# Stereo Electroencephalography

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# Drug-Resistant Epilepsy (DRE)

Epilepsy is a chronic neurological disease characterized by recurrent and unpredictable interruptions of normal brain functions, called **epileptic seizures**

- Epileptic seizures are **transient** phenomena thar are triggered by excessive **synchronous neuronal activity** in the brain
- In the world, patients with epilepsy are about $50$ million
- In Italy, patients with epilepsy are about $500'000$ $(\approx 8.5/1000)$

# Drug-Resistant Epilepsy (DRE)

Epileptic seizures strongly compromise the **Quality of Life (QoL)** of People with Epilepsy (PwE), increasing the probability of developing anxiety and depression

In the most critical cases, a seizure event leads to

- **Status Epilepticus (SE)**, i.e., a medical condition with abnormally prolonged seizures, either convulsive or non-convulsive

- **Sudden Unexpected Death in Epilepsy (SUDEP)**, i.e., death that is not due to known causes but is associated with an epileptic seizure

In most cases, epileptic seizures can be limited by pharmacological agents that block the rapid firing of neurons, known as **Anti-Seizure Medications (ASMs)**

# Drug-Resistant Epilepsy (DRE)

In the case of complex epilepsies, ASMs are not effective, and more than 30% of PwE are associated with **Drug-Resistant Epilepsy (DRE)**

- In DRE patients, the only effective option to ensure seizure freedom is **epilepsy surgery**, which is a surgical procedure that involves the resection of the area of the brain that generates epileptic seizures

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The goal of epilepsy surgery is to eradicate the **Epileptogenic Zone (EZ)**, which is *"the area of brain cortex indispensable for the generation of clinical seizures" (Rosenow and Luders, 2001)*

- The EZ localization is enabled by the joint analysis of electrophysiological and neuro-imaging information, including **Electroencephalography (EEG)** and **Magnetic Resonance Imaging (MRI)**

# Stereo-Electroencephalography (SEEG)

If seizures are triggered by a restricted brain area, as in the case of a tumor, the localization of the EZ is a relatively simple task → **Epileptogenic focus**

Complex epilepsies are associated with seizures that are generated from the interaction between multiple brain structures → **Epileptogenic network**

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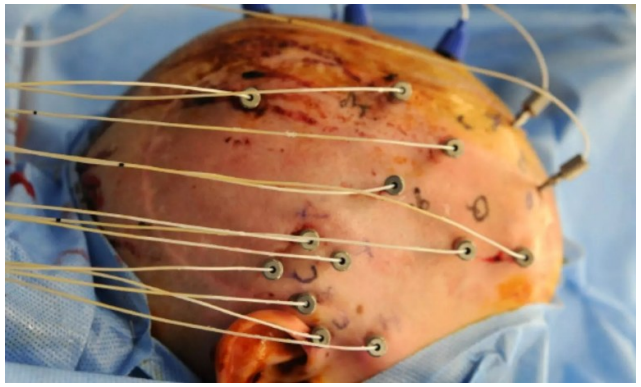
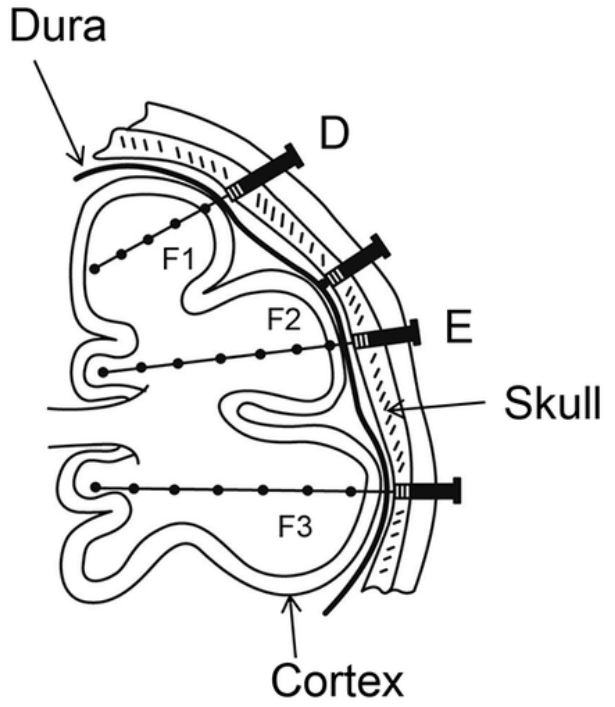
- In the second scenario, the localization of the EZ can be achieved via **Stereo-EEG**, which is a preliminary surgical intervention that enables the recording of electrical activities in deep cortical regions



# Stereo-Electroencephalography (SEEG)

A SEEG implant includes many **needle electrodes** that are inserted through the skull of the patient and explore the cortical sites that are suspected to be part of the EZ

Each SEEG electrode contains $\approx 10 - 20$ equispaced contacts, each recording the electrical activity of a distinct cortical site



