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Cross-frequency coupling studies of intracranial EEG data of epilepsy patients using time-frequency distributions

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Introduction

- **What is cross-frequency coupling in brain rhythms?**
- Why do we study it?
- What are time-frequency distributions?
- Why do we need them?
- How do we apply those time-frequency distributions to study cross-frequency coupling in brain disorder studies?

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Pause

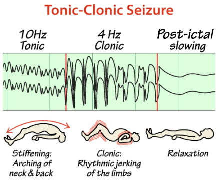


Figure 1: Tonic-clonic seizures

Figure 2: More or less an impared-awareness seizure

What are the intracranial EEG data?

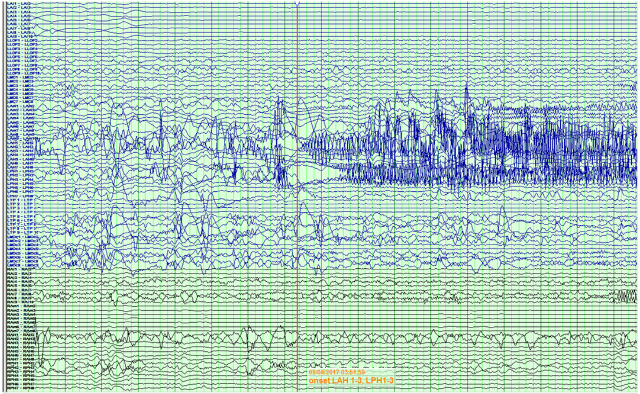


Figure 3: A screenshot of EEG waveforms in original software. The vertical red line demarcates the beginning of the seizure, called the onset.

Frequency Bands in Neuroscience

Delta: 1-3Hz — lowest frequencies with which information flows in the brain

Theta: 4-8Hz — focuses on memory and coordination

Alpha: 8-12Hz — sensory and motor systems

Beta: 12-30Hz — associated with our waking lives

Gamma: 25-120Hz * — the most important frequency in our waking lives

* Note that the gamma band is often broken into sections, i.e. 50-70Hz, 70-100Hz, 25-100Hz etc.

Also note that the edges of the bands aren't fixed, can overlap with one another, and that they vary from researcher to researcher even.

What is Cross-Frequency Coupling (CFC)? cont.

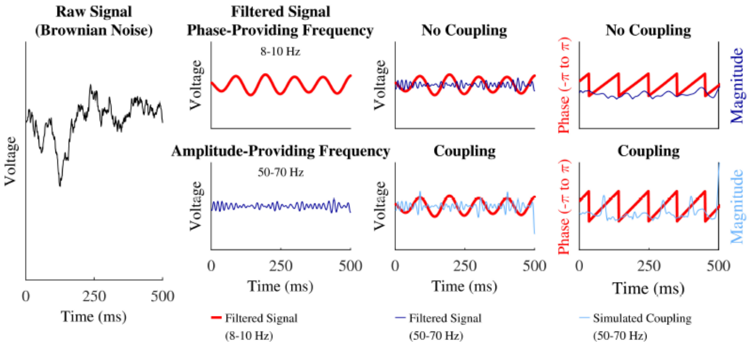
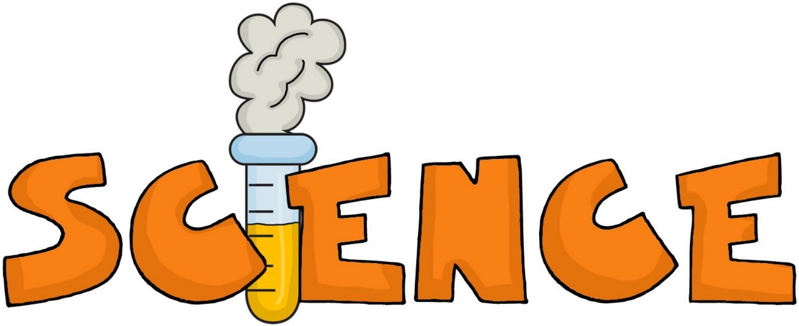


Figure 4: Taken from *Hülsemann M.J., Naumann E. and Rasch B.* — Quantification of Phase-Amplitude Coupling in Neuronal Oscillations: Comparison of Phase-Locking Value, Mean Vector Length, Modulation Index, and Generalized-Linear-Modeling-Cross-Frequency-Coupling. — // Front. Neurosci. — 2019. — Vol. 13 — P. 573.

