



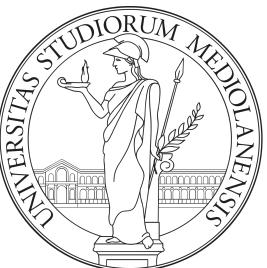
CENTER
COMPLEXITY
& BIOSYSTEMS

University of Milan

INFORMATION OPTIMIZED MULTILAYER NETWORK REPRESENTATION OF HIGH DENSITY ELECTROENCEPHALOGRAM RECORDINGS

29 07 2022

Lake Como School



DEPARTMENT OF
PHYSICS
“ALDO PONTREMOLI”



DEPARTMENT OF
ENVIRONMENTAL
SCIENCE AND POLICY

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www.oncolab.unimi.it

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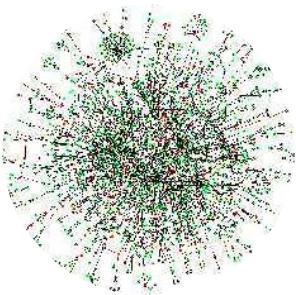


Alexander von Humboldt
Stiftung / Foundation

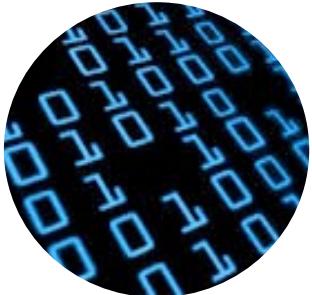


CC&B RESEARCH

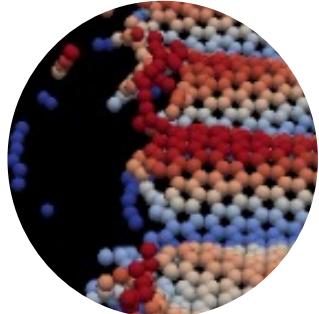
Network Medicine



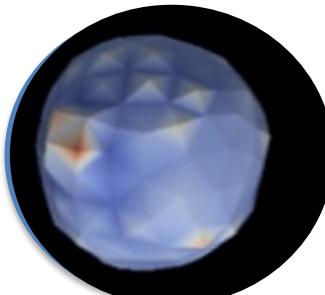
Data science



Disordered Systems



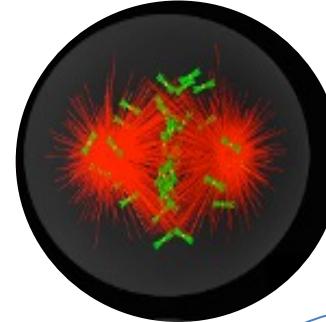
Cell biomechanics



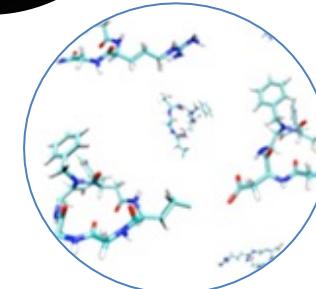
Neurodegenerative diseases



Cancer

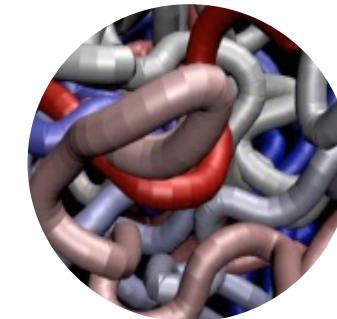


Protein simulations

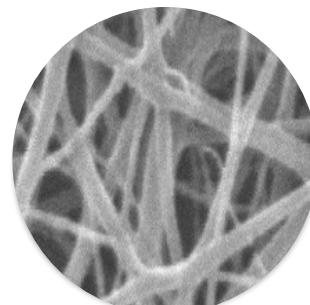


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University of Milan



Chromatin conformations



Bio-inspired
materials

OUTREACH

Newsletters

It is already one year for Complexity and I started its activities at University of Milan. A very difficult year. The corner was: colleagues from the Physics, Biosciences Sciences, to overcome disciplinary barriers. We will have a new forum to tackle problems at the frontier through an interdisciplinary approach based on complex systems in general, and biology in particular, more by an unprecedent data. However, extra knowledge from the quantitative analysis theoretical models, that combine the methods to address this task. Caterina La Porta brings cell biology and computer scientists Vigna and Paolo Belli large scale data analysis theory, and physicists

at the turn of the century the DNA sequence. Those see, but not all, of the future development. For instance, small number – the genes needed by the organism and in what type produced. Cells have a given necessity, and so the spatial organization within the cellular context is the approaching: the genome called a widespread message gene, and thus responding protein.

Having a picture, some parts are spatially nucleus can thus understand how and where are activated. And helps us to investigate

Scaling my world board of the silicon was undoubtedly a point in my academic career, but not all, of the major objective for the developer. For instance, small number – the genes needed by the organism and in what type produced. Cells have a given necessity, and so the spatial organization within the cellular context is the approaching: the genome called a widespread message gene, and thus responding protein.

Conventional strategies to study cancer usually try to characterize specific genetic/biological factors supposed to play a pivotal role in tumor progression with the aim of targeting them for possible therapeutic strategies. Tumors are, however, extremely heterogeneous and their growth depends on dynamical interactions among the cancer cells and between cells and the constantly changing microenvironment. All these interactive processes act together to control cell proliferation, apoptosis and migration. There is an increasing evidence pointing out that these interactions cannot be investigated only through biological experiments focusing on limited sets of genes, but require instead an integrative approach based on complex systems.

It is thus necessary to study cancer as a systemic disease in which the cancer phenotype emerges from the collective properties of complex regulatory networks. On the other hand, the enormous magnitude of tumor heterogeneity within individuals primary or metastatic tu-

mors and between patients has become particular relevant in view of a cancer precision medicine.

Therefore, nowadays there are two complementary aspects in tumors to understand: At microscopic level, it is important to identify the collective properties of tumors or subdivide each tumor into different subclasses using the new tools of computational analysis and machine learning. At microscopic level, research should focus on the heterogeneity of the tumors, to better understand the fluctuations inside the system and identify the signals from the background noise. Disentangling these aspects will lead to models that we can use to investigate the effect on cancer of external perturbations, from nutrition to the immune system. This is the central issue that we address at CC&B.

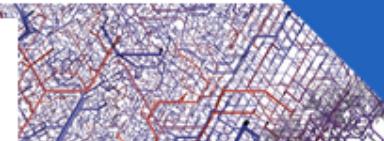
Machine learning-based intelligent systems take an input feature matrix that includes characteristic values of designated positive and negative samples, and self-trains the prediction model in the system via learning the patterns in the feature matrix to ultimately address classification problems with respect to a data set. It is clear that since there is an increasing amount of data in biology and medicine, it is becoming im-

WEB: www.complexitybiosystems.it



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→ THE PHYSICS OF
CANCER



WHO WE ARE
STEERING COMMITTEE
CORE MEMBERS

Social media (Youtube, twitter)

VIRTUAL SEMINARS ON COMPLEXITY

<https://sites.google.com/view/virtualeminarsoncomplexity>

SUMMER SCHOOL SERIES: Advances in Complex Systems



Advances in Complex Systems

Lake Como School of Advanced Studies, 29 June – 3 July 2015 (Como)



The school takes place every two years in July:

2015: <http://acss.lakecomoschool.org>

2017: <http://acst.lakecomoschool.org>

2019: <http://acse.lakecomoschool.org>

Topics: complex networks, chromatin, regeneration, morphogenesis, bioinspired materials....

NEXT SCHOOL July 2024



Lake Como School on Advances in Complex Systems

COMO, 3–7 JULY 2017

CC&B organises the second school on Advances in Complex Systems in Como. The first edition of the school took place in the summer of 2015. The scope of the school series is to present recent advances in

complex systems discussing applications of statistical mechanics of non-equilibrium and disordered systems, theories of complex networks and other stochastic systems to different topics in materials science, social sciences, biology and biomedical research. The broad choice of interdisciplinary topics is designed to expose the students to some of the multiple facets of complex systems theory. The 2017 edition of the school will focus on interdisciplinary approaches to tissue regeneration, chromatin conformations and telomeres, bio-inspired materials, protein aggregation and complex networks in health sciences. The school is open to graduate students and postdoctoral fellows working in complex systems and related fields.

