Prot. n. 0049170 del 31/05/2024 - [AOO: USGEUNI] Decreti 2740/2024

UNIVERSITÀ DEGLI STUDI DI GENOVA

AREA RICERCA, TRASFERIMENTO TECNOLOGICO E TERZA MISSIONE

SERVIZIO PER IL TRASFERIMENTO TECNOLOGICO E DELLE CONOSCENZE

SETTORE VALORIZZAZIONE DELLA RICERCA, TRASFERIMENTO TECNOLOGICO E RAPPORTI CON LE IMPRESE

IL RETTORE

Vista la Legge 9 maggio 1989, n. 168 - Istituzione del Ministero dell'Università e della ricerca scientifica e tecnologica e ss.mm.ii;

Visto lo Statuto dell'Università degli Studi di Genova;

Visto il Regolamento Generale di Ateneo;

Visto il Regolamento di Ateneo per l'Amministrazione, la Finanza e la Contabilità;

VISTA la legge 7 agosto 1990, n. 241 recante "Nuove norme in materia di procedimento amministrativo e di diritto di accesso ai documenti amministrativi" pubblicata sulla Gazzetta Ufficiale n. 192 del 18/08/1990 e s.m.i.;

VISTO il Decreto del Presidente della Repubblica 28 dicembre 2000, n. 445 (Disposizioni legislative in materia di documentazione amministrativa) e s.m.i.;

VISTO il Decreto Direttoriale MUR n. 341 del 15/03/2022 di emanazione di un Avviso pubblico per la presentazione di Proposte di intervento per la creazione di "Partenariati estesi alle università, ai centri di ricerca, alle aziende per il finanziamento di progetti di ricerca di base" nell'ambito del Piano Nazionale di Ripresa e Resilienza, Missione 4 "Istruzione e ricerca" – Componente 2 "Dalla ricerca all'impresa" – Investimento 1.3, finanziato dall'Unione europea – NextGenerationEU";

VISTO il Decreto Direttoriale MUR n. 1553 dell'11/10/2022 di concessione del finanziamento del progetto Codice identificativo PE00000006, Acronimo MNESYS, Titolo "*A multiscale integrated approach to the study of the nervous system in health and disease*", registrato alla Corte dei Conti il 23/11/2022 al n. 2948 e relativi allegati;

CONSIDERATO che l'Università degli Studi di Genova è leader dello Spoke 6, dal titolo "*Neurodegeneration, trauma and stroke*";

CONSIDERATO che gli Spoke possono emanare - nell'ambito dei limiti e con le modalità previste dall'Avviso - "bandi a cascata" finalizzati alla concessione di finanziamenti a soggetti esterni per attività coerenti con il progetto approvato;

VISTA la delibera della seduta del 27 settembre 2023 con cui il Consiglio di Amministrazione dell'Università degli Studi di Genova ha approvato l'emanazione del bando a cascata per organismi di ricerca nell'ambito del Progetto MNESYS - "*A multiscale integrated approach to the study of the nervous system in health and disease* - PNRR M4C2 per lo Spoke 6;

VISTO il Decreto del Direttore Generale n. 5418 del 14 novembre 2023 di nomina del Responsabile

del Procedimento;

VISTO il Decreto del Rettore n. 5439 del 14 novembre 2023 e il Decreto Rettorale n. 5474 del 15 novembre 2023 di emanazione del Bando a cascata per il finanziamento di proposte di intervento per le attività di ricerca svolte da Organismi di Ricerca nell'ambito del programma di ricerca PE MNESYS "*A multiscale integrated approach to the study of the nervous system in health and disease*", per lo Spoke 6 dal titolo "*Neurodegeneration, trauma and stroke*", nell'ambito del PNRR, Missione 4, Componente 2, Investimento 1.3 – finanziato dall'Unione europea – NextGenerationEU (CUP D33C22001340002);

CONSIDERATO che alla data di scadenza per la presentazione delle proposte progettuali, fissata entro e non oltre il giorno 14 dicembre 2023, per la **Tematica I – "Neural Network models of default activity patterns in the physiological and pathological (neurodegeneration or trauma) unconscious brain to design biomarker based on the microscopic cortical activity"** era pervenuta a mezzo PEC all'indirizzo air3@pec.unige.it la seguente proposta:

PROPONENTE: Istituto Superiore di Sanità
TITOLO PROPOSTA: NEMUS – Neurological Exploration through the Modeling of the Unconscious State

TENUTO CONTO che la Responsabile del procedimento, Ing. Patrizia Cepollina, ha ritenuto ricevibile, ammissibile e conforme la proposta sopra citata;

CONSIDERATO che nel Bando è previsto che la valutazione di merito tecnico-scientifico dei progetti pervenuti sia affidata ad una Commissione composta da almeno tre esperti esterni al Partenariato, indipendenti e competenti dell'Area tematica dello Spoke;

VISTO il Decreto Rettorale n. 6114 del 20 dicembre 2023 con cui è stato emanato l'Avviso di manifestazione di interesse per la costituzione di un albo di esperti indipendenti a supporto della valutazione di merito dei progetti PNRR presentati sui bandi a cascata del progetto MNESYS – A multiscale integrated approach to the study of the nervous system in health and disease;

VISTO l'Estratto del Verbale della Riunione del 12 febbraio 2024 del Comitato Scientifico del programma di ricerca MNESYS "*A multiscale integrated approach to the study of the nervous system in health and disease*" che ha approvato la "Rosa di Candidati" per le Commissioni di Valutazione dei Bandi a cascata sul Programma MNESYS;

VISTO il Decreto del Rettore n. 855 del 20 febbraio 2024 con cui è costituito l'Albo a supporto delle valutazioni dei progetti presentati in risposta al bando pubblico per la selezione di proposte progettuali da finanziare nell'ambito delle attività di ricerca dello Spoke n. 6 di cui al programma di "*A multiscale integrated approach to the study of the nervous system in health and disease*" – MNESYS, a valere sulle risorse del Piano Nazionale di Ripresa e Resilienza (PNRR), Missione 4 "Istruzione e Ricerca", Componente 2 "Dalla ricerca all'impresa", linea di Investimento 1.3 "Creazione di Partenariati Estesi alle università, centri di ricerca, alle aziende per il finanziamento di progetti di ricerca di base";

VISTO il Decreto del Rettore n. 1125 del 5 marzo 2024 con cui è stata nominata la Commissione di valutazione delle proposte pervenute in risposta al bando a cascata di cui al D.R. n. 5439 del 14 novembre 2023, indicato nelle premesse del presente decreto;

ACQUISITO il verbale della Commissione di Valutazione della seduta del 16 aprile 2024 (Prot. n. 37982 del 07/05/2024);

VISTO il Decreto del Rettore n. 2292 del 10 maggio 2024 con cui è stata approvata la graduatoria di merito per la Tematica I – "Neural Network models of default activity patterns in the physiological and pathological (neurodegeneration or trauma) unconscious brain to design biomarker based on the microscopic cortical activity", di cui al bando a cascata di cui al Decreto del Rettore n. 5439 del 14 novembre 2023, indicato nelle premesse del presente decreto;

TENUTO CONTO che in data 14 maggio 2024 è stata inviata all'Istituto Superiore di Sanità la comunicazione con prot. n. 41383 in cui si rendevano noti gli esiti della procedura e si richiedeva la documentazione propedeutica all'adozione del provvedimento di ammissione del finanziamento;

VISTO che in data 21 maggio 2024 con prot. n. 44429 la documentazione richiesta è stata ricevuta dall'Università degli Studi di Genova che l'ha ritenuta conforme a quanto previsto nel bando a cascata di cui al Decreto del Rettore n. 5439 del 14 novembre 2023 e il Decreto Rettorale n. 5474 del 15 novembre 2023 , indicato nelle premesse del presente decreto,

DECRETA

ART. 1

L'ammissione a finanziamento del progetto NEMUS – Neurological Exploration through the Modeling of the Unconscious State per la **Tematica I – "Neural Network models of default activity patterns in the physiological and pathological (neurodegeneration or trauma) unconscious brain to design biomarker based on the microscopic cortical activity"** con Soggetto proponente l'Istituto Superiore di Sanità – come rappresentato negli Allegati B e C alla proposta presentata con domanda di partecipazione prot. n. 74594 del 14 dicembre 2023.