Why do we need to study CFC?



Methods for detecting CFC

- **Mean Vector Length (MVL)**
  Canolty et al., and Tamanna T . K. Munia, Selin Aviyente
    - PAC
- **Modulation Index (MI)**
  Tort et al.
    - PAC
- **Generalized Linear Models (GLM-CFC)**
  Mark Kramer, Uri T. Eden, Jessica Nadalin
    - PAC
    - AAC

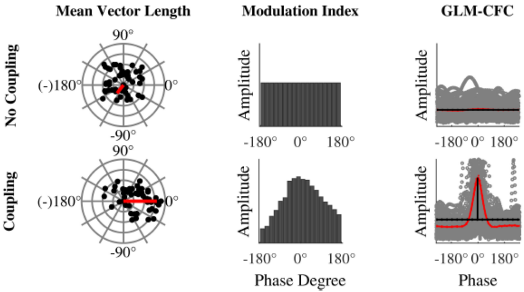


Figure 5: Taken (and modified) from *Hülsemann M.J., Naumann E. and Rasch B.* — Quantification of Phase-Amplitude Coupling in Neuronal Oscillations: Comparison of Phase-Locking Value, Mean Vector Length, Modulation Index, and Generalized-Linear-Modeling- Cross-Frequency-Coupling. — // Front. Neurosci. — 2019. — Vol. 13 — P. 573.

Methods for detecting CFC - MI

$$x_{f_p}(t) = LPF\{x_{raw}(t)\} \tag{1}$$

Phase-giving signal

$$x_{f_A}(t) = HPF\{x_{raw}(t)\} \tag{2}$$

Amplitude-giving signal

Methods for detecting CFC - MI cont.

$$\left[x_{f_p}(t)\right]_a = x_{f_p}(t) + j\mathcal{H}\{x_{f_p}(t)\} \tag{3}$$

Analytic signal representation of $x_{f_p}(t)$

$$\left[x_{f_A}(t)\right]_a = x_{f_A}(t) + j\mathcal{H}\{x_{f_A}(t)\} \tag{4}$$

Analytic signal representation of $x_{f_A}(t)$

Note: $j = \sqrt{-1}$ is the imaginary unit, common notation in electrical engineering and signal processing

Aside — Hilbert Transform

$$\mathcal{H}\{f(t)\} = \frac{1}{\pi}\int_{-\infty}^{\infty} \frac{f(\tau)}{t-\tau} d\tau$$

Aside — Convolution

$$(f * g)(t) = \int_{-\infty}^{\infty} f(\tau) g(t - \tau) d\tau$$

Methods for detecting CFC - MI cont. cont.

$$\phi_{f_p}(t) = \arctan\left[x_{f_p}(t)\right]_a \tag{5}$$

Instantaneous phase values

$$A_{f_A}(t) = \left|\left[x_{f_A}(t)\right]_a\right| \tag{6}$$

Instantaneous amplitude values

Methods for detecting CFC - MI cont. cont. cont.

$$\langle A_{f_A} \rangle_{\phi_{f_p}} \tag{7}$$

The mean of instantaneous amplitude values (A_{f_A}) over binned phases, with bins j.

$$P(j) = \frac{\langle A_{f_A} \rangle_{\phi_{f_p}}(j)}{\sum_{k=1}^{N} \langle A_{f_A} \rangle_{\phi_{f_p}}(k)} \tag{8}$$

$P(j)$ is the aforementioned amplitude distribution whose shape we need.

Note: $P(j) \geq 0 \, \forall j$ and $\sum_{j=1}^{N} P(j) = 1$

$$D_{KL}(P,Q) = \sum_{j=1}^{N} P(j) log\left[\frac{P(j)}{Q(j)} \right] \tag{9}$$

Kullback-Leibler (KL) distance.

Note: $D_{KL}(P,Q) \geq 0$ and $D_{KL}(P,Q) = 0 \iff P = Q$, in other words, when the distributions are identical.

