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Part B-1

1. Excellence #@REL-EVA-RE@#

1.1 *Quality and pertinence of the project's research and innovation objectives (and the extent to which they are ambitious, and go beyond the state of the art)*

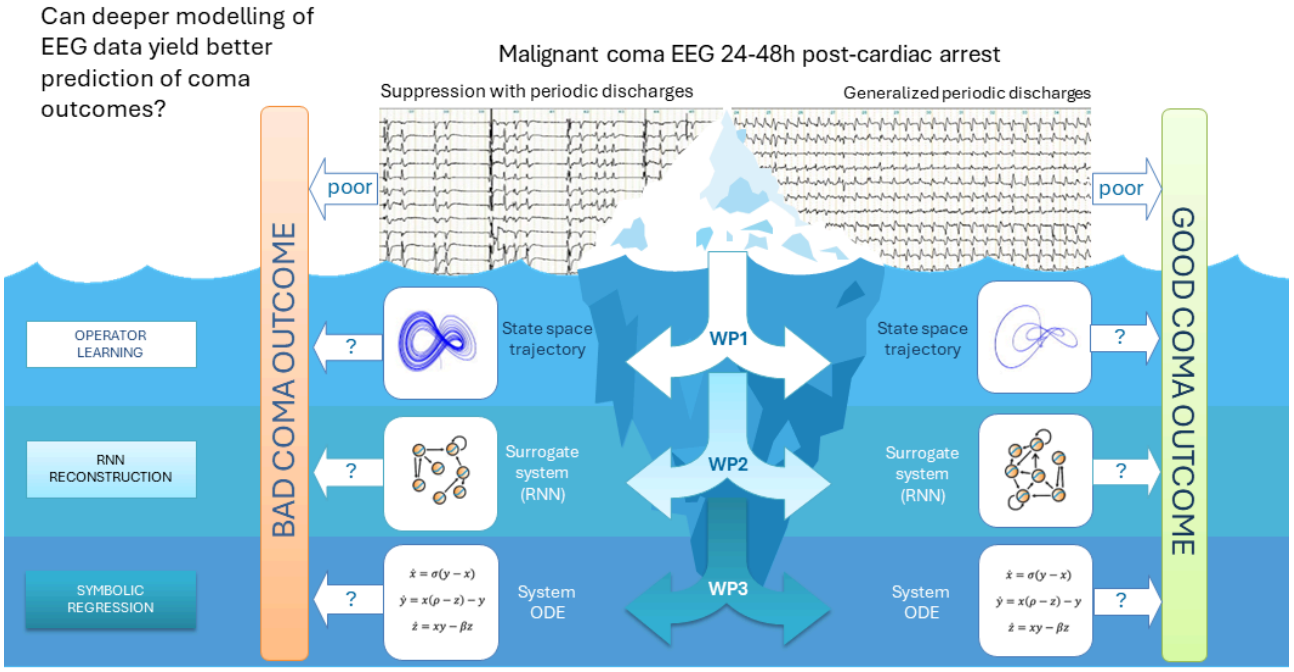
Context: The neurophysiological definition of consciousness is one of the most vexing theoretical and empirical questions facing modern neurosciences (Cogitate Consortium, 2023). So far the clinical classification of brain states in sleep and coma has mostly relied on "surface" features of the EEG waveform that can be visually detected by neurophysiologists. In sleep, for instance, the identification of sleep onset is typically associated with the disappearance of the alpha rhythm, and deeper sleep stages with the appearance of spindles, K-complex or slow waves (Lacaux et al. 2024). Similarly in coma, classification of vegetative vs minimally-conscious states, as well as prognosis, rely traditionally on the observation of "malignant" EEG features, such as discontinuities, reduced amplitude and rhythmic or periodic discharges (Benghanem et al. 2022; Figure 1). However, such features are highly variable both intra and inter-individuals, and may only reflect the "tip-of-the-iceberg" of the underlying state of the system. For instance, "benign" EEG that excludes any malignant feature still appears in 30% of bad-outcome patients (Fenter et al. 2023). Similarly, sleep researchers are starting to question the homogeneity of EEG appearance with sleep stages (Andrillon, 2023; Lacaux et al. 2024).

Aim, hypothesis and research objectives: The aim of project ARCADYA is to provide novel "bottom-of-the-iceberg" insights into what neurophysiological processes truly underlie altered states of consciousness in sleep and coma. To do so, we propose to capitalise on a recent series of advances in physics-informed machine learning (Kutz, 2016; Durstewitz et al. 2023; Brunton, 2016), which offer to treat the EEG waveform as the observation of a hidden, lower-dimensional dynamical system (in the sense of dynamical system theory, DST) and to learn its parameters and functional form from data. Our hypothesis is that, by focusing on the properties of reconstructed dynamical systems rather than on their highly-variable EEG observation, we will be able to improve both the definition and the prognosis of such states. Our **research objectives** are threefold:

- **RO1:** to evaluate the sensitivity of reconstructed DST parameters to the pre-existing clinical variables: do they correlate with coma severity and EEG malignancy, or with sleep stages
- **RO2:** to evaluate the capacity of reconstructed parameters to predict coma outcome, compared to other traditional predictors
- **RO3:** to look for novel mechanistic explanations for intra- and inter-individual EEG variability by measuring the similarity between the reconstructed systems between coma diagnostics and sleep stages.