ART. 2

L'entità dell'agevolazione concessa, a fondo perduto, ammonta a 99.251,33 euro complessivi come rappresentati nell'allegato C alla proposta presentata con domanda di partecipazione prot. n. 74594 del 14 dicembre 2023. L'agevolazione è pari al 100% dei costi di progetto trattandosi di attività di ricerca fondamentale per Organismi di Ricerca. L'agevolazione è concessa a valere sui fondi PNRR - Programma "*A multiscale integrated approach to the study of the nervous system in health and disease*" – MNESYS Codice PE00000006 a valere sulla Missione 4, Componente 2, Investimento 1.3, ai sensi del Decreto di concessione n. 1553 dell'11 ottobre 2022, registrato alla Corte dei Conti il 23/11/2022 n. 2948, iscritto al Bilancio di Ateneo sul progetto UGOV 100009-2022-TF-PNRR-PE_MNESYS_BAC_DINOGMI.

ART. 3

Le attività, come indicate dettagliatamente nell'Allegato B alla domanda di finanziamento, dovranno essere avviate a partire dalla data di sottoscrizione del Contratto e concluse entro e non oltre 12 mesi, affinché siano rendicontate in tempo utile per consentire la chiusura del Programma PE MNESYS, il cui termine è attualmente previsto al 31 ottobre 2025.
Potrà essere valutata e concessa una sola proroga in presenza di ritardi dovuti a circostanze eccezionali e non dipendenti da scelte del Beneficiario esclusivamente nel caso in cui il MUR, a sua volta, proroghi il termine del Programma MNESYS.

ART. 4

Il presente atto sarà pubblicato sul sito UniGe https://unige.it/progetti-finanziati-dal-pnrr e laddove la normativa vigente lo richiede.
Il documento informatico originale sottoscritto con firma digitale sarà conservato presso l'Area Ricerca, Trasferimento Tecnologico e Terza Missione.

ALLEGATI:

Allegato B – Proposta progettuale
Allegato C – Piano economico-finanziario

IL RETTORE
Prof. Federico DELFINO
(documento firmato digitalmente)

Finanziato dall'Unione europea NextGenerationEU
Ministero dell'Università e della Ricerca
Italiadomani PIANO NAZIONALE DI RIPRESA E RESILIENZA
MNESYS
Università di Genova

ANNEX B

PE00000006
"A multiscale integrated approach to the study of the nervous system in health and disease"

MNESYS

SPOKE N. 6

Research proposal

Topic (i): "Neural Network models of default activity patterns in the physiological and pathological (neurodegeneration or trauma) unconscious brain to design biomarker based on the microscopic cortical activity"

NEMUS - Neurological Exploration through the Modeling of the Unconscious State

- PIs' host institution: **Istituto Superiore di Sanità**
- Principal Investigators (PIs): **Maurizio Mattia & Cristiano Capone**
- Proposal duration in months: **12**

ROLE IN THE PROJECT	*NAME*	*SURNAME*	*DEPARTMENT*	*QUALIFICATION*	*YOUNG (under 40 al 31.12.2023)*	*F/M*
Principal Investigator	*Maurizio*	*Mattia*	*CN PRORA*	*Primo Ricercatore*		*M*
co-Principal Investigator (PI)	*Cristiano*	*Capone*	*CN PRORA*	*Ricercatore TD*	*Under 40*	*M*
Researcher	*Antonio*	*Pazienti*	*CN PRORA*	*Ricercatore*		*M*
Researcher	*Andrea*	*Galluzzi*	*CN PRORA*	*Ricercatore*		*M*
Researcher	*Gianni V.*	*Vinci*	*CN PRORA*	*Ricercatore TD*	*Under 40*	*M*

ABSTRACT

This research proposal focuses on the characterization of slow-wave activity (SWA) in the brain, a default activity pattern associated with both unconscious states like natural sleep, and pathological conditions. Our study aims to model and analyse SWA across different brain states, including wakefulness, sleep, and unconsciousness induced by anaesthesia. Utilizing low-dimensional networks of mean-field units modelling cortical networks, we plan to explore the phase transition between unconscious and conscious states.
A key aspect of our research is the investigation of the presence of SWA during wakefulness and its fragmentation in late stages of sleep, indicating a continuum rather than a monolithic brain state. It has indeed been observed that traces of SWA affects performance and are related to lapses in attention.
Additionally, we will extend our study to pathological contexts, where SWA is observed in brain lesions and is implicated in epileptic seizures. A major goal is to develop biomarkers based on the inferred network models for different brain states and neurological dysfunctions, including disorders of consciousness, stroke, and neurodegenerative diseases. To this purpose we will employ a combination of recurrent neural networks and networks of mean-field units, leveraging experimental data to infer models acting as digital twins of observed electrophysiological activity. These models will help us to single out the dynamical regimes and transitions between different states of consciousness of the probed cortical networks.
Collaborating with the MNESYS consortium, we will utilize advanced stimulation techniques and electrophysiological recordings from humans and animal models to validate and refine our models. Our approach promises to enhance the understanding of brain dynamics and aid in the development of new therapeutic interventions and diagnostics tools for neurological disorders.

RESEARCH PROPOSAL
Sections (a) and (b) should not exceed 4 pages. References do not count towards the page limits.

Section a. State-of-the-art and objectives

Unconscious state like natural sleep is a hallmark of physiological brains invariantly preserved across many species[1]. In this state, cortical neurons undergo a slow alternation between periods of depolarization and firing (Up states) and periods of almost-silent hyperpolarization (Down states)[2,3]. This quasi-rhythmic activity unfolds as propagating waves slowly travelling the cortical surface (namely the slow-wave activity, SWA) giving rise to a global synchronized brain state[4-6]. SWA is a default activity pattern[7] with a relatively low degree of complexity observed also in the anaesthesia-induced unconscious state[8-10]. Complexity arises as the awake conscious state is approached with an increasing enrichment of the propagation modes in the SWA[11-13].

Electrophysiological activity of sleep/anaesthesia-wake transitions can be faithfully reproduced by low-dimensional mean-field models of local networks/units as a phase transition due to the crossing of a critical point separating the unconscious and conscious global state[14-16]. Network of mean-field units offer an effective theoretical framework to control and predict the collective dynamics of spiking neuron networks in turn capable to match quantitatively the *in vitro* and *in vivo* recorded activity[12,17] (Fig. 1A). A key ingredient to reproduce SWA is a relatively strong synaptic excitation (E) capable to ignite the chain reaction leading neurons to fire self-consistently and persistently and giving rise to the active Up state. Self-inhibition is another mandatory feature, and it is often associated to adaptation (A) mechanism of the firing rate[14,18,19]. This allows to work out the "(E, A)" phase plane, i.e., a bifurcation diagram where different regimes of activity in model emerge varying independently these two parameters, and the transition from sleep-like SWA to the awake-like desynchronized state are represented as a trajectory (Fig. 1B). Models (Fig. 1C) and *in vivo* cortical activity (Fig. 1D) can be roughly matched looking at the average duration of Up and Down states[20,21], allowing to locate where the brain is positioned in the (E, A) plane. **Models can then be successfully used as a proxy to determine the brain state**. Such approach, however, have several limitations regarding the limited availability to detect Up and Down states during wakefulness. **This project aims to challenge these limitations developing new approaches of model inference from data** based on the reservoir computing approach[22,23].

