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Abstracts Book

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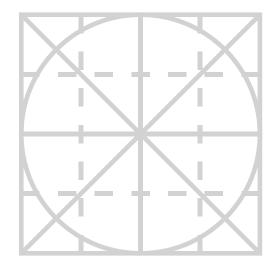
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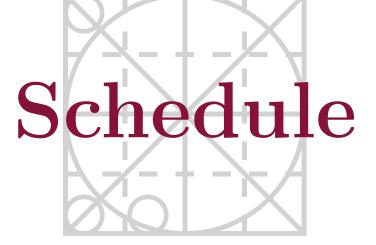


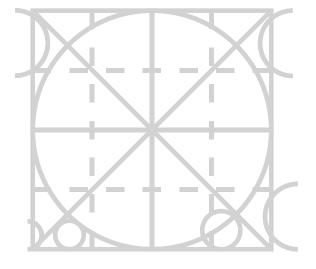
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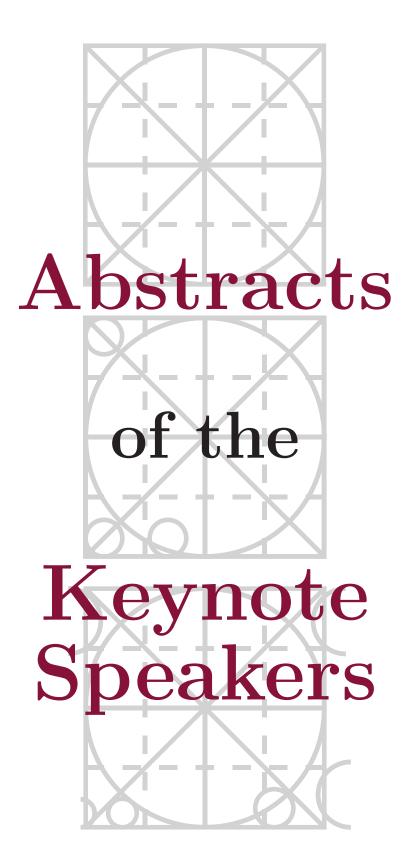
Monday 5th of July

9:00 - 9:30	REGISTRATION
9:30-9:45	Opening Remarks
9:45 - 10:35	Evaluating phase-based signal analysis techniques in electroencephalographic recordings from epilepsy patients
	Anaïs Espinoso, Universitat Pompeu Fabra
	Tuning synchrony in living neuronal networks through neuroengineering
	Jordi Soriano, Universitat de Barcelona
10:35 - 12:30	Poster Session 1
	GROUP PHOTO
	Coffee Break
12:30 - 13:30	From Input Statistics to Abstract Knowledge Learning from Speech
	Ruth de Diego-Balaguer, <i>Institució Catalana de Recerca i Estudis Avançats (ICREA); Universitat de Barcelona</i>
13:30 - 15:30	Lunch Break
15:30 - 16:25	Joint replay of correlated place maps in hippocampus
	Emma Roscow, Centre de Recerca Matemàtica
	Pre-training RNNs on ecologically relevant tasks explains sub-optimal behavioral reset
	MANUEL MOLANO-MAZON, IDIBAPS
16:30 - 17:30	What infants can think, maybe
	Luca Lorenzo Bonatti, <i>Institució Catalana de Recerca i Estudis Avançats (ICREA)</i> ; <i>Universitat Pompeu Fabra</i>
17:30 - 18:00	Coffee Break
18:00 - 18:50	Breadth versus depth: identifying close-to-optimal heuristics in human decision making with finite resources ALICE VIDAL, UNIVERSITAT POMPEU FABRA Brain mechanisms underlying auditory contributions to visual detection
	Alexis Pérez-Bellido, <i>Universitat de Barcelona</i>



Tuesday 6th of July

9:00 - 10:15	Specialized prefrontal circuits explain population dynamics during working memory encoding and maintenance
	Nicolás Pollán, Centre de Recerca Matemàtica
	When Working Memory fails: mechanisms underlying memory accuracy and errors
	Tiffany Oña Jodar, $IDIBAPS$
	Learning Cognitive Representations through Multitasking in Neural Networks
	Santiago Galella, <i>Universitat Politècnica de Valèn-</i> Cia
10:15-12:15	Poster Session 2
	Coffee Break
12:15 – 13:15	Macroscopic quantities of collective brain activity during wakefulness and anesthesia
	Adrián Ponce, Universitat Pompeu Fabra
13:15-15:15	Lunch Break
15:15 - 16:30	CHD8 whole-brain model: a mechanistic approach
	Laura Ulysse, Center for Brain and Cognition
	Structural brain connectivity and the paradox of weak links
	Gorka Zamora-López, Universitat Pompeu Fabra
	Emergence of complex spatiotemporal oscillations in large-scale brain networks
	Pau Clusella, <i>Universitat Pompeu Fabra</i>
16:30 - 18:30	Wine & Cheese
	Closing Remarks & Prizes





What infants can think, maybe

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Recent data suggest that preverbal infants possess remarkable capacities to process complex events and modify hypotheses about them facing inconsistent evidence. I will present data about the behavioral and neural correlates of some of these processes in infants and adults, focusing on elementary logical inferences. I will critically discuss various proposals about the mental representations underlying these capacities.



From Input Statistics to Abstract Knowledge Learning from Speech

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Speech is a very complex auditory stimulation. When trying to decode it to learn the Language conveyed in it a learner needs to compute the statistic relations between the specific sounds in this input. However it is also necessary at one point of learning to ignore these specific sounds in order to be able to create more abstract knowledge about classes of words (i.e. nouns, verbs, etc.) and their relations to be able to generalise and be fluent in a Language. In the talk I will review research providing evidence of how different aspects of attention from automatic capture to the ability highlight or ignore relevant information are essential in these different stages of learning. In this endeavour I will propose that the existence of concurrent cues in the statistic relations between elements are essential to be able to guide attention to generate abstract knowledge. I will also illustrate how different brain networks need to work in coordination at different stages for this learning to occur.

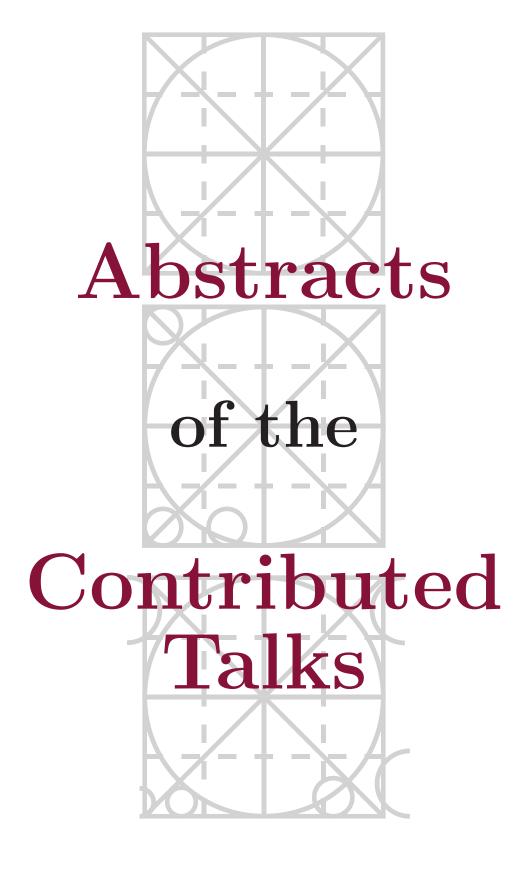


Macroscopic quantities of collective brain activity during wakefulness and anesthesia

Adrián Ponce

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The study of states of arousal is key to understand the principles of consciousness. Yet, how different brain states emerge from the collective activity of brain regions remains unknown. Here, we studied the fMRI brain activity of monkeys during wakefulness and anesthesia-induced loss of consciousness. We showed that the coupling between each brain region and the rest of the cortex provides an efficient statistic to classify the two brain states. Based on this and other statistics, we estimated maximum entropy models to derive collective, macroscopic properties that quantify the systems capabilities to produce work, to contain information and to transmit it, which were all maximized in the awake state. The differences in these properties were consistent with a phase transition from critical dynamics in the awake state to supercritical dynamics in the anesthetized state. Moreover, information-theoretic measures identified those parameters that impacted the most the network dynamics. We found that changes in the state of consciousness primarily depended on changes in network couplings of insular, cingulate, and parietal cortices. Our findings suggest that the brain state transition underlying the loss of consciousness is predominantly driven by the uncoupling of specific brain regions from the rest of the network.





Emergence of complex spatiotemporal oscillations in large-scale brain networks

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Neural oscillations constitute a primary indicator of brain and cognitive function. How certain types of complex oscillatory patterns emerge from the intricate and multi-scale structure of the brain is an open problem of great interest in the quest to understand neural encoding and treat cognitive disorders through external stimulation.

In this work we unveil the emergence of chaotic oscillatory regimes in a large-scale model of the human brain cortex. The model consists of 90 brain regions connected through a complex network obtained from tractography data. The activity of each brain area is governed by the dynamics of a Jansen–Rit neural mass model. Despite the absence of heterogeneities and noise, the system displays irregular spatiotemporal oscillatory dynamics for a wide range of coupling strengths and subcortical external input values.

In order to determine the dynamical landscape of the system and understand the onset of irregular behavior, we first consider a simplified formulation in which the total input received by each node is the same across brain areas. This simplification allows for the existence of different stationary and oscillatory states in which all nodes behave identically. We study the stability properties of these homogeneous solutions in detail. In particular, by means of the master stability function, we unveil a Turing-like instability of the synchronized solution which gives rise to heterogeneous oscillatory states that ultimately lead to spatiotemporal chaos through a cascade of period-doubling bifurcations.

Next, we perform extensive numerical simulations of the original system. The outcome reveals that irregular oscillations emerge through a mechanism similar to that of the simplified formulation, but differ on how the patterns synchronize and travel across the network.

Overall, our work characterizes a simple framework for the emergence of complex dynamics in systems composed of inter- connected neural mass models.



Evaluating phase-based signal analysis techniques in electroencephalographic recordings from epilepsy patients

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About 1% of the world population suffers from epilepsy, a severe neurological disorder. Electroencephalographic recordings (EEG) from epilepsy patients help clinicians in assessing the brain dynamics for a possible diagnostics. For patients who suffer from pharmacoresistant focal epilepsy, the purpose of EEG analysis is the localization of the brain area showing the firsts signs of the seizure. This area is the so-called seizure onset zone (SOZ) which can then be surgically resected provided that it does not overlap with functionally eloquent brain areas. We use the public domain Bern-Barcelona database, formed by two main groups of signals. One set is recorded from the hemisphere that contains the SOZ (focal signals) and the other set is recorded from the other hemisphere (nonfocal signals). The Bern-Barcelona database was composed and first analyzed by Andrzejak et al. applying nonlinear measures in 2012 [1]. The recordings from this database are seizure-free, meaning that we do not have the actual seizure activity which is otherwise used to localize the SOZ. In this research project we evaluate different analysis techniques based on the instantaneous phases extracted by means of the Hilbert transform from the signals. As a result, we can detect features induced by epilepsy that can sometimes be present in individual signals or manifest themselves between pairs of signals. Here we study the phase variability from individual signals, using the phase diffusion coefficient, and the phase synchronization from pairs of signals, using the mean phase coherence. We design a test from this phase-based signal analysis techniques jointly with the concept of surrogates. We first apply these phase-based techniques to the Rössler model system to understand how these measures work under controlled conditions. Our results from the EEG show that focal signals have more phase synchronization and less phase variability than nonfocal signals. The highest contrast is found applying the phase diffusion test. In conclusion, the phase-based measures which are obtained by simple definitions give relevant information about the underlying dynamics in EEG signals. Therefore, this study can be helpful for the presurgical evaluation of epilepsy.