These ROs are **measurable**, because they are associated with quantitative statistics such correlation coefficients (RO1), clinical measures of sensitivity/specificity (RO2) and machine-learning metrics of quality-of-fit such as mean sum of squared errors (MSE) or Kullback-Leibler (KL) divergence (RO3). They are also **verifiable**, because these metrics are either associated with well-understood statistical tests (RO1), or compared with predefined controls: other predictors of coma outcome from the clinical literature (RO2) or models within diagnostic and sleep stage (RO3). Finally, they are **realistically achievable** because we already have available datasets and well-defined computational strategies to achieve them (see Overall methodology, below).

Figure 1 (next page). Project ARCADYA aims provide novel "bottom-of-the-iceberg" insights into what neurophysiological processes underlie altered states of consciousness such as coma, by using dynamical system reconstruction techniques that treat the (variable and ambiguous) EEG waveform (top) as the observation of a hidden, lower-dimensional dynamical system with increasingly informative representations (WP1,WP2,WP3). Illustrations from Benghanem 2022; Durstewitz 2023



Position in relation to the state of the art: Project ARCADYA lies at the intersection of machine-learning, the physics of dynamical systems, and sleep and coma neurophysiology. The project goes beyond the state-of-the-art of this interdisciplinary perimeter in two major ways. First, while recent years have seen a lot of applications of machine learning to automatically detect/classify states of altered consciousness in coma or sleep (e.g. Ballanti et al. 2022), most of these use clinical EEG features (e.g. burst suppression; Zheng et al 2021) or learn these features with deep architectures (e.g. Pham et al. 2022) optimised to enhance the separability of the states. Our proposal departs from this approach by learning dynamical-system representations that are optimised to explain the temporal dynamics of the data, and to test the insights provided by these new representations. This is ambitious because it does not attempt to reproduce and automatize existing clinical expertise, but rather to derive novel insights into underlying physiological mechanisms. Second, several studies have already applied insights from DST or statistical physics to understand brain dynamics and consciousness. One prominent example is to model resting-state networks as networks of connected nodes (Deco, Jirsa & McIntosh, 2011) with techniques to infer both network connectivity and node-level dynamics. These models, when fit to resting-state fMRI activity of vegetative vs minimally-conscious patients, show a poorer and less flexible repertoire of configurations (Demertzi et al., 2019); in sleep, they may also explain EEG slow waves (Massimini et al., 2024). Our proposal departs from this approach because it does not postulate the explicit functional form of the model to fit it to data, but rather proposes to reconstruct this model in a purely data-driven manner. This development is ambitious because DS reconstruction has never been applied to EEG data in coma and sleep, nor with the ambition to go all the way to the clinic.

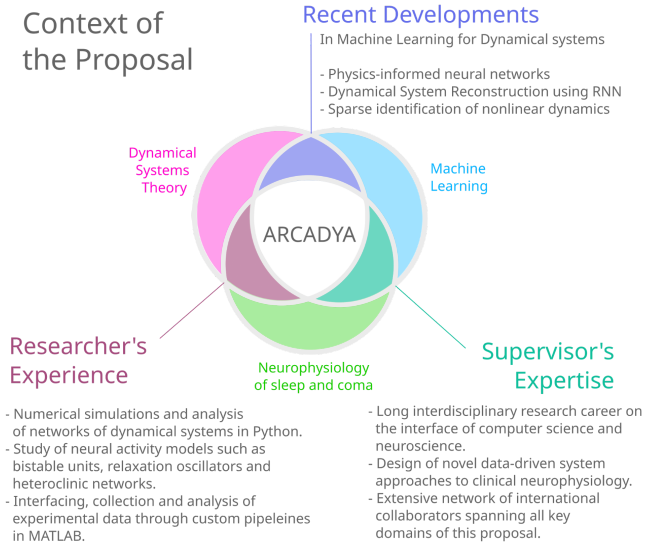
1.2 *Soundness of the proposed methodology*

The intuition behind our methodology is, while dynamical system theory (DST) provides a powerful mathematical toolbox to analyse physiological systems, that toolbox gets richer the more is known about the system's behaviour. If all is known is a single high-dimensional measurement of the system (e.g. the EEG waveform of an individual coma patient, Figure 1-top), then the researcher is left with model-agnostic time-series methods (however sophisticated) such as the ones used so far in machine learning. If, on the other hand, the system is known by its full functional form (e.g. a system of ordinary differential equations ODEs; Figure 1 - bottom), then DST offers tools not only to simulate arbitrarily large numbers of measurements from that system, but also to analytically study how they depend on its parameters in terms of bifurcations, fixed points, etc. Our rationale is to use DS reconstruction to progress along that continuum, abstracting away from the surface into depths where we can tap into the full power of DST to uncover otherwise unobserved properties of the underlying system.

