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## Unconsciousness reconfigures modular brain network dynamics

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In this work [1] we used complex network theory to study the dynamics of time-dependent functional brain networks obtained from functional magnetic resonance imaging (fMRI) data during both conscious wakefulness and states of reduced consciousness. In order to detect heterogeneous temporal networks communities, we developed a new temporal benchmark (Fig. 1 A) to set the optimal parameters (Fig. 1 B) of a multilayer modularity maximization algorithm [2]. We then defined the largest multilayer module (LMM) as the normalized size of the largest module in time and we measured its size (Fig. 1 C), nodes flexibility within the LMM (normalized number of times each node entered or left the LMM) and the regional probability of belonging to the LMM (Fig. 1 D). We observed that the majority of nodes decreased their flexibility during sleep, and that regions presenting decreased flexibility during sleep were related to sensory perception. We found that unconsciousness reconfigured network flexibility and reduced the size of the largest spatiotemporal module (Fig. 1 C), which we identified with the dynamic core. Our results represent a first characterization of modular brain network dynamics during states of unconsciousness measured with fMRI, adding support to the dynamic core hypothesis of human consciousness [3].

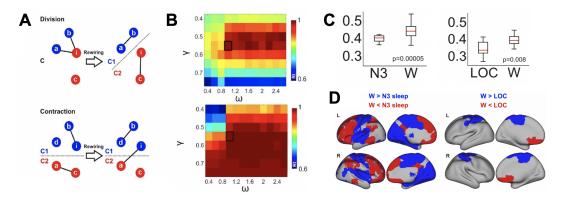


Figure 1: **A**. Dynamic benchmark rewiring steps. **B**. Grid of algorithm parameters performance (optimal parameters  $\gamma = 0.55$  and  $\omega = 1$ ). **C**. LMM size during N3 sleep stage, LOC (Loss of Consciousness) and W (Wakefulness) comparison. **D**. Regional probability of belonging to the LMM.

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## Monitoring the Depth of Anesthesia Using Parameter-free Features of a Single Prefrontal EEG Channel

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*Background and Objective*: Monitoring the depth of anesthesia (DoA) is necessary for preventing undesired awareness and inordinate anesthetic depth during a surgery [1]. Despite the popularity of bispectral index (BIS) system for the DoA monitoring, it is still not affordable for the developing countries. Alternatively, a low-cost single channel electroencephalogram (EEG) headband can be used.

*Materials and Methods*: Fig. 1(a) displays the block diagram of the proposed algorithm. Firstly, the signle channel EEG signal is filtered for the artifact removal. Secondly, the EEG is decomposed into its sub-bands and several parameter free features are extracted. Then, the prominent features are selected and fed to a random forest regressor. Here, we used EEG data recorded from 19 subjects during the general anesthesia.

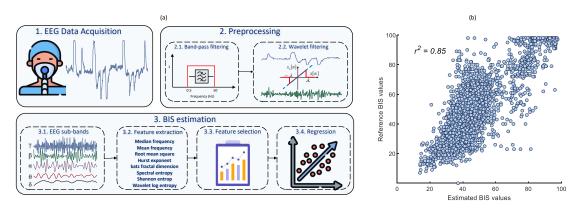


Figure 1: The block diagram of proposed algorithm (a) and the scatter plot of reference BIS values against the estimated BIS values (b).

*Experimental Results*: After excluding those EEG data with unknown BIS values, 19399 5s EEG signal segments were used for the analysis. The feature set was randomly divided into training-validation (70%) and unseen testing (30%) subsets, and fed to random forest regression model. Fig. 1(b) shows the scatter plot of reference BIS values against the estimated BIS values.

*Significance*: The most prominent advantage of our algorithm compared to the other studies is the employment of parameter free features, which eliminate the necessity of parameter tuning before the computation.

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## Robust Estimation of Long-Range Temporal Correlations in Electrophysiological Signals

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Accurate estimation of electrophysiological properties is crucial for understanding and finding treatments for numerous neurological disorders. Changes in long-range temporal correlations (LRTCs) were demonstrated to be associated with several conditions, for instance, epilepsy. Currently, LRTCs are primarily measured using either spectral methods in broad-band signals [1] or Detrended Fluctuation Analysis (DFA) in the envelope of oscillatory components [2]. However, theoretical work suggests that the Hurst exponent, a measure of LRTC, can be estimated using multiple methods [3]. Here, we compare spectral methods, DFA, auto-correlation, wavelet methods, and rescaled range analysis. Fig. 1 illustrates, for short signals, that the wavelet method and rescaled range analysis are more accurate than auto-correlation or spectral methods. However, spectral methods can handle oscillatory components explicitly [1]. Our goal is to develop a comprehensive framework that combines the strengths of different approaches to provide a robust estimation of LRTCs in electrophysiological signals.