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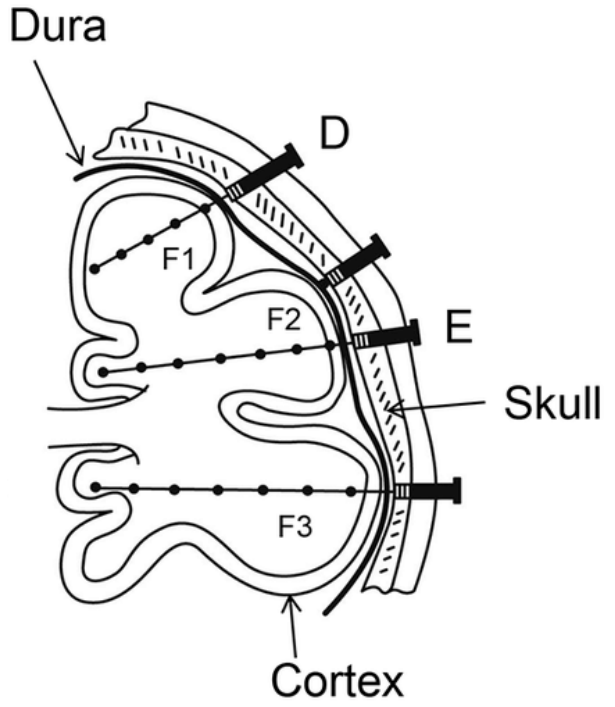
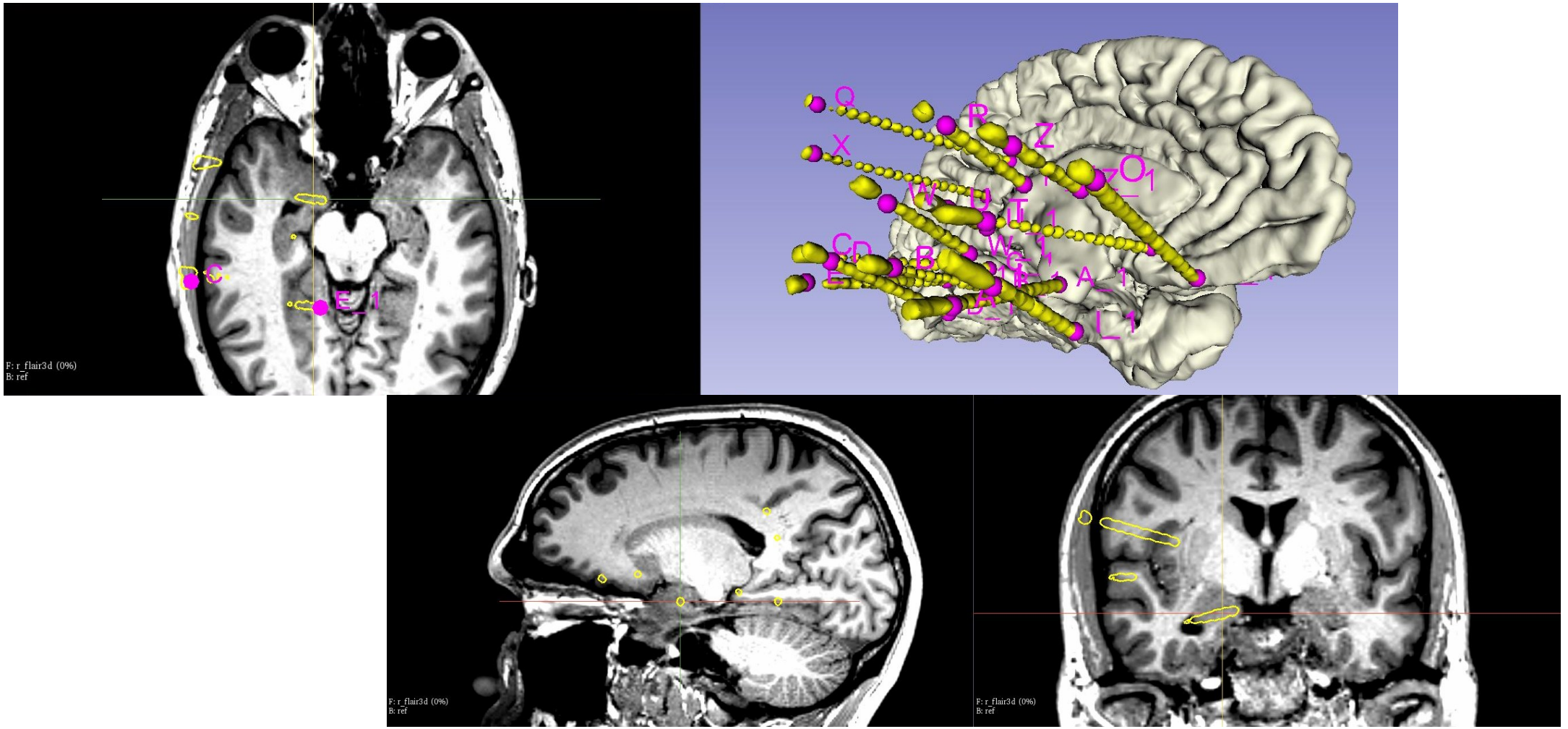
- The outcome is a **multi-dimensional signal**, whose components are named **channels**
- Each **electrode** is associated with a **letter**, and each **contact** with a **number**
- The deepest contact of an electrode is indicated by number $1$, while the others are numbered on a linear scale



# An Example of SEEG Recording



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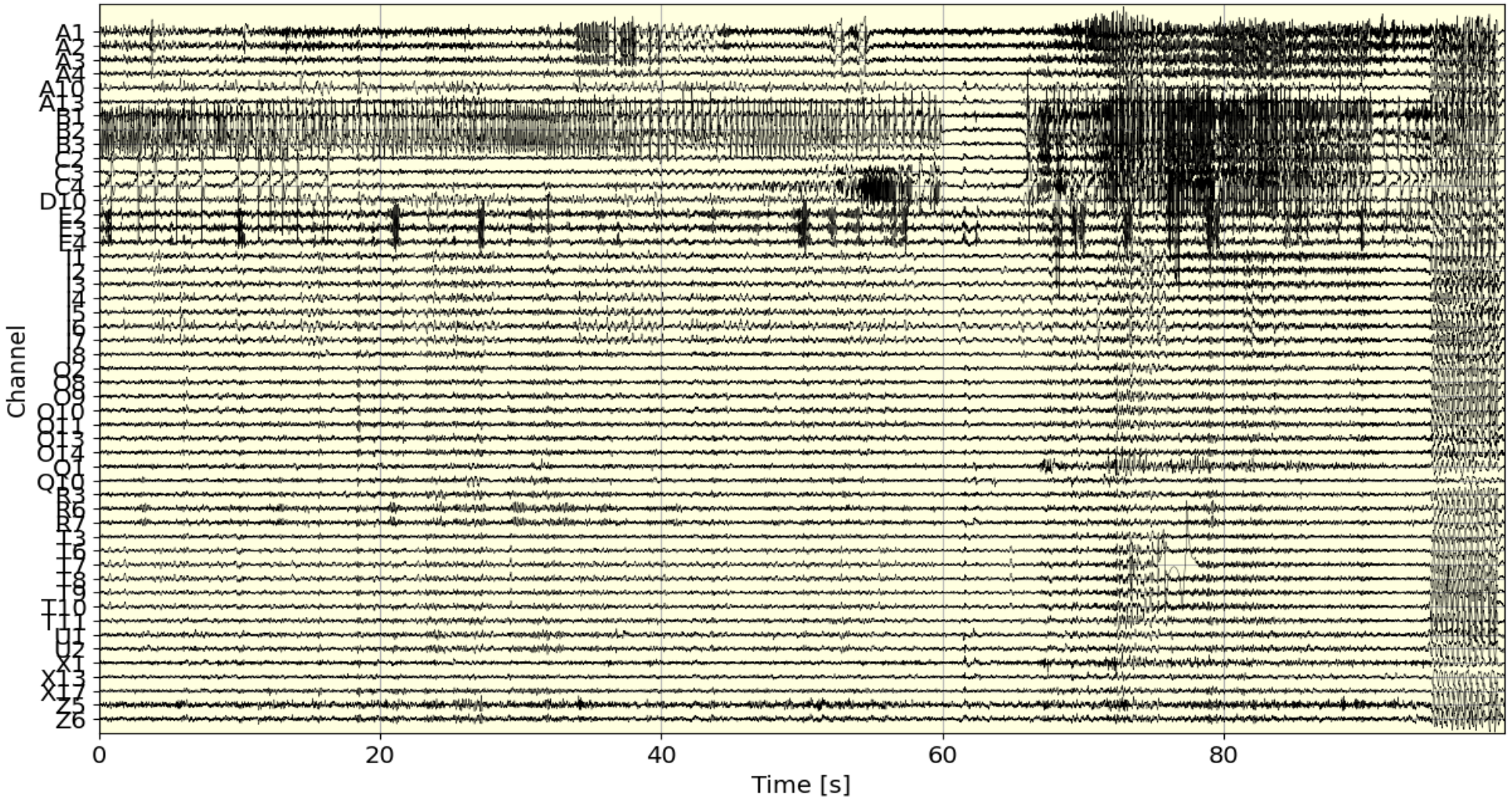

