Manfredo Atzori
Neuroscience Department, University of Padova, Italy

Knowledge Extraction from Multimodal Biomedical Data in Neuroscience

This presentation illustrates ongoing research activities focused on the extraction of biomedical knowledge from heterogeneous and multimodal data sources. The work addresses key challenges in the field, including data heterogeneity, complexity, variability, and the scarcity of annotated datasets, which collectively hinder the deployment of robust machine learning solutions in clinical practice. Central to this effort are several interdisciplinary projects—ExaMode, MedMax, and HEREDITARY—which develop and apply unsupervised and self-supervised learning approaches for disease phenotyping, prognosis prediction, and precision medicine, with a particular focus on neurological diseases. Methodological advancements include the integration of multimodal data, clustering of heterogeneous biomedical clinical data, harmonization of large-scale EEG repositories, and the development of explainable neural network architectures for EEG and MRI analysis. The presentation also emphasizes the importance of open-source software for reproducibility, generalizability, and scalable application of AI in biomedicine. Overall, this work contributes to the advancement of machine learning techniques tailored for complex biomedical datasets, with the ultimate goal of enhancing clinical decision-making and patient care.

Pietro Avanzini
Istituto di Neuroscienze, Consiglio Nazionale delle Ricerche, 43125 Parma, Italy

Giacomo Barzon[1], Daniel M. Busiello[2,3], Giorgio Nicoletti[4]
[1] *Padova Neuroscience Center, University of Padova, Padova, Italy*
[2] *Max Planck Institute for the Physics of Complex Systems, Dresden, Germany*
[3] *Department of Physics and Astronomy "G. Galilei", University of Padova, Padova, Italy*
[4] *Quantitative Life Sciences section, The Abdus Salam International Center for Theoretical Physics (ICTP), Trieste, Italy*

Information coding in excitatory–inhibitory populations: the roles of balance and plasticity

Understanding how the complex connectivity structure of the brain shapes its information-processing capabilities is a long-standing question. In this talk, we study how the neural activity of excitatory and inhibitory populations encodes information on external signals. We show that at long times information is maximized at the edge of stability, where inhibition balances excitation, both in linear and nonlinear regimes. For prolonged stimuli, however, stronger inhibition is required to maximize instantaneous sensitivity, revealing an intrinsic trade-off between short-time responses and long-time accuracy. We then extend this framework to include plasticity mechanisms acting on synaptic connections at different timescales. In this setting, long-term plasticity modulates circuit dynamics to steer neural activity toward regimes of optimal information encoding, with Hebbian or anti-Hebbian rules emerging depending on how external inputs are structured. Conversely, short-term plasticity enables discrimination of temporal sequences through the emergence of multistable attractor landscapes, with an optimal level of input variability enhancing discrimination. Together, these results provide a unified information-theoretic perspective on how excitation–inhibition balance and synaptic plasticity jointly shape the computational properties of neural populations, revealing fundamental trade-offs and adaptive strategies for efficient information processing across timescales.

Loredana Bellantuono
Dipartimento di Biomedicina Traslazionale e Neuroscienze (DiBraiN), Università degli Studi di Bari Aldo Moro, Bari, Italy

Brain Connectivity Biomarkers: A Complex Network & XAI Approach to Neurological, Developmental, and Age-Related Conditions

Understanding changes in brain connectivity patterns is a central challenge in neuroscience, especially when addressing complex neurological, neurodevelopmental, and age-related conditions. The present contribution discusses three case studies concerning the application of network models,
Machine Learning (ML), and eXplainable Artificial Intelligence (XAI) to the analysis of neuroimaging and genomic data.
The first study focuses on frailty, a critical geriatric syndrome impacting physiological reserve and vulnerability to stressors. Utilizing structural MRI scans from 310 participants (7 frail and 303 non-frail) from the IPREA collaboration, we construct individual brain networks where nodes represent regions and links denote structural similarities. Network centrality measures are used as features to train ML algorithms for classifying frail vs non-frail individuals. Our best model achieves an Area Under the Receiver Operating Characteristic curve (AUC) of 0.789±0.020. This result, particularly noteworthy given the significant class imbalance in the dataset, stems from integrating advanced oversampling techniques into our ML pipeline, including data-driven and synthetic data generation approaches specifically designed to preserve the underlying data structure and avoid overfitting. Crucially, the XAI analysis pinpoints the bilateral frontal gyri (Broadman Areas 10 and 11) as pivotal regions for prediction, offering promising neuroimaging biomarkers. Besides these clinical insights, this study provides a cutting-edge ML framework to address the automated recognition of rare conditions, characterized by an exiguous number of training examples available, representing a fundamental challenge in neuroscience and across all of medicine.
The second study explores the application of Exponential Random Graph (ERG) models within a complex network framework to characterize how Alzheimer's disease (AD) impacts brain connectivity. By defining brain connectivity networks from T1-weighted MRI scans of 126 normal controls (NC) and 92 AD patients, ERGs effectively outline both "global" and "local" disease patterns. This approach demonstrates high efficacy in highlighting AD-related connectivity alterations, achieving an overall classification accuracy of 0.82±0.08. Beyond classification, ERGs precisely delineate the brain regions most affected by the disease, proving a formidable tool for investigating pathological mechanisms. Significantly, as these effects are evaluated at the patient level, they offer a novel, explainable framework for designing innovative diagnosis support systems. The generality of this ERG-based approach also paves the way for broader applications in other diseases and with diverse data sources, or for exploring alternative network models.
Our third study addresses the profound genetic and clinical heterogeneity of autism spectrum disorder (ASD). Using a publicly available brain microarray dataset, we construct a gene co-expression network and identify stable communities of dysregulated genes through the Leiden algorithm. We thus integrate these communities within a robust ML framework to distinguish between autistic and control subjects, achieving a remarkable accuracy of 0.98±0.01. This performance is independently validated on a separate microarray experiment, yielding an accuracy of 0.88±0.03. Furthermore, we identify two specific gene communities, comprising 43 and 44 genes each, that are significantly enriched for ASD-associated variants and maintain a strong predictive power on the independent set, with accuracies of 0.78±0.05 and 0.75±0.04, respectively. Subsequent XAI analysis on these communities confirms the pivotal role of autism-specific variants, thereby validating our approach. Further investigation into these restricted sets of genes holds the potential to unveil essential mechanisms driving ASD.
The case studies presented in this contribution highlight the versatility and effectiveness of an integrative approach combining Network Science, ML, and XAI to identify novel brain connectivity biomarkers and gain clinical insights into the biological and neurological mechanisms underlying complex conditions. Our work

