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Transdisciplinary Research Linking Neuroscience, Brain Medicine and Computer Science

Ljubljana, Slovenia - February 14-16, 2018

BOOK OF ABSTRACTS

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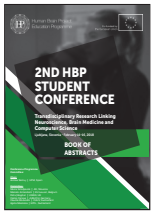

February 14–16, 2018, Ljubljana, Slovenia

Preface

We are pleased to present the proceedings of the 2nd Human Brain Project Student Conference–Transdisciplinary Research Linking Neuroscience, Brain Medicine and Computer Science–held in Ljubljana, Slovenia from 14 to 16 February 2018. The conference provided an open forum for exchange of new ideas among young researchers working on various aspects of neuroscience, brain medicine and computer science relevant to the Human Brain Project (HBP). Contributions emphasising theoretical and empirical foundations as well as novel approaches to specific problems of the HBP were welcome. We particularly encouraged submissions with a potential to inspire the research community by introducing new and relevant problems, concepts and ideas.

The contributions to this conference covered a wide variety of topics, including Mouse Brain Organisation, Human Brain Organisation, Systems and Cognitive Neuroscience, Theoretical Neuroscience, Neuroinformatics, Brain Simulation, High-Performance Analytics and Computing, Medical Informatics, Neuromorphic Computing, Neurorobotics, and Ethics and Society.

We would like to thank all authors for submitting their work to the 2nd HBP Student Conference. We hope that the readers will enjoy the selected set of abstracts and that these contributions will inspire and encourage new interactions, discussions, and opportunities beneficial to the authors, the Human Brain Project, and the whole scientific community.

February 14, 2018
Ljubljana

Andrea Santuy
Nikola Simidjievski
Marcelo Armendariz
Petrut Antoniu Bogdan
Claudia Modenato
Agata Mosinska-Domanska
Theresa Rass
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Table of Contents

Causal evidence of the involvement of the right occipital face area in face-identity acquisition

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Introduction/Motivation: Former research already highlighted that the occipital face area (OFA) might play a crucial role in face learning and recognition. However, whether this involvement includes low- or high-level processing remained unclear so far. To test whether the OFA is causally involved in face-identity acquisition, we conducted two experiments using a paradigm adapted by former experiments from Andrews et al. (2015) [1].

Methods: In the pilot study, we first explored options to ensure a learning effect for a computerised version of the paradigm used by Andrews et al., which is composed of a sequential sorting task for learning (Figure 1) and a matching task at test (Figure 2).

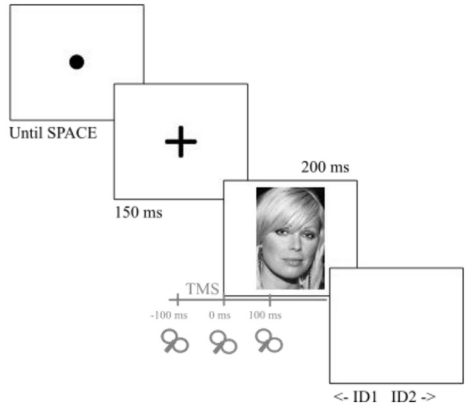

FIGURE 1: Sequential sorting task (Learning phase)

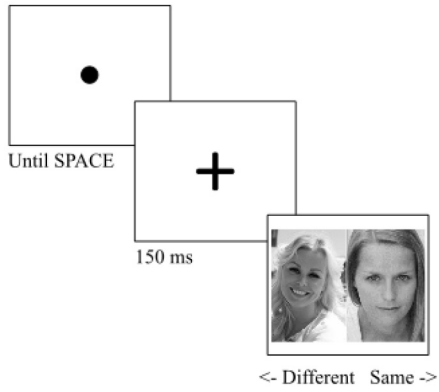

FIGURE 2: Face-matching task (Test phase)

To do so, we tested one control group without the sorting phase, one group with ten minutes and one with twenty-four hours delay, as well as one condition where subjects completed the learning and test phases straight after each other without any delay (16 participants in each condition; N=64). The no-delay condition obtained best results and was therefore used in the main experiment in combination with transcranial magnetic stimulation (TMS). Fourty-two subjects participated in this second experiment where during the learning phase, they performed the sorting task while stimulation was delivered either over the right OFA or, in a control condition, over the Vertex (Cz). Subsequently, performance for the face matching task consisting of already learned identities from the sorting task and two novel identities has been observed.

Results and Discussion: Results showed that accuracy at test was higher for trained than for novel identities in the control condition (Vertex stimulation), demonstrating a regular learning effect, whereas no such difference was found for the rOFA stimulation group (Figure 3). Rather, these indifferences match the performance pattern obatined by the control condition used in the pilot study that never performed the sorting task. These findings suggest that the OFA is not only relevant for the identification of low-level physical features of a face but also crucial for the formation of identity-specific face representations.

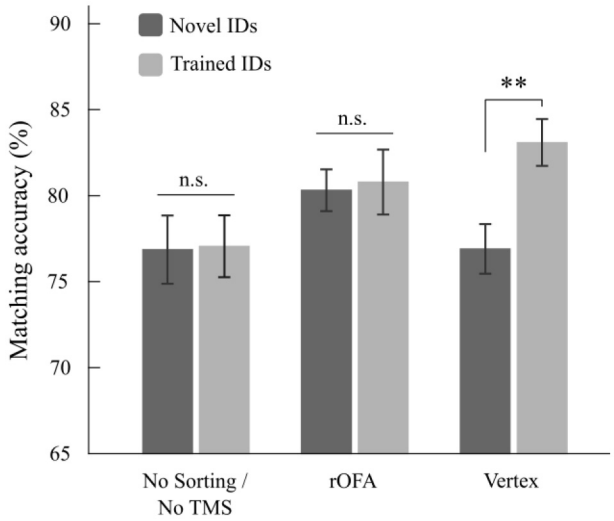

FIGURE 3: Face-matching accuracies for the test phase. The difference in performance for trained and novel identities in the Vertex condition demonstrates a learning effect. In the other two conditions, no such difference was observable.

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Fighting inactivity to prevent cognitive decline: The role of dopamine in modulating physical activity levels in older adults

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Introduction: Alzheimer's Disease (AD) is the world's leading cause of dementia. AD is a devastating neurodegenerative disease that progressively impairs cognition and ultimately results in dependence and death. Although great efforts have been made in the pursuit of a pharmaceutical compound effective at changing the course of disease, to date, these have failed. We now know that the neuropathological process underlying AD starts up to 20 years before the first clinical symptoms of the disease manifest. This could be one of the reasons behind the lack of progress in the search for a pharmacological treatment, since by the time AD is diagnosed, the extent of the damage is so widespread that little can be done. For these reasons, attention has moved towards AD prevention. Several different modifiable lifestyle factors have been

identified as potential tools to prevent AD or at least delay its onset. Physical activity is one of the most widely studied lifestyle factors, with evidence emerging from both cross-sectional and intervention studies. It is now widely accepted that physical activity is associated with reduced risk of AD and changes in AD markers such as brain volume, amyloid-beta deposition and cognitive performance. Furthermore, it is also imperative to identify individuals who are at greater risk of developing AD, such as carriers of the Apolipoprotein E gene (*APOE*) ε4 allele, and whether this genetic carriage alters the level of benefit gained from physical activity.

Methods: The purpose of the current study is to investigate the interaction between genetic factors and physical activity, and their contribution to risk of cognitive decline and AD. More specifically, efficient dopamine transmission has been claimed to be a powerful predictor of physical activity in several animal studies and a few human studies (Dang, 2017; Ebada, 2016; Luo, 2016; Park, 2016, Berse, 2015; Knab, 2010). We will calculate a genetic risk score of poor dopamine transmission, through the combination of different risk genotypes for genes encoding proteins involved in dopamine synthesis, transport and reception (Beeler, 2016; Papenberg, 2016; Pearson-Fuhrhop, 2014; Beaulieu, 2011). Once we have calculated the dopamine genetic risk score, we will apply moderation and mediation statistical analyses to examine the relationship between our genetic risk scores and different AD risk indicators (such as neuropsychological scores, amyloid-beta deposition or AD susceptible brain structure volumes) and whether such relationships are mediated (or moderated) by the amount of physical activity that the individual practices. *APOE* genotype, age, body mass index and sex will be included as possible confounding variables in the analyses. The sample used for these analyses will be cognitively healthy older men and women aged 60 years and over, from the Australian Imaging, Biomarker and Lifestyle study (AIBL). We will utilise genetic data, cognitive scores and self-reported measures of physical activity from a set of 883 participants, which have been followed up every 18 months for up to 9 years. Amyloid-beta (A**β**) deposition data (derived from Positron Emission Tomography Imaging), volumetric data (derived from Magnetic Resonance Imaging) and actigraphy data are also available from limited subsamples (259, 233 and 233 respectively).

Results: Expected results are outlined in Figure 1.

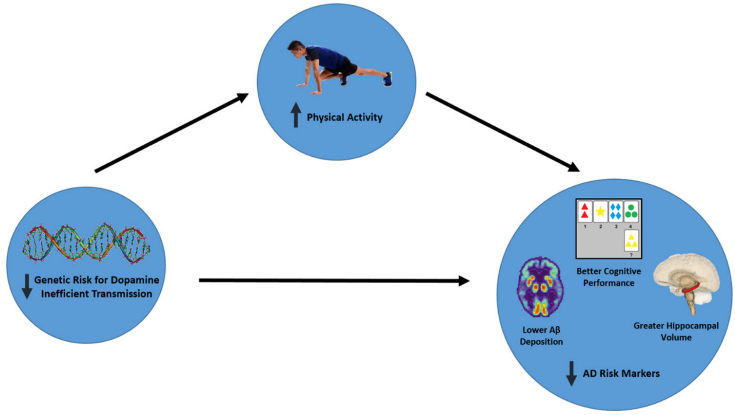

FIGURE 1: We hypothesize that people with more efficient dopamine transmission (as a result of the carriage of a greater number of beneficial alleles in genes involved in dopamine synthesis, transport and reception) will engage more in physical activity, which will reduce the risk of developing AD pathology (indicated by lower Aβ deposition, greater hippocampal volume and better cognitive performance).

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Detecting cognitive decline through dialogue processing

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Introduction/Motivation: Due to the severe incidence of dementia across the world, its care and prevention are increasingly demanded by public health [1], with a focus on early detection and improved caregiving. As language impairment is a common symptom of dementia and a good source of clinical information for its assessment [2–4], our research aims to characterise potentially disrupted communication patterns related to cognitive function and decline. Identifying such features will ultimately help us design assistive technologies able to automatically monitor cognitive status (i.e. adaptive interfaces, social robotics), in order to allow older people to live at home longer, and as independently as possible [5, 6]. In the present work, our hypothesis is that patients suffering from Alzheimer's Disease (AD) will show identifiable patterns during dialogue interactions (i.e. disrupted turn-taking patterns, differences in speech rate).

Methods: We employ spontaneous, conversational data gathered by the Carolina Conversations Collections [7] to train a machine learning model to differentiate AD and non-AD patients. Here, we included 21 patients and 17 controls, over 65 years old. The data was pre-processed to generate vocalisation graphs (Figure 1) and extract

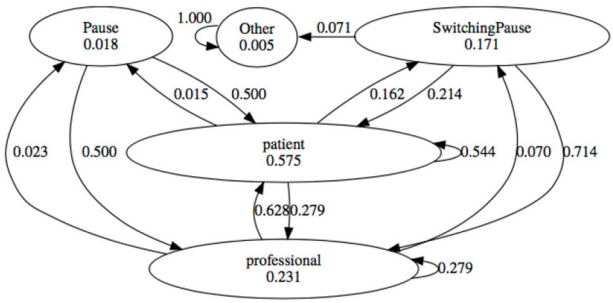

FIGURE 1: Vocalisation graph example.
(Markov diagrams describing the transition relationships between events like speech, pauses, joint talk, switching pauses).

speech rate information. These and the diagnostic annotations (AD vs. non-AD) were used for the supervised learning training of the model. Then, this classifier was evaluated on its ability to predict such annotations (AD vs. non-AD), implementing 10-fold cross-validation.

