

INFORMATION OPTIMIZED MULTILAYER NETWORK REPRESENTATION OF HIGH DENSITY ELECTROENCEPHALOGRAPH RECORDINGS



CENTER FOR
COMPLEXITY
& BIOSYSTEMS

University of Milan

29 07 2022
Lake Como School



DEPARTMENT OF
PHYSICS
“ALDO PONTREMOLI”

Stefano Zapperi
www.smmlab.it



DEPARTMENT OF
ENVIRONMENTAL
SCIENCE AND POLICY

Caterina A. M. La Porta
www.oncolab.unimi.it

Unterstützt von / Supported by


Alexander von Humboldt
Stiftung / Foundation

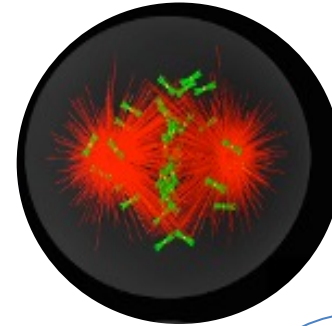


CC&B RESEARCH

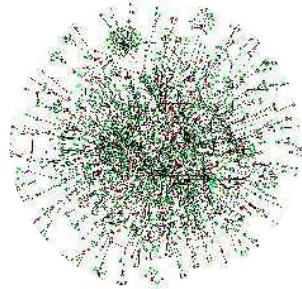
Neurodegenerative diseases



Cancer



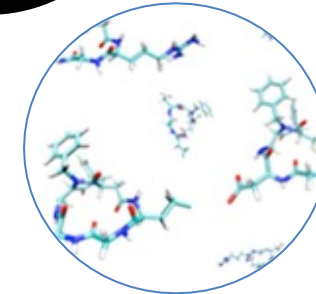
Network Medicine



Data science

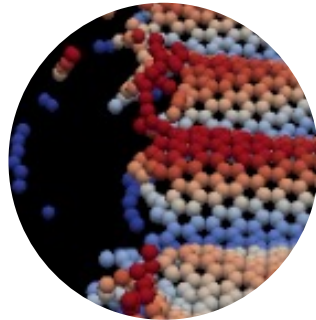


Protein simulations

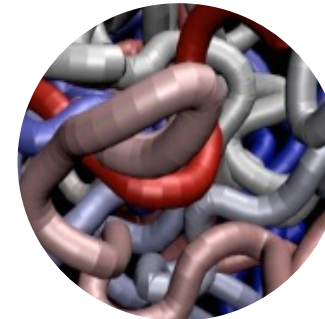


CENTER FOR
COMPLEXITY
& BIOSYSTEMS
University of Milan

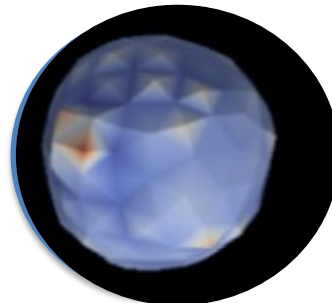
Disordered Systems



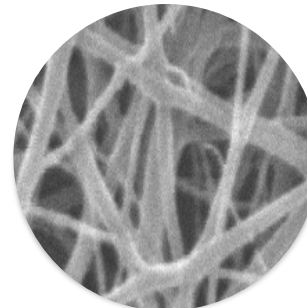
Chromatin conformations



Cell biomechanics



Bio-inspired materials



OUTREACH

Newsletters

ISSUE #2 / OCTOBER, 2016
NEWSLETTER

COMPLEXITYBIOSYSTEMS.IT
 COMPLEXITYBIOSYSTEMS.IT

Editorial

Picturing things in the cellular

Geometry, topology and mechanics

Cancer as an emerging complex phenomenon: the new frontiers of machine learning in biology

CATERINA LA PORTA
 CC&B founding member

It is already one year for Complexity and I started its activities of Milan. A very exciting journey. The corner was colleagues from the Physics, Bioscience Departments. We were a new forum to tackle problems at the front through an interdisciplinary approach based on complexity in general, and in particular, in the field of cell biology and computer science. Vigna and Paolo Bolognani large scale data analysis theory, and physics

The various groups at the turn of the DNA sequencing. These are not all, of course, for the development. For instance, small molecules - the genes - and in what type of produced. Cells in a given space, and so the spatial organization within the cellular genome, called it a widespread mechanism that genes, and thus responding precisely.

Having a picture of spatially organized cells can thus be a very interesting and helps us to investigate

Tumors are highly complex systems. Unraveling the biological dynamics that regulate their insurgence and growth is a major objective in biomedicine, and machine learning could provide a valuable help in such a challenge.

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-

ors and between patients has become particularly relevant in view of a cancer precision medicine.

Therefore, nowadays there are two complementary aspects in tumors to be tackled. At macroscopic level, it is important to identify the collective properties of tumors or subcategorize 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. Distinguishing 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 models 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-

portant to develop new machine learning/data science methods and tools, and to apply them to important problems in medicine. While Deep learning has been applied to genomic medicine, its impact has not yet reached its full potential. The genome is not always predictive of the phenotype and this fact prevents important advances in medicine. Deep learning can bridge the genotype-phenotype divide, by incorporating an exponential growing amount of data and accounting for the multiple layers of complex biological processes that relate the genotype to the phenotype. In general, deep learning is successful in application where the humans are naturally adept, i.e. image speech etc., but it is not intrinsically designed to understand the genome. To achieve these results, the interdisciplinary approach of CC&B provides a common answer to the language barriers between the different disciplines from physics and computer science to biology and biomedicine.

In this way it would be possible to approach the study of heterogeneous and dynamic systems like cancers, by investigating the emergence of tumorous phenotype from the interactions and properties of complex biological networks.

WEB: www.complexitybiosystems.it

C&B
 CENTER FOR COMPLEXITY & BIOSYSTEMS
 University of Milan

→ **THE PHYSICS OF CANCER**

WHO WE ARE
 STEERING COMMITTEE
 CORE MEMBERS

Social media (Youtube, twitter)

YouTube IT

Search

C&B
 CENTER FOR COMPLEXITY & BIOSYSTEMS
 University of Milan

CC&B Unimi

Home About

C&B
 CENTER FOR COMPLEXITY & BIOSYSTEMS
 University of Milan

Tweets
481

VIRTUAL SEMINARS ON COMPLEXITY

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

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 telomers, 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

Mikko J. Alava
/ Aalto University
Caterina A. M. La Porta
/ University of Milan
Alessandro Vespignani
/ Northeastern University
Stefano Zapperi
/ University of Milan

LECTURERS

Luis Amaral / Northwestern University
Martine Ben Amar / UPMC, Paris
Nikolay Dokholyan / UNC, Chapel Hill
Jack Griffith / UNC, Chapel Hill
Jeff Holly / University of Bristol
Sui Huang / Institute for Systems Biology, Seattle
Tim Liedt / LMU, Munich
Michel Labouesse / UPMC, Paris
Fred MacKintosh / Rice University
Leonid Mirny / MIT, Cambridge
Guido Tiana / University of Milan
Jeffrey S. Urbach / Georgetown University
Alessandro Vespignani / Northeastern University

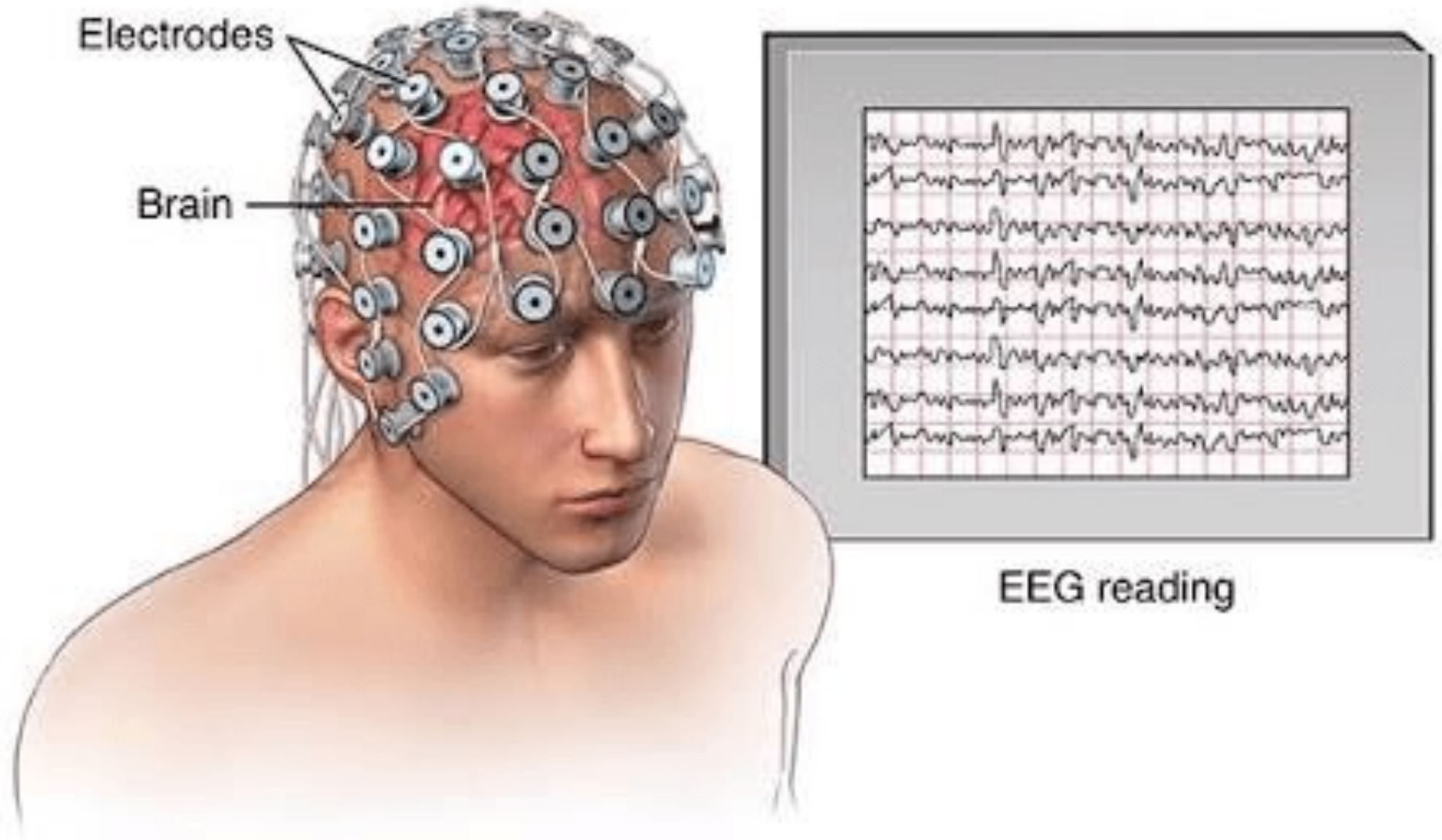
Two fellowships available,
please look at the website:
acst.lakecomoschool.org