SCHOOL DIRECTORS

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Guido Tiana / University of Milan
Jeffrey S. Urbach / Georgetown University
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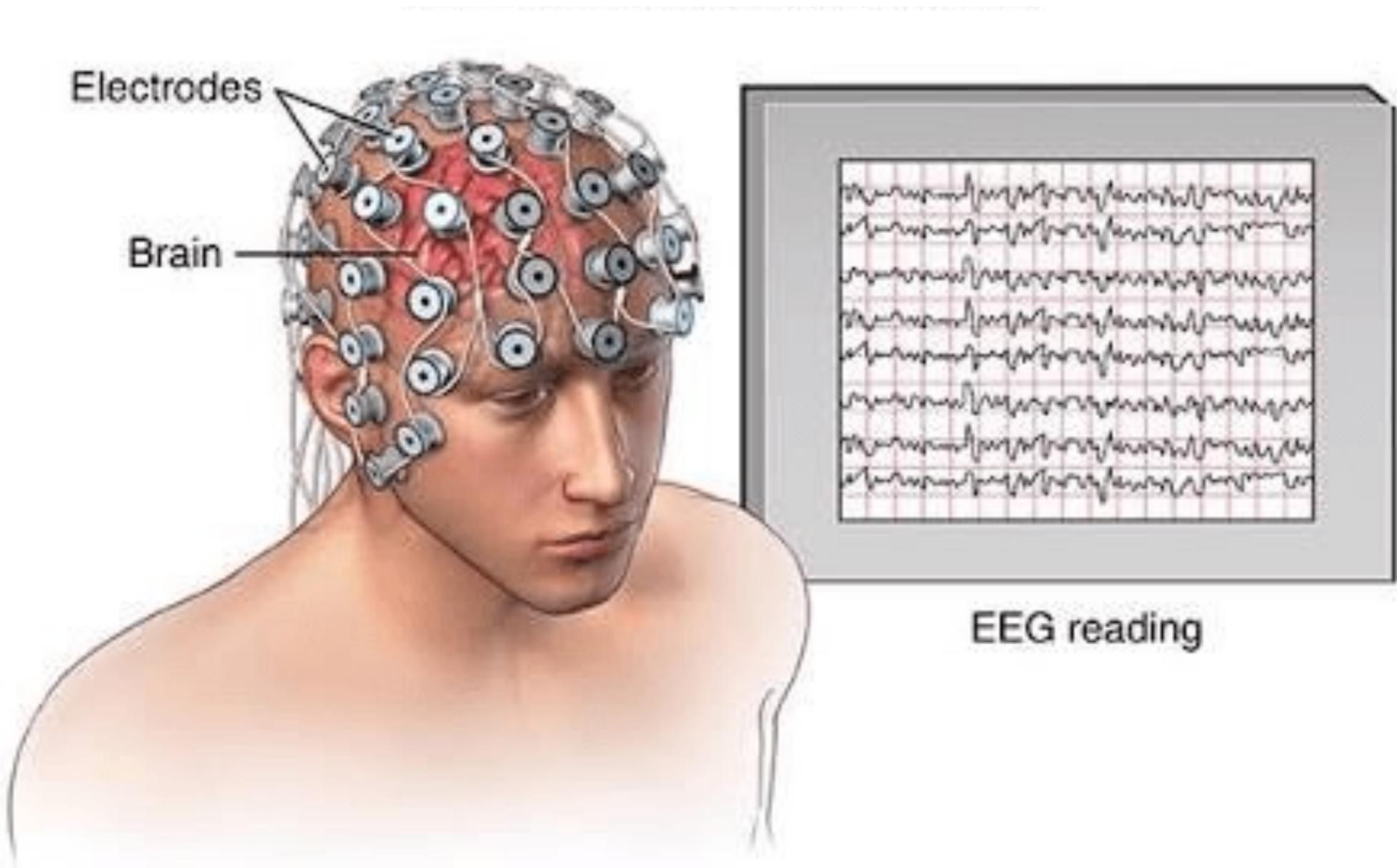
Two fellowships available,
please look at the website:
acst.lakecomoschool.org



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DEADLINE FOR
APPLICATIONS
1 MARCH 2017

ELECTROENCEPHALOGRAPH (EEG)



CAN WE USE EEG SIGNALS TO DETECT CLINICAL CONDITIONS IN PATIENTS?