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Learning Cognitive Representations through Multitasking in Neural Networks

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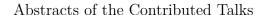
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Biological neural networks learn upon prior knowledge and are capable of responding to inputs differently based on contextual information. Artificial neural networks in common supervised tasks, on the other hand, learn without previous knowledge and learning is targeted specifically to a single task of interest.

In this study, we inspect artificial neural networks under a multitasking learning paradigm, where the network learns to differently classify a set of inputs according to the current task, specified by context units. Inputs are said to be congruent (incongruent) if they produce a same (different) responses for different tasks.

We focus on different tasks involving digit recognition, and categorize those according to parity and magnitude. Our results show that networks can solve both tasks with high accuracy. A further analysis on the activations reveals how classification occurs in the downstream layers of the network, suggesting that the first layers mainly process sensory information. In addition, highly anticorrelated weights from context inputs further suggest that the network learns to apply contextual information only for incongruent inputs, whereas for congruent inputs contexts are neglected. This means that the network learns to solve the tasks differently and independently for congruent and incongruent inputs. This is in clear contrast with how humans process context-dependent and rule-based decisions. For example, when showed a digit and asked about the parity or relative magnitude, we first recognize the digit and then recall its parity or relative magnitude. The network does not recognize the number. Instead, it has learned to categorize it as congruent or incongruent and map the input to the correct output category.

This analysis proves that a simple artificial network that learns to classify digits according to their parity and magnitude, will hardly invoke the concept of numerosity as a solution to answer the task. In reality, the network just learns to map input images to some desired outputs. This exposes the different ways of solving a cognitive





problem. To facilitate the learning constructed upon prior knowledge, we trained AI algorithms using curriculum learning. After learning to recognize digits, the learning of parity and magnitude is faster and more efficient. In this way, we can assist continuous learning and prevent catastrophic forgetting.

Keywords Neural networks; Multitask learning; Congruency Effect; Continuous learning

Acknowledgments: This work was supported by the Generalitat Valenciana Pla Gen-T Program [Ref. CIDEGENT/2019/043]



Pre-training RNNs on ecologically relevant tasks explains sub-optimal behavioral reset

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When faced with a new task, animals' cognitive capabilities are determined both by individual experience and by structural priors evolved to leverage the statistics of natural environments. Rats can quickly learn to capitalize on the trial sequence correlations of two-alternative forced choice (2AFC) tasks after correct trials, but consistently deviate from optimal behavior after error trials, when they waive the accumulated evidence. To understand this outcome-dependent gating, we first show that Recurrent Neural Networks (RNNs) trained in the same 2AFC task outperform animals as they can readily learn to use previous trials' information both after correct and error trials. We hypothesize that, while RNNs can optimize their behavior in the 2AFC task without a priori restrictions, rats' strategy is constrained by a structural prior adapted to a natural environment in which rewarded and non-rewarded actions provide largely asymmetric information. When pre-training RNNs in a more ecological task with more than two possible choices, networks develop a strategy by which they gate off the across-trial evidence after errors, mimicking rats' behavior.

Our results suggest that the observed suboptimal behavior reflects the influence of a structural prior that, adaptive in a natural multi-choice environment, constrains performance in a 2AFC laboratory task.

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When Working Memory fails: mechanisms underlying memory accuracy and errors

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Working memory (WM) is an essential brain function, which is central for cognition and severely impaired in multiple brain disorders. To investigate the underlying mechanisms limiting WM we developed a two-alternative delayed response task in which head-fixed mice are presented with an acoustic stimulus coming from either a left or a right side speaker. Animals had to remember the prospective response during a variable delay (duration D=0, 1, 3 and 10s) after which, they had to lick the corresponding side port. To understand how the length of the delay period affected the mice accuracy, we fitted a Generalized Linear Model that quantified the impact of the different factors on choice. The fitted model captured the forgetting process that took place during the delay as a reduction of stimulus impact on choice as D increased. Mice also showed (1) an idiosyncratic fixed bias showing a preference for one choice that was affected by the delay and (2) a delay-independent history bias favoring the previously rewarded side and opting away the previously unrewarded side. To recapitulate these two biases and their dependence (or lack of) on memory, we propose a two-state hidden Markov Model in which animals switch between a WM and a history-based module (H). The WM module is a double well potential where the information about the planned response is degraded during the delay. Since the double well is asymmetric, this introduces a modulation of the side bias with the delay.

The H one is a logistic function that only depends on previous response and is thus unaffected by the delay.

Also, we observed an increase in the weights of history regressors with trial index within a session and a reduction of stimulus importance. This suggests that the transitions to the H module are more frequent towards the end of the session. Moreover, we performed pharmacological manipulations where we inhibited NMDA receptors using NR2B antagonists. These animals showed a decrease of stimulus relevance that was taken over by a more prevalent presence of reinforcement learning strategies.

Finally, we took advantage of electrophysiological recordings to be able to access the anterolateral motor cortex (ALM) of behaving mice in order to find neural correlated of the described modules, something that is still under analysis.



Brain mechanisms underlying auditory contributions to visual detection

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How auditory information interacts with visual detection is a recurrent question in visual neuroscience. Whereas some studies propose that sounds interact automatically with incoming visual input, others instead claim that audiovisual interactions are dependent on top-down controlled processes like attention. In this study, we recorded magnetoencephalography (MEG) data while participants performed a visual detection task (where the audiovisual events were task-relevant) or a working memory task (where the audiovisual events were task-irrelevant). We trained multivariate pattern analysis classifiers and tested them at different time points to characterise how auditory information shaped visual stimulus representations over time in each task. Our results showed that sounds interact with visual detection via two different mechanisms. First, a mechanism by which observers actively used the auditory stimulus to orient their attention to the target onset, maintaining a stable representation of the visual stimulus along the whole trial. This mechanism allowed participants to improve their visual sensitivity and it was not automatic, as it required participants to attend the audiovisual signals. Second, a mechanism by which sounds elicit a neural response pattern akin to the one evoked by an actual visual stimulus. This latter mechanism was associated with an increase in false alarms and it is automatic since it was independent of participants attention to the audiovisual signals. This work shed light on a classic debate in regard to the automaticity of auditory dependent modulations of visual detection by showing that

- 1. sounds improve visual detection sensitivity via a top-down controlled mechanism
- 2. changes in criterion (i.e. signal detection theory parameter) due to sound presentation in visual detection tasks might not merely reflect decisional biases

Instead, our results suggest that sounds automatically evoke neural activity patterns that could be interpreted by the brain as a veridical visual stimulus.



Specialized prefrontal circuits explain population dynamics during working memory encoding and maintenance

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Neuronal population activity recorded from primate prefrontal cortex (PFC) carries information about the presented stimulus during working memory tasks. During cue presentation and in the beginning of the delay period the population code is dynamic [1], before it stabilizes and remains stable throughout the rest of the delay period. The circuit mechanisms underlying this dynamic-to-stable transition in the code are not yet understood. Here, we show that a spiking network model composed of three specialized attractor circuits can explain the experimentally observed transition. Each conceptual ring circuit represents a specialized PFC sub-population (encoding, storage and readout neurons). Based on experimental findings [2] we structured the model such that the external input excites the encoding population while it suppresses the storage population. When a cue stimulus is presented, a bump forms in the encoding population. Since its recurrent connections are not strong enough, the activity fades upon stimulus removal. When the strongly connected storage units are released from stimulus suppression, they form the stable bump which will maintain the memory. The readout circuit receives input from the other two populations and is thus active during cue and delay periods even without strong recurrency. Cross-temporal decoding analysis fails to generalize across cue and delay periods because different neuronal subsets are most informative during the respective epochs. These results agree with similar analysis of PFC recordings from a visual and memory task. Finally, from a functional point of view, the network model shows increased robustness to distractors once the activity bump has formed in the storage population, a prediction that can be tested experimentally. In sum, our findings suggest that the presence of a highly dynamic cue to delay transition



originates mainly from different neuronal subpopulations. After this initial transient, a stable state is reached, and memory maintenance is achieved through attractor dynamics.

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Joint replay of correlated place maps in hippocampus

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Place cells in the mammalian hippocampus show tuning to location. During rest and sleep, when immobile, the hippocampus replays place cell sequences which represent recent trajectories taken through the environment. Such replay is enabled by attractor dynamics in the CA3 area of the hippocampus, where bursts of excitation push the network towards recently active states characterised by newly strengthened synapses between excitable place cells. Hippocampal replay is believed to play an important role in memory consolidation, generalising across episodes, and more.

On constrained, linear paths, place cells also exhibit directional tuning, which means that trajectories in different directions are ended by different activity patterns. Replayed trajectories can therefore be decoded to one direction only, or both directions; however, models and analysis of replay typically consider just one direction at a time.

To address this, we re-analysed previously published single-unit recordings from CA1 in five rats during exploration of novel linear tracks. Place cells quickly developed directionally modulated tuning, forming two correlated place maps corresponding to runs in opposite directions. During brief rest periods between runs, we could detect offline reactivation of the place maps, whose Bayesian decoding often revealed a clear trajectory along the track. Joint replay, reflecting replayed patterns which are decodable to both place maps at once, appeared more than could be predicted by chance, suggesting that they form mixed attractors in the hippocampal network.

To test whether mixed attractors can explain the prevalence of joint replay, we extended a previous computational model of CA3 to produce spontaneous replay of correlated place maps. We found that only a small overlap between place maps is sufficient to produce attractor dynamics that reflect coherent replay in both place maps at once. This has implications for how hippocampal replay enables generalisation between distinct episodes for flexible navigation.



Tuning synchrony in living neuronal networks through neuroengineering

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Neuronal cultures are a highly versatile platform to study the relationship between activity and connectivity in living neuronal networks. Standard neuronal cultures grown on a homogeneous surface show a typical bursting behavior in which all neurons activate in a quasi-synchronous manner in a short time window, remaining silent in between bursts [1]. This behavior is similar to epileptic states in the brain. To tune a richer repertoire of activity patterns, and therefore approach brain-like dynamics in vitro, an interesting strategy that we have developed consists in restricting and directing the connectivity of the neurons through neuroengineering [2, 3, 4]. Two main configurations are explored. On the one hand, we use stamps to print modular circuits of about 1 mm total size on a substrate, and where the connectivity among modules can be tuned by allowing multiple connectivity paths among modules [2]. The higher the number of paths, the stronger the overall connectivity. This allows us to investigate the gradual transition from independent modular activity to intermodular synchrony as connectivity grows. On the other, we use physical obstacles such as parallel lines to induce strong directionality and anisotropy in the neuronal cultures [3]. The lines are designed as 50-micron high, 100-micron wide bulges in a polymer mold 8 mm in diameter. In either configuration, spontaneous neuronal activity is recorded through fluorescence imaging with genetically encoded calcium indicators, allowing for the monitoring of about 1000 neurons at high spatial and temporal resolution, and along different days in vitro. By studying the properties



of the emerging activity patterns and the functional connectivity of the circuits, we show that neuroengineering facilitates the emergence of a richer collective dynamics. We also show that small chemical perturbations suffice to move from a global synchronous dynamics to a local, richly patterned one, indicating that it is possible to design circuits with the same structural connectivity but very different functional one.

