Developing Mathematical and Physical Tools for Multiscale Dynamical Systems

Applications to Neurophysiological Data

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Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET)

Achucarro Basque Center for Neuroscience

Breaf CV

EDUCATION

- **Ph.D. in Physics** | FaMAF - UNC (2015)
- **Lic. in Physics** | FaMAF - UNC (2011)

RESEARCH POSITIONS

- **2016 – 2018:** Postdoctoral Fellow, SickKids Hospital (Canada)
- **2018 – 2020:** Adjunct Professor, Universidad Autónoma de Entre Ríos
- **2019 – Present: Independent Researcher**, CONICET (Argentina)
- *Founded the **Neuroimage Group** at IMAL*
- **2023 – Present:** Research Fellow, Achucarro (Spain)

FaMAF

Sick Kids Hospital

IMAL

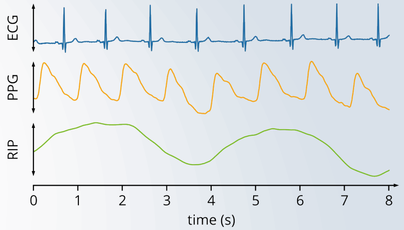
Achucarro

Neuroimage Group

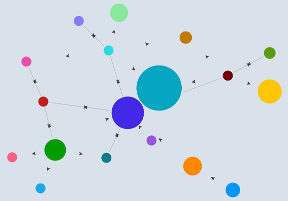
Overview

- **Introduction**

- **Time Series Analysis**
  Extracting insights from sequential data.



- **Complex Networks**
  Mapping the interactions and structure of the system.



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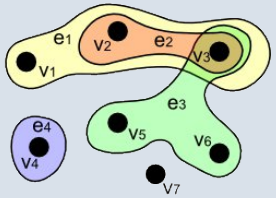
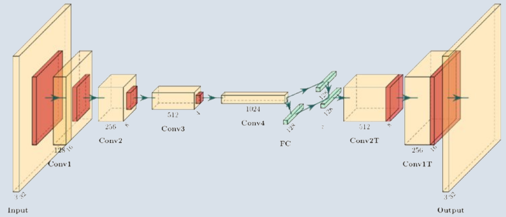
  Moving beyond pairwise connections to understand complex group dynamics.



- **Explainable AI (XAI)**
  Making the predictions of AI models transparent and interpretable.



- **Future Directions**
  Exploring new ideas and applications.

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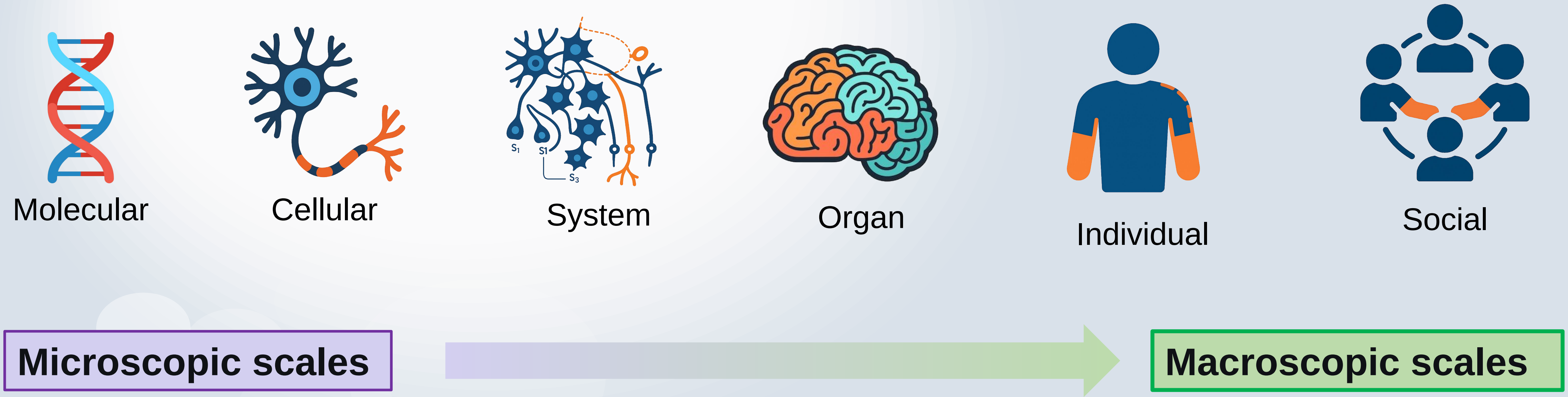
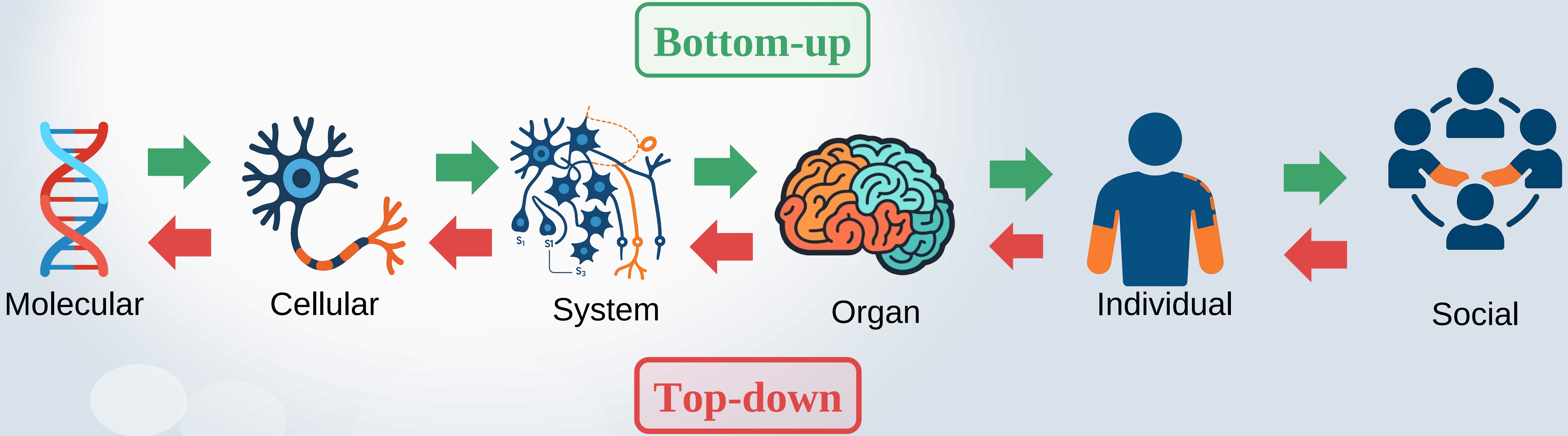
Multiples Level of Organization



Multiples Level of Organization

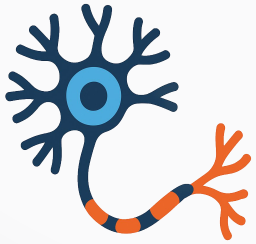


Interactions at one level can **drive** changes at other levels

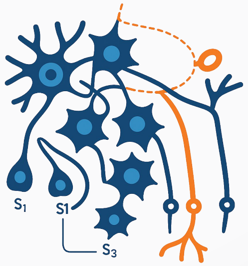
Multiples Level of Organization

Each scale of a complex system has its own unique **properties** requiring different and specific **measurement techniques**

Molecular



Cellular

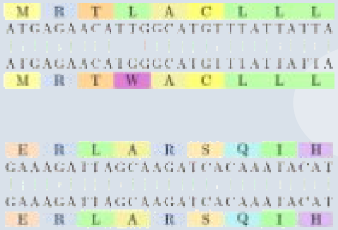


System

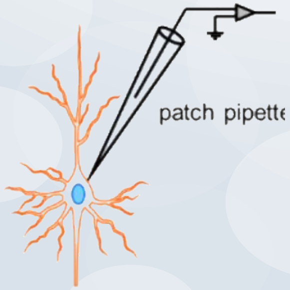
Organ

Individual

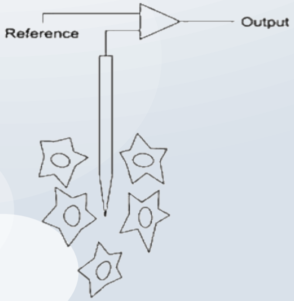
Social



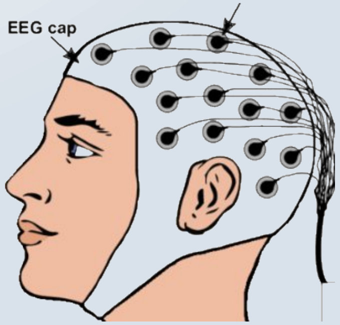
DNA sequencing



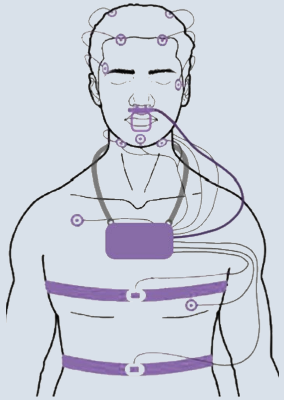
Ion Currents



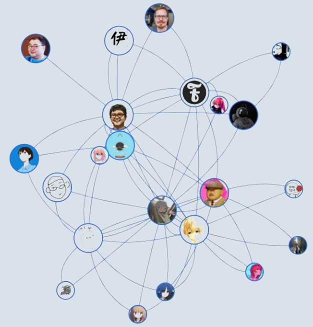
LFP



EEG



Polisomnography



Networks

Scientific Goal

Because the signals obtained from these different levels are **highly complex**, it is necessary to develop **innovative specific tools** to extract the maximum amount of **information** from the dynamical systems we study.

This is precisely where the fields of **Physics and Mathematics** become essential, providing the powerful **theoretical and computational framework** needed to **model, analyze, and understand** this complexity**.**

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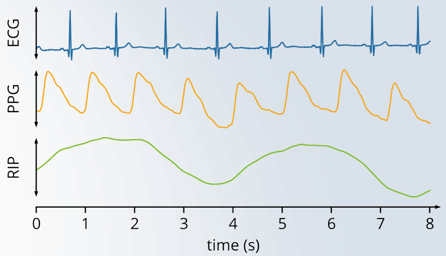

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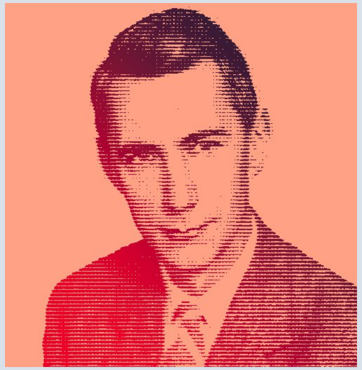
Shannon Entropy

Entropy quantifies the degree of **uncertainty or unpredictability** in a system.

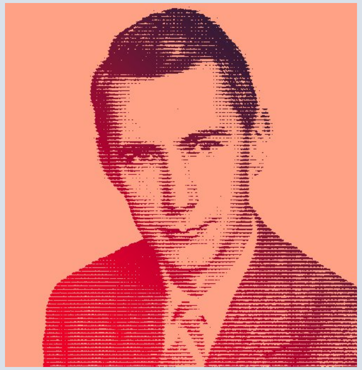


C.E. Shannon - *The Bell system technical journal, 1948*

Shannon Entropy

Entropy quantifies the degree of **uncertainty or unpredictability** in a system.

Two state system = Coin (“head” or “Tail”)



Normal Coin

50 % head
50 % tail
High Uncertainty

Maximun H

Magic Coin

100 % head
0 % tail
Non Uncertainty

H=0

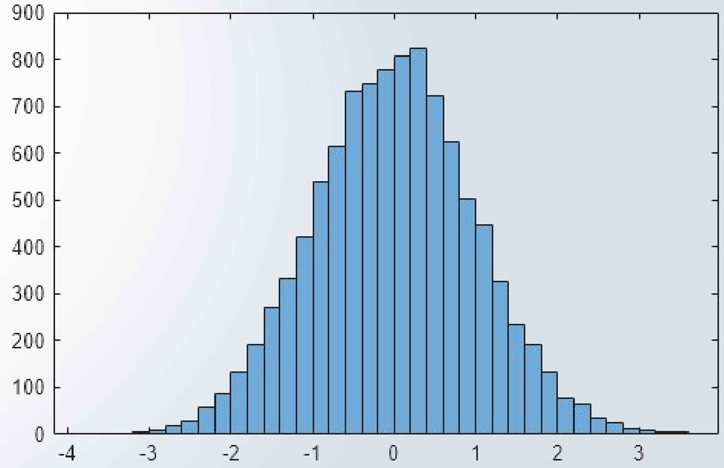
C.E. Shannon - *The Bell system technical journal, 1948*

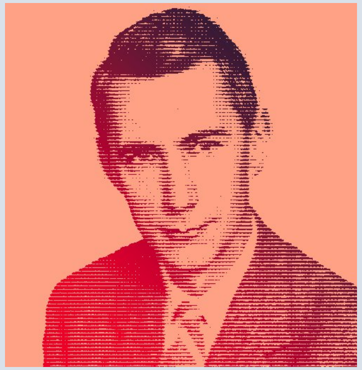
Shannon Entropy

Entropy quantifies the degree of **uncertainty or unpredictability** in a system.

System with probability distribution **P**

$$P = \{P_1, P_2 ..., P_n\}$$





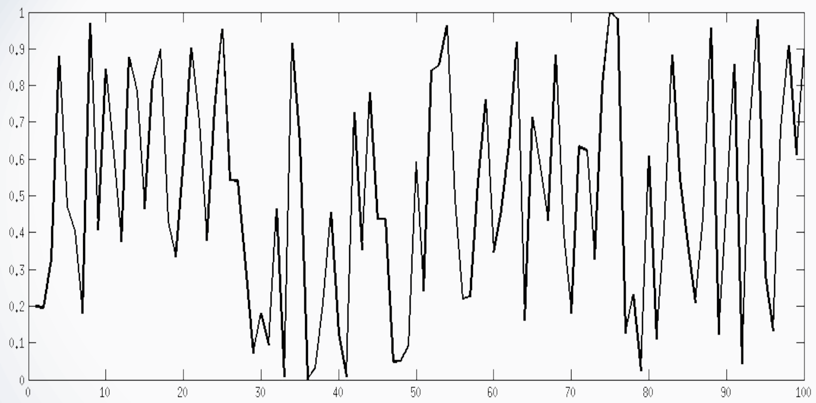
Shannon entropy

$$H[P] = -\sum_i P_i log(P_i)$$

C.E. Shannon - *The Bell system technical journal, 1948*

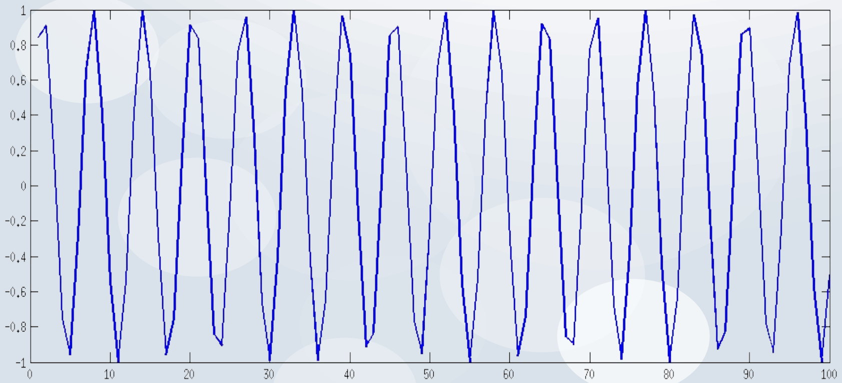
How we see this concept in signals

Highly **Fluctuating** signals. (White nosie or Brain signal in Awake state)



→ **High** uncertainty about its future behavior → High H

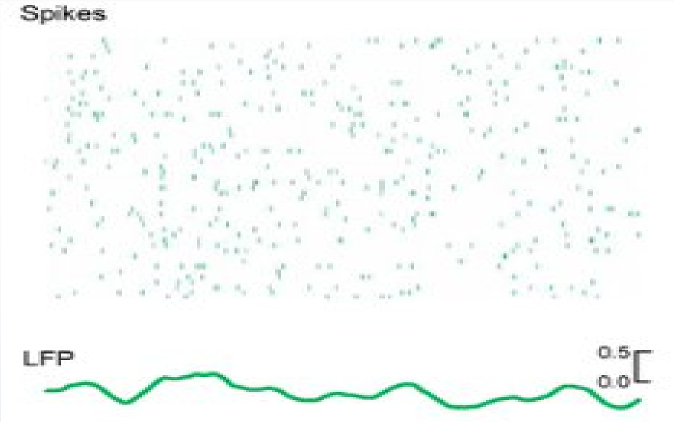
Highly **Periodic** signals. (Sine or Brain signals in Sleep state)



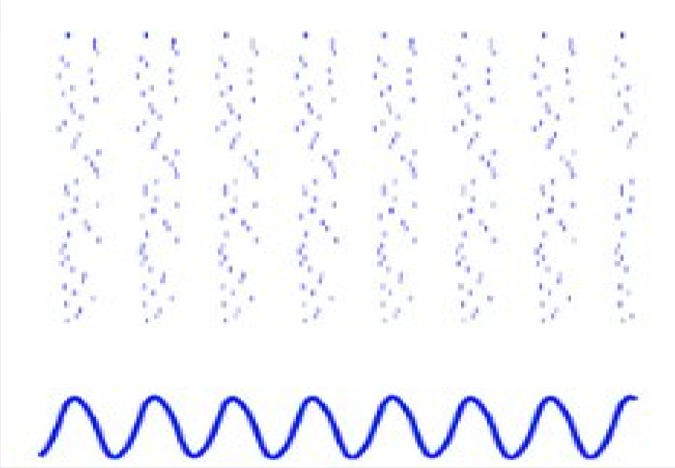
→ **Low** uncertainty about its future behavior → Low H