paves the way for the development of next-generation diagnostic tools and personalized therapeutic strategies in neuroscience and geriatric care.

Danilo Benozzo[1], Egidio D'Angelo[1,2], Claudia Casellato[1]
[1] Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy
[2] Digital Neuroscience Center, IRCCS Mondino Foundation, Pavia, Italy

Linking time-lagged functional dynamics to structural constraints in resting-state fMRI

Linear state-space models have been shown to effectively reproduce large-scale brain dynamics. We applied this approach to resting-state fMRI data acquired from 20 mice, focusing on the system's Jacobian matrix, i.e. the effective connectivity, and specifically on its component encoding nonzero-lag interactions: the differential covariance matrix. Within this matrix, we concentrated on the off-diagonal elements (dC-Cov), which reflect endogenous time-lagged correlations. Our aim was to investigate the relationship between dC-Cov and structural constraints imposed by the spatial placement and white matter connectivity between brain areas. Because dC-Cov captures the rotational component of signal trajectories, we employed Schur decomposition to identify 2D rotational modes, each characterized by a pair of orthogonal vectors (the source and sink projections), and an associated angular velocity. We found that among the leading eigenvectors of the structural distance matrix, one consistently aligned with one of the faster Schur modes. Notably, in 15 out of 20 mice, the strongest alignment occurred with the Schur vector associated with the sink component, echoing with the role of in-degree in shaping directed nonzero-lag interactions.

Andrea Brovelli
Institut de Neurosciences de la Timone UMR 7289, Aix Marseille Université, CNRS, 13005, Marseille, France

Intrinsic motivational signals for information seeking and causal learning

A key aspect of human agency is the capacity to learn causal relationships between actions and their consequences. This capacity relies on a balance between reward maximization and information-seeking mechanisms. Whereas reward-maximization signals have been extensively studied, the computations and neural substrates supporting information seeking remain less well understood. In my talk, I will present two studies investigating intrinsic learning signals and the associated neural interactions. To this end, we combined information-theoretic approaches with human magnetoencephalography (MEG) to examine how intrinsic learning signals are encoded and broadcasted across cortical circuits. In the first study, we demonstrated that information gain—the reduction in uncertainty about the causal relationship between actions and outcomes—is represented in the visual, parietal, lateral prefrontal, and ventromedial and orbitofrontal cortices. Cortico-cortical interactions encoded information gain synergistically, both at pairwise and higher-order levels, including triplet and quadruplet interactions. These higher-order synergistic interactions were characterised by long-range dependencies centred on the ventromedial and orbitofrontal cortices, which served as a " receiver" in the network. In the second study, we showed that expected information gain and empowerment gain function as intrinsically motivational neural computations that drive information seeking during causal learning. These signals were represented in the visuomotor system, with a predominant role played by sensorimotor regions. Overall, my talk will provide evidence on how intrinsic neural signals are encoded and broadcasted across distributed cortical networks.

Victor Buendia
Department of Decision Sciences, Bocconi University, Milan

Modularity in excitatory-inhibitory networks controls the dynamical regime and optimizes their computational capabilities

Structural modularity is a ubiquitous feature of biological neural networks and has been associated with rich dynamics that can impact computational performance. Brain networks are characterized by diverse neuron types with distinct connectivity patterns. In this talk, I will discuss the information processing capabilities of modular E/I networks with different excitatory-inhibitory connectivity patterns, and how such information can be extracted from them. We will consider two different but related scenarios, synaptic plasticity and reservoir computing. I will leverage tools from statistical physics of disorder systems to link the network modularity with its dynamical states and computational capabilities.

Valentina Carabelli[1], Giulia Tomagra[1], Chiara Cambini[1], Claudia Stella[2], Elena Losero[2], Sofia Sturari[3], Adam Britel[3], Ettore Bernardi[2], Ivo Pietro Degiovanni[2], Ekaterina Moreva[2], Paolo Traina[2], Emilio Carbone[1], Andrea Marcantoni[1], Marco Genovese[2], Federico Picollo[3]
[1] *Drug Science Department, Torino University*
[2] *Istituto Nazionale di Ricerca Metrologica, Torino*
[3] *Physics Department, Torino University*

Diamond-based multiarrays and NV centers in nanodiamonds as probes for monitoring neuronal activity down to the nanoscale