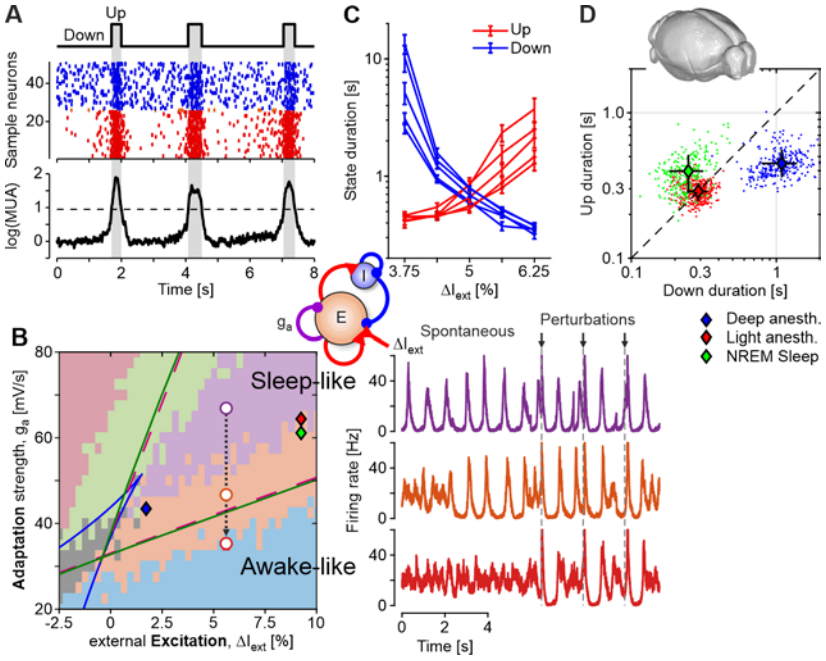


Figure 1: SNN (**A**) and mean-field models (**B**) describe sleep-wake transition (dotted vertical line). Synaptic excitation and firing rate adaptation determine a (E, A) diagram where the sleep- and wake-like phase emerge (**B**). Alternation between Up and Down states can be modulated by adaptation strength and excitation, changing their durations (**C**). Measuring duration of such states in anesthetized and sleeping mice allows to map *in vivo* brain states in the (E, A) diagram (**D**, coloured diamonds in **B**). Perturbations like TMS stimulation can elicit Down states even in the awake-like state (B-right). From refs. [20,24].

Slow-wave activity is not only a hallmark of the unconscious state. Indeed, an increasing body of literature is documenting the presence of local sleep islands also during wakefulness[25,26]. Fragmentation in space and time of SWA starts to be visible also in late stages of sleep[27]. This is in line with the hypothesis that the default activity pattern associated to unconsciousness is not a monolithic brain state, but it is rather a continuum[7,12].

Indeed, approaching wakefulness SWA displays a wider repertoire of propagation modes[12], and an increased capability of global integration arise due to the strengthening of long-distance interactions between brain regions[28,29]. A complexity reaching its maximum in the desynchronized activity associated with the conscious state, which can be seen as a dynamic exploration of functional brain configurations departing from anatomical constraints[30]. Fragments of SWA during wakefulness can temporarily disrupt such richness as the occurrence of Down states travelling across cortical networks operates a break in the functional connectivity[31], thus making more segregated and synchronized cortical activity hindering the integration of information behind conscious processing[32]. Accordingly, the occurrence of K-complexes in scalp EEG, known to be correlated with intracortical Down states and thus to EEG delta-waves[33], have been found to predict lapses of attention[34] becoming more frequent when the pressure for sleep increases[26]. Intracortical slow-waves are ubiquitous not only in physiological brains. For instance, EEG delta-waves are produced by brain lesions[35]. Sleep-like waves in the awake brain emerge nearby focal lesion induced by therapeutical thermo-coagulation[36] similarly to what found in perilesional cortical tissue after focal injury[37]. Not only, slow-waves seem to play an active role in eliciting epileptic seizure[38].

Inspecting local and global SWA or its fragmented occurrences during wakefulness and in pathological cortical networks can then offer a window of opportunity to the models capable to reproduce the unconscious state and the sleep-wake transition. In this framework **we aim to prove that a new generation of data-driven models can match electrophysiological recordings in physiological brain networks and the ones altered by focal traumas and tissue degeneration**. We can this with an 'opening the box' approach which will allow us to inspect the excitation and the self-inhibition adaptation degree of the inferred model bringing to map experimental activity of probed cortical network onto the normative (E, A) phase diagram.

Developing a reliable model that accurately reproduces experimentally recorded brain data is a significant challenge in neuroscience, given the intricate nature of neural dynamics. Challenges arise from the fragmented and multiscale nature of the data, as well as the limited accessibility (undersampling) to brain activity in terms of spatial extent of probe areas and temporal resolution. Undersampling leads to inferring effective (and thus biased) generative models, compromising its ability to generalize to new conditions. Reservoir computing (RC) has the potential to address these challenges. This approach utilizes recurrent neural network (RNN) architectures with fixed, random structure (the reservoir) to capture and process complex temporal patterns in data[22,23]. RC is particularly well-suited for handling sparse and biased datasets, as it relies on the reservoir intrinsic dynamics to map input data to high-dimensional spaces. These **RNNs result to be general computational machines capable to replicate any low dimensional dynamical systems: a kind of digital-twin of the observed system**. It is important to stress that the inference approach of RC is 'observational'. This means it does not rely neither on exogenous perturbations of the system[39] and nor on large amount of data needed by machine learning approaches[40].

While RC presents a promising approach for addressing challenges in modelling experimentally recorded brain data, they lack the direct capability to describe the dynamical properties of the replicated cortical networks in terms of biological parameters. On the other hand, this can be effectively done resorting to mean-field approaches successfully applied to replicate SWA and the unconscious-wake brain transition (Fig. 1). In this modelling framework the collective dynamics of a population of neurons is associated to a set of microscopic biological parameters (such as receptors, recurrent connectivity, or neuronal excitability), as the case of (E, A) plane. For this reason, here **we aim to develop a mapping mechanism that establishes a connection between reservoir models and mean field models**. This mapping will create a comprehensive framework capable to take the benefits of both the fields, allowing to successfully describe and predict the temporal dynamics of the probed cortical network from which to extract biologically relevant parameters. **The inferred digital-twins will be an effective proxy to inspect and characterize physiological and pathological changes of probed brain networks**.

Our proposal will push forward our capability in diagnosing and treating conditions determined by neurological dysfunctions like disorder of consciousness, stroke and neurodegenerative diseases. **The parametric information readable from the inferred digital-twins will possibly allow to design new**

biomarkers characterizing the multiscale cortical activity based on the mechanistic understanding of their dynamics rather than on a "black box" approach. Our data-driven RNNs can in principle also replicate electrophysiological recording in experimental setting where electric, magnetic and/or sensorial perturbations are administered. In principle, **this will allow us to investigate *in silico* which stimulation protocol may optimize the capability to move the cortical network from one point of the $(\boldsymbol{E}, \boldsymbol{A})$ plane to another** thus recovering some physiological functional states, paving the way to the advance the capability to treat patients.

Our vision is to take this challenge by coordinating our research activity with the competences and datasets from the various experimental settings already present in MNESYS. We will focus on brain functions and resting/unconscious states and the consequences of focal brain lesions explored through advanced stimulation techniques (optical, transcranial electric and magnetic) and electrophysiological recordings (intracellular and multiunit in cultured neuronal networks and from *in vivo* intracranial EEG in both Humans and animals). Developed tools, and RNN inference methods, and simulations will be also made available.

Section b. Methodology

b.1 Experimental data

We will rely on data available in open source repositories for both *in vivo* multi-electrode recordings from wild-type and knock-out mice modelling several neurological diseases (EBRAINS Knowledge Graph[41-43]) and intracranial/scalp EEG from Human epileptic patients (MNI Open iEEG Atlas[44] and G-Node[45]). Further data acquisition will be provided from experimental collaborators such as Prof. M. Massimini (Univ. Milan, Italy), Prof. M. V. Sanchez-Vives (IDIBAPS, Barcelona, Spain) and Prof. S. Ferraina ("Sapienza" Univ. Rome, Italy).

The acquired data define the spatiotemporal activity $S_i(t)$ (where i is the electrode and t is time) of an individual, in a specific condition and brain state (physiological resting state, sleep and awake, and anesthesia, and pathological states like minimally conscious and vegetative states, i.e., MCS and VS respectively). The whole spatiotemporal recording is defined as $\boldsymbol{z} = \{z_i(t), i = 1,..N, 1, ...T\}$, where N is the number of node and T the number of temporal acquisitions.