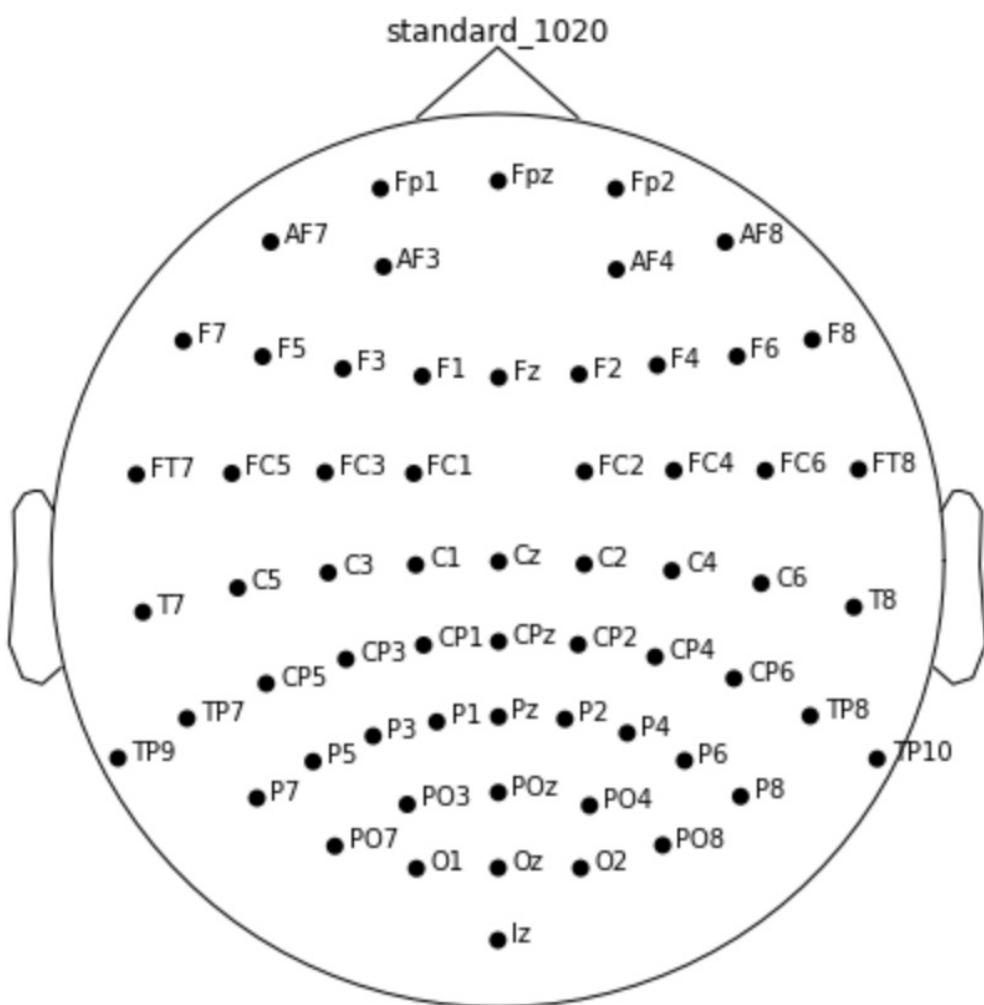
e.g. Patients with mental health issues

EXPERIMENTAL DATA

64 electrodes

500 Hz frequency

8 hours recording during sleep



32 PATIENTS:

7 Bipolar Disorder (BD)

12 First Episode Psychosis (FEP)

13 Control subjects

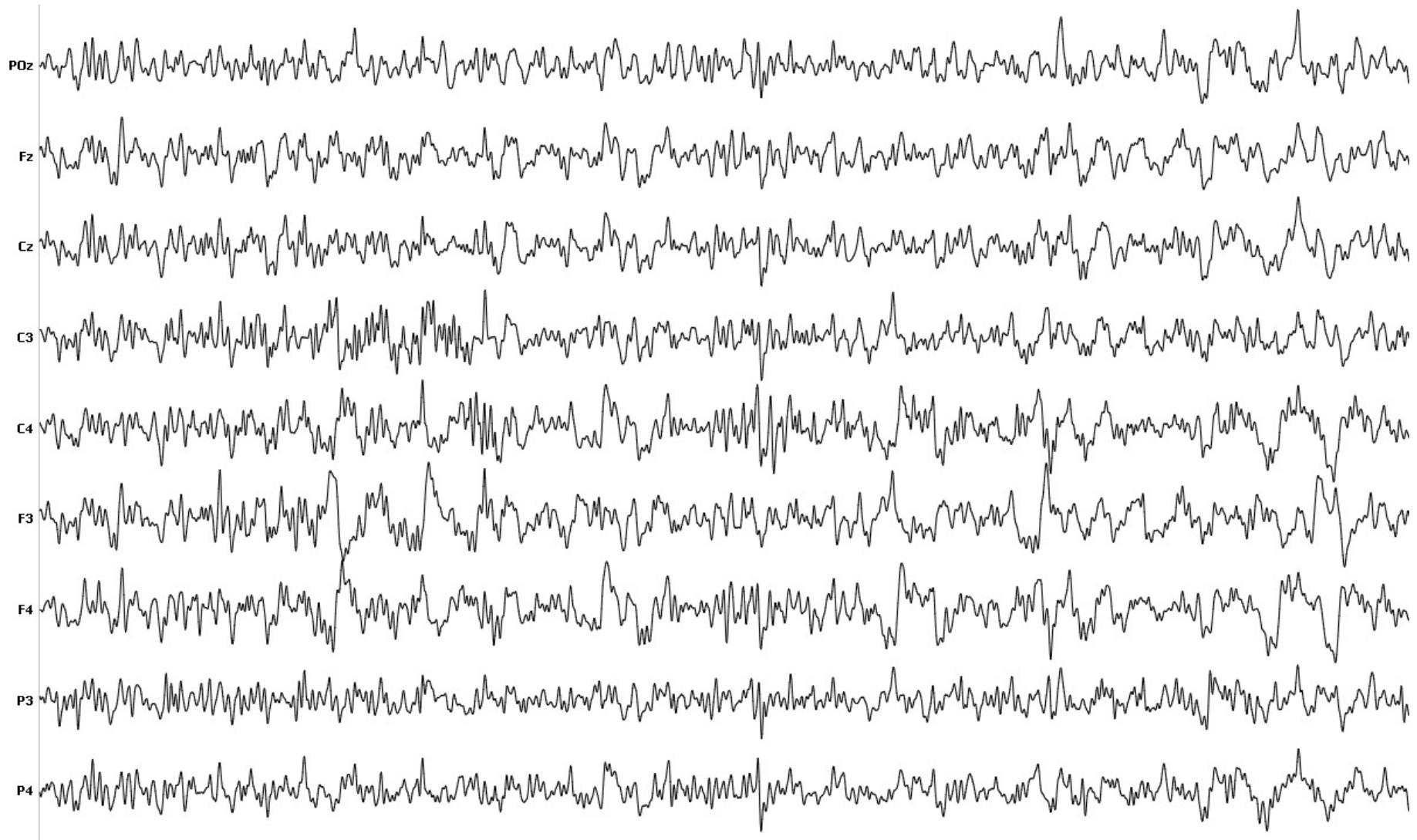
Sistema Socio Sanitario



Regione
Lombardia

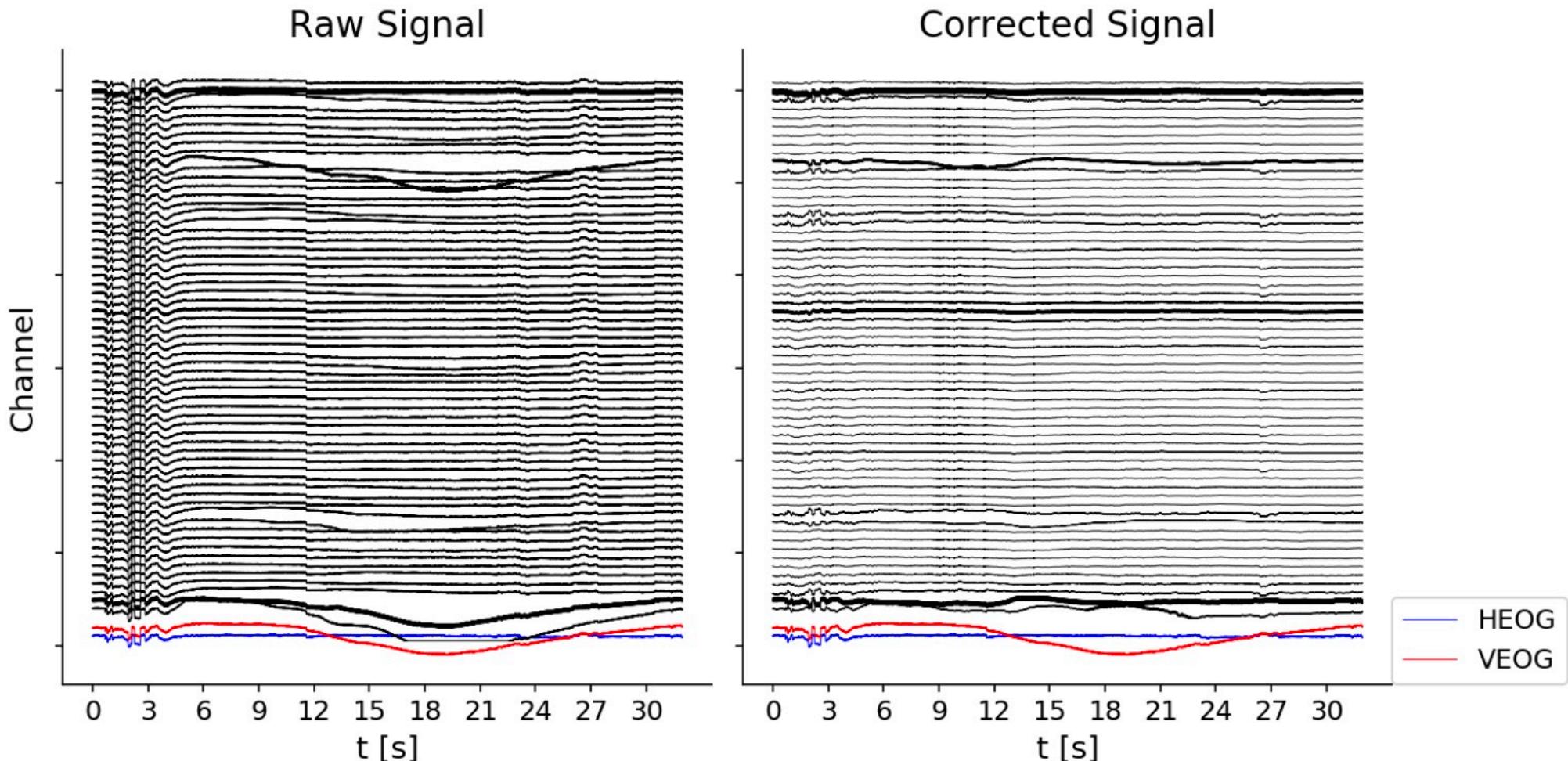
ASST Santi Paolo e Carlo

RAW EEG SIGNALS



DATA PREPROCESSING

Eye Movement Correction

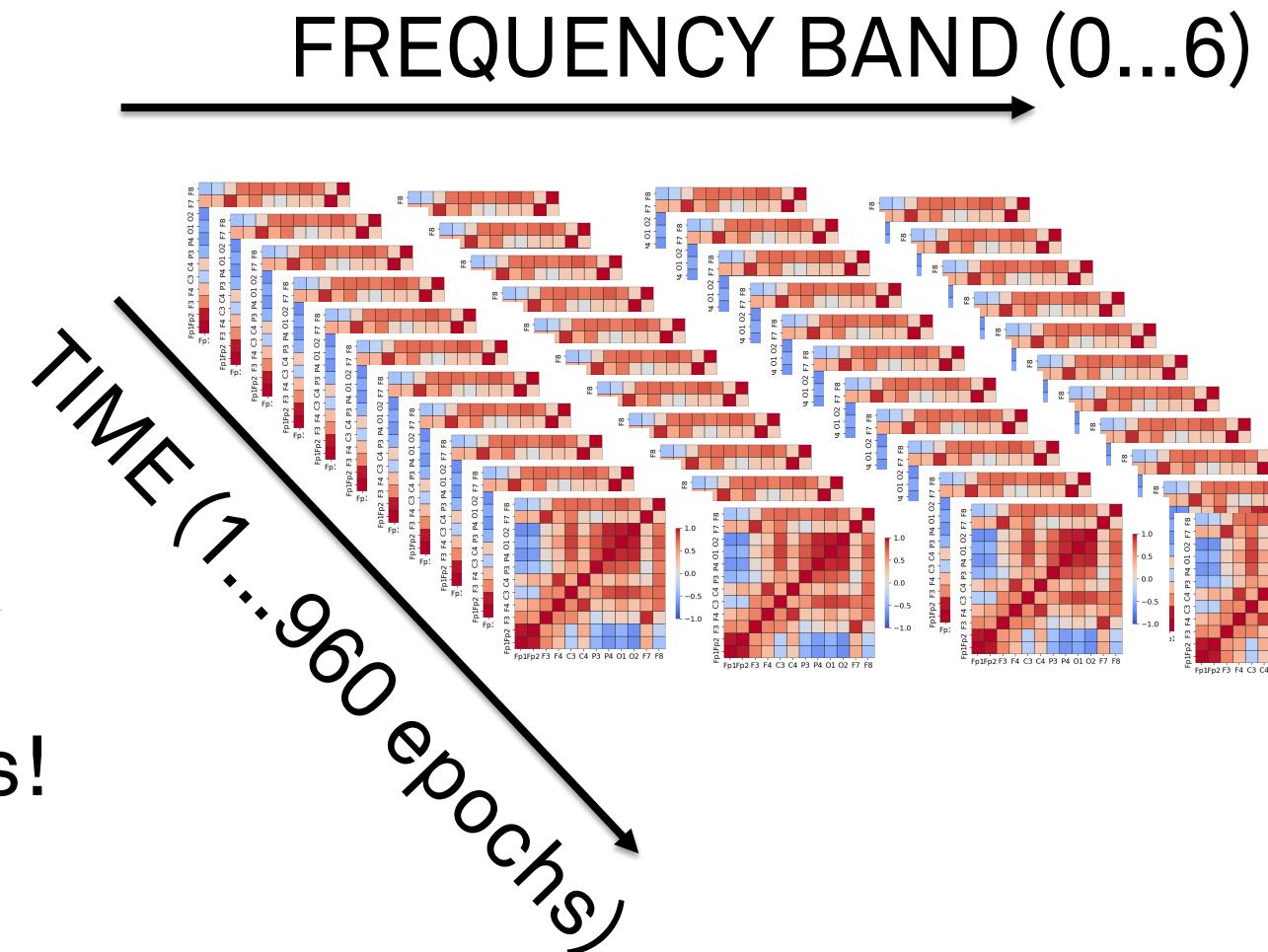
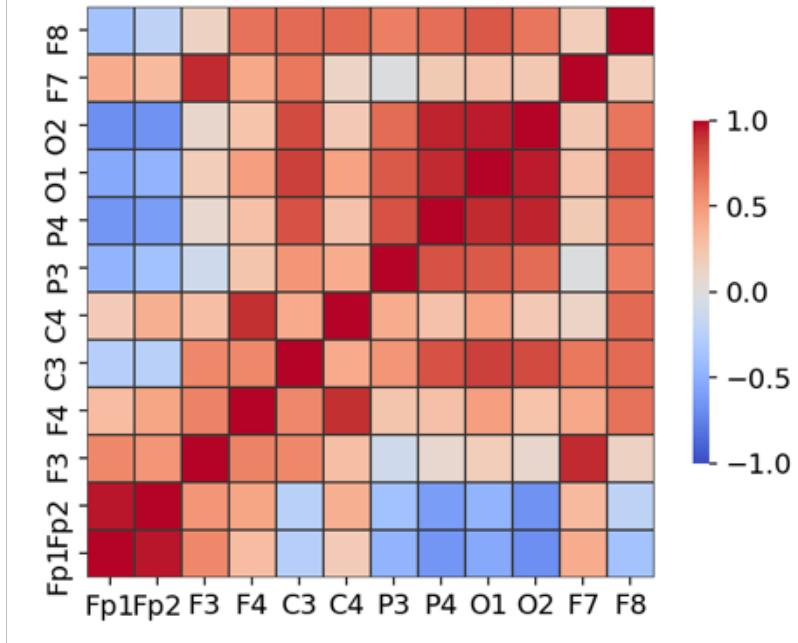


SIGNAL COVARIANCE MATRICES

$$C_{ij} = \frac{\text{cov}(x_i, x_j)}{\sigma_{x_i} \sigma_{x_j}}.$$

30 seconds timesteps

7 bands: [0.5-1],[1-2],[2-4],[4-8],[8-16],
[16-32], [32-64] Hz

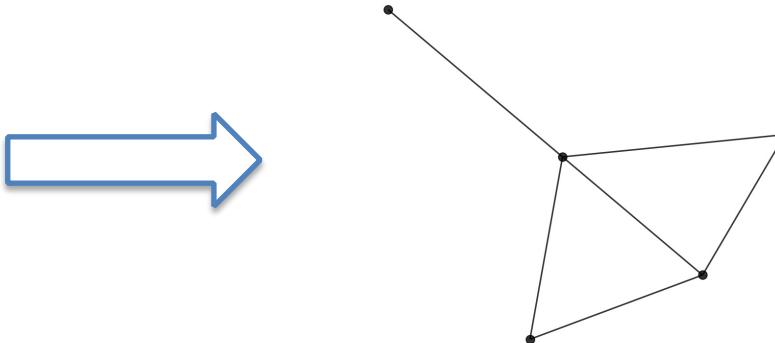


6720 62x62 matrices!