Data: Our proposed data for this work are, for coma, an internally-available dataset of 20min resting-state EEG (13 scalp electrodes) recorded in 181 post-cardiac-arrest comatose patients, associated with neurological outcome (Coma Recovery Scale CRS-R at 7 days, Cerebral Performance Category, CPC at 3 months; Hermann et al. 2024); and for sleep, a recent public dataset of overnight sleep polysomnograms of 29 healthy adults (83 scalp electrode EEG, ECG, EMG, EOG), with annotations of N1,N2,N3 and REM sleep stages (Wei et al., 2024). Both datasets are already used at the host institution, and the main contributor of the coma dataset (S.B.) is part of the project team.
Overall methodology: Given this available data, we propose three methodological routes (and work packages) towards our ROs, which exemplify 3 families of techniques that have recently emerged from the community of physics-informed machine learning, and let us explore complementary aspects of the reconstructed DS.

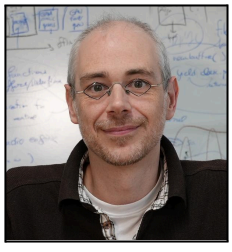
- **Operator learning** (WP1) is a family of techniques inspired by linear algebra which aim to approximate the relation between successive measurements of the system (i.e. its delay embedding) as a linear matrix operator A: $x_{k+1} \approx A.x_k$. This operator can be approximated, for instance, by the eigenmodes of a low-rank singular value decomposition (SVD) of x (dynamic mode decomposition, DMD; Kutz, 2016), or with variational autoencoders (VAE) trained on the delay embedding matrix (Raut et al. 2023). In the project, we use operator learning to transform the raw EEG time-series of each individual into a lower-dimensional trajectory in the state-space of a linear dynamical system that approximates the system's true dynamics. To address the project's ROs, we will then analyse that trajectory instead of the original waveform to provide indicators of its complexity (e.g. its fractal dimension), and the transformation mapping (e.g. SVD matrix), to provide indicators of system dimensionality and topology (RO1,RO2). Finally, we will measure system similarity across coma diagnostics and sleep stages (RO3) based on how well the measurement of a system can be decoded from the embedded trajectory of another (Raut et al. 2023).
- **RNN reconstruction** (WP2) is a family of techniques that use recurrent neural networks (RNNs) to learn a model from the data and then analyse that model as a surrogate for the true system. Several RNN architectures and training procedures have been proposed to fit the particular dynamics of neurophysiological data, including piecewise-linear recurrent neural network (PLRNN) or neural ordinary differential equations (ODEs; see Durstewitz et al. 2023). To address the project's ROs, we will train separate RNN models for each individual's data, then analyse each model in terms of its observation layer, its connectivity matrix, and its reduced dynamical graph (see Turner et al. 2021). We will then compare these parameters and measures against clinical parameters (RO1) and outcome (RO2). We will also compute measures of system similarity between coma diagnostics and sleep stages (RO3), based on how well trajectories simulated from one model overlap the trajectories of another using KL divergence.
- Finally, **Symbolic regression** (WP3), also known as the Sparse Identification of Non-linear Dynamics algorithm (SINDy; Brunton, Proctor & Kutz, 2016), attempts to directly write the differential equations of the system by approximating its vector field $dx/dt = f(x)$ by a large library of nonlinear basis functions (x, x^2, x^3, etc.) that are linearly combined with regularised (LASSO) regression. In the project, we will use SINDy to learn the functional form f(x) of each individual's time series. To address the project's ROs, we will then compare the parameters of each equation against clinical parameters and outcomes (RO1,RO2), as well as apply DST stability analysis on the obtained equations to look for common geometric and time-invariant properties across coma diagnostics and sleep stages (RO3).