Mean-field models inferred from data are networks of interconnected nodes. Each node describes the dynamics of a single electrode and can be modeled as the activity of a population of spiking neurons.

b.2 Model Fitting (parameters and position/trajectory in the phase diagram)

The average activity of the i-th node at time t can be described in the framework of the mean-field theory through a non-linear current-to-rate gain function $F(\mu_i)$ dependent on the total synaptic mean-field input $\mu_i(t)$, the node receives. In turn, $\mu_i(t)$ is a function of the activity of the other (pre-synaptic) nodes *via* a connectivity kernel. The strength of this formulation is that the shape of the function $F(\mu_i)$ depends analytically on the microscopic and cellular parameters $\vec{m}$ of the neurons composing the node-related population (e.g., number of synaptic connections, the local balance between excitation-inhibition and other), allowing for the integration of microscopic and mesoscopic scales in our model. We can thus write $F(\mu_i) = F(\mu_i, \vec{m})$, allowing to naturally integrate microscopic features in the large-scale model.

There are many possible approaches to estimate the network parameters capable of reproducing the experimental data. One common choice is to write an error function $E(\vec{m}|\overrightarrow{\mathrm{MUA}}) = \sum_i(\mathrm{MUA_i} - F(\mu_i))^2$, comparing the electrophysiological activity (in this case the multi-unit activity $\mathrm{MUA_i}(t)$ of electrode i at time t) to the model state $F[\mu_i(t)]$, and then to find the parameters $\vec{m}$ minimizing this function (an approach previously used from the co-PI to successfully reproduce slow waves propagation in the whole hemisphere of the mouse under anaesthesia[16]). The major issue in this setup is the large number of parameters that can induce overfitting and optimization instabilities. Alternatively, we introduce an inference approach relying on reservoir computing (RC). In this framework we consider a RNN composed of N linear units evolving with the following dynamics: $\dot{x}_i(t) = -x_i(t) + \sum_j W_{ij}x_j(t) + \sum_j G_{ij}\mathrm{MUA}_j(t)$, where the recurrent weight matrix $\boldsymbol{W}$ is a random matrix with zero mean and variance $0.9/\sqrt{N}$, and the input weight matrix $\boldsymbol{G}$ has zero mean and

variance 0.1. Here only the parameters R_{ij} of the linear readout $z_i(t) = \sum_j R_{ij}\, x_j(t)$, necessary to decode the correct $\mathrm{MUA}_i(t)$ must be estimated minimizing the error between $\mathrm{MUA}_i(t)$ and $z_i(t)$.

As output of the project we derive a theoretical equivalence between the RNN dynamics and the mean-field model (exact in the case of a linear $F(\mu_i)$), allowing to work out analytically the recurrent and input weights of the latter from the inferred parameters of the former. This approach drastically reduces the number of free parameters and the computational cost for optimization, retaining remarkable model performances as digital-twin with the availability of a straightforward interpretation of the RNN dynamics, and thus of the emulated cortical network.

In a preliminary study from our group, we leverage this methodology to estimate cortico-cortical connectivity from data (Fig. 2A) by replicating the MUA from a 32-channel μECoG in anesthetized mice (Fig. 2B). By "opening the box", the strength of cortical assembly couplings can be estimated highlighting the presence of both short-range and sparse long-range connections (Fig. 2C). Notably, both the effectiveness of the connectivity and local excitability increase as anaesthesia fades out approaching the awake state.

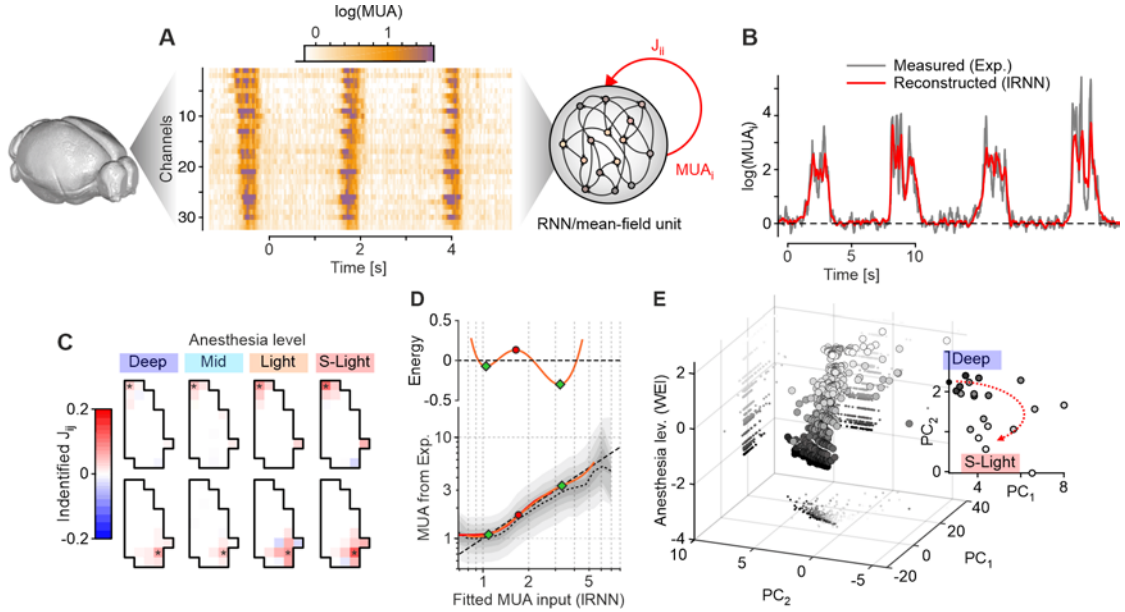


Figure 2: Reconstructing in RNN the multi-unit activity (MUA) from ECoG recordings of in vivo cortical networks of anesthetized mice: preliminary results. (**A**) MUA estimated from multi-electrode arrays placed on the cortical surface (μECoG, micro electrocorticography) capturing from electrophysiological signals at high frequency (>200 Hz). Dataset from Ref. [41]. (**B**) The MUA(t) trace at the following time step is predicted (red) using a recurrent model fitted and then compared against the experimental data (gray). (**C**) Afferent inferred connections for two channels (marked by a black dot), as the anesthesia levels decrease, showing that listening volume and self-interaction increase. (**D**) The data-inferred model highlights the enhancement of input from presynaptic MUA, demonstrating the current-to-rate gain function and providing an energy profile for the preferred working conditions of the system. (**E**) Analyzing the current-to-rate gain function of each channel across different anesthesia levels reveals how anesthesia variations affect neural assembly modulation of incoming currents. This is depicted in the main plot using the first two principal components, with an inset showing average values for each anesthesia level (gray shadings).

In the theoretical work package WP1 we aim to advance beyond linear models by developing new theoretical insights throughout the project. A key focus will be on understanding and modelling the linear-nonlinear amplification of input from presynaptic MUA, allowing to position each cortical assembly in the (E, A) plane across physiological and pathological brain states. As a preliminary result in this direction, we estimated the shape of the current-to-rate gain function $F(\mu_i)$ (Fig. 2D) and the change of its features at different levels of anaesthesia as emerge in the low-dimensional representation shown in Fig. 2E.

Section c. Available instrumentations and resources

Our group has a robust array of computing resources, designed to handle a variety of computational needs.

Firstly, we have a Computing Cluster that comprises four nodes, each powered by the Intel® Xeon® CPU E5-2650 0, clocking in at 2.00GHz. With each node boasting 16 cores.

We are in the process of acquiring a second Computing Cluster, that is set to feature two nodes, each equipped with the AMD Epyc 9654 processor, running at 2.4 GHz. The standout feature here is the 96 cores per node.

