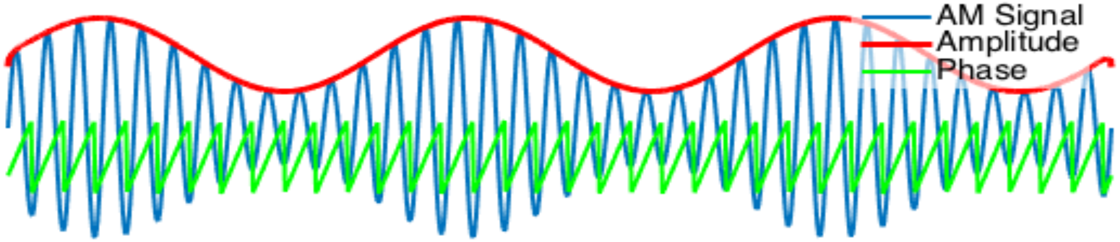
By means of the **Hilbert transform** a signal can be expressed as its **analytic signal**

$$S_{m_t} = |S_t|$$

Instantaneous amplitude (or the envelope)

$$\phi_t = arg[S_t]$$

Instantaneous phase.



$abs(hilbert(S_t))$

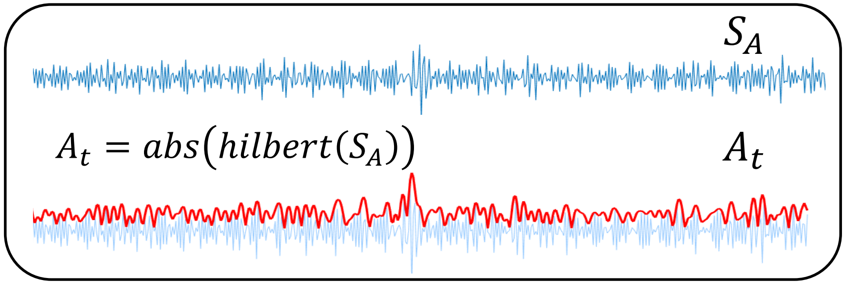
$angle(hilbert(S_t))$

Computing PAC

Electrophysiological signal

Band-pass Filter

High frequency band f_{Amp} (e.g: 30-50Hz)

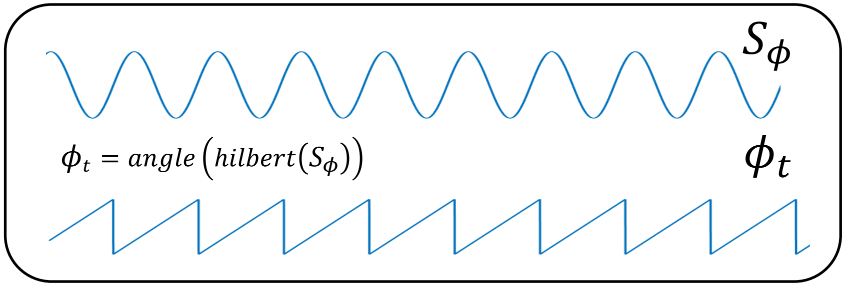


S_A

$A_t = abs\left(hilbert(S_A)\right)$

A_t

Low frequency band f_{phase} (e.g: 5-12Hz)



S_ϕ

$\phi_t = angle\left(hilbert(S_\phi)\right)$

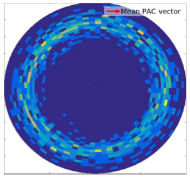
ϕ_t

Mean Vector Length

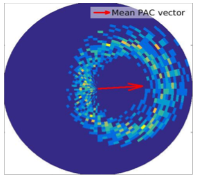
Canolty et al. 2006

- Composite vectors $z_t = A_t e^{i\phi_t}$
- Mean vector length

$$MVLmi = \left|\frac{1}{N}\sum_{t=1}^{N} z_t\right|$$



No Coupling



Coupling

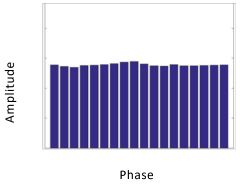
Kullback-Leibler Modulation Index

Tort et al, 2010

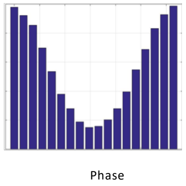
$$P(j) = \frac{\left\langle A_{f_A}\right\rangle \phi_{f_p}(j)}{\sum_{k=1}^{N}\left\langle A_{f_A}\right\rangle \phi_{f_p}(k)}$$

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

Compute the Kullback-Leibler with a uniform distribution



No Coupling



Coupling

GLM Measure

Penny et al. 2008

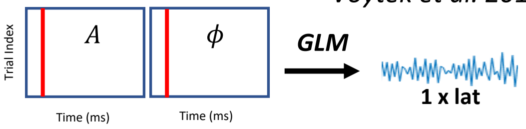
$$A_t = X\beta + e$$

$$X = \begin{vmatrix} cos\phi_1 & sin\phi_1 & 1 \\ \vdots & \vdots & \vdots \\ cos\phi_N & cos\phi_N & 1 \end{vmatrix}$$

Explained variance as an index of PAC

ERPAC

Voytek et al. 2013



Time resolved '*average*' PAC by applying ***GLM Measure*** for each latency in event related data

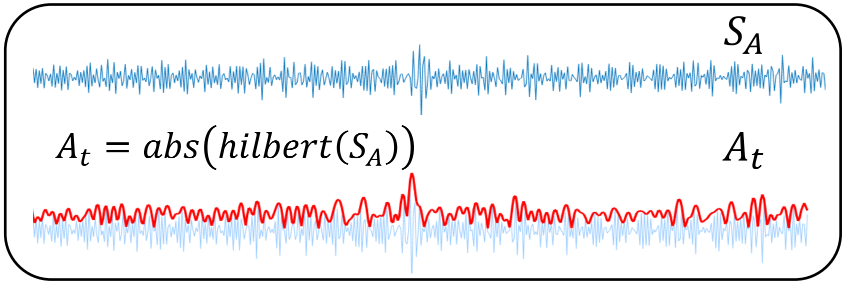
Computing PAC

Electrophysiological signal

High frequency band f_{Amp} (e.g: 30-50Hz)

Low frequency band f_{phase} (e.g: 5-12Hz)

Band-pass Filter



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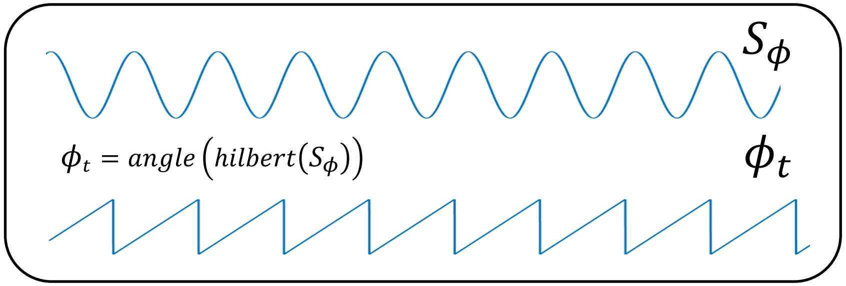

$$\phi_t = angle\left(hilbert(S_\phi)\right)$$

Mean Vector Length

Canolty et al. 2006

- Composite vectors $z_t = A_t e^{i\phi_t}$
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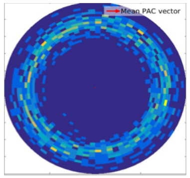
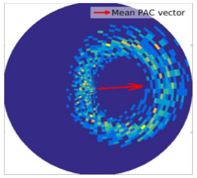


No Coupling



Coupling

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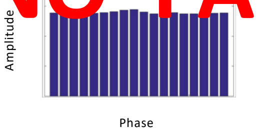
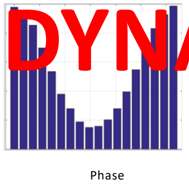
Compute the Kullback-Leibler with a uniform distribution

NO PAC DYNAMIC



No Coupling



Coupling

GLM Measure

Penny et al. 2008

$$A_t = X\beta + e$$

$$X = \begin{vmatrix} cos\phi_1 & sin\phi_1 & 1 \\ \vdots & \vdots & \vdots \\ cos\phi_N & cos\phi_N & 1 \end{vmatrix}$$

Explained variance as an index of PAC

ERPAC

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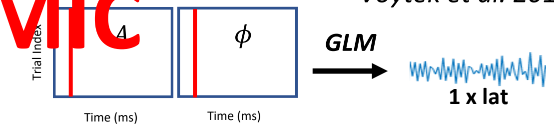


Time resolved '*average*' PAC by applying ***GLM Measure*** for each latency in event related data

Can we do better than this?