Dimensional reduction
by network representation

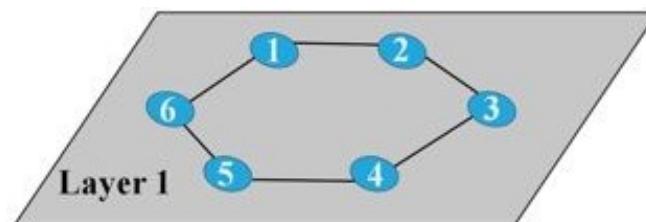
SIMPLE NETWORK CONSTRUCTION (EXAMPLE)

$$A = \begin{pmatrix} 0 & 0 & 1 & 0 & 1 \\ 0 & 0 & 0 & 0 & 1 \\ 1 & 0 & 0 & 1 & 1 \\ 0 & 0 & 1 & 0 & 1 \\ 1 & 1 & 1 & 1 & 0 \end{pmatrix}$$

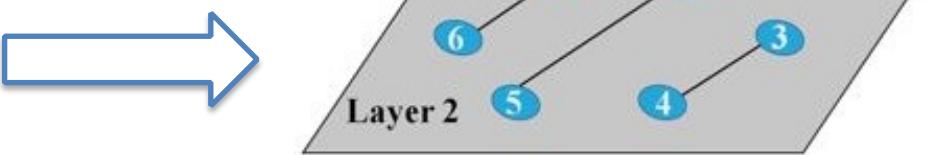


MULTILAYER NETWORK (EXAMPLE)

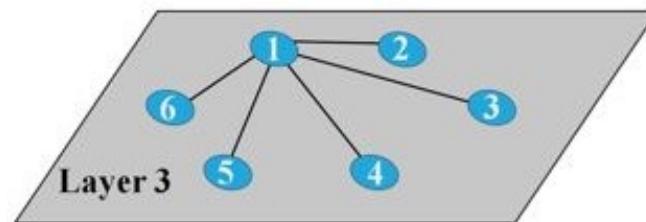
$$A^1 = \begin{pmatrix} 0 & 1 & 0 & 0 & 0 & 1 \\ 1 & 0 & 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 & 0 & 1 \\ 1 & 0 & 0 & 0 & 1 & 0 \end{pmatrix}$$



$$A^2 = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

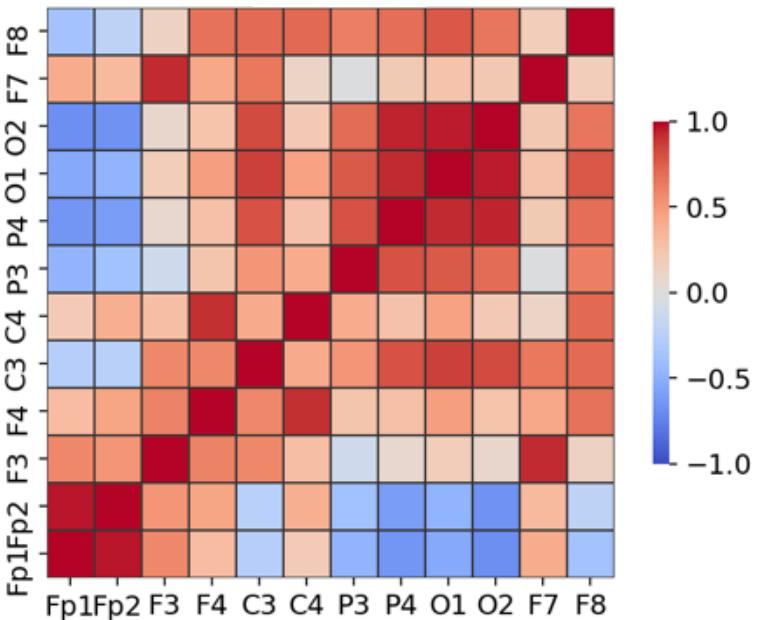


$$A^3 = \begin{pmatrix} 0 & 1 & 1 & 1 & 1 & 1 \\ 1 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$



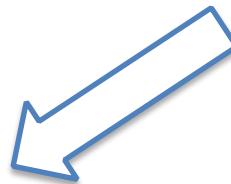
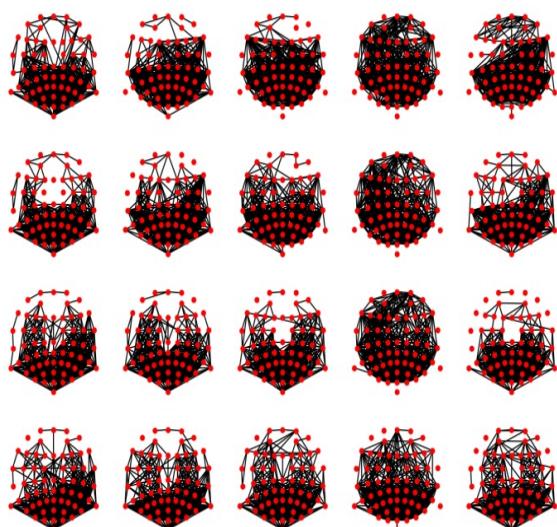
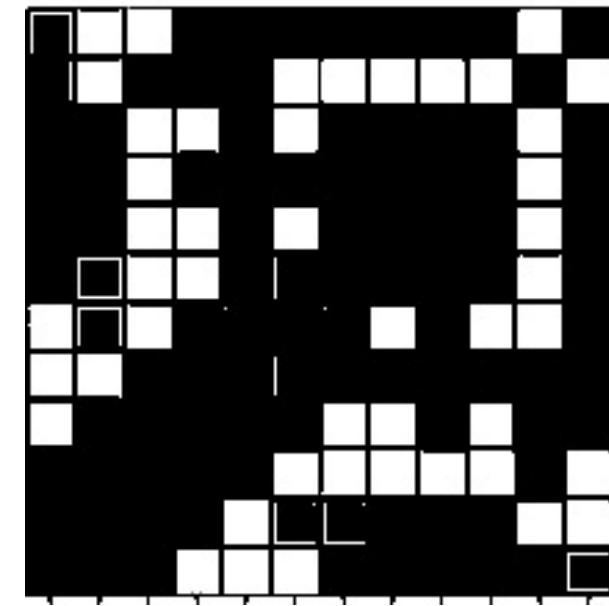
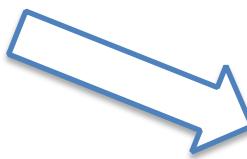
FROM COVARIANCE MATRIX TO NETWORK

$C_{ij}^b(t)$



$$A_{ij}^b(t) = \begin{cases} 1 & \text{if } |C_{ij}^b(t)| \geq \theta^* \\ 0 & \text{else} \end{cases}$$

Θ^*



How to chose θ^* ?

NETWORK JENSEN-SHANNON DIVERGENCE

De Domenico & Biamonte 2016

$$\rho = \frac{e^{-\tau L}}{Z}$$

NETWORK “DENSITY MATRIX”

$$Z = \text{Tr}[e^{-\tau L}] \quad \text{DIFFUSION PROPAGATOR AT TIME } \tau$$

$$S(\rho) = \log_2 Z + \frac{\tau}{\ln 2} \text{Tr}[L\rho] \quad \text{NETWORK “ENTROPY”}$$