Results and Discussion: The classifier reached up to 83% accuracy, based on turn-taking patterns and speech rate. Precision, recall and F_1 scores were also calculated (Figure 2). These are preliminary results of a research in progress, as we are currently pre-processing the rest of the dataset and will be trying different methods for dialogue analysis and natural language processing in the short term.

All in all, there are several linguistic parameters that are promising to be helpful in the assessment of cognitive functioning [2–4]. Our approach does not rely on speech transcription content, but on speech-silence patterns and basic prosodic information extracted from spontaneous spoken dialogue. Still, it obtains levels of accuracy comparable to state-of-the-art systems that rely on more complex features. This opens the possibility of devising mental health monitoring methods which would be non-invasive and low-cost in terms of time and resources.

Acknowledgments: We acknowledge C. Pope and B. H. Davis, from the Medical University of South Carolina, host to the Carolina Conversation Collection [15]. Our research is supported by the UK Medical Research Council.

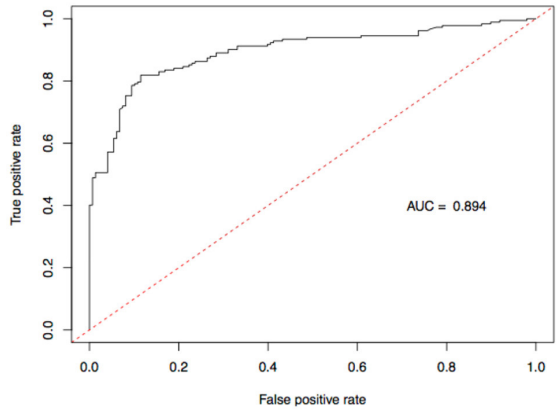

FIGURE 2: VROC curve representing precision and recall (sensitivity) of the classifier.

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Synaptology of the mesial temporal cortex in Alzheimer's disease

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Alzheimer's disease (AD) is the main cause of dementia, accounting for 60–80% of all cases. During the course of the disease, three main neuropathological alterations occur: cerebral atrophy, intracellular neurofibrillary tangles and extracellular amyloid plaques. Early loss of episodic memory in AD patients is closely associated with the progressive degeneration of medial temporal lobe structures, including the hippocampal formation and adjacent cortex. In addition, neurofibrilar tangles are first observed in the transentorhinal (TEC), entorhinal cortex and hippocampal CA1 field. Synapse loss has also been reported, but relatively few detailed studies have been performed using electron microscopy. This is important because elucidation of the changes that affect synapses is crucial for better understanding the pathogenic mechanisms underlying AD.

Brain tissue from 5 AD patients and 6 control subjects with no neurological alterations were used in this study. These human brain samples had less than 3h postmortem delays. A 3D ultrastructural analysis of the neuropil in layer II of the TEC and superficial pyramidal layer of the medial CA1 was performed. We used an instrument that combines a high-resolution field-emission SEM (scanning electron microscopy) column with a focused gallium ion beam (FIB), which mills the sample surface on a nanometer scale. The sequential and automated use of FIB milling and SEM imaging allows us to obtain large image stacks that represent a three-dimensional sample. Customized analysis software was used for the reconstruction of synapses, which allowed their number, morphology (surface area of the synaptic apposition surface) and spatial distribution to be calculated. These spatial and morphological data are of great interest in terms of synaptic function.

Our preliminary results show that the total number of synapses per volume in AD patients was lower than in controls, both in CA1 and TEC. However, we have not found differences in the morphology of the synapses in AD patients compared with control subjects. Furthermore, the spatial organization of synapses showed a nearly random 3D distribution, regardless of the subject group and the region analyzed. In conclusion, these data show a decrease in the density of synapses in these brain regions in AD patients but both the spatial distribution and size of the synapses remain unchanged. Further studies will be performed to extend these observations to other brain areas of AD patients and to try to elucidate the functional consequences of these synaptic changes.

Ordinal synchronization: A novel approach for quantifying synchronization

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Introduction/Motivation: Synchronization measures depending on Fourier analysis, such as Spectral Coherence and variations on it, typically demand the time series to be stationary and the correlation between spectra to be linear [3]. On the other hand, phase indexes (e.g., phase locking value PLV or phase lag index PLI), require, in addition to stationarity, that instantaneous phases of the signals follow a Von Mises distribution. Measures based on Information Theory entail large datasets to estimate properly the underlying distribution of values, and the procedure to construct the bins from which to build distributions is not trivial [2]. However, most dynamical systems are strongly nonlinear, nonstationary, and, in many cases, we only have access to short length time series [4]. Thus, synchronization analysis based on these procedures could potentially yield to misleading results. Here we propose Ordinal Synchronization (OS) as a new measure of synchronization, based on the correlation of temporal ordinal patterns extracted from any pair of time series, in a natural development from Bandt and Pompe's method [1].

Methods: To assess the validity of the measure, and to unveil which is the best length of the ordinal patterns extracted to quantify synchronization, we analyze datasets coming from unidirectionally coupled electronic Lorenz and Rössler oscillators (in a master-slave configuration), varying the strength of the coupling and perturbing the system with noise signals of different amplitude (see Figure 1) in different conditions: equal noise in both oscillators, noise in the master node, and noise in the slave node. A benchmark is conducted to compare OS with other common measures of synchronization: Spectral Coherence (SC), Mutual Information (MI), Phase Locking Value (PLV) and Pearson Correlation (Rho). We are especially concerned about the application of OS to the analysis of brain imaging. Thus, we also study resting state MEG datasets, both at broad-band and filtered in the most common frequency bands: θ, α1, α2, β1 and β2.

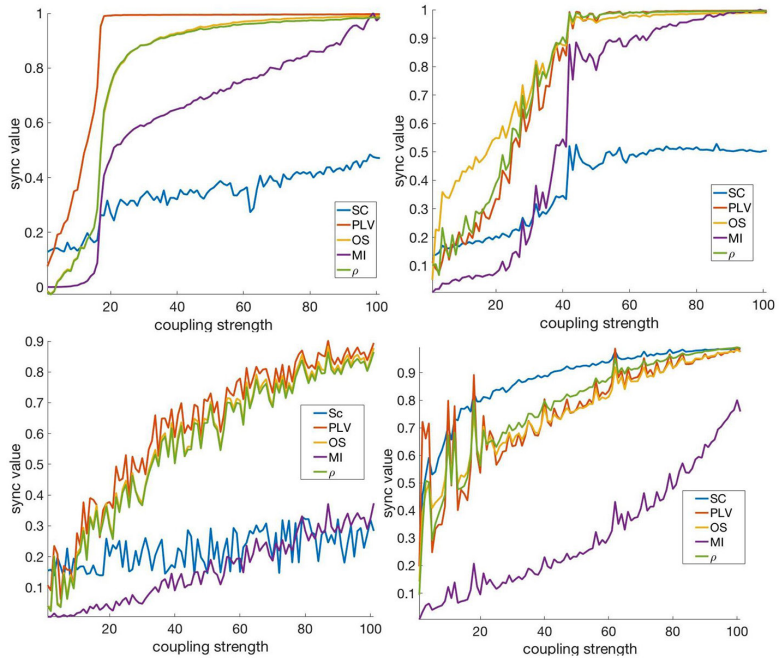

FIGURE 1: Evolution of the synchronization (y-axis) as the coupling strength increases (x-axis) in Rössler (upper and bottom left) and Lorenz oscillators (upper and bottom right), for the smallest (upper, right and left) and largest (bottom, right and left) noise amplitude considered. All cases correspond to the condition in which only the master oscillator is perturbed by noise.

Results: OS provides a fast and robust-to-noise tool to assess synchronization, without any implicit assumption about the distribution of data nor its dynamical properties. Nonetheless, as it ranges from [−1, 1], it captures anti-phase synchronization, where two coupled nodes act synchronously in an inverse fashion, a plausible mechanism in the brain, neglected by many other metrics. We found a relation between the width of the studied frequencies and the length of the ordinal patterns, as well as a good concordance between OS and the other classical synchronization measures. OS seems to be robust to noise and gives a good resolution capturing synchronization (see Figure 1).

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Communication optimisation in distributed Spiking Neural Network simulations

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Introduction/Motivation: In distributed computation, higher parallelism is desirable to split the computation into independently executable parts. Ideally such parts do not require any synchronisation to speed-up execution time. In Spiking Neuron Network (SNN) simulations, this is not realistic due to the high level of interconnectivity amongst neurons. Thus, higher parallelism increases communication overhead, limiting scalability [1].

There are two ways of mitigating parallel overhead in neuronal simulations: communicating more efficiently (targeted propagation); and decreasing the amount of data to be sent (number of spikes going across partitions). This work proposes solutions to the scale of communication at both levels.

Methods: Sending every spike to all processes has been shown to scale poorly for large parallel sims and be wasteful because not all partitions require all spike data [3,4]. Thus, by only sending the relevant data to the interested processes, communication volume can be reduced. Two alternative point-to-point strategies are proposed, based on how the inter-process messages are coordinated at each time step.

Parallel simulators that have considered the mapping of neurons to processes have focused on computational load balance alone [5]. To date, state-of-the-art parallel simulators are not considering communication amongst neurons to inform the mapping of neurons to processes. Authors have suggested the impact of neuron connectivity would have [2,6], but not on actual network activity. The proposed approach models the SNN as a graph, where the vertices (neurons) are weighted proportional to their activity during simulation (neurons with high activity spike frequently, hence communicating more often with post-synaptic neurons). Multilevel k-way partitioning is used to minimise the volume of communication between vertices and map them to processes. To gather results, simulations of a Cortical Microcircuit model [7] are performed across both experiments.

Results and Discussion: Figure 1 shows poor scalability of the collective all-to-all communication strategy and the reduction in communication volume when using point-to-point strategies with respect to an all to all pattern. Not only the communication is reduced, but it scales linearly with the number of processes.

The distribution of workload based on the communication volume of neurons is shown to reduce communication in distributed simulations in Figure 2. Two baselines are shown: random allocation and static partitioning (graph partitioning with equal weights edges and vertices). Repartitioning based on network activity shows an improvement of ~40% over random and ~12–15% over static partitioning.

As the total communication during simulation is reduced, simulations are expected to run faster, particularly given the scale of the communication volume in spiking neuron simulations. Further work could look into dynamic partitioning and graph analysis to inform partitioning in heterogeneous architectures (where processes can accept different workload).

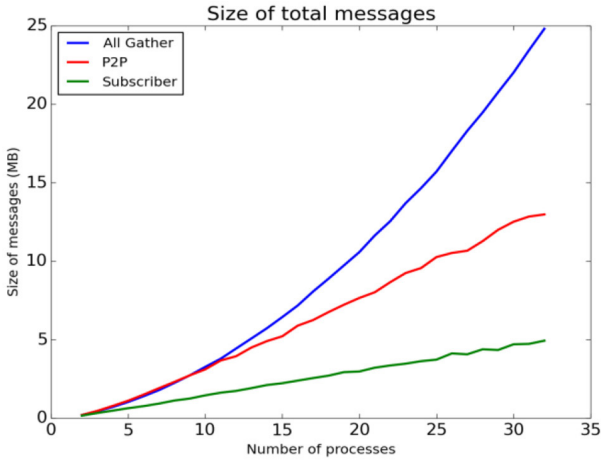

FIGURE 1: Scaling of the number and weight of messages sent across during distributed simulations using three different communication strategies.