Integration of methods and disciplines: Project ARCADYA operates at the interface of three disciplines. Classical physics brings more than 300 years of experimentally validated models of macroscopic phenomenon. Machine learning yields the ability to learn and predict processes, from large amounts of data, through model agnostic algorithms. Neurophysiology brings precise, high throughput experimental data that can be used to learn correlations in brain activity and causal links to behaviour. The new methods of physics-informed machine learning (PIML) that we employ in all three parts of our proposal, enhance the ability of traditional ML systems to learn measurements from physical processes. Though mathematical models describing neurophysiological data is standard practice, using these cutting edge PIML techniques to analyse EEG data from sleep and coma is a novel endeavour. My extensive experience in the analysis and experimental study of dynamical systems, along with the



supervisor's expertise in modelling neurophysiological data makes this possible. • **Gender and diversity:** AI approaches to medicine have a critical risk of providing biased decisions for groups of the human population that are misrepresented or absent in existing biomedical datasets (Larrazabal et al. 2020). To avoid algorithmic bias due to possible misrepresentation in these datasets, project ARCADYA was designed on the idea of modelling brain activity at the individual level (i.e. each individual EEG observation yields its own reconstructed DS). As a result, in no stage of the project will we group the results of majorities with minorities or otherwise enforce similarities or categories on these individuals. In terms of data, our two proposed datasets clearly specify both the biological sex (sleep: 13F/16M; coma: 65F/116M) and age (sleep: 20-44, M=34; coma: 50–72, M=61) of each individual. Neither of them includes information about gender and ethnicity. • **Artificial intelligence**: We understand and acknowledge that AI systems are not politically neutral and their deployment in societies and in the environment has non-neutral consequences (McQuillan, 2022). This is markedly so in systems aiding diagnosis and decision making in critical care. Our work here specifically focuses on alleviating the "black-box" nature of these AI systems by introducing algorithms that use "known physics". This helps in two ways, first by making these systems more explainable and transparent so they can be useful aids in human decision making; second by reducing the amount of brute-force computations (used by the likes of LLMs for instance) by taking advantage of physical intuition. The aim is to augment human understanding of these phenomena, and not to replace human expertise at the expenses of environmental resources.• **Open science practices and research data management**: Finally, open science is an important part of how I'd like to carry my research forward. In this regard, the host lab's long tradition of sharing their results and data to the public and other experts in an accessible format (https://neuro-team-femto.github.io/publications/) will be an important learning. All papers in the project will be published in green open access and all code will be shared on public repositories. Finally, since our proposal seeks predictability in clinical neurophysiological data, we pledge to develop accessible toolboxes (possibly with web services) that can be used by medical experts, if we find clinically meaningful insights. The host lab has already developed such a utility for voice synthesis that is routinely used in the GHU hospital to test coma patients with the sound of their name (https://rec.alta-voce.tech/).

1.3 *Quality of the supervision, training and of the two-way transfer of knowledge between the researcher and the host*



Jean-Julien Aucouturier is a CNRS Directeur de recherche (equiv. Full Professor) at the FEMTO-ST Institute in Besançon, France, where he directs the NEURO research group (https://neuro-team-femto.github.io). Trained in machine learning at SONY Computer Science Laboratories Paris with François Pachet (PhD, 2006), JJA then received postdoctoral training in cognitive and clinical neuroscience at the University of Tokyo (2008), RIKEN Brain Science Institute (2011) and the University of Lille, France (2017). JJA's experience with computer modelling in coma research includes being the PI of the Sounds4Coma consortium, an ongoing collaboration with the GHU Hospital in Paris on novel approaches towards coma prognostication. The project has so far received 1M€ of funding from Agence Nationale de la Recherche and Direction Générale de l'Offre de Soin, has produced 5 ongoing clinical trials, a novel clinical platform in the GHU ICU, and lead to supervision of 3 PhD theses. Over his career with CNRS, JJA has published more than 50 peer-reviewed papers in both computer science and neuroscience journals, incl. PNAS, Current Biology, Nature Communications, Cognition and Cortex (2024

H-index 34). He has supervised 9 PhD students and 7 postdocs, many of whom are now permanent researchers with institutions such as CNRS, Sorbonne Université or the University of Glasgow. JJA also has sizeable experience with EU funding, having been the PI of two ERC projects (CREAM StG 2014-2019 and ACTIVATE PoC 2019-2021) and, most recently, one MSCA Doctoral Network (LULLABYTE, 2023-2027) on music and sleep neurophysiology. JJA's extensive network of international collaborators spans all key domains of the current proposal, incl. coma science (Prof. Lionel Naccache, Tarek Sharshar, Martine Gavaret, France; Prof. Athina Tsovara, Switzerland; Dr Athina Demertzi, Belgium), sleep neurophysiology (Dr Thomas Andrillon, France; Prof. Björn Rasch, Switzerland; Prof. Martin Dresler, Netherlands) and physics-informed machine learning (Prof. Patrick Gallinari, France; Prof. Nathan Kutz, USA).• Beyond direct supervision by JJA, the researcher will also benefit from training and scientific collaboration with 3 members of the FEMTO-ST community, whose expertise are directly relevant for the project. **Noura Dridi,** Assistant Professor of Applied Mathematics at FEMTO-ST will