How we see this concept in signals

In signals like LFP, which we can consider a **mesoscopic system**. The entropy of the LFP signal gives us a information about the behavior of the **underlying neuronal firing groups (microscopic system).**



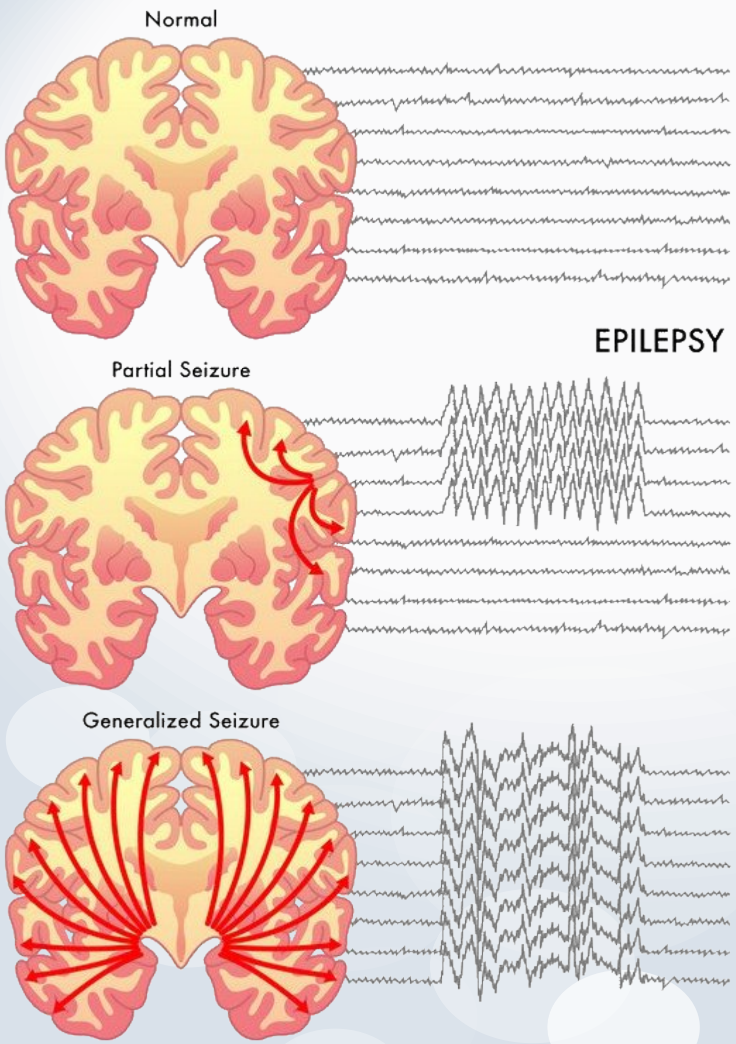
→ Neural Desynchronization → High H

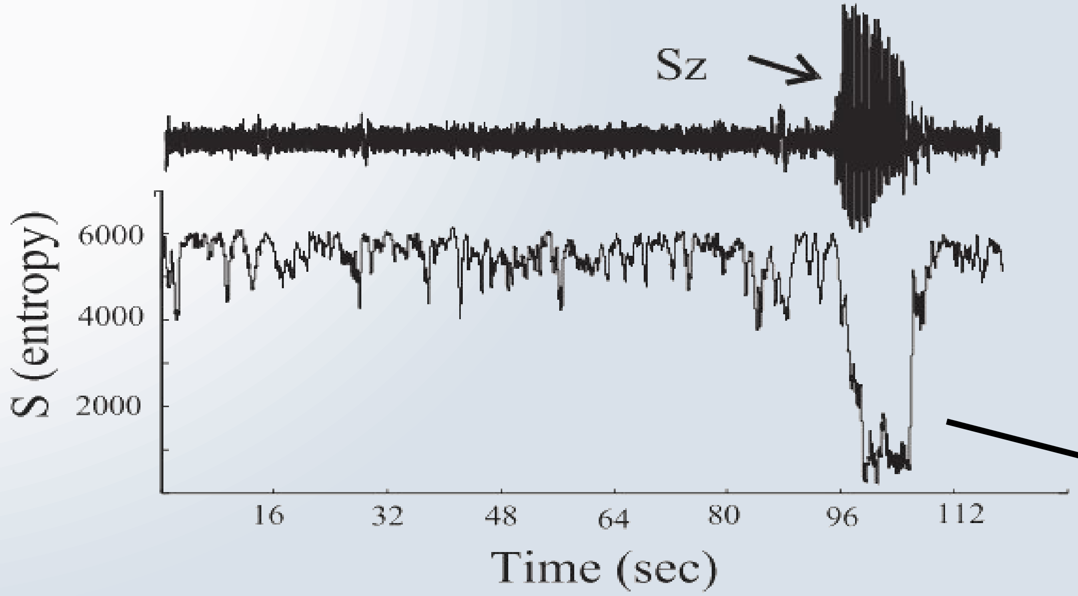


→ Neural Synchronization → Low H

Entropy can changes...

During a Seizure



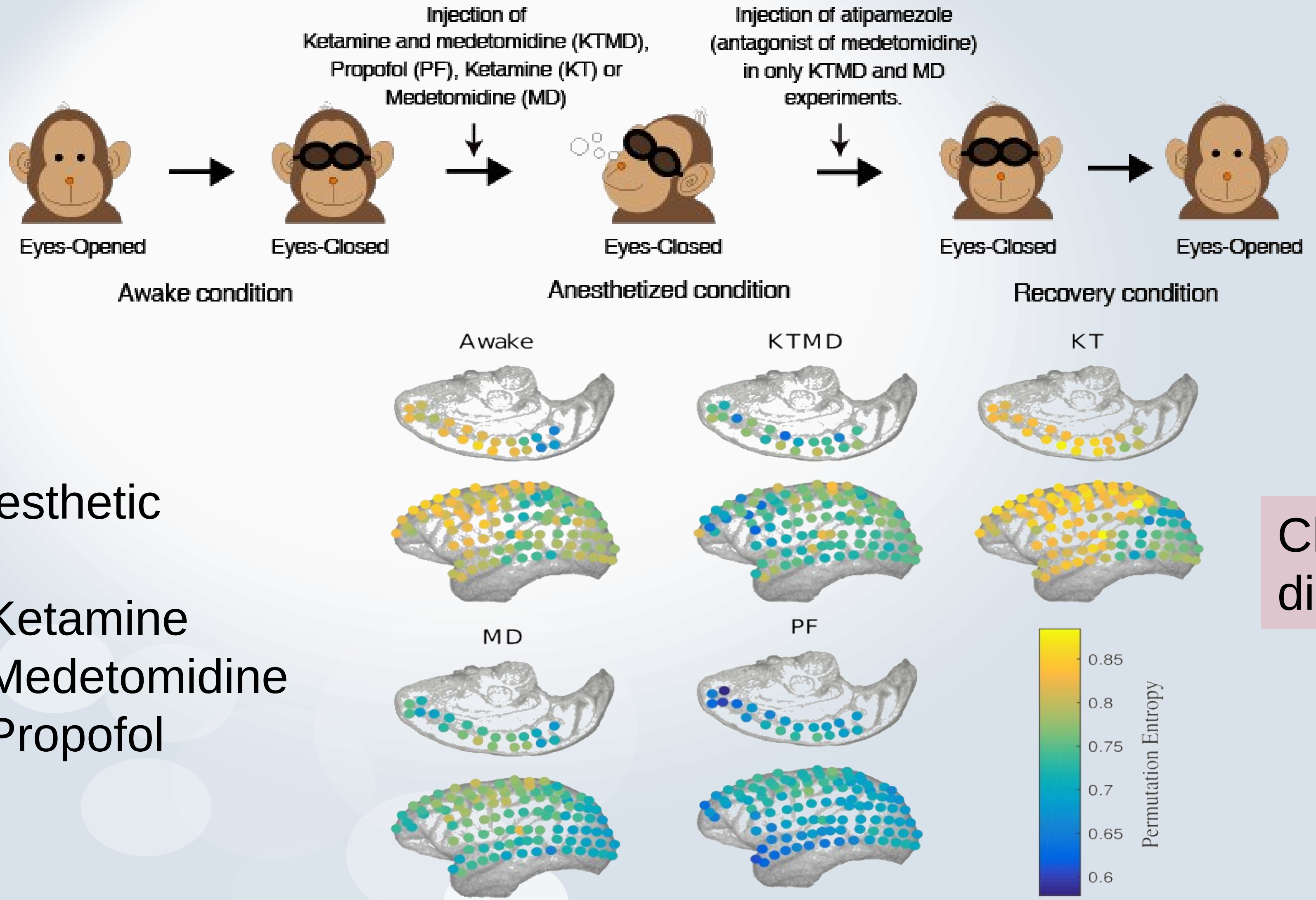


Entropy Drop

Mateos D.M et al. *PRE, 2016*

Entropy can changes...

Under different Anesthetics



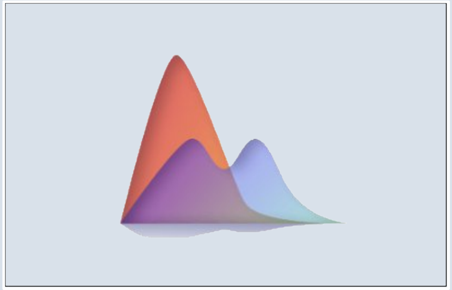
Anesthetic

- Ketamine
- Medetomidine
- Propofol

Changes in the Entropy distribution among the brain

Fuentes N,..., Mateos D. *Neuroinformatic 2023*

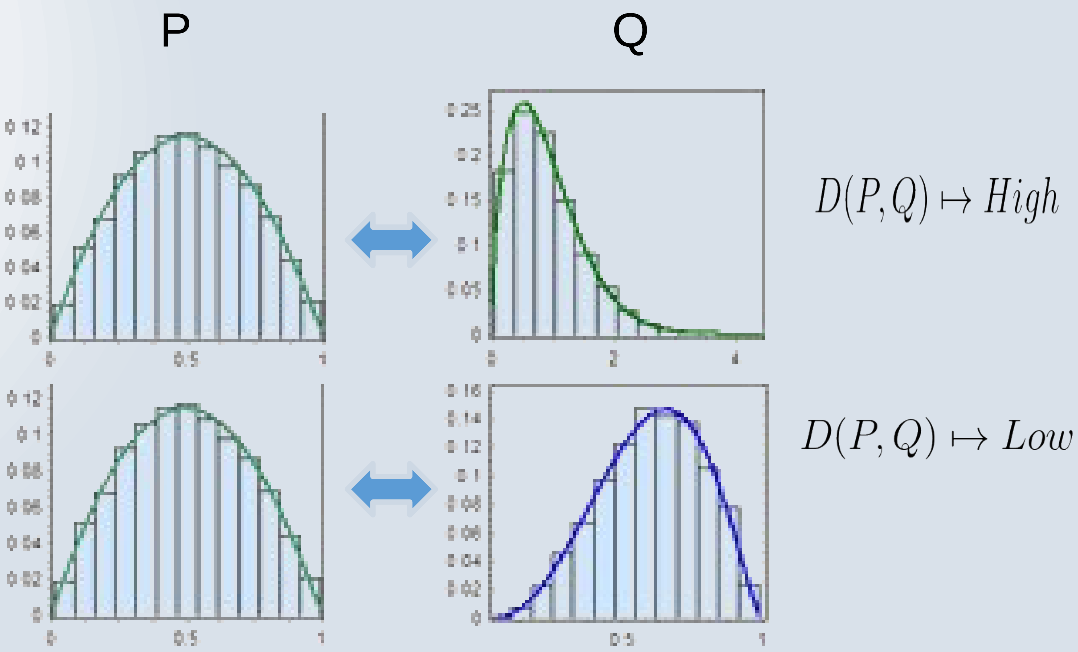
Divergences



Divergence are mathematical measures used to quantify the ***difference*** *or* ***distance*** *between* ***two probability distributions P, Q.***

Kullback-Leible Divergence (KLD)

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



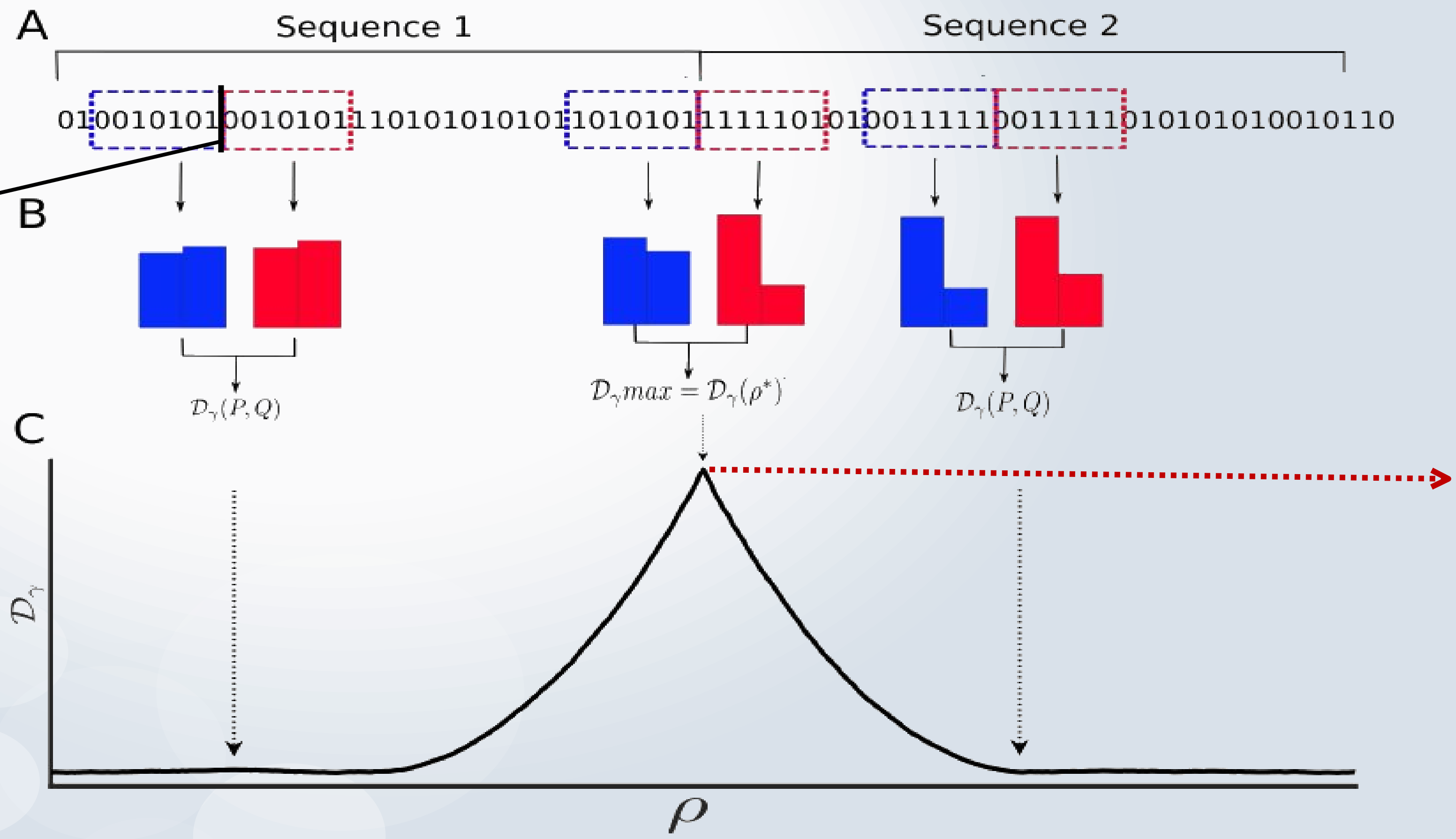
Symmetrising KLD we obtain...

Jensen-Shannon Divergence (JSD)

$$D_{JS}(P,Q) = H\left[\frac{(P+Q)}{2}\right] - \frac{1}{2}H[P] - \frac{1}{2}H[Q]$$

Sliding windows method

Detect **changes in the dynamics** of a single signal over time.