YES WE CAN

Goal:
Estimating PAC temporal dynamics

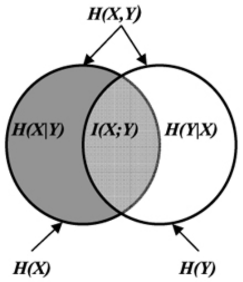
Information Theory Definitions

Shannon Entropy: average amount of uncertainty associated to any measure x of X

$$H(X) = -\sum_{x} p(x) \log_2 p(x)$$

Mutual Information: average reduction in uncertainty about X given the knowledge of the value of Y

$$I(X,Y) = H(X) - H(X|Y)$$



Non-linear form of correlation !!!!!!

$$I(X,Y) = -\sum p(x,y) log_2 \frac{p(x,y)}{p(x)p(y)}$$

KSG Mutual Information Estimator

(Kraskov, Stogbauer and Grassberger)

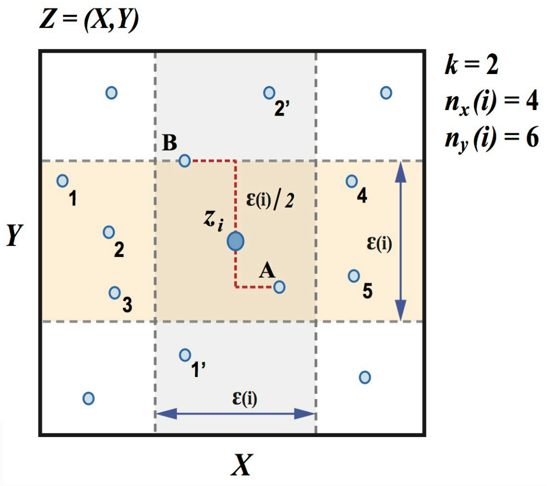
- Extension of Kozachenko-Leonenko estimator of Entropy
- Non-parametric estimator
- Data efficient
- Minimal bias

Assume the joint space $Z = (X, Y)$

Determining *k*-nearest neighbors for each z_i

$$\|z - z'\| = max\{\|x - x'\|, \|y - y'\|\}$$

- Find K-nearest neighbor of z_i (a distance $\frac{\varepsilon}{2}$)
- Count the number of points $n_x(i)$ and $n_y(i)$ in the marginal space within a row (and column) of width ε



Estimate Mutual Information

$$I(X,Y) = \psi(k) - \langle \psi(n_x + 1) + \psi(n_y + 1) \rangle + \psi(N)$$

Kraskov et al. 2004

Estimating local Mutual Information

Lizier et al. 2008, considered the estimation of Local MI from the KSG estimator

Estimate Mutual Information

Kraskov et al. 2004

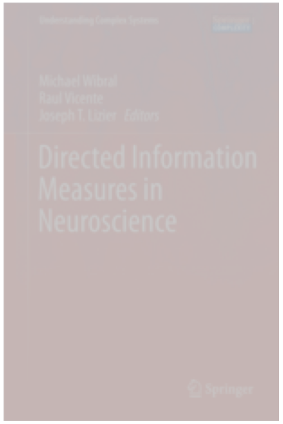
$$I(X,Y)=\psi(k)-\langle\psi(n_x+1)+\psi(n_y+1)\rangle+\psi(N)$$

Unrolling expectation

Estimating Local Mutual Information

$$i(x,y)=\psi(k)-\psi(n_x+1)-\psi(n_y+1)+\psi(N)$$

Lizier, J. T. Directed Information Measures in Neuroscience. Springer, 2014



Directed Information Measures in Neuroscience

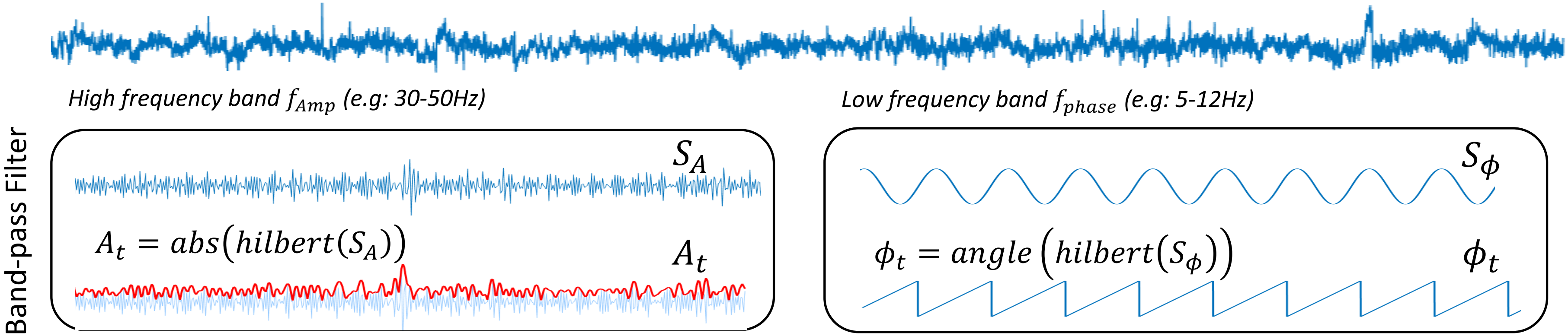
Goal:
Estimating PAC using local Mutual Information

Instantaneous MIPAC

UC San Diego
Jacobs School of Engineering

Data model:

Continuous data $(1\times N_{lat})$



High frequency band f_{Amp} (e.g: 30-50Hz)

Low frequency band f_{phase} (e.g: 5-12Hz)

Band-pass Filter

S_A

$A_t = abs(hilbert(S_A))$

A_t

S_ϕ

$\phi_t = angle\left(hilbert(S_\phi)\right)$

ϕ_t

Assume the joint space $Z = (A_t, \phi_t)$

$$\|z - z'\| = max\{\boxed{\|\phi - \phi'\|}, \boxed{\|A - A'\|}\}$$

Circular norm Euclidean norm

$$i(x,y) = \psi(k) - \psi(n_x + 1) - \psi(n_y + 1) + \psi(N)$$

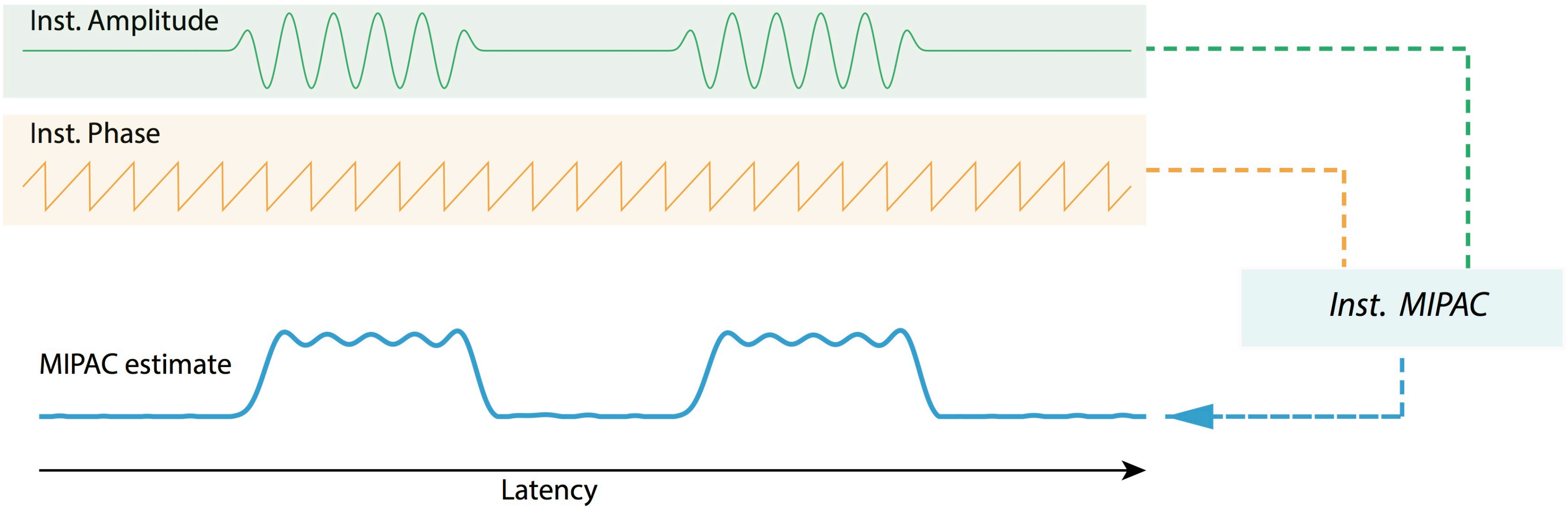
Inst. MIPAC

% Single trials or continuous

```
$\Delta_{var}$ = Inf ; % Initialize Percentage variance reduction
c = 1;
while  $\Delta_{var\_threshold} < \Delta_{var}$
        Estimate $i(A_t, \phi_t)$ for k=c ;
        Compute $\Delta_{var}$ ;
        c = c+1 ;
End
MIPAC = Low-pass filter $i(A_t, \phi_t)$ at $f_{phase}$ ;
```