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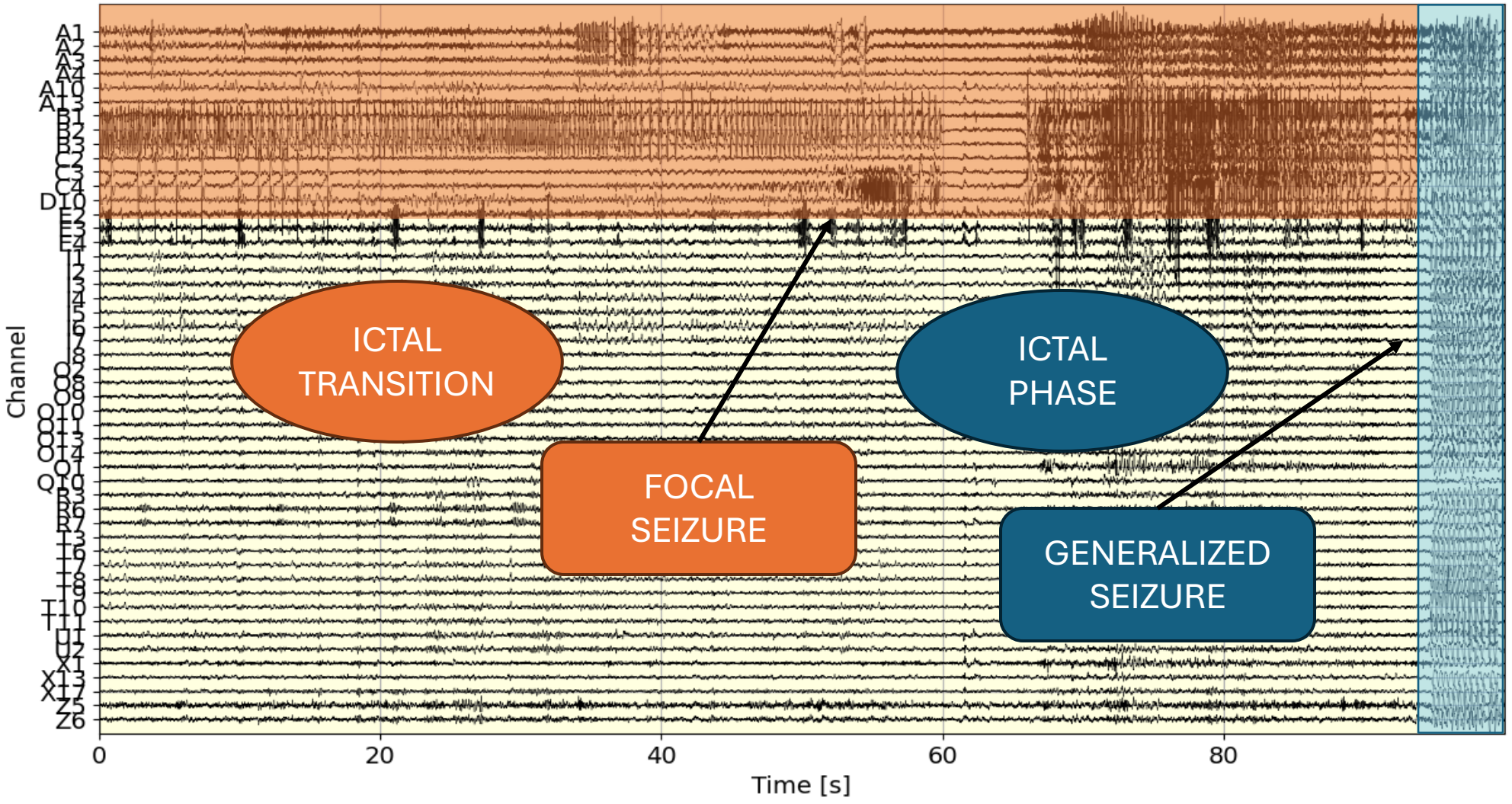

# Low-voltage Fast Oscillations

In SEEG analysis, the main target is to identify the **epileptogenic channels**, which are the channels that explore part of the EZ

- An epileptogenicity biomarker is given by **low-voltage fast oscillations**, which are electrical discharges spanning beta and gamma frequencies

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- An epileptogenicity biomarker is given by **low-voltage fast oscillations**, which are electrical discharges spanning beta and gamma frequencies

- By calculating the energy of a channel $x(\cdot)$ from its short-time Fourier transform $\mathcal{X}(\cdot)$, we can determine the strength of specific oscillations as a function of time

$$E_{[f_a,f_b]}(t) = \int_{f_a}^{f_b} |\mathcal{X}(t,f)|^2 \, df, \qquad [f_a, f_b] \in \{[12,30],[30,100]\}\, Hz$$

# Low-voltage Fast Oscillations

During the ictal transition, the **hyper-synchronization** of the neurons within the EZ results in an increase in the strength of fast oscillations in epileptogenic channels

- We can quantify the epileptogenic level of a channel by computing the **ratio** $ER(\cdot)$ between the energies associated with **fast** and **slow oscillations**

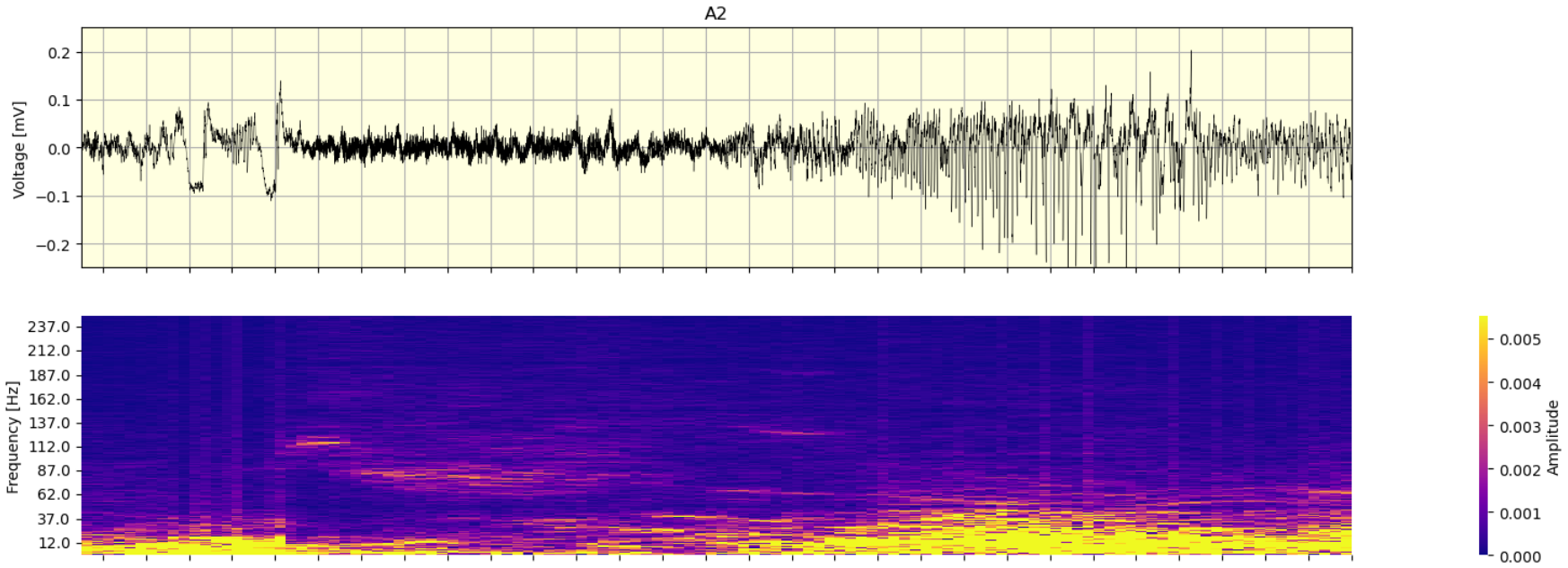
$$E_{\beta+\gamma}(t) = \int_{12}^{70} |\mathcal{X}(t,f)|^2 \, df, \qquad E_{\theta+\alpha}(t) = \int_{4}^{12} |\mathcal{X}(t,f)|^2 \, df$$

$$ER(t) = \frac{E_{\beta+\gamma}(t)}{E_{\theta+\alpha}(t)}$$

# Low-voltage Fast Oscillations

During the ictal transition, the **hyper-synchronization** of the neurons within the EZ results in an increase in the strength of fast oscillations in epileptogenic channels