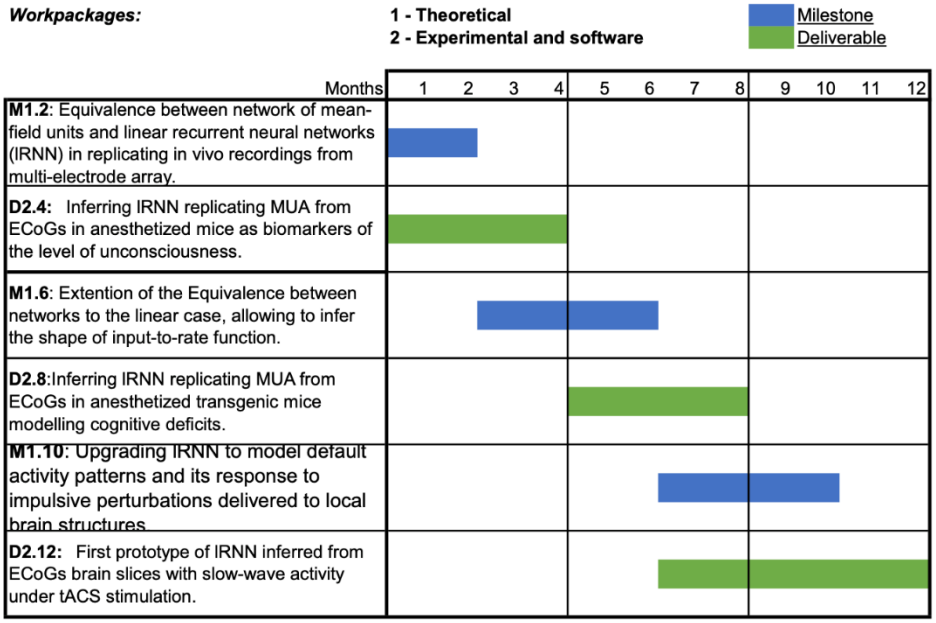
We have seven workstations, each configured to meet demanding workloads. These workstations are equipped with processors running at 2.1 GHz (13th Gen Intel® Core i7-13700 x 24) with 8 cores, ensuring smooth and efficient handling of tasks. Storage-wise, each workstation is equipped with a 2.5TB, and they are generously provisioned with 64GB of RAM to handle large datasets and intensive applications with ease.

Lastly, we're proud to mention our access to high-performance computing (HPC) platforms. Notably, we have been allocated one million core hours at CINECA. This access is through our involvement in the EBRAINS-Italy IR00011 PNRR Project (CUP B51E22000150006). This opportunity is not just a testament to our computational capabilities but also to our active participation in cutting-edge research and development.

We will also provide specific in-house analysis and theoretical tools to further tune and develop the specific instances of the models of interest for the MNESYS consortium. The available library of tools (Python, Julia and Matlab scripts) consists in cutting-edge algorithmic solutions to detect spatiotemporal patterns of activity and to decode task relevant information from multi-electrode electrophysiological recordings both *in vitro* and *in vivo* (anesthetized and behaving rodents and primates). This library of scripts will also include the ones we will develop to integrate numerically the dynamics of our recurrent neural networks and to infer their parameters to generate a statistically equivalent electrophysiological activity recorded in experiment.

Section d. GANTT diagram

The program is organized in 2 Work Packages (WP) and is structured in Deliverables (D) and Milestones (M).



WP1: the theoretical work package having the role to develop the analytical tools.

WP2: the experimental/data analysis work package, having the role to apply theoretical tool to data, and to produce the software to be released to the community.

M1.2: Equivalence between network of mean-field units and linear recurrent neural networks (lRNN) in replicating *in vivo* recordings from multi-electrode array.

D2.4: Inferring lRNN replicating MUA from ECoGs in anesthetized mice as biomarkers of the level of unconsciousness.

M1.6: Extension of the equivalence between networks to the linear case, allowing to infer the shape of input-to-rate function.

D2.8: Inferring lRNN replicating MUA from ECoGs in anesthetized transgenic mice modelling cognitive deficits.

M1.10: Upgrading lRNN to model default activity patterns and its response to impulsive perturbations delivered to local brain structures.

D1.12: First prototype of RNN inferred from ECoGs in brain slices with SWA under tACS stimulation.

References

1. Hobson, J. A. (2009). REM sleep and dreaming: towards a theory of protoconsciousness. Nat. Rev. Neurosci., 10(11), 803–813.
2. Steriade, M., Nuñez, A., and Amzica, F. (1993). A novel slow (< 1 Hz) oscillation of neocortical neurons in vivo: depolarizing and hyperpolarizing components. J. Neurosci. 13, 3252–3265.
3. Vyazovskiy, V.V., Olcese, U., Lazimy, Y.M., Faraguna, U., Esser, S.K., Williams, J.C., Cirelli, C., and Tononi, G. (2009). Cortical firing and sleep homeostasis. Neuron 63, 865–878.
4. Steriade, M., McCormick, D.A., and Sejnowski, T.J. (1993). Thalamocortical oscillations in the sleeping and aroused brain. Science 262, 679–685.
5. Destexhe, A., Contreras, D., and Steriade, M. (1999). Spatiotemporal analysis of local field potentials and unit discharges in cat cerebral cortex during natural wake and sleep states. J. Neurosci. 19, 4595–4608.
6. Massimini, M., Huber, R., Ferrarelli, F., Hill, S., and Tononi, G. (2004). The sleep slow oscillation as a traveling wave. J. Neurosci. 24, 6862–6870.
7. Sanchez-Vives, M. V, Massimini, M., & Mattia, M. (2017). Shaping the default activity pattern of the cortical network. Neuron, 94(5), 993–1001.
8. Mohajerani, M.H., McVea, D.A., Fingas, M., and Murphy, T.H. (2010). Mirrored bilateral slow-wave cortical activity within local circuits revealed by fast bihemispheric voltage-sensitive dye imaging in anesthetized and awake mice. J. Neurosci. 30, 3745–3751.
9. Stroh, A., Adelsberger, H., Groh, A., Rühlmann, C., Fischer, S., Schierloh, A., Deisseroth, K., & Konnerth, A. (2013). Making waves: initiation and propagation of corticothalamic Ca2+ waves in vivo. Neuron, 77(6), 1136–1150.
10. Sheroziya, M., and Timofeev, I. (2014). Global intracellular slow-wave dynamics of the thalamocortical system. J. Neurosci. 34, 8875–8893.
11. Dasilva, M., Camassa, A., Navarro-Guzman, A., Pazienti, A., Perez-Mendez, L., Zamora-López, G., Mattia, M., and Sanchez-Vives, M.V. (2021). Modulation of cortical slow oscillations and complexity across anesthesia levels. Neuroimage 224, 117415.
12. Pazienti, A., Galluzzi, A., Dasilva, M., Sanchez-Vives, M. V, & Mattia, M. (2022). Slow waves form expanding, memory-rich mesostates steered by local excitability in fading anesthesia. iScience, 25(3), 103918.

13. Liang, Y., Liang, J., Song, C., Liu, M., Knöpfel, T., Gong, P., and Zhou, C. (2023). Complexity of cortical wave patterns of the wake mouse cortex. Nat. Commun., 14(1), 1434.

14. Mattia, M., and Sanchez-Vives, M. V. (2012). Exploring the spectrum of dynamical regimes and timescales in spontaneous cortical activity. Cogn. Neurodyn., 6(3), 239–250.

15. Tort-Colet, N., Capone, C., Sanchez-Vives, M.V., and Mattia, M. (2021). Attractor competition enriches cortical dynamics during awakening from anesthesia. Cell Rep. 35.

16. Capone, C., De Luca, C., De Bonis, G., Gutzen, R., Bernava, I., Pastorelli, E., Simula, F., Lupo, C., Tonielli, L., Resta, F., Allegra Mascaro, A. L., Pavone, F., Denker, M., and Paolucci, P. S. (2023). Simulations approaching data: cortical slow waves in inferred models of the whole hemisphere of mouse. Commun. Biol., 6(1), 1–14.

17. Capone, C., Rebollo, B., Muñoz, A., Illa, X., Del Giudice, P., Sanchez-Vives, M. V, and Mattia, M. (2019). Slow waves in cortical slices: How spontaneous activity is shaped by laminar structure. Cereb. Cortex, 29(1), 319–335.

18. Compte, A., Sanchez-Vives, M.V., McCormick, D.A., and Wang, X.-J. (2003). Cellular and network mechanisms of slow oscillatory activity (<1 Hz) and wave propagations in a cortical network model. J. Neurophysiol. 89, 2707–2725.

19. Destexhe, A. (2009). Self-sustained asynchronous irregular states and Up-Down states in thalamic, cortical and thalamo-cortical networks of nonlinear integrate-and-fire neurons. J. Comput. Neurosci. 27, 493–506.

20. Torao-Angosto, M., Manasanch, A., Mattia, M., and Sanchez-Vives, M. V (2021). Up and Down states during slow oscillations in slow wave sleep and different levels of anesthesia. Front. Syst. Neurosci. 15, 609645.

21. Levenstein, D., Buzsáki, G., and Rinzel, J. (2019). NREM sleep in the rodent neocortex and hippocampus reflects excitable dynamics. Nat. Commun. 10, 2478.