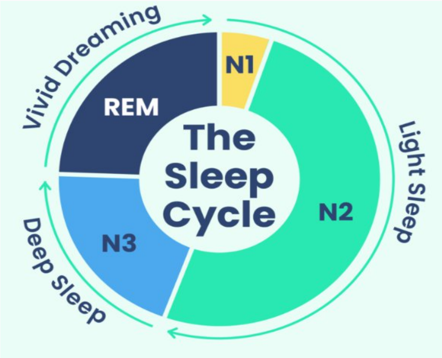
Pointer

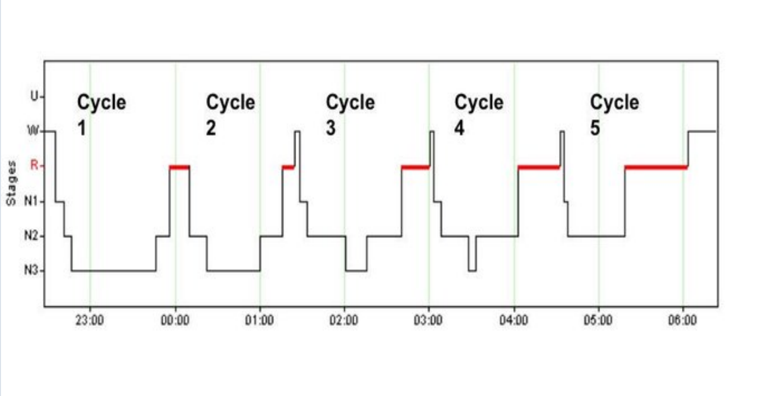
Changes in the dynamics

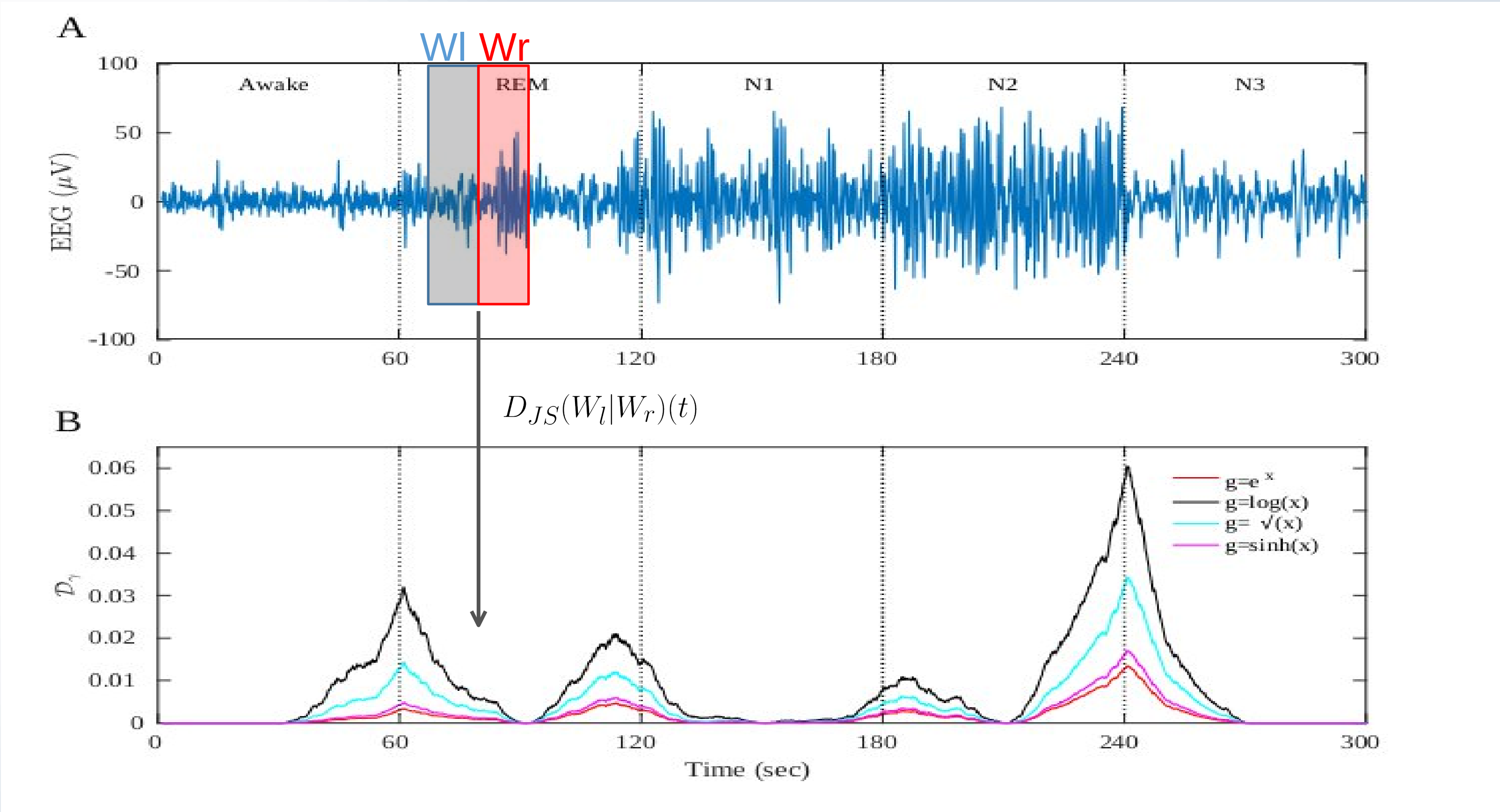
Riveaud E, **Mateos D**. *et al. Chaos 2018*

Sliding windows method

Detecting Changes in EEG Dynamics During Sleep







*Riveaud E, **Mateos D.** et al. Chaos 2018*

Now, Let see this example...

S1= 0 1 0 1 0 1 0 1 0 1 0 1 0 1 0 1 0 1

S2= 0 0 0 0 0 0 0 0 0 1 1 1 1 1 1 1 1 1

$$P_0 = 0.5 \quad P_1 = 0.5 \longrightarrow H_{S1} = H_{S2}$$

Entropy cannot distinguish between the two sequences, because it don't care the **order of the values** in the serie.

Lempel - Ziv Complexity

It is an algorithmic complexity that quantifies **non-redundant information** in a sequence.

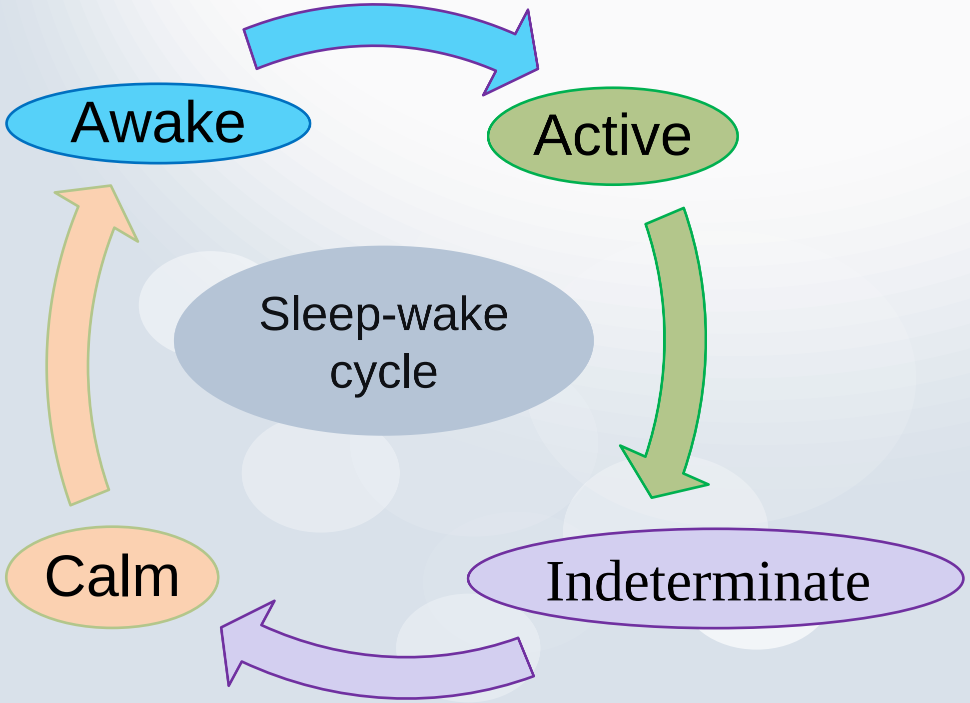
The idea is to reproduce a signal using the **least amount of information**.
It is based on the idea of **Production** and **Reproduction** of the sequence.

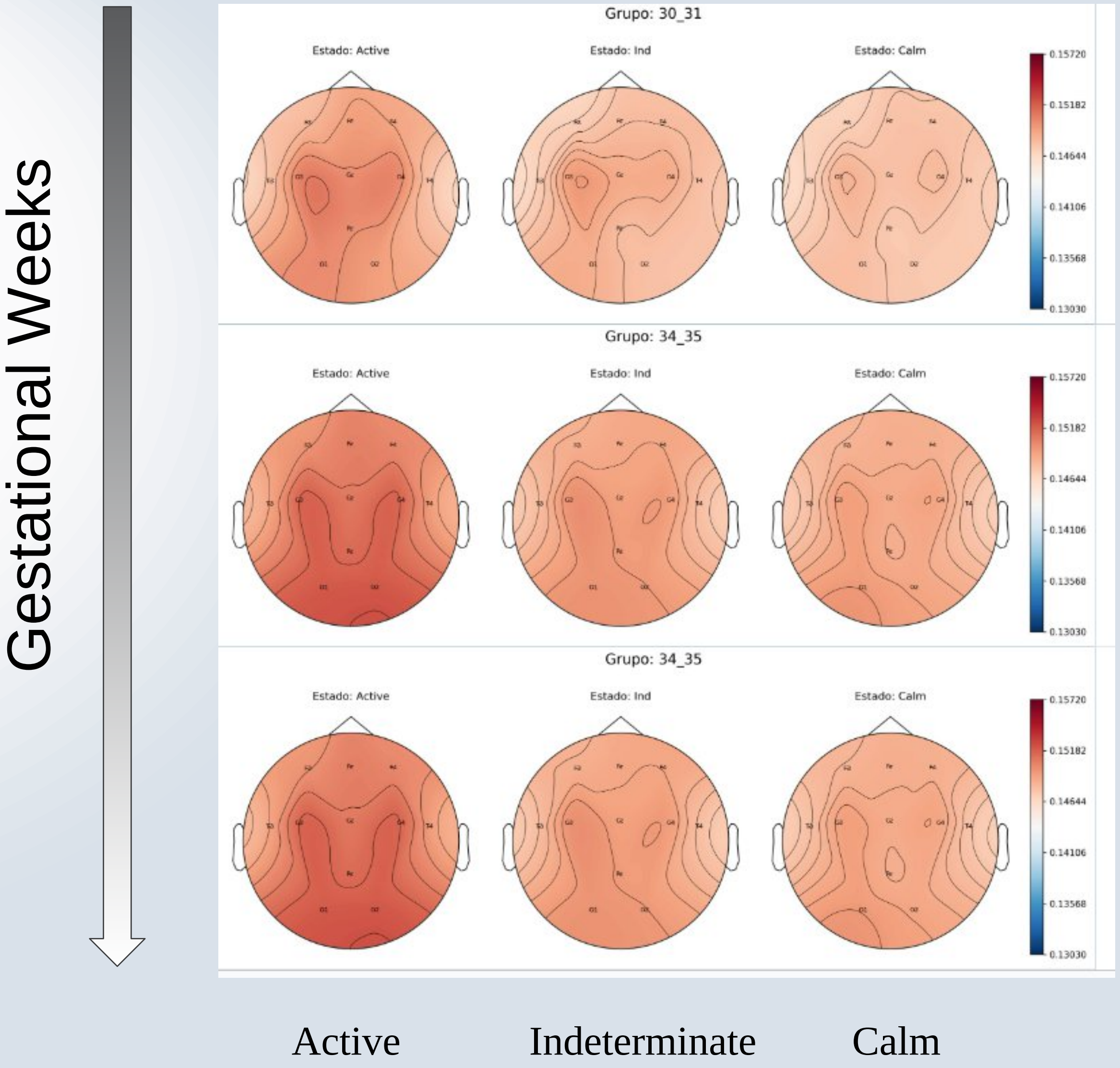
0 1 0 0 1 1 0 1 0 1	
0	Production of a new word
0 | 1	Pro
0 | 1 | 0	Reproproduction of a word
0 | 1 | 00	Pro
0 | 1 | 00 | 1	Repro
0 | 1 | 00 | 11	Pro
0 | 1 | 00 | 11 | 0	Repro
0 | 1 | 00 | 11 | 01	Prod

$C_{LZ}=5$

Lempel and Ziv. *Trans in Inf Theory, 1978*

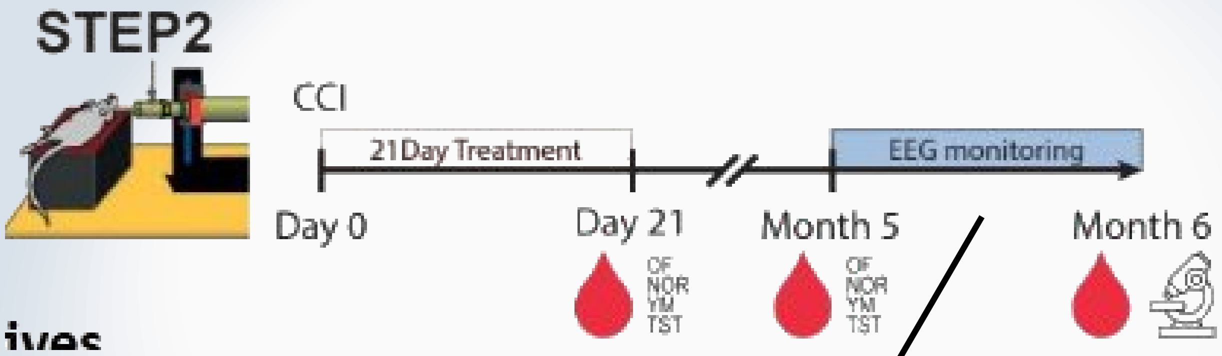
Study of neuronal dynamics in the sleep-wake cycle in **premature infants.**



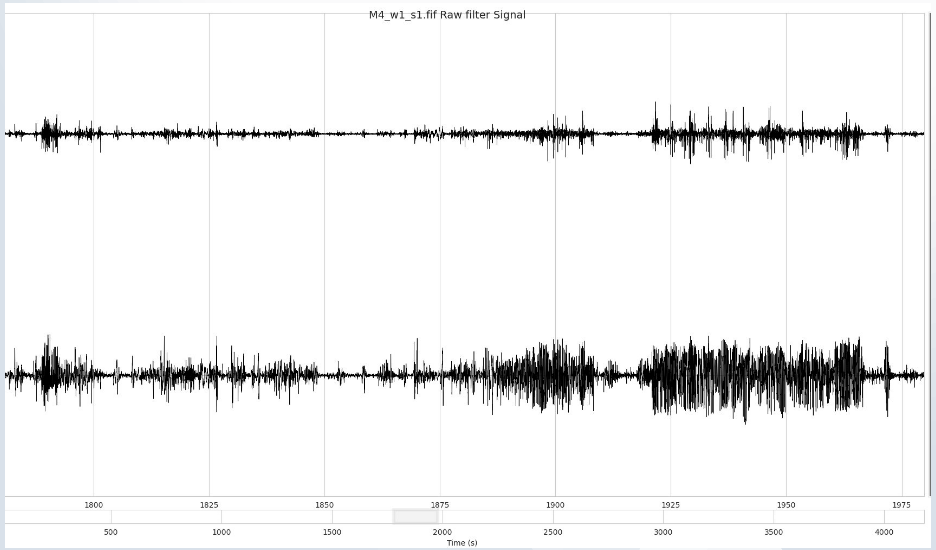


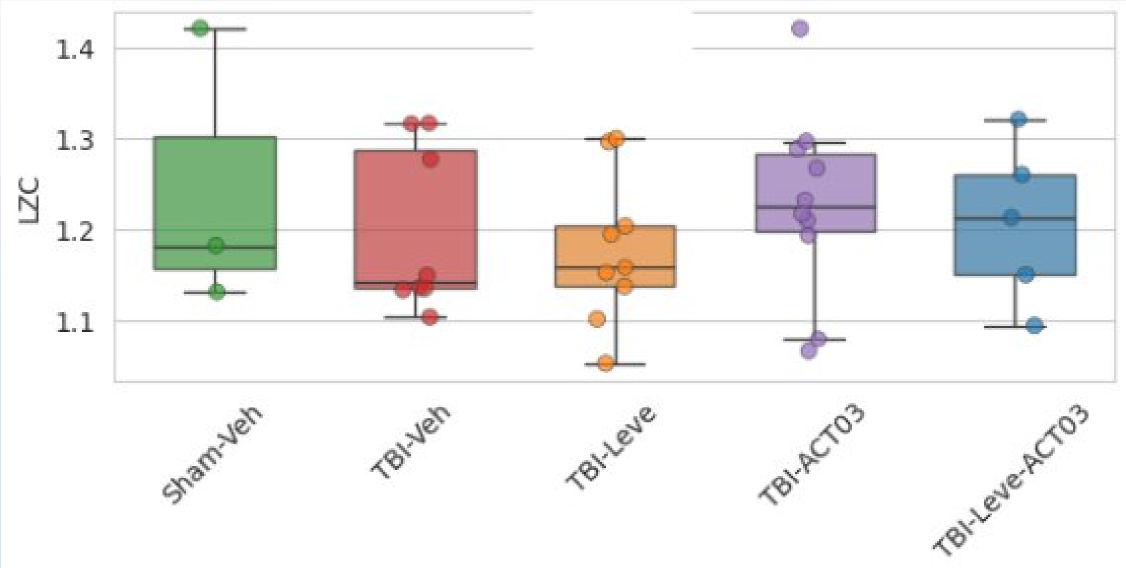
(Under Preparation)

Changes in Brain Dynamics during Pharmacological Treatment for **Traumatic Brain Injury (TBI)**