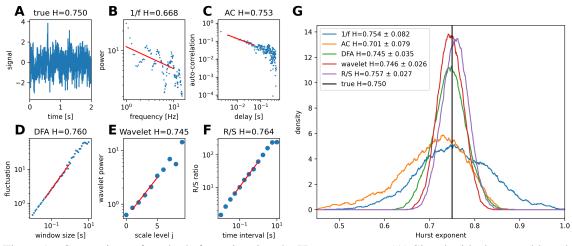


Figure 1: Comparison of methods for estimating the Hurst exponent. (A) Signal with short total length of 10s, generated as colored noise. (B-F) Illustration of Hurst exponent estimation using spectral analysis (B), auto-correlation (C), fluctuation analysis (D), wavelet method (E), and rescaled range analysis (F). (G) distribution of 1000 estimations obtained from different methods with mean  $\pm$  std indicated.

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## Mesoscale structural differences in the connectome of schizophrenia patients revealed by topological data analysis

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Topological data analysis (TDA) has opened new possibilities for understanding neurodegenerative diseases such as schizophrenia[1]. Although TDA methods offer a new perspective on connectivity pattern analysis, the outcomes are frequently challenging in interpretation. This study uses TDA to reveal differences in brain connectivity between individuals with schizophrenia and healthy controls. The authors apply the weight rank clique filtration (WRCF)[2]to brain connectivity matrices obtained from a probabilistic fiber-tracking algorithm run on the COBRE dataset[3] (DTI images, N=44 SCH, N=44 HC).

The results of the filtration are a set of topological cycles that are shared among many subjects (Fig. 1-C). These cycles were clustered together based on their anatomical structure using agglomerative clustering (Fig. 1-A,B). The authors then investigated connectivity differences between groups by studying average persistence landscapes [4]. The findings show that the two groups have statistically different connectivity patterns for several clusters with distinct anatomical characteristics. These clusters of cycles for the SCH group tend to 'die' later than those for the HC group, indicating longer lifetime (p<0.05, landscapes permutation tests with Benjamini-Hochberg correction, significance is shown in pink in the Fig.1-D and Fig.1-E). The authors also found that the functional correlates of brain regions involved with those connectivity patterns have different functional and structural properties.

The research provides insights into the mechanisms underlying schizophrenia and highlights the potential of TDA in investigating neurodegenerative diseases.

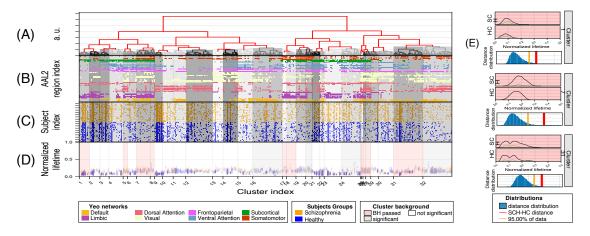


Figure 1: A: Hierarchical clustering of persistent cycles based on brain regions; B: Brain region (AAL2 atlas) participation in cycles; C: Subject participation in cycles; D: Normalised lifetimes of cycles; E: Average persistence landscapes;

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## Bio-inspired Reflex System for Learning Visual Information for Resilient Robotic Manipulation

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#### Abstract

Humans have an incredible sense of self-preservation that is both instilled, and also learned through experience. One system which contributes to this is the pain and reflex system shown in Fig. 1a), which both minimizes damage through involuntary reflex actions and also serves as a means of 'negative reinforcement' to allow learning of poor actions or decision. Equipping robots with a reflex system and parallel learning architecture could help to prolong their useful life and allow for continued learning of safe actions. Focusing on a specific mock-up scenario of cubes on a 'stove' like setup, we investigate the hardware and learning approaches for a robotic manipulator to learn the presence of 'hot' objects and its contextual relationship to the environment. By creating a reflex arc using analog electronics that bypasses the 'brain' of the system we show an increase in the speed of release by at least two-fold. In parallel, we have a learning procedure illustrated in Fig. 1b) which combines visual information of the scene with this 'pain signal' to learn and predict when an object may be hot, utilizing an object detection neural network. Finally, we are able to extract the learned contextual information of the environment by introducing a method inspired by 'thought experiments' to generate heatmaps that indicate the probability of the environment being hot.