Methods for detecting CFC - MI cont. x6

$$H(P) = -\sum_{j=1}^{N} P(j) log\left[P(j)\right] \tag{10}$$

Shannon Entropy

Methods for detecting CFC - MI cont. x7

$$D_{KL}(P, U) = log(N) - H(P) \tag{11}$$

Relationship between Shannon entropy and KL distance

Methods for detecting CFC - MI cont. x8

$$MI = \left[\frac{D_{KL}(P, U)}{log(N)} \right] \tag{12}$$

Definition of MI

Methods for detecting CFC - MI cont. x9

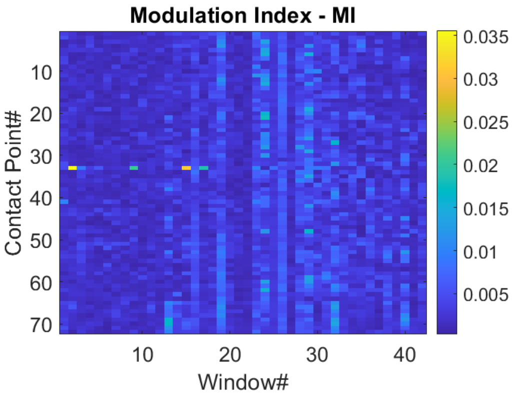


Figure 6: An example of values of MI, found by filtering all waveforms into low and high frequency components, and comparing components from one waveform. Distribution of colours of colormap is unaltered.

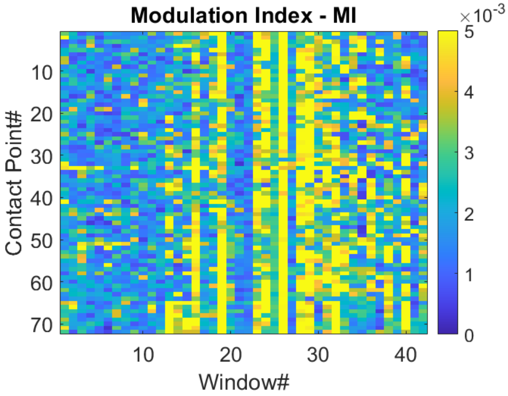
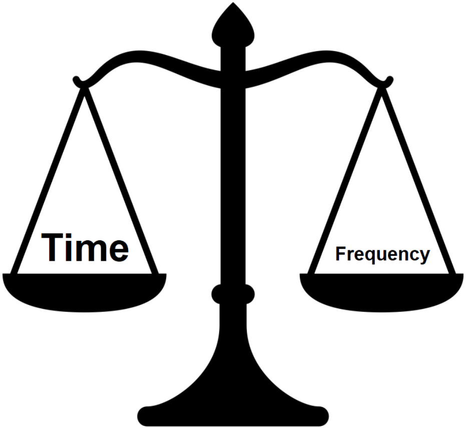


Figure 7: An example of values of MI, found by filtering all waveforms into low and high frequency components, and comparing components from one waveform. Distribution of colours of colormap is maxed at 0.005, a value indicative of PAC.

Problems with current methods

What is time-frequency analysis? And what are time-frequency distributions?



Problems with time-frequency analysis today

Let y(t)=cos(2 $\pi f_1 t) + cos(2\pi f_2 t)$ $\begin{cases} f_1 = 10, f_2 = 15 & 0s \leq t < 1s \\ f_1 = 20, f_2 = 25 & 1s \leq t < 2s \\ f_1 = 30, f_2 = 35 & 2s \leq t < 3s \\ f_1 = 40, f_2 = 45 & 3s \leq t < 4s \end{cases}$

Problems with time-frequency analysis today cont.

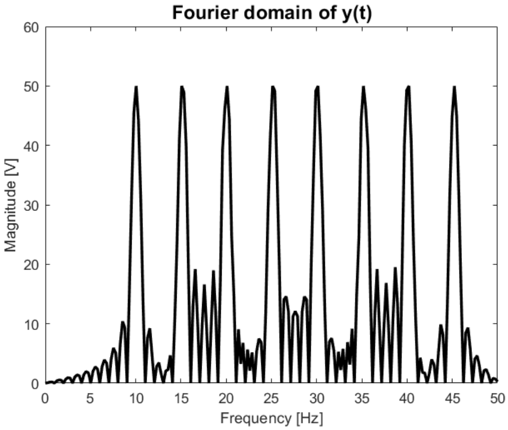


Figure 8: Traditional Fourier transform methods fail to account for changing frequencies. Also, spectral noise has been introduced.