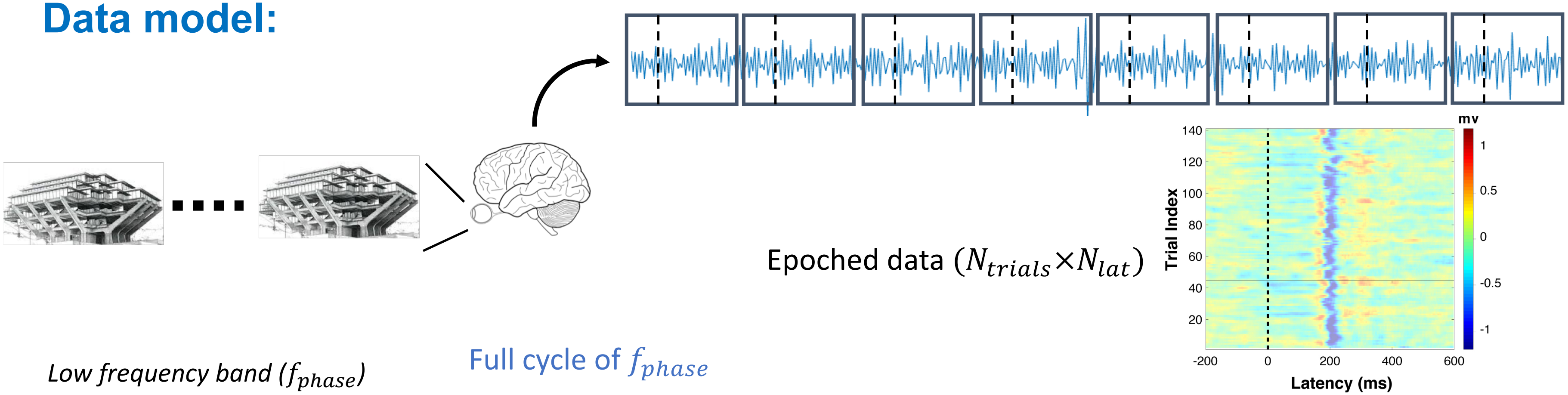
Martinez-Cancino et al , **Neuroimage** Volume 185, 2019

Inst. MIPAC in a nutshell



Event-related MIPAC

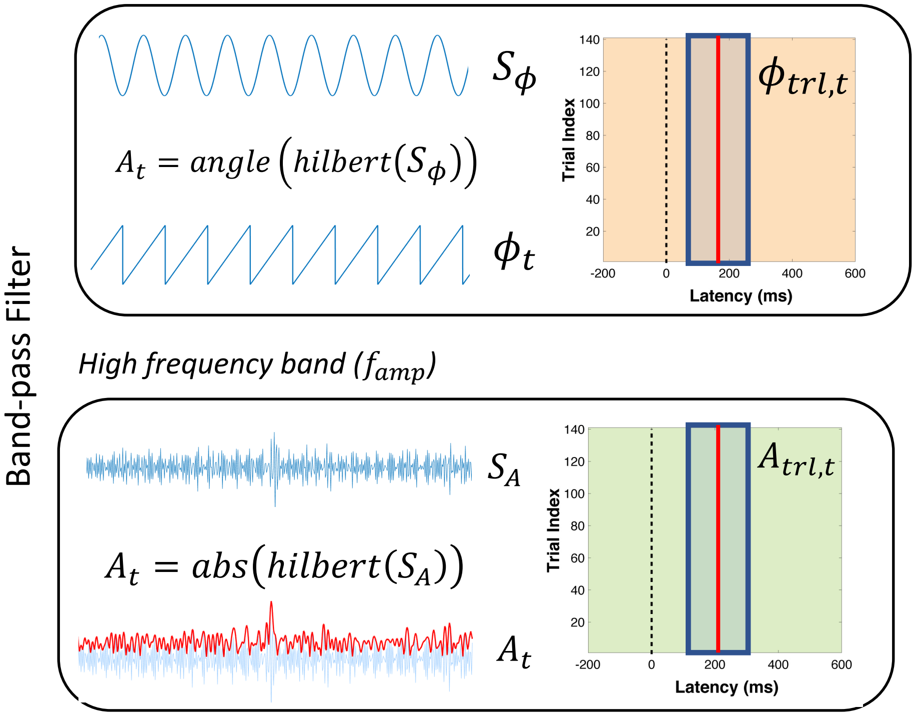
Data model:



Epoched data $(N_{trials} \times N_{lat})$

Low frequency band (f_{phase})

Full cycle of f_{phase}



$A_t = angle\left(hilbert(S_\phi)\right)$

High frequency band (f_{amp})

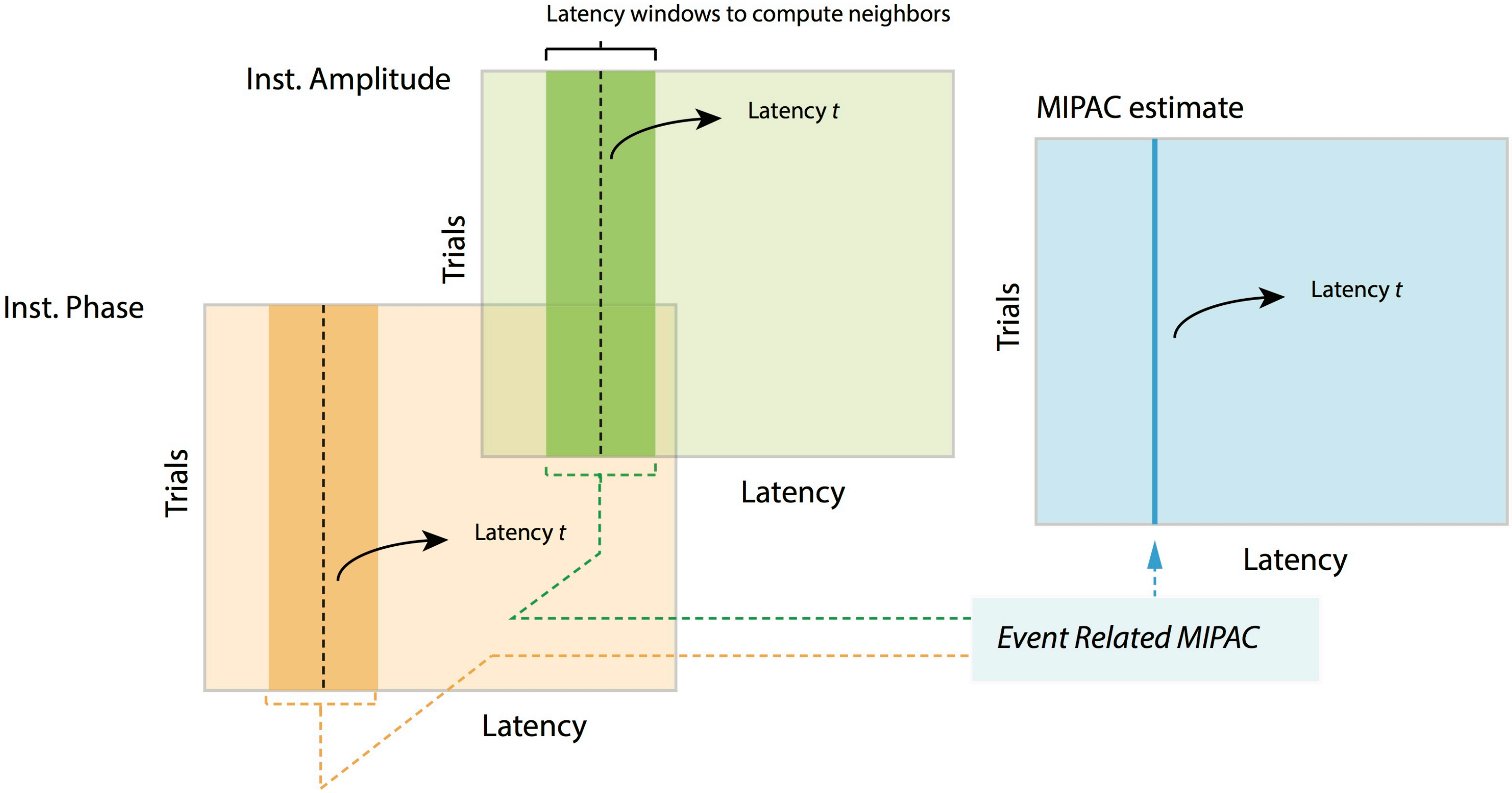
$A_t = abs\left(hilbert(S_A)\right)$

Event Related MIPAC (cyclostationary)

```
% Epoched data
for $t = 1: N_{lat}$
    $\Delta_{var}$ = Inf ; % Initialize Percentage variance reduction
    c = 1;
    while  $\Delta_{var\_threshold} < \Delta_{var}$
            Estimate $i\left(A_{trl,t}(:,t), \phi_{trl,t}(:,t)\right)$ for k=c ;
            (Neighbors are count in a latency window)
            Compute $\Delta_{var}$ ;
            c = c+1;
    end
end
MIPAC = Low-pass filter  $i\left(A_{trl,t}, \phi_{trl,t}\right)$  at $f_{phase}$.
```