Understanding the brain complexity relies on the challenging production of biosensing probes with high spatial- and time-resolution and suitable for detecting multiple parameters of neuronal activity. Taking advantage of the cutting edge diamond technology, we developed different prototypes of diamond-based microelectrode arrays (D-MEAs) that have been patterned with different geometries of graphitic microelectrodes. D-MEAs were able to detect, in real time, both neuronal firing and also quantal dopamine release from cultured SN neurons. This approach has been proven useful for monitoring the progressive network impairment caused by the presence of exogenous alpha-synuclein oligomers, mimicking the early onset of neurodegeneration in Parkinson disease. More recently, using ion beam implantation with boron doping instead of graphite we also developed transparent D-MEAs, with the aim of providing a simultaneous detection of neuronal firing activity and intracellular Ca2+ transients.
On the other side, we exploited the fluorescence of nitrogen-vacancy (NV) centers in nanodiamonds (approximately 100 nm diameter). Atomic-scale defects (centers), combined with the optically detected magnetic resonance (ODMR) technique, are pivotal for sensing at the nanoscale, in particular for detecting intracellular temperature changes with a sensitivity < (1-2)K/Hz^1/2. As localized temperature gradients are strictly coupled to neuronal activity and cell metabolism, we aimed at correlating the firing activity of cultured hippocampal neurons with localized temperature variations, under resting condition and after the silentiation of GABAergic transmission. Our results prove that NV-centers in the nanodiamonds represent a potent tool for mapping neuronal spiking activity changes with high sensitivity and spatial resolution.

Claudia Casellato
Dipartimento di Scienze del Sistema Nervoso e del Comportamento, University of Pavia, Italy

Multiscale cerebellar circuit models

There is a strong need for developing an open-source canonical cerebellar circuit model, able to flexibly include multiple features by easy reconfigurations, in order to unveil the structure-function-dynamics relationships in cerebellum. The canonical olivocerebellar model has been developed by exploiting the Brain Scaffold Builder (BSB) component-based framework. The pipeline to interface BSB cerebellar models with Allen Mouse Atlas has been optimized. The circuit is geometrically reconstructed by defining the placement and the connectome, using the full morphologies properly oriented when available. The models are validated against the population-specific firing frequencies, considering in-vitro and awake states. Multiple versions are generated by introducing i) receptor-specific synaptic transmission, ii) connection-specific short-term synapse dynamics, iii) bilateral asymmetric long-term learning rules at proper connections. The version including the long-term plasticity rules is embedded in brain-control systems interfacing with neurorobotic platforms challenged in sensorimotor learning tasks, so linking cellular-level phenomena to brain architecture. Some pathological cases are under studies, e.g. autism by multicompartmental cerebellar microcircuit models, and ataxia by point-neuron cerebellar circuit models, also simulating Transcranial Magnetic Stimulation treatments. The cerebellar point-neuron models are then transformed in the equivalent mean-field with population-specific properties, and embedded in virtual brain frameworks to shed light on whole-brain dynamics.

Marco Celotto[1,2], Gabrielle Drummond[3], Arundhati Natesan[1], Jiho Park[3], Yuma Osako[1], J Samuel Sooter[1,4], Giselle Fernandes[1], Stefano Panzeri[2], Mriganka Sur[1,3]

Astrocyte-norepinephrine interactions tune cortical neuronal encoding to guide behavioral adaptation

[1] Picower Institute for Learning and Memory, Massachusetts Institute of Technology, Cambridge, MA, 02139, USA
[2] Institute for Neural Information Processing, Center for Molecular Neurobiology (ZMNH), University Medical Center Hamburg-Eppendorf (UKE), 20251 Hamburg, Germany
[3] Department of Brain and Cognitive Sciences, Massachusetts Institute of Technology, Cambridge, MA, 02139, USA
[4] UA Integrative Systems Neuroscience Group, Department of Physics, University of Arkansas, Fayetteville, AR 72701, USA

Decision-making in adaptive behavior relies on internal models refined by reinforcement learning (RL). Biological organisms outperform artificial RL in many contexts, suggesting undiscovered brain mechanisms. Emerging evidence implicates astrocytes - once relegated to metabolic support - in regulating neural circuits over long timescales. Here, we combine computational analyses and modeling to show how astrocytes transform transient neuromodulatory signals into sustained, context-dependent cortical modulation, enabling real-time RL. We focused on norepinephrine (NE)-driven behavioral adaptation following unexpected outcomes. Using a go/no-go task in mice, we showed that surprising outcomes with different valences triggered distinct updates in behavior. Phasic locus coeruleus (LC)-NE release transiently encodes reward prediction errors (RPEs). Cortical astrocytes extend NE-RPE signals to modulate neuronal population activity at the single-trial level over long inter-trial intervals. Crucially, disrupting LC activity, astrocyte dynamics, or astrocyte-neuronal signaling abolished post-surprise behavioral adaptation. Notably, astrocytes modulated neuronal responses in a context-specific way. After an unexpected punishment, NE-astrocyte signaling enhanced cortical stimulus information, increasing behavioral sensitivity on subsequent trials. Conversely, unexpected rewards caused astrocytes to suppress action-related neuronal signals, driving adaptive reductions in action execution. To formalize these mechanisms, we are developing computational models that integrate astrocytes into recurrent neural networks (RNNs). We hypothesize that such models could improve policy updates in real-time RL tasks by retaining contextual information across delays - a known weakness in conventional RNNs. Altogether, our work reveals a unified principle for astrocytes in flexibly converting transient neuromodulatory cues into sustained, task-relevant tuning of cortical neuronal encoding, providing biological insights for real-time RL.

Simona Cocco
Département de Physique, École Normale Supérieure, Paris, France

Data driven models in zebrafish navigation: combining neural and behavioral data.

In this talk I will first introduce effective connectivity (or Ising) models inferred from neural data. I will use them to model the spontaneous activity in neural recordings of the anterior rhombencephalic turning region (ARTR), a circuit that controls zebrafish swimming. The Inferred Ising model is able to reproduce the emergence of long time time scales related to the behavioral persistence. To describe dynamics both form the trajectories and from the neural recordings and combine them I will then use Hidden Markov models.