Problems with time-frequency analysis today cont. cont.

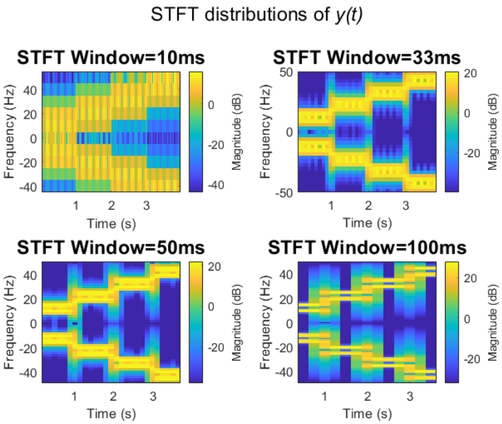


Figure 9: Better resolution in the time domain results in worse resolution in the frequency domain and vice-versa.

Solutions to the aforementioned problems

$$C(t,\omega) = \frac{1}{\sqrt{2\pi}} e^{-j\omega t} x(t) X^*(\omega) \tag{13}$$

Rihaczek Distribution — introduced in 1968

Solutions to the aforementioned problems

$$C(t, \omega) = \frac{1}{\sqrt{2\pi}} e^{-j\omega t} x(t) X^*(\omega) \tag{13}$$

Kernel function

Solutions to the aforementioned problems

$$C(t,\omega) = \frac{1}{\sqrt{2\pi}} e^{-j\omega t} x(t) X^*(\omega) \tag{13}$$

Time-series

Solutions to the aforementioned problems

$$C(t,\omega) = \frac{1}{\sqrt{2\pi}} e^{-j\omega t} x(t) X^*(\omega) \tag{13}$$

Complex conjugate of Fourier Transform

Solutions to the aforementioned problems cont.

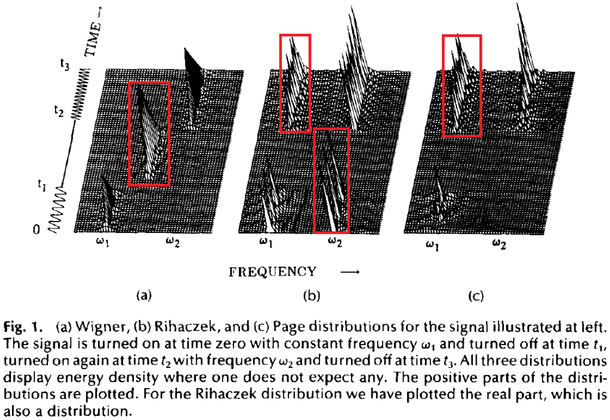


Figure 10: Taken from *Cohen L.* — Time-frequency distributions-a review. — // Proceedings of the IEEE. — 1989. — Vol. 77, no. 7. — P. 941–981.

Solutions to the aforementioned problems cont. cont.

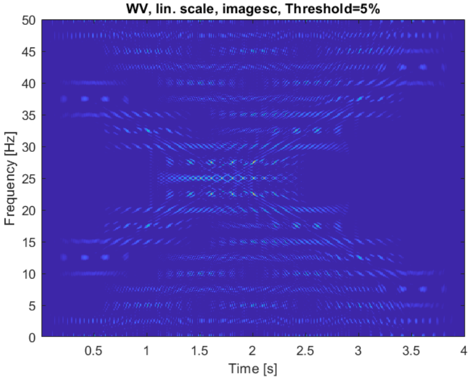


Figure 11: Wigner-Ville TFD performed on $y(t)$ using the Time-Frequency Toolbox. Downloadable from: `http://tftb.nongnu.org/`

Solutions to the aforementioned problems cont. cont. cont.