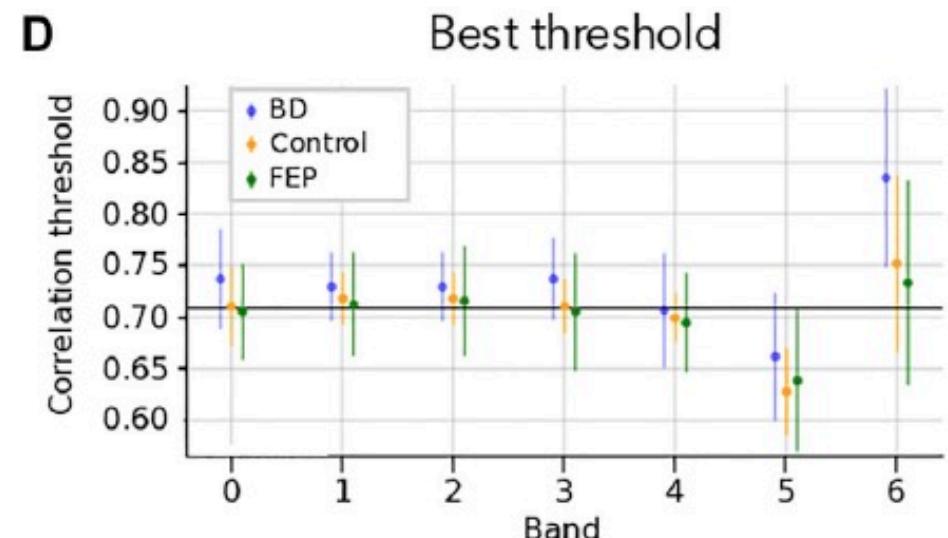
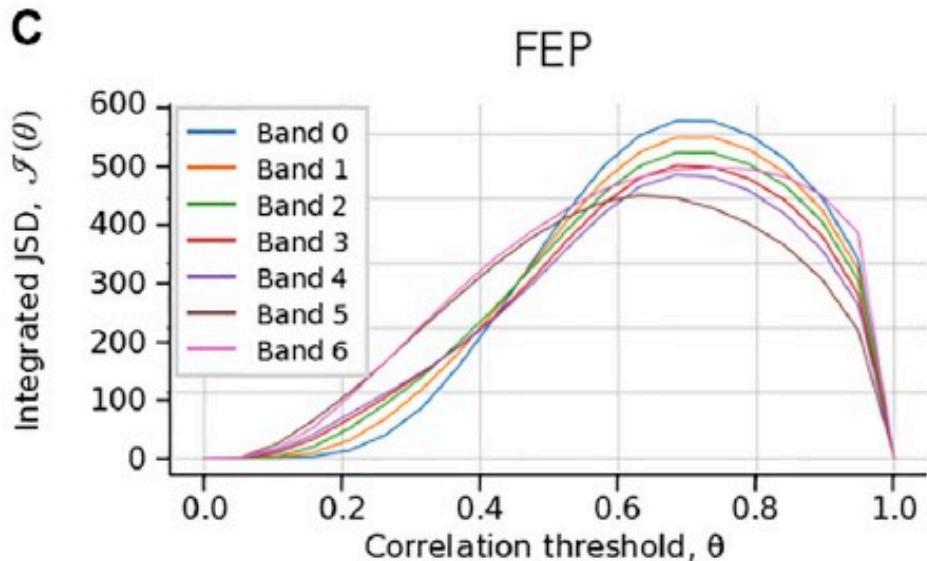
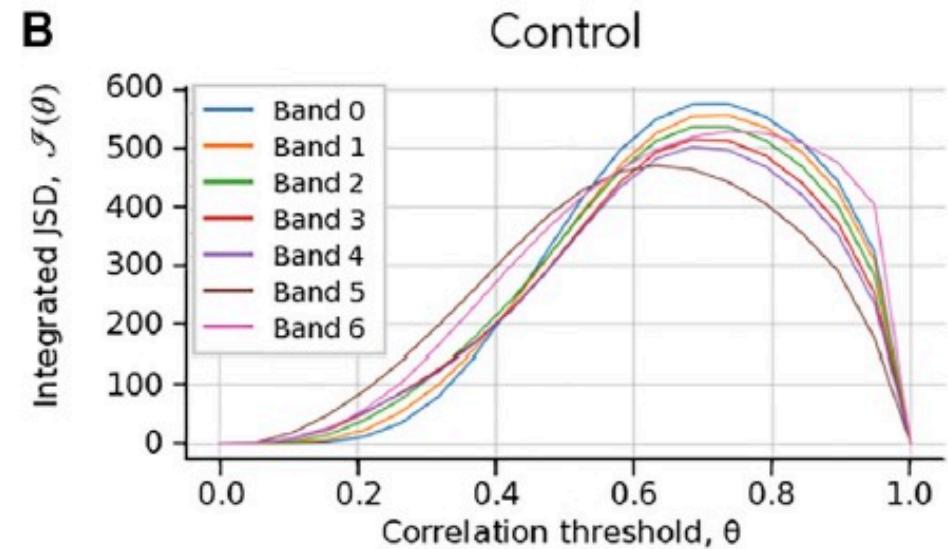
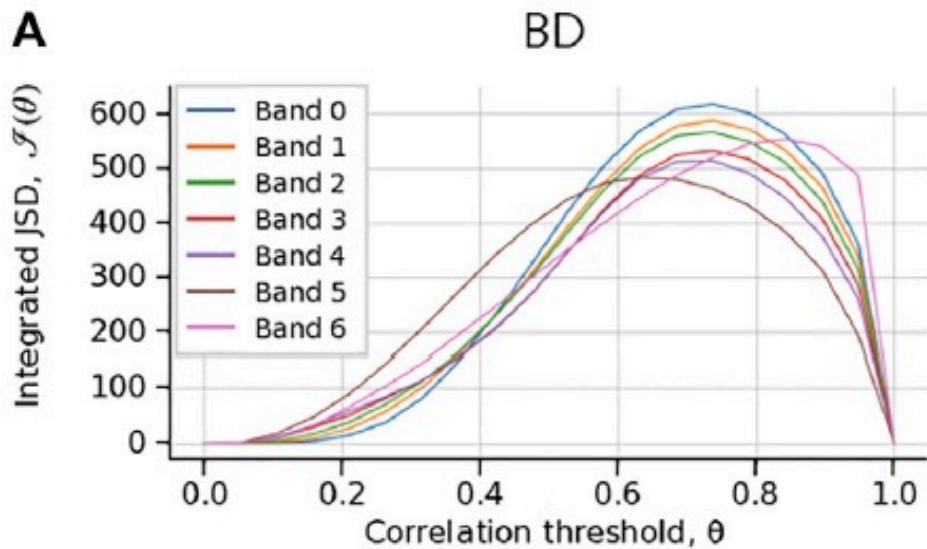
$$J(\rho|\sigma) = S\left(\frac{\rho + \sigma}{2}\right) - \frac{1}{2}(\rho + \sigma) \quad \text{J-S DIVERGENCE}$$

$$\mathcal{I}(\theta) = \sum_{t=1}^T J(\rho_t(\theta) | \rho_{t-1}(\theta)) \quad \text{INTEGRATED J-S DIVERGENCE}$$

MAXIMIZE INTEGRATED J-S DIVERGENCE

$$\theta_{b,p}^* = \operatorname{argmax}_{\theta \in [0,1]} \mathcal{I}_{b,p}(\theta)$$

$$\theta^* = \langle \theta_{b,p}^* \rangle_{b,p}$$



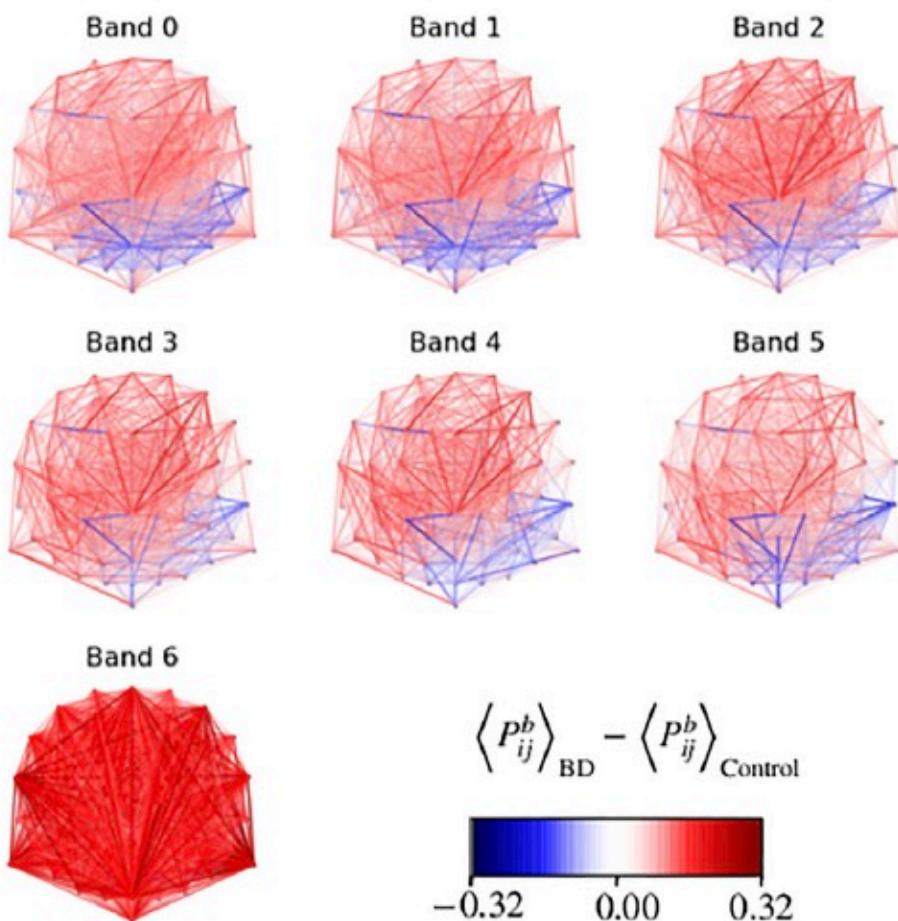
EEG MULTILAYER NETWORKS



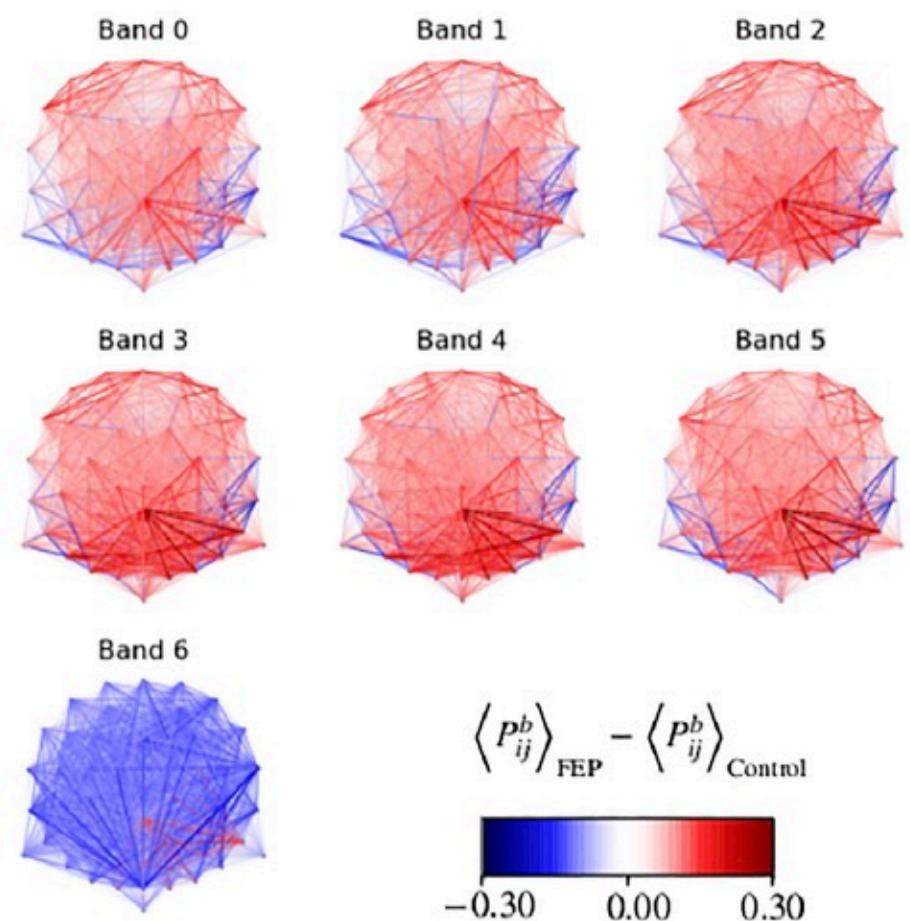
NETWORK EDGE PRESENCE

$$P_{ij}^b = \langle A_{ij}^b(t) \rangle_t$$

C Fixed Threshold



D Fixed Threshold



NETWORK MEASURES

Betweenness Centrality:

$$BC = \frac{1}{N} \sum_{i=1}^N c_B(i)$$

$$c_B(i) = \frac{2}{(N-1)(N-2)} \sum_{j,k \in V} \frac{\sigma(j,k|i)}{\sigma(j,k)}$$