Federico Del Pup[1,2,3], Andrea Zanola[1,2,3], Louis Fabrice Tshimanga[1,2,3], Livio Finos[3,4,5], Henning Muller[6], Alessandra Bertoldo[1,2], Manfredo Atzori[2,3,6]

[1] Department of Information Engineering, University of Padova, Padova, Italy;
[2] Department of Neuroscience, University of Padova, Padova, Italy;
[3] Padova Neuroscience Center, University of Padova, Padova, Italy;
[4] Department of Statistical Sciences, University of Padova, Padova, Italy;
[5] Department of Developmental and Social Psychology, University of Padova, Padova, Italy;
[6] Information Systems Institute, HES-SO Valais-Wallis, Sierre, Switzerland

Addressing Generalizability Issues in Deep Learning-Based Electroencephalography Data Analysis

Deep learning is significantly advancing the analysis of electroencephalography (EEG) data, with recent studies reporting extremely high accuracy in various applications. However, impressive accuracies are often the result of methodological errors that produce unrealistic performance estimates. When properly evaluated, state-of-the-art EEG deep learning models demonstrate poor generalizability. This issue stems from several steps in the training pipeline, including data preprocessing, data partitioning, random seed selection, and cross-validation strategy. Generalizability issues and methodological errors are detrimental to the field, as they produce inflated performances estimates and create unrealistic expectations. Thus, proper analyses are fundamental to reframe recent results and direct research towards reliable outcomes. The aim of this presentation is to thoroughly describe common methodological errors in deep learning-based EEG data analysis and to provide easy-to-follow guidelines for understanding and avoiding them. The presentation showcases findings from multiple studies conducted within the large Horizon Europe-funded HEREDITARY project. First, a comprehensive analysis of EEG preprocessing for deep learning applications will be presented, offering valuable insights into how this step can significantly influence model performance and the quality of the features learned. Second, data partitioning strategies will be examined in detail. This section emphasizes how incorrect cross-validation methods can lead to data leakage and misuse of inherent signal characteristics (e.g., biometric features), ultimately resulting in overestimated model accuracy. In conclusion, this presentation provides an important opportunity to discuss current challenges and future directions of deep learning-based EEG data analysis. It also helps researchers who are not experts in deep learning identify reliable contributions.

Ambra Ferrari
Center for Mind/Brain Sciences, University of Trento, Italy

How the brain binds information across the senses

Adaptive behaviour in a complex, dynamic, and multisensory world presents some of the brain's most fundamental computational challenges, including sensory binding, perceptual inference, and decision-making. I will first discuss how the brain integrates sensory signals from a common source by weighting them according to their relative reliabilities. Next, I will examine how observers solve the binding problem—deciding whether signals originate from a common cause and should therefore be integrated, or else segregated. Finally, I will assess how multisensory perceptual inference interacts with higher-level cognitive functions such as attention and language.

Alessio Fracasso
Department of General Psychology, University of Padova

Modelling cortical oculo-motor planning and execution at high-field, a 7T approach

The posterior parietal cortex (PPC) is a central hub for attention-related and movement-related responses. Within the context of oculo-motor responses, the human posterior parietal cortex sensitivity to eye movement planning and execution has been shown using classic methodology introduced by Sereno and colleagues to measure the response to delayed saccades, based on phase-encoded designs, and taking advantage of the lawful relationship between the signal phase and saccade direction. Using this approach, it is possible to derive estimates of preferred saccade orientation (preferred tuning direction) for each cortical location. However, phase-encoded designs only provide detailed information about preferred tuning direction, but they do not provide information about tuning width: how broad or narrow is a response around the preferred saccade direction. First, it is not clear whether allowing tuning width to change would yield a better goodness-of-fit than the classic approach. Moreover, it is not known whether tuning width is topographically arranged along human PPC, following a general principle of cortical organization seen for example within the domain of vision. Furthermore, the relation between tuning width and tuning direction in PPC at the population level is not known, and results from non-human primate neurophysiology are surprisingly conflicting. Here we tackle these questions using a forward modelling approach coupled with high-field (7Tesla) functional magnetic resonance imaging acquisitions, probing large scale organizational principle of preferred tuning direction and, specifically, tuning width, for the first time, in vivo, in humans.

Silvia Gini[1, 2], Loren Kocillari[3], Valeria Bedin[1, 2], Marco Celotto[3], Ludovico Coletta[4], Stefano Panzeri[3], and Alessandro Gozzi[1]

[1] *Functional Neuroimaging Laboratory, Istituto Italiano di Tecnologia, Center for Neuroscience and Cognitive Systems @UniTn, Rovereto, Italy*
[2] *Center for Mind and Brain Sciences, University of Trento, Rovereto, Italy*
[3] *Institute for Neural Information Processing, University Medical Center Hamburg-Eppendorf (UKE), Hamburg, Germany*
[4] *Fondazione Bruno Kessler, Trento, Italy.*

Brain state shapes the intrinsic sender-to-receiver architecture of the mouse brain

Resting state fMRI (rsfMRI) is widely used to study the functional organization of brain networks in health and disease. Functional relationships between regions are typically mapped using undirected, zero-lag temporal correlation of their rsfMRI signals, a measure known as functional connectivity (FC). While FC has yielded valuable insights into brain organization, it cannot reveal the directionality of these relationships. To address this limitation, we validated a measure of directed functional connectivity known as Transfer Entropy (TE) to characterize intrinsic information transfer in the mouse brain. Using TE, we identified a robust sender-to-receiver organization that flexibly reconfigures depending on brain state. Specifically, in anesthetized mice, cortical regions such as retrosplenial, anterior cingulate and somatosensory cortices act as sources of information, while the motor cortex and insula serve as sinks. Notably, this organization does not trivially mirror the architecture of the directed structural connectome. Moreover, in a genetic mouse model of autism, the directionality of regional information flow appears altered in the absence of white matter alterations, corroborating a functional rather than structural origin of this phenomenon. Indeed, this sender-to-receiver axis is rearranged in the awake state, where arousal-related areas including the basal forebrain emerge as sources, whereas the retrosplenial and entorhinal cortices as sinks. A significant reversal in the basal forebrain's role in awake mice following ablation provided additional support for the functional relevance of TE. These findings suggest that the mammalian brain is intrinsically organized along a flexible, state-dependent sender-to-receiver axis of information flow.