22. Jaeger, H., and Haas, H. (2004). Harnessing nonlinearity: predicting chaotic systems and saving energy in wireless communication. Science (80). 304, 78–80.

23. Vyas, S., Golub, M.D., Sussillo, D., and Shenoy, K. V (2020). Computation through Neural Population Dynamics. Annu. Rev. Neurosci. 43, 249–275.

24. Cattani, A., Galluzzi, A., Fecchio, M., Pigorini, A., Mattia, M., and Massimini, M. (2023). Adaptation shapes local cortical reactivity: From bifurcation diagram and simulations to human physiological and pathological responses. ENeuro 10, ENEURO.0435-22.2023.

25. Vyazovskiy, V. V, Olcese, U., Hanlon, E.C., Nir, Y., Cirelli, C., and Tononi, G. (2011). Local sleep in awake rats. Nature 472, 443–447.

26. Nir, Y., Andrillon, T., Marmelshtein, A., Suthana, N., Cirelli, C., Tononi, G., and Fried, I. (2017). Selective neuronal lapses precede human cognitive lapses following sleep deprivation. Nat. Med. 23, 1474–1480.

27. Nir, Y., Staba, R.J., Andrillon, T., Vyazovskiy, V. V, Cirelli, C., Fried, I., and Tononi, G. (2011). Regional slow waves and spindles in human sleep. Neuron 70, 153–169.

28. Barttfeld, P., Uhrig, L., Sitt, J. D., Sigman, M., Jarraya, B., and Dehaene, S. (2015). Signature of consciousness in the dynamics of resting-state brain activity. Proc. Natl. Acad. Sci. USA, 112(3), 887–892.

29. Demertzi, A., Tagliazucchi, E., Dehaene, S., Deco, G., Barttfeld, P., Raimondo, F., Martial, C., Fernández-Espejo, D., Rohaut, B., Voss, H. U., Schiff, N. D., Owen, A. M., Laureys, S., Naccache, L.,

and Sitt, J. D. (2019). Human consciousness is supported by dynamic complex patterns of brain signal coordination. Sci. Adv., 5(2), eaat7603.

30. Koch, C., Massimini, M., Boly, M., and Tononi, G. (2016). Neural correlates of consciousness: progress and problems. Nat. Rev. Neurosci., 17(5), 307–321.
31. Massimini, M., Ferrarelli, F., Huber, R., Esser, S. K., Singh, H., and Tononi, G. (2005). Breakdown of cortical effective connectivity during sleep. Science, 309(5744), 2228–2232.
32. Luppi, A. I., Craig, M. M., Pappas, I., Finoia, P., Williams, G. B., Allanson, J., Pickard, J. D., Owen, A. M., Naci, L., Menon, D. K., & Stamatakis, E. A. (2019). Consciousness-specific dynamic interactions of brain integration and functional diversity. Nat. Commun., 10(1).
33. Cash, S.S., Halgren, E., Dehghani, N., Rossetti, A.O., Thesen, T., Wang, C., Devinsky, O., Kuzniecky, R., Doyle, W., Madsen, J.R., et al. (2009). The human K-complex represents an isolated cortical down-state. Science 324, 1084–1087.
34. Andrillon, T., Burns, A., Mackay, T., Windt, J., and Tsuchiya, N. (2021). Predicting lapses of attention with sleep-like slow waves. Nat. Commun. 12, 1–12.
35. Gloor, P., Ball, G., and Schaul, N. (1977). Brain lesions that produce delta waves in the EEG. Neurology 27, 326–333.
36. Russo, S., Pigorini, A., Mikulan, E., Sarasso, S., Rubino, A., Zauli, F. M., Parmigiani, S., d'Orio, P., Cattani, A., Francione, S., Tassi, L., Bassetti, C. L. A., lo Russo, G., Nobili, L., Sartori, I., & Massimini, M. (2021). Focal lesions induce large-scale percolation of sleep-like intracerebral activity in awake humans. NeuroImage, 234, 117964.
37. Sarasso, S., D'Ambrosio, S., Fecchio, M., Casarotto, S., Viganò, A., Landi, C., Mattavelli, G., Gosseries, O., Quarenghi, M., Laureys, S., Devalle, G., Rosanova, M., & Massimini, M. (2020). Local sleep-like cortical reactivity in the awake brain after focal injury. Brain, 143(12), 3672–3684.
38. Sheybani, L., Vivekananda, U., Rodionov, R., Diehl, B., Chowdhury, F.A., McEvoy, A.W., Miserocchi, A., Bisby, J.A., Bush, D., Burgess, N., et al. (2023). Wake slow waves in focal human epilepsy impact network activity and cognition. Nat. Commun. 14, 7397.
39. Casali, A. G., Gosseries, O., Rosanova, M., Boly, M., Sarasso, S., Casali, K. R., Casarotto, S., Bruno, M.-A., Laureys, S., Tononi, G., & Massimini, M. (2013). A theoretically based index of consciousness independent of sensory processing and behavior. Sci. Transl. Med., 5(198), 198ra105.
40. Lee, M., Sanz, L. R. D., Barra, A., Wolff, A., Nieminen, J. O., Boly, M., Rosanova, M., Casarotto, S., Bodart, O., Annen, J., Thibaut, A., Panda, R., Bonhomme, V., Massimini, M., Tononi, G., Laureys, S., Gosseries, O., & Lee, S. W. (2022). Quantifying arousal and awareness in altered states of consciousness using interpretable deep learning. Nat. Commun., 13(1), 1–14.
41. Sanchez-Vives, M. (2020). Propagation modes of slow waves in mouse cortex [Data set]. Human Brain Project Neuroinformatics Platform. https://doi.org/10.25493/WKA8-Q4T
42. Sanchez-Vives, M. (2019). Cortical activity features in transgenic mouse models of cognitive deficits (Fragile X Syndrome) [Data set]. Human Brain Project Neuroinformatics Platform. https://doi.org/10.25493/ANF9-EG3
43. Sanchez-Vives, M. (2019). Cortical activity features in transgenic mouse models of cognitive deficits (Williams Beuren Syndrome) [Data set]. Human Brain Project Neuroinformatics Platform. https://doi.org/10.25493/DZWT-1T8
44. Frauscher, B., Von Ellenrieder, N., Zelmann, R., Doležalová, I., Minotti, L., Olivier, A., Hall, J., Hoffmann, D., Nguyen, D.K., Kahane, P., et al. (2018). Atlas of the normal intracranial

electroencephalogram: Neurophysiological awake activity in different cortical areas. Brain 141, 1130–1144. https://mni-open-ieegatlas.research.mcgill.ca

45. Boran E, Fedele T, Steiner A, Hilfiker P, Stieglitz L, Grunwald T, Sarnthein J (2019) Dataset of simultaneous scalp EEG and intracranial EEG recordings and human medial temporal lobe units during a verbal working memory task. G-Node. https://doi.org/10.12751/g-node.d76994

1 - Curriculum Vitae, Maurizio Mattia (PI)

PERSONAL INFORMATION

Family name, First name: Mattia Maurizio
Researcher unique identifier(s) (ORCID): 0000-0002-2356-4509
Date of birth: 15/09/1968
Nationality: Italian
URL for web site: https://scholar.google.com/citations?user=GEyFcaQAAAAJ&hl=en&oi=ao

- **EDUCATION**

2010	PhD in Neurophysiology, Dept. of Neurophysiology, "Sapienza" University of Rome, Italy Supervisor: S. Ferraina
1997	Master in Physics Dept. of Physics, "Sapienza" University of Rome, Italy Supervisor: D. J. Amit

- **CURRENT POSITION(S)**

2022 – now	Senior Researcher (equivalent to Full Professor). Natl. Center for Radiaprotection and Computational Physics, Istituto Superiore di Sanità (ISS), Rome, Italy
2019 – now	Adjunct professor of Neural Networks (6 CFU, 60 hours, FIS/02, LM-17) Dept. of Physics of the "Sapienza" University of Rome, Italy

- **PREVIOUS POSITIONS**

2002 – 2022	Researcher position. Lab. of Physics/Dept. of Technologies and Health/Natl. Center for Radioprotection and Computational Physics, Istituto Superiore di Sanità (ISS), Rome (Italy).
2006	Scientific research collaborator with S. Fusi. Institute for Neuroinformatics (INI), UNI-ETH, Zurich (Switzerland).
1998 – 2002	Postdoc research position. Physics Lab., ISS, Rome (Italy).
1997 – 1998	Postdoc research position. Physics Dept., University of Genoa, Genoa (Italy).