- The Energy Ratio (ER) adapts the energy of fast oscillations to those of slow oscillations, and, thus, is independent of the specific cortical site analyzed



# Epileptogenicity Index (EI)

Given that the ictal phase starts at time $t_0$ and a channel $x(\cdot)$ starts generating fast oscillations at time $t_x$, we define the **Epileptogenicity Index (EI)** of $x(\cdot)$ as

$$ER_x = \frac{1}{(t_x - t_0)} \int_{t_x}^{t_x+T} ER_x(t)dt$$

- The **delay** $t_x - t_0$ is inversely proportional to the timing of the fast oscillations with respect the seizure onset
- The **tonicity** $\int_{t_x}^{t_x+T} ER_x(t)dt$ is directly proportional to the energy of the fast oscillations during the seizure onset

Bartolomei, F., Chauvel, P., and Wendling, F., «Epileptogenicity of brain structures in human temporal lobe epilepsy: a quantified study from intracerebral EEG. Brain: a journal of neurology,» Vol. 131, No. 7, pp. 1818–1830, 2008.

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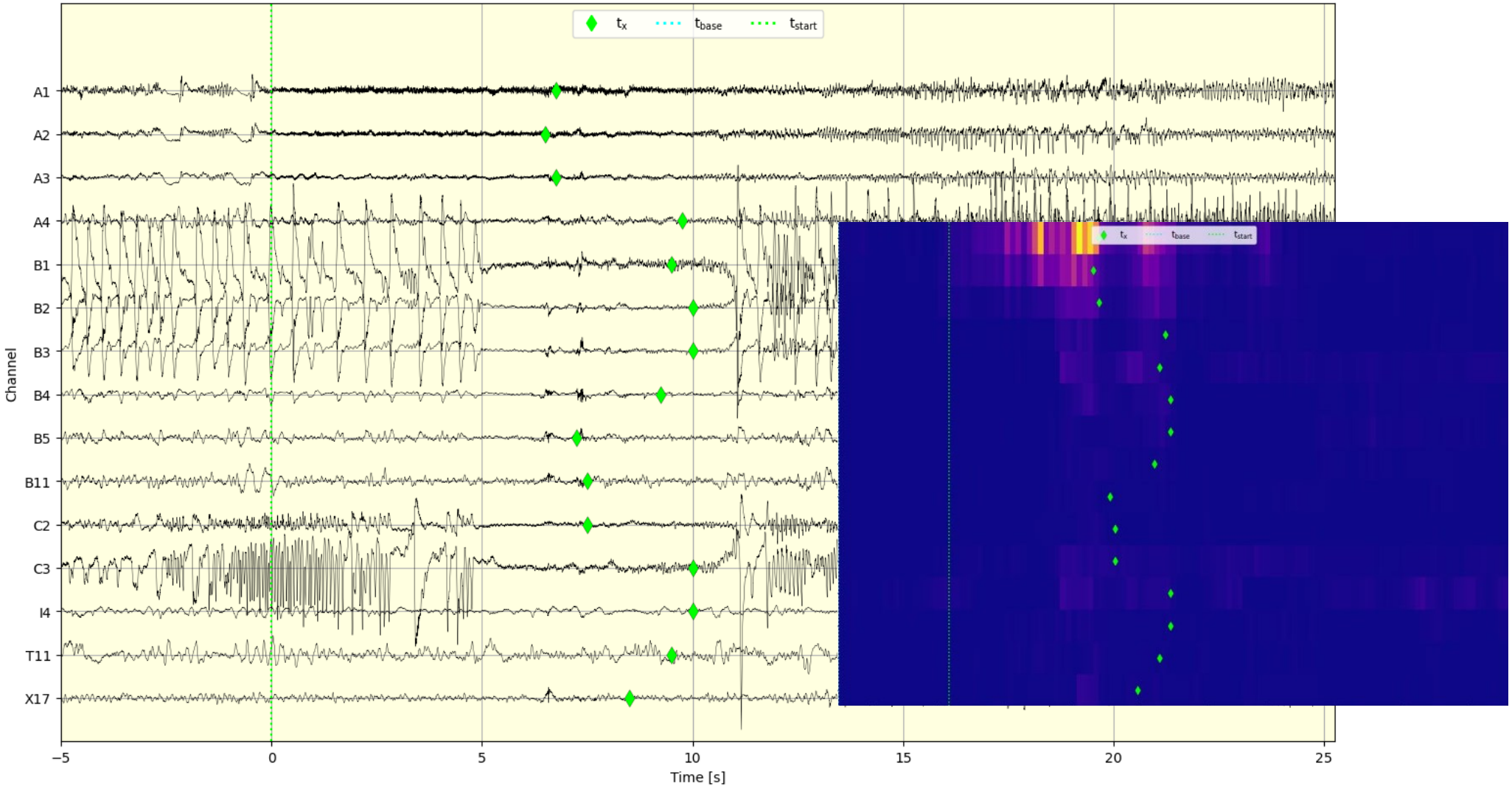

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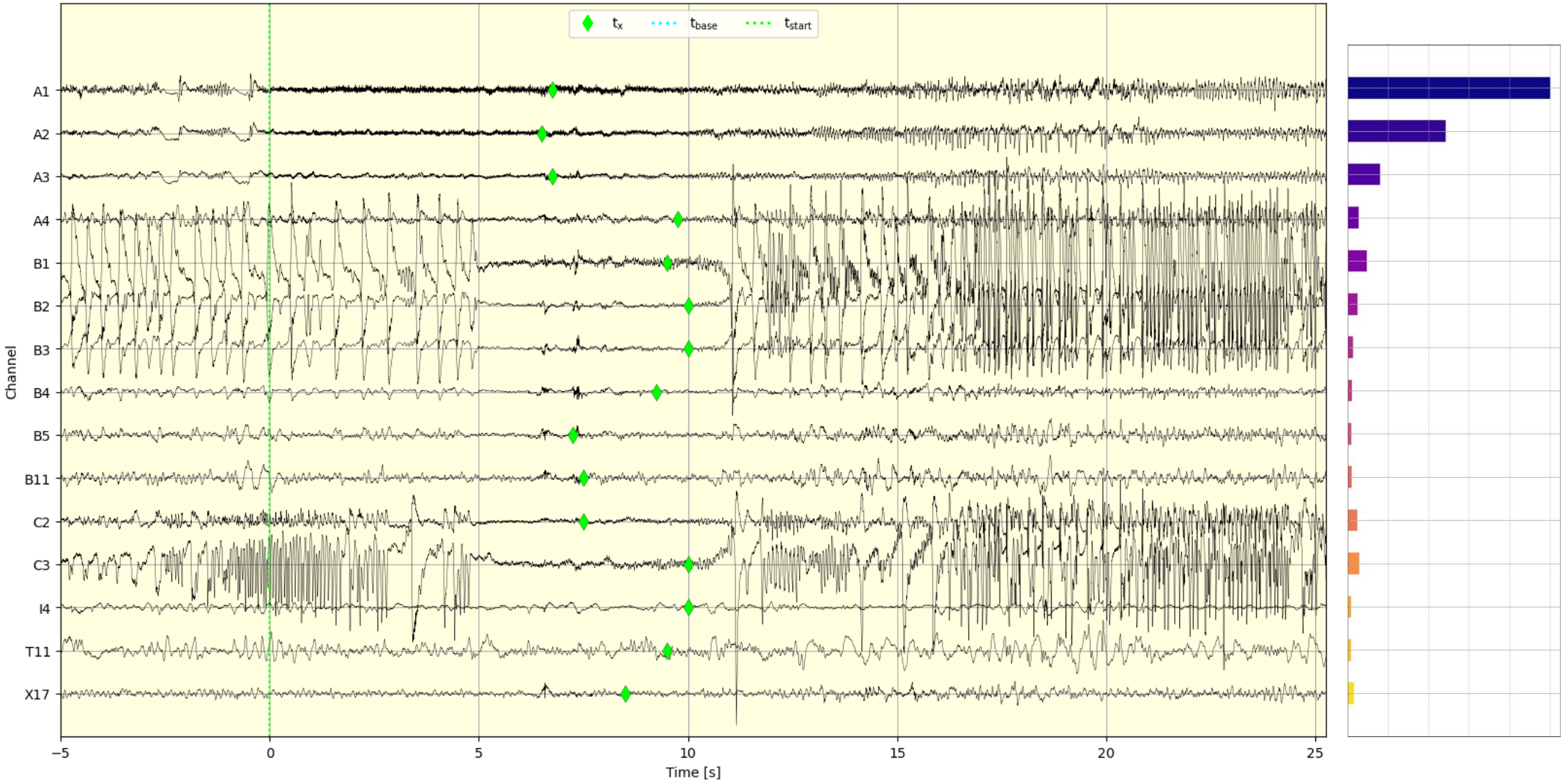