DEADLINE FOR
APPLICATIONS
1 MARCH 2017



Villa del Grimaldo
Via per Cernobbio 11 — 22100 Como, Italy
T +39 031 570610 | F +39 031 573365

ELECTROENCEPHALOGRAPH (EEG)



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

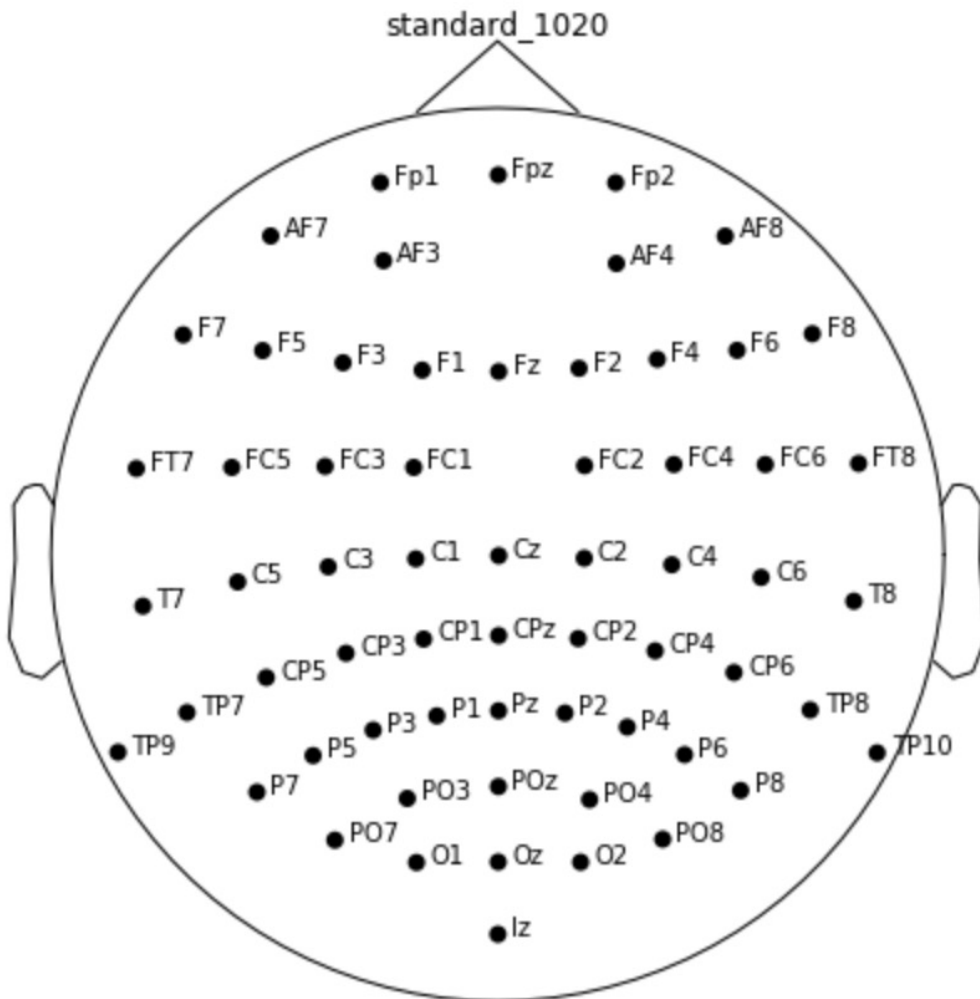
e.g. Patients with mental health issues

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

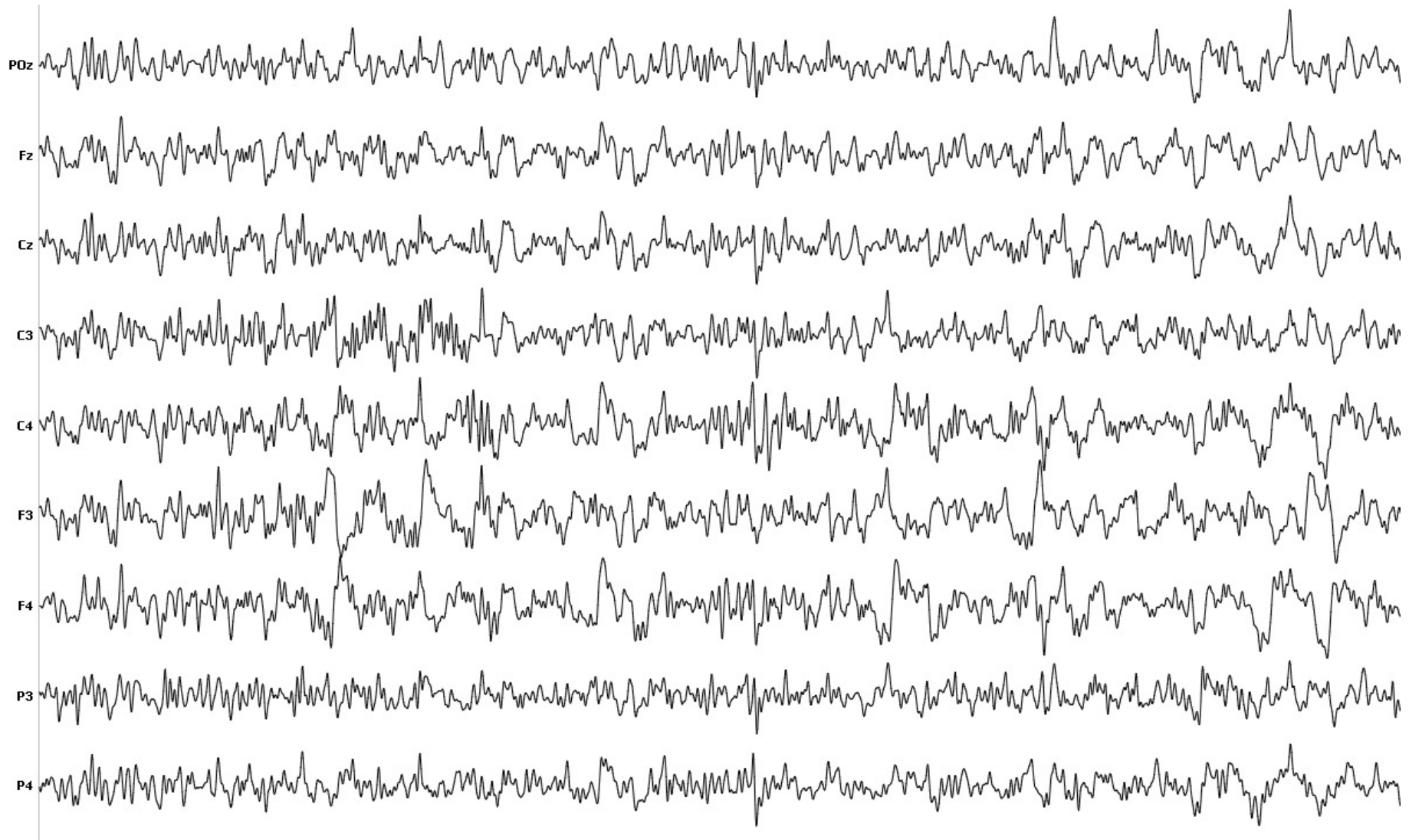
Sistema Socio Sanitario



Regione
Lombardia

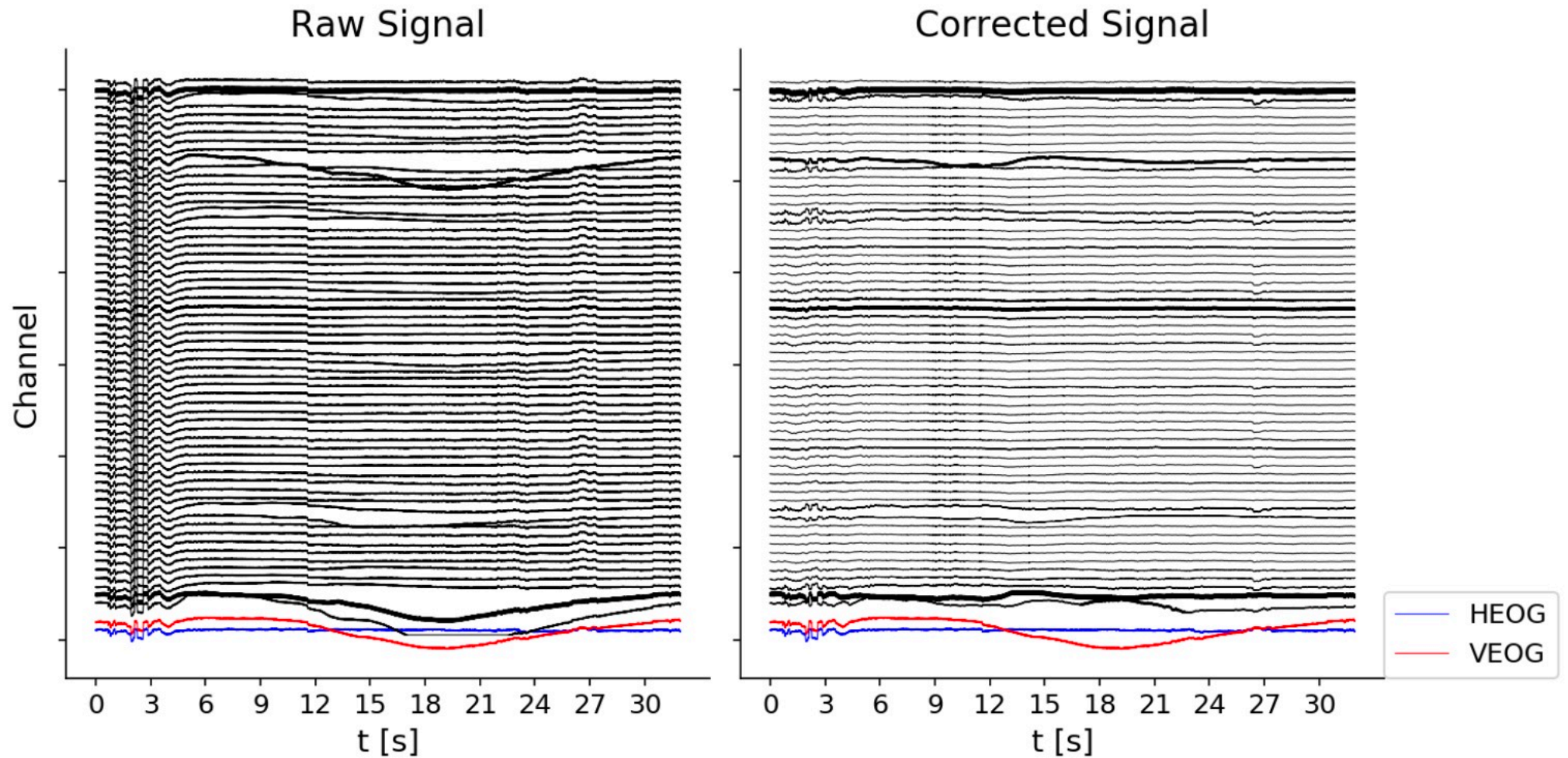
ASST Santi Paolo e Carlo

RAW EEG SIGNALS



DATA PREPROCESSING

Eye Movement Correction