contribute expertise in the methodology of WP2 (RNN Reconstruction). **Sarah Benghanem (**M.D.) intensivist and neurologist at our partner hospital GHU in Paris, contributes the dataset of coma EEG used in the project (Hermann et al., 2024) and, as our consultant clinician, will host the researcher for short visits in the GHU ICU. **Mathieu Triclot**, Prof. of Philosophy of Technique in FEMTO-ST, is a specialist of ethnographic studies of how new AI technologies are deployed in social environments and will contribute expertise when designing clinical workshops at the end of the project. • **Planned training activities for the researcher**: During my time at FEMTO-ST, I will lay out a career development roadmap towards establishing myself as a PI working at the interface of brain dynamics, complex systems and machine learning. First, I'll receive hands-on training in the collection and handling of neurophysiological data, through short visits at the GHU hospital in Paris. Second, I will gain experience in organising scientific meetings and establish a network of collaboration with researchers working in these areas by organising a special session on "*Coma: A dynamical systems perspective*" at the NICIS conference that the host lab co-organizes in Paris every year. Third, I will receive formal training in machine learning via the FEMTO-ST Graduate School (EIPHI). Finally, I will obtain mentorship experience by supervising a MSc student in the project's second year. • **Two-way transfer of knowledge:** The researcher and the host lab possess key complementary skills that, when combined, enable the realisation of this project. I come from a physics background with experience simulating, characterising and modelling dynamical systems. This includes models that are regularly used to model neural activity such as heteroclinic networks and relaxation oscillators (Aravind 2023, Murali, 2021). I would like to add modern machine learning methods into my scientific repertoire. At the host lab, supervisor Jean-Julien and his team have extensive experience modelling EEG activity using data-driven techniques, and would like to incorporate DST into their models. This complementarity of knowledge between me and the host lab creates a special opportunity to learn, collaborate and execute such an ambitious project.

1.4 Quality and appropriateness of the researcher's professional experience, competences and skills

I am a physicist with a background in both the computational and experimental study of dynamical systems. My work so far has yielded 9 (incl. 7 first-author or corresponding-author) publications in leading journals of the field (*Physical Review Applied, Physical Review E, Chaos, Proceeding of the Royal Society A etc.*). During my PhD (IISER Mohali, 2020) I focussed on utilising coupled networks of dynamical systems to yield better computing. This theme of work has given me a strong grounding in theoretical analysis of dynamical systems, such as linear stability analysis, basin stability, bifurcation analysis, and study of emergent phase transitions (Physics Review E, 2021, 2022)- all of which will be important to analyse and critically evaluate the DS reconstructed by the project. In my subsequent postdocs in IIT Bombay and Constructor University in Bremen (DE), I have turned to studying large networks of coupled dynamical systems through numerical simulations, and have acquired experience with systems that are

used to model neural activity such as bistable systems (Chaos, 2021), relaxation oscillators (Physical Review E, 2024) and heteroclinic networks (Chaos, 2023), as well as key scientific programming experience in Python. Finally, I have been involved in a number of experimental studies of complex dynamical systems, for which I have developed a taste for constructing custom data acquisition pipelines (Eur. Phys. J. Spec. Top, 2022) and electronic circuits (Physical Review E, 2024). This rare combination of skills spanning DST theory, scientific programming and experiment design makes me an ideal researcher to carry out this project.

2. Impact #@IMP-ACT-IA@#

2.1 Credibility of the measures to enhance the career perspectives and employability of the researcher and contribution to his skills development

Specific measures to enhance career perspectives and employability: Securing a MSCA grant for my research project at FEMTO-ST will provide me with a valuable platform to develop a rare combination of skill sets. First, I get to apply modern machine learning techniques to my field of expertise (dynamical systems) and be part of a small thriving community of researchers working in 'learning for dynamics'. Attending key conferences in this field (L4DC, ERNSI, possibly submissions at NeurIPS and ICML) will help connect with key researchers. In addition, the host lab has started a monthly invited seminar series this year on 'Learning & Dynamics' (https://neuro-team-femto.github.io/learning2425), which I will take on organising next year. Second, I'll attain leadership in building novel research programs with direct social/clinical impact. The proposed work will provide first-hand experience communicating with medical doctors and the opportunity to publish and present results to the vast neuroscience community (in conferences such as ASSC, Brain-Body Waves) as well as publish my first articles in neuroscience and neurology journals. This unique combination of skills will greatly aid my career as a long term research leader. Third, the host lab co-organizes a master's course in computational physics and engineering, where I'll get teaching opportunities necessary to access lectureship positions in France. Lastly, my time at the host lab will firmly establish my commitment to open software development and help me develop my github page (https://github.com/man-aravind) on the model of the host lab's (https://github.com/neuro-team-femto).