Alessandro Gozzi
Italian Institute of Technology, Rovereto, Italy

Mechanisms of fMRI (dys)connectivity

Human brain disorders are characterized by dysfunctional communication among brain regions. Yet, the biological mechanisms underlying this “functional dysconnectivity” remain unclear. In my talk, I will highlight recent cross-species research aimed at decoding patterns of brain dysconnectivity into their molecular and neurophysiological underpinnings. In particular, I will illustrate how targeted perturbational approaches can reveal fundamental physiological principles underlying the organization of large-scale functional connectivity, and its disruption in brain disorders. By bridging findings across species and investigational scales, this emerging approach opens new avenues for modelling and interpreting functional connectivity in both healthy and in neuropathological states.

Cosimo Lupo[1], Alessandra Cardinale[1,2,3], Federico Marmoreo[1], Gianluca Gaglioti[4,5], Thierry Nieus[6], Sofia Karvounari[7], Eleni Mathioulaki[7], Robin Gutzen[8], Andrea Pigorini[9,10], Simone Sarasso[4], Marcello Massimini[4,11,12], Pier Stanislao Paolucci[1], Michael Denker[13], Giulia De Bonis[1]

[1] Istituto Nazionale di Fisica Nucleare (INFN), Sezione di Roma, Rome, Italy
[2] Università Campus Bio-Medico, Rome, Italy
[3] Istituto Superiore di Sanità (ISS), Rome, Italy
[4] Dept. of Biomedical and Clinical Sciences, University of Milan, Italy
[5] Dept. of Philosophy "Piero Martinetti", University of Milan, Italy
[6] Dept. of Environmental Science and Policy, University of Milan, Italy
[7] "Athena" Research and Innovation Center in Information, Communication and Knowledge Technologies, Athens, Greece
[8] Dept. of Psychology and Center for Data Science, New York University, New York, USA
[9] Dept. of Biomedical, Surgical and Dental Sciences, University of Milan, Italy
[10] U.O.C. Maxillo- facial Surgery and dentistry, Fondazione IRCCS Cà Granda, Ospedale Maggiore Policlinico, Milan, Italy
[11] IRCCS Fondazione Don Carlo Gnocchi ONLUS, Milan, Italy
[12] Azrieli Program in Brain, Mind and Consciousness, Canadian Institute for Advanced Research, Toronto, Canada -
[13] Institute of Neuroscience and Medicine (INM-6) and Institute for Advanced Simulation (IAS-6) and JARA-Institute Brain Structure-Function Relationships (INM-10), Jülich Research Centre, Jülich, Germany

Cobrawap: studying the wave dynamics as a tool for understanding brain networks

Cobrawap (Collaborative Brain Wave Analysis Pipeline) [1,2] is an open-source, modular and customizable data analysis tool developed in the HBP/EBRAINS context, with the aim of enabling standardized quantitative descriptions of cortical wave dynamics observed in heterogeneous data sources, both experimental and simulated. The tool intercepts the increasing demand expressed by the Neuroscience community for reusability and reproducibility, offering a software framework suitable for collecting generalized implementations of established methods and algorithms, and for embracing innovative procedures. Inspired by FAIR principles and leveraging the latest findings in software engineering, Cobrawap is structured as a collection of modular Python3 building blocks - flexibly arrangeable along sequential stages - implementing data processing steps and analysis methods, directed by workflow managers (Snakemake or CWL). Latest Cobrawap progresses include the enlargement of the set of scientific usecases and applications, aimed at increasing both the software robustness and its potential for discoveries. Among the latest scientific developments, we present: (a) a recursive algorithm ("HOS", Hierarchical Optimal Sampling) designed for dealing with high-resolution recordings from brain imaging, able to dynamically tune the resolution across the field of view, locally optimizing the signal-to-noise ratio; (b) the study of simulations of neuronal dynamics in the human brain obtained from TVB-implemented models [3], paving the pathway to analyze human brain data (e.g. from EEG) with Cobrawap; (c) the study of spiking simulations of human hippocampus, extending the application of Cobrawap to brain regions other than the cortex, and enabling the analysis of spiking activity from analog signals to train spikes.

Wolfgang Maass
Institute of Machine Learning and Neural Computation, Graz University of 5 Technology, Graz, Austria

Clues for the implementation of brain intelligence

Eleonora Maggioni
Dipartimento di Elettronica, Informazione e Bioingegneria, Politecnico di Milano, Italy

Integrating electrophysiological and neuroimaging techniques to study brain-body interactions in physiology and psychiatry.

Despite continuous advances in imaging and signalling techniques, our knowledge of the human nervous system is still incomplete. In the study of the fascinating yet complex neural connectome, only by integrating complementary techniques we can achieve a fuller picture and extend our spatio-temporal domain coverage. This talk aims to provide an overview of areas of integration of neuroimaging and electrophysiological techniques and processing pipelines for the study of the brain and brain-body interactions. We will describe the advantages and challenges of integrating techniques such as functional magnetic resonance imaging (fMRI), electroencephalography (EEG) and electrocardiography (ECG), and present exemplary applications of these integrated approaches in the study of physiology and psychiatric disorders.