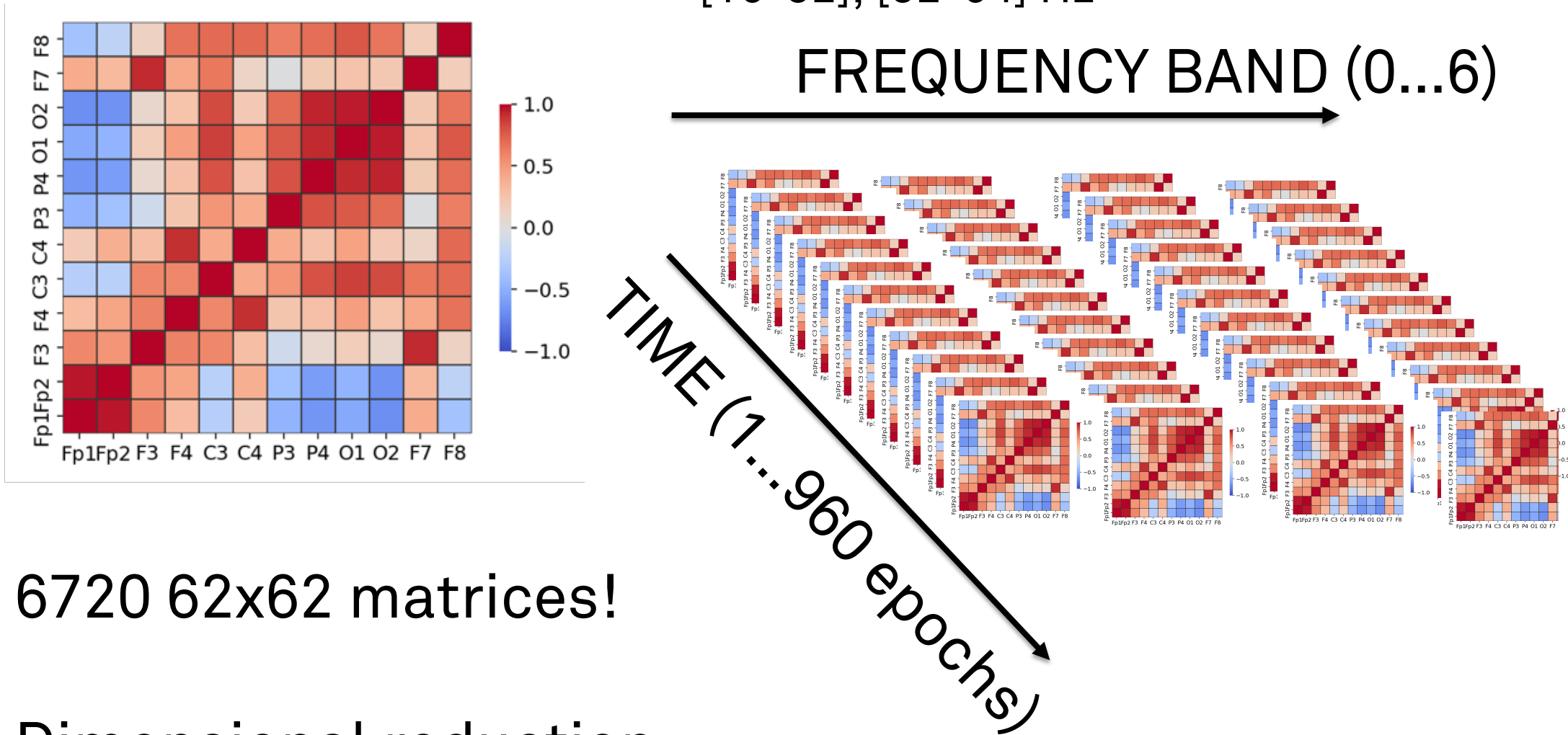


SIGNAL COVARIANCE MATRICES

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

30 seconds timesteps

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

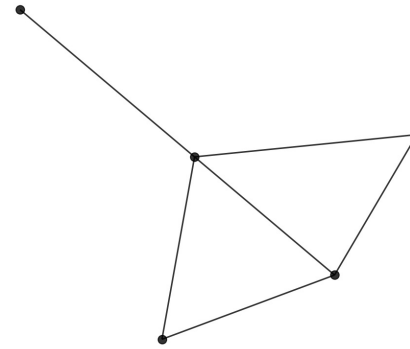


6720 62x62 matrices!

Dimensional reduction
by **network representation**

SIMPLE NETWORK CONSTRUCTION (EXAMPLE)

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

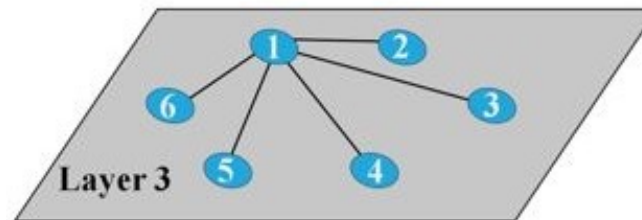
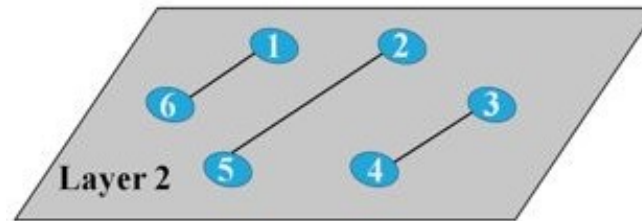
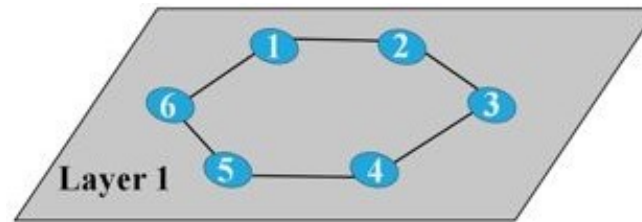


MULTILAYER NETWORK (EXAMPLE)