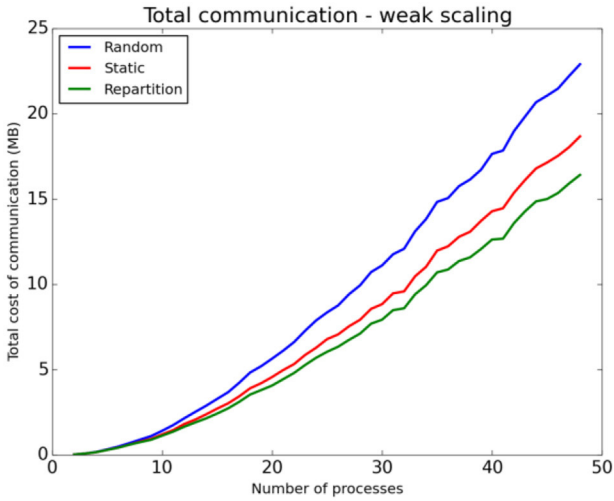

FIGURE 2: Communication costs with different workload allocation strategies (SNN model is scaled with the number of processes).

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Dynamic resource management for interactive supercomputing in neuroscience

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Supercomputers, as High Performance Computing systems grow in complexity every year. These systems are composed of many nodes interconnected with a very fast network, which allows to use them together for very complex computations. Nowadays we see that the capacity of each node is also growing: much more cores are available (e.g. up to 72 in Intel KNL [1]), specific purpose computing units such as GPUs [2], and also different memory hierarchies (e.g. Non-Volatile Memories [3]). Having so many resources available in a single node makes very unlikely that a single application is able to exploit all of them, and if the node is reserved for that application, the situation ends up in a poor utilization of the system. This is something system administrators want completely to avoid, since the ideal case is that the supercomputer is used at its 100% capacity. Considering this, it is clear that sharing resources between applications becomes a must in the near future.

In addition, commonly used techniques to enable Interactive Supercomputing capacities to applications (i.e. the ability to interact with a running simulation, analysing partial results with visualization or intermediate results processing, and even steer the running simulation according to these partial insights) do not care much about where resources are obtained, for instance to run the in-situ visualization or the analytics [4]. The most common assumptions are that "extra" resources are available somehow to do these interactive tasks, or that the main application is halted so the interactive tasks can proceed, at the penalty of stopping the original application. In the Interactive Supercomputing scenario, sharing resources also becomes ideal, since a big simulation using all available resources can lend some of them to the interactive task to be started immediately, and when the interactive task finishes, resources can be given back to the big simulation, as it can be seen in Figure 1.

To achieve the resource sharing we mention, our proposal is to enable what we call Dynamic Resource Management (malleability) in the different layers of the system: Job level, Node level, Application level and Kernel level. We have especially worked in the Job level, by modifying the SLURM job scheduler to include malleability options

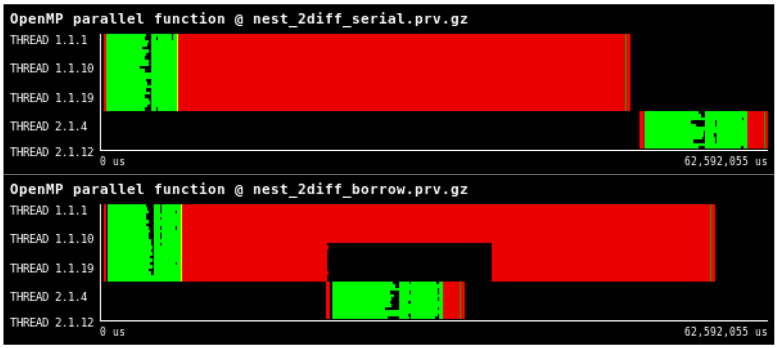

FIGURE 1: Interactive Supercomputing example

[5], and at Node level, providing a library called DLB (Dynamic Load Balancing) that is able to share resources between different applications running in the same node, or even in the same application to speed up the processing [6]. We have successfully applied DLB in the CFD domain [7].

Our modifications made to SLURM enable jobs to increase or decrease the number of resources they are using, so a reduction of resources used by a job can allow a new job to enter to run in the system, decreasing its wait time. With respect to DLB, it is a library linked with the application that is able to lend the unused CPUs from an application to another one running in the same node, therefore speeding up the execution of the second one. DLB keeps a fair control of resources, returning them to the original owner when they are needed. Besides, DLB is able to interface with the job scheduler with its DROM API, to exchange knowledge about resource needs and resources available.

In the framework of the HBP, in particular in WP7.4, we have been able to enable malleability for both NEST [8] and CoreNeuron [9] simulators, allowing them to change the resources they use at runtime. The use case motivating this need comes from CDP2, where CoreNeuron is used as a service, and when many different users start to submit different simulations (e.g. typically in a course or tutorial), the wait time in the queue becomes a problem due to the lack of capacity of the jobs to share resources. Our tests demonstrate that on one hand, adding malleability to the simulators does not cause a penalty in their execution time, and on the other hand, malleability helps to reduce wait time of the jobs, ending up in a better response time for users, and a higher system utilization.

Acknowledgements: This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 720270 (HBP SGA1), from the Spanish Ministry of Economy and Competitiveness under the project Computación de Altas Prestaciones VII (TIN2015-65316-P) and the Departament d'Innovació, Universitats i Empresa de la Generalitat de Catalunya, under project MPEXPAR: Models de Programació i Entorns d'Execució Parallels (2014-SGR-1051).

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Analysing dialogue to support detection of Alzheimer's disease

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Introduction/Motivation: As well as memory loss and linguistic impairment, changes in behaviour and decreased interactional skills in conversation are also symptoms for Alzheimer's Disease (AD). Recent work has shown that **linguistic** features can be used within natural language processing (NLP) and machine learning (ML) methods to provide computational tools with potential for automatic detection of AD [1]; however, few studies have applied these techniques to investigate the predictive power of **interactional** symptoms. Automatic diagnosis of AD aids assessment and allows for earlier diagnosis. Interactional features are linguistically and culturally independent, allowing the automation to be applied across languages and borders.

Methods: We investigate the use of interactional features (IFs) to predict AD, and compare performance against and in addition to known predictive linguistic (but non-interactional) features (Non-IFs) [1]. IFs investigated are chosen to encode known symptoms of AD observable in conversation transcripts, such as turn-taking, filler term frequency and trailing-off mid-sentence. Following [1], we examine the task of discriminating patients with dementia from controls in the DementiaBank Pitt corpus [2]; we assess the overall utility of features via classification accuracy using logistic regression. Non-IFs & IFs were compared by ranking the features based on ANOVA F-value, and we use correlation analysis on the IFs as a sense check and to investigate the direction in which each variable correlates with the diagnosis.

Results and Discussion: Initial results suggest that interactional features (IFs) can assist in computationally classifying AD. IFs are amongst the top features in terms of predictive power. Feature combinations including IFs can improve accuracy by nearly 5% over the state of the art [1]. Features encoding turn-taking and clarification behaviour between speakers are amongst the most predictive.

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Exponential first passage time approximations of neuron model with conductance-based dynamics

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Introduction/Motivation: The first-passage time problem of the stochastic leaky-integrate-and-fire (SLIF) neuron model remains a challenge despite a large amount of work on the topic. Apart from the work on escape noise in the time-homogeneous case most approaches focus on numerical methods (Buonocore et al., 2011). Large Deviation Theory (LDT) and in particular the Freidlin-Wentzell-Theory (Freidlin and Wentzell, 1984) provides a framework in which we can treat stochastic processes such as the SLIF analytically in the small-noise limit, i.e. when large deviations from the deterministic path become rare. In this work, we apply the LDT to a leaky integrate and fire model with conductance-based dynamics to analyse one of its major qualitative features, as described in Kuhn, Aertsen, and Rotter, 2004: the non-monotonic firing rate response to balanced scaling of input firing rates.

Methods: We use a diffusion approximation of the leaky integrate and fire model with conductance-based dynamics (Richardson and Gerstner, 2005) and investigate its firing response curve under balanced excitation and inhibition with simulations in NEST and R, see Figure 1. We then cast the resulting Itô diffusion process into a normal form which induces an action functional. This functional associates to each possible voltage trajectory a cost, measured by how much the trajectory deviates from the unperturbed dynamics. Freidlin-Wentzell-Theory now tells us that the probabilities of certain events F, such as a first passage through a constant boundary, scale as the *most likely*, i.e. *least costly*, event from this set. Effectively, this reduces to solving an optimal control problem with constrained end-points.

Results and Discussion: We derive an expression that explains the non-monotonic response described by Kuhn, Aertsen, and Rotter, 2004, see Figure 2. Unser some additional simplifying assumptions, this expression reduces to

$$E\left(T^{\sigma}\right) \approx \exp\{\frac{V^{2}_{th}\left(2R_{E}+1\right)^{2}}{2R_{E}}\} \cdot$$

Despite the asymptotic nature of the estimator, the resulting expressions manage to capture the qualitative characteristics to a high level of accuracy. However, most quantitative features concerning the exact scaling of the curve are not represented correctly. The diffusion approximation and some additional approximations in the derivation cause this scaling discrepancy, but they do not interfere with the qualitative characteristics.

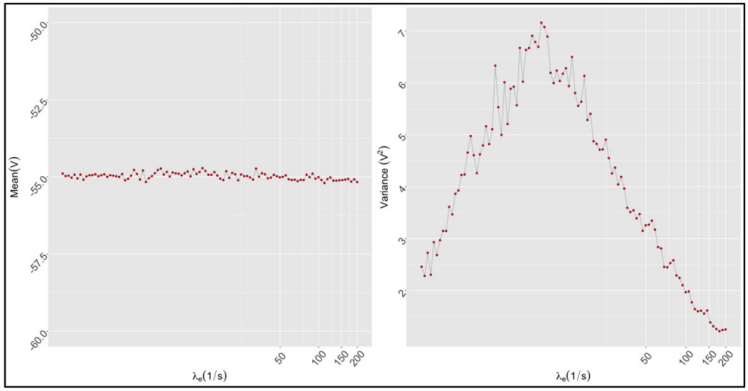

FIGURE 1: λ_E is the rate of incoming excitatory spikes. For these plots, the inhibitory rate λ_I was varied accordingly to maintain balanced input. Left: The free mean potential was kept constant at approximately –55 mV. Right: The free variance displays non-monotonic behaviour.

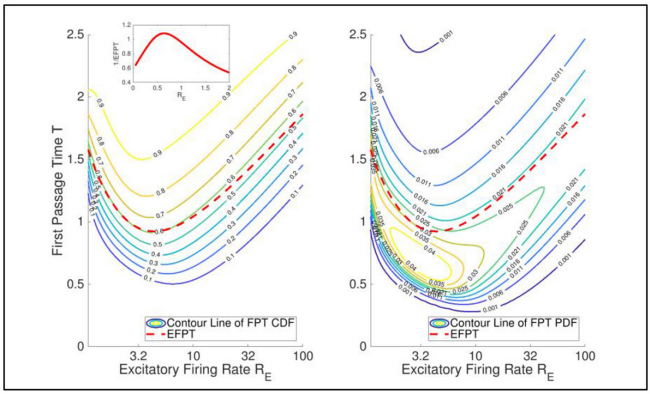

FIGURE 2: LDT approximation of the First Passage Time cdf (left) and pdf(right). Expected Value $E(T^k)$ in red and $1/E(T^k)$ as an inset for comparison with Figure 1.

This hints at a stronger theoretical relationship between optimal control and neuron models than the Freidlin-Wentzell theory predicts and this connection warrants further investigation.

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Using network analysis to speed up semantic data mining

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Introduction: For many data mining tasks incorporation of domain knowledge is essential. The field of Semantic Data Mining (SDM) studies how to systematically incorporate domain knowledge into the learning process. In SDM context, ontologies are used as formal definitions of the semantics of knowledge and data. The ontology networks can be very large (e.g., gene ontology [1]) and for such cases most SDM algorithms fail. On the other hand, many efficient network analysis approaches exist which are able to handle huge networks. We describe the NetSDM algorithm which uses network analysis as a preprocessing for SDM algorithms allowing them to efficiently extract interesting patterns.