Francesca Mastrogiuseppe
Data Science Sector, SISSA, Trieste

Input-dependent Directionality of Interactions Between Cortical Areas

A long-standing question in neuroscience is how different brain areas communicate. One approach to studying information flow is to analyze the covariation of activity across areas, with the temporal structure of this covariation offering clues about the directionality of signaling. Recent studies applying this method to large-scale single-cell recordings across areas have revealed that the directionality of interactions can shift rapidly, depending on stimuli and task demands. These findings suggest that experimentally measured covariation metrics reflect not only the underlying synaptic connectivity but also dynamic influences such as inputs from other regions. Understanding how these metrics relate to circuit-level mechanisms remains a challenging task that warrants theoretical approaches.

Here, we develop a theoretical framework for the emergence of directional interactions in recurrent circuits, based on recurrent neural network models driven by stochastic inputs. We use this framework to understand how external inputs can flexibly shape the directionality of inter-area communication in mesoscopic cortical circuits. Our analysis reveals that inputs targeting excitatory (E) and inhibitory (I) populations play different roles in inter-areal interactions. Specifically, inputs to E significantly influence directionality by inducing a systematic bias from the area receiving the strongest input, while inputs to I regulate the amplitude and timescale of activity with minimal impact on directionality. In circuits with feature-specific connectivity and inputs, the effect of inputs to E on directionality is most apparent at the level of latent variables reflecting global co-fluctuations between stimulus-tuned and untuned units. This analysis offers a number of biological insights that could be used to guide the re-analysis of experimental data to constrain the underlying circuitry.

Overall, our work provides a theoretical foundation for the interpretation of experimentally measured covariation metrics and advances our understanding of how to link the functional and anatomical substrates of neural interactions.

Sergio Martinoia
Dipartimento di Informatica, Bioingegneria, Robotica e Ingegneria dei Sistemi, Università di Genova, Italy

Biological and digital brain twins: in-vitro and in-silico brain models

The advent of engineered neuronal networks (both 2D and 3D) derived from human- Induced Pluripotent Stem Cells coupled to large-scale, high-density electronic devices that can be used to study the dynamics of complex neuronal populations opens new avenues in the field of in-vitro brain models for patient-specific applications. The availability of new data, computational models, and computing power together with simulation-based inference, enables the creation of hybrid models (both biological and digital) of a specific disease of a specific patient. The hybrid brain twin for neural disease, in the framework of the personalized and precision medicine, could be within reach in the next few years.

Emanuele Menegatti
Information Engineering Department, University of Padova, Italy

Neurorobotics: how brain and muscles can control a robot

Gianluca Martelloni[1], David Angulo-Garcia[2], Alessandro Torcini[3], **Simona Olmi**[1,4]
[1] Istituto dei Sistemi Complessi, Consiglio Nazionale delle Ricerche, Sesto Fiorentino Italy (2)
[2] Departamento de Matemáticas y Estadística, Universidad Nacional de Colombia (UNAL), Manizales, Colombia
[3] Laboratoire de Physique Théorique et Modélisation, UMR 8089, CY Cergy Paris Université, CNRS, Cergy -Pontoise, France
[4] INFN, Sezione di Firenze, Sesto Fiorentino, Italy

Relaxation oscillations in next-generation neural masses with spike-frequency adaptation

Spike-frequency adaptation (SFA) is a fundamental neuronal mechanism taking into account the fatigue due to spike emissions and the consequent reduction of the firing activity. We have studied the effect of this adaptation mechanism on the macroscopic dynamics of excitatory and inhibitory networks of quadratic integrate-and-fire (QIF) neurons. In particular, we have studied the population activities by employing an exact mean-field reduction, which gives rise to next-generation neural mass models. This low-dimensional reduction allows for the derivation of bifurcation diagrams and the identification of the possible macroscopic regimes emerging both in a single and in two identically coupled neural masses. In single populations SFA favors the emergence of population bursts in excitatory networks, while it hinders tonic population spiking for inhibitory ones. In two populations, the addition of SFA leads to new collective dynamical regimes exhibiting cross-frequency coupling (CFC) among the fast synaptic timescale and the slow adaptation one, ranging from antiphase slow-fast nested oscillations to symmetric and asymmetric bursting phenomena. The analysis of these CFC rhythms in the $\theta - \gamma$ range has revealed that a reduction of SFA leads to an increase of the θ frequency joined to a decrease of the γ one. In a PING configuration, where SFA affects the excitatory population only, it is possible to observe the emergence of relaxation oscillations due to the interplay between the nonlinear dynamics of the firing rate and the self-inhibition modulated by SFA. A characterization of Up and Down states, together with that of the spike adding process, is provided in the PING configuration for different parameters.

Eugenio Piasini
Cognitive Neuroscience Sector, SISSA, Trieste

How sharp is your razor? Quantifying the bias for simpler explanations in human decision-making

Occam's razor is the principle that, all else being equal, simpler explanations should be preferred over more complex ones. This principle is thought to play a role in human perception and decision-making, but the nature of our presumed preference for simplicity and its underlying computational mechanisms are unclear. In this talk I will describe recent behavioral experiments performed by our group, guided by formal theories of statistical model selection. We show that, when faced with uncertain evidence, human subjects exhibit preferences for specific, theoretically grounded forms of simplicity of the alternative explanations. These preferences persist even when they are maladaptive, and their dependence on the amount of available data suggests the involvement of lower-level cognitive processes related to numerosity perception. Thus, these preferences are not mere optimizations for particular task conditions but rather a more general feature of human decision-making. Our results imply that principled notions of statistical model complexity have direct, quantitative relevance to human behavior.