Martinez-Cancino et al, **Neuroimage** Volume 185, 2019

Event-related MIPAC in a nutshell



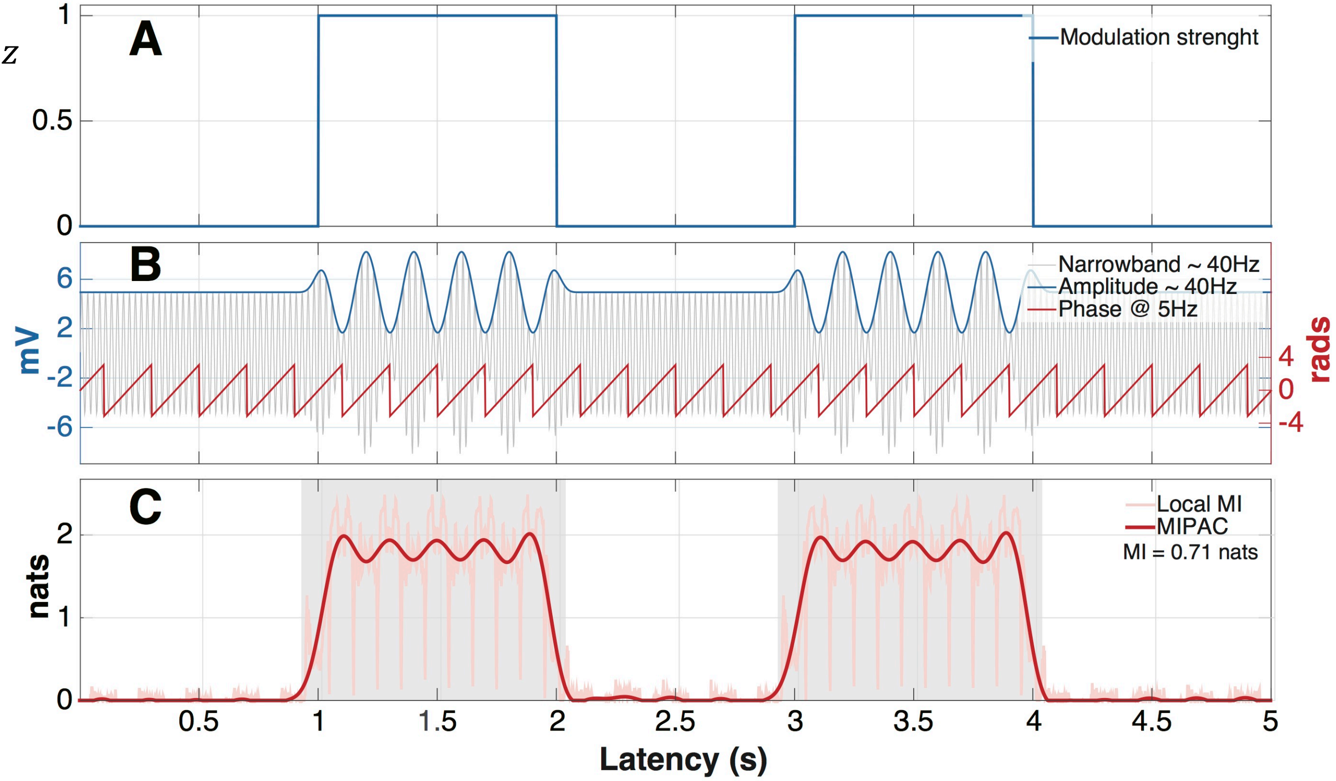
MIPAC Simulations

Simulation 1.1: Instantaneous MIPAC

$f_{mod} = 5Hz$

$f_{carr} = 40Hz$

$S_{rate} = 500Hz$



(A) Block-shaped waveform modulation strength.
(B) Simulated signal
(C) Estimated MIPAC (red), and local MI (light red)

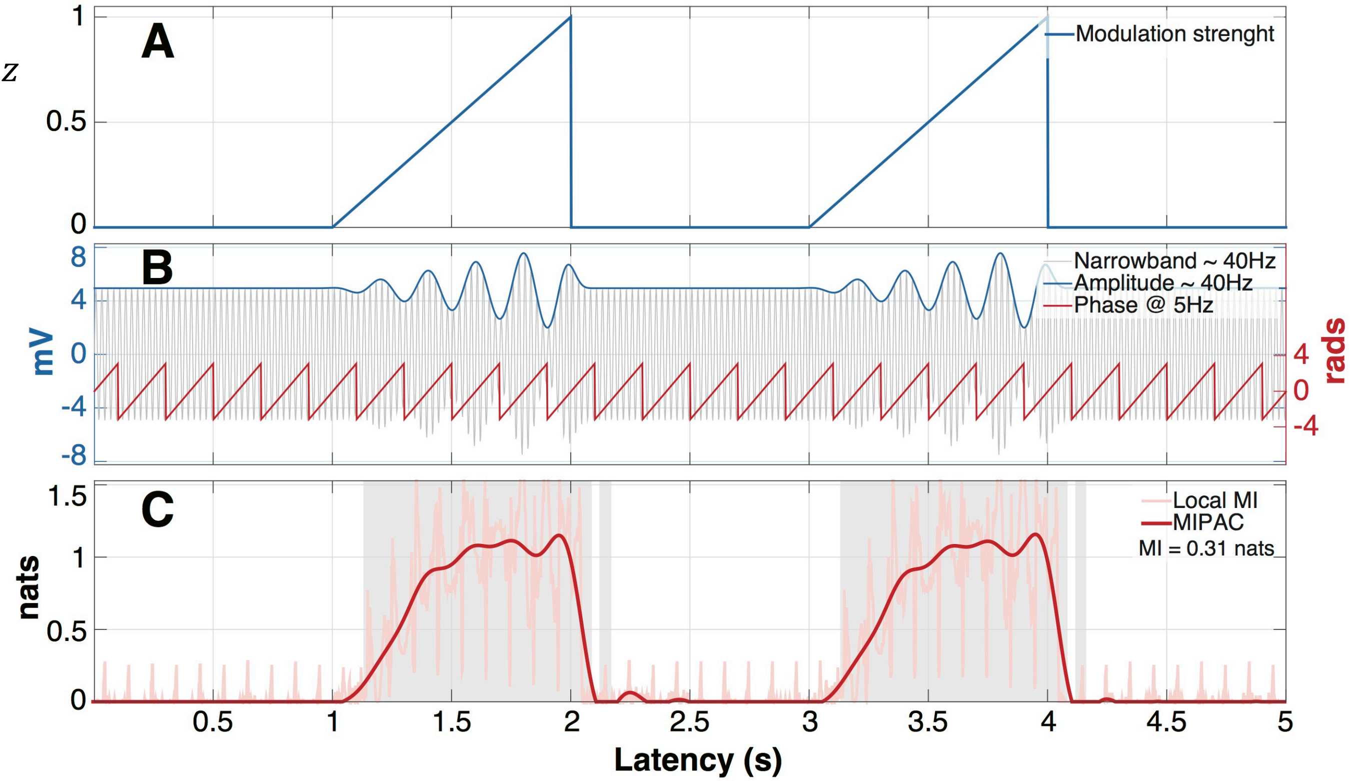
(Martinez-Cancino et al., 2019)

Simulation 1.2: Instantaneous MIPAC

$f_{mod} = 5Hz$

$f_{carr} = 40Hz$

$S_{rate} = 500Hz$



(A) Saw-tooth shape waveform modulation strength.
(B) Simulated signal
(C) Estimated MIPAC (red), and local MI (light red)

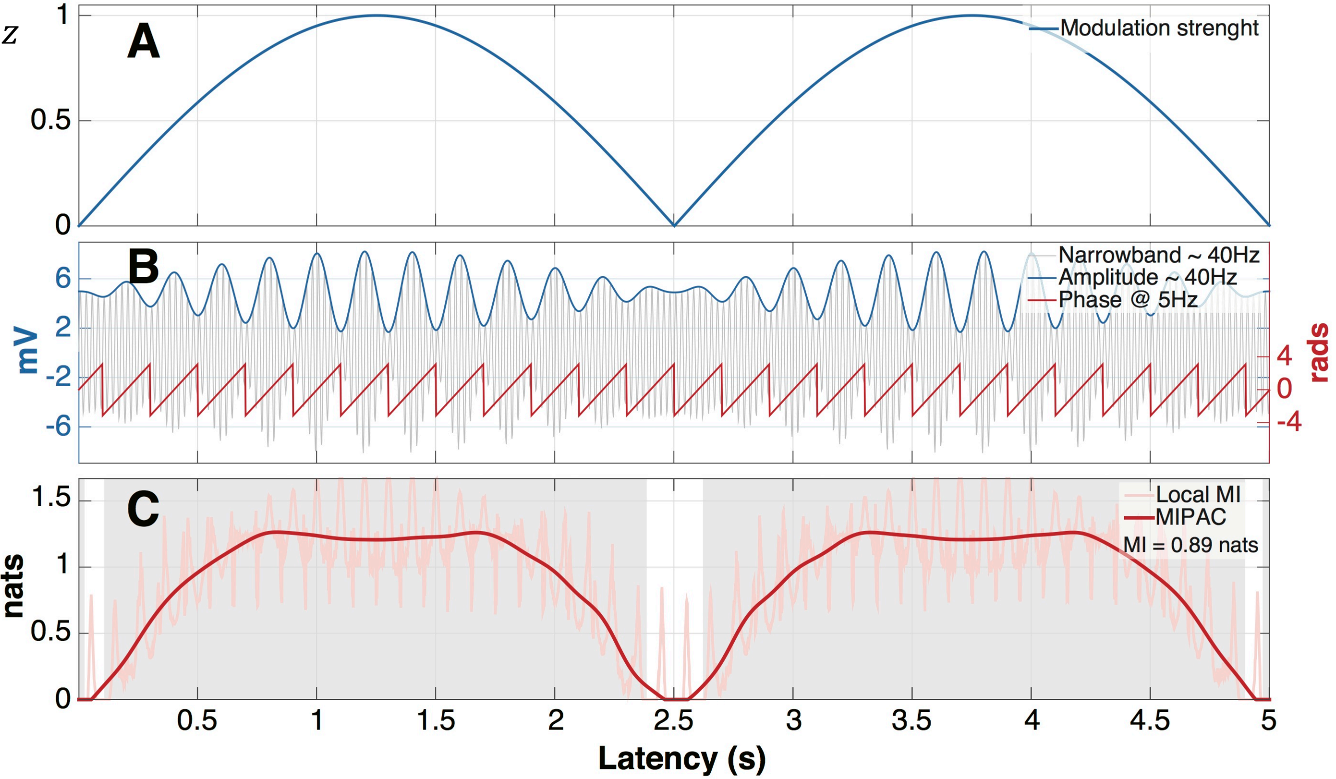
(Martinez-Cancino et al., 2019)