Methods: When constructing if-then rules characterizing groups of target class instances, the SDM algorithm Hedwig [2] uses a computationally demanding beam search approach. The goal of the NetSDM methodology (outlined in Figure 1) is to

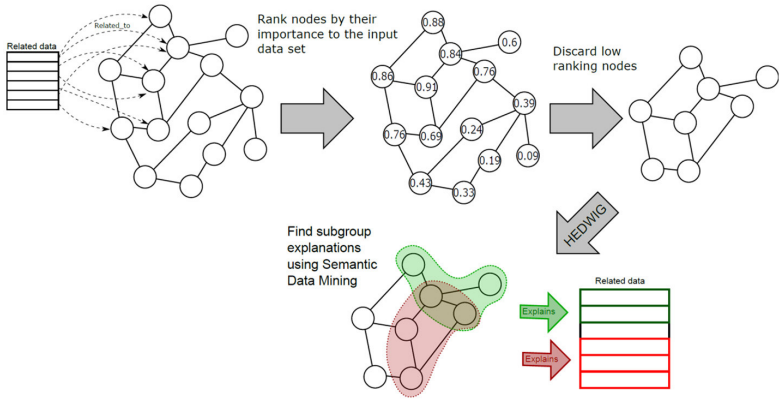

FIGURE 1: An overview schema, outlining of the proposed netSDM methodology.

improve the efficiency of the Hedwig algorithm by using a pre-pruning step in which we filter out background knowledge terms that are not likely to appear in significant rules. A scoring function used in pruning should (i) be able to evaluate the significance of terms based on data, and (ii) be efficiently computed. We used the Personalized PageRank (P-PR) [3] function to score the ontology terms. The output of the scoring function is a vector which, for each term in the background knowledge, contains a score estimating its significance. We use the computed scores to prune the background data and get a smaller background data set using a selected threshold value. We construct the pruned background ontology by keeping only the proportion *c* of nodes with the highest scores. For example, if the pruning threshold *c* is set to 0.4, the new network consists only of terms in the background knowledge which are in the top 40% of all terms according to the scoring function.

Results: The netSDM methodology was tested on two data sets previously used to examine properties of SDM algorithms [4]. For each pruning threshold *c* ranging from 0.005 to 1, we ran Hedwig with 8 different parameter settings on the data sets. The result of all settings is that when setting the pruning threshold to 0.03, Hedwig is able to discover the same rule as when no pruning is done at all. In some cases, including the two most computationally demanding parameter settings, the pruning threshold can be set even lower, to 0.02 and 0.01, without decreasing the quality of the rules.

Figure 2 shows the average times the Hedwig algorithm took to discover the best rules describing the data set for each parameter setting. The figure shows an almost linear connection between the pruning parameter and the time taken. This means that setting the pruning parameter to 0.01 reduces the time Hedwig needs to discover the rules

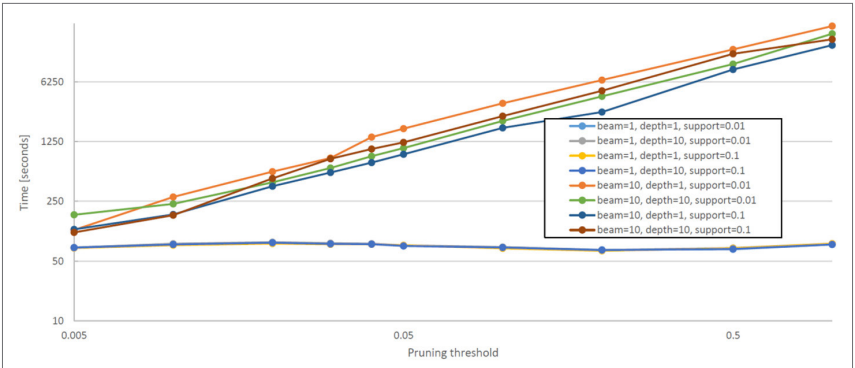

FIGURE 2: Average times, taken by NetSDM, to discover rules describing the positively expressed genes in the data set.

from approximatelly 7 hours to a matter of minutes. The resulting rules are the same, meaning that using network scoring to prune the ontology allows us to greatly reduce the search time of the SDM algorithm.

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Assesing readability with deep neural language models

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Introduction: Readability is concerned with the relation between the text and the cognitive load for a user to comprehend it. Traditionally, readability is defined as a degree of lexical sophistication in the text [1] and most of the readability formulas measure that by taking into an account various statistical factors, such as sentence length and word difficulty [2]. This approach has been criticized in the past because of its shaky statistical bases and because it ignores some factors that influence readability (e.g., discourse cohesion, background knowledge required, etc) [2]. To overcome this problem, we propose a new approach that uses deep neural language models and their perplexity, which measures how well a probability model predicts a sample, as a tool to assess readability. This approach takes background knowledge and discourse cohesion into account and can not only assess the level of text difficulty but also contextualize the readability because of the trainable nature of neural networks. The approach will be tested in the scope of the development of a new system for automatic quality evaluation of Slovenian textbooks. We believe that the textbook quality is strongly dependant on its level of readability, while the age of pupils and the topic of the textbook should also be taken into account.

Methods: We implemented a character-aware neural language model [3] appropriate for languages with rich morphology. The model employs a convolutional neural network combined with a highway network over characters, whose output is given to a reccurent neural network language model. In initial experiments, the model was trained on the collection of Slovenian magazines for young children (Ciciban and Cicido) and teenagers (PIL, Smrklja, Cool, Frka) from the KRES corpus [4] and tested for perplexity on separate samples of these magazines.

Results and Discussion: Results in Table 1 show a gap between the perplexity calculated for children magazines and perplexity calculated for teenagers' magazines, suggesting correlation between perplexity and readability. This suggests that the perplexity of the implemented language model can be used as a new readability measure capable

Table 1: Perplexity of the language model on different test sets

Magazine	Audience	Perplexity
Pil	Teenagers	22.19
Smrklja	Teenagers	22.27
Cool	Teenagers	38.04
Frka	Teenagers	31.92
Cicido	Young children	11.00
Ciciban	Young children	14.12

of detecting the trend of text difficulty progression. In the future, we plan to test this model on a corpus of Slovenian textbooks.

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Staging brain research: Framings of scientific visions in the film *Transcendence*

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Introduction/Motivation: Scientific knowledge travels. Through its journeys, it is reshaped and recontextualized and at the same time it shapes what the recipients of such knowledge understand to be fact. One major public arena in which this happens is Hollywood films. Through the depiction of novel technology and science embedded within powerful narratives, Hollywood films provide a space for the audience to "make sense of science [...] in the context of [their] everyday lives, preexisting knowledge, experience, and belief structures" (Kirby, 2011, p.15). There is a long genealogy of Hollywood films in which the intersection of neuroscience and computer technologies has a primary role, but this project will focus on one particular film, *Transcendence* (2014). It was released in April 2014, at a time when visions of computationally constructing a human brain were prominent with the selection of the Human Brain Project as a flagship project and the announcement of the U.S. BRAIN initiative. Thus the film may be understood as one of the vehicles through which "technoscientific imaginaries" related to neuroscience is formed. But how do representational practices in Hollywood movies enact scientific visions as feasible realities? How are these visions framed and how do they shape imaginations and expectations of the future? How are ethical views rehearsed and contextualized?

Methods: This study analyzes the metaphors and framings used in the film *Transcendensce* (2014) and additional material such as published interviews with scientific advisors and articles and YouTube videos analyzing the scientific background of the film. These stagings and framings are instrumental in the process of stabilizing novel technologies as existing or imminent, while they constrain imaginations and discourses of the possible along pre-existing frames of reference (Luokkanen, 2014). It also employs visual analysis to unearth resonances with such framings. Images do not only depict particular realities. They equally take part in creating 'new' realities—they enact a vision of how the world should be (Rose, 2012). This study is an attempt to understand one of the "multiple uses and arenas of facts-in-the-world [and] [...] the ways that they have built-in, presupposed notions of human nature" (Dumit, 2004, p.169). We believe this to be crucial for any attempt to critically engage with the development of new technologies, and hence of possible futures, pertaining to brain research.

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A software pipeline for efficient processing of 3D high-resolution microscopy images of large brain samples

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Introduction/Motivation: Imaging large biological specimens or whole organs such as whole mouse brains through state of the art microscopy techniques – such as Light-Sheet Fluorescence Microscopy (LSM) and Two-Photon Fluorescence Microscopy (TPFM) – poses significant challenges in terms of data processing and analysis. In particular, high-resolution tomographies acquired with such techniques can produce datasets as big as 10^{12} voxels, or several TB in terms of storage. To extract meaningful information out of these datasets, high-throughput analysis tools are needed [1–3]. As a first step, the mosaic of volumetric data produced by these instruments needs to be stitched and fused to produce the reconstructed volume. Depending on the specimen, the fused volume can then be aligned to a reference atlas, or undergo further analysis such as vasculature segmentation, cell classification, cell counting.

Methods: We focus primarily on imaging whole mouse brains and human brain tissue. To meet the unique needs of processing this kind of datasets, we have put in place a high-throughput software pipeline for image analysis. In particular we have developed a stitching tool that allows us to reconstruct and query the fused volume [4]. The software is written in Python and is able to cope well both with teravoxel-sized datasets and multichannel datasets. An Application Programming Interface (API) can be used to perform queries on the stitched datasets and extract subvolumes for further processing. After stitching, we perform manual annotation of cell centroids, cell contours and cell classification. This data is used as the ground truth to train a neural network on the GPU that allows us to perform automatic segmentation and classification. Finally, we are also exploring both lossless and lossy video compression (HEVC/MP4) for permanent storage and easier processing of the experimental datasets.

Results and Discussion: The stitching software is currently being used successfully on production datasets. We are able to produce high-resolution tomographies of whole mouse brains and human brain tissues (see Figures below). Through machine learning we are able to reconstruct 3D maps of selected cell types in the whole mouse brain, highlighting the spatial distribution of neurons in a macroscopic cerebral volume [1].

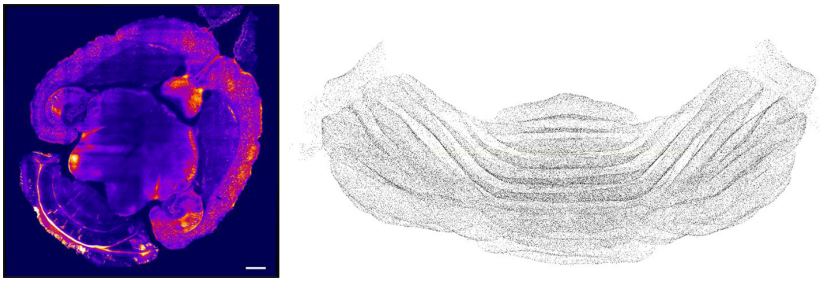

FIGURE 1: Left: a single frame of a high-resolution tomography of a whole mouse brain. Scale bar: 1 mm. Right: Purkinje cells automatically localized in the cerebellum of a L7-GFP mouse using semantic deconvolution.

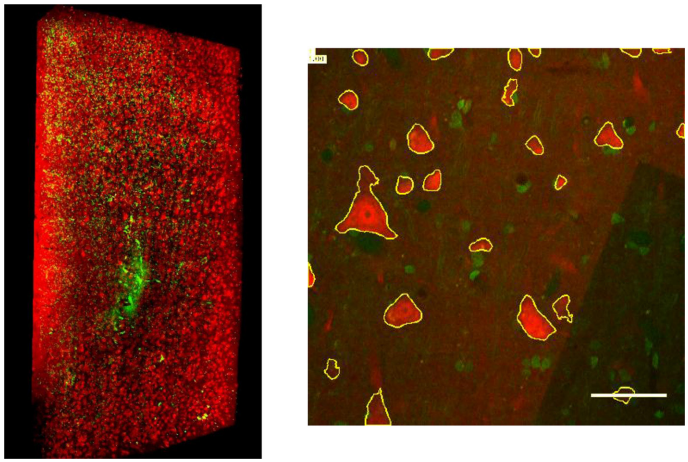

FIGURE 2: Left: a 2 x 7 x 0.5 mm^3 volume of human brain cortex stained with NeuN (red) and DAPI (green). Right: automatic cell segmentation.Scale bar: 50 µm.