• **Expected contribution:** By the end of the project, I expect to have published between 3 to 6 first-author journal articles or preprints, one per work package, divided among the sleep and coma datasets. I will have spread roots in the machine learning for dynamics and the neurophysiology communities, manifested by the organised lectures series and special session (NICIS). I expect to gain at least 10-20 hours of experience teaching a master's level dynamical systems course at a French University. Finally, the results obtained from this proposal will serve as pilot results to apply for a CNRS permanent researcher position and an ERC Starting Grant (for which I'm eligible until 2027).

2.2 Suitability and quality of the measures to maximise expected outcomes and impacts, as set out in the dissemination and exploitation plan, including communication activities #@COM-DIS-VIS-CDV@#

Plan for the dissemination and exploitation activities, including communication activities: Scientific results from the project will be disseminated with publications in general-science journals (e.g. from the host lab's previous work, PNAS, Nature Communications, Current Biology) and medical journals (e.g. from the host lab's previous work, Clinical neurophysiology, Critical Care). To ensure the timely dissemination of results, results will also be published as preprints as soon as available, and sent out for communication in scientific conferences. Finally, results will also be disseminated by making the project's new software tools available as open-source libraries or web services (deliverable D1.2, D2.2, D3.2) on the researcher's github page. • The clinical potential of the project's results will be explored at the end of the project by organising workshops with staff neurophysiologists at our partner hospital GHU, in which we will discuss how insights derived from the project's methodology can be integrated in the expert decision-making process and facilitate conversations with patients and their families.• Artist residency: dynamical systems as reconstructed by the project have a unique potential for artistic visualisation (Peitgen & Richter, 1986). At the end of the project, we will fund a 2-month residency for a visual artist to produce artistic renderings of the dynamic trajectories uncovered from sleep and coma. These renderings will be used to

communicate the project to the general public (in events such as Fête de la Science, Nuit des Chercheurs) as well as provide e.g. proposals of cover images for the project's scientific publications. • Finally, the media platform for disseminating the project's result is broad and has been nurtured by previous projects of the host lab. Supervisor JJA was the 2014 laureate of Association des Journalistes Scientifiques de la Presse d'Information (AJSPI) and spent one month as resident scientist at the science dept. of the Agence France Presse (AFP) news agency, which lead to strong relations with the science media community which continue to this day. • **Strategy for the management of intellectual property, foreseen protection measures**: If outcomes show any specific commercialization potential, these will be explored at the end of the project using the maturation services of our host institution CNRS (CNRS Innovation) and FEMTO-ST (FCInnov), incl. IP protection to the extent that they are compatible with our commitment to open science, and a possible MSCA-track to an EIC Transition application.

2.3. The magnitude and importance of the project's contribution to the expected scientific, societal and economic impacts

Scientific impacts: The scientific impact of our project will be both theoretical and methodological. First, the project will change what we know of the neurophysiological processes that underlie altered states of consciousness such as sleep and coma (e.g. *"are successive sleep stages bifurcations of a single dynamical system ?"*; *"are the coma brain dynamics lower-dimensional than the healthy brain's ?"*). Second, it will introduce novel physics-informed machine learning methods for analysing raw EEG data, and disseminate it with new open-source tools that simplify their use in the lab as well as the clinic (deliverables D1.2, D2.2, D3.2). • **Clinical impacts:** The incidence of coma in the general population is estimated at 8.5 per 100,000 for traumatic causes (59% of which involve car accidents) and an additional 6 per 100,000 for non-traumatic causes (e.g. infection), per year (Masson et al. 2003). This represents more than 110,000 patients per year in Europe alone, 40% of whom will evolve to vegetative and minimally-conscious states, or death (Luaute et al. 2005). For these patients and their family, our findings will provide new procedures for better informed diagnosis and more ethically-acceptable life-support decisions. • **Economic/technological:** The machine learning procedures developed in the project have potential to improve the efficiency and effectiveness for health care services, and to be in high demand by patient families. They will be considered for IP protection and commercialization, using the maturation services of our host institution CNRS (CNRS Innovation) and FEMTO-ST (FCInnov). • **Societal:** Beyond science, modelling the individual brain dynamics of patients will initiate a shift of paradigm from the typical application of AI for medical decision making, which tends to abstract individual diversity into broader statistical categories of patients with similar outcomes. This may have potentially important ethical and legal implications (e.g. "*what is the status of a patient which can't pass the CRS-R, but whose brain nevertheless shows intricate dynamical trajectories*"?). • **Cultural:** Finally, from Marcel Proust to Philip Glass, the scientific and philosophical question of consciousness has long been a source of inspiration for the arts. Because it promises to uncover visually compelling dynamical trajectories of consciousness in sleep and coma, the project has a high potential to entertain rich relations with the artistic community, something we explicitly address by funding a 2-3 month art residency at the end of the project.