# Graph Representation of SEEG Signals

A SEEG signal can be naturally described as a graph, where each channel represents a **node** and the synchronization between different channels determines the **edges**

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- To estimate the synchrony between different channels, we can consider the instantaneous phase, which is retrieved by the channel's analytical representation

$$x_a(t) = x(t) + j\mathcal{H}\{x\}(t) = x(t) + j\frac{1}{\pi}\int_{-\infty}^{+\infty}\frac{u(\tau)}{t-\tau}d\tau$$

$$x_a(t) = \mathcal{R}e\{x_a(t)\} + j\mathcal{I}m\{x_a(t)\} = A_x(t)e^{j\theta_x(t)}$$

$$\theta_x(t) \in [0, 2\pi], \qquad A_x(t) \in \mathbb{R}$$

# Graph Representation of SEEG Signals

A SEEG signal can be naturally described as a graph, where each channel represents a **node** and the synchronization between different channels determines the **edges**

- Given two channels $x(t)$ and $y(t)$, we can compute their **functional connectivity** via the **mutual information** between $\theta_x(t)$ and $\theta_y(t)$

$$I(\theta_x, \theta_y) = H(\theta_x) + H(\theta_y) - H(\theta_x, \theta_y)$$

$$H(\theta_x, \theta_y) = \sum_{\vartheta_x, \vartheta_y} -Prob(\theta_x = \vartheta_x, \theta_y = \vartheta_y) \log\big(Prob(\theta_x = \vartheta_x, \theta_y = \vartheta_y)\big)$$

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A SEEG signal can be naturally described as a graph, where each channel represents a **node** and the synchronization between different channels determines the **edges**

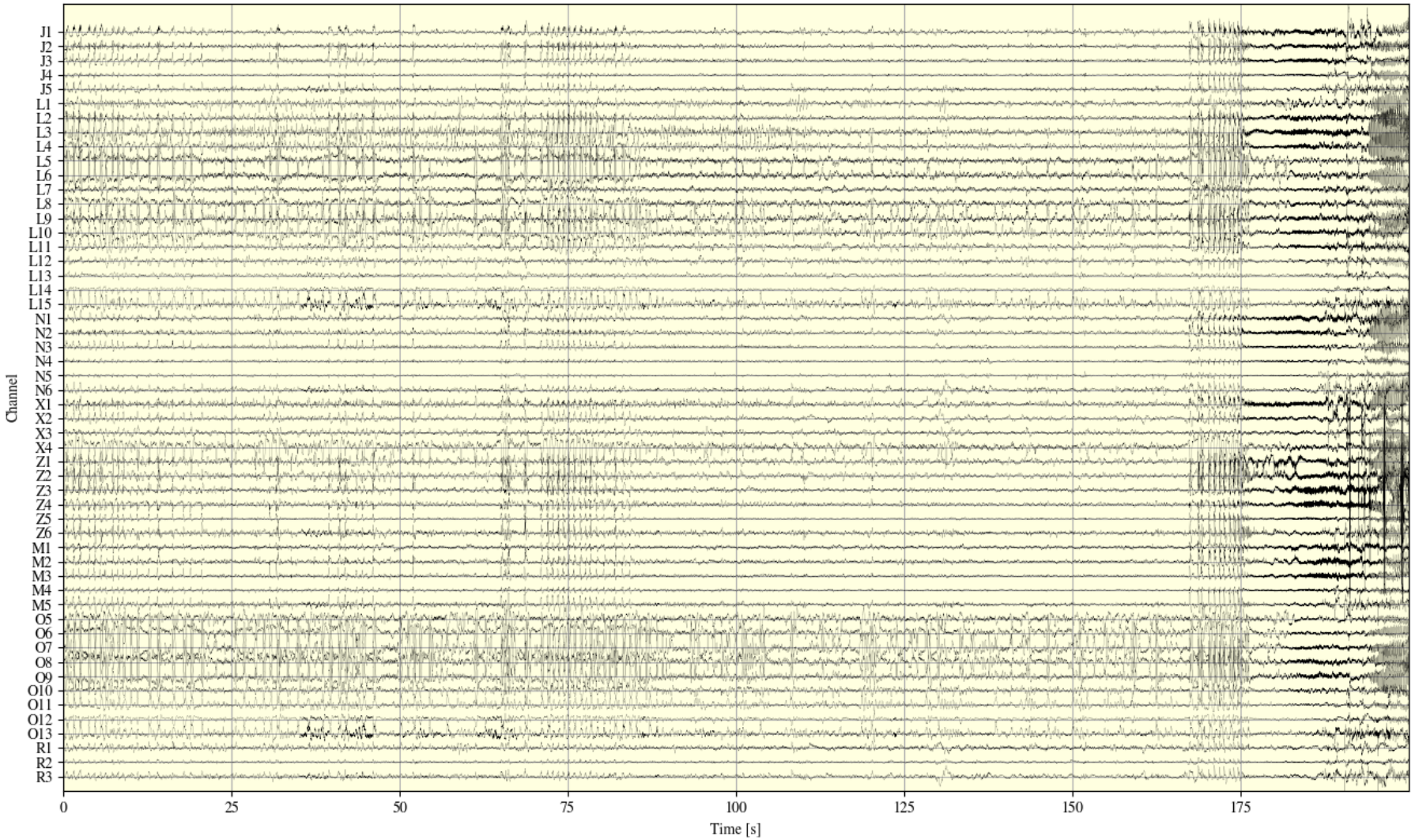
- Given two channels $x(t)$ and $y(t)$, we can compute their **effective connectivity** via the **phase-transfer entropy** between $\theta_x(t)$ and $\theta_y(t)$

$$PTE(\theta_x, \theta_y) = \max_{\tau} H(\theta_y, \theta_{y_\tau}) + H(\theta_x, \theta_y) - H(\theta_y) - H(\theta_x, \theta_y, \theta_{y_\tau})$$

where $\theta_{y_\tau}(t) = \theta_y(t + \tau)$

- In general, we have that $PTE(\theta_x, \theta_y) \neq PTE(\theta_y, \theta_x)$ and the resulting graph is directed