Besides being a valuable reference for neurobiologists, these datasets can be used to build realistic point-neuron simulations of the entire brain inside the HBP. In samples of optically-cleared [5] human brain cortex, we reconstruct the 3D structural organization of neurons to investigate how cells, dendrites and axons are distributed throughout the cortex. The microscopy techniques that we use represent a remarkable advance, in that they allow to acquire 3D images of the cellular spatial distribution in whole mouse brains and of the cellular and laminar structures in the human brain, with the molecular specificity that is needed to build accurate models and atlases.

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The assessment of brain responses to sexual and nonsexual affective stimuli: Applying inter-subject correlations to fMRI data in couples

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Introduction: Sexual stimuli are well-suited for neuroscience studies on reward, positive affect, and mixed emotional states (Janssen & Prause, 2017). Although functional brain imaging methods have been applied to the study of couples (e.g. in response to partner images), as yet, no research exists in which these techniques are used to assess couple similarity in brain activation to erotic and other affective stimuli and its relevance to sexual couple processes. We propose a new design using inter-subject correlation techniques in couple fMRI time series.

Aim: To assess similarity and dissimilarity in fMRI time series in response to affective stimuli on the level of the dyad and its correlation to behavioural and affective measures of relationship and sexual satisfaction.

Methods

Participants

40 couples (n = 80) participants will undergo Magnetic Resonance Imaging (MRI) to measure brain responses to sexual and nonsexual affective stimuli.

Analyses

MRI data will be analyzed using the ISC Toolbox (Kauppi et al., 2014), an open source toolbox implemented in MATLAB, for computing various inter-subject correlation-based analyses. Whereas GLM compares individual fMRI time series with a predefined model voxel-wise, and then combines the results to one multi-subject statistic, inter-subject correlation (ISC; Hasson et al., 2004) combines voxel-wise correlations between subject pairs to one single multi-subject statistic in a non-parametric way. The acquired data will be analyzed using this approach and similarity/dissimilarity, defined

as the correlation coefficient between the hemodynamic activity time series on the level of the dyad, is measured using the absolute angular distance between the time-series of two subjects. The theoretical framework is based on the neurophenomenological model of sexual arousal (Stoléru et al., 2012).

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Detection of pathological ageing with artificial neural networks

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Introduction/Motivation: Gradual detriment in cognitive functions is common during normal ageing. In addition, in some cases learning impairment derive in later cognitive impairment, which represents a transition between normal ageing and dementia. It has been highlighted that the prevalence and incidence of dementia has increased in the past few years [1,2]. Dementia is defined as a cognitive disease with gradual and progressive development that interferes with the functioning of daily life, affecting the autonomy and independence of patients [2]. Drawings are used to diagnose different forms of dementia through the analysis of components such as shapes, visuospatial organization and tendencies to omit or to perseverate in certain elements. The most commonly used drawing assessments are the rey complex figure, interlocking pentagons, cube, and clock [3]. Clock tests show high sensitivity for mild dementia, and for the differential diagnosis between cognitive impairment and dementia. Moreover, it has been used to identify cognitive impairment six years before it becomes dementia [4,5]. However, some researchers claim that it should not be used as an exclusive tool for diagnosis [6]. Furthermore, it has been proved that the rey complex figure is a more accurate diagnose instrument [7]. Over the last few years, artificial neural networks (ANN) have been used to correlate neural imaging, questionnaires and clock drawings data with clinical diseases as dementia, building predictive models to identify cognitive dysfunctions [8,9]. This work proposes an ANN to classify between normal and pathological ageing using the rey complex figure and the clock draws done by tested patients as only inputs.

Methods: Elderly adults with and without pathological ageing diagnoses (cognitive impairment and dementia) are going to be tested with the rey complex figure and the clock assessments. As a guideline for the application of the assessments Ardila handbook is going to be used [10]. Additionally, data of each patient clinical diagnosis is going to be retrieved from medical professionals with the standardized scales of both applied assessments [11]. The ANN will be train to classify the patients into two groups: normal and pathological ageing. Data from drawings is will be used as inputs to train the ANN. A convolutional neural network (CNN) is going to be used since it has shown good properties for images analysis [12].

Results and Discussion: Diagnoses for dementia are not often performed, even though early diagnoses are needed in order to give treatment with better prognosis for the patient quality of life [8]. Therefore, the aim is to design an ANN model with the ability to process elderly adults drawings to identify whether the patient has a normal or pathological ageing. This is intended to improve the early identification of cognitive impairments.

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Detection of normal speech development using artificial neural networks

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Introduction/Motivation: Speech is defined as the production of complex coordinated movements of meaningful sounds through breathing, phonation, and articulation. Infants with ages between 0–12 months process auditory inputs from their environments, and produce random vocal sounds as explorations during speech development. Cooing, gooing, squealing and babbling are some of these vocal sounds [1–3]. Recognition of speech patterns gives information about infants normal development. Currently, pediatricians and other professionals use global scale assessments (GSA) or clinical observation to distinguish between normal and non-normal speech development. In spite of this, early diagnoses of speech delays are rarely done and the parents are unable to recognize such problems [4]. Infants vocalization can be recorder and studied with computational models to understand speech behavior and development. Nevertheless, more data and research are needed in order to design models that can analyze the vocal sounds produced by infants [5]. Artificial neural networks (ANN) are learning methods that has been successfully applied in speech recognition [6]. Consequently, the detection of normal speech development is proposed as an ANN model trained with infant vocal sounds and data retrieved from clinical records.

Methods: With the purpose of detecting normal development and early warnings of developmental impairments, the vocal sounds of two hundred infants (between 0 and 12 months of age) of Antioquia-Colombia are going to be studied. The data needed to train the ANN will be obtained by means of audio files from infants vocal sounds [5], which are going to be recorded by their parents at home. Each vocal sound is will be tagged based on the absence or presence of early warnings known from the clinical record. Moreover, the vocal sounds will be also tagged according to the infants age. The acquired data will be classified into two categories according to early warnings outcomes: (i) normal and (ii) non-normal speech development. Addiotionally, the topology of the ANN will be built taking the vocal sounds as input and the early warnings as output.

Results and Discussion: This work aims to design an artificial neural network model with the ability to process infant's vocal sounds and the biological age to identify whether the infant has a normal speech development or not. Design an accurate real data-based system will help health professionals and parents to monitor the speech development. Finally, improving early diagnoses of delays in speech development will increase early treatments [5].

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Semantic annotation of data on neurodegenerative diseases in patients using ontologies

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In this work, we propose a mid-level ontology for representing various types of data on patients with neurodegenerative diseases. The proposed ontology can be used for semantic annotation of datasets that contain different diagnostic data (clinical, imaging, biomarker, etc) about neurodegenerative diseases and its progression, collected on patients by the hospitals. Having an ontology for describing data on patients with neurodegenerative diseases is important from two different perspectives: (1) from a viewpoint of ontology-based data access (ODBA) [1] it would allow federation queries on data produced and stored at different hospitals; (2) from viewpoint of data analytics it would allow (semi) automatic creation of data analysis workflows based on the datatypes that occur in the datasets, annotated with ontology terms.

The proposed ontology was constructed following best practices from ontology engineering. This involved the use of a top level ontology (Basic Formal Ontology [2]) as a template, and a set of standard formally defined relations. We heavily reused classes and identified mappings to domain terms that are defined in previously developed biomedical ontologies and vocabularies available at BioPortal (http://bioportal.bioontology.org/). This included domain terms from ontologies and vocabularies covering general medicine (such as SNOMED, NCIT, MESH, LOINC, ICD10), neuroscience (such as NIF, BRCT, NeuroMorpho.org) and neurodegenerative diseases (such as ADO, PDON).

The ontology was constructed in a hybrid fashion (see Figure 1). For this purpose, we used two instances of datasets on patients with neurodegenerative diseases [3,4], originating from two well-known studies concerning neurodegenerative diseases:

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‡ Data used in preparation of this article were obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database (adni.loni.usc.edu). As such, the investigators within the ADNI contributed to the design and implementation of ADNI and/or provided data but did not participate in analysis or writing of this report. A complete listing of ADNI investigators can be found at: http://adni.loni.usc.edu/wp-content/uploads/how_to_apply/ADNI_Acknowledgement_List.pdf

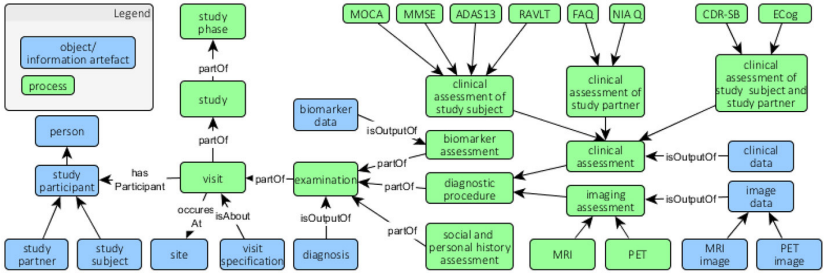

FIGURE 1: Part of the structure of the constructed ontology for representing data on patients with neurodegenerative diseases. The arrows that are not labeled represent IS-A relations.

Alzheimer's Disease Neuroimaging Initiative (ADNI) [5] and Parkinson's Progression Markers Initiative (PPMI) [6]. We also used the domain terms that appear documentation of ADNI and PPMI studies (study objectives, study protocols, study procedures, schedule of activities and others) [7–11], as we believe that the data produced by the hospitals in the project will most probably be subsets of types of data that occur in ADNI and PPMI studies. To address the data analytics perspective, we also reused and extended our previously developed ontology of data types (OntoDT) [12] and ontology of core data mining entities (OntoDM-core) [13] to represent specific domain datatypes that occur in the datasets from the domain of neurodegenerative diseases. The ontology construction and the semantic annotation of the two instances of neurodegenerative diseases datasets was performed using semantic web technologies (RDF, OWL, RDFS), which are currently a popular solution to data and knowledge sharing and integration.

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Research; Neurotrack Technologies; Novartis Pharmaceuticals Corporation; Pfizer Inc.; Piramal Imaging; Servier; Takeda Pharmaceutical Company; and Transition Therapeutics. The Canadian Institutes of Health Research is providing funds to support ADNI clinical sites in Canada. Private sector contributions are facilitated by the Foundation for the National Institutes of Health (www.fnih.org). The grantee organization is the Northern California Institute for Research and Education, and the study is coordinated by the Alzheimer's Therapeutic Research Institute at the University of Southern California. ADNI data are disseminated by the Laboratory for Neuro Imaging at the University of Southern California. Data used in the preparation of this work was also obtained from the Parkinson's Progression Markers Initiative (PPMI) database (www.ppmi-info.org/data). For up-to-date information on the study, visit www.ppmi-info.org. "PPMI – a public-private partnership – is funded by the Michael J. Fox Foundation for Parkinson's Research and funding partners, including list the full names of all of the PPMI funding partners found at www.ppmi-info.org/fundingpartners.We also acknowledge the European Commission's support through the Human Brain Project (Grant No. 604102).

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Big data for HPC: The Human Brain Project

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Motivation: A typical workflow in the HBP project consists of analyzing a dataset after it has been transformed or generated through simulation. Given the complexity of the brain, high volumes of data are used in this process, causing this workflow to last for hours. As a result, examining partial results and confirming that parameters are appropriate can save hours of computation.