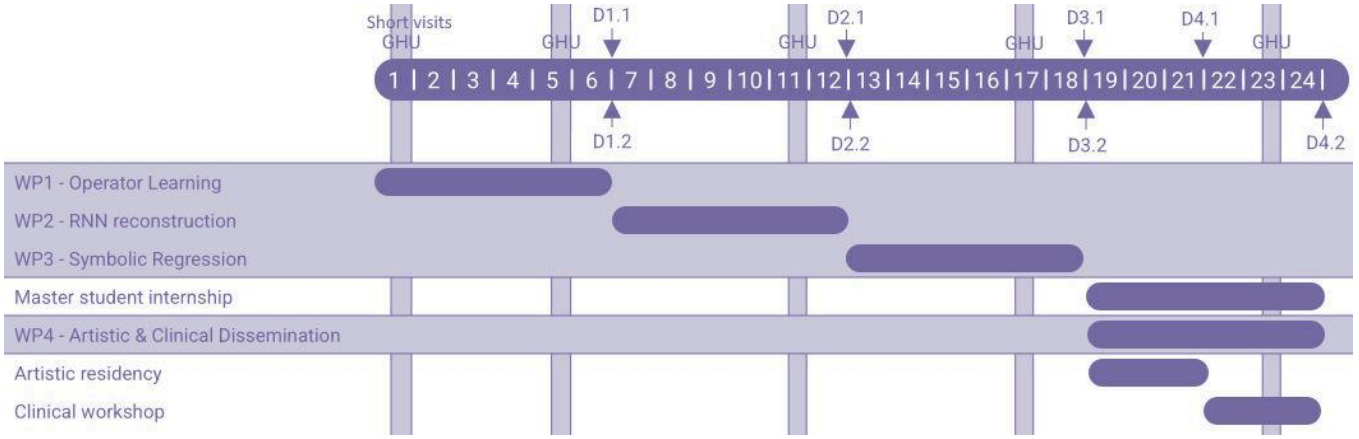
#§COM-DIS-VIS-CDV§# #§IMP-ACT-IA§#

3. Quality and Efficiency of the Implementation #@QUA-LIT-QL@# #@WRK-PLA-WP@# #@CON-SOR-CS@# #@PRJ-MGT-PM@#

3.1 Quality and effectiveness of the work plan, assessment of risks and appropriateness of the effort assigned to work packages

Project ARCADYA (24M) is organised in 3 scientific (WP1-2-3) and one artistic & clinical dissemination work package (WP4). • **WP1-2-3** correspond to the three techniques of Operator Learning, RNN Reconstruction and Symbolic Regression (see Methodology, above). Together, they provide 3 complementary routes to achieve the project's ROs. They will be carried out in sequence for a duration of 6M each. WP1 is studied first because it is simpler, and its outcome (a dimension reduction procedure) can be reused in WP2 and WP3 (i.e. on can apply RNNs and SINDy on the state-space trajectory learned in WP1, see e.g. Champion et al. 2019). In each WP1-2-3, work can be done independently on two datasets (sleep and coma), yielding different potential findings. Because it

is unrealistic to conduct thorough work addressing both fields with all 3 methodologies within the scope of the project, we will prioritise work in this way: WP1 will be carried out for both sleep and coma datasets (because it is simpler, it is reusable in WP2-3, and it is a good way to create intuitions about the dimensionality of the problem); WP2 and WP3 will be carried out on the sole coma dataset in months M6-M18 (because it is based on a privileged internal dataset, has more clinical implication, and we have more internal expertise), unless we reach a critical impossibility in which case the sleep dataset will serve as risk mitigation (see below) • In addition, the project includes a final 6M internship by a MSc student (supervised by the researcher), which will complement the work program in this way: if the initial work of WP2 or WP3 is considered successful on coma, the student will apply the same methodology on the sleep dataset, providing more coverage; if the initial work of WP2 or WP3 needs extra work on coma, the student will pursue this work, providing extra time to reach the project's ROs. • **WP4** (artistic and clinical dissemination) is placed at the end of the project, and includes two independent phases. First, we will fund a visual artist to work on artistic renderings of the project's reconstructed trajectories ("dynamics of consciousness"). The artist will be hosted in FEMTO-ST (M19-21) under an existing format of artist residency, and the produced visualisations will be used for general-public dissemination, journal cover images, and for the subsequent clinical workshops. Second, we will organise a series of clinical workshops with staff neurophysiologists at our partner hospital GHU (M21-24), where outcomes of the project will be discussed for their potential of integration in research practice. The workshops will be co-organized by our consultant clinician S.B. and FEMTO ethnographer M.T.