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CHD8 whole-brain model: a mechanistic approach

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Abstract

The Chd8 Haploinsufficient Syndrome involves a downregulation of the Chd8 transcription de novo gene $(Chd8^{+/-})$, a well known mutation in the ASD aetiology [1]. However the mechanistic relationship between the alteration of the gene expression and the behavioral consequences is still unclear. To do so, we examine the brain activity in order to bridge the gap. In fact, because brain regions are mapped with functions, altered activity in those regions can be linked to behavioral malfunctions, in particular those in the ASD phenotype. More precisely, evidences suggest that this mechanism might be related to the maintaining of the brain region' synchrony [4]. GABAergic interneurons are essential neural entities for the control of the global network excitability and the synchronisation of the pyramidal cells further documented to be deregulated in the $Chd8^{+/-}$ genotype suggesting this celltype as a plausible target of this genetic mutation [11, 9, 10, 6, 8, 12, 3, 5]. Then, gating defects in the global dynamical synchrony patterns related to changes in local E/I balance are expected to be observed [7]. Here, we investigate the specific question whether computationally decreasing the synaptic strength of the feedbackinhibitory-control (FIC) coupling in each brain regions within a biologically plausible



whole-brain model [2], can reproduce the brain dynamics of the heterozygous mice at the global and local scale. Our results confirm the possibility to reproduce both healthy $(Chd8^{+/+})$ and unhealthy $(Chd8^{+/-})$ states before and after the induced synaptic perturbation on the distributed FIC couplings strength, proportionally to the excitatory drives, within a whole-brain rsfMRI mice model. Those results demonstrate for the first time that FIC strengths deficits can be one of the mechanisms underlying the $Chd8^{+/-}$ mutation. This perturbation leads to local E/I imbalance, global oversynchrony patterns and global long-range overconnectivity in $Chd8^{+/-}$ compared to $Chd8^{+/+}$ rsfMRI mice model.

Keywords: rsfMRI mice, Chd8, whole-brain model, synchrony, E/I ratio.

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Breadth versus depth: identifying close-to-optimal heuristics in human decision making with finite resources

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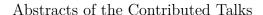
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Planning a holiday trip, selecting university courses or investing in stock options, these situations require the allocation of finite resources (time, money) in the absence of immediate feedback.

Such cases can be described under the framework of the breadth-depth dilemma; a multi-alternative risk-taking problem where optimality requires striking a delicate balance between pure depth concentrating all your capacity in one alternative and pure breadth spreading your capacity across the most alternatives. Do humans choose optimally in these situations? How do we manage the breadth-depth (BD) trade-off depending on the resources available? Although this question has been previously discussed (Halpert, 1958; M, 1981; Schwartz, Sadler, Sonnert, & Tai, 2009; Turner, Bettis, & Burton, 2002), only recently it has been formalised through a finite sample capacity model (Moreno-Bote, Ramírez-Ruiz, Drugowitsch, & Hayden, 2020) that makes quantitative predictions defining optimal choice behaviour as a function of available resources (sampling capacity) and likelihood of reward (environment richness).

Here, we set up a novel paradigm to test the model predictions empirically by manipulating these two variables. Finite capacity was defined as a number of samples (between 2 to 32) which had to be dispatched between several alternative options in order to gather information about their probability of success. After the sampling phase, participants had to make a final choice and select one of the alternatives sampled. The outcome corresponded to the probability of success of the chosen alternative and participants goal was to maximize the outcome accumulated throughout the experiment. The richness of the environment corresponded to the probability of success overall for the alternatives presented. This was modelled with a beta distribution characterising the environment: poor $(\alpha=1/3, \beta=1)$, neutral $(\alpha=1/3, \beta=1)$ and rich $(\alpha=1/3, \beta=1)$. We defined participants sampling strategy as the number of sampled alternatives (M) as a function of capacity.





As predicted by the model, we found that (1) at low capacities pure breadth predominates, whilst at high capacities participants sample just a few alternatives in depth, and intentionally ignore the rest, (2) the number of different alternatives sampled increases with capacity following a power law with an exponent close to 1/2, and that (3) rich environments promote depth over breadth, so that participants tend toward depth as the probability of success increases overall. Interestingly, some divergences between empirical data and predictions also stand out. First, we predominantly observe a gradual transition of the BD trade-off rather than the sharp transition predicted by the model. Second, we identify a bias to sample homogeneously, meaning that samples tend to be equally dispatched among the selected alternatives, which deviates from optimal BD strategies.

To conclude, our study provides a novel framework to investigate multi-alternative decision-making under finite resources, it reveals near-optimal choice behaviour, and identifies some heuristics that simplify computations at the cost of optimality.



Structural brain connectivity and the paradox of weak links

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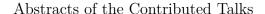
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Over the last three decades the study of structural brain connectivity has revealed several features which are consistently found across species. Structural brain connectomes are modular and small-world, with the cross-modular pathways centralised through a set of densely interconnected hubs, which form a rich-club. These conclusions have been mainly achieved by considering the unweighted binarised connectivity matrices derived from tract-tracing or tractography. However, if the strength of individual interactions were heterogeneous these network properties could be seriously altered.

In practice, the connectivity maps derived from both tract-tracing and tractography return weighted connections. It has been reported that (i) these weights are largely heterogeneous with values spanning over orders of magnitude, and (ii) the weights rapidly decay with the fiber length. Taken together, these observations result paradoxical because, on the one hand, the small-world property requires that long-distance fibers act as shortcuts facilitating the quick propagation of information across distant brain regions. But on the other hand, if long fibers are much weaker than shorter fibers, this renders the long-distant shortcuts irrelevant at the eyes of any dynamical process propagating along the brain.

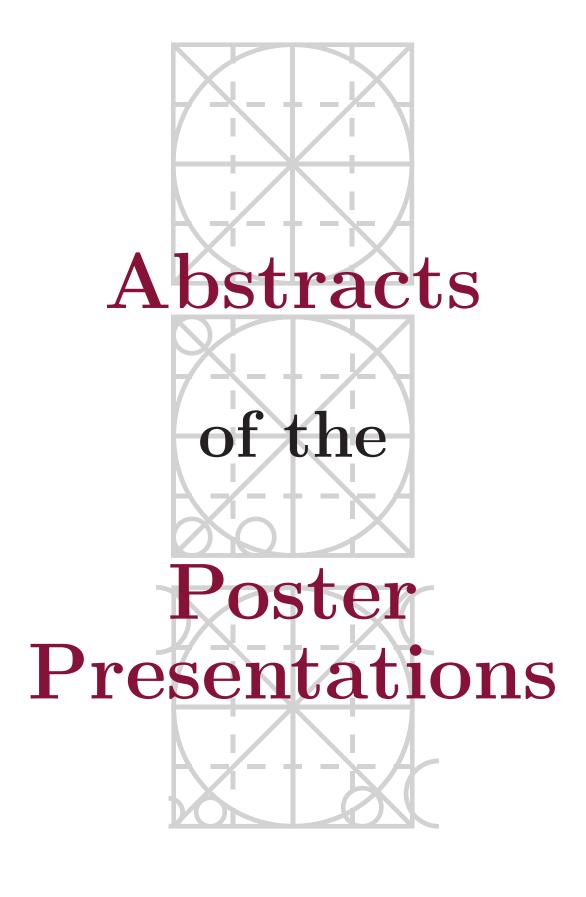
Here, we aim at understanding this paradox. For that, we compare the properties of whole-brain structural (SC), effective (EC) and functional (FC) connectivites as derived from neuroimaging. SC was obtained via diffusion imaging and probabilistic tractography in healthy participants. EC and FC were derived from resting-state fMRI. In accordance with previous diffusion imaging studies we find that the weight of structural links sharply decreases with the (euclidean) distance between brain regions. However, this behaviour is not corresponded neither by FC nor by EC. Indeed, the strength of functional and effective connections are independent of the distance between the brain regions. These observations reinforce the paradoxical situation in which, despite long anatomical fibers have negligible weight, strong associations are common between distant regions.





In order to investigate the influence of the weight distributions on the dynamical behaviour of the brain we perform a comparative network analysis between the SC and the EC. Therefore, we employ a recently developed approach to characterise complex networks that is based on the resulting network flows after a perturbation. Unlike standard graph theory, this approach naturally accounts for the strength of the connections. We find that the weighted SC is rather inefficient for the propagation of information on the network since its architecture is dominated by short connections, forming a spatial 3D grid without distant shortcuts. However, the small-worldness of the network is recovered when considering the weighted EC as the proxy for brain connectivity.

Our results evidence that the interpretation of the tractography weights as the "coupling strength" of SC is misleading and paves the way for future solutions.





Towards Data Driven MorphoNeural Models

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In the last decade, whole mouse brain 3D-images acquired at the resolutions of single neurons have become a reality due to recent advances in clearing techniques and microscopy technologies. Our approach aims to extract key anatomical information from those large images that, in turn, will be used to generate data driven morphoneural models that should help us to understand new fundamental aspects of brain computations.

In this context, we have started to develop a set of open source tools that aim to overcome the computing challenges that arise when dealing with 3D-images of tens of terabytes. For this purpose, we have been developing a cell detection tool that computes, in a reasonable time, the spatial location, size and orientation of neurons from whole brain images acquired at the mesoscopic scale. The algorithm is able to detect the soma of neurons in datasets with a high variability of sizes and fluorescent intensity values. Once the spatial location of a neuron is known a tracking algorithm that was also developed can follow automatically the processes that come out from the soma.

These tools are able to manage images acquired with different resolution across the xyz axes (anisotropic images). A special effort has been made to provide user friendly tools which can be managed through a Graphical User Interface (GUI) or a Command Line Interface (CLI). In addition, our tools were designed to achieve (1) computational tractability to prevent runtime out-of-memory errors and (2) computational scalability to adjust the execution to the available computing resources. This means that the tools can be executed on a regular laptop, a workstation, or a computer cluster.



Synaptic extension of the bump attractor model predicts target-distractor onset asynchrony effects

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Distractor filtering is fundamental to achieve an efficient management of working memory (WM). The capacity of a distractor to impair WM performance depends on its time separation with the target stimulus, the target-distractor onset asynchrony (TDOA). Distractors are more disruptive for short than long TDOA. This fact suggests a period of relative memory instability at early stages of the WM delay period, but its exact mechanisms remain elusive. The bump attractor model of WM explains memory maintenance through elevated firing activity during the delay period, and it can explain the TDOA effect by assuming a slow, gradual formation of the attractor in the delay. Here, we propose an alternative model based on the interplay of persistent activity and short-term synaptic plasticity. The combination of synaptic depression and facilitation at the onset of persistent activity induces a dip in the firing rate of memory-selective neurons in the early delay period. We tested this specific prediction by reanalyzing single-neuron recordings in macaque dorsolateral prefrontal cortex (dlPFC) while performing a visuo-spatial WM task with distractors presented with TDOAs of 100, 200, 300 and 900ms [1]. Consistent with the model, we found that neurons selected based on their target stimulus selectivity at the end of the delay displayed this early-delay dip with robust cue period elevated firing. We also tested the validity of the model in human participants performing a more complex task where, besides manipulating the TDOA, distractors were presented not just prospectively but also retrospectively to the target. Behavioural, modeling and electrophysiological results point towards a dlPFC population that combines circuit-reverberation and short-term synaptic plasticity mechanisms to achieve memory maintenance.