# Epileptic Seizures as Connectivity Outages



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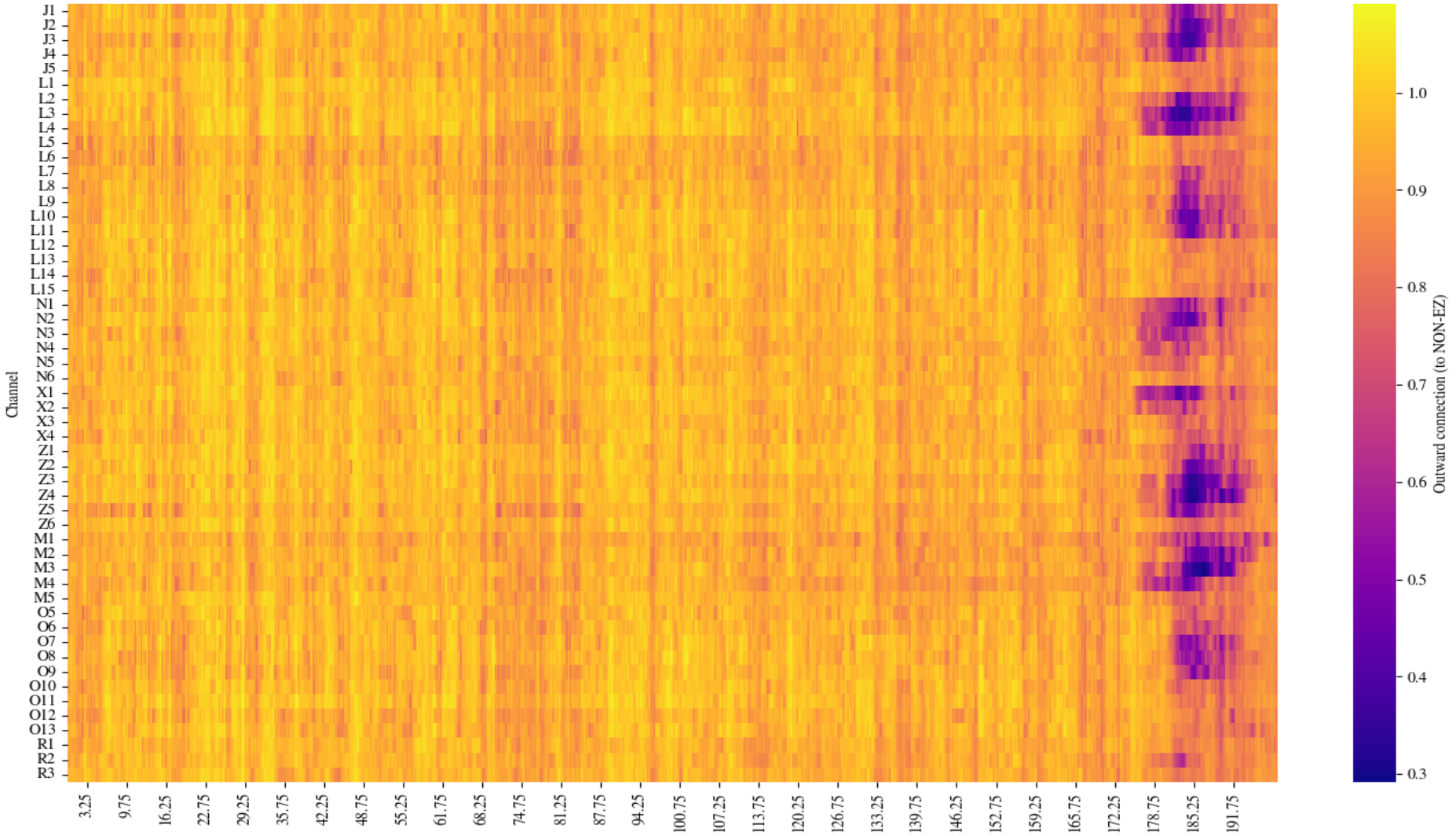
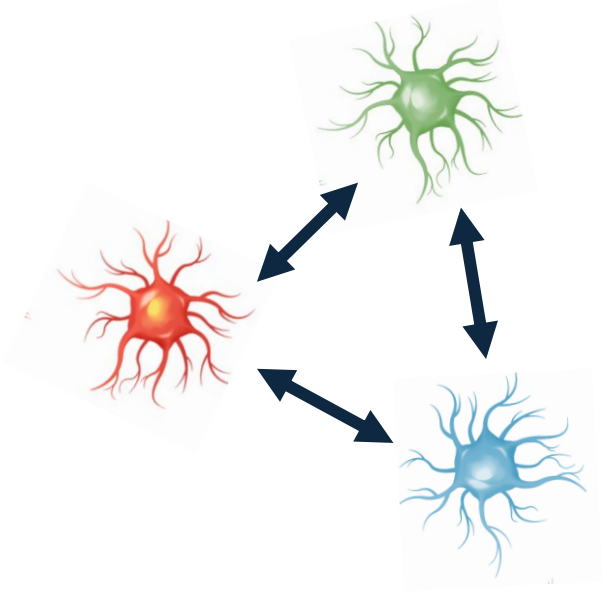


# From Graphs to Hyper-Graphs

The mutual information and the phase transfer entropy allow us to compute **pairwise connectivity measures** that, however, are not enough to represent all the possible synchronization phenomena in SEEG networks

- Let us consider that three neurons (or three groups of neurons) whose phase relationship is described by the **exclusive OR (XOR) function**

| | | |
|---|---|---|
| 0 | 0 | 0 |
| 0 | 1 | 1 |
| 1 | 0 | 1 |
| 1 | 1 | 0 |



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$$H(x) = H(y) = H(z) = 1\ bit$$

$$H(x,y) = H(x,z) = H(y,z) = 2\ bit$$

$$I(x,y) = H(x) + H(y) - H(x,y) = 0\ bit$$

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# From Graphs to Hyper-Graphs

The mutual information and the phase transfer entropy allow us to compute **pairwise connectivity measures** that, however, are not enough to represent all the possible synchronization phenomena in SEEG networks

- To analyze high-order phenomena, we need to introduce the **interaction information**

$$I(x, y, z) = H(x) + H(y) + H(z) - H(x, y) - H(x, z) - H(y, z) + H(x, y, z)$$

- $I(x, y, z) < 0$ → **Negative interaction information** denotes synergistic phenomena
- $I(x, y, z) > 0$ → **Positive interaction information** denotes redundant phenomena

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$$I(x,y) = I(x,z) = I(y,z) = 0\ bit$$

$$I(x,y,z) = -1\ bit$$

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The interaction information $I(x, y, z)$ can be defined as the difference between the **total correlation** $TC(x, y, z)$ and the **dual total correlation** $DTC(x, y, z)$

- The total correlation denotes the amount of information that is **jointly shared** among the target variables

$$TC(x, y, z) = H(x) + H(y) + H(z) - H(x, y, z)$$

- The dual total correlation is the amount of information that **emerges** when the target variables are analyzed together