Deliverables: Each of the 3 scientific work packages WP1-2-3 is associated with 2 deliverables: one report (possibly in the form of a journal preprint), and one open-source code repository hosted on github. WP4 is associated with 2 deliverables: one report on artistic residency, and one report on clinical workshops. • **WP1: D1.1** Report on using operator learning techniques to achieve RO1-2-3 on coma and sleep; **D1.2** Code repository that implements the corresponding techniques; both due M6. • **WP2: D2.1** Report on using RNN reconstruction techniques to achieve RO1-2-3 on coma (in priority); **D2.2** Code repository that implements the corresponding techniques; both due M12. • **WP3: D3.1** Report on using symbolic regression techniques to achieve RO1-2-3 on coma (in priority); **D3.2** Code repository that implements the corresponding techniques; both due M18. • **WP4: D4.1** Report on artistic residency, due M21; **D4.2** Report on final clinical workshops, due M24. • **Short visits:** Throughout the project, 5 short visits will be planned in the GHU hospital (3hour-train ride in Paris), in months M1, M5, M11, M17 and M23. In the first visit at M1 (2 weeks), the researcher will shadow our consultant clinician in the GHU intensive care unit to get first-hand experience in coma management and EEG diagnosis. Visits at M5, M1 and M17 (1w each) are planned to discuss the results of, resp., WP1, WP2 and WP3 and learn about clinical statistics. Finally, the visit at M23 (2w) is dedicated to the clinical workshops.

Mechanisms in place to assess and mitigate risks: All three scientific WPs provide alternative and complementary routes to the three ROs, so they serve as risk mitigation for one another. Additionally, ROs can be investigated both for coma and sleep datasets. We put priority on coma, and use sleep when necessary as risk mitigation.

Work package	Risk and fall-back
WP1 - Operator Learning	1. **Cannot find a low-rank embedding** (because resting-state data is too diverse) **->** use additional ECG/EOG data to constrain the state space (Raut et al. 2023) **2. Lack of time to analyse trajectory parameters by M6 ->** Carry on with WP2, and consider returning to WP1 in MSc internship **3. Trajectory parameters do not correlate with coma or sleep parameters by M6 ->** not a risk but an outcome. Carry on with WP2
WP2 - RNN Reconstruction	1. **Structural reason why coma data cannot be learned** (e.g. dimension, etc.) -> pivot to sleep dataset 2. **Low reconstruction accuracy** -> embed RNN with dimension reduction from WP1 3. **Difficulty analysing RNN structure for ROs** -> sample trajectories and use WP1 metrics 4. **Lack of time to analyse RNN structure by M12** -> Carry on with WP3, and consider returning to WP2 in MSc internship 5. **RNN parameters do not correlate with coma parameters by M12 ->** not a risk but an outcome. Carry on with other work packages, and consider revisiting with sleep dataset in MSc internship
WP3 - Symbolic Regression	1. **Structural reason why coma data cannot be learned** (e.g. dimension, etc.) -> pivot to sleep dataset 2. **Low reconstruction accuracy** -> embed SINDY with dimension reduction from WP1 3. **Difficulty analysing functional form for ROs** -> sample trajectories and use WP1 metrics 4. **Lack of time to analyse functional form structure by M18** -> Carry on with WP4, and consider returning to WP3 in MSc internship 5. **Functional form does not correlate with coma parameters by M12 ->** not a risk but an outcome. Carry on with WP4, consider revisiting with sleep dataset in MSc internship

3.2 Quality and capacity of the host institutions and participating organisations, including hosting arrangements

Hosting arrangements: The researcher will be hosted in the FEMTO Neuro group, an interdisciplinary group of scientists exploring data-driven control and dynamical approaches to the analysis of human sensory electrophysiology. The group currently consists of 2 PIs, 2 postdocs and 5 PhD students, all working in related fields to the present proposal. The group is part of the larger *System Data Science* team, a concentration of 7 faculty and about 30 postdoctoral and doctoral students working on data-driven analysis, pronostic and health management of natural, industrial and environmental systems, and based in the Department of Automation and Robotics of the FEMTO-ST Institute in Besançon, France. • **Quality and capacity of the participating organisations**: The Neuro group is highly committed to hosting this project, and supervisor JJA has been closely involved in grant writing and preparation. FEMTO-ST offers an ideal infrastructure for efficiently conducting the present study because (1) Dept. secretarial staff will help with administrative tasks, (2) the researcher will benefit from expertise of colleagues covering all key fields of the project, including critical clinical expertise with partner hospital GHU (3) all the technical facilities needed for the project (datasets, machine-learning pipelines) are available in the group (4) FEMTO-ST and HI CNRS has hosted many international graduate students and postdoctoral researchers, and the infrastructure to handle administrative issues is well in place. (5) FEMTO-ST will provide a dedicated desk space in the supervisor's lab, as well as access to IT resources, datasets and computing resources.

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#§CON-SOR-CS§# #§PRJ-MGT-PM§# #§QUA-LIT-QL§# #§WRK-PLA-WP§#

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