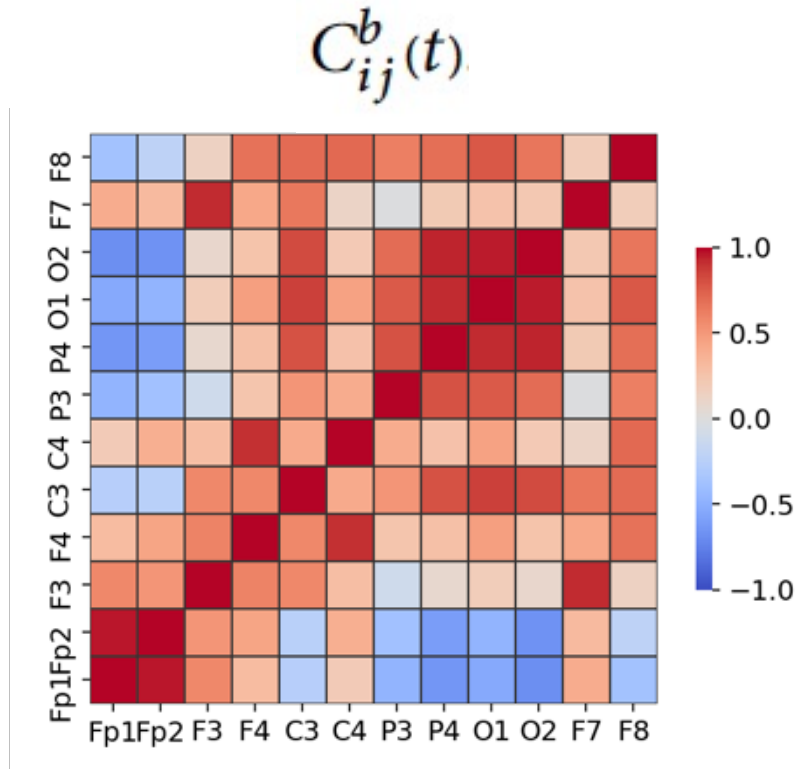
$$A^1 = \begin{pmatrix} 0 & 1 & 0 & 0 & 0 & 1 \\ 1 & 0 & 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 & 0 & 1 \\ 1 & 0 & 0 & 0 & 1 & 0 \end{pmatrix}$$

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

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

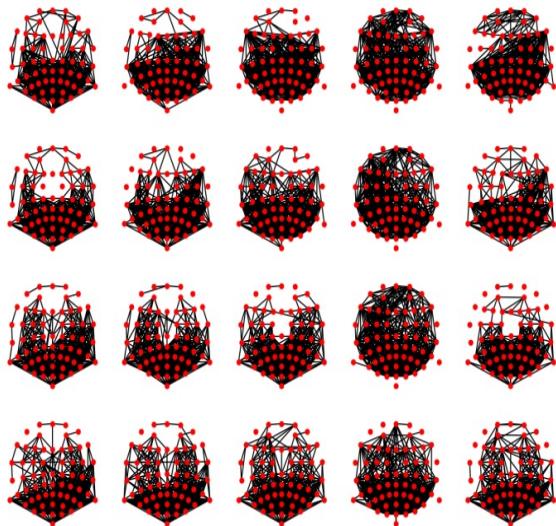
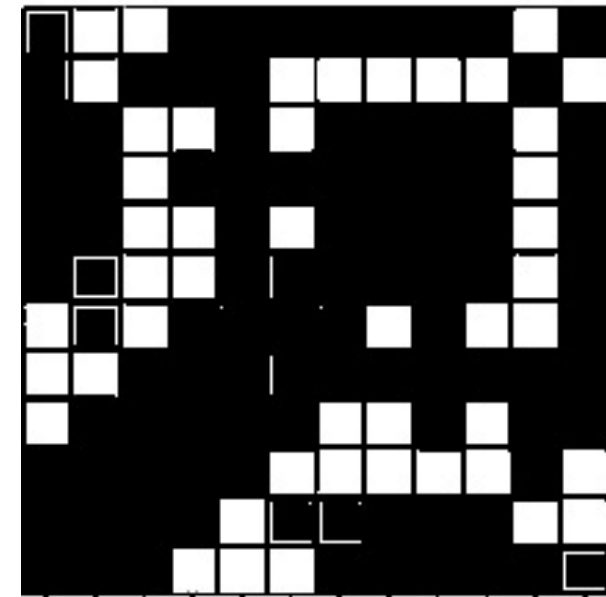


FROM COVARIANCE MATRIX TO NETWORK



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

θ^*



How to choose θ^* ?

NETWORK JENSEN-SHANNON DIVERGENCE

De Domenico & Biamonte 2016

$$\rho = \frac{e^{-\tau L}}{Z} \quad \text{NETWORK "DENSITY MATRIX"}$$

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

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

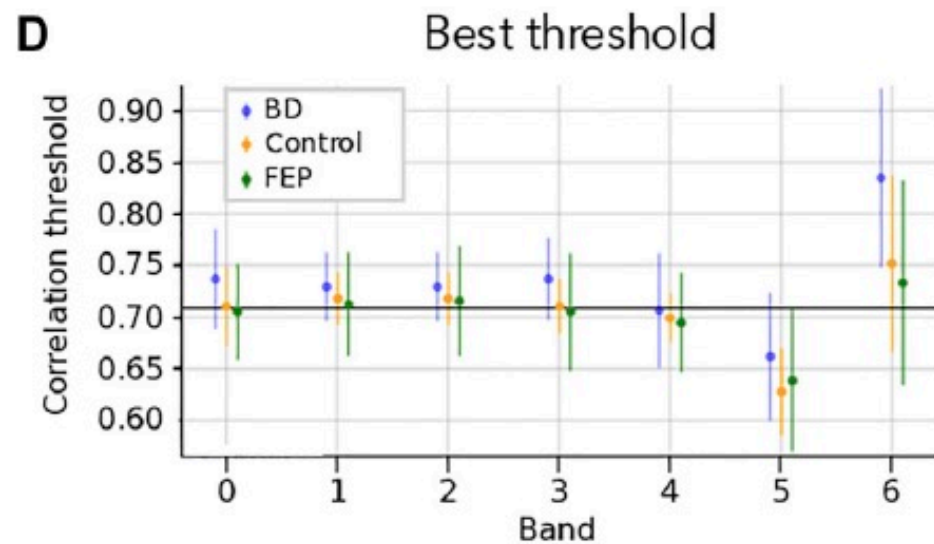
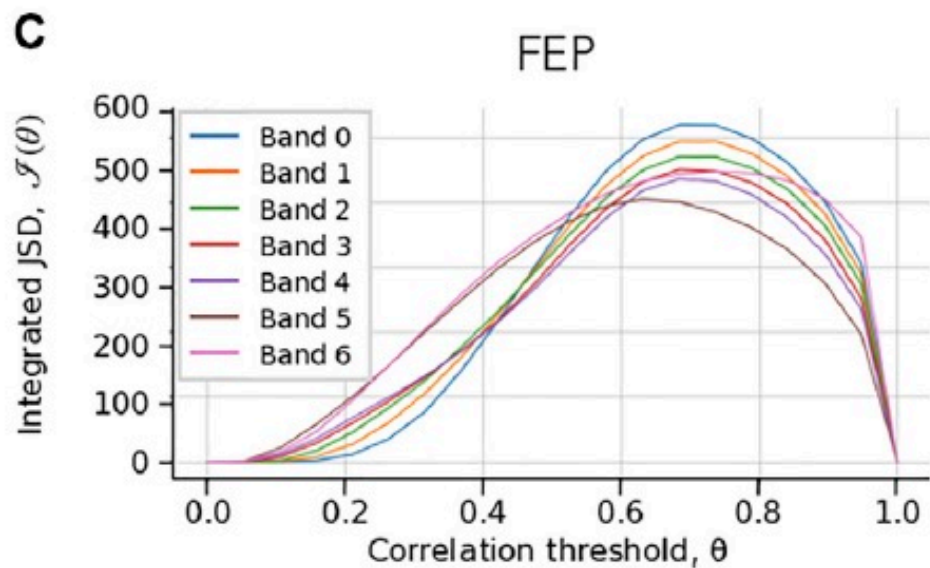
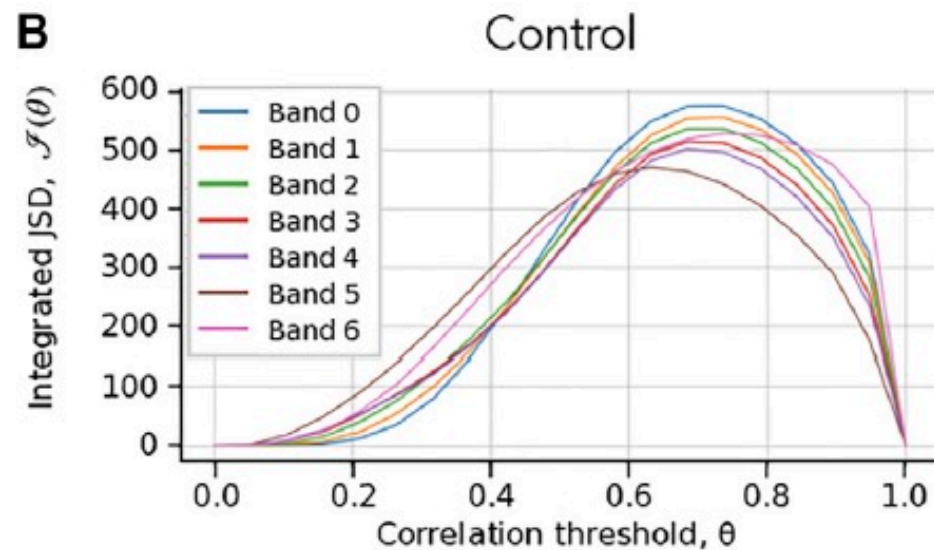
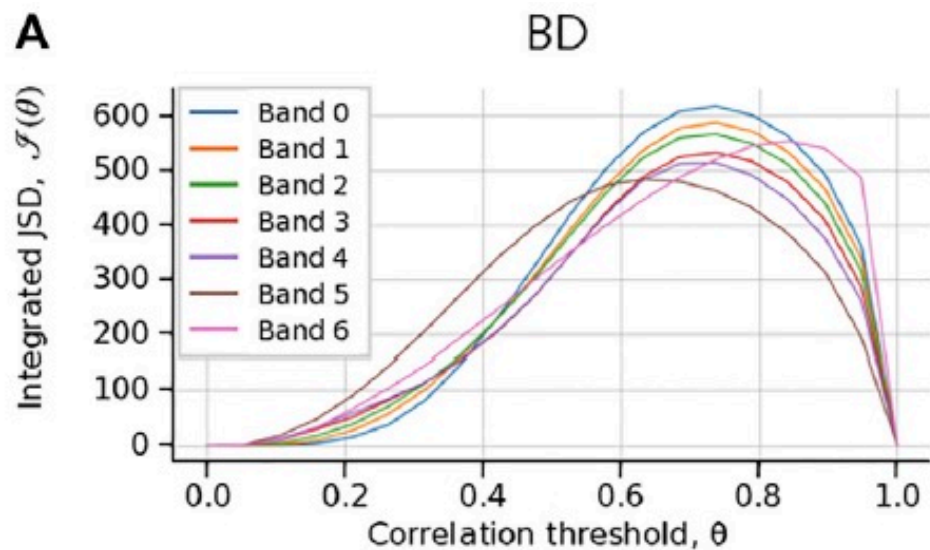
$$J(\rho|\sigma) = S\left(\frac{\rho + \sigma}{2}\right) - \frac{1}{2}(\rho + \sigma) \quad \text{J-S DIVERGENCE}$$