Number of shortest paths between j and k

passing from node i

Clustering Coefficient:

$$c = \frac{1}{N} \sum_{i=1}^N c_i$$

$$c_i = \frac{2 \cdot t_i}{k_i \cdot (k_i - 1)}$$

Number of triangles involving node i

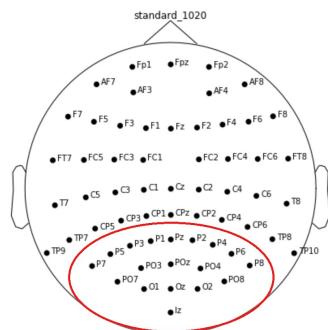
Degree of node i

Average Path Length:

$$a_G = \frac{1}{N \cdot (N-1)} \sum_{i \neq j} d(i,j).$$

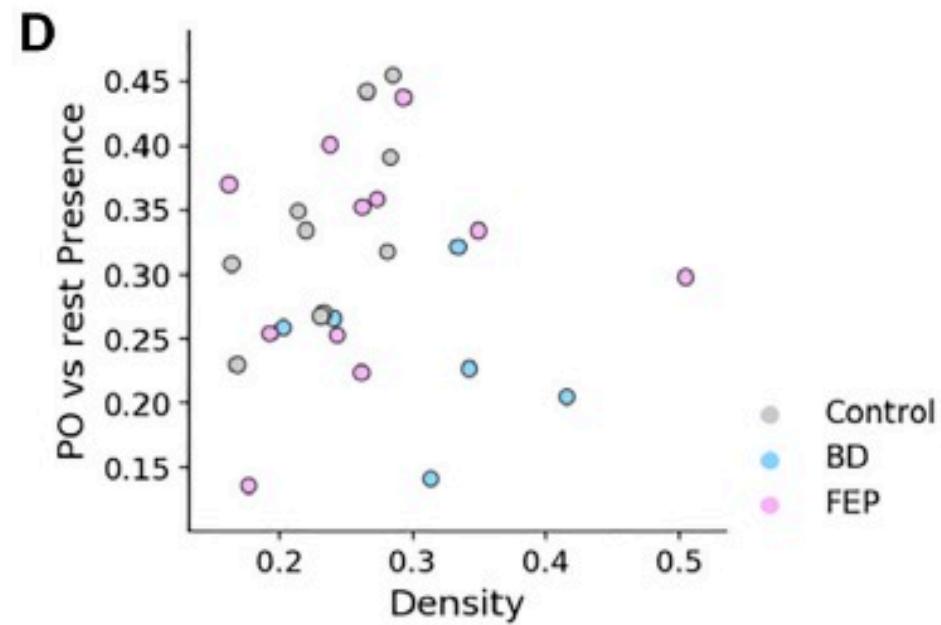
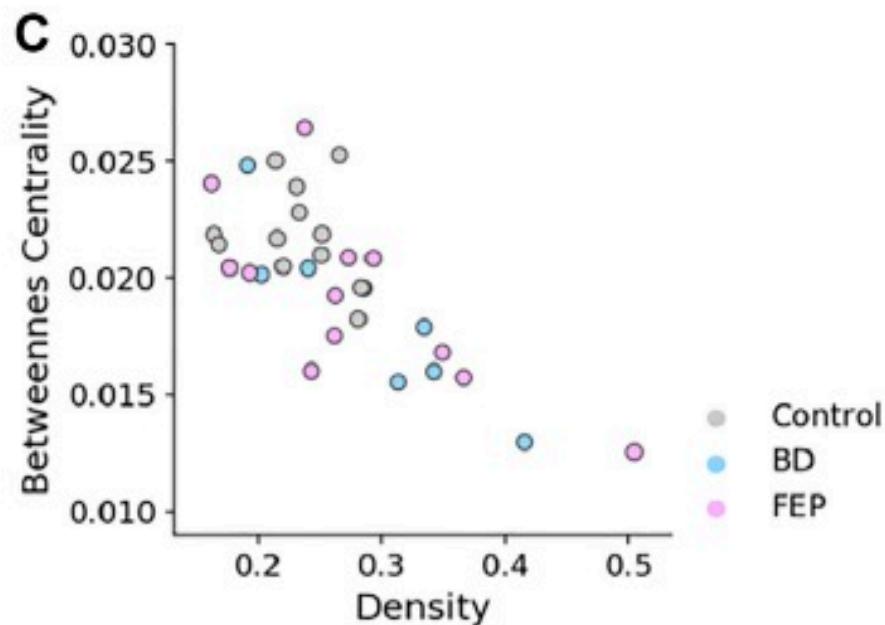
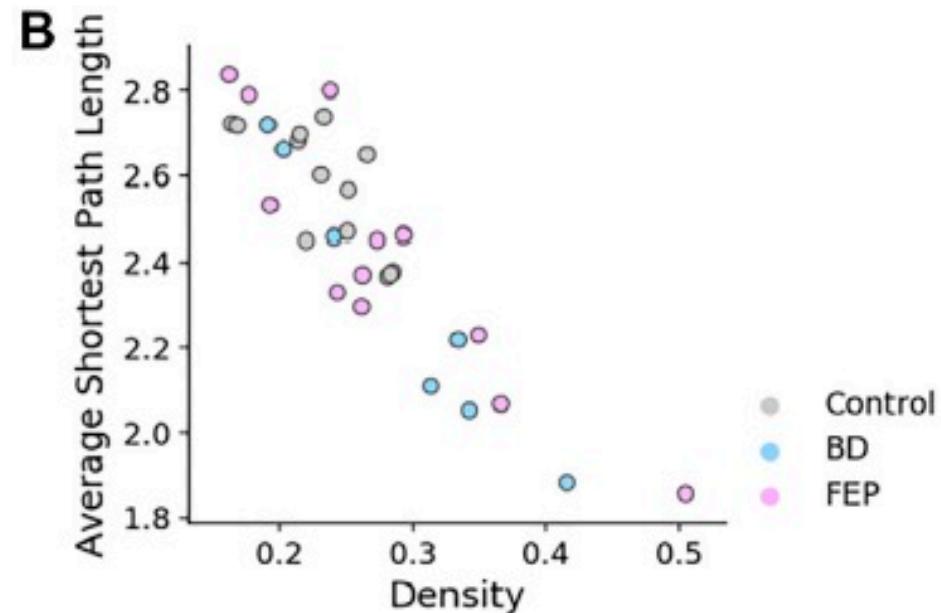
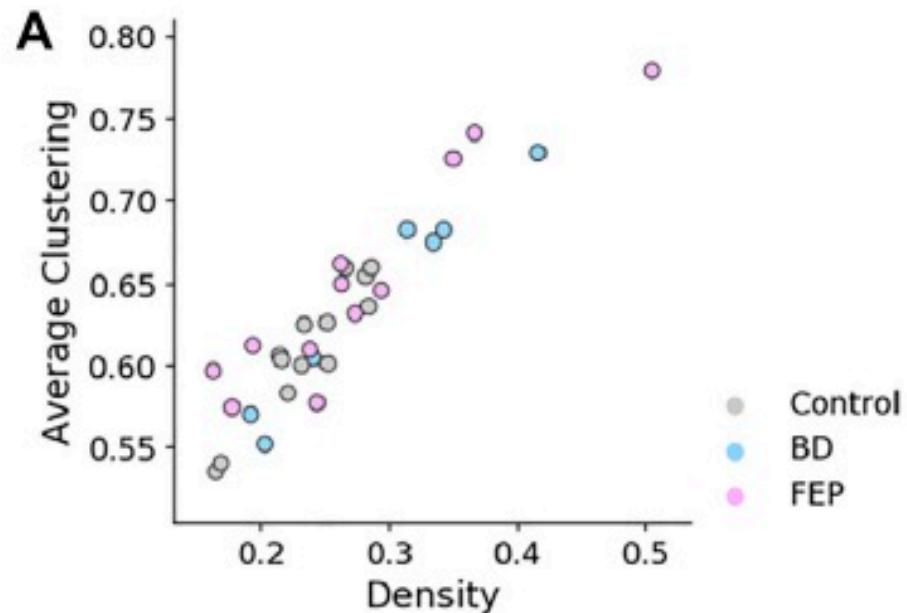
Length of shortest path between i and j

Parieto-Occipital Edge Presence:



$$P_{PO} = \langle P_{ij}^b \rangle_{(ij) \in PO} - \langle P_{ij}^b \rangle_{(ij) \notin PO} \quad P_{ij}^b = \langle A_{ij}^b(t) \rangle_t$$