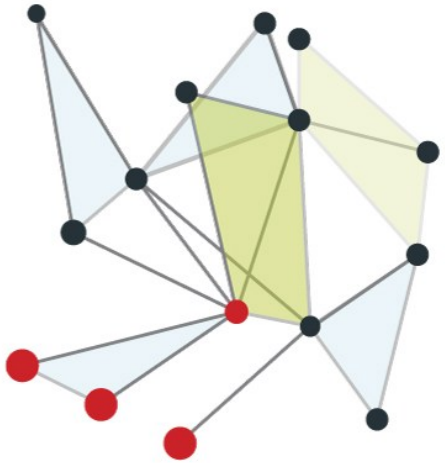
$$DTC(x, y, z) = H(x, y, z) - H(x|y, z) - H(y|x, z) - H(z|x, y)$$

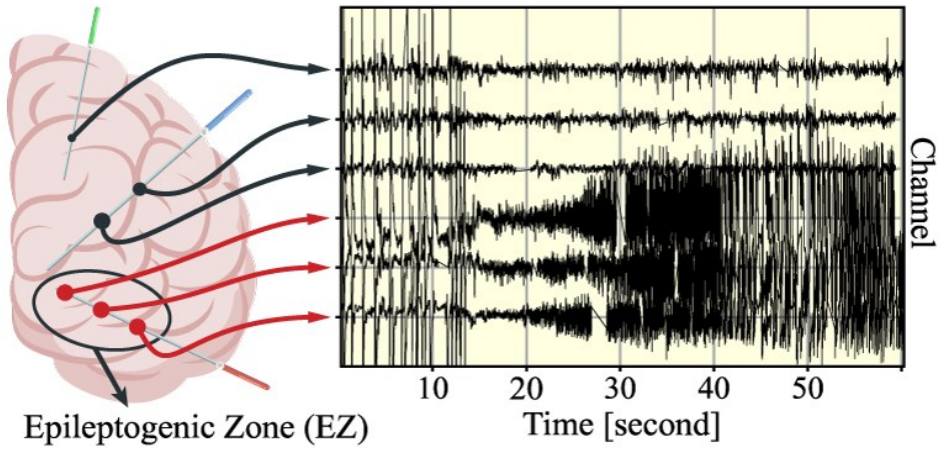
$$= H(x, y) + H(x, z) + H(y, z) - 2H(x, y, z)$$

# From Graphs to Hyper-Graphs

We can thus represent SEEG signals as hypergraphs, where:

- Each node corresponds to a different channel
- The strength of each edge is determined by the **mutual information** between the edge vertices
- The strength of each hyper-edge is given by the **interaction information** (or the total correlation, or the dual total correlation) between the hyper-edge vertices





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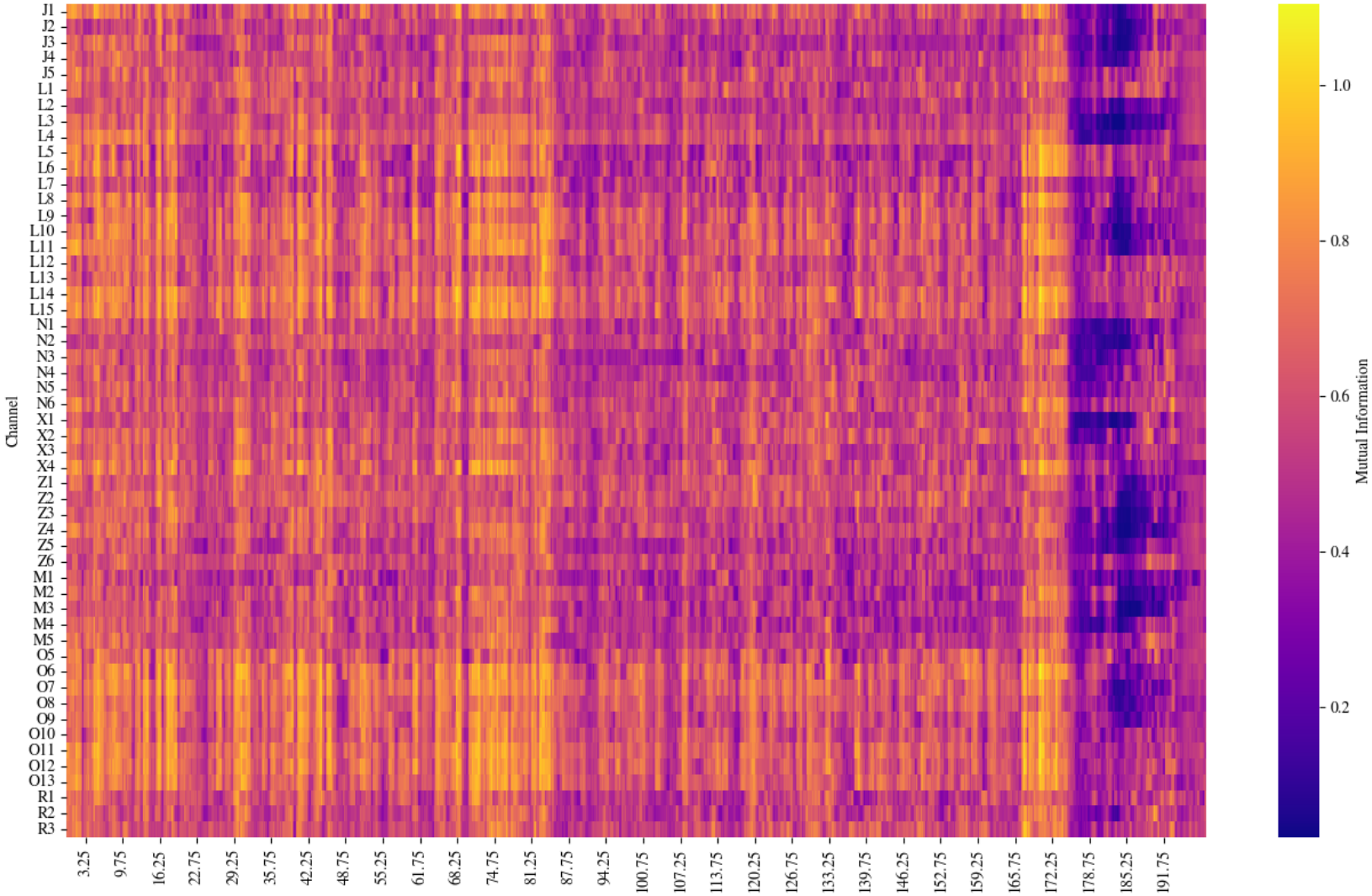