Simulation 1.3: Instantaneous MIPAC

$f_{mod} = 5Hz$

$f_{carr} = 40Hz$

$S_{rate} = 500Hz$

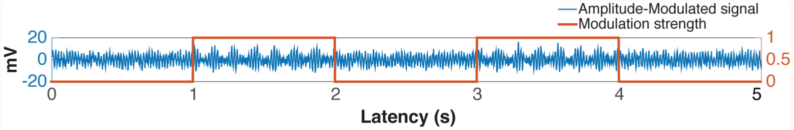


(A) Absolute value of a sinusoid used as modulation strength.
(B) Simulated signal
(C) Estimated MIPAC (red), and local MI (light red)

(Martinez-Cancino et al., 2019)

Simulation 2: Event-related MIPAC

ER PAC data simulation



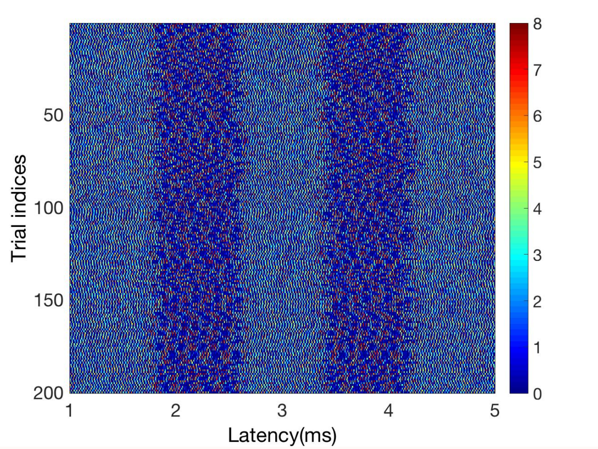
$f_{mod} = 5Hz$

$f_{carr} = 40Hz$

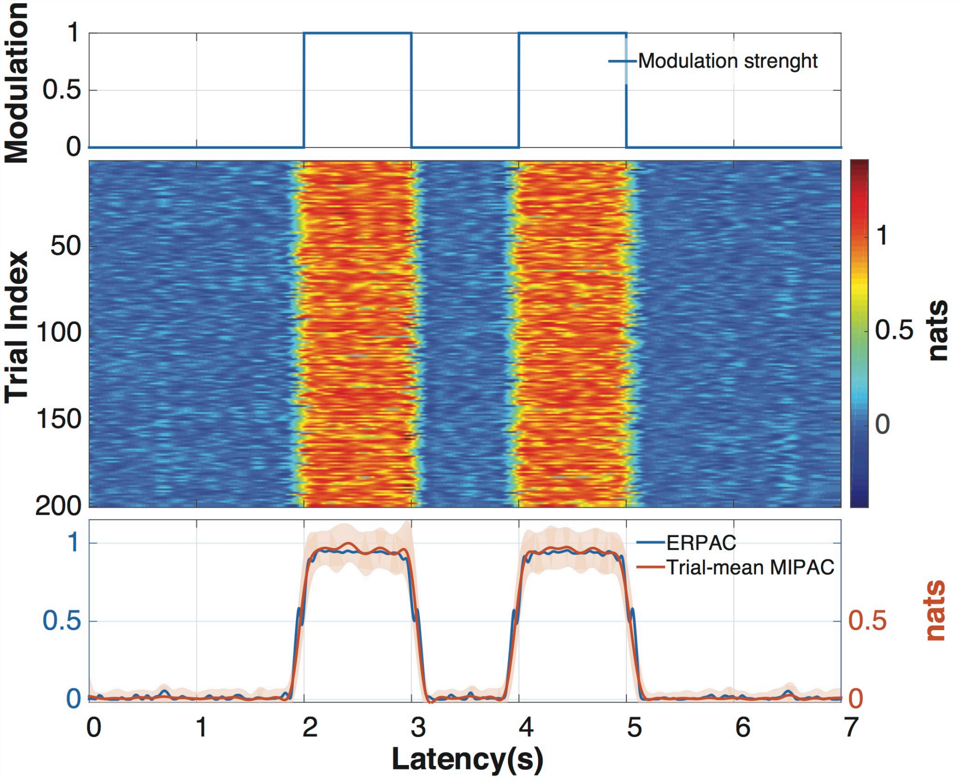
$S_{rate} = 500Hz$ $SNR = 10$

x200

Each trial was shifted 1-100 pts



Event related MIPAC and ERPAC (*Voytek et al, 2013*) were used to estimate PAC



(Martinez-Cancino et al., 2019)