- **FELLOWSHIPS AND AWARDS**

1996 – 2009	INFN (Italian Institute of Nuclear Physics) fellowship at the "Roma I" Section of the Sapienza University of Rome and ISS.
2016 – 2018	PI for ISS of the "Human Brain Project – Special Grant Agreement 1" (HBP-SGA1). EC Horizon 2020, Grant n. 720270. Funding: 330.625,00 €
2018 – 2020	PI for ISS of the "Human Brain Project – Special Grant Agreement 2" (HBP-SGA2). EC Horizon 2020, Grant n. 785907. Funding: 323.762,50 €
2020 – 2023	PI for ISS of the "Human Brain Project – Special Grant Agreement 3" (HBP-SGA3). EC Horizon 2020, Grant n. 945539. Funding: 406.250,00 €

2022 – 2025 PI for ISS of "EBRAINS-Italy – European Brain ReseArch InfrastructureS-Italy" MUR PNRR and EC NextGenerationEU (2022CALL_PNRR:M4/C2/L3.1.1) (CUP: B51E22000150006). Funding: 446.250,00 €

- **SUPERVISION OF GRADUATE STUDENTS AND POSTDOCTORAL FELLOWS**

2013 – now 5 Postdocs / 12 PhD students / 17 Master Students
Dept. of Physics / "Sapienza" University of Rome / Italy
Dept. of Mathematics / Sapienza University of Rome / Italy
Dept. of Physics / "Tor Vergata" University of Rome / Italy
Faculty of Medicine and Health Sciences / Universitat de Barcelona / Spain

- **ORGANISATION OF SCIENTIFIC MEETINGS**

2015 "Metastable Dynamics of Neural Ensembles Underlying Cognition" CNS Workshop, Prague, Czech Republic.
2022 "Inquiring (the) mind – Talking science to remember Paolo Del Giudice", Rome, Italy

- **INSTITUTIONAL RESPONSIBILITIES**

2016 PhD evaluation committee, Yasmina Seamari, Universidad de Malaga, Spain
2017 PhD evaluation committee, Augusitn Moritz, Technische Universitat of Berlin, Germany
2018 PhD evaluation committee, Noe V. Gallice, EPFL, Lausanne, Switzerland
2018 PhD evaluation committee, Julia F. Weinert, Universitat de Barcelona, Spain
2020 PhD evaluation committee, Melody Torao-Angosto, Universitat de Barcelona, Spain
2020 Scientific project evaluator, Agence Nationale de la Recherche, France
2021 Scientific project evaluator, Human Brain Project-ICEI proposals, Germany
2021 PhD evaluation committee, Farzaneh Darki, University of Friburg, Germany
2022 PhD evaluation committee, Brijesh Modi, European Brain Research Institute, Italy
2022 PhD evaluation committee, Leonardo Della Porta, Universitat de Barcelona, Spain
2022 PhD evaluation committee, Surabhi Ramawat, Sapienza University of Rome, Italy
2022 Scientific project evaluator, Human Brain Project Partnering Projects, Germany
2022 Scientific project evaluator, Dutch Research Council (NOW), Netherlands

- **REVIEWING ACTIVITIES**

2002 – now Referee for more than 100 papers on peer-review international journals including Physical Review Letters, Neuron, Nature Communication, PNAS, Cerebral Cortex and PLoS Computational Biology.
2018 Guest Editor for Neural Computation
2019 – now Associate Editor for Frontiers in Computational Neuroscience
2019 – now Guest Associate Editor for Frontiers in Systems Neuroscience
2019 Guest Editor for PLoS Computational Biology
2021 – now Associate Editor for Journal of Computational Neuroscience

- **MAJOR COLLABORATIONS**

M.V. Sanchez-Vives, In vivo and in vitro recordings in rodents, IDIBAPS, Spain
S. Ferraina, In vivo recordings in non-human primates, Sapienza Univ. Rome, Italy
N. Brunel, Theoretical and computational neuroscience, Bicocca Univ. Milan, Italy

2 - Curriculum Vitae, Cristiano Capone, Co-PI

PERSONAL INFORMATION

Family name: Capone
First name: Cristiano
Researcher unique identifier(s): https://orcid.org/0000-0002-9958-2551
Date of birth: 03/01/1989
Nationality: Italian

- **EDUCATION**

2013 – 2016 PhD
Physics Department , "La Sapienza University", Rome, Italy
Title: Emergent dynamics of cortical networks: From slow-wave activity to wakefulness.
Tutors: Maurizio Mattia, Paolo Del Giudice

2011 – 2009 Master
Physics Department , "La Sapienza University", Rome, Italy
Title: The role of time scales in synaptic inference based on inverse Ising methods applied to neural networks.
Tutors: Paolo Del Giudice, Federico Ricci Tersenghi

- **CURRENT POSITION(S)**

2023 – now Postdoctoral Researcher
"Natl. Center for Radiation Protection and Computational Physics, Istituto Superiore di Sanità"/ Rome/ Italy

- **PREVIOUS POSITIONS**

2018 – 2023 Postdoctoral Researcher
"INFN, Sezione di Roma"/ Rome/ Italy
2017 – 2018 Postdoctoral Researcher
"European Institute for Theoretical Neuroscience", CNRS, Paris/ France
2017 – 2017 Postdoctoral Researcher
"La Sapienza University", Physics Department / Rome/ Italy

- **FELLOWSHIPS AND AWARDS**

2022 – 2023 Fenix-ICEI allocation of computational resource, FENIX grant n. icei-hbp-2022-0012

- **ORGANISATION OF SCIENTIFIC MEETINGS**

2021 Organizer of the Workshop: "Energy and entropy-based concepts to characterize brain activity". EITN, Online. https://www.eitn.org/index.php/calendar-event/eventdetail/742/-/workshop-on-energy-and-entropy-measures-in-neural-systems
2018 Organizer of the Workshop: "The many flavors of Effective connectivity". EITN, Online. https://www.eitn.org/index.php/calendar-event/eventdetail/693/-/the-many-flavors-of-effective-connectivity-from-neuronal-cultures-to-fmri

- **REVIEWING ACTIVITIES**

2018 – now Reviewer for the journal "Physical Review E"
2019 – now Review panel member for FENIX ICEI
2022 – now Review for the journal "Frontiers in Neuroscience"
2022 – now Review for the journal "Nature Computational Science"
2023 – now Review for the journal "Plos Computational Biology"

- **MAJOR COLLABORATIONS**

- Alain Destexhe, Theoretical Neuroscience, EITN, Paris, France
- Maria Victoria Sanchez-Vives, Experimental data of cortical dynamics, DIBAPS, Barcellona, Spain
- Marcello Massimini, University of Milan, Italy
- Federico Ricci Tersenghi, Statistical Mechanics, La Sapienza University, Rome, Italy
- Francesco Pavone, Experimental data of cortical dynamics, LENS, Florence, Italy
- Michael Denker, Data analysis, Institute of Neuroscience and Medicine, Julich, Germany
- Pier Stanislao Paolucci, Computational Neuroscience, INFN, Rome, Italy
- Maurizio Mattia and Paolo Del Giudice, Theoretical Neuroscience, ISS, Rome, Italy
- Giacomo Indiveri, "University of Zurich and ETH Zurich", Institute of Neuroinformatics/ Zurich/Switzerland

- **INSTITUTIONAL RESPONSIBILITIES**

2022 – 2023 Master Student co-Advisor, Ingo Blakowski, Model-based reinforcement learning on neuromorphic chip.
"University of Zurich and ETH Zurich", Instituto of Neuroinformatics/ Zurich/Switzerland

2022 – 2023 Graduate Student co-Advisor, Luigi Rosati, Learning temporal sequences in bio-inspired neural networks.
"La Sapienza University"/ Physics Department/ Italy

2020 – 2021 Graduate Student co-Advisor, Gabriele Mancini, Inference as an engine of a Renormalization Group approach to investigate neural networks properties at different spatial scales.
"La Sapienza University"/ Physics Department/ Italy