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Disconfirmation bias as a perceptual strategy to deal with repeated sensory experiences

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In our daily lives we interact in repeated occasions with the same perceptual information. Often, each of these repeated interactions lead to different decisional outcomes between one occasion to the other. In this project we wanted to study which mechanisms determine participants changes of mind in a decision-making task where the same information was presented to the participants multiple times. To test these hypotheses, we designed an experiment where participants had to estimate the average orientation of 6 sequentially presented Gabor patches. Participants saw the same sequence three times and were allowed to change their mind between repetitions. We hypothesized that after a perceptual decision, participants might be more sensitive to confirmatory evidence, while reducing sensitivity to disconfirmatory evidence (Talluri et al., 2018), or simply repeat the same response regardless of the new gathered information (i.e. decision bias). The results showed that participants responses improved after repeated exposure to the same stimuli sequence and were biased towards previous responses, in line with confirmation bias predictions.

However, reverse correlation analyses showed that participants weighted more in their final decision those information samples that disconfirmed their previous decision. Our results demonstrate that humans, when faced several times with exactly the same information, distribute their perceptual resources asymmetrically, overweighting that information that is incongruent with their previous beliefs.



Studying population coding in the human tactile afferents

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Introduction The spiking activity of tactile receptors in the human skin has been widely investigated, from their responses to simple or complex tactile stimuli to the relationship between spiking activity, brain processing, and elicited sensations of touch. The vast majority of these studies only explore the activity of individual or a handful of afferents, due to the technical limitation imposed by the commonly used acquisition tools. However, the glabrous skin of the human hand is covered with approximately 17,000 afferents [1], thus natural mechanical interaction is expected to activate hundreds of receptors. The glabrous skin is innervated by four classes of tactile afferents, which traditionally have been viewed as functionally segregated. This notion has lately been challenged with evidence that most stimuli excite all classes of afferents, and most tactile percepts are shaped by multiple submodalities. Still, our understanding of tactile information encoding on a population level remains primitive [2]. In this study, we employ computational methods to study tactile afferents' activity at the population level. We simulated the simultaneous activity of thousands of tactile afferents innervating the hand in response to precise and well-defined stimuli. Then we used information theoretic and decompositional tools to explore synergies and redundancies among different afferent classes.

Methods Spiking activity of the tactile afferents was simulated using Touchsim [3]. Firing activity of the afferents is sparse and suitable for a lower dimensionality representation. Non-negative matrix factorization (NMF) linearly decomposes single-trial population spike trains into non-negative basis functions and coefficients [4]. Then a generalized linear model (GLM) was fed with the compact representation found by NMF. to decode the stimulus.

To capture all types of interaction, linear and nonlinear, at all possible orders, we turned to information theoretic methods, which are model independent, statistically robust and mathematically well-grounded [5]. The probabilities of classification provided by the GLM were used to compute mutual information as a proxy of the



information content of the spiking activity [6]. Following this insight, we take into account how much likely each stimulus is given the activity. Also, by using this approach, we avoid single-cell methods and focus on population coding, given that the GLM was trained on the entire neural populations.

Results First, we tried to find a lower-dimensional representation that compactly captured all sensory information carried by the neural population. By means of NMF, we identified stereotypical co-activation patterns across different stimulus conditions. Second, we asked in how afferents of different classes and at different locations on the hand signalled redundant or complementary information to the brain. With the GLM and information theoretic methods, we highlight that a significant portion of the encoding is shared among different afferent classes, that still have unique and synergistic information, suggesting that segregated coding seems an unlikely candidate code. Conclusion Due to the technical limitations in the acquisition tools, literature has been focused in the analysis of single afferents, finding evidence of segregated coding. In contrast, our population-based analysis found synergies and redundancies among tactile afferent classes, suggesting that analyses based on single afferents might not be enough to unveil the complexity of the tactile coding strategies. These results will pave the ground for a deeper understanding of the convergence and integration of tactile submodalities in the brain.

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Mean-field model of consequential reward-driven decision making

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Despite the rich literature in decision-making, the computations underlying its neuro-physiology, as a function of how complex options are and of their potential consequence, remain to be well understood. Our hypothesis is that although consequence is a critical concern in our daily decision-making processes, the dynamics of its operation have not yet been incorporated into typical state-of-the-art formulations such as the Wang attractor model. Here we introduced a parsimonious extension thereof that accommodates consequence in the context of a novel experimental design for the study of consequence and adaptation.

To this end, we developed a mean-field model of neuronal dynamics. In partic- ular, we modelled the firing rates of two competing populations of neurons, each sensitive to one of two stimuli. We assumed that the commitment for an option is made when the difference of firing rates between pools crosses a certain threshold. Furthermore, to incorporate consequence and to test it in a fitting scenario, we included the well-known paradigm of Wang attractor models, into a wider network scheme that considers not only single decisions, but rather the overall decision strategy across several trials. In particular, the dynamics of the decision-making process are captured by two pools of neurons representing the saliency of each option. Furthermore, an additional strategy pool was designed and incorporated into the model to oversee consequence and to learn from the rewards obtained from each decision. This feedback was also incorporated into the decision-making process to maximize overall reward. In conclusion, we offer a novel model that explains reward-driven decision-making, incorporating consequence and learning in a parsimonious fashion.



Long-term turnover dynamics in area CA1 of hippocampus are consistent with plasticity of non-spatial inputs

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Recent chronic imaging experiments in mice have revealed that the hippocampal code exhibits non-trivial turnover dynamics over long time scales [1]. Specifically, the subset of cells which are active on any given session in a familiar environment changes over the course of days and weeks. While some cells transition into or out of the code after a few sessions, others are stable over the entire experiment. The mechanisms underlying this turnover are unknown. Here we show that the statistics of turnover are consistent with a model in which non-spatial inputs to CA1 pyramidal cells readily undergo plasticity, while spatially tuned inputs are largely stable over time. The heterogeneity in stability across the cell assembly, as well as the decrease in correlation of the population vector of activity over time, are both quantitatively fit by a simple toy model with Gaussian input statistics. In fact, such input statistics emerge naturally in a network of spiking neurons operating in the fluctuation-driven regime. This correspondence allowed us to map the parameters of a large-scale spiking network model of CA1 onto the simple statistical model, and thereby fit the experimental data [2] quantitatively.

Our model suggests that the internal representation of space in the hippocampus evolves over time mainly due to changes in non-spatial inputs, which may represent changing contextual cues, or simply the passing of time. It also suggests that the locus of plasticity underlying turnover may be in the inputs from the entorhinal cortex, and not necessarily CA3.

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Sensory independent history choice biases in auditory categorization tasks in rats

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To make adequate decisions, animals need to evaluate not only the current sensory information but also recent actions and outcomes. In trial-based perceptual categorization tasks, both humans and rats can develop three main history choice biases:

- 1. the win-stay/lose-switch bias, which reflects a tendency to repeat previous rewarded actions and avoid unrewarded ones;
- 2. a repulsive aftereffect caused by previous stimuli and related to sensory adaptation;
- 3. the transition bias, a tendency to repeat or alternate the previous response based on an internal estimate of the repeating probability of the sequence of events.

While the first is known to be an action-reward bias, the last two are assumed to be sensory-related, but few studies have validated this hypothesis. To do it, we trained rats on two tasks which only differ in the existence of sensory information. First, to test if the Aftereffect bias is affecting the perception of upcoming stimuli, we trained rats in an auditory categorization task (Sound task) with a 10% of Silent catch trials. With this design, animals could generally use sounds to guide their choices. We found that animals still exhibited an Aftereffect bias in Silent trials, suggesting the bias does not require the perception of a stimulus to impact consequent choices. Second, to elucidate which is the contribution of sensory stimuli to generate the Transition bias, we trained rats in a free-choice task (Foraging task) in which there were no acoustic stimuli to guide their choices, and animals had to rely solely on the serial correlations of the sequence of previous choices to obtain reward. We found that rats developed the same Transition bias as in the Sound task, suggesting that it reflects the prediction of the rewarded response rather than an expectation of future stimuli.





These results suggest that the three more prevalent history biases observed in rats performing a decision-making task -win-stay/lose-switch, transition and aftereffect-can all be manifested in the absence of a sensory stimulus.



Bump attractor dynamics underlying stimulus integration in perceptual estimation tasks

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Perceptual decision and continuous stimulus estimation tasks involve making judgments based on accumulated sensory evidence. Network models of evidence integration usually rely on competition between neural populations each encoding a discrete categorical choice. By design, these models do not maintain information of the integrated stimulus (e.g. the average stimulus direction in degrees) that is necessary for a continuous perceptual judgement. Here, we show that the continuous ring attractor network can integrate a stimulus feature such as orientation and track the stimulus average in the phase of its activity bump. We reduced the network dynamics of the ring model to a two-dimensional equation for the amplitude and the phase of the bump. Interestingly, these reduced equations are nearly identical to an optimal integration process for computing the running average of the stimulus orientation. They differ only in the intrinsic dynamics of the amplitude, which affects the temporal weighting of the sensory evidence. Whether the network shows early (primacy), uniform or late (recency) weighting depends on the relative strength of sensory stimuli compared to the amplitude of the bump and on the initial state of the network. The specific relation between the internal network dynamics and the sensory inputs can be modulated by changing a single parameter of the model, the global excitatory drive. We show that this can account for the heterogeneity of temporal weighting profiles observed in humans integrating a stream of oriented stimulus frames [1, 2]. Our findings point to continuous attractor dynamics as a plausible mechanism underlying stimulus integration in perceptual estimation tasks.

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Abstracts of the Poster Presentations



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Approaching brains *in vitro*: dynamics and functional organization in three–dimensional neuronal cultures

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Due to the difficulty and ethical limitations of in vivo approaches for brain research, in vitro neuronal cultures have emerged as a powerful tool to study the structure, dynamics and functional organization of neuronal circuits in a controlled environment. Until now, research has primarily focused on two-dimensional cultures (2D), i.e. flat substrates on which neurons grow and connect to one another [1]. However, this 2D environment typically shapes a rigid dynamic behavior characterized by network bursts, in which all neurons fire synchronously in a short time window [1]. Additionally, 2D cultures cannot replicate the physical organization, cell morphology and biochemical richness of neurons grown in the brain. To overcome this limitation, three-dimensional (3D) neuronal cultures were introduced in the last decade as a new paradigm for brain-on-a-chip investigations [2]. These 3D cultures typically



consist of a structural support (scaffold) that facilitates neuronal positioning and physical stability, and without blocking neuronal connectivity [3]. In our laboratory we use "PEGylated–fibrinogen" as scaffold, a transparent hydrogel that shapes truly 3D circuits of few mm³, and where ~1000 neurons can be individually monitored with fluorescence calcium imaging. Compared to 2D cultures, and with the assistance of numerical simulations, we observed that the 3D networks exhibit a very rich repertoire of activity patterns, in which complex spatio–temporal waves coexist in the volume, similar from a quantitative point of view to what is observed in the brain. The analysis of functional connectivity in these 3D cultures revealed a more intricate functional organization, characterized by functional modules that cover distinct spatial regions of the culture, and a neuron–to–neuron communication that balances short– and long–length scales. Our results show the promising potential of 3D cultures as a living model system for both physics of complex systems and biomedical research.