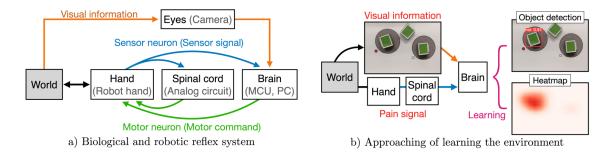


Figure 1: a) Biological interaction to an external signal from the world and their robotic counterparts (in brackets). b) Overview of the learning approach where visual information about hot objects is learned to allow for prediction of hot objects and generation of heatmaps.

<sup>&</sup>lt;sup>\*</sup> These authors contributed equally to this work.

## Differential effects of depression and anxiety on reward and punishment processing: a machine learning analysis

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Impaired reward-seeking and punishment-avoiding have been systematically linked to depression. The evidence comes from reward positivity (RewP) in event-related potentials studies. RewP is a rewardpunishment feedback difference wave that picks 250-350 ms after feedback. Numerous studies have shown that RewP amplitude is attenuated in adults with depressive symptoms compared to non-depressed controls. However, there is evidence that depression is specifically linked with rewards whereas anxiety, often comorbid with depression, is linked with punishments [1]. To test this hypothesis, we classify depression versus control and anxiety versus control based on feedback-locked electroencephalogram (EEG) recordings. We expected varying results depending on the group and the type of feedback tested.

The reward-locked and punishment-locked activity were quantified as the delta (0.1 - 2.0 Hz) and theta (4.0 - 10.0 Hz) activity from 200 to 300 ms after reward (FP) and punishment (FN) feedback respectively. We were interested mainly in theta activity. The signal was filtered with Common Spatial Patterns and classified with Support Vector Classifier (SVC). The models were trained using 3-fold cross-validation (CV) and were compared in terms of 10x10 CV balanced accuracy scores.

All DEP and ANX classifiers yielded significant results. The DEP and control groups were slightly better differentiated by theta and delta reward activity than by punishment activity (Fig. 1A). Punishment theta slightly better differentiated the ANX from the control group (Fig. 1B). A comparison of classification metrics of all models is shown in Table 1.

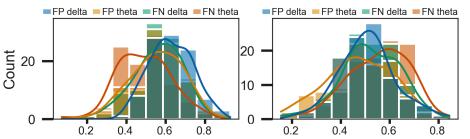


Figure 1: Histograms of depression models' (panel A) and anxiety models (panel B) 10x10 CV scores.

	Depression				Anxiety			
	ACC	<i>p</i> -value	Precision	Recall	ACC	<i>p</i> -value	Precision	Recall
FP delta FP theta FN delta	.64 .58 .62	.005 .036 .005	.67 .58 .60	.57 .59 .79	.57 .67 .59	.068 .001 .065	.55 .67 .58	.81 .69 .69
FN theta	.61	.009	.61	.59	.60	.015	.61	.59

Table 1: Results of depression and anxiety classification tasks.

The presented results support the dimensional hypothesis for depression and anxiety. The ANX/DEP groups were differentially associated with FP-theta and FN-theta. This suggest altered positive feedback processing in depression and negative feedback processing in anxiety.

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## Brain injury measured with electrophysiology – why it matters, the rationale for the methodology and results from a pilot study

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Traumatic brain injury (TBI) is a relatively frequent (incidence of 200–600 per 10<sup>5</sup> persons per year) and often underestimated health condition. The majority (75–98%) of injuries are *mild* TBI (mTBI), also referred to as *concussion*. mTBI, while generally not life-threatening, is associated with persistent symptoms among 10–60% of casualties [1,2]. Research evidence pointing towards a subtle, but chronic pathology ensuing even after mild TBI, has been accumulating [1]: notable results include hazard ratios on the order of 1.5 for dementia among footballers habitually heading [3], as well as small decrements in event-related potentials and neuromotor function detectable up to 30 years post injury [1,4].