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

MAXIMIZE INTEGRATED J-S DIVERGENCE

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

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

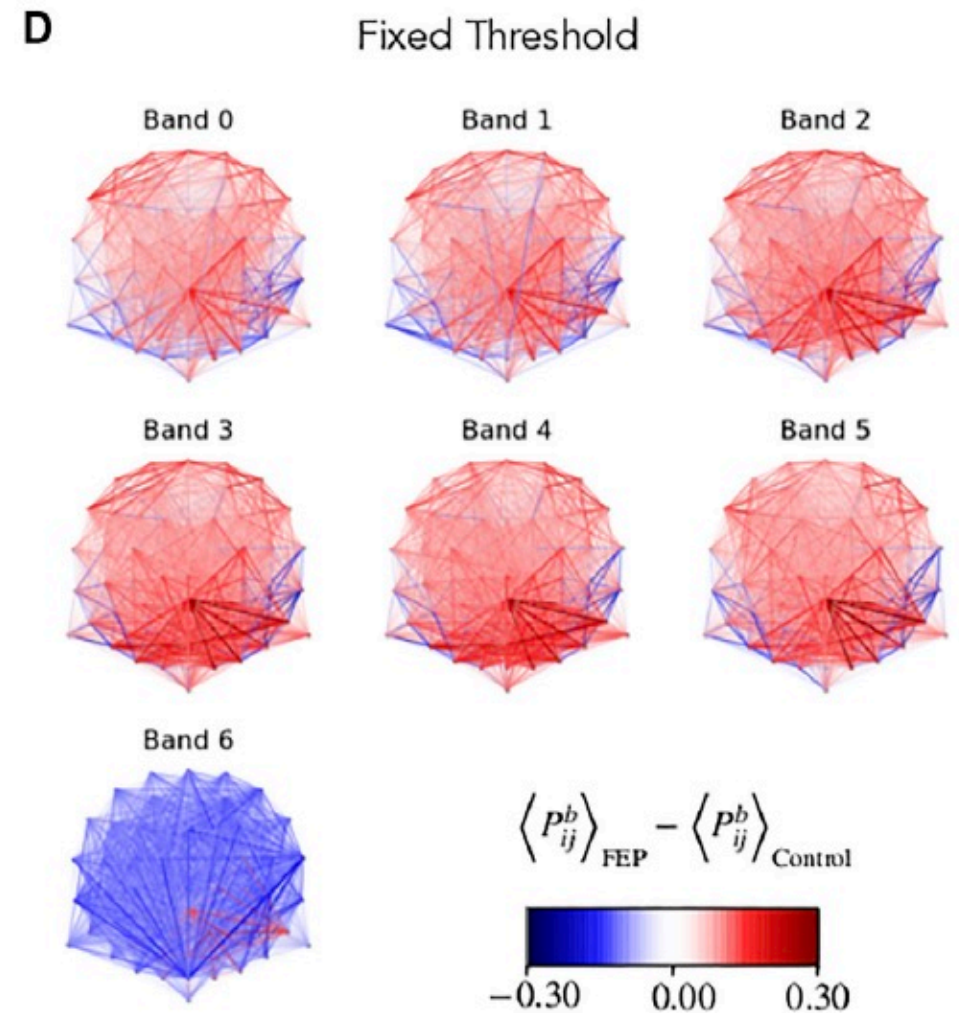
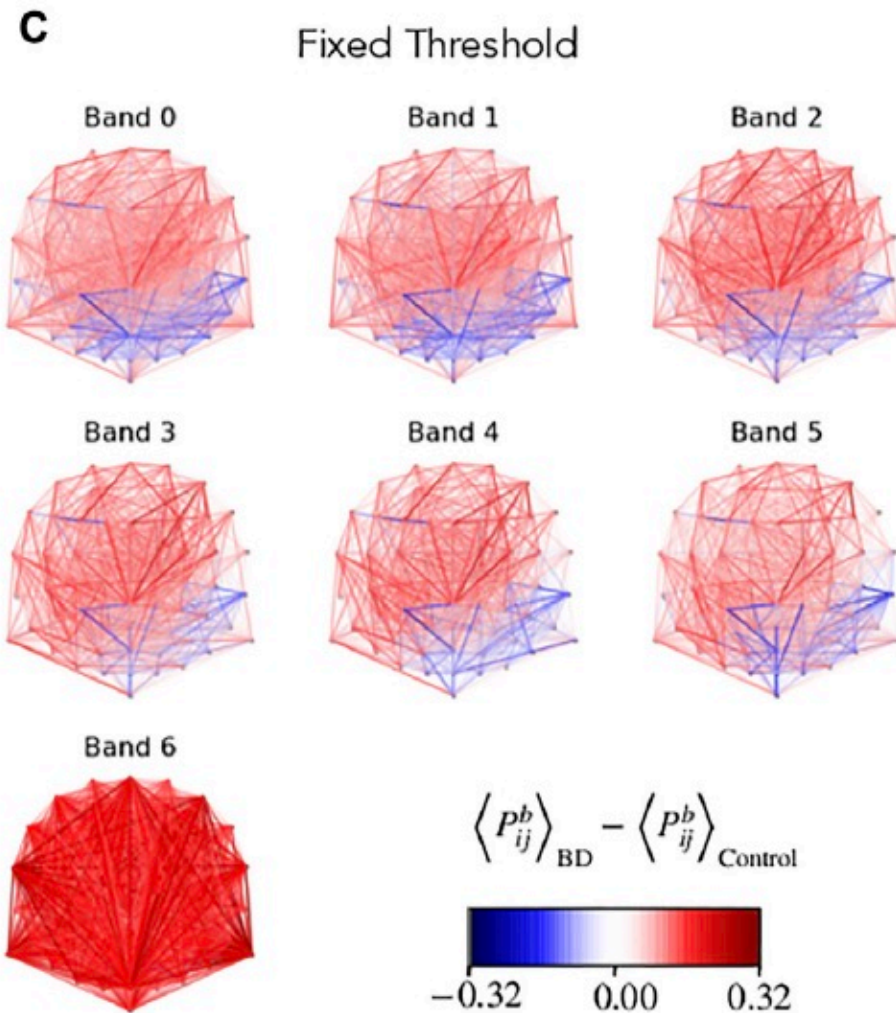


EEG MULTILAYER NETWORKS



NETWORK EDGE PRESENCE

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



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

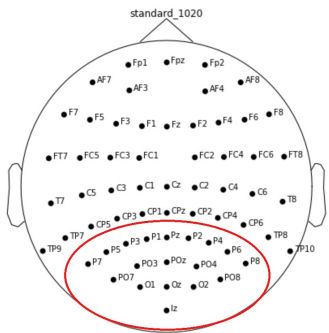
Degree of node i

Average Path Length:

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

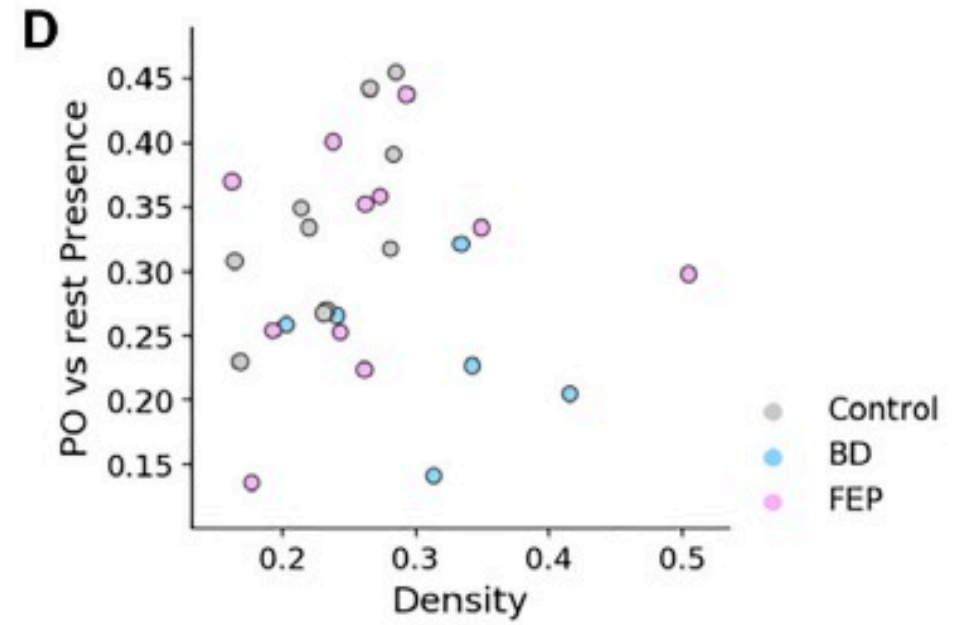
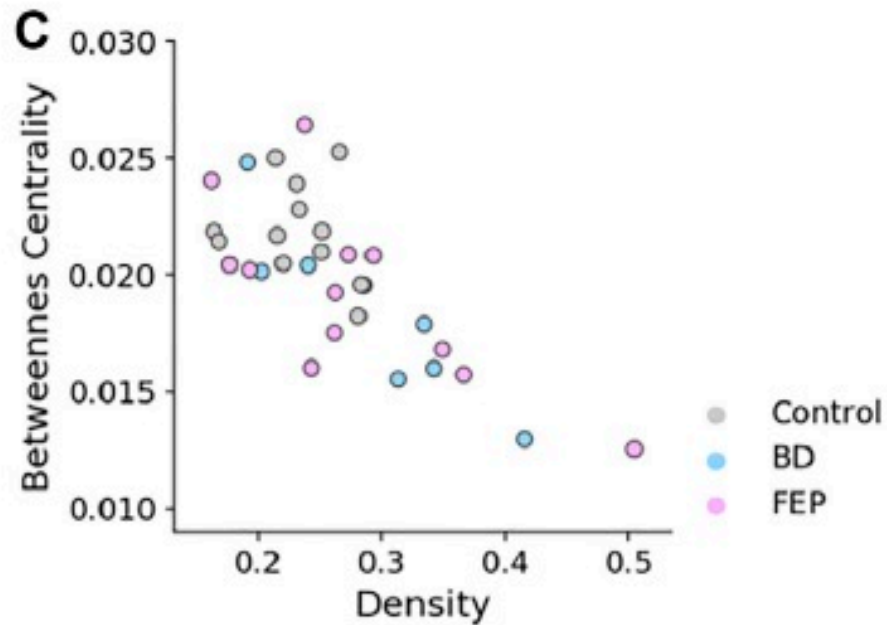
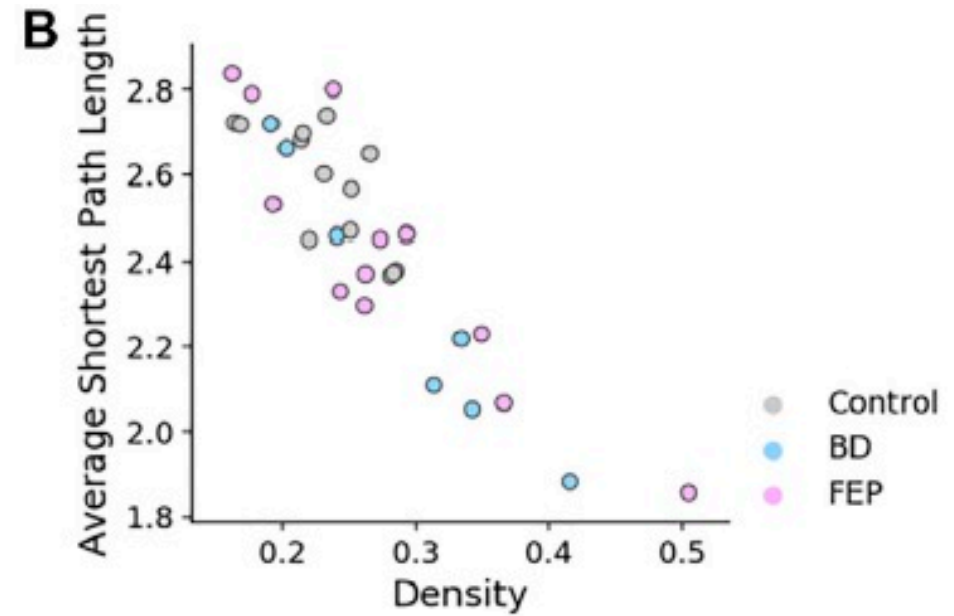
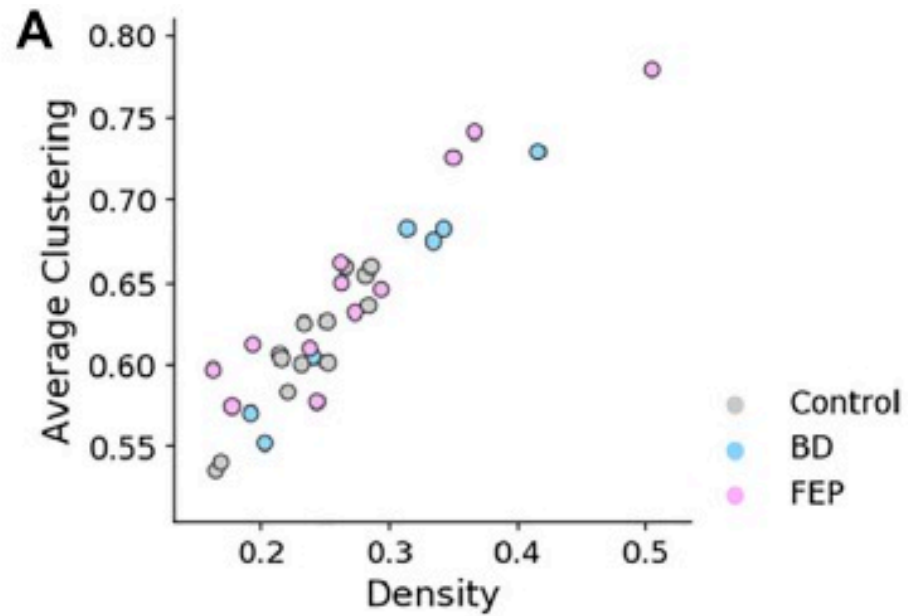
Length of shortest path between i and j

Parieto-Occipital Edge Presence:



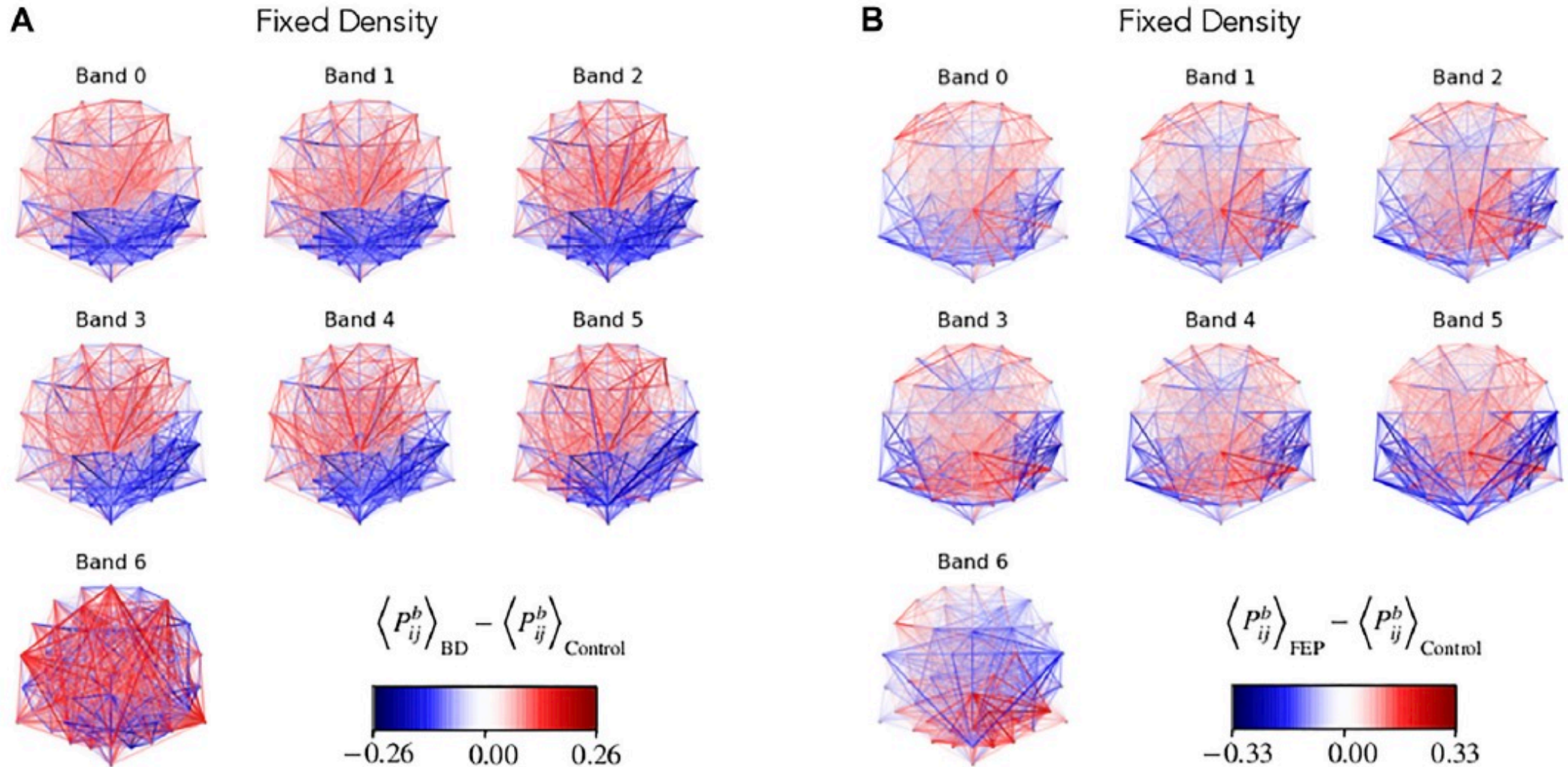
$$P_{PO} = \langle P_{ij}^b \rangle_{(ij) \in PO} - \langle P_{ij}^b \rangle_{(ij) \notin PO} \quad P_{ij}^b = \langle A_{ij}^b(t) \rangle_t$$