DENSITY DEPENDENCE OF NETWORK MEASURES

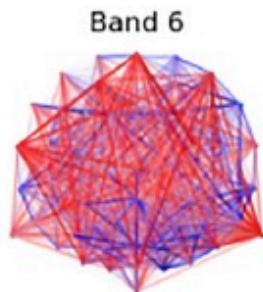
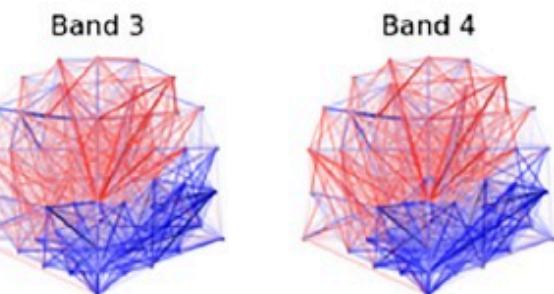
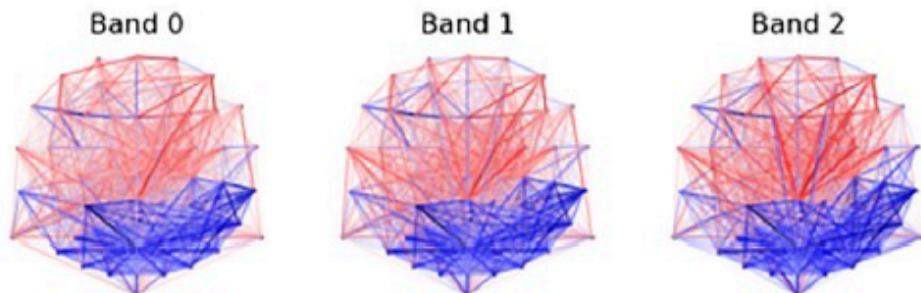


NETWORK EDGE PRESENCE (FIXED DENSITY)

DENSITY IS CONSTANT AND CORRESPONDS
TO THE AVERAGE DENSITY OF FIXED THRESHOLD NETWORKS

A

Fixed Density

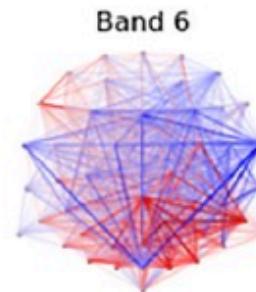
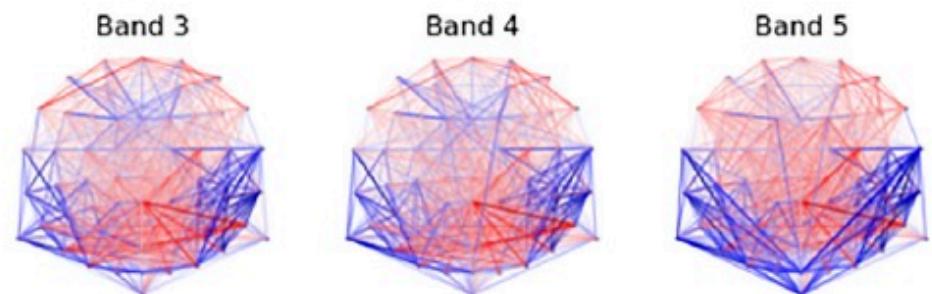
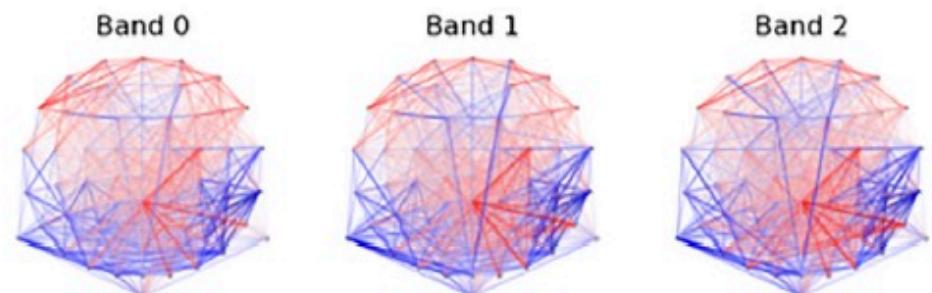


$$\left\langle P_{ij}^b \right\rangle_{BD} - \left\langle P_{ij}^b \right\rangle_{Control}$$

-0.26 0.00 0.26

B

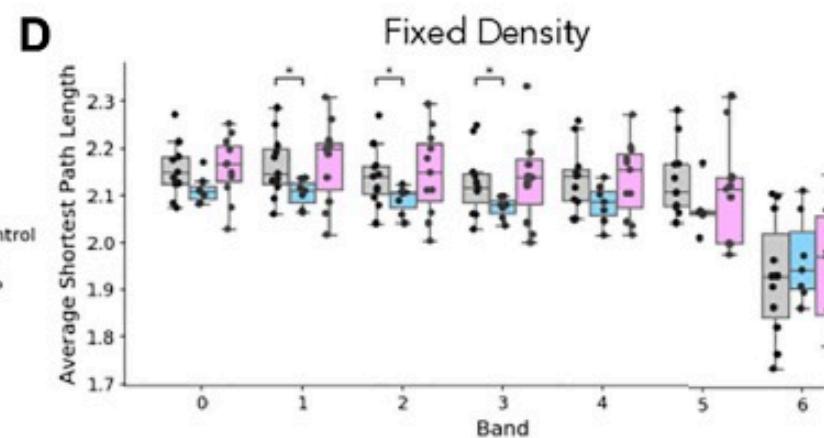
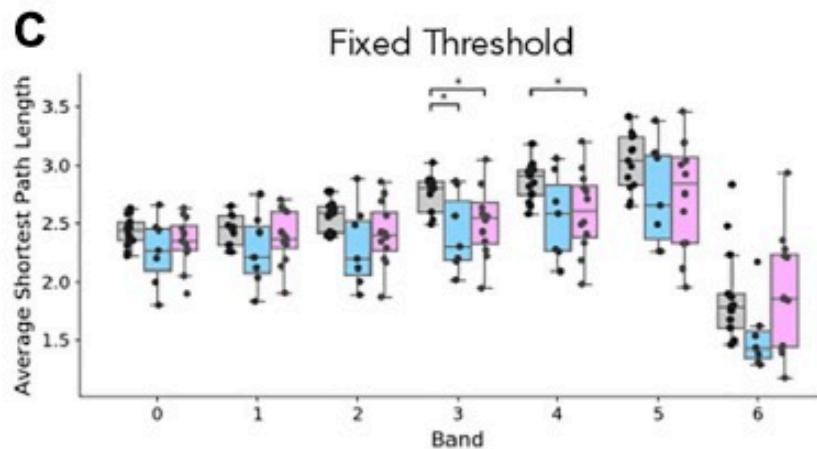
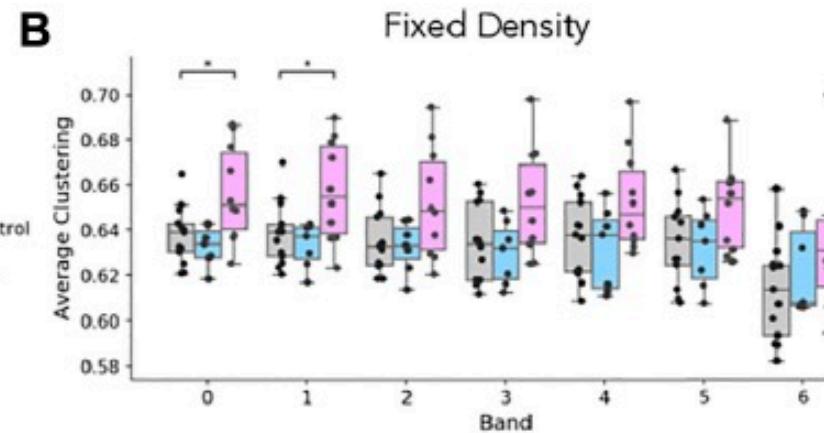
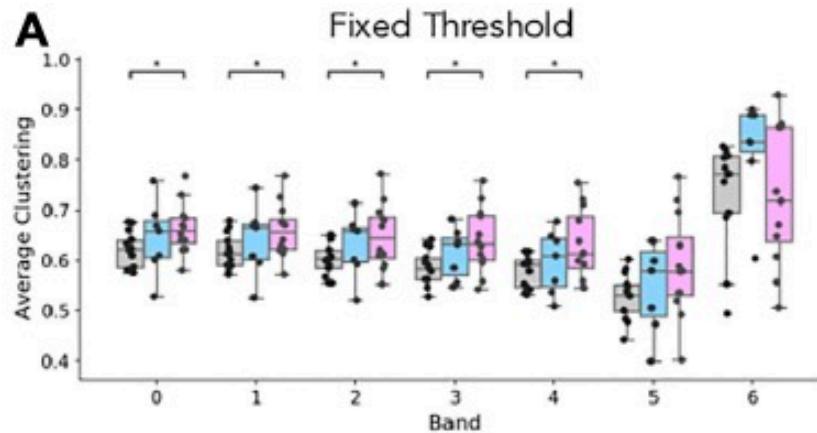
Fixed Density