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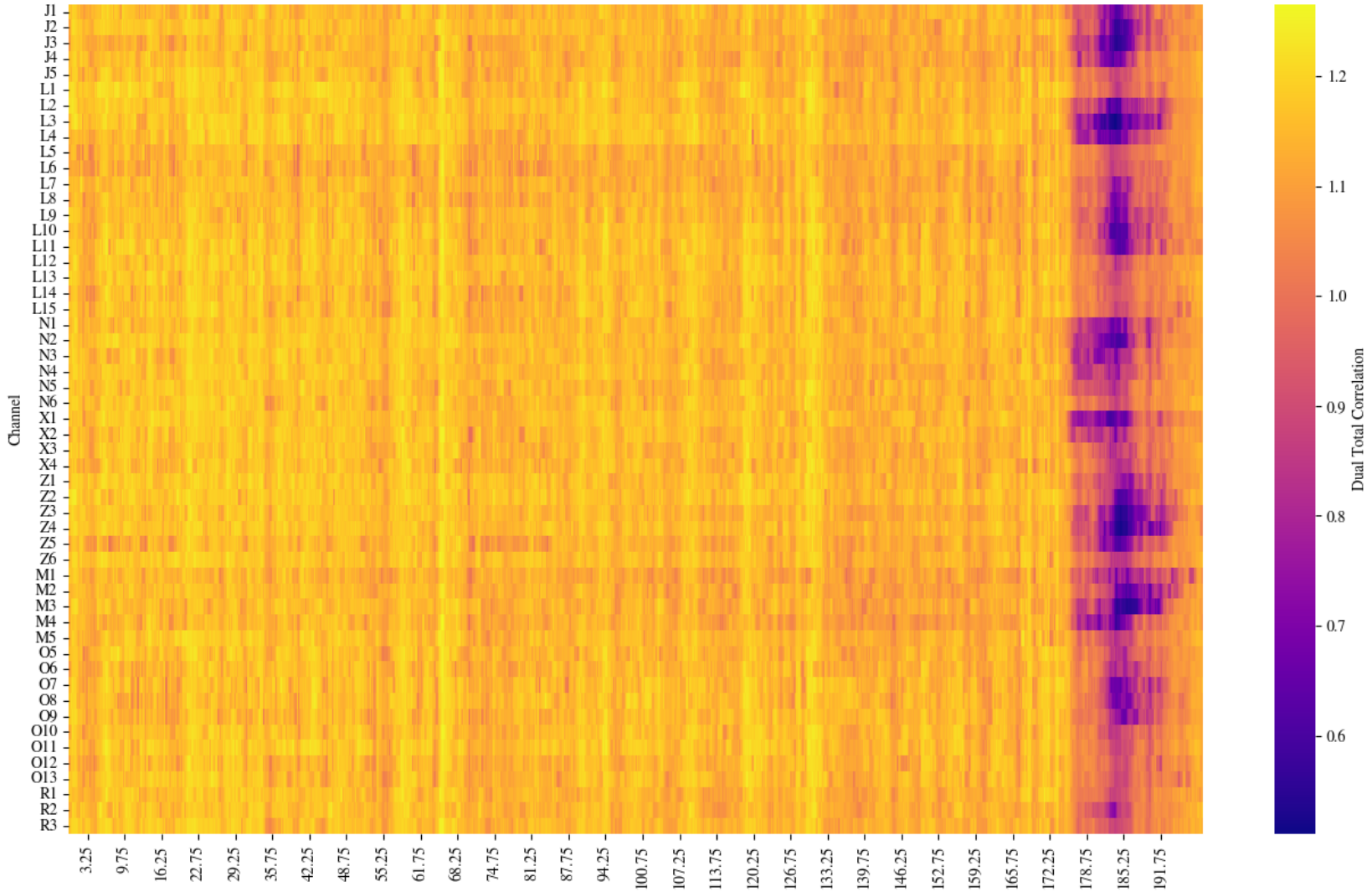

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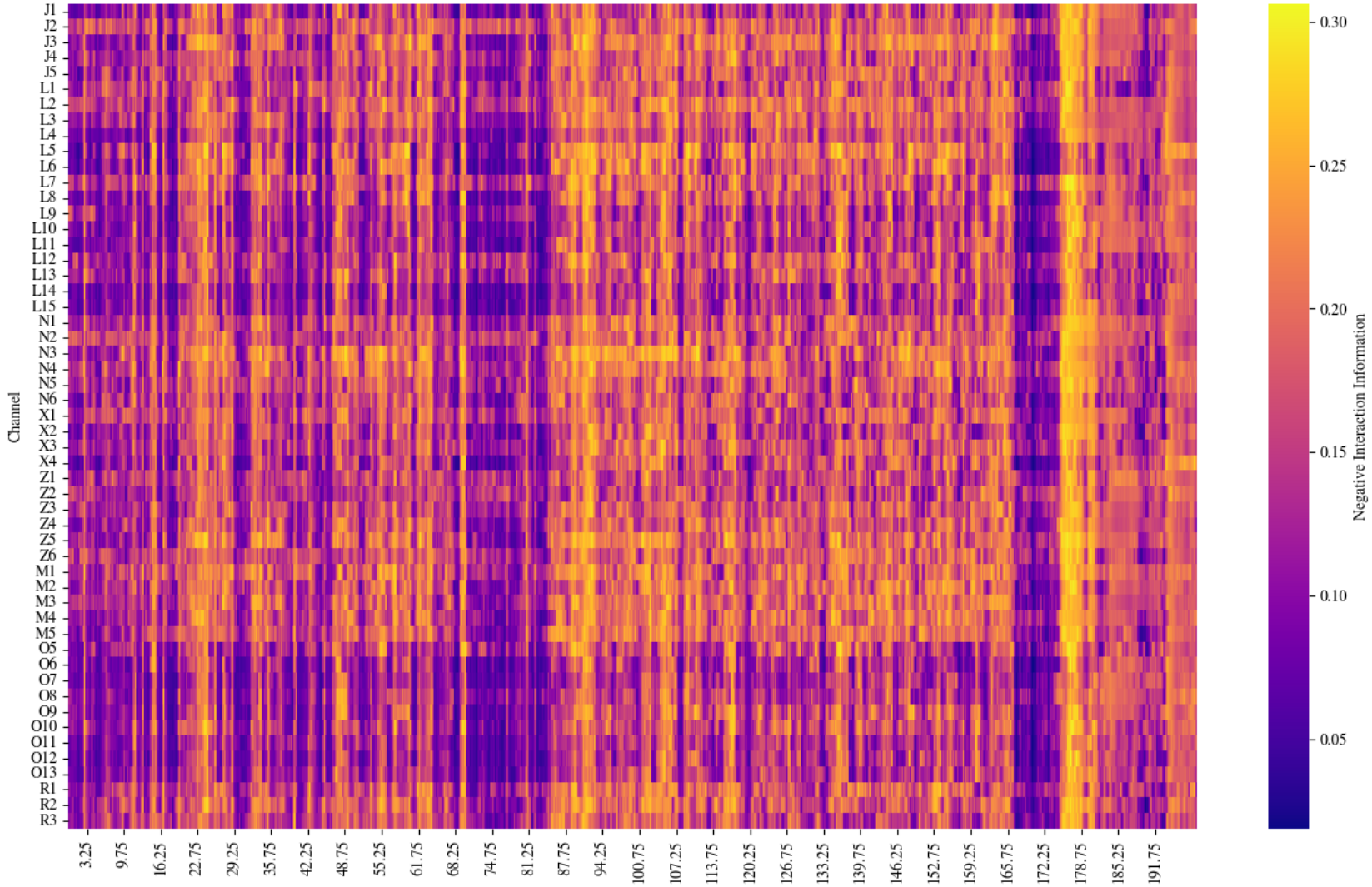

# Questions?


If you are interested in this topic, contact me!

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# References


- Isnard, J., et al., “French guidelines on stereoelectroencephalography (SEEG),” in Neurophysiologie Clinique, Vol. 48, No. 1, pp. 5-13, February 2018.
- Bartolomei, F., et al., “Defining epileptogenic networks: contribution of SEEG and signal analysis,” in Epilepsia, Vol. 58, No. 7, pp. 1131-1147, July 2017.
- Bartolomei, F., et al., “Epileptogenicity of brain structures in human temporal lobe epilepsy: a quantified study from intracerebral EEG,” in Brain, Vol. 131, No. 7, pp. 1818-1830, July 2008.
- Santoro, A., et al., “Higher-order organization of multivariate time series,” in Nature Physics, Vol. 19, No. 2, pp. 221-229, February 2023.