DENSITY DEPENDENCE OF NETWORK MEASURES

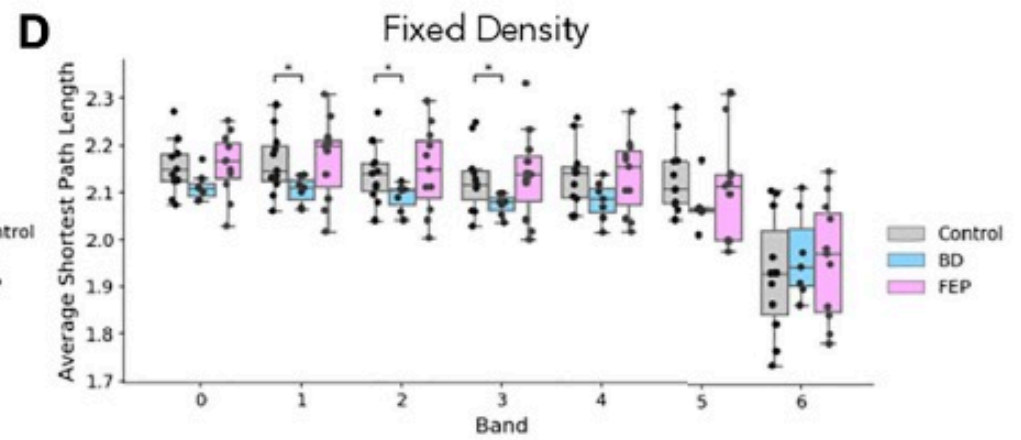
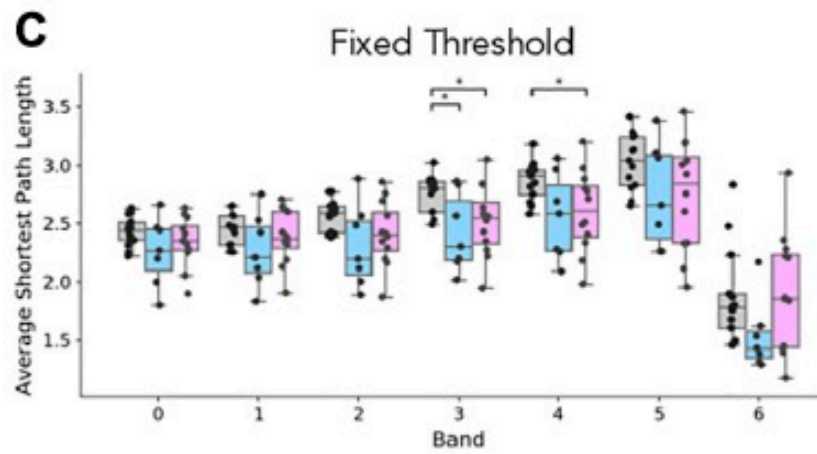
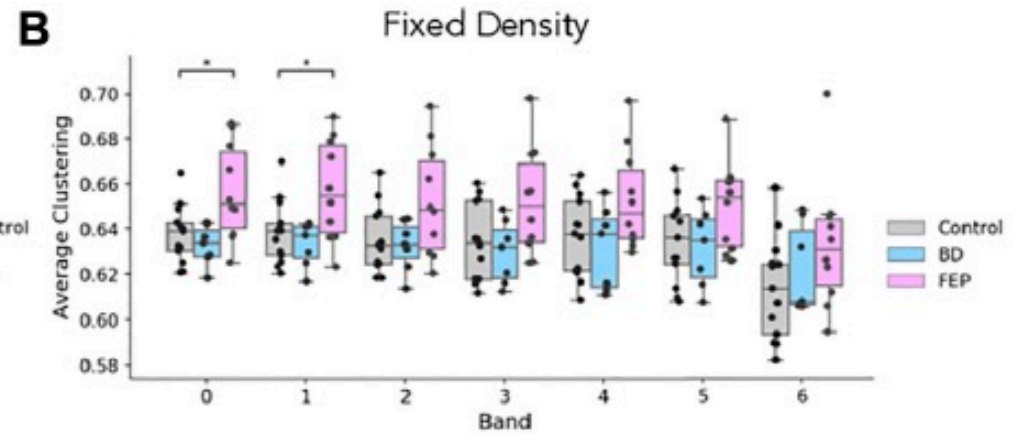
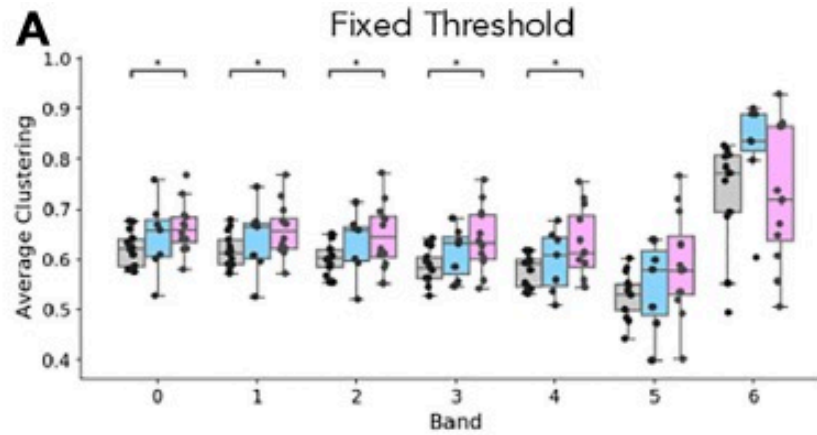


NETWORK EDGE PRESENCE (FIXED DENSITY)

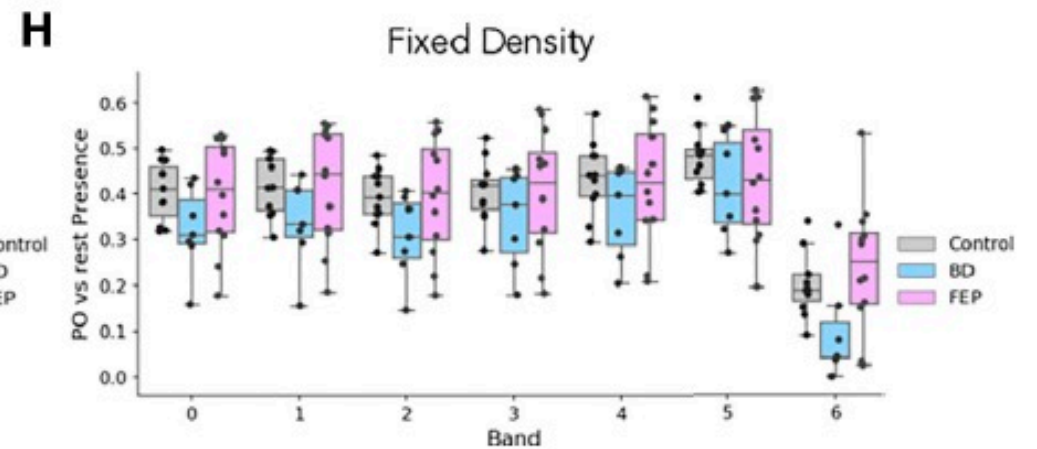
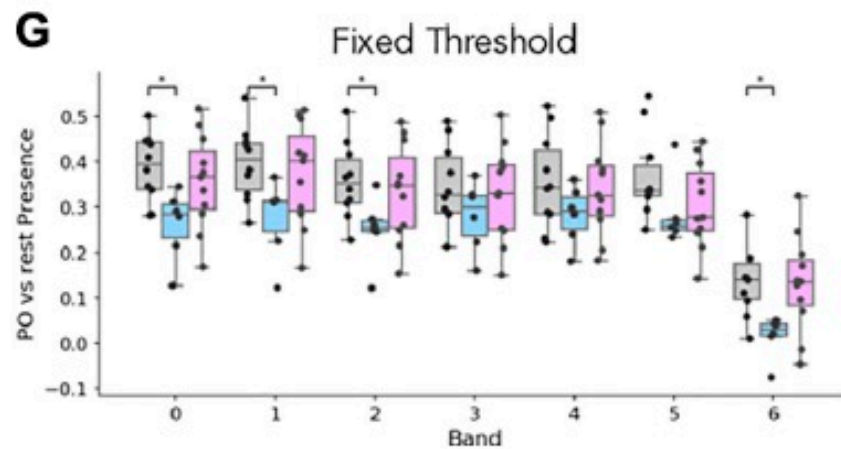
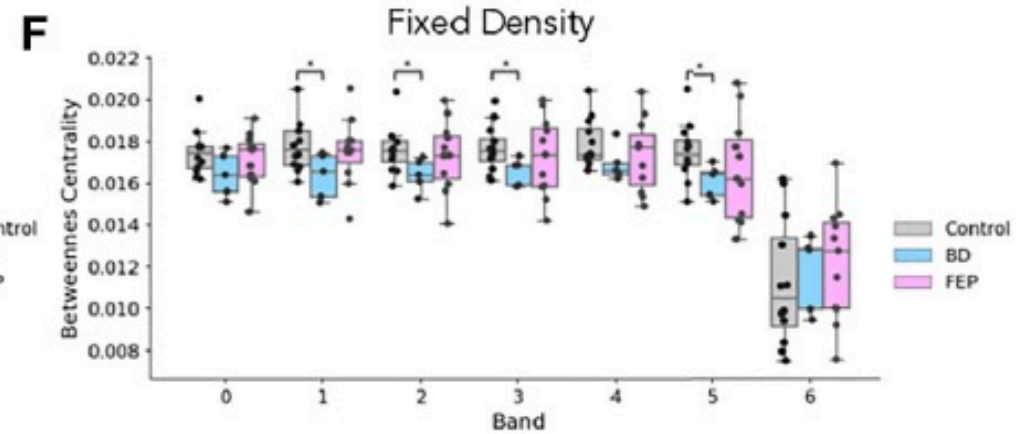
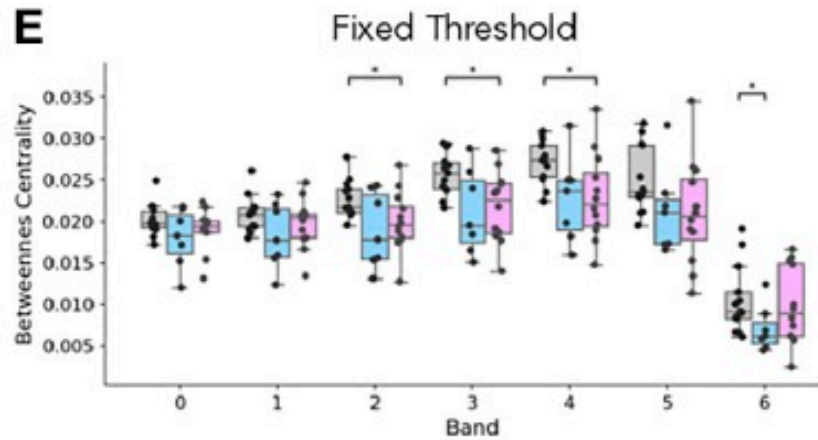
DENSITY IS CONSTANT AND CORRESPONDS TO THE AVERAGE DENSITY OF FIXED THRESHOLD NETWORKS