Margherita Premi[1], Carlo Andrea Sartori[1], Victor Buendía[2], Alessandra Pedrocchi[1], Alessandro Sanzeni[2], Alberto Antonietti[1]

A Computational Pipeline for Simulating Mouse Visual Cortex Microcircuits with Spiking Neural Networks

[1] NeuroEngineering and Medical Robotics Laboratory - Department of Electronics, Information and Bioengineering - Politecnico di Milano, Milan, Italy
[2] Department of Computing Sciences, Bocconi University, Milan, Italy

Understanding neural circuit function requires accurate structural connectivity models that include both neurons and astrocytes. The visual cortex serves as an ideal system for investigating these interactions, yet computational models often lack realistic connectivity or overlook astrocytic contributions to network dynamics. Therefore, we developed a computational pipeline to simulate spiking neural networks encompassing both neurons and astrocytes using the MICrONs dataset, the largest electron microscopy reconstruction from a cubic millimeter of mouse visual cortex. However, automatic reconstruction suffers from known limitations, resulting in incomplete synapse detection due to artifacts and algorithm constraints. Given insufficient synapse density and incorrect connectivity assignments, we implemented two solutions:
1. We increased the number of synapses by generating a cluster of synapses placed in a sphere centered on the original location, validated through layer densities analyses.
2. We improved the connectivity using proofread astrocytes and neurons to establish connectivity patterns for non-proofread cells.
We successfully matched physiological synapse counts while maintaining layer-specific synaptic organization. A geometric approach was developed that defines ellipsoidal domains containing all synapses belonging to each proofread astrocyte. The extracted ellipsoids' parameters were generalized and applied to non-proofread astrocytes. Finally, we verified the connectivity patterns between Layer 2/3 neurons, Layer 4 neurons, and interneurons. Our methods corrected connectivity data, enabling accurate mouse visual cortex modeling. The network was simulated as a spiking neural model generating biologically realistic responses to visual stimuli. This framework allows testing alternative architectures against accurate structural connectivity. Future work will expand astrocyte-neuron interaction models.

Tommaso Proietti
Bioelectronics and Bioengineering Area, Scuola Superiore Sant'Anna, Pisa, Italy

Implantable and wearable neurotechnologies to understand and restore neural functions

Recent advances in implantable and wearable neurotechnologies are transforming both clinical practice and basic neuroscience. Implantable systems allow highly selective and stable restoration of motor and sensory functions, while soft wearable robotics provide lightweight, portable, and accessible solutions for assistance and rehabilitation. Beyond their clinical applications, these devices are also powerful research tools: they enable the acquisition of rich behavioral and physiological data, fostering the development of computational models that improve our understanding of neural function and motor control. In this talk, I will present recent technological and clinical results across both research directions, with a focus on the integration of neural interfaces, sensory feedback, and soft robotics. By combining assistive applications with neuroscience-driven insights, these complementary approaches open to next-generation neurotechnologies that both restore function and deepen our knowledge of the human nervous system.

Elisa Tentori[1], George Kastellakis[3], Marta Maschietto[2], Alessandro Leparulo[2], Panayiota Poirazi[3], Michele Allegra[4], Stefano Vassanelli[2] and Luca Mazzucato[5]

[1] *Padova Neuroscience Center, University of Padova, Padova, Italy*

[2] *Department of Biomedical Sciences, University of Padova, Padova, Italy*

[3] *Institute of Molecular Biology and Biotechnology, Foundation for Research and Technology – Hellas (FORTH), Heraklion, Crete, Greece*

[4] *Department of Physics and Astronomy "G. Galilei", University of Padova, Padova, Italy*

[5] *Departments of Biology and Mathematics and Institute of Neuroscience, University of Oregon, Eugene, 97403, Oregon, USA*

Prediction and Modulation of Network Responses in Spiking Neuronal Cultures via Effective Connectivity and Latent State Dynamics

Causal control of neuronal networks remains a key challenge in neuroscience and neuroengineering. While high-density electrophysiology allows for precise observation of spiking dynamics, predicting the effect of targeted perturbations remains largely heuristic. Can we instead infer the network's response to perturbation directly from its spontaneous dynamics? To address this question, we employ dissociated rat hippocampal cultures interfaced with high-density microelectrode arrays (MaxOne HD-MEAs, 26k electrodes, 1k simultaneously addressable), enabling fine-grained electrical stimulation and sub-millisecond, spatially resolved recordings. We design a protocol to sequentially stimulate individual electrodes and quantify the resulting network-wide response, thus reconstructing the perturbome – the map of evoked effects across the network. Perturbation responses are structured, revealing reproducible activation motifs and spatially localized modules. We show that these responses can be predicted from spontaneous activity alone. Using simple, model-free Effective Connectivity (EC) measures we estimate directed interaction maps that reproduce the modular structure of the perturbome, supporting the hypothesis that spontaneous activity encodes latent causal pathways. EC-based predictions are robust across replicates and stimulation protocols.
To study how perturbations reshape network dynamics, we then fit a Hidden Markov Model (HMM) to both spontaneous and evoked activity. The inferred latent states reflect recurring patterns of cluster activation. Post-stimulation state sequences depend on the pre-stimulus state only when EC hubs are targeted; otherwise, transitions mirror spontaneous dynamics. This strategy allows us to identify stimulation-sensitive sites and guide the network toward desired states through adaptive monitoring.

Alberto Testolin
Information Engineering Department, University of Padova

Modeling numerosity perception with generative neural networks

Generative models have a long history in AI and cognitive science: Boltzmann machines have been one of the earliest attempts to simulate the emergence of internal representations of the environment through statistical learning, and served as building blocks for the development of the first unsupervised deep learning models. In this talk I will overview the main concepts behind generative neural networks, focusing on deep belief networks and variational autoencoders, and discuss how they can be used to investigate the nature of our numerical representations.