Traditionally, data has been stored in plain text or HDF5 [1] files among other mechanisms. They condition the programming model and force the user to be aware of the storage backend. Besides, existing interfaces make challenging to write into a unique dataset in parallel. Furthermore, files might be not consistent during the execution, making inconvenient - or even impossible - to analyze partial results. Other relevant issues include the availability of data or the risk of corruption.

For all the reasons mentioned above, distributed storage systems are currently being evaluated in the WP7.2. As a starting point, we identified structures of data used in the HBP project. Then, defined nice-to-have features to evaluate storage systems including horizontal scalability, ease of use, good performance on handling continuous data such as time series, space indexation, mechanisms to avoid corruption and maintain coherence, high availability, and portability between backends.

Proposed solution: In the context of storage, BSC introduces an architecture comprised of a key-value distributed storage system with a simple interface to handle data transparently. One of its main benefits is simultaneously accessing and updating the results, accelerating the traditional workflow. By inspecting the partial results, control and verification of the correct execution are applied.

Our proposed interface allows accessing stored data as regular memory objects. In this way, users can ignore the storage backend and programs are adapted performing minor changes. The system named Hecuba [2] is designed to be run with Cassandra [3], a NoSQL database, though it is natively compatible with

ScyllaDB [4]. They are designed with the aim of making data available without corruption obtaining good performance.

Results: We successfully applied this solution to an HBP use case based on a Python program responsible for analyzing brain sections and individualize neurons. In particular, we demonstrated that traditional approaches do not reduce processing times linearly as resources are added, while Hecuba nearly did. During the execution, we have been able to access and verify the results. Moreover, there hasn't been a penalty on performance, and the adaptation of code implied minor modifications.

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A framework for robot control with multi-modal motion activation using spiking neurons

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Motivation: Flexible and robust robotic motor control is an active field of research. Even though nature has numerous examples of sophisticated mechanisms concerning this matter, only a small fraction of the presented approaches regarding robot control exhibit properties of biological systems. Mammals, especially humans, are remarkably capable of adapting to changes in their environment, reacting to unforeseen events or learning new skills. These features, in particular adaptation, are desirable for robots in closed-loop scenarios and are induced by two biological principles. Firstly, the hierarchical and distributed way motion is represented by the vertebrate nervous system. This concerns the involvement of the brain, the cerebellum, the spinal cord and the muscles in diverse sub-tasks of motor-control [1] [2]. Secondly, three different kind of activation modalities for movements exist; voluntary, rhythmic and by reflexes. Their combination enables reuse and switching between motions. Furthermore, networks of spiking neurons, the third generation of Artificial Neural Networks, are distinctly closer to the biological model and also in theory more powerful [3] [4]. Hence, Spiking Neural Networks (SNN) are well suited for motor control inspired by nature.

Methods: In this approach, a SNN is used to control motions, represented with motor primitives, in a hierarchical manner. The network is capable of combining the different modalities in various ways, leading to reuse, combination and parametrization of motions. Additionally, learning new motions on previous knowledge is possible. The hierarchical architecture, inspired by [2], is illustrated in Figure 1. From right to left, the layers are arranged in increasing order of abstraction. The first level, motor control, provides the representation including motor primitives [5] [6], motor activation through motor neurons and the mapping to the robot embodiment. This is followed by low-level and high-level representations of the three activation modalities voluntary, rhythmic and by reflexes. The low-level motor control, governed by higher layers, is responsible for activating primitives rhythmically in a continuous way as shown in [7]. In addition, reflexes implemented for robots in [8], are realized within this layer. They incorporate proprioception to inhibit a currently executed primitive or to trigger a one time execution of a primitive. Besides voluntary activation of primitives, the high-level control provides parametrization of rhythmic motions. Supplementary,

higher brain areas represent e.g. action selection, motion planning and visual input, but these topics are intended for future work. Joint positions are transformed into neural input by stochastic population encoding, with a Gaussian tuning curve. In order to represent the effort on a joint rate coding, similar to the decoding used for muscle activation [9], is applied.

Results and Discussion: A novel, biologically plausible way of robotic motor control with SNNs was presented. In contrast to conventional robot control, our method exhibits interesting properties of biological systems like a hierarchical architecture and different activation modalities. We were able to use multi-modal activation to perform different complex movements, using motor primitives as fundamental building blocks. Primitives represent arbitrary trajectories and can be learned using previous knowledge. Combination of the three modalities has lead to reuse, switching, superimposition, combination and parameterization of motor primitives. Furthermore, the network could be activated with a single motor primitive as a rhythmic motion, combined with a voluntary motion triggering a reflex in case of a collision.

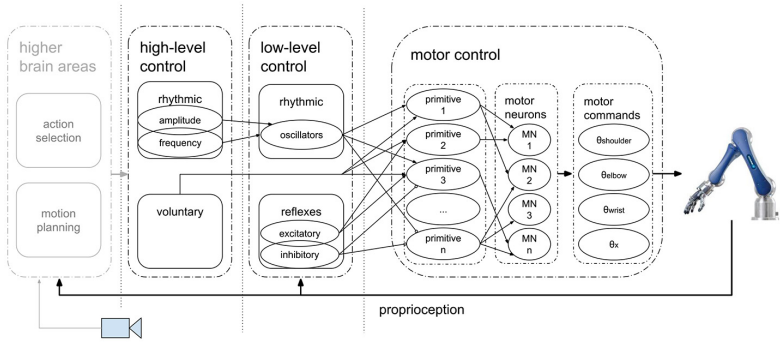

FIGURE 1: Detailed map of hierarchical architecture. The motor control layer consists of the representation of primitives, motor neurons and the mapping to motor commands. In the low-level control layer we have oscillators for rhythmic activation, and inter-neurons and neural circuits for reflexes. The high-level control layer represents voluntary activation and the parametrization of the oscillators. The proprioception includes joint states and efforts. For sake of completeness we included visual input, and in the higher brain areas a mechanism for action selection and motion planning. This figure was adapted from [10].

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The effects of computer based cognitive rehabilitation in patients with symptoms of visuospatial neglect or hemianopsia after stroke: A randomized, controlled, unblinded cross-over pilot-study

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Purpose: To address the effects of Computer Based Cognitive Rehabilitation (CBCR) in patients with visuospatial neglect and/or hemianopia in the subacute phase after stroke.

Method: CBCR was delivered by a commercially available program: 'Scientific Brain training PRO' designed to train visuospatial attention and mental rotation. Fourteen patients were randomly assigned to early or late CBCR intervention targeting visuospatial symptoms in a cross-over design. All patients were included within 40 days of stroke onset. The early intervention group (EI group) received CBCR starting immediately after inclusion for three weeks, and the late intervention group (LI group) started a 3-week CBCR intervention 3 weeks after inclusion. Attention was assessed by the CABPad Butterfly test at baseline, 3 weeks and 6 weeks.

Results: Groups were balanced on baseline characteristics. The EI group showed a significant reduction in neglect score between baseline and after training ($p = 0.018$), while the neglect score did not change significantly in the LI group, neither during the waiting list period nor during training, though an insignificant trend in this direction was observed. The LI group did not improve during their no-training period ($p = 0.237$) nor during their CBCR intervention period ($p = 0.116$). The difference in improvement during training periods was not significant between the EI and LI group ($p = 0.259$).

Conclusion: CBCR improved visuospatial symptoms after stroke significantly, especially when administered early in the subacute phase after stroke. The study was small and confirmation is needed.

Integrating multiple data sources for predicting the mouse mesoconnectome

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One of the original goals of the Human Brain Project was the development of a large-scale cellular level model of the human brain which could be used for understanding fundamental mechanisms of brain diseases and cognition (H. Markram et al, 2011). The achievement of such a goal requires sufficient information about the brain strucrture, including structural connectivity. Extensive research reporting the connectome of various species has been made, with the closest to the human brain being the mouse connectome at a mesoscale level (S.W. Oh et al, 2014). However, the connectivity coverage is not complete for all brain areas. The goal of this study is the integration of multiple brain data sources for predicting missing connectivity data by employing machine learning classification techniques and a bayesian framework.

A structural connectivity dataset was used in the analysis in which information about the connectivity strength between sending and receiving mouse brain areas was estimated using the anterograde tracing method. Gene expression data corersponding to the receiving areas and estimated with the in situ hybridization (ISH) method were used as a further data source (C. O'Connor, 2008). Both sources were registered into the Allen Brain Atlas. Before utilizing multiple data sources, prediction of connectivity between brain areas using gene expression data was investigated. Classification models based on the Random Forest and Logistic Regression methods were constructed at which combinations of gene expression values were trained to match the known connectivity patterns (T. Hastie et al, 2015, P. Tan et al, 2005). The classification performance was tested with the leave-one-out cross validation method while the evaluation measures used were average accuracy and area under the ROC curve (R. Kohavi, 1995, D.M. Powers, 2011).

The classification models were constructed and evaluated for each sending area separately. The average accuracy over all sending areas estimated was 84% for Random Forest and 87% for Logistic Regression (Figure 1). The average area under the roc curve over all sending areas was 89% for Random Forest and 92% for Logistic Regression (Figure 2). For some areas, both measures exceeded 95% (Figure 2).

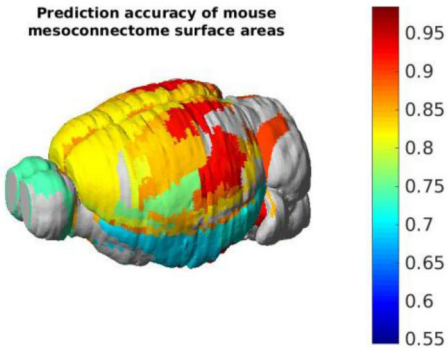

FIGURE 1: 3D plot displaying average prediction accuracy of the surface brain areas. The colors to the right represent the prediction accuracy according to the legend. The plotted surface areas are receiving ones. The classification model used is Random Forest. The accuracy of an area is estimated by averaging the prediction accuracy of the model for the connection between the corresponding area and all sending ones. The 3D tool being used is the Scalable Brain Atlas (Rembrandt Bakker, Paul Tiesinga, Rolf Kötter, 2015), (https://scalablebrainatlas.incf.org/composer/).

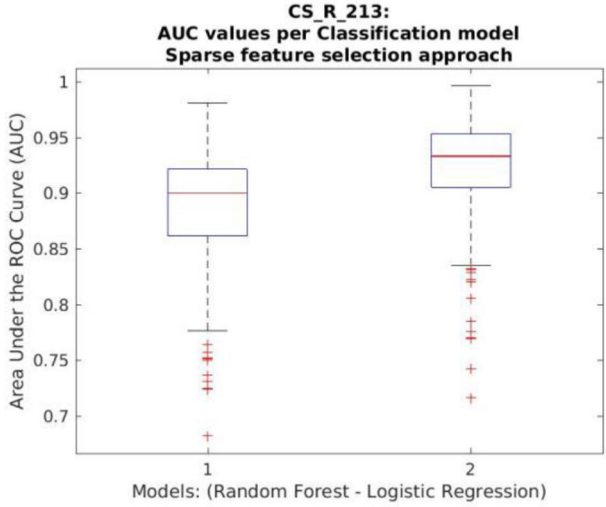

FIGURE 2: Area Under the ROC curve (AUC) values for all sending brain areas. X-axis: the two classification approaches: Random Forest (left) – Logistic Regression (right). Y-axis: AUC values (Work in progress).

As a future work reference, a Bayesian Generative framework will be implemented for estimating the posterior probabilities of brain region pairs being connected given the distributions of multiple data souces like single-cell RNA sequencing, Diffusion Tensor Imaging (DTI), cell density and morphological data (M. Hinne et al, 2014, A. Zeisel et al, 2015, D.K. Jones & A. Leemans, 2011). The posterior probabilities will be used for missing value imputation and network reconstruction. Taken together, these approaches demonstrate how different sources of information can be combined into a single estimate of the mesoconnectome and lead to its completion.