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Efficient pattern recognition in the hippocampus with a phase-order code

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The existence of place cells in the rodent hippocampus, together with their phase precession throughout the ongoing theta oscillation in the local field potential, suggests the coexistence of both a rate and a phase code to support spatial navigation. Yet, the properties of both neural codes have not been formally compared in the context of hippocampal dynamics. Here, by using an encoder-decoder framework representing the CA3-CA1 circuit, we characterize two plausible coding schemes for pattern recognition: one based on spatially distributed firing rates, and another based on phase-ordered spike sequences. Whereas the former transforms incoming analog input patterns into theta-confined firing rates, the latter recasts them into a theta-gamma phase format. Thus, while both codes rely on orthogonal ensembles firing throughout self-generated theta oscillations in CA3, they predict different but physiologically plausible-readout mechanisms in CA1. Moreover, we show that, while both codes predict opposite distributions of the CA3-CA1 readout weights, they are both learnable via STDP in a one-shot supervised learning scenario. Then, after matching both codes in terms of information rate, we show that the phase-order code is much more energy-efficient than the rate code, with the spikes per second scaling well with the number of ensembles. Hence, while a trade-off between information rate and energy efficiency, that determines the optimal number of ensembles, is identified for the rate code, the phase-order code seems to be unbounded, thus leaving open the question of what the underlying cost function is that determines hippocampal dynamics.



Is your gaze your aim? Eye position in reward gambling and the role of OFC in encoding the value of visually cued offers

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A wealth of studies has revealed how cells in frontal brain areas are involved in higher cognitive control functions. Of crucial interest is the understanding of how the activity of neural cells relates to the processing of external stimuli features bound in abstract entities of behavioral relevance. Working memory mechanisms reveal their most fundamental importance when they are functional to the selection of behavioral options for the achievement of alternative goals as in decision making. For behavioral tasks with sequential reward offers presentation, neurons in the orbitofrontal cortex (OFC) have been associated with the coding and maintenance of the estimated value of a firstly presented offer so that it can be later compared with the estimated value of a later presented one. Importantly, it is yet to be assessed what is the role of perceptual features of visually presented offers such as the order of presentation and their spatial location. Our research aims to investigate the role of task variables in eve movement behavior and the role of neural activity in OFC during the execution of a two-alternative gambling task with sequential visual offer presentation. Interestingly, we report that eye movements consistently fell within the visual screen side with best offer expected value, thus showing how eye position can be used as a marker of readout of the actual best guess. In addition, despite the subjects were left with blank screen and free to direct gaze at their will, we found that they most frequently reached the side of best offer at each time during task execution. We find evidence for this behavior soon after the first offer was presented and, very consistently, soon after the second offer presentation. Lastly, we investigated the role of cells in OFC, revealing how a significant portion of cells shows linear tuning in their firing rate





with respect to offer features. In particular, we report spatial selectivity to the side of presentation, to the order of presentation of offers with different values, and to the value of rewards achieved in previous trials.



Sequential Episodic Control

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State of the art deep reinforcement learning algorithms are sample inefficient due to large number of episodes they require to achieve asymptotic performance. Episodic Reinforcement Learning (ERL) algorithms, inspired by the mammalian hippocampus, typically use extended memory systems to bootstrap learning from past events to overcome this sample-inefficiency problem. However, such memory augmentations are often used as mere buffers, from which isolated past experiences are drawn to learn from in an offline-fashion (e.g., replay). Here, we demonstrate that including a bias in the acquired memory content derived from the order of episodic sampling improves both sample and memory efficiency of an episodic control algorithm. We test our Sequential Episodic Control (SEC) model in a foraging task to show that storing and using integrated episodes as event sequences leads to faster learning with less memory requirements as opposed to a control model, which buffers isolated events only. Furthermore, we link our approach to the transition of deliberate-to-habitual behaviour in mammals, showing how hippocampal-like fast episodic learning with cortical deliberation can bootstrap striatal-like slow habit learning to serve adaptive behaviour.



Spherical harmonics based model of electric field effects on neocortical neurons

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Transcranial electrical stimulation (tES) is a non-invasive method consisting of the injection of currents through the scalp and resulting in the generation of externally induced electric fields inside the brain. The injection of constant (DC) currents, referred to as transcranial direct current stimulation (tDCS), generates a constant electric field in the different tissues that can be estimated through biophysical head models based on the electrical properties and geometry of the different tissues obtained from neuroimaging data. The effect that these generated electric fields have on single neurons can be approximated as a membrane potential perturbation that is proportional to the membrane length constant (lambda) as described in the cable equation. This is referred to as the lambda-E model [1] and is a simple mechanistic approach that assumes that the membrane perturbation can be modeled as the dot product of a vector parallel to the orthodromic direction of cortical neurons with the electric field, multiplied by lambda. This approach has been used mostly to model the effect of tDCS on pyramidal cells. Here we propose to represent in a more general way the model of the membrane perturbation as a function of the magnitude and angular orientation of the E-field, using a spherical harmonics expansion that can better capture the dependence of the perturbation on electric field direction. In this representation, the lambda-E model corresponds to the first-order degree (l=1) term of the expansion. This approach can be used to represent the three-dimensional response of a specific cell part, obtained experimentally. Here we employ it using synthetic data from realistic neocortical cell models in a DC field in the tDCS regime, fitting the coefficients for the membrane responses. We use realistic reconstructions of the rat somatosensory cortex from the Blue Brain Project [2] to simulate the response of different pyramidal cells and interneurons to electric fields of 1 V/m as a function of the orientation of the field with respect to the cell using the NEURON simulation environment [3]. Using this procedure, we report values of membrane perturbation comparable to those in the literature [4,5], extend it to different cell types, and provide the spherical harmonic coefficient profile for each neuron. Finally, since in general the azimuthal orientation of a specific cell type is not readily accessible, we provide an azimuth-independent version of the model that



can be used for realistic non-invasive stimulation simulations, providing an averaged response that only depends on the angle between the electric field vector and the cortical surface.

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Dynamics of elementary NMM circuits

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Neural mass models (NMM) have been widely used to study the meso- and macroscopic dynamics of populations of neurons, especially related to oscillations [1, 2], and more recently, in whole-brain models [3, 4]. Over the years, a great variety of NMM have been introduced, some more complex than others, and each aimed at representing some aspects of neural behavior (e.g. spontaneous activity, epilepsy, predictive coding). Most models also present different regimes e.g. sinusoidal oscillations vs no oscillations depending on the external input and the initial conditions, and their analysis is extremely complex.

In this work, we aim to get a better insight into how these regimes appear. In an effort to create conceptual tools to deconstruct and analyze the behavior of complex networks, we study a total of four elementary circuits, all consisting of two populations of neurons interconnected and one of them receiving an external input, which may be tuned to change the dynamics regime of the system.

First, we focused on 3-synapses systems, consisting of a pyramidal population connected to another pyramidal $(P \leftrightarrow P)$, an inhibitory to inhibitory $(I \leftrightarrow I)$, and a pyramidal receiving an external input to an inhibitory $(P \leftrightarrow I)$. An initial analytical study of the fixed points and stability of the systems allowed us to understand under what conditions (set of parameters and types of populations) oscillations can arise. In particular, we found that only the case of a $P \leftrightarrow I$ circuit can present oscillations and as a direct result of a Hopf bifurcation. Additionally, near the bifurcation point, we observed coherence resonance, i.e. the appearance of oscillations when noise is added in the external input. In both cases, we were also able to get an analytical expression for the eigenfrequency in terms of the parameters of the system.

Moreover, these results were verified by drawing the bifurcation diagram of each circuit and calculating numerically the frequency using a dedicated software (XPPaut [5]).

The change of dynamics under a sinusoidal electric field was also studied by drawing an Arnolds tongue diagram for each circuit. The plots were coherent with the previous results, observing only resonance phenomena for the pyramidal to inhibitory circuits.



Finally, we extended the study to a 4-synapses system, focusing on the pyramidal to inhibitory circuit with an additional self-inhibitory loop on the inhibitory population. In this case, we failed to obtain a complete analytical expression for the eigenfrequency, although we did investigate how it changes with the variation of the circuit parameters. The dynamics of this circuit resemble those in the simpler one the pyramidal to inhibitory without the self-loop. The main difference is a wider range of frequencies at which the system oscillates as the external input changes (while the rest of the parameters are fixed).

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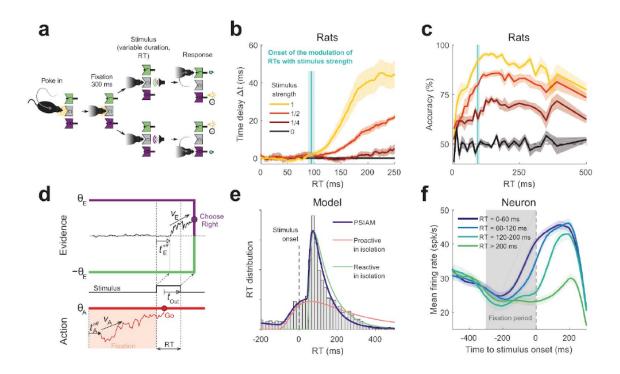
Neural signatures of competing proactive and reactive processes during perceptual decisions in dorsomedial striatum

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Standard models of perceptual decision-making postulate that a response is triggered in reaction to stimulus presentation when the accumulated stimulus evidence reaches a decision threshold. This framework excludes however the possibility that informed responses are generated proactively at a time independent of stimulus2. Here, we find that, in a free reaction time (RT) auditory discrimination task in rats (Fig. 1a), the timing of the fastest responses does not depend on the stimulus strength (Fig. 1b), although the choices do (Fig. 1c). This unveils the coexistence of reactive and proactive responses, also for longer RTs, suggesting that choice selection and motor initiation, commonly viewed as serial processes, are decoupled in general. We capture this behavior by a novel model in which proactive and reactive responses are triggered whenever either of two competing processes, respectively Action Initiation or Evidence Accumulation, reaches a bound (Fig. 1d-e). In both types of response, the choice is ultimately informed by the Evidence Accumulation process. To investigate where the Action Initiation process may be implemented in the brain, we performed population recordings in the dorsomedial striatum (DMS) of four rats (total of n= 652 well isolated single units). A preliminary analysis of neural activity revealed that a large fraction of neurons (40%) encoded choice side from the response initiation until the next trial response. Another subpopulation of neurons (20%) displayed stimulus-independent ramping activity before response onset whose slope correlated with RT, suggestive of the Action Initiation ramping process (Fig. 1f). Overall, these results fundamentally extend standard models of evidence accumulation in decision making by showing that proactive and reactive processes compete for the generation of responses, and that dorsomedial striatum





may play an important role in generating the proactive process. Figure 1. a, Task sketch. b, Delay between RT cumulative distributions, mean across 10 rats, shaded areas are s.e.m. c, Tachometric curves; legend as in b. d, Sketch of PSIAM with parallel Evidence and Action processes. Example of a proactive response where the bound of the AI process is reached before any bound of the Evidence Accumulation is reached, prompting the animal to respond. The choice is determined by the sign of the EA. e, Model fit to RTs for an example rat. f, Peri-stimulus time histograms conditioned on RT bins for an example neuron in dorso-medial striatum, shaded areas are s.e.m.