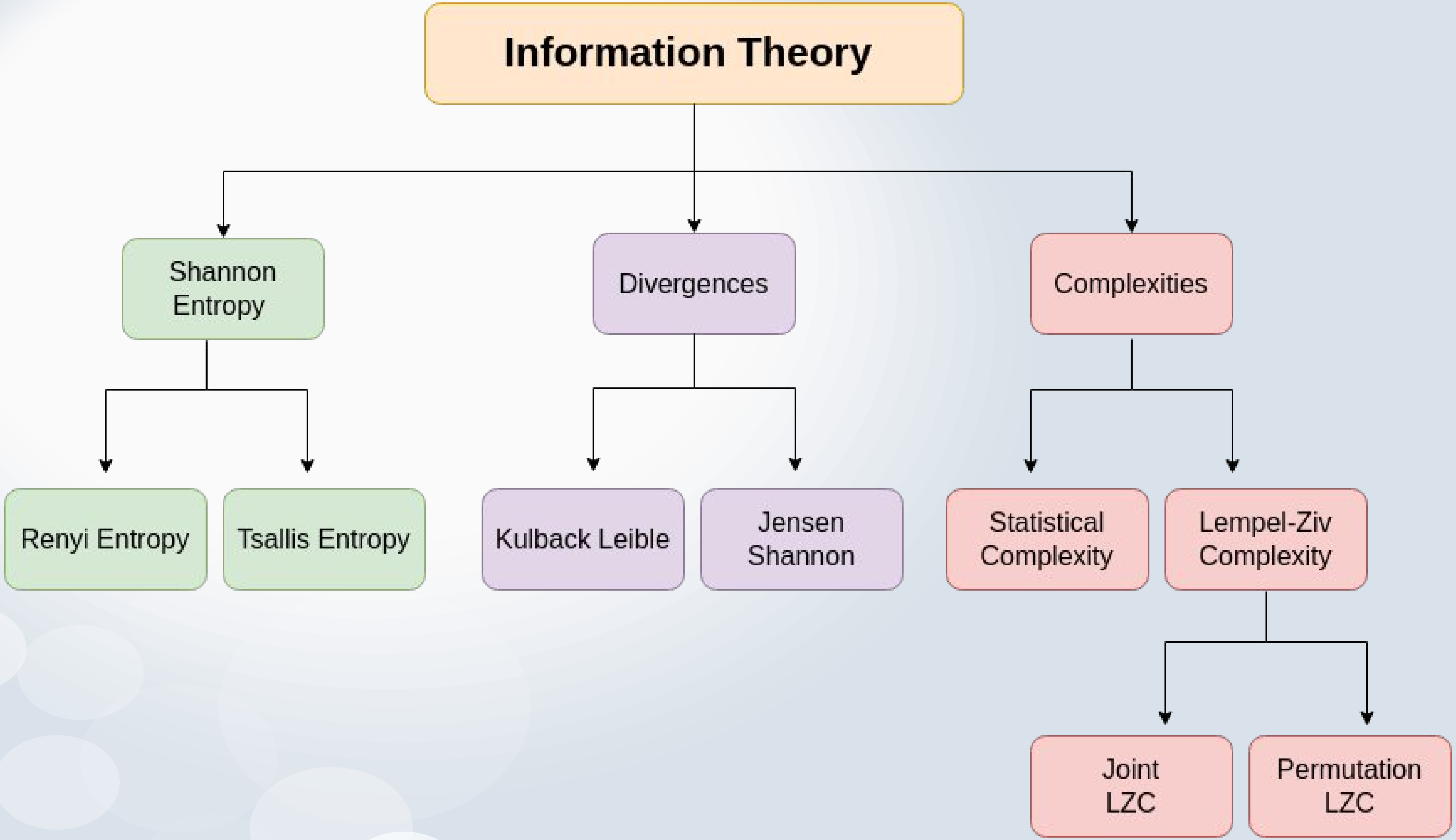


LFP hipocampus





Summary of information theory-based signal analysis techniques



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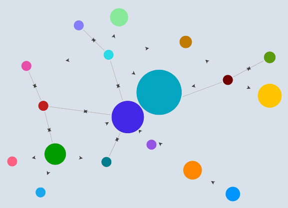

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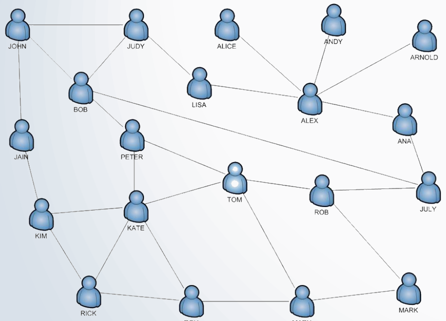
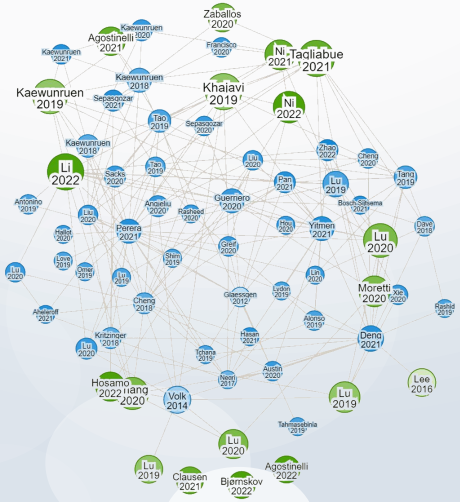
Complex Networks

A **complex network** is a graph that represents a real-world system and exhibits **non-trivial topological features**.

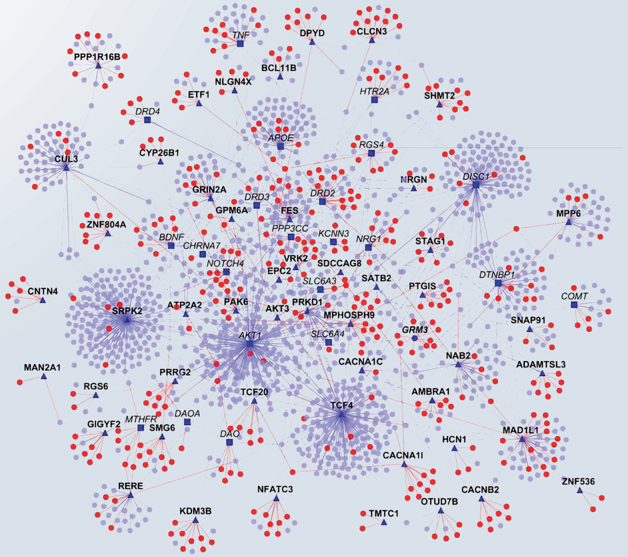
- **Non-trivial Topology**
- **Large-Scale**
- **Evolution**
- **Emergence**



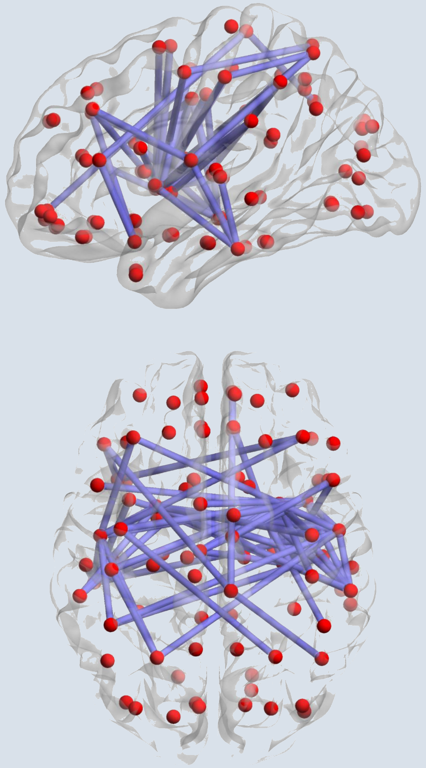
Social Network



Citation Network

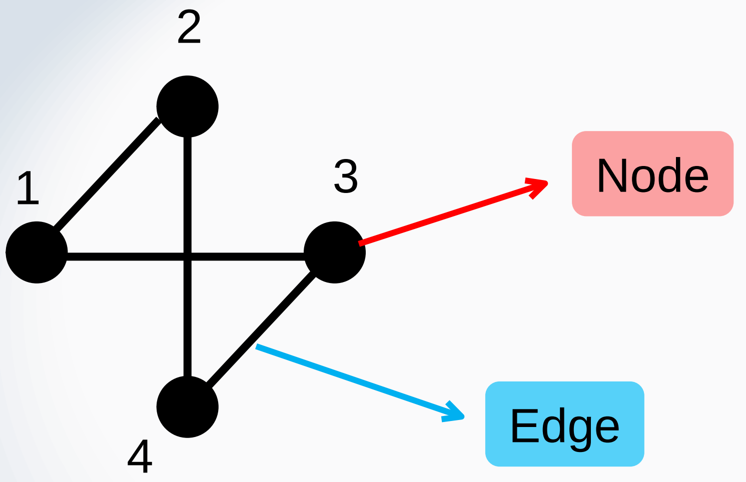


Protein Network

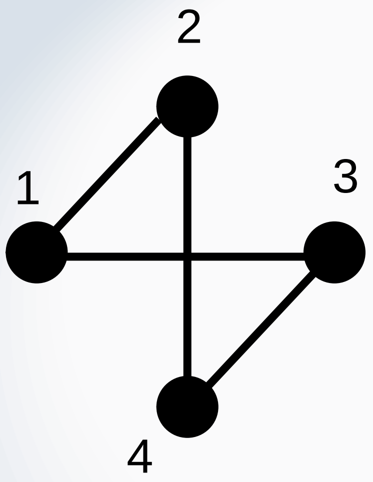


Brain Network

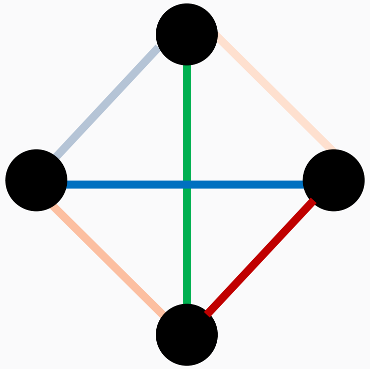
The interation on a systems can be modelated as **graph**



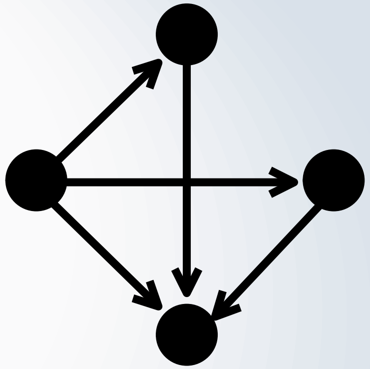
Graph classification



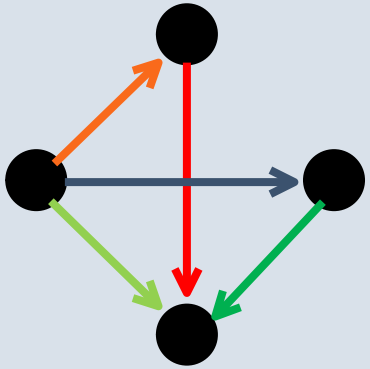
Undirected
Binary



Undirected
Weighted

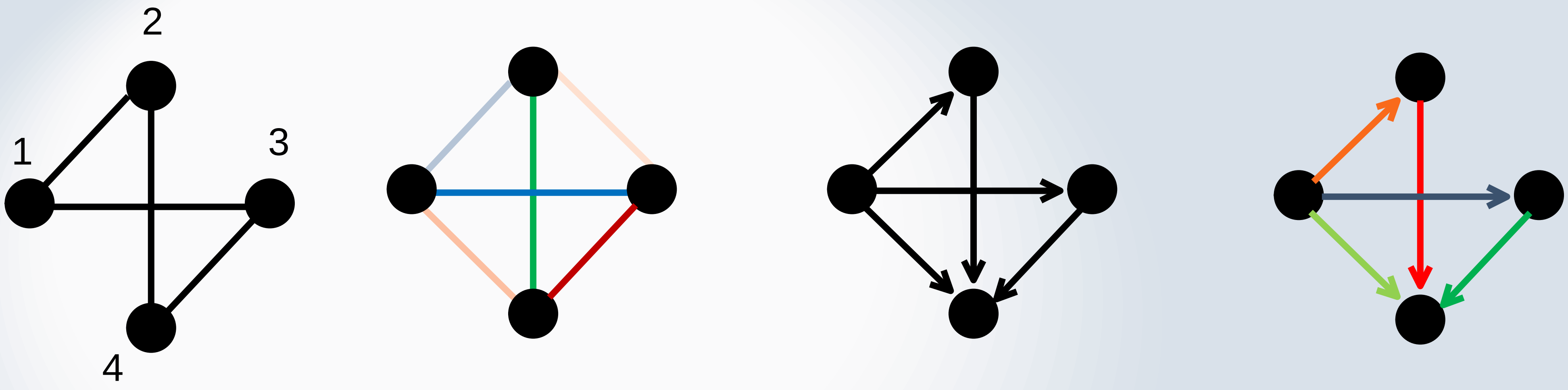


Directed
Binary



Directed
Weighted

Mathematical reprecentation of a graph: **Adjacency Matrix (A)**



Undirected Binary

Undirected Weighted

Directed Binary

Directed Weighted

0	1	1	0
1	0	0	1
1	0	0	1
0	1	1	0

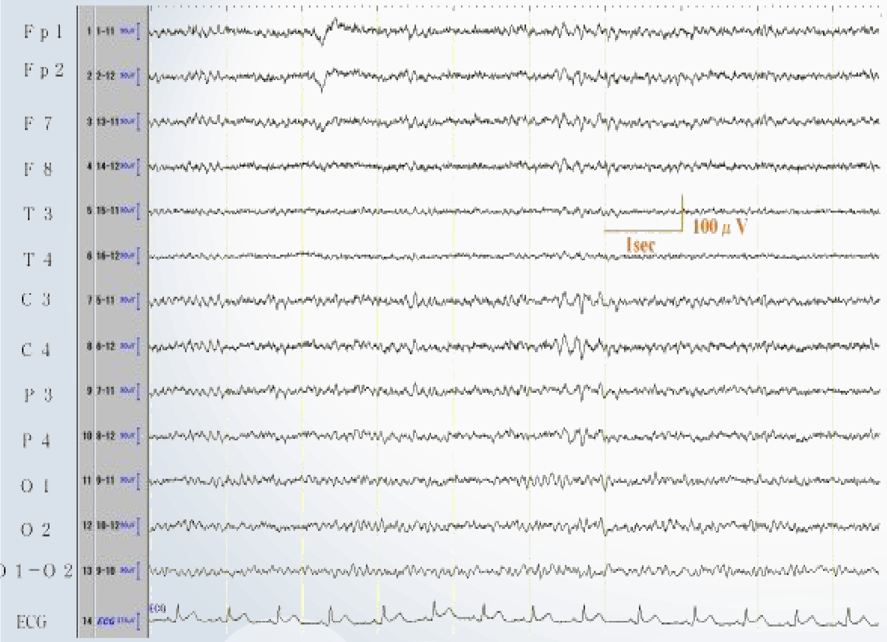
0	2	3	0
2	0	0	5
3	0	0	9
0	5	9	0

0	1	1	1
0	0	0	1
0	0	0	1
0	0	0	0

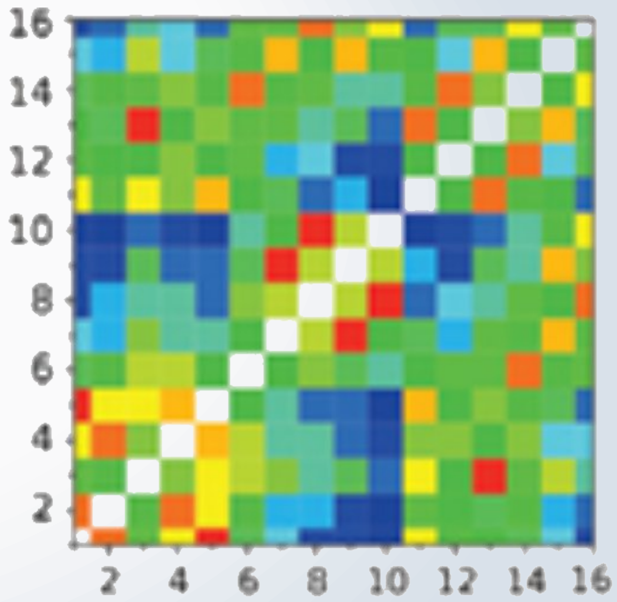
0	2	3	4
0	0	0	9
0	0	0	4
0	0	0	0

How we measure this interaction in signals ?