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Cultured neuronal networks as complex systems

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Introduction/Motivation: Having simulated various network topologies[1], as well as having dealt with several dynamical models taking [2] into account the spiking character of neurons, the next natural step is to culture real neuronal networks [3].

The goal of this line of research is to compare the theoretically-based simulations with the experimental data acquired, both from electrical activity and from structure; moreover, the idea is then to compare the interrelation, which we found in our simulations, between the dynamical output of a particular neuron and its place in the network.

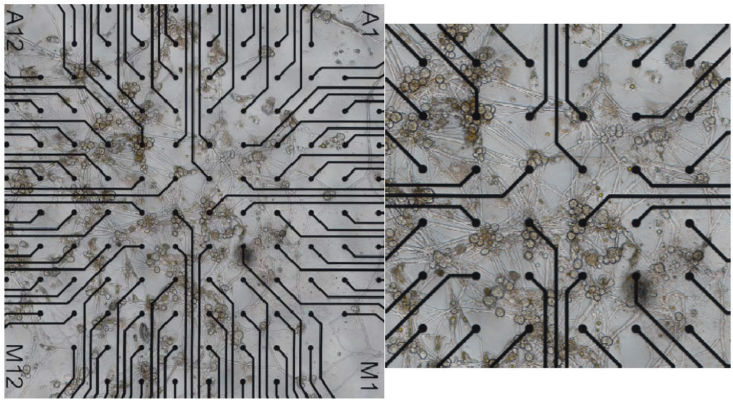

FIGURE 1: Example of a cultured neuronal network (left) and a zoomed version (right). We notice the electrodes (solid black lines) and the neurons (greenish blobs) with their connections clearly.

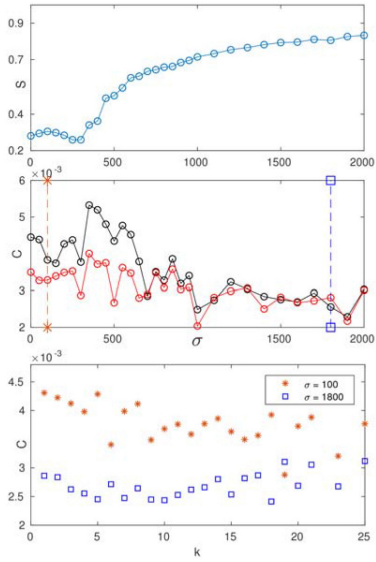

FIGURE 2: Results of simulating the Morris-Lecar neuron model on top of an experimentally obtained network structure. This is the previous step to the full experiment. This experimental network is made of 301 nodes (neuronal aggregates). It is interesting to note that although a similar behavior is attained in the second plot, the third one is the exact reverse of the simulated version, which is at least surprising.

Methods: For the first part of the work (i.e., the simulation part), we used numerical integration of several nonlinear models of neuronal spiking (specifically: Morris-Lecar [2], Fitzhugh-Nagumo and Rössler), for various network dispositions [1] (Scale-Free, Erdös-Rènyi, Star and Geometric), based on physiological observations of the brain and mathematical simplifications.

Regarding this part, we have cultured (see Figure. 1) neuronal networks [3] extracted from *Schistocerca gregaria.* We remove every part of the connective tissue and let the neurons "find each others" to explore and record the growth of the network. We let the network grow in a Petri dish about 200 electrodes inserted in it (called Micro Electrodes Array, i.e. MEAs), which enable us the recording of the electrical activity of small groups of neurons.

Results and Discussion: In this ongoing experiment we will compare and, ideally, try to classify: firstly to which of the selected network topologies, if to any, the cultured version corresponds; secondly, we want to discriminate between oscillatory models in this particular species, hopefully achievable with some complexity analysis techniques.

Our current results (Figure 2) have to do with an intermediate step: we have simulated the mathematical model on top of the experimental network, having obtained some interesting results such as the possibility of correlating the dynamical and the structural complexities, although the network is highly variable and, for sure, non-Scale Free.

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Longitudinal representation learning with deep networks for image retrieval applied to Alzheimer's disease

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Introduction/Motivation: Early diagnoses and prognosis of Alzheimer's disease (AD), monitoring the patient's condition or the disease progression, finding powerful biomarkers, identifying the patients who are most probable to ultimately develop AD, as well as treatment reaction are considered as key challenges in the research regarding AD. Considering Magnetic Resonance Imaging (MRI) as a key and powerful diagnostic tool for AD, it is very beneficial for physicians and researchers to provide efficient and reliable image retrieval and access to the medical cases to which they belong. These data might be used for knowledge discovery and could improve the diagnostic and therapeutic processes. The main concern here is to find a relevant image representation. Considering that AD is a progressive disease, finding a proper information representation from longitudinal images is even more challenging in this domain.

Methods: The stacked deep polynomial network (SDPN) is a powerful deep learning concept, which has shown good performance in learning and fusion of neuroimaging data [1]. In this study, a longitudinal two-stage SDPN algorithm, is proposed to refine and learn feature representation from longitudinal MRI data for AD, by adapting and expanding the architecture given in [1]. The proposed architecture is depicted on Figure 1. The first stage contains n+1 SDPNs, where n is the number of the available scans (acquired at n separate time points) for each patient. They are used to learn high-level features for each time point, and from the statistics that represent longitudinal changes (rate of change, percent change and symmetrized percent change). These features are than given to the second stage SDPN to fuse the information from the available time points and from the longitudinal changes. The proposed architecture is aimed to be applied to the ADNI dataset [2] to perform the longitudinal image retrieval task.

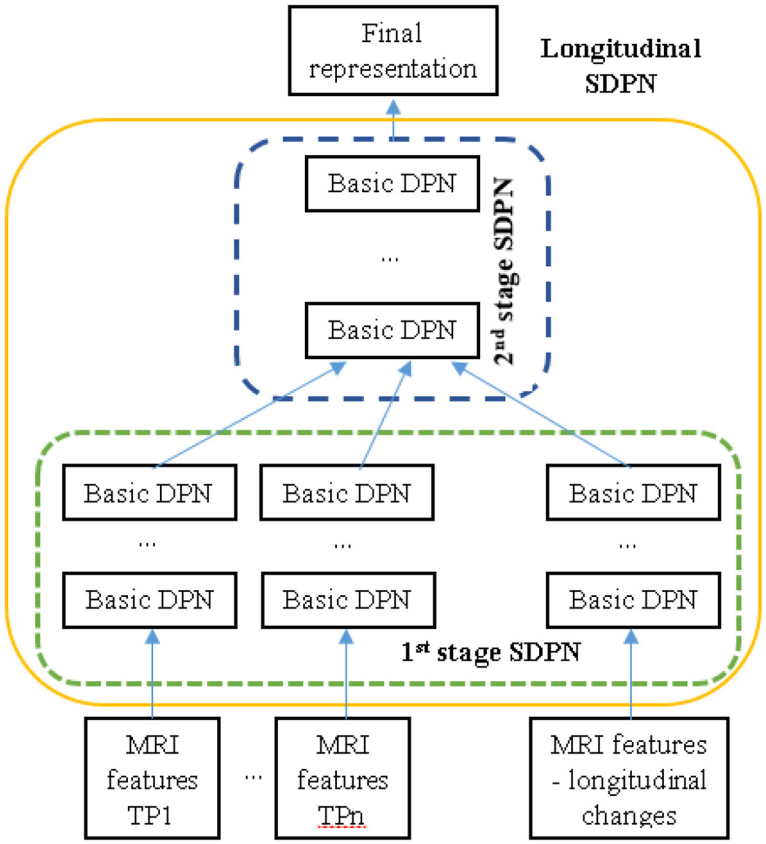

FIGURE 1: Longitudinal SDPN architecture
Abbreviations: MRI – Magnetic Resonance Images, DPN - deep polynomial network, SDPN - stacked deep polynomial network, TPx – MRI scan acquired at the time point x.

Results and Discussion: The proposed method is based on the state-of-the-art concepts proven to be powerful in feature learning. We believe that the proposed architecture will provide more comprehensive and reliable feature representation because of three main reasons: (1) the layer-wise stacking often yields better representations in deep learning [1], (2) longitudinal data provide information on temporal dynamics of the disease progression, and (3) the DPN performs well on both large-scale and

small-size datasets [1]. This might be very useful with regards to the image retrieval for Alzheimer's disease. The evaluation of this architecture is certainly needed to approve its suitability for the application domain.

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Synaptology of the somatosensory cortex in the adult mouse

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Most cortical synapses are established in the neuropil, which is composed of dendrites, axons and glial processes. There are two basic types of synapses: asymmetric or type I synapses, usually excitatory (glutamatergic), and symmetric or type II synapses, usually inhibitory (GABAergic). Most synapses in the neuropil (75–95%) are excitatory, while a minority (25–5%) are inhibitory. Synapses can be established either on the dendritic spines of excitatory neurons or on the dendritic shaft of both excitatory and inhibitory neurons. It is important to describe the morphology of excitatory and inhibitory synapses, as well as their density and location, because these parameters have a functional correlate. In addition, we have studied the possible correlation between mitochondria, multivesicular bodies (MVBs) and synapses.

For that purpose, we used three-dimensional electron microscopy with combined focused ion beam milling and scanning electron microscopy (FIB/SEM), a method that allows us to obtain long series of consecutive sections in an automated way. These stacks of serial sections can later be examined and segmented in 3D. We obtained seven stacks of serial sections from the neuropil of the six layers of the mouse somatosensory cortex. Using dedicated software (Espina), we have studied over 3550 synapses within these stacks.

Preliminary data show that the mean synapse density is 1.43 synapses/μm^3, ranging from 0.93 synapses/μm^3 in layer I to 1.69 synapses/μm^3 in layer Vb. We found that most synapses were excitatory (95%). Regarding the location of synapses, the vast majority of them were excitatory synapses located on spines (83%), followed by excitatory synapses on dendritic shafts (12%), inhibitory synapses on dendritic shafts (3%) and

inhibitory synapses on spines (2%). Therefore, it is to be noted that there are different preferences on synapse location depending on the type of synapse.

This work provides accurate quantitative data that helps understand the mouse cortical circuitry and will be useful to refine current cortical models.

Design of a bio-inspired compliant quadruped robot for research on closed-loop locomotion control

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Motivations: Research on adaptive locomotion has been conducted for many years, especially through neurophysiological and biomechanical studies generally carried independently. However, those complex motor behaviours originate from interactions between the neural system, the musculoskeletal system and the environment which makes exhaustive research in vivo hard to realize in practice. In this work-in-progress, we are developing different robotic platforms embedding classical hardware or a neuromorphic SpiNNaker board to investigate emergence of gait patterns on a quadruped and their relation with body morphology. In contrast with most of the classical robots, animals use tendon-driven actuators whose dynamical properties like stiffness or damping can be tuned in real-time depending on the usage and present unequalled performance in energy consumption and robustness. This aspect is mainly rendered by using compliant deformable and soft parts in the robot mechanics inspired from the cat. A simple model of brain functions is realized with Central Pattern Generators (CPGs) that are modelled with recurrent neural networks.

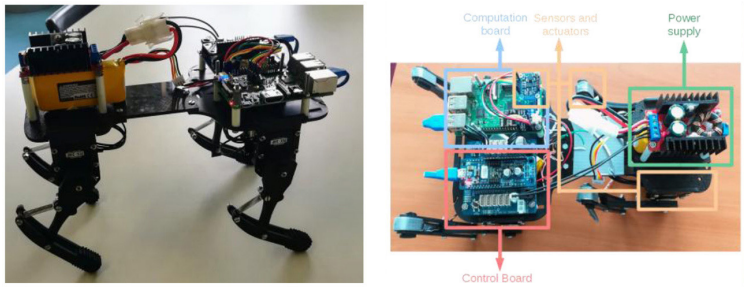

FIGURE 1: The Tigrillo robot and its electrical schema in the current prototype configuration.