NETWORK MEASURES



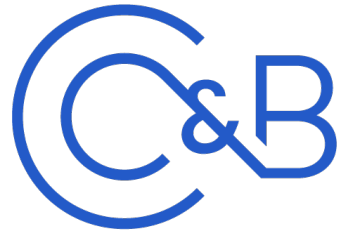
NETWORK MEASURES



SUMMARY

EEG network representation
Network measures
Patients stratification

COWORKERS:



CENTER FOR
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



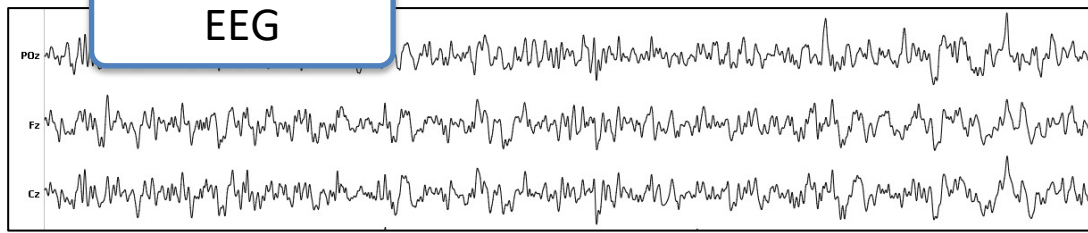
Regione
Lombardia

ASST Santi Paolo e Carlo

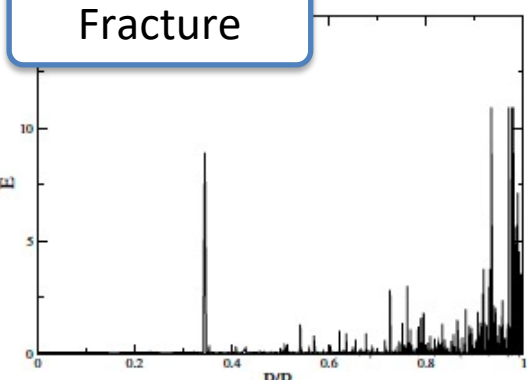
PAPER:

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.

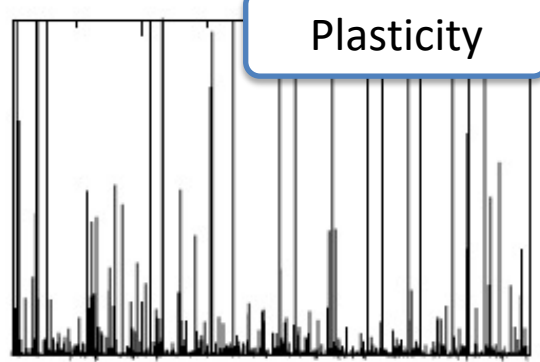
EEG



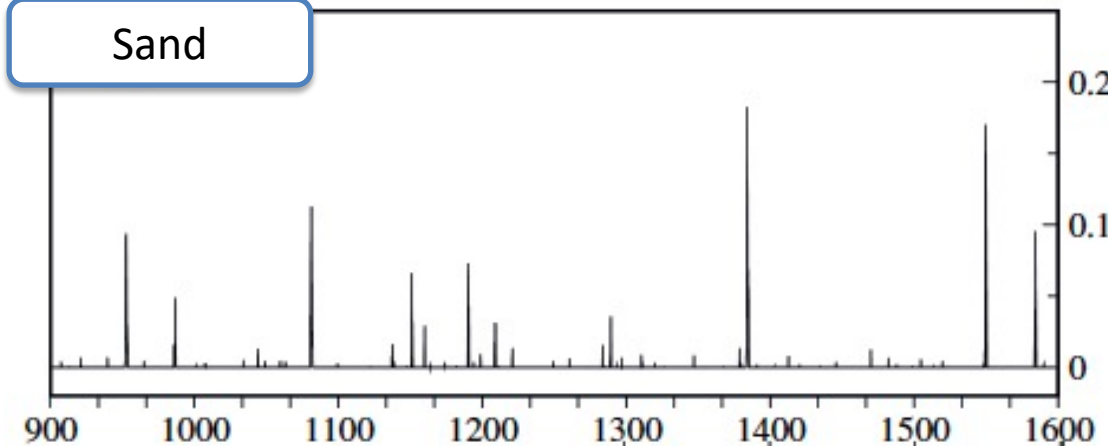
Fracture



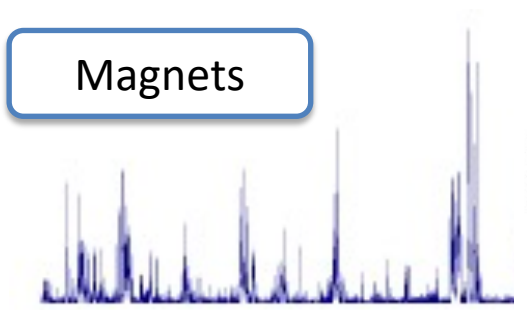
Plasticity



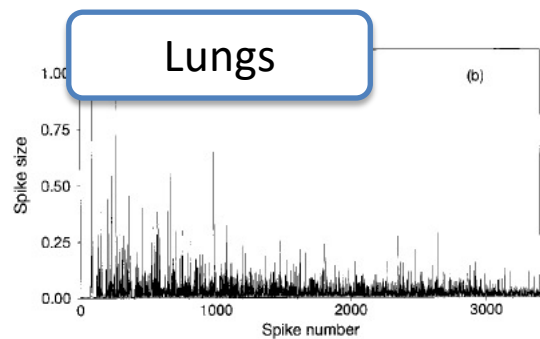
Sand



Magnets

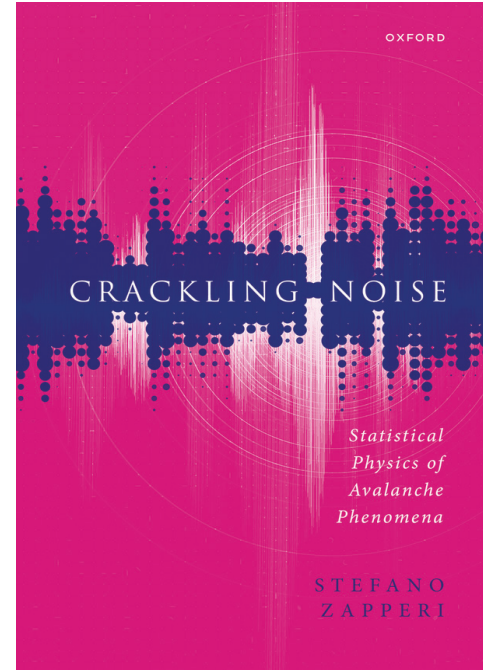


Lungs



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.

Order online at www.oup.com with promotion code ASPROMP8 for 30%

June 2022

Hardback

9780192856951

£65.00 £45.50

\$85.00 \$59.50

240 pages

**THANK YOU
FOR YOUR
ATTENTION!**