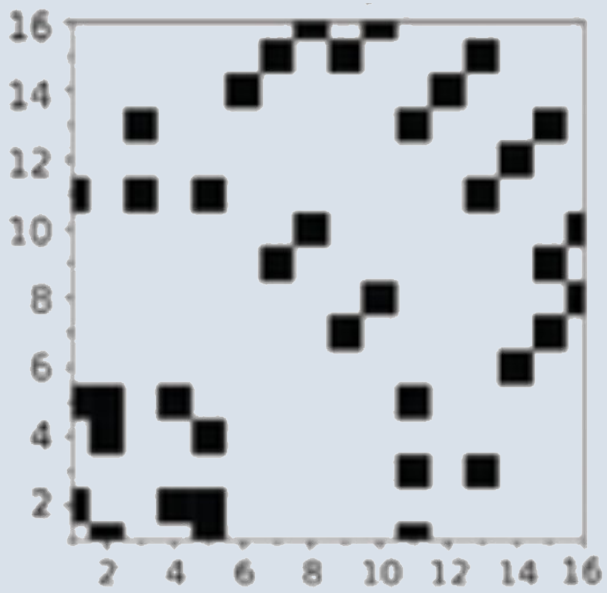
Recording



Correlation Matrix



Conectivity Matrix



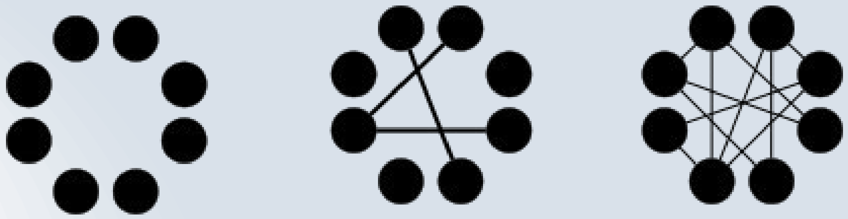
- **Statistical**: Pearson Correlation
- **Power Spectrum:** Coherence
- **Phase signal:** Phase Lag Index (PLI)

Threshold
Baseline
Phase Surrogate

Complex Networks Features

Link Density

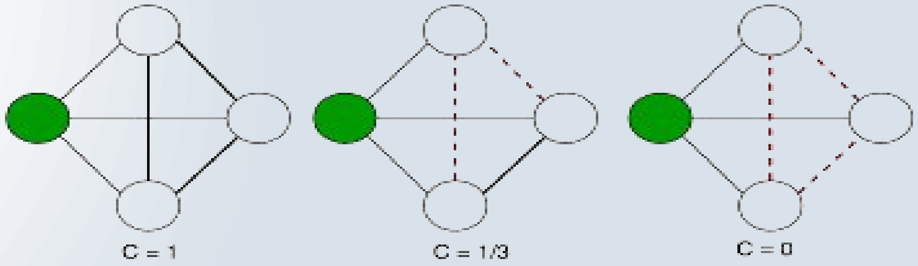
$$\delta = \frac{2e}{N(N-1)}$$



$\rho = 0$ $\rho = 0.1$ $\rho = 0.35$

Cluster Coefficient

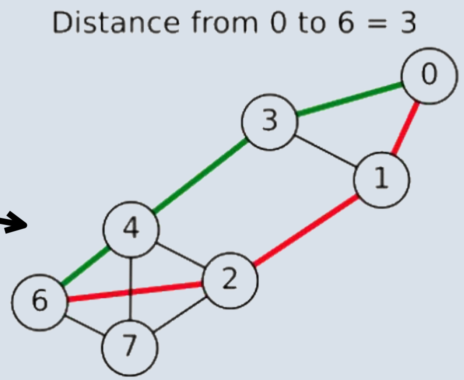
$$\mathcal{C} = \sum_{i=1}^{N} \frac{2n_v(i)}{n_c(i)(n_c(i)-1)}$$



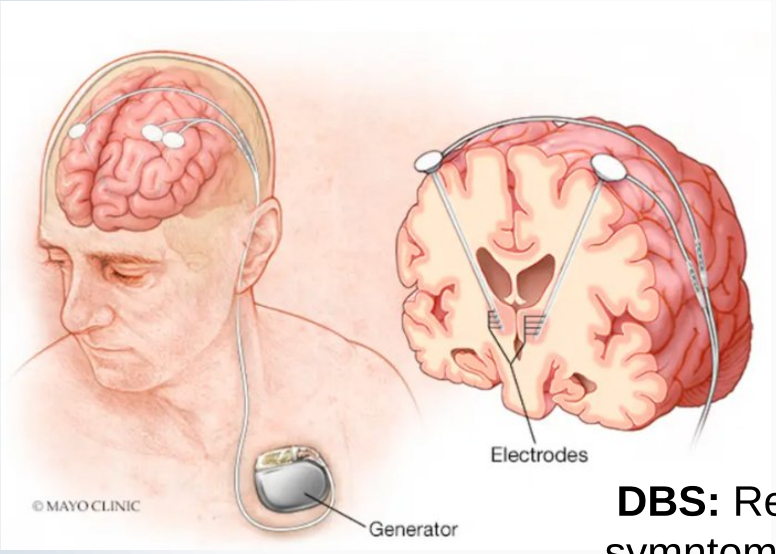
Global Efficiency

$$E_{\text{global}} = \frac{1}{N(N-1)} \sum_{i \neq j} \frac{1}{d_{ij}}$$

Shorter Path Length



The Effects of Deep Brain Stimulation on Neural Dynamics in Parkinson's Disease



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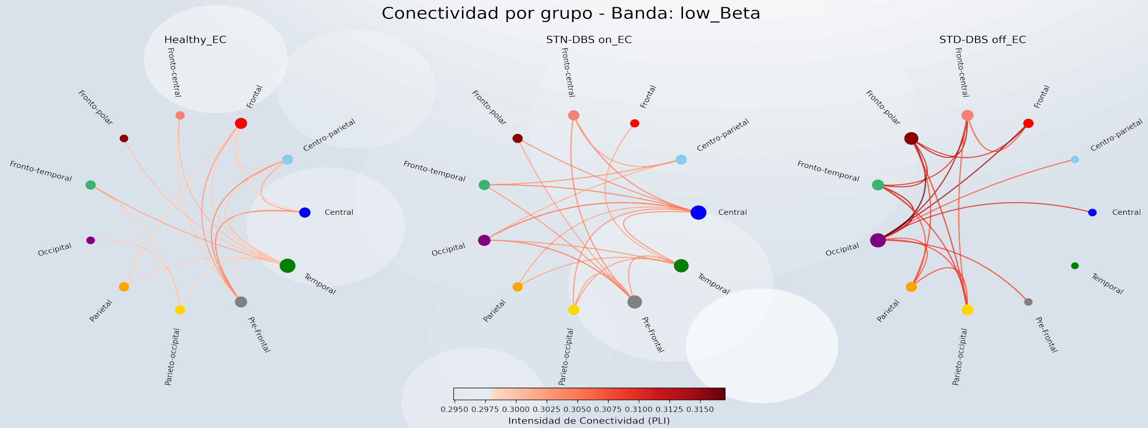
INSTITUTO DE INVESTIGACIÓN E INNOVACIÓN BIOMÉDICA DE CÁDIZ

DBS: Reduce motor symntoms as tremor:

Control DBS-on **DBS-off**

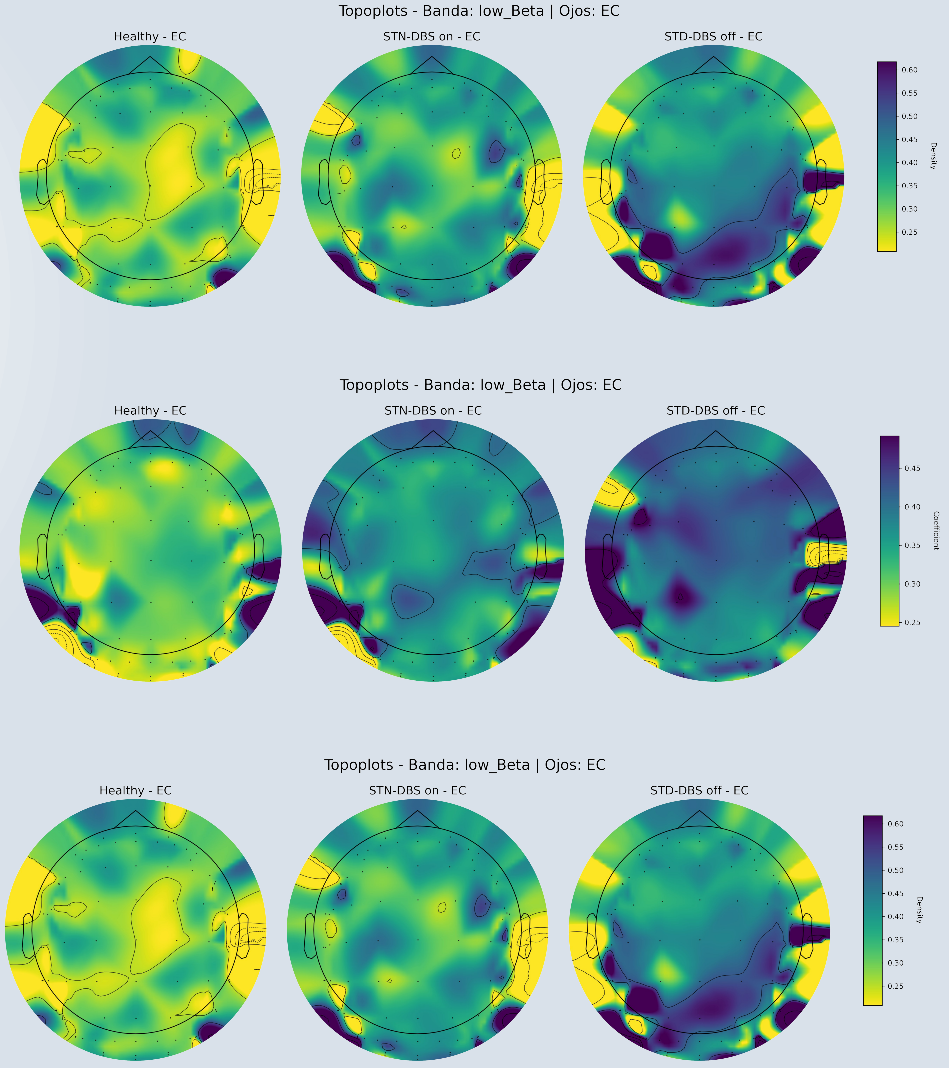


Control DBS-on DBS-off

Link Density

Clustering Coefficient

Ranck Page



Jimenez Armas L..,...,Mateos D. (*In preparation*)

Laplasian Spectral Analysis

From an adjacency matrix **A**, we can compute the **Graph Laplacian operator, L**

$$\mathcal{L} = \mathcal{A} - D$$

$$D = diag(\delta(1), ..., \delta(n))$$

$$\delta(i) = \sum_i w_{i,j}$$

and the associated **eigenvalues spectrum**

$$\{\lambda_1, \ldots, \lambda_n\} \; 0 = \lambda_1 \geq \lambda_2 \geq, ..., \geq \lambda_n$$

von Newman Entropy

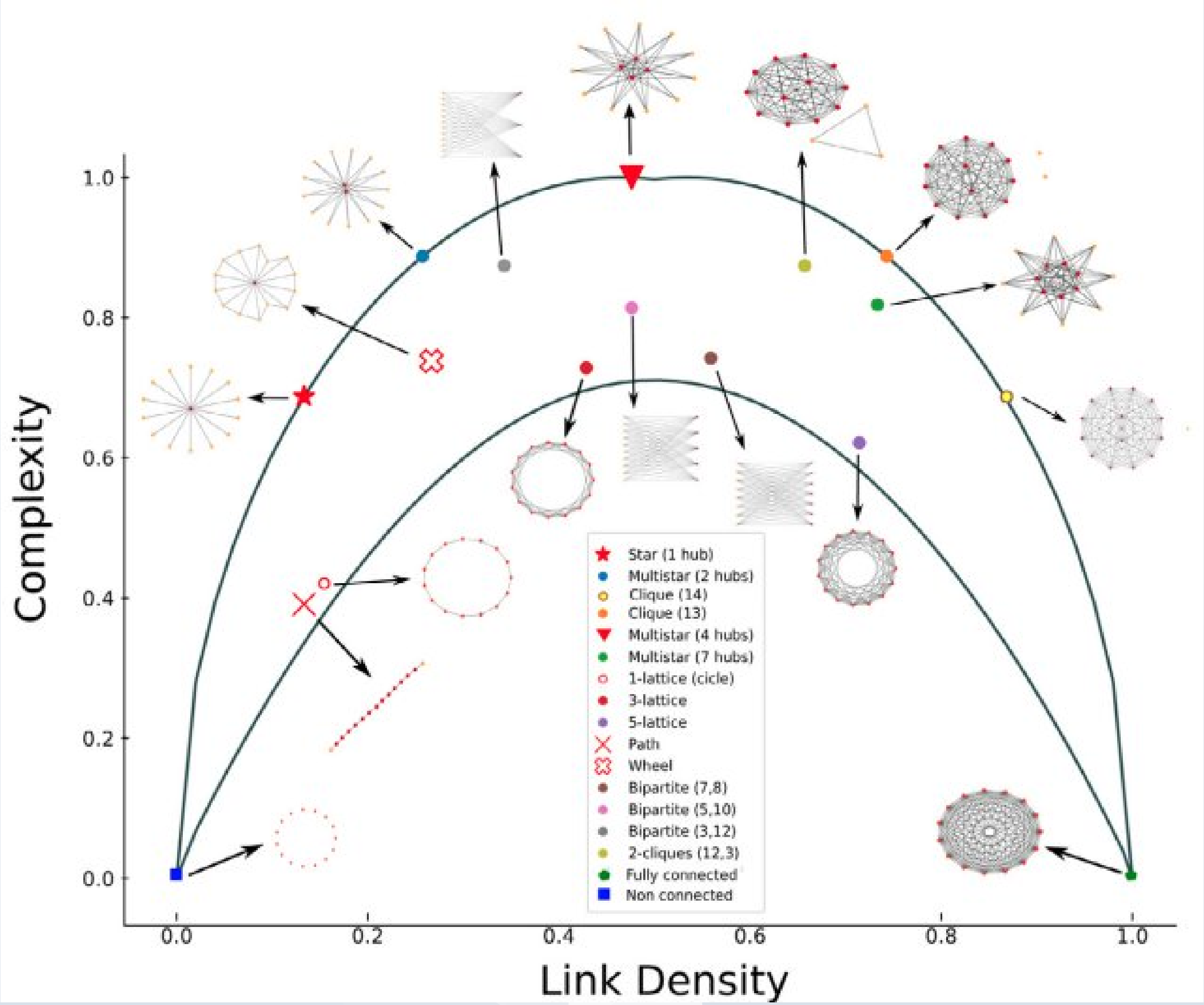
$$\mathcal{H}_{VN} = -\sum_i \lambda_i log(\lambda_i)$$

Spectral Complexity

$$C_s(G) = d_s(G, Z).d_s(G, F) = \|\lambda_G - \lambda_Z\| \, \|\lambda_G - \lambda_F\|$$

Mateos D., et al. *Chaos, Solitons & Fractals, 2022*

Spectral Complexity vs Link Density plane

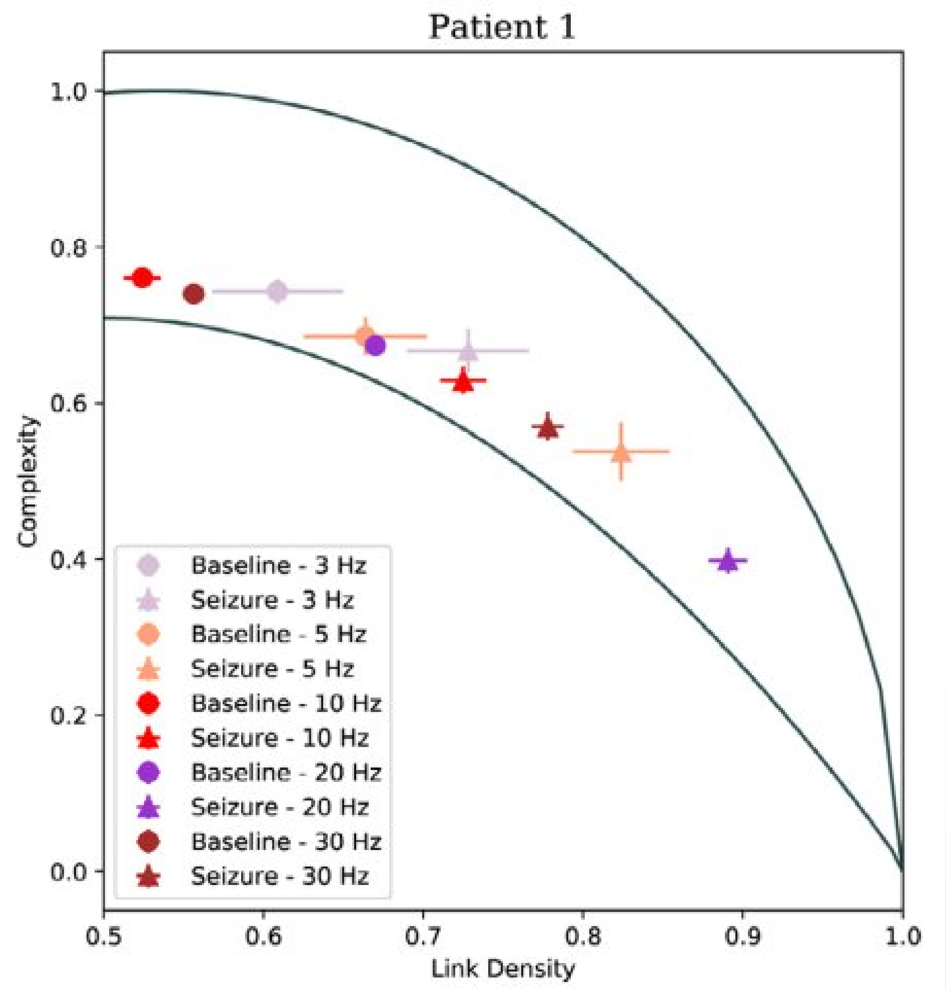


Given a fixed Number of node

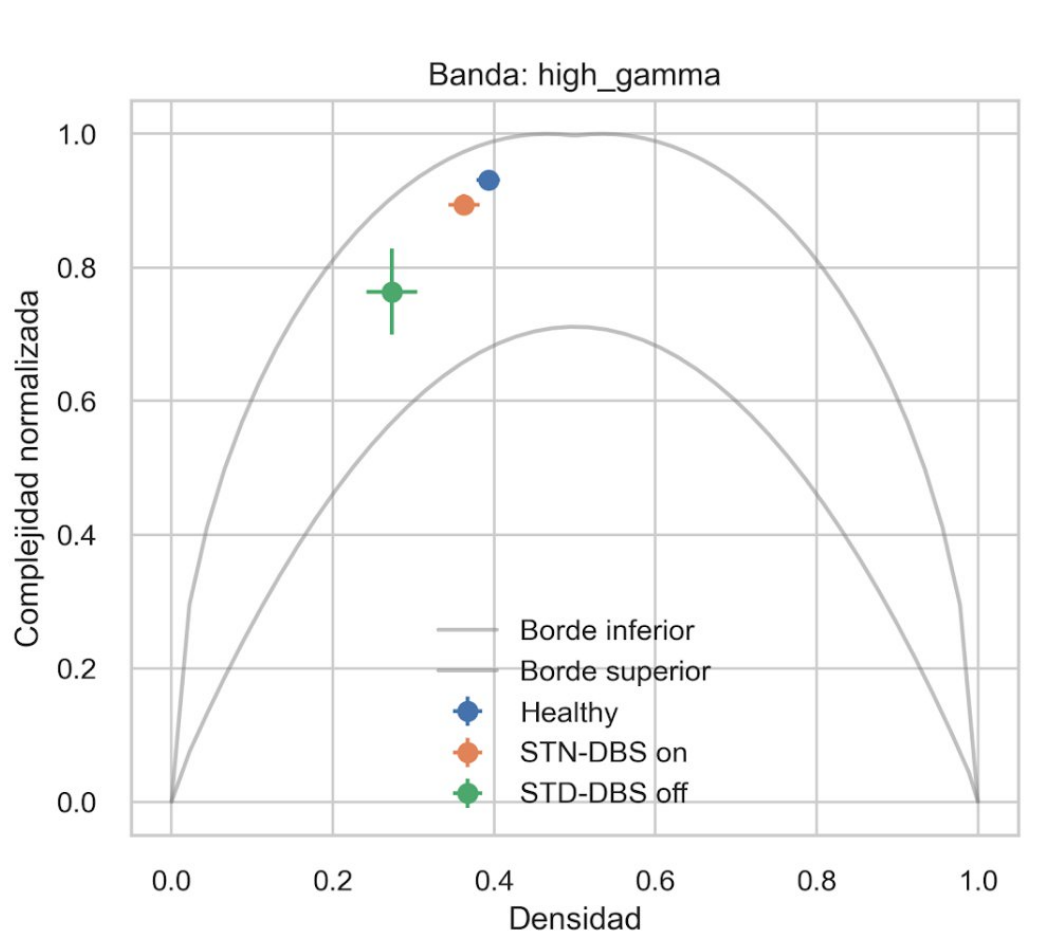
All possible network topologies must reside within a bounded croasant-shaped region