Methods: The platform has been designed with focus on four key features: cost, simplicity, versatility and compliance. The compliance is a key element in this research as it is believed to add efficiency and robustness to locomotion, as observed in bio-mechanics. However, it also challenges classical control techniques as the dynamics of the robot is then governed by equations with a higher complexity level. On the current platform, the compliance is mainly ensured by using damper-spring systems in under-actuated legs. This version embeds classical processing hardware (relying on a RaspberryPI computer board and an OpenCM control board for sensing and actuation) and is a step toward a version integrating neuromorphic hardware like a SpiNNaker board. A general overview of the mechanical state and the electrical architecture is presented on Figure 1.

MultiMap: An application to visualize, edit and analyze spatial data

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Introduction: The increasing availability of automatic segmentation and counting methods [1][2] and the introduction of new procedures and tools to examine the organization of the nervous system [3][4] require the development of tools allowing researchers to visualize, analyze and share the obtained results. In the process of building an interactive map of synapses in the mouse hippocampal region we developed a desktop application (and related libraries and tool) that permits the creation, visualization and analysis of maps with various layers of information.

Methods: MultiMap is a multi-platform desktop application developed with javascript using electron [5] and NodeJS [6]. At the core of MultiMap there is a novel map-rendering tool [7] based on Leaflet [8], an open-source library for interactive maps.

Maps are stored as json [9] and can comprise several different kinds of layers: tiled images (tileLayer, deepZoom), cloud of points stored in csv files, regions of interests and markers. The layers information (images and csv files) can be stored both locally on the user machine or remotely on a server thus facilitating collaborations and the dissemination of research findings.

Users can draw regions of interest (see Figure 1) and retrieve basic statistics (area, volume and densities of points in the region). Moreover it is possible to annotate with markers any point in the map. MultiMap was planned as an extensible application leveraging the npm package manager. We already developed extensions to use ImageJ [10][11], BioFormats [12] and GraphicsMagick [13].

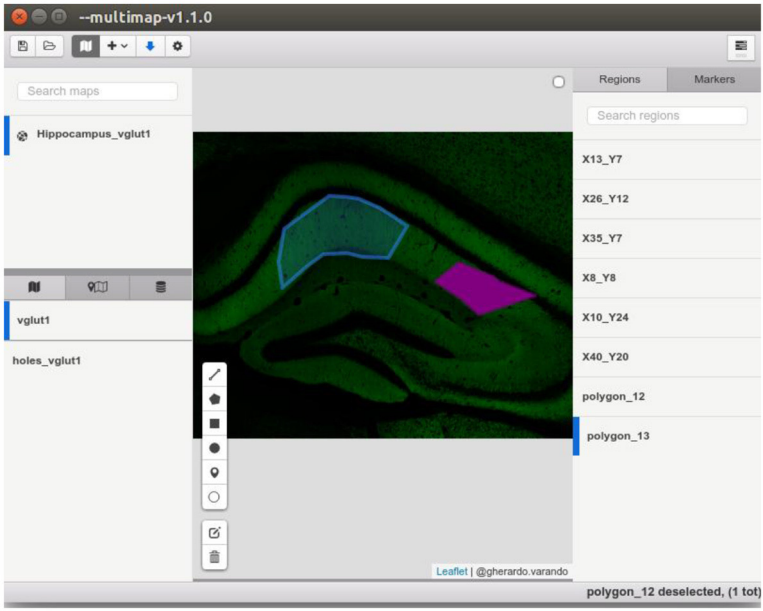

FIGURE 1: MultiMap interface.

Results and Discussion: We developed a new software [14] to visualize and analyze spatial data. MultiMap was inspired by applications that involve large amounts of spatial data to process. In particular we focus on analyzing spatial densities and visualize clouds of points with several billions of coordinates tiled across thousands of files. MultiMap can be a valuable tool in building brain atlases including spatial data in a standardized but flexible format that is well suited both for desktop that web-based applications. We think that the developed application and the related tools can be used as a valuable proof-of-concept for more complex and complete software products.

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Towards grasping with spiking neural networks for anthropomorphic robot hands†

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Motivation: The way movement is represented and executed in biology is an active field of research. The human hand is a complex system that can perform a wide range of motions with great flexibility and adaptation, for example, playing the piano or grasping unknown objects. Humans can remember grasp motions and modify them during execution based on the shape and the interaction with objects. However, studies show that only a small grasp repertoire is actually used [2]. Furthermore, a principle component analysis revealed that the first two components determine the 80% of the variance of all grasps [3]. A generally accepted hypothesis is that the central nervous system (CNS) uses motor building blocks when performing motion tasks [4]. These building blocks are called *motor primitives* [5] and are formed by *muscle synergies* [6]. In this context, the term synergy refers to the coupling of motor activation. A common assumption is that these primitives are linearly combined by the CNS in a hierarchical manner to compose complex motions [7]. These insights have been successfully transfered in robotics, for instance in the concepts of *eigengrasps* [8] and *dynamic movement primitives* [9].

Spiking neural networks (SNN) focus on biological plausibility [10]. Plasticity is used for learning by changing the synaptic weights. In a neuro-robotics context, there are approaches of SNNs using spike time dependent plasticity (STDP). For instance, to learn transformations of spatio-temporal data between coordinate systems [11], [12]. Inspired by this research, approaches for learning robot kinematics in simulation [13] and with a real robotic arm [14] were developed.

Methods: Our SNN approach is inspired by the biological concepts of hierarchical motion representation [7] and motor primitives [4] for grasping using muscle synergies [6]. We make the following assumptions for the fingers and for the hand. The hand makes different types of grasp motions when picking a pen from a table (pinch) than

† *Presentation of the work in Tieck et al.* [1]

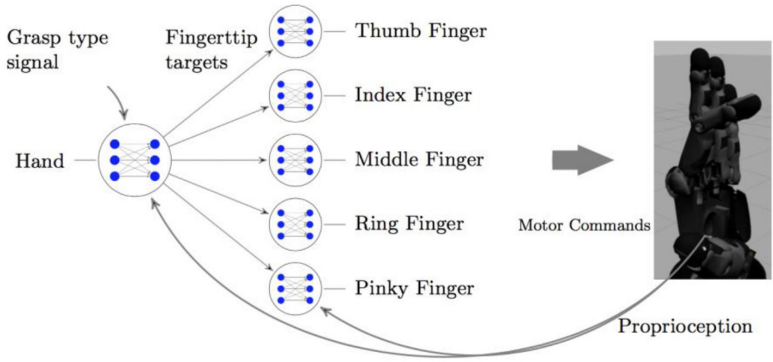

FIGURE 1: Complete architecture. The hand network (*left*) receives the proprioception of all fingers and a grasp type signal to generate fingertip targets. Each finger network (*middle*) receives its proprioception and fingertip target to generate motor commands [1].

when holding a tennis racket (cylinder). The motion of a single finger, in the examples above, is represented by the synergies between its joints and defines a motor primitive. Consequently, the motion representation and control movements are modelled using two types of networks, one for the fingers and one for the hand (see Figure 1). The finger networks control the movements of single fingers independent of the task, while the hand network coordinates the activation of the finger networks to resemble a specific grasp motion. Training data is recorded from human demonstration to train the SNN.

Results and Discussion: In this work, we present a model of a hierarchical SNN with a biologically inspired architecture that is able to learn and perform different grasp motions. Our model combines two different network types, one for the fingers and one for the hand. The finger networks learn different motor primitives as synergies between the joints. The hand network efficiently represents different grasp types coordinating the finger networks reusing the learned motor primitives. Both, the hand and the finger networks, are trained independently using STDP. Finally, we incorporate a mechanism for tactile feedback in the finger networks to stop the motion on contact. We evaluate our model with two different grasp types, i.e. pinch and cylinder [2]. After learning from human demonstration, the SNN is evaluated in simulation and on a real anthropomorphic robot hand.

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The structure of complex neural networks and its effects on learning

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Introduction: Reservoir Computing (RC) is one of the rare computing paradigms which can be used both as a theoretical neuroscience model [2] and as a machine learning tool [1]. The key feature of the RC paradigm is its reservoir a directed and weighted network that represents the connections between neurons. Despite extensive research efforts, the impact of the reservoir topology on the RC performance remains unclear. In this work [3] we explore this fundamental question and show, both analytically and computationally, how structural features determine the type of tasks that these recurrent neural networks can perform.

Methods: Computational methods: We create large recurrent networks of sigmoidal neurons test them in different tasks: capacity to retain previous inputs, precision in forecasting time series and voice recognition. The training is done by feeding the network a signal input and then using linear regression on the states of the neurons to obtain an output that matches our training data. The performance is then measured as an error function on test data.

Analytical methods: We consider every network as a dynamical system with high dimension space in which each dimension –corresponding to a neuron-- has a probability distribution which depends on the network structure. Then we derive the effects of changing some parameters of the network structure. And we combine this with the tasks studied by taking the error function associated to each task and derive the effects that different probability distributions will have.

Results and Discussion: We focus on two network properties: First, by studying the correlations between neurons we demonstrate how the degree distribution affects the short-term memory of the reservoir (Figure 1). And second, after showing that adapting the reservoir to the frequency of the time series to be processed increases

the performance we demonstrate how this adaptation is dependent on the abundance of short cycles in the network (Figure 2). Finally, we leverage those results to create an optimization strategy to improve time series forecasting performance. We validate our results with various benchmark problems, in which we surpass state-of-the-art reservoir implementations (Figure 2, dotted line).

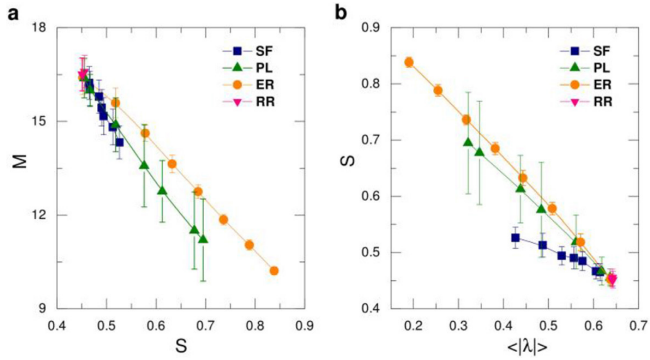

FIGURE 1: Relationship between memory capacity, neuron correlation and the network spectrum. (a) Short-term memory capacity M vs neuron state correlation S. (b) Neuron state correlation S vs average eigenvalue modulus <|λ|>. The different lines represent various network topologies with a wide range of parameters, but a fixed number of nodes.

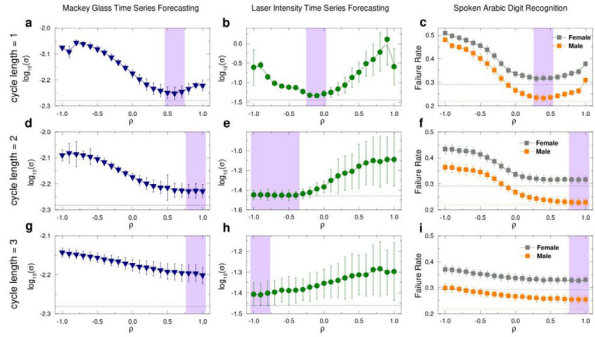

FIGURE 2: We plot the ESN error σ, for the tasks of forecasting Mackey-Glass (a, d, g), Laser Intensity (b, e, h), and recognizing Spoken Arabic Digits (c, f, i). The variable ρ accounts for fraction of cycles. Our figure shows that the optimal ρ is not 0, as it is in all previous literature. Spectral analysis allows us to obtain an optimization strategy which improves the performance (dotted black line).

Our approach provides a new way of designing more efficient recurrent neural networks and to understand how the computational role of common network properties.

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