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Oscillatory network dynamics and neuronal communication for exact firing rate models

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Macroscopic oscillations in the brain have been observed to be involved in many brain tasks but their role is not completely understood. The Communication Through Coherence (CTC) theory (Fries, 2005,20015) establishes that neural communication is much effective if the underlying oscillatory activity of the emitting and receiving populations is properly phase locked, so that inputs arrive at the peaks of excitability of the receiving population. We study the phase-locked states of a neuronal Excitatory-Inhibitory (E-I) network under external periodic forcing, simulating the input from other neural groups. We use recently developed mean-field models (Montbrió et al., 2015; Dumont & Gutkin, 2019), which provide an exact description of the macroscopic activity of a network and are amenable for mathematical analysis. We identify the conditions for optimal phase-locking and selective communication. Namely, we find that inputs with higher frequency and coherence have an advantage to entrain the network and we quantify how robust are to distractors.



Impact of age-related changes in axon myelination on working memory

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Behavioral studies have shown that aging leads to an impairment in working memory performance. Working memory crucially relies on persistent neuronal activity in prefrontal and parietal cortex as the underlying mechanism. Normal aging also leads to a combination of structural and functional changes in cortical pyramidal neurons and in white matter pathways, with particularly significant white matter (myelin) dystrophy. In order to understand the relationship between neuronal and behavioral changes, we aim to develop a network model comprising a visual cortical circuit, a posterior parietal circuit, and a lateral prefrontal cortical circuit, constrained by in vitro and MRI data from rhesus monkeys across the adult lifespan. Here we present initial results towards this goal, with a focus on the effects of age-related myelin alterations. Electron microscopy studies have shown extensive axon demyelination and remyelination in the lateral prefrontal cortex pyramidal neurons in the rhesus monkey, and MRI studies of both monkeys and humans have shown a loss of white matter from the cerebral hemispheres with age. We modified a single-neuron model of pyramidal neurons to study the effect of age-related myelin alterations on action potential conduction. Applying empirical data-based demyelination and remyelination alterations to a cohort of "young model neurons", we quantified a reduction in action potential propagation speeds in some cases and action potential failure before the distal end of the axon in others. Equipped with these results, we then studied the effects of action potential failures in a spiking neural network model of an oculomotor working memory task in PFC. We found significant demyelinationrelated impairment of network performance during the task. Remyelination worked





as a compensatory mechanism: it did not totally counteract demyelination effects but reduced the amount of impairment to a level more comparable with the task performance observed empirically. This model allows us to make predictions that can be tested against the empirical data and that will be later incorporated into a more complex multi-area network model.



Mouse Village: A novel automated high-throughput platform for behavioral tasks in freely moving mice

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Mice are preferred species for biomedical research and have been used for a long period because of their both anatomical and physiological similarities to humans. Using this species is advantageous due to their size and abundant behavioral and imaging tools to measure and monitor their behavioral and biological responses. However training mice in cognitively complex tasks is a difficult enterprise: it typically takes several months of daily behavioral experiments and large groups of animals to reduce behavioral variability across sessions, which can be a large limiting factor in this species.

Here, we present a novel, fully-automatized, behavioral platform, the Mouse Village, that works 24/7 without any intervention from the experimenter. We test this platform with a novel visuospatial working memory (WM) task but that is suitable to almost any mouse tasks in freely moving animals. This platform allows the homecage, where animals are housed in groups, to be connected to the behavioral box so that animals can access it freely. The platform is programmed in Python and uses Bpod controllers which are based on Arduino boards (Sanworks) providing high temporal precision to the responses and behavior of the mice.

Because of the connection of the homecage to the maze, mice can enter the maze when they are motivated to do the task. This connection reduces the training time because mice can train themselves during the day and night. Another benefit of the set-up is that it reduces the stress caused by handling. Moreover, it eliminates unconscious biases introduced by the experimenter. Therefore, the advantages of using the Mouse Village are using standardized training and test procedures, minimizing the experimenters interference and thus, lowering the stress caused by them and collecting highly precise data. Working memory refers to the capacity to temporarily represent information for a short period of time while being processed and manipulated. There are several visuospatial working memory tasks used with primates and humans to investigate the underlying neural mechanisms. However, there



is no similar working memory task for mice which are suitable models used in behavioral research. In our WM task, mice are trained to remember the location of a visual stimulus which is briefly presented in random order. There are three stimulus positions on a horizontal axis of a touchscreen.

Mice are expected to respond to the location of the visual stimulus by poking after a delay period. In one trial, a mouse fixates behind a transparent door for 2s and the stimulus is presented on the touchscreen during 2 second. After stimulus offset there is a delay period in which animals maintain the stimulus location in memory. After the delay period, the door opens and a mouse is expected to touch the stimulus position on the touchscreen where the stimulus is presented. After a correct response, water is given as a reward. The next trial starts after the collection of the reward from the lick port. Throughout the trials, the position of the mouse is recorded by using infrared beams and a video camera.

A group of 9 C57BL/6 mice was trained in this task using the Mouse Village. Three different delay lengths were used: -0.4s, -0.1s (meaning that the door opens 0.4 or 0.1 s before stimulus offset), and +0.3s (meaning that the door opens 0.3 s after stimulus offset). A one-way analysis of variance yielded a significant difference among three delay lengths in accuracy of responses, F(2,16) = 486.41, p < .01.

A post-hoc Tukeys HSD test showed that -0.4s, -0.1s, and +0.3s delay lengths differed from each other significantly, p < .05.

Mice were given three different reward values (5, 10, and 20 μ l) each session in random order; within a session, reward value did not change. During the period in which mice were presented with 3 different reward values, subjects conducted 38, 66.57, and 73.7 trials per session in sessions with the value of 5, 10, and 20 μ l respectively.

In the MV, mice conducted this task both during the day (709 sessions) and night (803 sessions) cycle completing an average number of trials per session of 63 during the day and 64 during night. Our results show that the MV is a valid platform to train animals in a fast and reliable way in WM tasks.



Dynamics of aggregated vs homogeneous 3D neuronal cultures

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Introduction

According to Graph Theory, complex networks can be defined as a set of nodes V, and a set of links, L, that describe the connections between nodes [1]. In our case, the nodes will be the neurons of our culture; whereas the links will be their synaptic connections.

Model

Structural model

The structural networks are created following a generalization of the method put forward by Orlandi et al. [2]. With this model we are able to emulate the growth of a biological culture of neurons in a volume for any level of aggregation. One of the most important features of this model is that a connection between neurons takes place with a connection probability α whenever the axon of one neuron intersects the dendritic tree of another.



Dynamical model

To describe the dynamics we will use the Izhikevich model [3]:

$$\tau_c \dot{v}_j = k[v_j - v_t][v_j - v_r] - u_j + I_j + \eta , \qquad (1)$$

$$\tau_a \dot{u}_i = b[v_i - v_r] - u_i , \qquad (2)$$

$$I_j = g \sum_{i=1}^N A_{ij} \sum_{t_m < t} D(t_m, t) \exp\left(-\frac{t - t_m}{\tau_A}\right) \Theta(t - t_m) , \qquad (3)$$

which depicts the neuron through two variables: the membrane potential, v, which describes the generation of action potentials, and the inhibitory current, u, which introduces a negative feedback to the membrane potential. It also considers the influence of synaptic currents through the term I.

Homogeneous vs aggregated cultures

Measure of aggregation: Gini coefficient Λ

The aggregation, Λ , of the cultures is measured through the Gini coefficient, given by the normalized area between the bisector and the Lorentz curve, as defined in [4], but modified to adapt it to 3D cultures. Typically, the best homogeneous cultures presented a degree of aggregation of $\Lambda \approx 0.4$, while the clustered ones could exhibit up to $\Lambda \approx 0.9$.

Synchronization dynamics

We describe the dynamics through raster plots. With them we observe that homogeneous cultures display on-and-off dynamics, with very well defined global avalanches [5]. On the other hand, the more aggregated ones have a much richer behavior, presenting both local and global coherent activity.

Functional vs structural networks

Finally we study this difference in the dynamics through the functional network of the cultures, which we also compare to the structural networks.



Conclusions

This work sheds light on two central results:

- I Aggregated cultures display richer dynamics than homogeneous cultures, which is manifested in both their raster plots and functional networks.
- II The functional networks of the cultures are able to capture the skeleton of the structural network.

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Rotations of prefrontal working memory representations to protect from task interference in a dual-task paradigm

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Recent studies involving complex working memory (WM) tasks or tasks with distracting inputs have suggested that stimulus representations before and after distractors are orthogonal, thus allowing for the protection of stimulus information from interferences. However, whether orthogonalization is a general mechanism for WM preservation remains an open question. Moreover, the specific network mechanisms that could allow for such an orthogonalization are unknown. Here, we investigated orthogonalization as an instrument of WM control on calcium imaging data from the medial prefrontal cortex (mPFC) and the anterior cingulate cortex (ACC) in behaving mice performing a recently developed olfactory dual-task. The dual-task - the ultimate WM interference condition - consists of an outer delay-paired association task (DPA) combined with an inner Go-NoGo task. We studied how the representation of the sample stimulus of the DPA was affected by presenting the Go/NoGo cue of the inner task. Specifically, we examined how the memory of the stimulus was transformed across the delay period of the outer task. We focused on inferring low-dimensional coding directions to evaluate angles between WM representations at different epochs of the delay period. In mPFC, we found a significant change in the directions representing DPA sample information before and after the Go/NoGo cue. This result indicates a rotation of the representation of the sample information in the early delay period into a more orthogonal direction after the Go/NoGo cue and in the late delay period. In contrast, in ACC, memory rotations occurred after completion of the inner task. We finally investigated how the WM representations in mPFC depended on the cue of the inner task. We found that the WM representations of the DPA sample between each trial type (no cue, Go, or NoGo trial) followed similar rotational dynamics. After cue presentation, the coding directions between no cue trials and Go or NoGo trials became more and more orthogonal. Altogether, our results suggest that rotation of WM representation in mPFC is a fundamental mechanism for maintaining WM information against interfering tasks.



BrainX3: A neuroinformatic tool for interactive exploration of multimodal brain datasets

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BrainX3 is a neuroinformatic tool for exploration, analysis, modelling and simulation of brain data using interactive visualizations that facilitates exploration and discovery of new insights by scientist and clinicians. We describe the design principles and architecture of the platform and the general features of the software. We present BrainX3 Radiology, an application built on top of the platform that targets the localization of brain lesions and the analysis of their impact on brain function for rapid and efficient access to high-quality integrated multi-modal brain data together with tools for analysis and semantic interpretation.