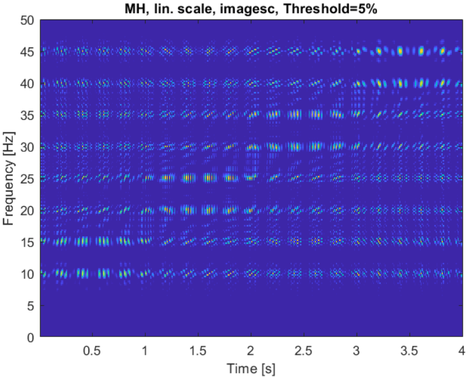


Figure 12: Rihaczek (but really Margenau-Hill) TFD performed on $y(t)$ using the Time-Frequency Toolbox. Downloadable from: `http://tftb.nongnu.org/`

Solutions to the aforementioned problems cont. x4

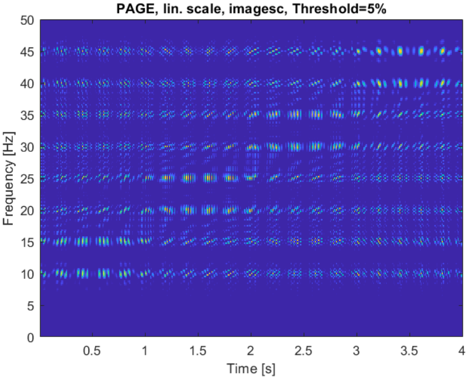


Figure 13: Page TFD performed on $y(t)$ using the Time-Frequency Toolbox. Downloadable from: `http://tftb.nongnu.org/`

Solutions to the aforementioned problems cont. x5

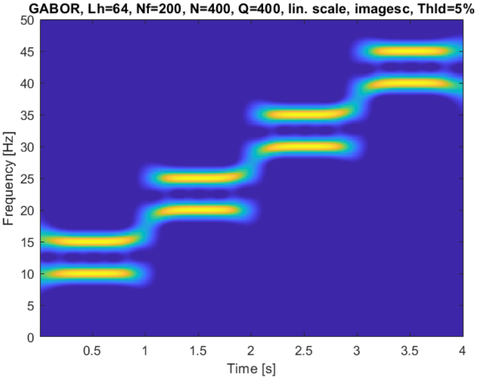


Figure 14: Gabor TFD performed on $y(t)$ using the Time-Frequency Toolbox. Downloadable from: `http://tftb.nongnu.org/`

Solutions to the aforementioned problems cont. x6

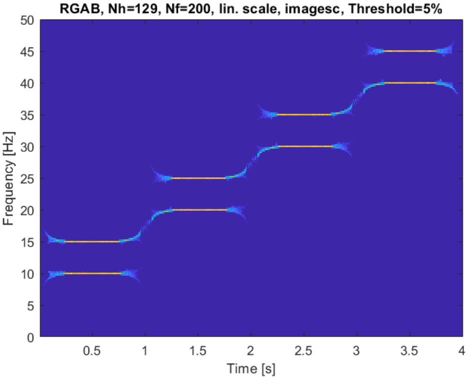


Figure 15: Reassigned Gabor TFD performed on $y(t)$ using the Time-Frequency Toolbox. Downloadable from: `http://tftb.nongnu.org/`

$$C(t,f) = \iint exp\left(- \frac{(\theta\tau)^2}{\sigma}\right) exp\left(j\frac{\theta\tau}{\sigma}\right) A(\theta,\tau) e^{-j(\theta t + 2\pi f \tau)}\, d\tau\, d\theta \tag{14}$$

Reduced-Interference (RID) Rihaczek Distribution — introduced by Selin Aviyente and Ali Yener Mutlu in 2011

$$C(t,f) = \iint exp\left(- \frac{(\theta\tau)^2}{\sigma} \right) exp\left(j\frac{\theta\tau}{\sigma} \right) A(\theta,\tau) e^{-j(\theta t + 2\pi f\tau)}\, d\tau\, d\theta \tag{14}$$

Reduced-Interference (RID) Rihaczek Distribution — introduced by Selin Aviyente and Ali Yener Mutlu in 2011

Choi-Williams Kernel — reduces cross-interference terms by acting as a LPF

Solutions to the aforementioned problems cont. x8

$$A(\theta, \tau) = \int x\left(u + \frac{\tau}{2}\right)x^*\left(u - \frac{\tau}{2}\right)e^{j\theta u}\,du \tag{15}$$

Ambiguity Function — reduces cross-interference terms in the TFD by pulling them towards one central location.

Where I stand now

Wanderer above the Sea of Fog by Caspar David Friedrich