Mild injuries are usually undetectable on conventional structural brain imaging (CT, MRI) [1] (under some definitions this is their defining characteristic contra moderate or severe injury), which motivates the exploration of other diagnostic modalities. Electrophysiology, such as EEG, can provide valuable information on the *functional* characteristics of the injured brain with relatively low equipment cost and higher availability, compared to e.g. functional MRI (fMRI).

I present the results of a pilot animal study (n = 5 + 1 sham) utilizing an angular acceleration injury model [5]. Peak accelerations close to the histological injury threshold of 0.8–0.9 Mrad/s<sup>2</sup> [5] were applied. Resting state activity in anesthetized animals pre and post injury was recorded from the brain surface. The most salient differences seen against the sham trial are an acute reduction in signal amplitude, particularly for higher frequencies, which partially normalizes over time. The FOOOF parametrization (Eq. 1) [6] of the power spectral density unfortunately did not yield consistent results. I discuss our results on the canvas of the current literature on electrophysiological diagnostics of concussion.

$$\log PSD(f) = \underbrace{b - a_0 \log(f)}_{\text{aperiodic component}} + \underbrace{a_1 \exp\left(\frac{-(f - c_1)^2}{2w_1^2}\right) + a_2 \exp\left(\frac{-(f - c_2)^2}{2w_2^2}\right) + \dots}_{\text{periodic components}}$$
(1)

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## Normalizing flows for nonlinear dimensionality reduction of electrophysiological recordings

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Even though the cortex has many active neurons, neuronal populations for different brain areas should dwell on a low-dimensional manifold [1]. Principal component analysis versions are used to estimate this manifold and its dimension. Although successful, these methods assume that the data is well described by a Gaussian distribution and ignore features like skewness and bimodality. Therefore, they perform poorly as generative models.

Normalizing Flows (NFs) allow us to learn neural activity statistics and generate artificial samples [2, 3]. These neural networks learn a dimension-preserving estimator of the data's probability distribution. They are simpler than generative adversarial networks (GANs) and variational autoencoders (VAEs) since they learn only one bijective mapping and can compute the likelihood correctly due to tractable Jacobians at each building block.

NFs are trained to distinguish relevant (in manifold) from noisy dimensions (out of manifold). To do this, we break the original symmetry of the latent space by pushing maximal variance of the data to be captured by as few dimensions as possible — the same idea underpinning PCA, a linear model, adopted here for nonlinear mappings. NFs' unique characteristics allows us to estimate the neural manifold's dimensions and describe the underlying manifold without discarding any information.

Our adaptation is validated on simulated datasets of various complexity created using a hidden manifold model with specified dimensions. Reconstructing data with a few latent NF dimensions shows our approach's capability. In this case, our nonlinear approaches outperform linear ones. We identify manifolds in high-gamma EEG recordings using the aforementioned technique. In the experiment of [4], 128 electrodes recorded during four movement tasks. These data show a heavy-tailed distribution along some of the first principal components. NFs can learn higher-order correlations while linear models like PCA are limited to Gaussian statistics. We can also better match features to latent dimensions by flattening the latent space. We now have fewer latent dimensions that explain most data variance.

#### Acknowledgements

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## Non-invasive tDCS stimulation and advanced network connectivity methods in investigating the role of the vmPFC in affective perception

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The ventromedial prefrontal cortex (vmPFC) plays a critical role in emotional appraisal, and disruptions in its activity have been linked to psychiatric disorders such as major depressive disorder (MDD) [1]. To investigate how changes in vmPFC activation affect emotional processing, we assumed that it modulates and is modulated by other brain regions, specifically dorsolateral prefrontal (dlPFC) and temporoparietal (TPC) cortical regions, and is responsible for processing positive valence.

To better understand how vmPFC affects attentional bias and reward processing through direct stimulation, researchers conducted a study with 40 participants. They examined visual perception of happy, fearful, and neutral faces using 275-channel MEG after excitatory or inhibitory tDCS. Data were preprocessed using a custom software called the Atlantis toolbox, partly based on FieldTrip routines [2], and effective connectivity was estimated for theta and alpha frequency bands using a Directed Transfer Function[3,4]. Functional connectivity was analyzed using a mixed model implemented with the lme4 package in R.