Physical Effort Modulates Urgency and Speed-Accuracy Tradeoff in Perceptual Decision Making

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Urgency is an important aspect of the decision-making process, which optimizes overall reward rate by accounting for the time-related costs and hence modulates the speed accuracy trade-offs (SAT) (Ditterich, 2006, Drugowitch, et al., 2012). Recent findings suggest that primary motor areas of the brain show activity reflecting sensory evidence and urgency to act (Thura & Cisek, 2014) and that urgency influences movement execution (Thura, et. al., 2014). These two pieces of evidence are gradually depicting urgency as a general arousal signal that modulates both decision and motor processes. Consistent with this, we hypothesize that motor costs of accumulating evidence impact urgency in a similar fashion as time-related costs, and that this may be observable through SAT adjustments in peoples performance. To test this, we modified the classical random dot motion (RDM) task (Britten, et. al., 1992) by making the stimulus viewing period contingent on continuous hand press. In the experimental conditions, participants (N=12) had to press a hand dynamometer (two levels of intensity, high and low) to be able to see the RDM stimulus on the screen, upon which they had to make a left/right decision. In the baseline condition (no effort), participants were shown the stimulus whilst holding the dynamometer. By manipulating the physical effort (no, low, high) of the hand press and trial deadlines (short = 1.5s & long = 4s), we aimed to test whether effort induces a change in SAT similar to deadline manipulations, and whether their respective effects can be dissociated. The results showed that physical effort shortened RTs in both long deadline (no effort = 1.82, low effort = 1.57, high effort = 1.39, p = 0.002) and short deadline (no effort = .91, low effort = .89, high effort = .77, p < 0.001) conditions. Physical effort significantly reduced proportion of correct responses in short



deadline (no effort = .69, low effort = .68, high effort = .65, p = 0.013) but not in long deadline (no effort = .71, low effort = .7, high effort = .69, p = 0.54) blocks. Since accuracy is strongly modulated by motion coherence, we also looked at the psychophysical threshold (motion coherence at 75% accuracy) as a proxy of performance. We found a significant effect of both deadline (p = 0.005) & effort (p = 0.026) on psychophysical threshold. These results are consistent with physical effort inducing changes in SAT (summarised in Figure 1). In order to assess the accuracy drop per unit of time (1s), we calculated Rate Correct Score (RCS, number of correct responses from a condition divided to total RT) for each participant and condition. We found that RCS is significantly predicted by motion coherence ($\beta = 1.69$, p < (0.001) and deadline ($\beta = -0.3$, p < (0.001) but not by physical effort ($\beta = 0.001$, p = .97). Although physical effort speeds up RT and reduces performance, the correct response in a unit time is not modulated by it. We conclude that physical effort can influence the urgency signal, however its effect on performance is different than a typical deadline manipulation in terms of keeping the RCS stable. This study offers a general understanding of urgency as a signal that represents both time-related & effort-related costs during decision making and opens new questions about how different sources of urgency end up in different performance effects in perceptual decision making.

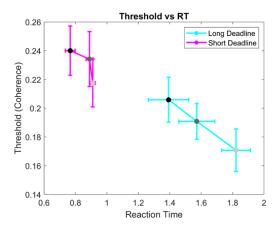


Figure 1. Psychophysical Performance and Reaction Time. The colour of the markers indicates the level of effort (black=high, dark grey=low, light grey=no). Lines represent the two deadline conditions (cyan=long, magenta=short). Error-bars indicate SEM.



Plan, initiate and update: a model for rats choice and reaching in 2AFC task

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Standard decision-making models postulate that a response is triggered once the accumulated evidence reaches a decision bound. We have recently shown that rats in a free reaction time (RT) auditory discrimination task trigger their response before stimulus is processed or even presented in a considerable fraction of trials. However, accuracy in those expressed responses is influenced by stimulus strength, suggesting they are not guesses but sensory informed choices. A new model, the Parallel Sensory Integration and Action Model (PSIAM), explained this phenomenon by proposing the parallel processing of response initiation and evidence accumulation processes [1]. Here we build on this model by characterizing the precise response trajectories exhibited by our subjects revealing aspects of the decision process beyond canonical descriptions.

We first extract the rats response orienting trajectories while performing the task using DeepLabCut. Average trajectories of the decision coordinate as a function of time exhibit a sigmoidal shape which we quantify by the time at which they cross a decision threshold right before the side ports and the peak velocity with which they cross.

Using catch trials with no stimulus we find that prior expectations modulate trajectories in absence of stimulus by reducing the crossing time of the decision thresholds and increasing the peak velocity. In regular trials, stimulus strength also modulates average trajectories peak velocity. The point in the trajectory where we could first detect the impact of the stimulus ranges from 40 ms to 80 ms after movement onset, depending on the RT imposesing bounds on the motor efferent latency and the sensory afferent latency.

Finally, we explore trials in which expectations are incongruent with the presented stimulus and find a significant fraction of trajectories in which the initial choice is reversed. Several additional analyses indicate that these trajectories may represent



changes of mind: their rate increases with prior-stimulus incongruency, decreases with RT and is mostly correcting reversals.

We expand the PSIAM model to describe the full trajectory of the animals. In reactive trials, responses are triggered by the stimulus accumulated evidence hitting the decision bound and the trajectory is ballistic towards the port associated port. In proactive responses, however, animals initiate an a priori trajectory, whose velocity depends on the prior expectation, which is updated en route by the stimulus. Importantly, the update depends parametrically on the final value of the accumulated evidence: it can confirm and accelerate the original trajectory or reverse it if the final evidence is at odds with the end goal of the original trajectory.

Together, our analysis and modeling results put into question ballistic models of decision making and illustrate how response trajectories reveal the timely superposition of two processes, prior and sensory evidence, which compete asynchronously to dictate the subjects choices.

References

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Interference-based forgetting in a goal-directed spatial navigation task for rodents

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To avoid catastrophic accumulation of information during learning the brain needs to forget to retain only what is subjectivity relevant to each individual. Interference-based forgetting occurs when new information acquired before or after a learning event attenuates memory strength. In our daily life we are continuously exposed to new associations, each with its own value and volatility, which limits the interpretation of results obtained in lab conditions using only few associations. For this reason, we developed a novel task that allows us to observe the effect of memory interference in more ethological conditions.

We utilized our high-throughput behavioral task where animals learn the location of the reward among 8 possible positions, that randomly changes across days. We test the memory recall of the location of the reward position 2 hrs after the training session and we observe how memories from previous sessions (i.e. days) interfered with this recently learned memory. To manipulate the interference between previously learned memories, we infused human N-Methyl-D-aspartic (NMDA) receptor and Leucine-rich glioma-inactivated 1 (LGI1) antibodies into animals brain ventricles to mimic a partially anterograde amnesic state.

We confirmed that continuous learning of new associations decreases the strength of recent memories due to the interference with previous ones. We showed for the first time the effect of interference from all previous memories up to 3 days in the past. We also found that antibodies mediated amnesia is capable of reducing interference significantly (p<0.01) enhancing recent memories at the cost of considerably reducing (40%) the strength of old ones. Our findings support the theory of retroactive interference as the mechanism to eliminate memories from associations with high volatility.



Magic number five: The breadth-depth dilemma in accumulator and decision-tree models of decision making

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Decision-makers are often faced with the opportunity to allocate their liited information-gathering capacity between several options before receiving feedback. Current formalizations of uncertain choice, such as the explore-exploit dilemma, do not apply well to decisions in which a limited sampling capacity can be allocated to each option in variable amounts. Such choices confront decision-makers with the need to trade off between breadth - allocating a small amount of capacity to each of many options and depth - focusing capacity only on a few options.

We formalize the breadth-depth dilemma through two finite sampling capacity models. First, we study the optimal allocation of limited sampling time to multiple options with the objective of choosing the most profitable one. The options here are modelled as accumulators of noisy evidence, its rates of accumulation are drawn from a given prior distribution, and the rate of the chosen option determines the reward. We show that the available time, the noise and the discriminability of the options define the intrinsic capacity of the decision maker, and their optimal policies undergo a sharp transition as a function of it. For small capacity, it is best to allocate time evenly to exactly five options and to ignore all the others, regardless of the prior distribution. For large capacities, the optimal number of sampled accumulators grows sublinearly, closely following a power law for Gaussian, uniform and bimodal priors. Furthermore, we show that allocating equal time to the sampled accumulators is better than using uneven time allocations.

Secondly, we apply a finite sampling capacity model on infinite decision trees. Many decisions in real life involve choosing the expected best path from a tree-like structure, but the exponential number of options in trees makes the full evaluation of all



the possibilities a hard problem for agents experiencing limited capacity. We formalize this problem as a one-shot allocation of the available resources over the nodes of a tree, whose rewards are hidden and can be discovered through sampling. The probability of collecting a positive reward from each node of the tree defines the 'richness' of the environment. Once again, decision-makers need to balance breadth and depth, as they could use their finite sampling capacity to collect information over many short paths of the tree, or they could focus only on a few but exploring them deeply. In the limit of large capacity, we find that the optimal solution is to always consider ~ 5 paths, a policy which corresponds to very deep allocations. We also find depth dominating over breadth for small capacity, as long as the environment is rich enough, while a transition in the optimal policy can be observed moving to poor environments, where wide allocations of many short paths are favoured. Interestingly, in those cases, little loss would occur by always allocating again ~ 5 paths. Therefore, deep allocations are found to be close-to-optimal policy in almost all the different conditions analyzed.

Our work highlights how breadth-depth tradeoffs emerge from the presence of limited resources in different models of decision-making. It demonstrates, for a wide range of capacities and environments, and both in tree-structure and multi-alternative decisions, that the optimal solution is to narrow down the large number of options to very few. This result showcases that a depth heuristic which ignores many options can be a sign of optimal behavior under limited sampling resources.

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Patterns of endogenous recruitment of top-down circuits linking cingulate cortex to primary visual cortex during visually guided behaviour

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The cingulate cortex (Cg) provides long-range retinotopically targeted top-down signals to the primary visual cortex (V1) in mice. The signals relayed through this projection have been proposed to function as an attentional spotlight and previous studies have provided evidence that optogenetic stimulation of this circuit can enhance visual discrimination. Other work has argued for a role of this projection in relaying predictive motor signals to sensory cortex. In this study we sought to characterise the endogenous recruitment of this circuit during visually guided discrimination behaviour. Two-photon microscopy was used to longitudinally image activity of GCaMP6s labelled axons originating from Cg in layer 1 of V1 while animals performed a Go/Nogo visual discrimination task.

We found that many axons exhibited reproducible elevated activity in different phases of the task including during visual stimulation and behavioural response.

Increased endogenous recruitment of this circuit was not however associated with improved discrimination performance. This was true at a range of degrees of task difficulty, controlled by altering stimulus contrast, or degrees of stimulus position predictability. Instead, we found that activity of Cg>V1 axons was associated with reward in a way that could not be explained by reward associated motor activity, and with a degree of specificity to the sensory cortex hemisphere currently processing the discriminated stimulus.



Perceptual saliency induces persistent information integration biases

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Making decisions generally involves integrating evidence over multiple sources of information. It is often assumed that humans are optimal decision makers that weight each source of information accordingly to its reliability. However, an increasing body of the literature shows that human decisions often deviate from such optimality assumption, and are biased towards previous decisions or perceived information (e.g. confirmatory biases, serial dependency effects, etc.). Here, we extend this question to evaluate whether information saliency alters the way that we process new incoming information. In our experiments, participants had to integrate and estimate the mean orientation of six gratings in two repeated occasions. Crucially, during the first presentation and in half of the trials, three of the six gratings were presented with a lower contrast than the others (mixed contrast). We expected participants to base their decision to a larger degree on salient stimuli (those with a higher contrast) in the first presentation but we wondered how participants would process the information in the second if all of the gratings had the same level of contrast. Our results showed that, as expected, participants were biased to weight more those gratings with higher contrast. Interestingly, we found that such bias persisted in the second repetition despite having complete access to all the information. This work suggests that increasing the saliency of information sources induces long-term biases in how subsequent information is integrated. This is an apparently suboptimal behavior, as in our experiment the six stimuli were always equally relevant and should be equally weighted when presented with the same contrast. Based on our results, we discuss on the possible adaptive role of biasing attention to a subpart of the stimuli set when the sources of information are noisy.