Alessandro Torcini
Laboratoire de Physique Théorique et Modélisation, UMR 8089, CY Cergy Paris Université, CNRS, Cergy -Pontoise, France

A theory for self-sustained balanced states in absence of strong external currents

The human brain is constantly active. This ongoing activity is not random but follows complex patterns that emerge from the interactions between billions of neurons. Understanding how these patterns arise is a fundamental question in neuroscience. One influential idea is that the brain maintains a delicate balance between excitatory and inhibitory signals, preventing runaway activity while allowing rich, flexible dynamics. However, classic models of this balance often require an external input to sustain realistic firing rates, which may not align with biological observations.
In this work, we propose an alternative mechanism based on a process called short-term synaptic depression. This process weakens excitatory connections when neurons fire too much, acting as a natural self-regulating mechanism. Using Dynamical Mean Field Theory and computer simulations, we show that this mechanism can maintain stable and irregular activity without external input. Furthermore, we identify different ways in which the system transitions from stable activity to chaotic dynamics, similar to what is observed in the brain. Our findings suggest that internal synaptic adaptation may play a key role in shaping neural activity, offering new perspectives on how the brain organizes its complex dynamics.

Alessandro Treves[1,2]
[1] *Cognitive Neuroscience Sector, SISSA, Trieste*
[2] *University of Agder, Kristiansand*

Disorder and Frustration in Spatial Cognition: The Demise of an Old Map

I paraphrase the title "Disorder, Frustration and Metastability: The Development of a New Era" of a 1987 chapter by David Sherrington in the proceedings of the Heidelberg Colloquium on Glassy Dynamics, to wonder how much Computational Neuroscience has really assimilated, over the past 40 years, these foundational concepts in statistical physics. In particular in the domain of spatial cognition, our thinking is still heavily biased by functionalist prejudices, a neopositivist make-it-work, or make-it-work-optimally attitude, in which disorder and frustration have limited breathing space. I will argue that to understand learning about space we need to consider disorder from the start.

Gianni Valerio Vinci[1], Cristiano Capone[1], Andrea Galluzzi[1], Roberto Benzi[2] & Maurizio Mattia[1]

[1] *National Center for Radiation Protection and Computational Physics Istituto Superiore di Sanità, 00161 Roma, Italy*

[2] *Department of Physics and INFN, "Tor Vergata" University of Rome, 00133 Roma, Italy*

Noise induced phase transition in cortical neural field: the role of finite-size fluctuations

Mean-field models of neural population dynamics are central to theoretical neuroscience. However, cortical columns consist of a finite number of neurons , requiring realistic models to account for finite-size fluctuations. This endogenous noise can induce transitions and coherence, phenomena well-studied in isolated or coupled populations but less understood in spatially extended systems. We investigate a two-dimensional cortical field, where each lattice node is a population composed of N excitatory spiking neurons. Each neuron has a membrane potential integrating with leakage the input current due to both the pre-synaptic barrage of spikes it receives, and the inhibitory potassium flow determining the adaptation phenomenon of spike frequency. Populations are interconnected with a probability that decays exponentially with distance. For optimal population sizes, finite-size fluctuations coupled with spatial interactions generate coherent oscillations absent in the limit. We characterize this novel noise-induced phase transition and explore the system's dynamics in the bifurcation diagram of local excitability versus adaptation strength. Our findings depend primarily on global and local connectivity parameters therefore, we expect them to be general and ubiquitous. Based on these results we address the transition from sleep, dominated by slow global waves, to the asynchronous state characteristic of wakefulness, using our cortical field model offering insights into this fundamental problem in neuroscience, challenging the current understanding. Finally, we comment on how recent rigorous results make it possible to drastically reduce the dimensionality leading to a massive reduction in computational cost.

Riccardo Zecchina, D. Badalotti, C. Baldassi, M. Mézard, M. Scardecchia,
Department of. Computing Sciences, Bocconi University, Milan

Dynamical Deep Learning in Asymmetric Recurrent Networks

We introduce a statistical physics framework for learning in neural architectures composed of single or interconnected asymmetric attractor networks. These systems can exhibit a manifold of global fixed points capable of implementing sophisticated input-output mappings, which we characterize analytically. Learning from extensive datasets is achieved through the stabilization of fixed points via a fully distributed and local learning process, implemented at the single-neuron level. This simple mechanism yields performance comparable to that of conventional feedforward deep neural networks trained using gradient-based methods. The effectiveness of the model stems from the dense and accessible manifolds of stable fixed points, which encode the internal representations of data. Unlike other approaches to deep learning without backpropagation, our method does not attempt to estimate gradients.

Lubomír Kostal[1], Laura Sacerdote[2], **Cristina Zucca**[2]
[1] *Institute of Physiology, Czech Academy of Sciences, Prague, Czech Republic*
[2] *Department of Mathematics, University of Torino, Via Carlo Alberto 10, 10123 Torino, Italy*

Uncovering Input-Output Dynamics in Single Neuron Model through Mutual Information

We investigate how information about an unknown neuronal input can be inferred from output spike timing in stochastic integrate-and-fire models. Specifically, we study Brownian motion and Ornstein–Uhlenbeck processes with oscillating thresholds, comparing the effectiveness of different boundary shapes in transmitting information. Mutual information and mutual information per time are computed between the input, modeled as a Gamma-distributed random variable, and the first passage time. Some preliminary results are unexpected. For instance, mutual information shows a non-monotonic dependence on the input variance when the input mean is fixed. While increasing the noise level of the model generally reduces mutual information, in the Ornstein–Uhlenbeck case, higher noise can increase the mutual information per unit time. These findings contribute to the understanding of stimulus encoding efficiency in noisy neuronal systems.