Excitatory stimulation of the vmPFC has a significant impact on functional networks involved in attention and emotional processing, especially when participants view fearful faces. The connectivity analysis indicates interaction effects in specific areas, including the perigenual and posterior parts of the vmPFC (emotional content processing control) [5], the Right Temporal Area (emotional reactions, particularly emotional tension) [6], and the Visual area (visual processing).

These findings demonstrate the potential for non-invasive brain stimulation targeting the vmPFC and suggest that further research is warranted to explore its clinical applications beyond MDD.

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## **P.10**

## Olfactory matching reveals optimized time for accurate decisions

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Matching of various sensory stimuli involves neural signaling at the periphery as well as higher cognitive functions. Different decision processes such as detection and discrimination, and holding the perceived information are involved during this course of action. In the context of increasing reports of olfactory dysfunctions under infectious and non-infectious disease conditions, establishing precise methods for quantifying olfactory fitness has become an emerging need. To probe sensory and cognitive functions involving olfactory system, we have developed a novel olfactory matching paradigm using an automated custom-built olfactory-action meter. With precise and consistent odor delivery and realtime data analysis, our system automates the entire process without any intervention of the experimenter, making it usable in clinical conditions. We have optimized all experimental parameters by quantifying olfactory detection and matching abilities in over 300 healthy subjects [1]. With a mean detection accuracy around 90%, we observed significantly better olfactory matching performance for simple odors, in comparison to complex odor mixtures. Odor matching accuracy remained unaltered across varying interstimulus intervals. However, the olfactory matching time shown by the subjects for correct responses were significantly lower than the incorrect responses. This optimized paradigm offers quantification of sensory and cognitive deficits under various neurological disorders with olfactory impairments.

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# Ambient Particulate Matter (PM<sub>2.5</sub>) exposure contributes to cognitive and motor dysfunction that mimics Parkinson's Disease

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## Objective

To explore the mechanism of Particulate Matter ( $PM_{2.5}$ ) in inducing bidirectional olfactory-brain inflammation and neurodegeneration leading to motor and cognitive dysfunction in C57BL/6 mice.

## Background

Air pollution has been linked to cause detrimental health problems such as respiratory, cardiovascular and neurological diseases. Polyaromatic hydrocarbons (PAHs) and heavy metals present in abundant amounts in  $PM_{2.5}$  could be the primary factory to contributing neurodegenerative diseases and further affecting cognition and motor functions [1]. Elaborate and in-depth mechanisms mediating neurodegeneration in the olfactory bulb and brain could play a crucial role in preventing the initiation and progression of the disease [2].

## Methods

Intranasal  $PM_{2.5}$  exposure to C57BL/6 mice at a dose of 100 and 200 µg/animal (n=10) for 30-days showed significant impairment in the cognitive and motor functions as evidenced from Open Field Test (OFT), Novel Object Recognition Test (NORT), rotarod and Morris Water Maze (MWM). Olfactory function tests were assessed by buried pellet test, olfactory preference/avoidance test (OPT/OAT). These results were further correlated with walking pattern analysis in which the PM<sub>2.5</sub> exposed animals had impaired movement and reduction in the stride length compared to control. Further Nissl staining of the brain revealed reduced neuronal density and structure in the olfactory bulb and SNpc regions of the mice brain corelating with the neurobehavioral impairment. Increased microglial and astrocyte activation was observed in the regions along with marked increase in the inflammatory markers and reduced neuronal plasticity was observed.

## Results

Our in-vivo results suggest the impaired olfactory function was well corroborated with loss in the nigral and hippocampal neurons thus resulting in impaired cognitive and motor functions in C57BL/6 mice. Similarly, a marked reduction in the neuronal density in the olfactory bulb and brain correlates with the initiation and progression of neurodegeneration and neuroinflammation caused by  $PM_{2.5}$  exposure to the mice. Astrocyte (GFAP) and microglial activation (iba-1 and CD-68) further explores the glial cells associated inflammation and progression of the disease through the olfactory-brain axis.

## Conclusion

Our current study explores the role of APM<sub>2.5</sub>-100 and 200  $\mu$ g/animal in initiating the loss of olfactory function and neurons along with progression of the neuroinflammation and neuronal loss to other parts of the brain regions causing loss of cognitive and motor functions. Acknowledgements The authors thank and acknowledge Department of Pharmaceuticals, Ministry of chemical and fertilizers, Government of India.

## References

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