Mateos D., et al. *Chaos, Solitons & Fractals, 2022*

Epilepsy



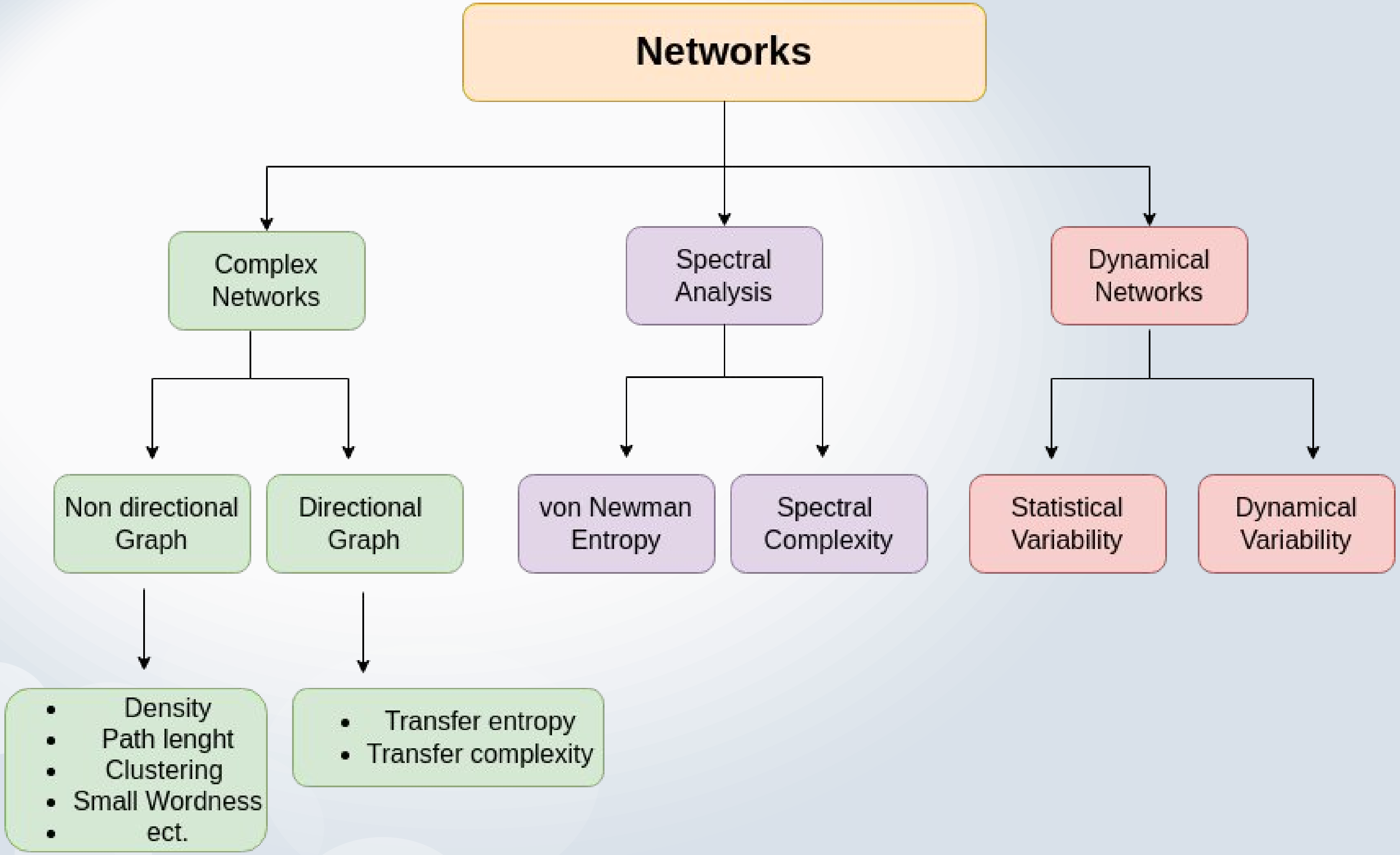
Parkinson DBS



Mateos D., et al. *Chaos, Solitons & Fractals, 2022*

Jimenez Armas L..,...,Mateos D. (*In preparation*)

Summary of Networks Analysis techniques



Overview

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- **Time Series Analysis**
  Extracting insights from sequential data.
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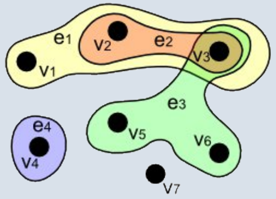
  Mapping the interactions and structure of the system.
- **Higher-Order Interactions**
  Moving beyond pairwise connections to understand complex group dynamics.



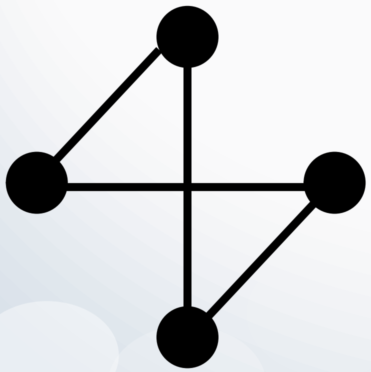
- **Explainable AI (XAI)**
  Making the predictions of AI models transparent and interpretable.
- **Future Directions**
  Exploring new ideas and applications.

High Order Interaction

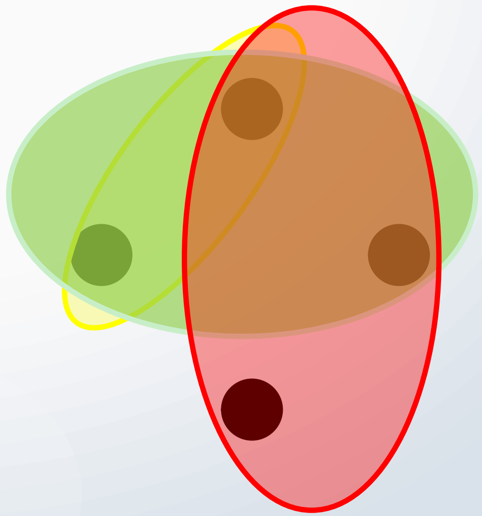
High-Order Interactions (HOI) capture the collective behavior of groups of **three or more elements** in a system, which cannot be explained or reduced to the sum of their pairwise interactions.

Pairwise Interaction

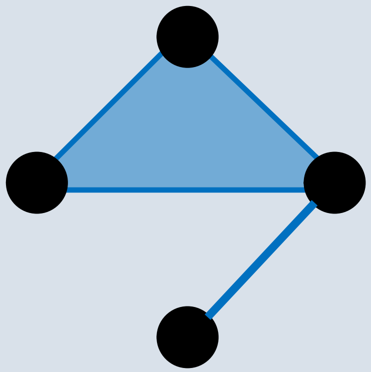
HOI



Graph



Hypergraph



Clique or simplex

Hypergraph

A **hypergraph** is a generalization of a graph in which an **edge** (called a **hyperedge**) can connect **any number of vertices**

Hyperedge
Email={M1, M2, M3}

Vertices={Diego, Magui, Santiago, Lijo, Hugo }

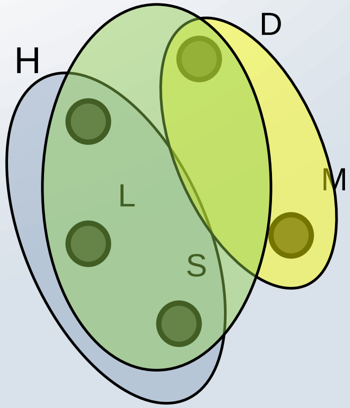
M1={D, M}
M2={S, L, H}
M3={D, S, L, H}

Incidence matrix

	M1	M2	M3
D	1	0	1
M	1	0	0
S	0	1	1
L	0	1	1
H	0	1	1

$\mathcal{I}(v, e)$

Hypegraph



$\mathcal{H}$

Adjacency Matrix

$\mathcal{A}$

	D	M	S	L	H
D		1	1	1	1
M	1		0	0	0
S	1	0		2	2
L	1	0	2		2
H	1	2	2	2	

Relationships between nodes and hyperedges

Hypergraph Quantifiers

Vertex degrees

$$d(v) = \sum_e \mathcal{I}(v, e)$$

$$D_v = \{d(v_1), d(v_2), \ldots, d(v_n)\}$$

Hyperedge degrees

$$\delta(e) = \sum_v \mathcal{I}(v, e)$$

Adjacency Matrix

$$\mathcal{A} = \mathcal{I}.\mathcal{I}^T - D_v$$

⬇

Laplacian Spectral Analysis

$\delta(e)$ →

$d(v)$ ↓

	M1	M2	M3
D	1	0	1
M	1	0	0
S	0	1	1
L	0	1	1
H	0	1	1

Hypergraph Quantifiers

Vertex degrees

$$d(v) = \sum_{e} \mathcal{I}(v, e)$$

$$D_v = \{d(v_1), d(v_2), \ldots, d(v_n)\}$$

Hyperedge degrees

$$\delta(e) = \sum_{v} \mathcal{I}(v, e)$$

Adjacency Matrix

$$\mathcal{A} = \mathcal{I}.\mathcal{I}^T - D_v$$

⬇

Laplasian Spectral Analysis

Distance between hypergraph

Vertex centrality distance

$$D^{\mathcal{C}_{\mathcal{V}}}(\mathcal{H}, \tilde{\mathcal{H}}) = \max_{v \in \mathcal{V}} \left| \sum_{e \in \mathcal{E}} I(v, e) - \sum_{\tilde{e} \in \tilde{\mathcal{E}}} \tilde{I}(v, e) \right|$$

Hyperedge centrality distance

$$D^{\mathcal{C}_{\mathcal{E}}}(\mathcal{H}, \tilde{\mathcal{H}}) = \max_{i=1,\ldots,m} \left| \sum_{v \in \mathcal{V}} I(v, e_i) - \sum_{\tilde{v} \in \tilde{\mathcal{V}}} \tilde{I}(v, e_i) \right|$$

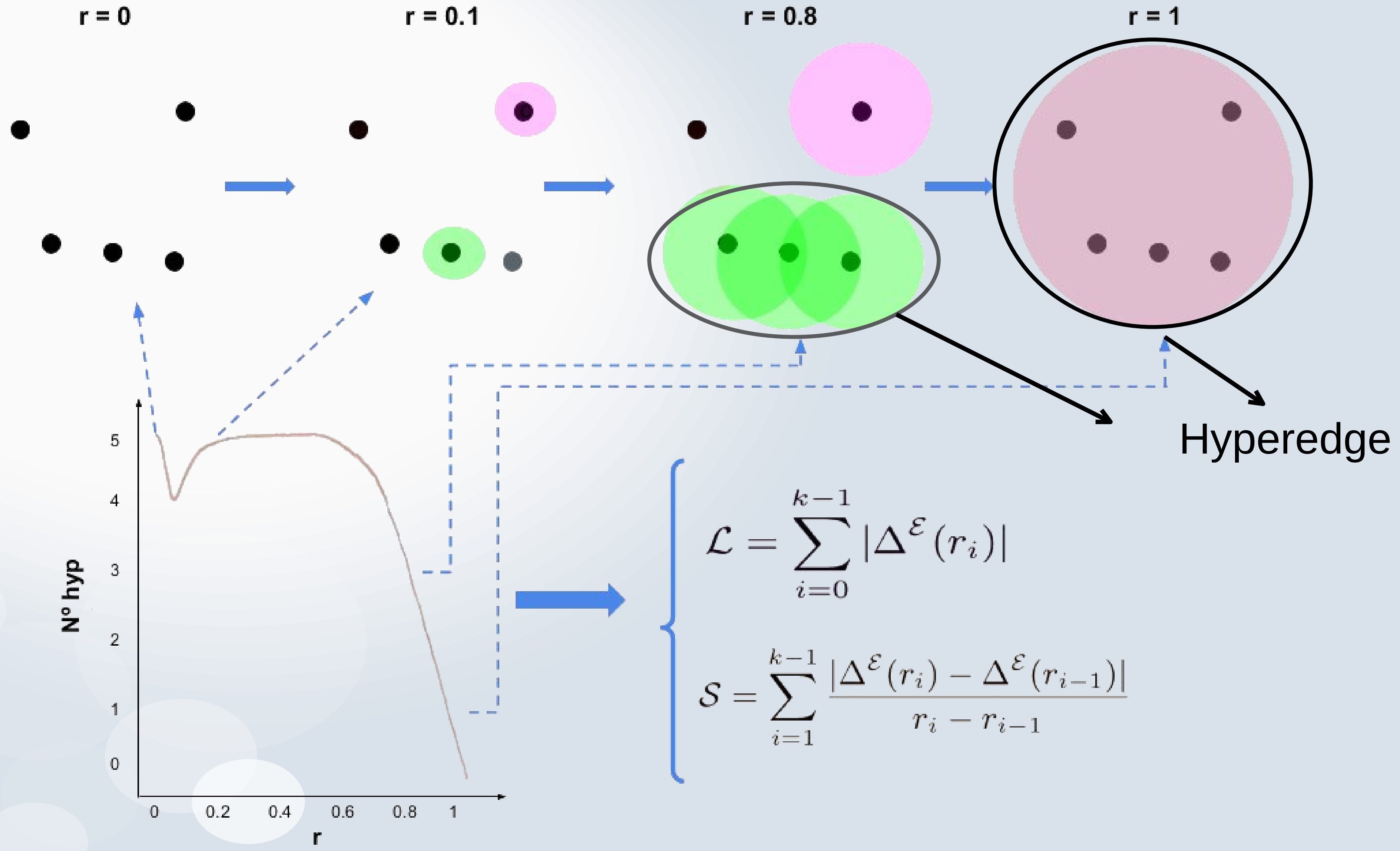
Spectral distance

$$D_p^s(\mathcal{H}, \tilde{\mathcal{H}}) = \left(\frac{1}{n} \sum_{i=1}^{n-1} |\lambda_i - \tilde{\lambda}_i|^p \right)^{\frac{1}{p}}.$$