Simulation 4: MIPAC & MImi

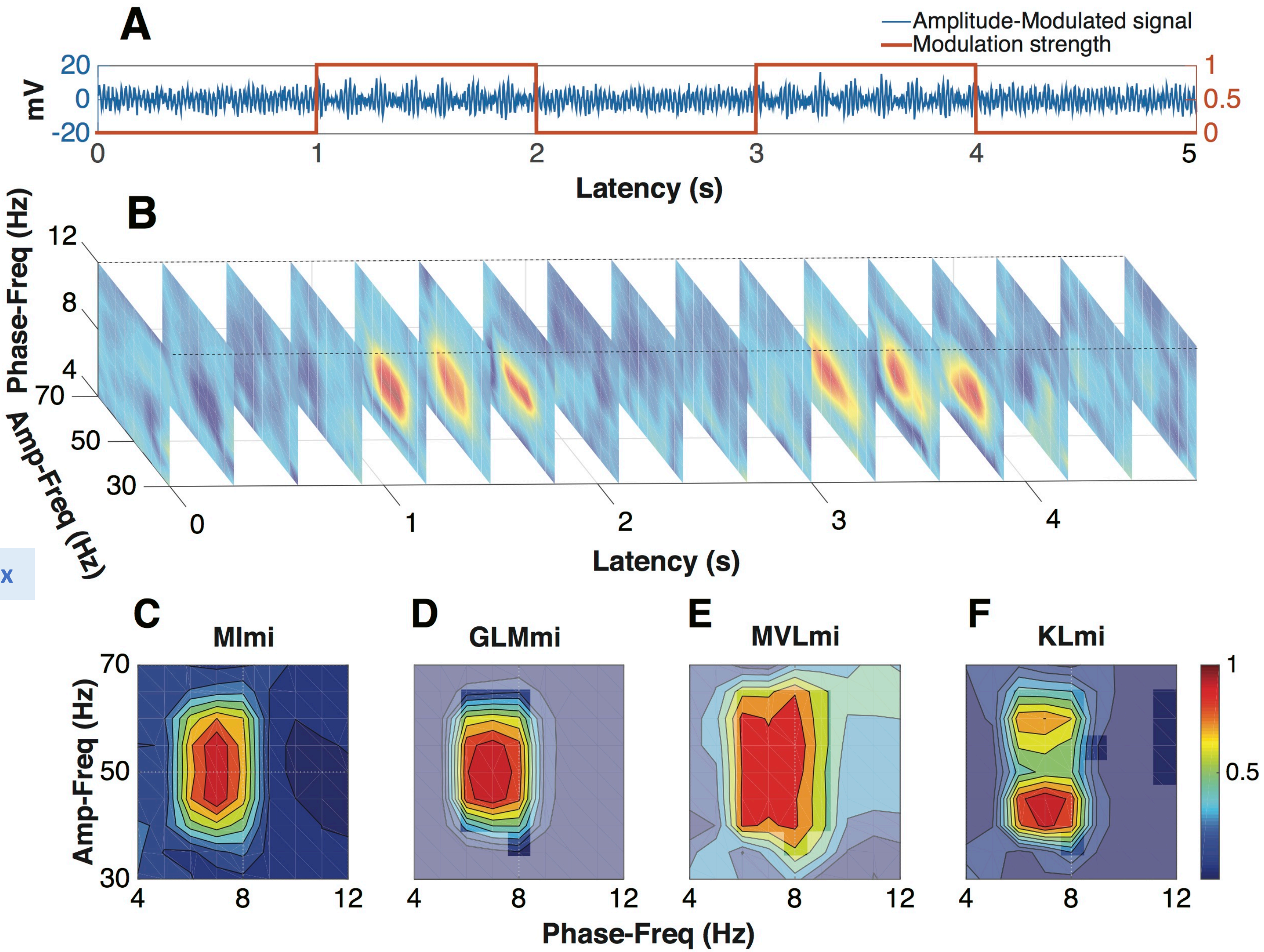
$f_{mod} = 7Hz$

$f_{carr} = 50Hz$

$S_{rate} = 500Hz$

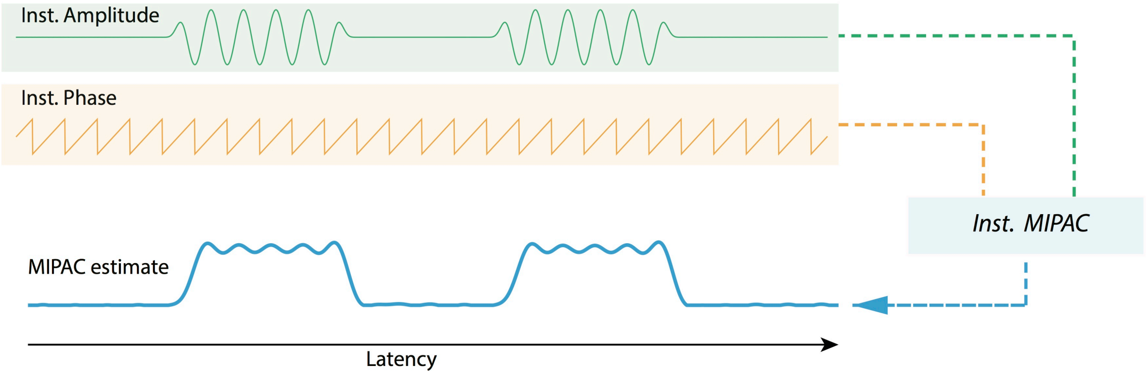
Grand Mean

MI modulation index

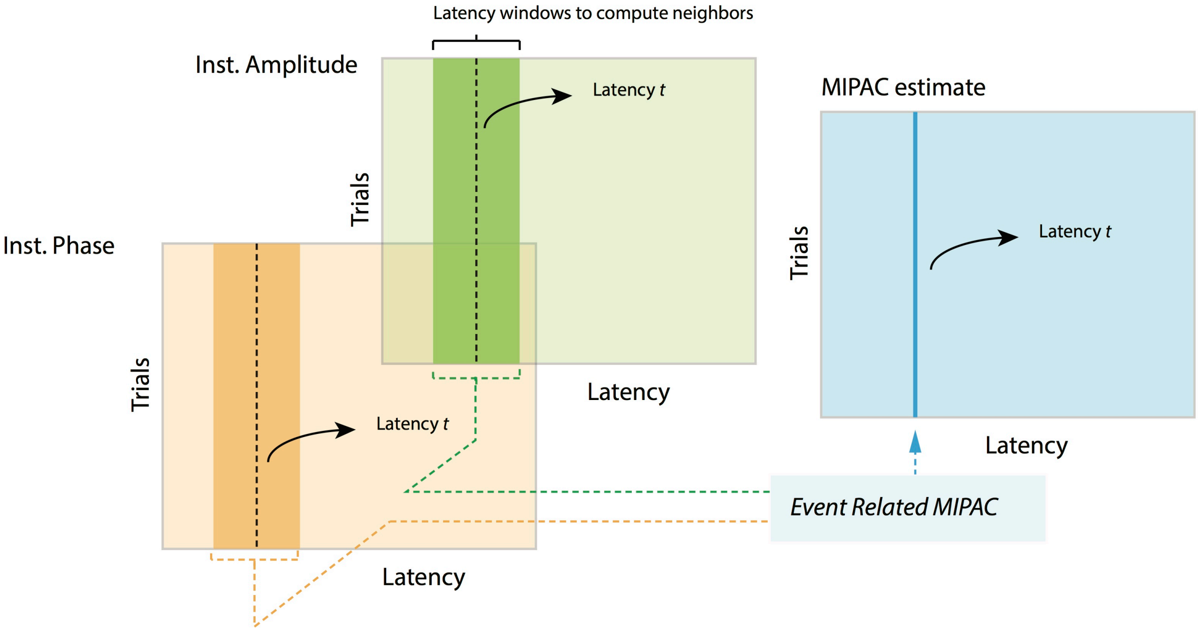


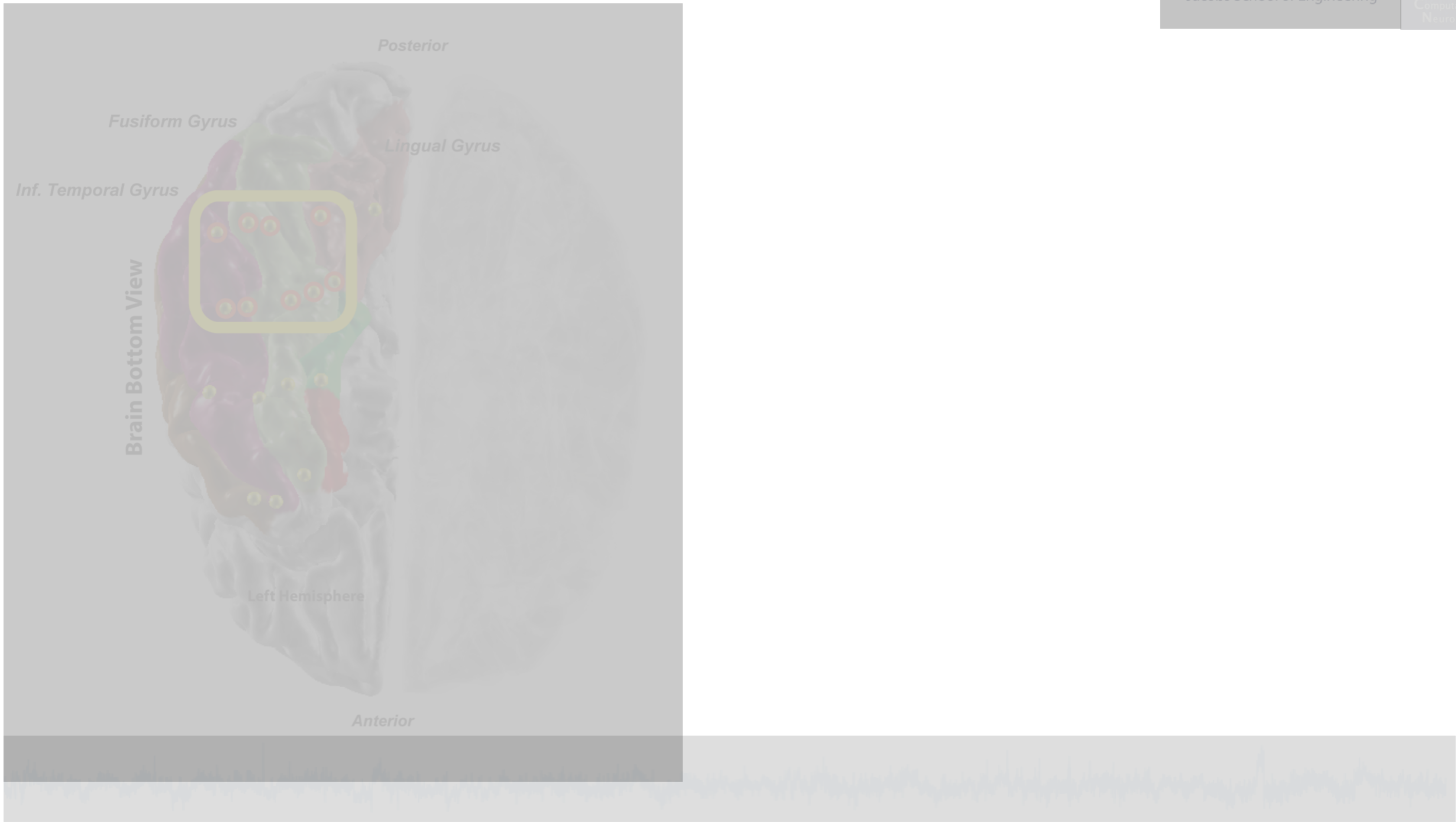
Inst. MIPAC and Event-related MIPAC

MIPAC



Event-related MIPAC



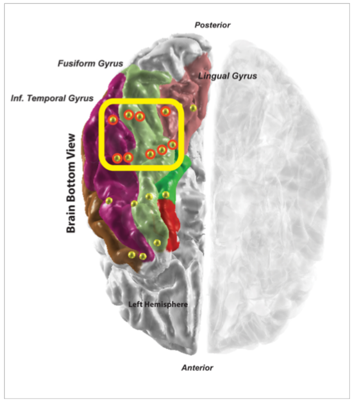


MIPAC application to real data

ECoG Data

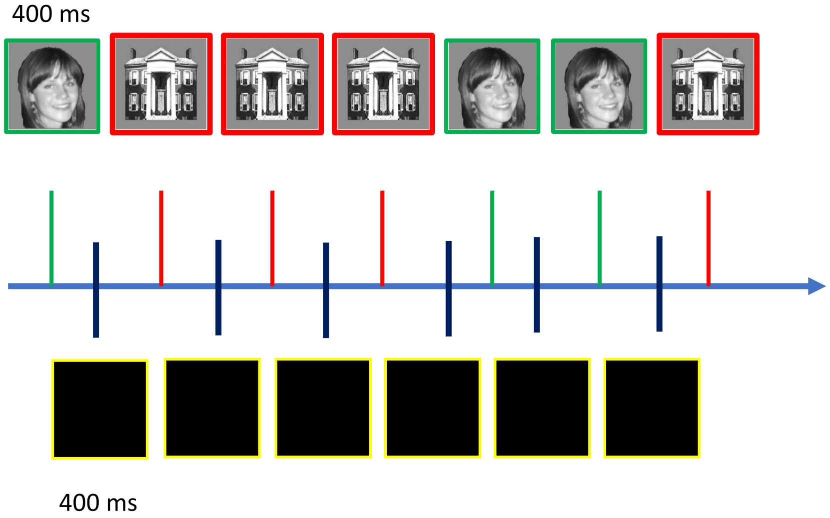
Subject

- Clinical monitoring and localization of seizure foci
- 1 subject (mv)
- ECoG channels in: Inf. Temp. Gyrus
  Lingual Gyrus
  Fusiform Gyrus