2018 – 2019 Graduate Student co-Advisor, Paolo Muratore, Maximum Likelihood Methods for Biologically Plausible Learning in Recurrent Spiking Networks. "La Sapienza University"/ Physics Department/ Italy

2018 – 2019 Graduate Student co-Advisor, Chiara De Luca, Learning and sleep in a thalamo-cortical multi-area model.
"La Sapienza University"/ Physics Department/ Italy

- **PERIODS ABROAD**

2017-2018 Alain Destexhe Lab. EITN, Paris, France

3 - Curriculum Vitae, Antonio Pazienti

PERSONAL INFORMATION

Family name, First name: **Pazienti, Antonio**
Researcher unique identifier: ORCID 0000-0002-3834-5501
Date of birth: 16/01/1976
Nationality: Italian

- **EDUCATION**

2003 – 2007	Institute of neurobiology, Free University Berlin / University of Potsdam PhD (Dr. Re. Nat.) in theoretical physics (magna cum laude)
1995 – 2001	University La Sapienza, Rome, Italy Diploma in Physics
1998 – 1999	University of Paris Denis Diderot, France Exchange student in the Erasmus European program

- **CURRENT POSITION**

2017 – now	Full-time researcher National Center for Radiation Protection and Computational Physics Italian National Institute of Health, Roma (Italy)

- **PREVIOUS POSITIONS**

2014 – 2016	European Brain Research Institute, Rome, Italy Post-doctoral research in computational neuroscience / neurophysiology
2009 – 2014	European Brain Research Institute, Rome, Italy Post-doctoral research in neurophysiology / computational neuroscience
2007 – 2007	Institute of neurobiology, Free University Berlin Research Assistant in the group Neuroinformatics/Theor. Neuroscience
2006 – 2007	RIKEN Brain Research Institute, Saitama, Japan Technical staff in the laboratory of Prof. Dr. Sonja Gruen and Prof. Dr. Markus Diesmann
2003 – 2006	Institute of neurobiology, Freie Universitaet Berlin PhD fellow in computational neurobiology

- **FELLOWSHIPS AND AWARDS**

2006	Fellowship from the Computational Neuroscience Society for the participation to CNS Meeting di Madison, WI, USA
1998 – 1999	Fellowship at the physics department, university "Paris 7 – Denis Diderot", Paris, France in the program “Socrates-Erasmus”

- **ORGANISATION OF SCIENTIFIC MEETINGS**

2019	Organization of the workshop: “Dynamical richness of cortical networks: role and modulation across brain states”. Bernstein Conference 2019, Berlin, Germany
2006	Organization of the workshop: “Spatio-temporal scales of cortical interaction”, Le Cannelle, Monte Argentario, Italia.

- **INSTITUTIONAL RESPONSIBILITIES**

2020 – 2022 ISS responsible for the task "Scientific and technical integration in EBRAINS" (T2.11), Human Brain Project (HBP)

- **REVIEWING ACTIVITIES**

2009 – now Reviewer for Springer Series in Computational Neuroscience
2009 – now Reviewer for the journal Frontiers in cellular neuroscience.
2009 – now Reviewer for the journal Frontiers in system neuroscience.

MEMBERSHIPS OF SCIENTIFIC SOCIETIES

2006 – 2008 Associate member, Bernstein Center for Computational Neuroscience (BCCN)

- **MAJOR COLLABORATIONS**

- Participant in project EU Future and Emerging Technologies, Human Brain Project 2019 – 2021
- Participant in project EC Future and Emerging Technologies, 2017 – 2019
- Wavescaling Experiments and Simulations (WaveScalES)
- Participant in project FILAS-RU-2014-1040 "La microscopia in super-risoluzione: una nuova tecnologia per lo studio e la divulgazione delle dinamiche cellulari e molecolari nella ricerca biomedica" 2016
- Participant in project FIRB FIRBRBAP10L8TY 2011-2014
- Participant in project ERC "Project 200808 CORTEXSELFCONTROL" 2009-2011

4 - Curriculum Vitae, Andrea Galluzzi

PERSONAL INFORMATION

Family name, First name: Galluzzi Andrea
Researcher unique identifier(s) (such as ORCID): https://orcid.org/**0009-0001-9994-7055**
Date of birth: 19/02/83
Nationality: Italy

- **EDUCATION**

2016 Ph.D. Degree
La Sapienza University of Rome / Mathematics / Italy
Name of PhD Supervisor: E. Agliari

2011 Master's degree
La Sapienza University of Rome / Physics/ Italy
Name of Supervisor: A. Barra, F. Guerra.

2007 Bachelor's degree
La Sapienza University of Rome / Physics/ Italy

Name of Supervisor: D. J. Amit.

- **CURRENT POSITION(S)**

2016 –2023 Researcher
"Italian National Institute of Health" (ISS-Istituto Superiore di Sanità)

- **PREVIOUS POSITIONS**

2012– 2012 co.co.co
La Sapienza University of Rome / Physics/ Italy

- **FELLOWSHIPS AND AWARDS**

2015 2015-Highlights of JPA IOP (best papers of 2015),
Journal of Physics A: Mathematical and Theoretical 48 (1), 015001.
2015 2015-Progetti per avvio alla ricerca- La Sapienza University of Rome.

- **REVIEWING ACTIVITIES (if applicable)**

2017 –2023 Reviewer, ScientificReport
2023 –2023 Reviewer, NeuralNetwork
2018 –2023 Reviewer, Neural Computation
2019 –2023 Reviewer, JPhysA
2020 –2023 Reviewer, Frontiers
2021 –2023 Reviewer, Neuromorphic Computing and Engineering

- **MAJOR COLLABORATIONS (if applicable)**

Project: EU Project FET (Future and Emerging Technology) Flagship projects:
Human Brain Project (HBP)

5 - Curriculum Vitae – Ganni Valerio Vinci

PERSONAL INFORMATION

Family name, First name: Vinci, Gianni Valerio
Researcher unique identifier(s): ORCID: 0000-0002-1199-4907
Date of birth: 12/03/1996
Nationality: Italian

- **EDUCATION**

2023 PhD in Physics
University of Rome Tor Vergata
Roberto Benzi & Maurizio Mattia

2019 Master degree in Theoretical Physics
University of Rome Tor Vergata

- **CURRENT POSITION**

2023 – now Researcher

Istituto Superiore di Sanità – Centro per la Protezione dalle Radiazione e Fisica Computazionale

Appendix: All current grants and on-going and submitted grant applications of the PI (Funding ID)

Mandatory information (does not count towards page limits)

Current grants (Please indicate "No funding" when applicable):

Project Title	*Funding source*	*Amount (Euros)*	*Period*	*Role of the PI*	*Relation to current proposal*
EBRAINS-Italy	EC NextGenerationEU – MUR PNRR	446.250,00	11/2022 – 04/2025	PI for ISS	Computational Neuroscience RI
In2PrimateBrains	ITN European Commission (EC)	No funding	07/2020 – 06/2024	Collaborator	International Training Network
Rome Technopole	EC NextGenerationEU – MUR PNRR	84.152,52	07/2022 – 06/2025	Collaborator	Machine Learning tools

ALLEGATO C

TABELLA COSTI PERSONALE STANDARD				COSTO DEL PERSONALE
FASCIA DI COSTO /LIVELLO	**NUMERO SOGGETTI**	**COSTO ORARIO vedi nota**	**MONTE ORE**	
Basso				- €
Medio	**4**	33 €	507	16.720 €
Alto	**1**	55 €	253	13.933 €
TOTALI	**5**		**760**	**30.653 €**

COSTO ORARIO: si deve far riferimento al Decreto Interministeriale n. 116 del 24/1/2018

ALLEGATO C

BUDGET DI PROGETTO	COSTO DEL PERSONALE	OVERHEAD	Costi per servizi di Consulenza Specialistica	Costi per licenze direttamente imputabili al progetto	Costi per materiali e attrezzature direttamente imputabili al progetto	Costi per altre tipologie di spese direttamente imputabili al progetto	COSTO TOTALE
	30.653,33 €	4.598,00 €	0,00 €	7.000,00 €	36.000,00 €	21.000,00 €	99.251,33 €