Building hypergraph from data. Filtration hypergraph

Any kind of data embedded in a **metric space.**

We define a Ball with readious r



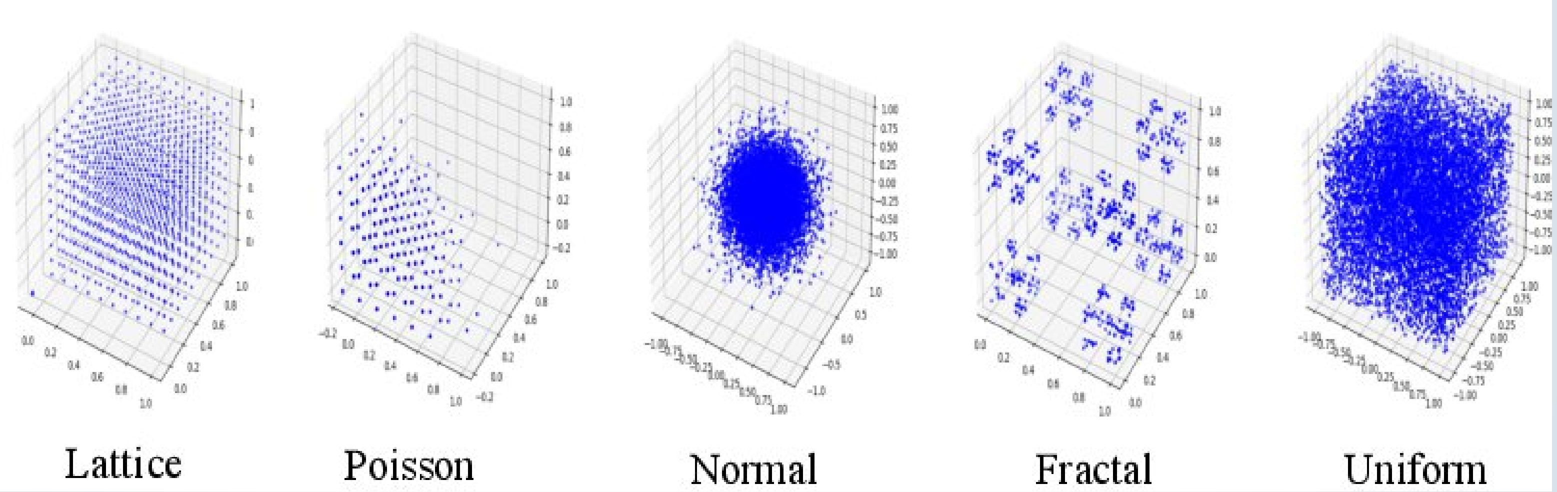
$$
\begin{cases}
\mathcal{L} = \sum_{i=0}^{k-1} |\Delta^{\mathcal{E}}(r_i)| \\
\mathcal{S} = \sum_{i=1}^{k-1} \frac{|\Delta^{\mathcal{E}}(r_i) - \Delta^{\mathcal{E}}(r_{i-1})|}{r_i - r_{i-1}}
\end{cases}
$$

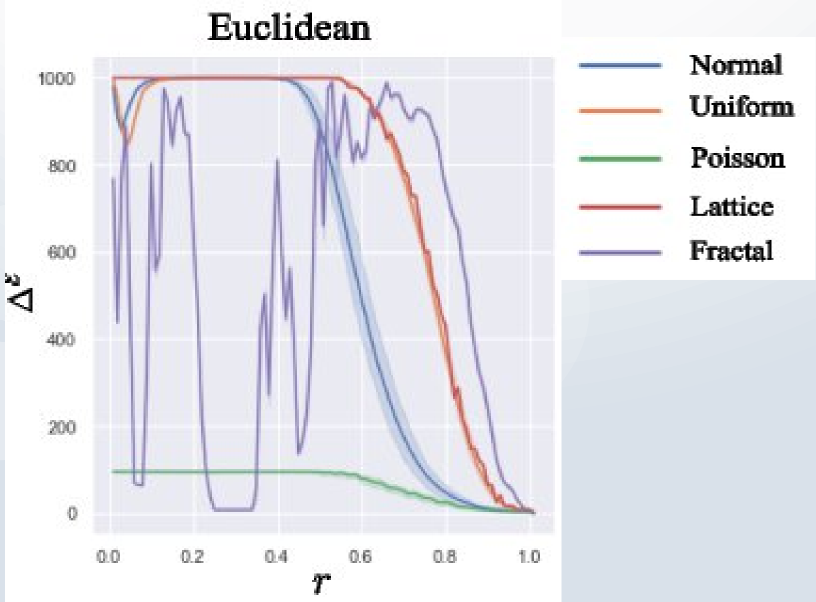
Bilbao D., ..., Mateos D. *Chaos, 2024*

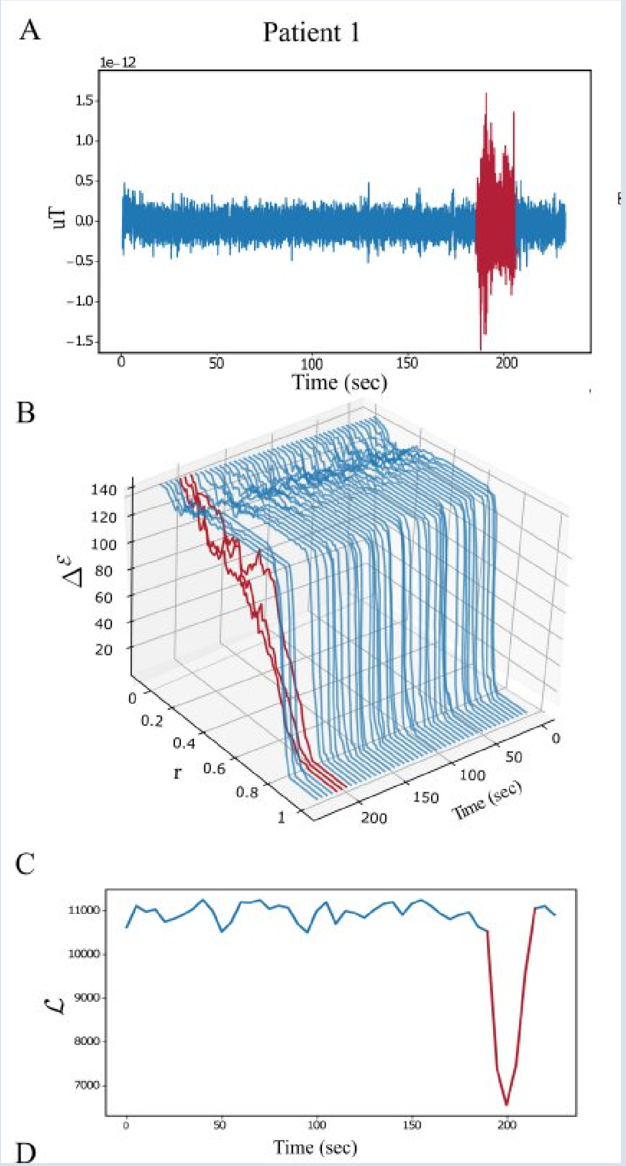
Building hypergraph from data **Filtration hypergraph**

Signals

Data Distribution

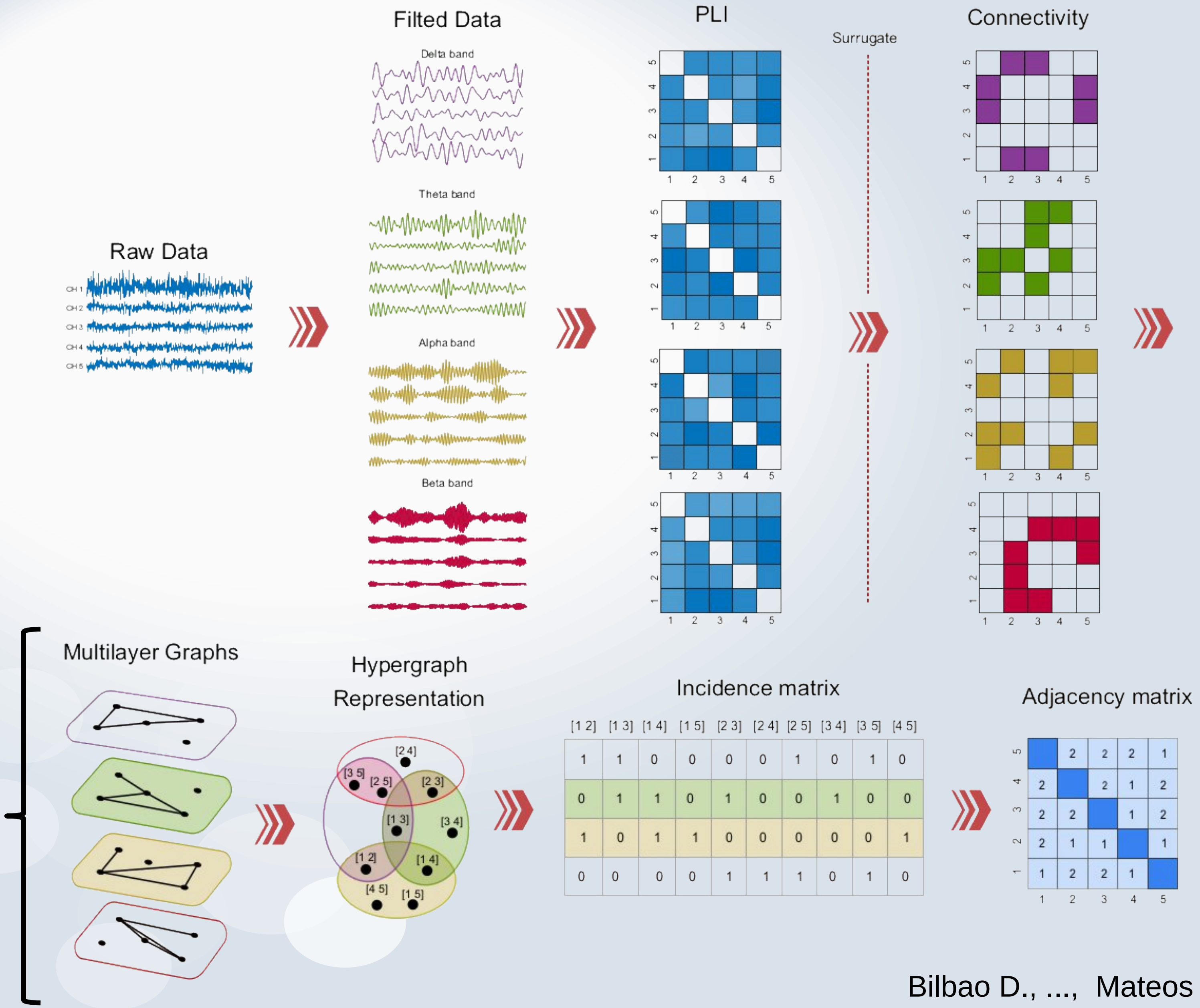






Bilbao D., ..., Mateos D. *Chaos*, *2024*

Building hypergraph from multilayer graphs



Same set of vertices connected by different types of edges

Bilbao D., ..., Mateos D. *Biol Signal Pros and Control, 2025*

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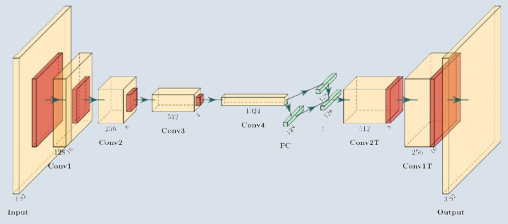
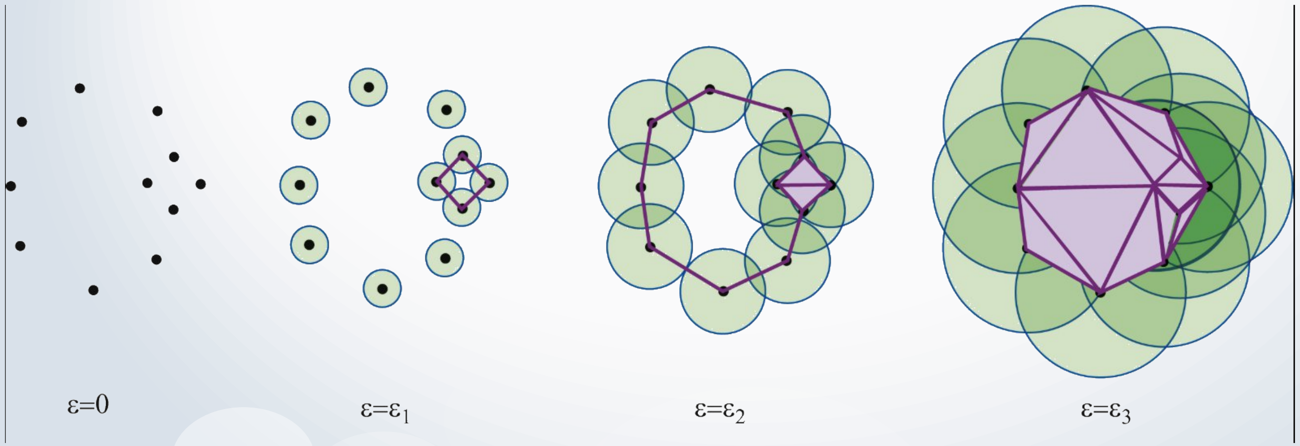


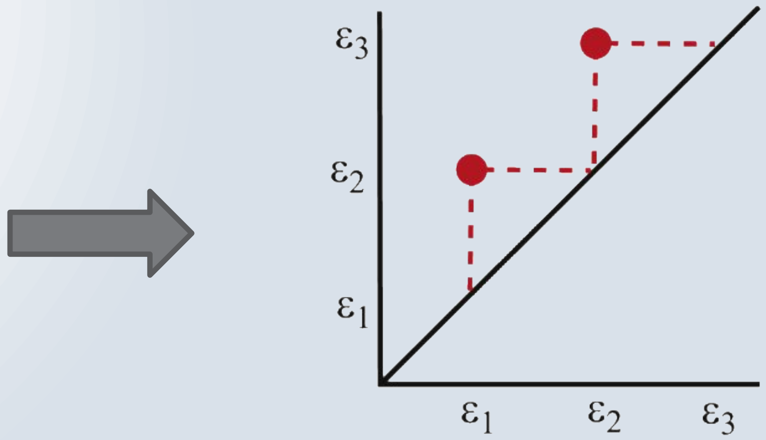
- **Future Directions**
  Exploring new ideas and applications.

Topological Data Analisis (TDA)

Analysed the complex, high-dimensional datasets by characterizing their intrinsic shape, connectivity, and holes, which **persist across multiple scales**



Vietoris - Rips Filtration



Persistence Diagram

Persistence Homology quantification

Wasserstein distance

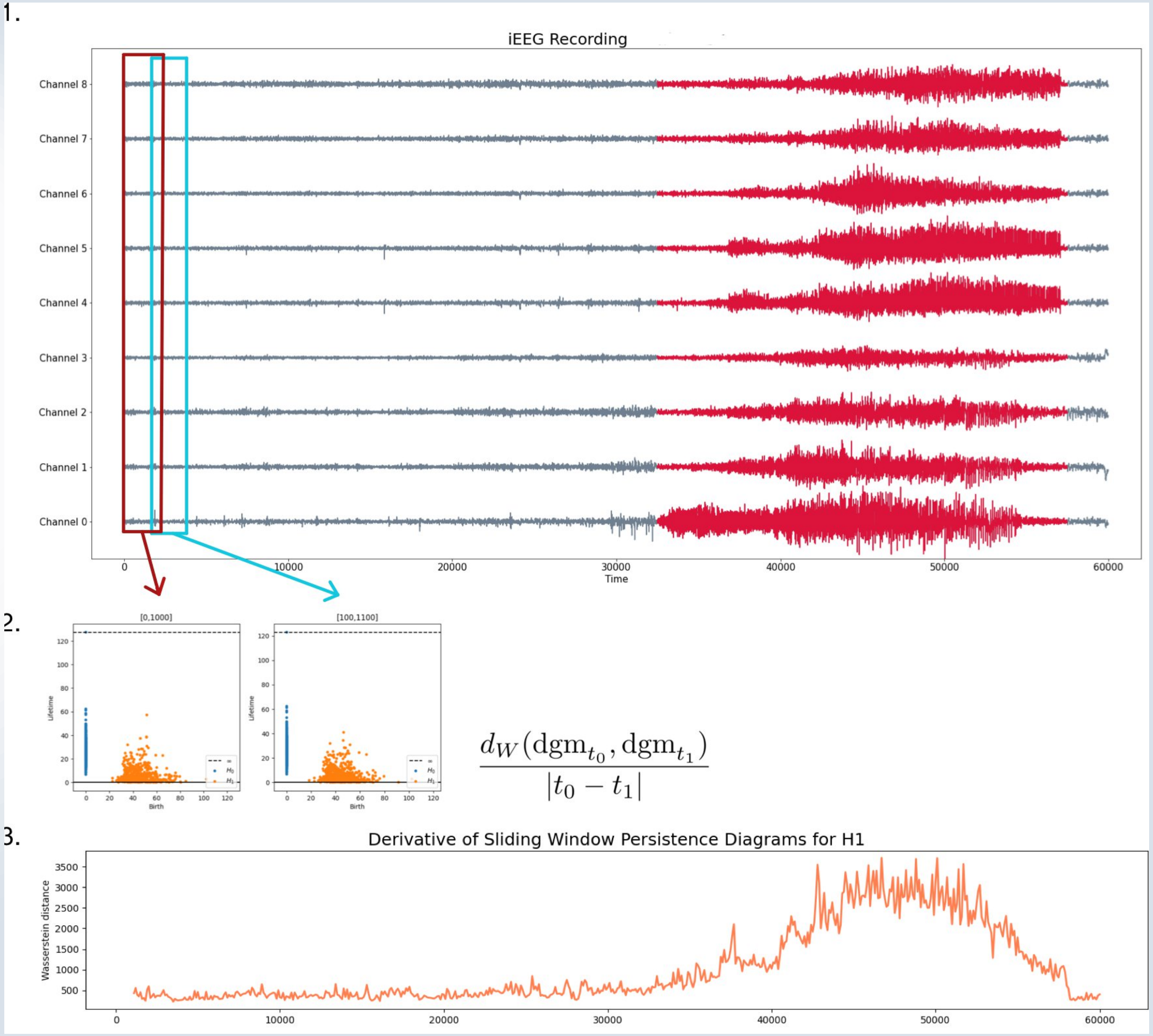
$$d_{W,p}(D,D') = \inf_{\psi: D \to D'} \left(\sum_{(x,y) \in D} ||(x,y) - \psi(x,y)||_\infty^p \right)^{1/p}$$