Experimental design

- Images of Houses and Faces were presented randomly
- 3 runs 100 presentations each (50 H / 50F)



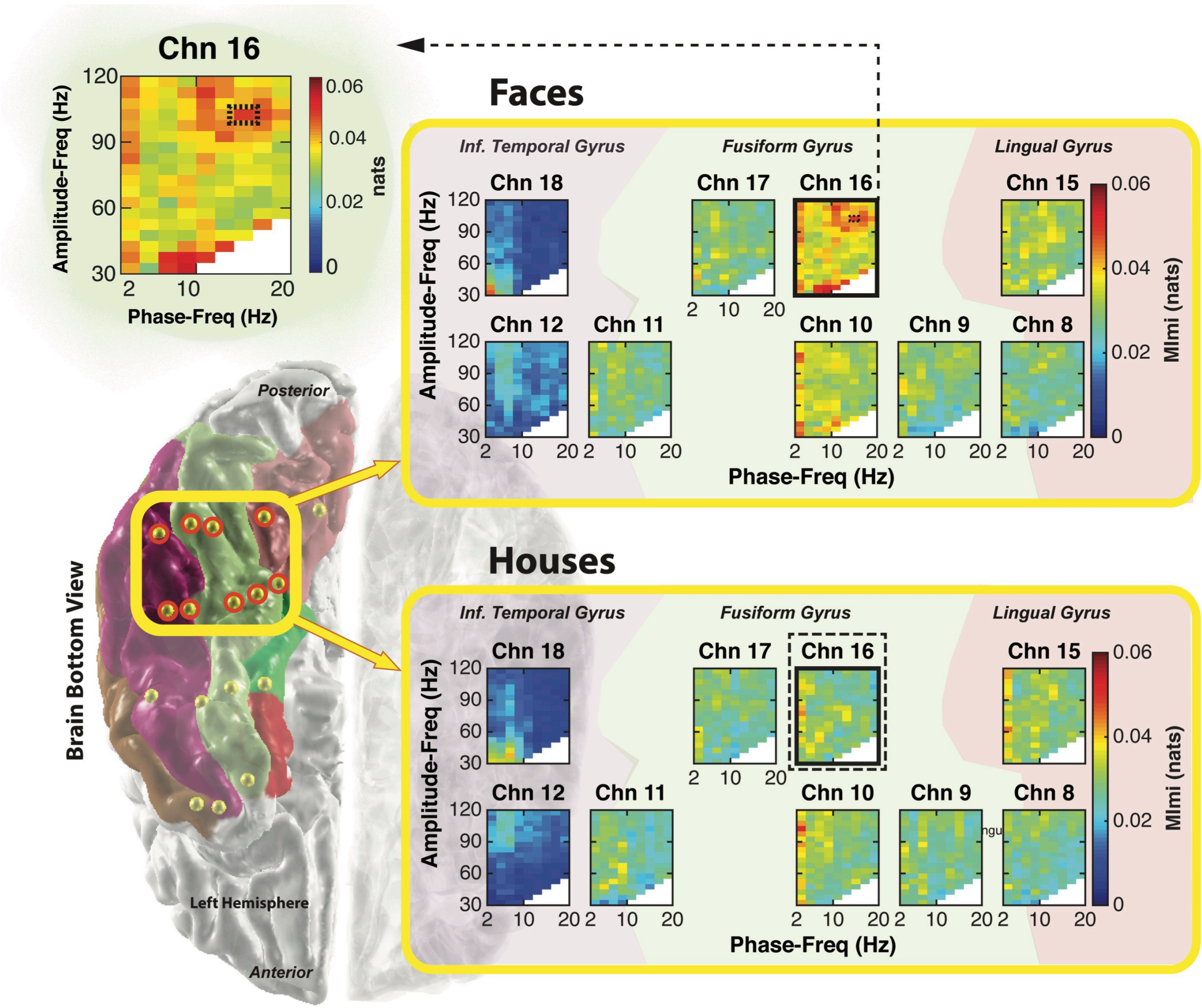
Preprocessing

Performed in EEGLAB ***(Delorme and Makeig, 2004)***

1. Artifact removal
2. CAR
3. Resampling to 512Hz
4. Line noise removal ~(60, 120) Hz
   Hamming-windowed FIR notch filter
5. Extract epochs time-locked to stimulus presentations [-400,800] *ms*

Original publication:
The physiology of perception in human temporal llobe is specialized for contextual novelty
Kai J. Miller, Dora Hermes, Nathan Witthoft, Rajesh P. N. Rao, Jeffrey G. Ojemann

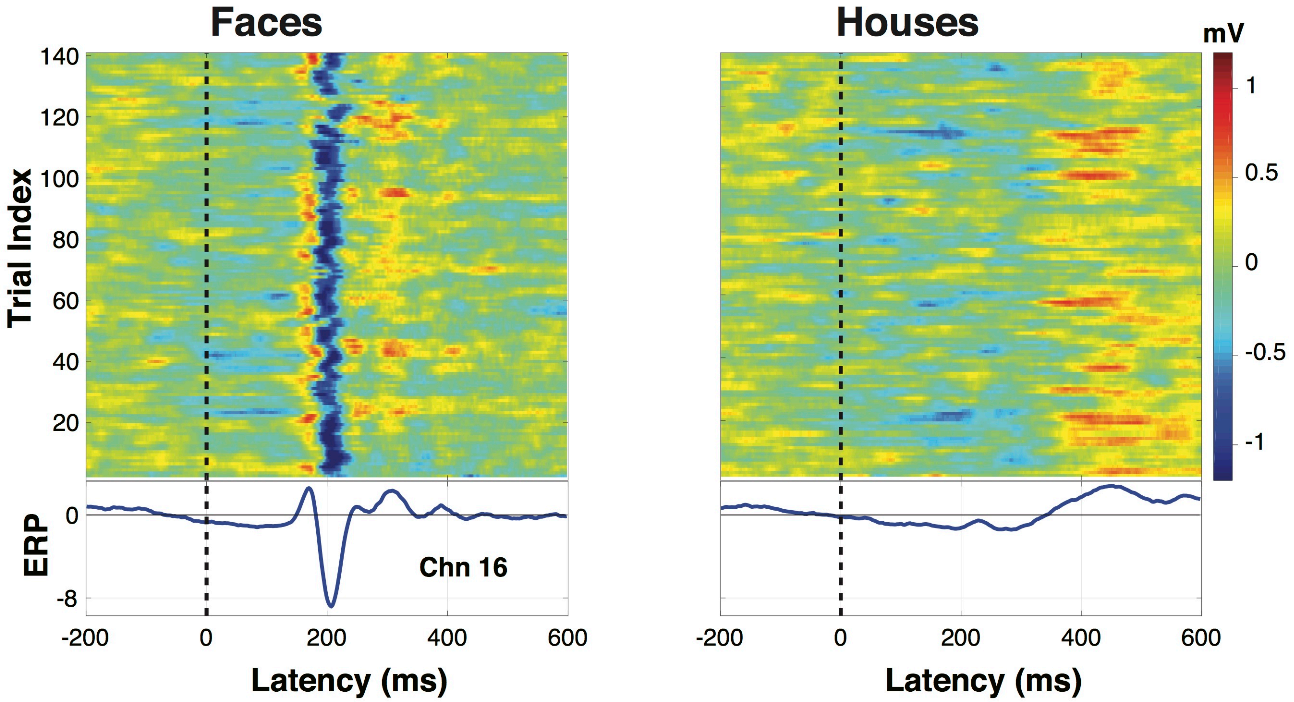
ECoG Data: MImi in action



(Martinez-Cancino et al., 2019)