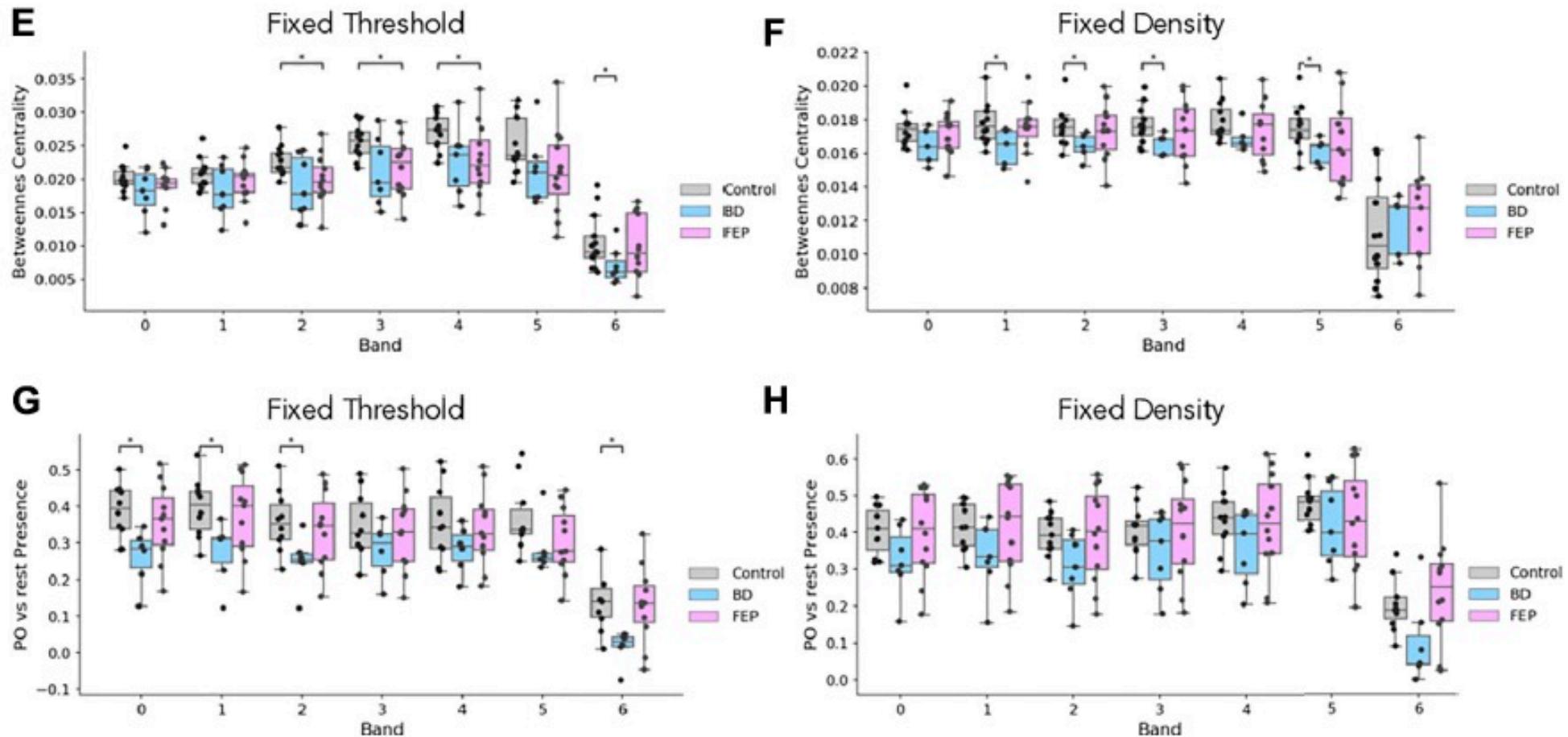
$$\left\langle P_{ij}^b \right\rangle_{FEP} - \left\langle P_{ij}^b \right\rangle_{Control}$$

-0.33 0.00 0.33

NETWORK MEASURES



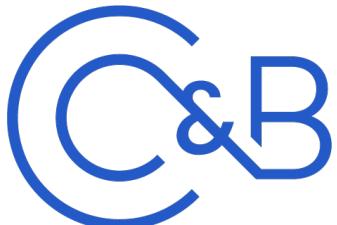
NETWORK MEASURES



SUMMARY

EEG network representation
Network measures
Patients stratification

COWORKERS:



CENTER
COMPLEXITY
& BIOSYSTEMS

University of Milan



Francesc
Font-Clos



Benedetta
Spelta

CLINICAL COLLABORATORS:

Armando D'Agostino
Francesco Donati
Simone Sarasso
Maria P. Canevini

Sistema Socio Sanitario



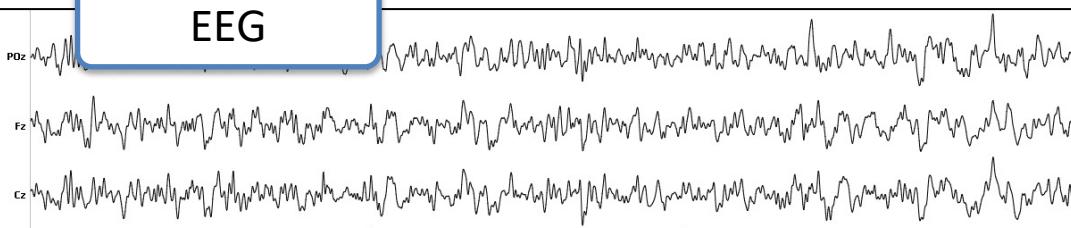
Regione
Lombardia

ASST Santi Paolo e Carlo

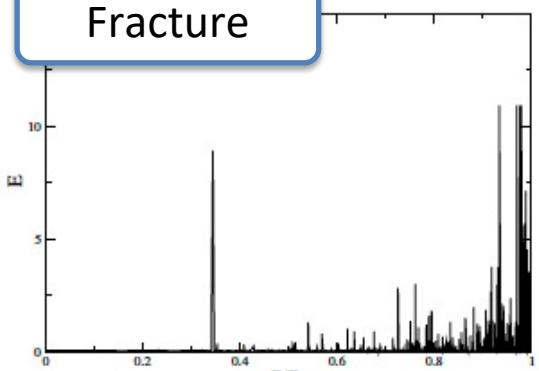
PAPER:

Font-Clos, F., Spelta, B., D'Agostino, A., Donati, F., Sarasso, S., Canevini, M.P., Zapperi, S. and La Porta, C.A., 2021. Information optimized multilayer network representation of high density electroencephalogram recordings. *Frontiers in Network Physiology*, p.8.

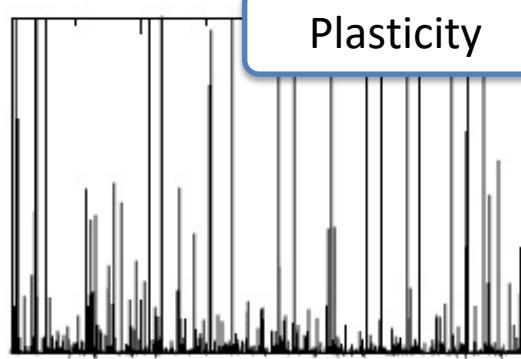
EEG



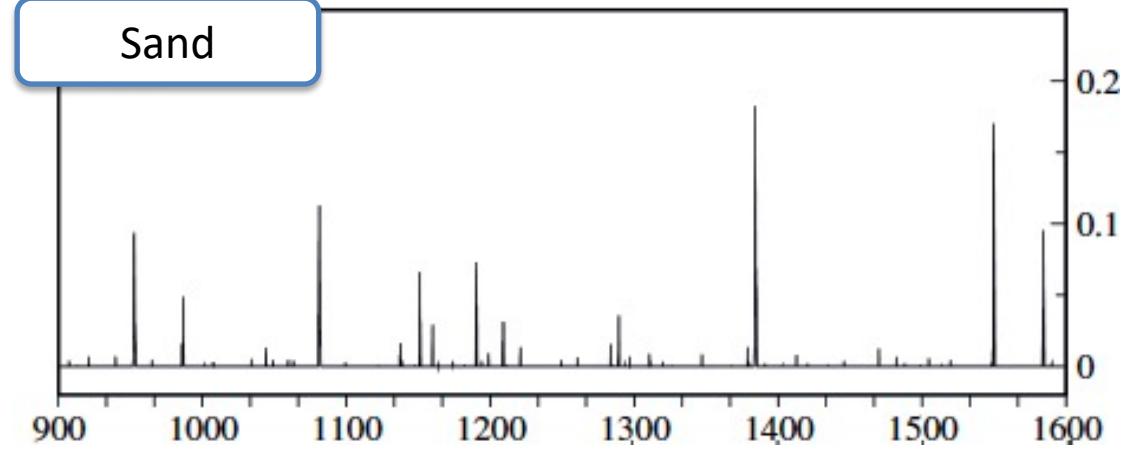
Fracture



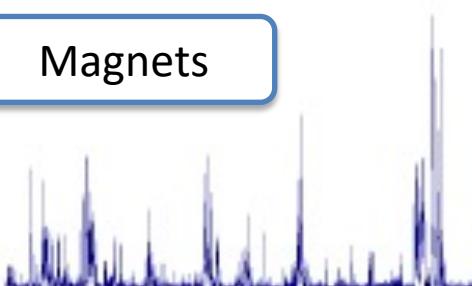
Plasticity



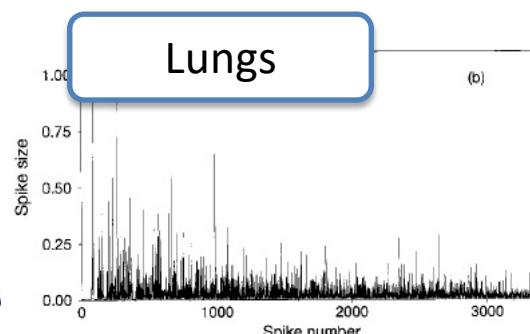
Sand



Magnets

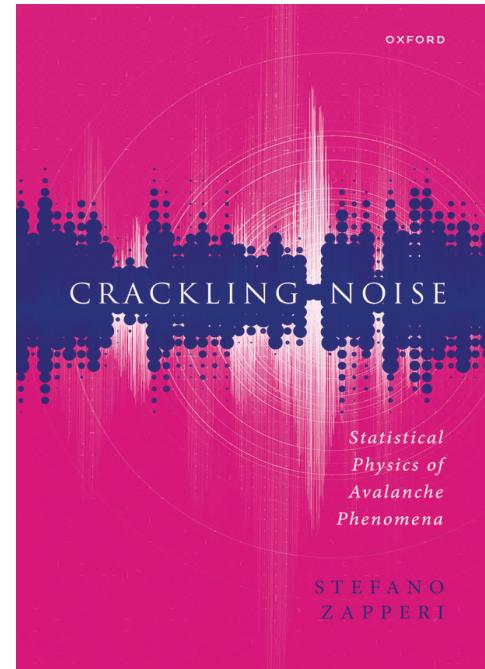


Lungs



Crackling Noise

Statistical Physics of Avalanche Phenomena



The response of materials and the functioning of devices is often associated with noise. In this book, Stefano Zapperi concentrates on a particular type of noise, known as crackling noise, which is characterized by an intermittent series of broadly distributed pulses. While representing a nuisance in many practical applications, crackling noise can also tell us something useful about the microscopic processes ruling a material's behavior.

Features

- Provides a comprehensive overview of key concepts and theoretical models
- Explores the many applications of the theory of crackling noise in materials science
- Includes expansive discussions considering implications for the life sciences

THE AUTHOR: STEFANO ZAPPERI

Stefano Zapperi is Professor of Theoretical Condensed Matter Physics and Coordinator of the Center for Complexity and Biosystems at the University of Milan.

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