Total Persistence

$$Pers_{tot}(D) = \sum_{(x,y) \in \mathcal{D}} pers(x,y)$$

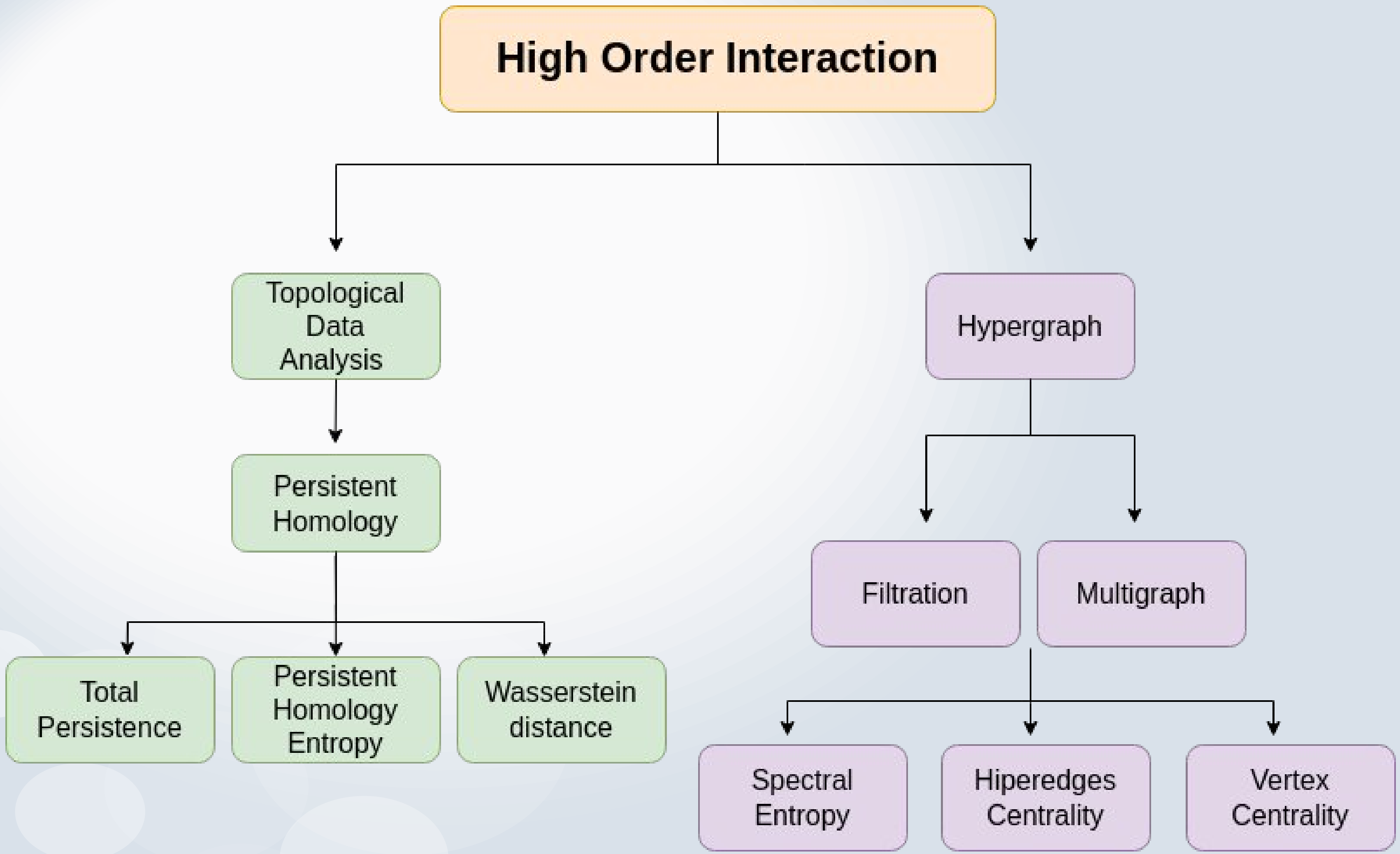
Persistent homology Entropy

$$PHE(\mathcal{D}) = - \sum_{(x,y) \in \mathcal{D}} \frac{\text{pers}(x,y)}{Pers_{total}} \log \left(\frac{\text{pers}(x,y)}{Pers_{total}} \right)$$



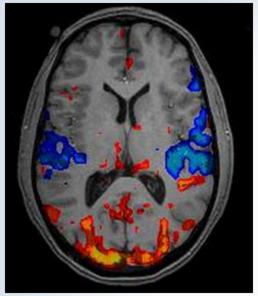
Fernandez X. & Mateos D. *ArXiv, 2025*

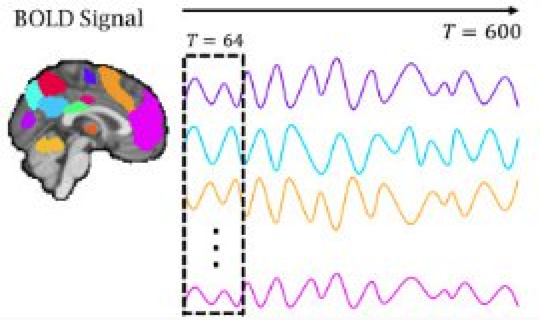
Summary of HOI Analysis techniques



Beta Variational Autoencoder

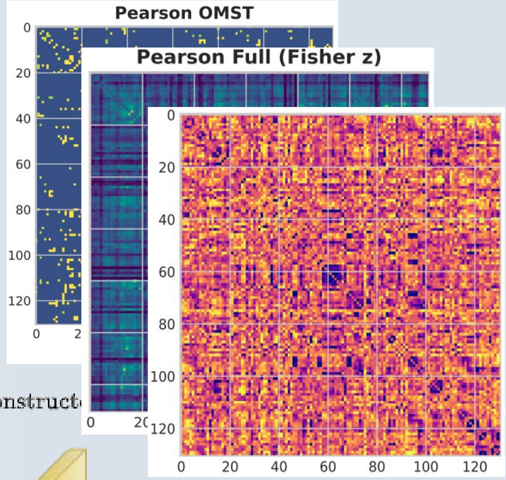
fMRI





Preprocessing

Connectivity Matrix



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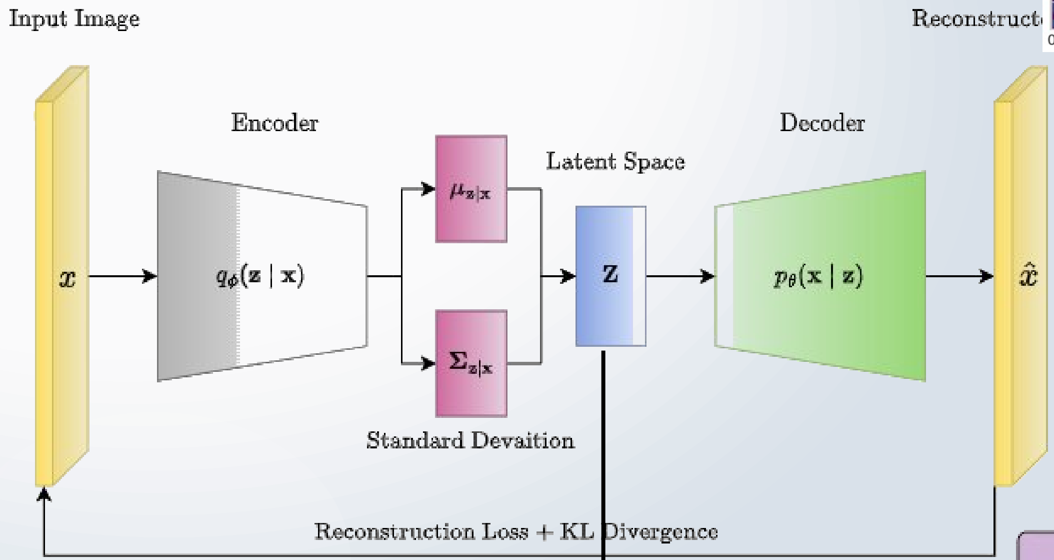


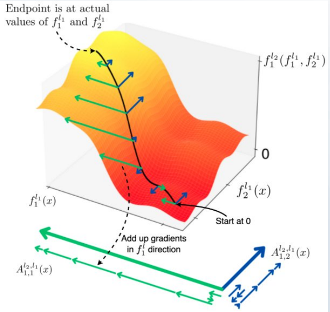
Supervised classification nrame

Pipeline	Hyperparamter tuning
(StandardScaler + SMOTE)	Optuna RF, SVM, LightGBM XGBoost ot cross-vaidat

Normal

AD

XAI Models

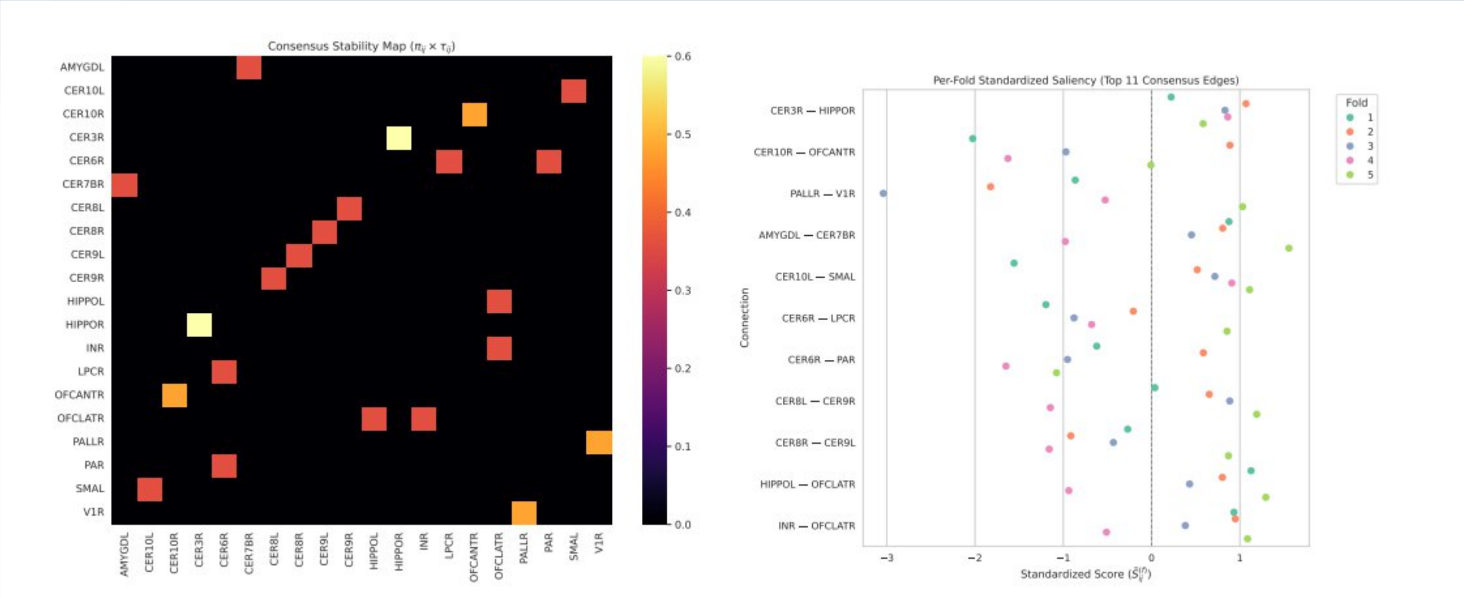


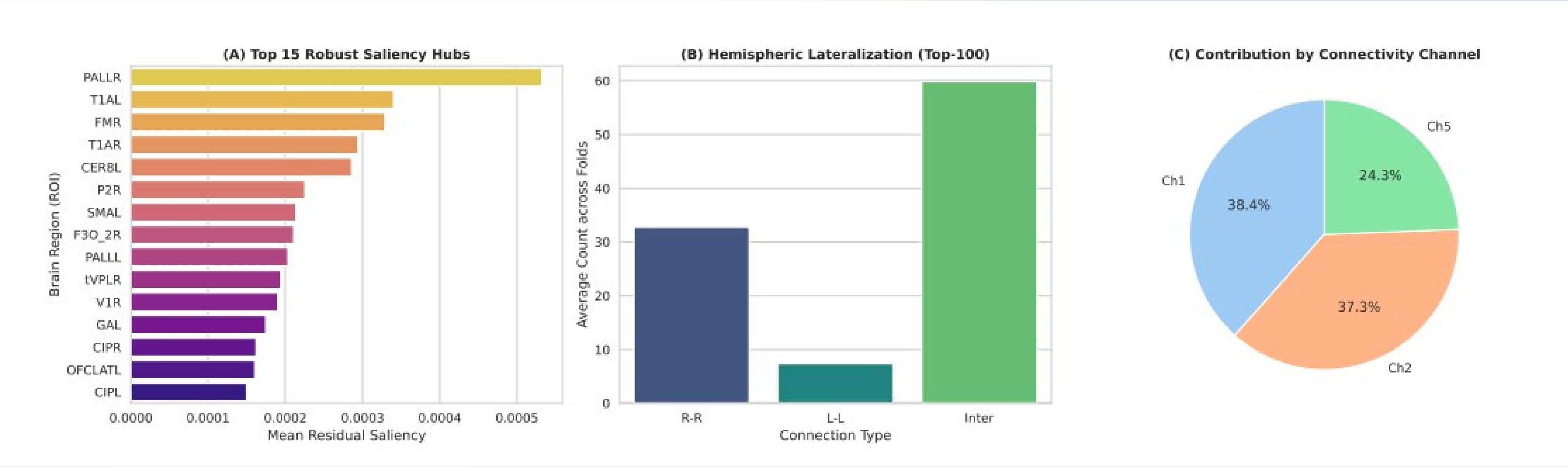
SHAP

Integrated Gradients

Blas S., ..., Mateos D. *(in process) 2025*

This allow us to Identifying the **most critical connections** for decision-making





XIA can provide interpretable insights into the system's dynamics

Blas S., ..., Mateos D. *(in process) 2025*

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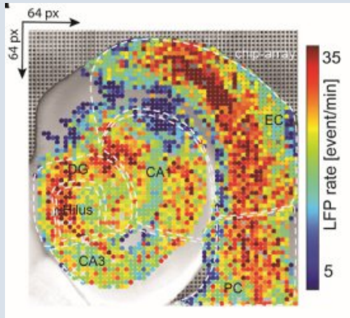
Ongoing projects

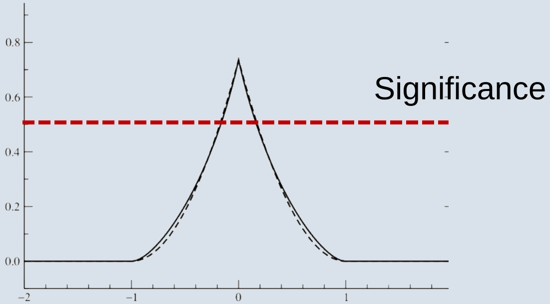
- Development of an **open-source Python package** for time-series analysis using **Lempel-Ziv** complexity.

- Investigating dynamic network alterations in a Kainic **epilepsy** model using **high-density Microelectrode** Arrays (hdMEA).



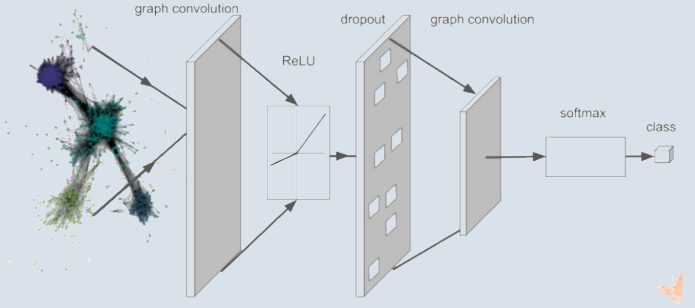
- Generalization of **phase-based correlation** metrics via the Riesz transform for the analysis of **high-dimensional datasets.**

- Extending the framework for **statistical significance** in Permutation Jensen-Shannon divergence.

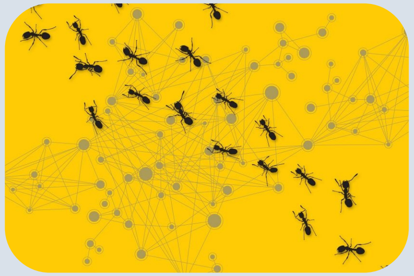


Future Research Directions

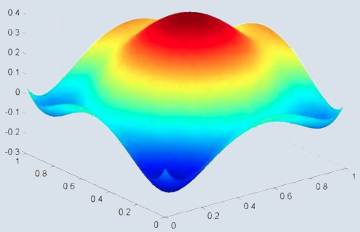
- Development of a novel **seizure forecasting** framework integrating **Graph Neural Networks (GNNs)** and explainable **AI (XAI)** for EEG and iEEG analysis.



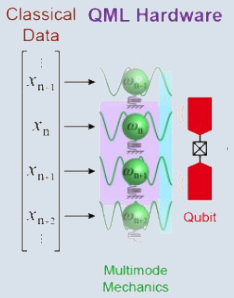
- Application of spectral complexity metrics to characterize dynamics in **ecological networks**.



- Designing a novel **information-geometric** framework for the analysis of high-dimensional neurophysiological data.



- Exploring the application of **Quantum Machine Learning** (QML) algorithms to model neurophysiological dynamics.



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Thank You

For Your Attention

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