ECoG Data: Event Related Potential Image

Channel 16



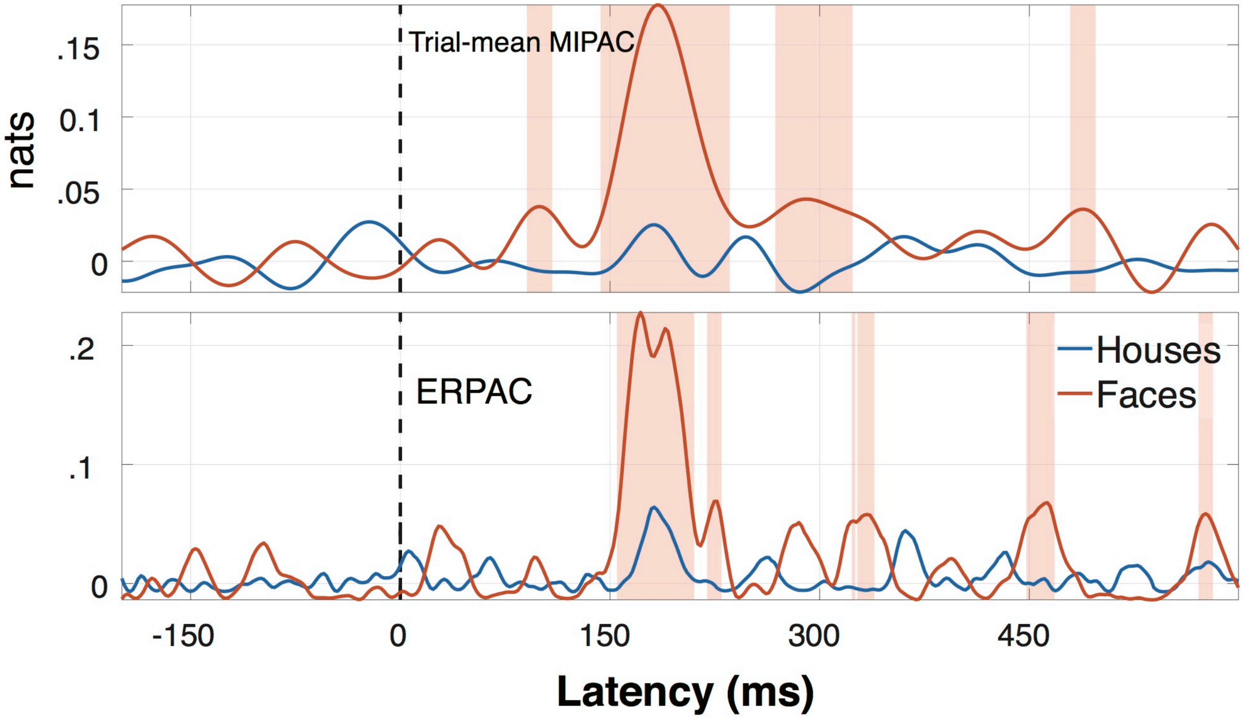
(Martinez-Cancino et al., 2019)

ECoG Data: MIPAC vs ERPAC

Event-related MIPAC and ERPAC (***Voytek et al. 2014***) were computed

$$f_{phase} = 16\ Hz$$

$$f_{amp} = 95Hz$$



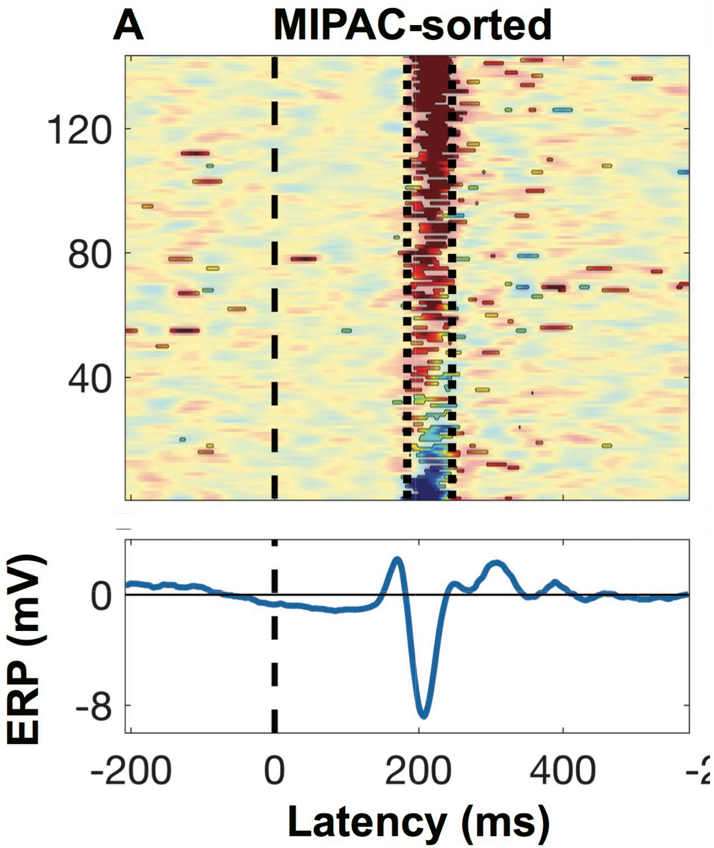
(Martinez-Cancino et al., 2019)

ECoG Data: MIPAC Image

ER-MIPAC computed for ***Faces*** presentation

$$f_{phase} = 16\ Hz$$

$$f_{amp} = 95Hz$$



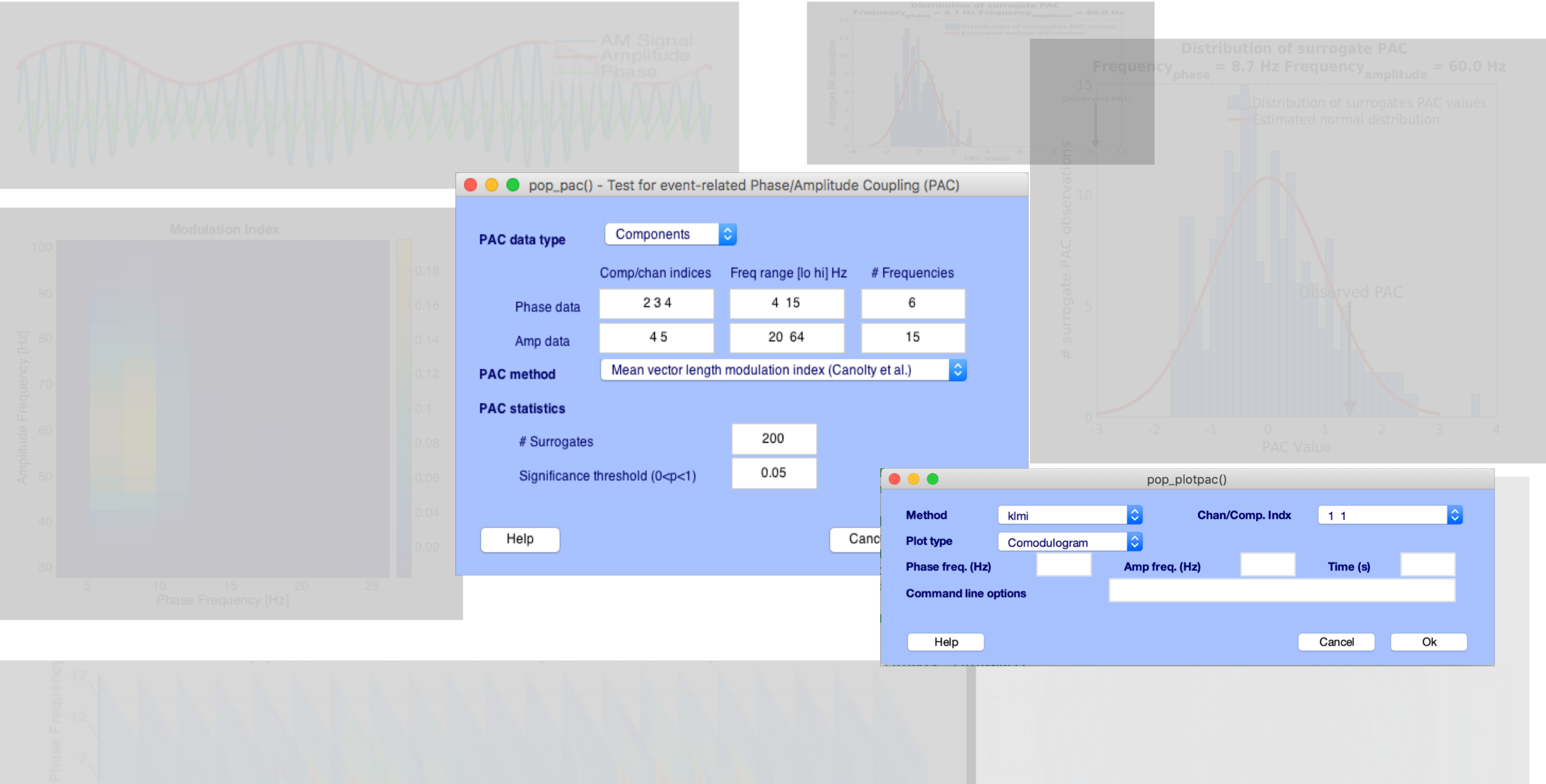
(Martinez-Cancino et al., 2019)

Conclusions

- The method was validated on simulated PAC signals
- Application to human ECoG data showed positive results

Future Direction

ERPAC Tools



pop_pac() - Test for event-related Phase/Amplitude Coupling (PAC)

PAC data type: Components

	Comp/chan indices	Freq range [lo hi] Hz	# Frequencies
Phase data	2 3 4	4 15	6
Amp data	4 5	20 64	15

PAC method: Mean vector length modulation index (Canolty et al.)

PAC statistics

Surrogates: 200

Significance threshold (0<p<1): 0.05

pop_plotpac()

Method: klmi

Chan/Comp. Indx: 1 1

Plot type: Comodulogram

Phase freq. (Hz)

Amp freq. (Hz)

Time (s)

Command line options

Available from: https://github.com/nucleuscub/pop_pac

Acknowledgments

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