High frequency activity in the human hippocampus for encoding and retrieval of sequential episodic memories

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Hippocampal Gamma activity (30-120 Hz) in the local field potential have long been implicated in learning and memory. Human studies of episodic memory have generally focused on single item encoding or retrieval, showing sometimes mixed evidence about the role of hippocampal high frequencies in encoding, retrieval or immediate reinstatement. Here, we recorded direct intracranial EEG from the hippocampus as human participants performed a sequential memory task. For each sequence at encoding and offset (the short amount of time right after each sequence encoding) we derived time-frequency resolved representational patterns of high frequency in the hippocampus and compared the extent of pattern reinstatement for different mnemonic outcomes (accurate or non accurate series retrieval during a test 24 hours later) Results show that successful recall of a series event is predicted by event-specific reinstatement at the boundary right after series encoding. Moreover, we found that encoding sequences seem to be modulated by gamma power increases (40-100Hz) in the hippocampus. These results show that immediate reinstatement in the hippocampus is an early process of long term memory storage, and that the encoding of memories is modulated by stable gamma bursts at each item of the sequences.



A novel full-automated visuospatial working memory task in mice

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Working memory (WM), defined as the ability to maintain and process information in our brain for a short time, is a cornerstone of cognition. It is involved in many cognitive processes and is impaired in multiple mental disorders. Despite decades of study, the neural circuit mechanisms underlying this key brain function remain debated.

Aiming to better understand limits of WM, we have developed a visuospatial WM task in mice inspired by classical work carried out in primates. Subjects are trained to look and memorize the location of a visual stimulus displayed in a touchscreen. After a variable delay period, mice had to report the remembered position by touching the screen.

In this task, animals made two types of errors: non-memory dependent, present in visually-guided trials; and memory dependent, they increase gradually with delay length. Part of these memory dependent errors are caused by idiosyncratic biases that increase as a function of delay. We hypothesize that idiosyncratic biases are induced by discrete attractor dynamics pulling memories towards a few stable representations in mnemonic space.

We also analyzed the repeating bias, defined as the excess of probability of making a particular response $r_t = X$ after the previous choice $r_t - 1$ is also X:



$$Rep.Bias = \left\langle \frac{P_{rep}(X) - P(X)}{P(X)} \right\rangle \qquad P(X) = p(r_t = X)$$

$$P_{rep}(X) = p(r_t = X | r_{t-1} = X)$$

We fit a linear mixed model to the repeating bias data and we observed a significant increase with delay length (p = 0.004) suggesting that this type of choice bias could be a bias in WM caused by previous stored locations (Fig. 1d).

This novel task presents an opportunity to investigate visuospatial WM in mice, an animal model suited for circuit level electrophysiology, genetic and pharmacologic manipulations and models of mental disorders associated with a WM malfunction such as schizophrenia.

Figure 1: a) Fraction correct responses 0 0.5 Delay (sec) ۷Ġ -0.2 1.5 b LMM c) d) + (1 + delay|subject) 0.3 0.2 Repeating Bias P = 0.00370.1 -0.1



The causal role of the striatum in the encoding of flexible expectation-based choice biases

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Actions and their outcomes can generate expectations that modulate perceptual decisions, but the underlying neural circuits are poorly understood. To promote the use of expectations, we used a two-alternative auditory discrimination task with serial correlations in the stimulus sequence in the form of repeating and alternating trial blocks. Recent work showed that rats leverage on these correlations to estimate the probability that the previous rewarded side is repeated, and bias their choices accordingly.

Here we asked what brain region(s) implements such repeating bias, and particularly the transition bias component that rests on computing the local pattern of sequential rewards. We focused in the associative striatum (i.e. DMS), which funnels limbic cortical inputs to the midbrain, and it has been involved in value encoding of the different options. We first performed unit recordings in the DMS during the task and found different neural correlates of the animals behavior. Around 20% of the neurons encoded the trial-to-trial latent estimate of the repeating probability provided by a model fit of their previous choices. Moreover, the last choice was also sustainably represented in the activity of many neurons, but only when that choice was rewarded. To investigate the causal role of the DMS in these computations, we virally expressed the opsin stGtACR2 in medium spiny neurons to silence their somata in the millisecond scale. Bilateral photostimulation during the intertrial interval (ITI; $\sim 20\%$ trials), i.e. before stimulus onset, significantly reduced the repeating bias compared with light-off trials. Notably, ITI inhibition increased or decreased response accuracy depending on the congruence of the stimulus with the accumulated evidence. In contrast, ITI inhibition had no effect on accuracy after an error response when rats temporarily waived prior evidence, stressing the specificity of inhibition. Strikingly, unilateral ITI inhibition was equally effective at ablating





the repeating bias for ipsi- and contralateral responses, clearly departing from the ipsiversive effect of unilateral inhibition during action selection. A generalized linear model fitted to rats choices suggested that single-trial ITI inhibition reduces the weight of all previous transitions on choice. Likewise, transitions ending with an illuminated trial were not properly integrated into the accumulated transition evidence, reducing their impact on all future choices.

Together, our new findings show that pre-stimulus activity in the DMS plays a causal role in the accumulation and encoding of rule-based expectations on perceptual decisions.



Assessing the influence of local neural activity on global connectivity fluctuations: Application to human intracranial EEG during a cognitive task

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Cognitive-relevant information is processed by different brain areas that cooperate to eventually produce a response. The relationship between local activity and global brain states during such processes, however, remains for the most part unexplored. To address this question, we designed a simple face-recognition task performed in drug-resistant epileptic patients with intracranial EEG. Based on our observations, we developed a novel analytical framework (named local-global framework) to statistically correlate the brain activity in every recorded gray-matter region with lowfrequency regional-average connectivity measures as proxy to assess the level of influence of local neural activations into the brains global state during cognition. The application of our analysis to intracranial recordings from two subjects was able to detect the local activity in task-relevant brain areas including the primary visual and motor cortices. Despite substantial differences in the recorded regions of each subject, connectivity-based functions consistently showed a significant global desynchronization occurring a few hundred milliseconds after the stimulus onset. In this context, the local-global framework revealed that the reported desynchronization was better explained by the local activity of brain areas involved in face information processing, providing evidence that the global measures might be a novel signature of functional brain activity reorganization taking place when a stimulus is processed in a task context. Overall, the findings of this study urge to re-examine task-driven fluctuations of global brain connectivity in light of their intimate relationship with the more interpretable local neural activity.



Serial dependence across visual hemifields

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It has been shown that previously perceived working memory (WM) items have an effect on current WM reports. This effect is called serial dependence and has been shown to rely on the interaction of active neural representations and long-lasting activity-silent mechanisms in prefrontal cortex (PFC) [Barbosa, Stein et al, 2020]. Furthermore, it has been shown that WM representations are more frequent for contralateral than for ipsilateral memorized locations in PFC [Funahashi et al, 1989] and that active representations transfer between hemispheres when midline-crossing saccades occur in the delay [Brincat et al, 2021]. This indicates the consistent specialization of each hemisphere for the corresponding visual hemifield in WM. However, serial dependence challenges this view as it is unclear how it can emerge when consecutive stimuli appear in different hemifields, which engage independent neural substrates. Here, we investigate the transfer of serial dependence between visual hemifields, in order to shed light on the mechanisms of integration of lateralized WM storage. We collected behavioral data of 3 monkeys and analyzed two further data sets of human participants performing an oculomotor visuospatial delayed response task. We analyzed responses from all three studies in relation to serial dependence and evaluated the dependence on the presentation of stimuli in same and opposite hemifields. We found that serial dependence of stimuli presented across hemifields was diminished in comparison to trials within the same hemifield. We conclude that small biases towards previous memories in WM show a partial lateralization between hemifields. This hints towards an incomplete continuity of serial dependence in WM, which is in line with the activity-silent theory for serial dependence but needs further support through the analysis of neural data in the future.



Neural network dynamics underlying the adjustment of temporal evidence weighting in perceptual decisions

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During perceptual decision making, sensory information can be accumulated using distinct strategies; weighting some stimulus epochs more heavily than others. A recent study has shown that primates can flexibly adapt their temporal weighting strategy to the stimulus statistics (Levi et al., Eneuro 2018). Sensory stimuli with more information at the beginning of the trial produced early weighting, while stronger sensory evidence in later stimulus epochs caused a switch to a late weighting strategy.

To shed light on how this flexible adjustment can be mechanistically implemented at a neuronal level, we used a two-area firing rate model composed of a sensory and a decision circuit with bottom-up and top-down connectivity (Wimmer et al., Nat. Commun. 2015). We included a time-varying modulation signal, ("choice commitment" signal), that altered the attractor dynamics of the decision circuit. This modulation signal affected the decision circuit in two ways. Firstly, it initiated the decision process by pushing the network into a competition regime. Secondly, it changed the decision dynamics by accelerating or delaying the choice, similar to an urgency signal.

The model could reproduce the experimentally observed primacy weighting for early and flat stimulus statistics and late weighting for late stimulus conditions when the time-course of the modulation signal reflected the stimulus statistics. We reasoned that the modulation signal may be related to the subject's task engagement, which we measured as the time needed to execute a successful fixation at the start of the





trial. Consistent with the model, we found that the subject's engagement was higher (faster fixation) in the early weighting condition and lower (slower fixation) for the late condition.

Preliminary analysis of neural data recorded from areas MT and LIP indicated that the neurons' pre-stimulus activity was correlated with task engagement, providing further evidence for the modulation signal.



Episodic sequences are rapidly reinstated post-encoding to promote their integration in long-term memory

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In episodic encoding, the unfolding experience can be selectively transformed into different event memory traces that have the potential to be recollected. Work in rodents have provided evidence that offline reinstatement plays an important role in stabilizing memory beyond initial learning processes. Our recent work also revealed the evidence for rapid neural reinstatement after the completion of an individual episodic to promote memory representation formation after one-shot exposure. Here, to further explore the hypothesis supporting reinstatement as a crucial process for binding separate episodic elements into an integrated memory trace, we asked participants to encode series of episodic-like triplets formed by three categories of unique images, namely a famous face, a well-known place and a common object. We used representational similarity analysis of scalp electroencephalography recordings during encoding and found evidence for memory reactivation of the just encoded episodic elements of triplets after encoding, i.e., at the offset following the image presentation. And importantly, the magnitude of the reactivation predicted the memory strength of encoded triplets during later free recall phase. These results indicate that episodic offset memory reinstatement is a mechanism engaged to support integration of episodic elements in long term memory.



One-shot learning in recurrent networks using behavioral time-scale plasticity

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The formation of episodic memory requires fast and potent plasticity mechanisms which allow for one-shot association of events on a time-scale of seconds or longer. Traditional Hebbian plasticity rules rely on the concurrence of pre- and post-synaptic spiking and typically lead to plasticity windows of only tens to hundreds of milliseconds. Furthermore, such rules tend to lead to instabilities unless the learning occurs slowly, making them inappropriate for one-shot learning.

However, recent in-vivo experiments in area CA1 of mouse hippocampus have revealed a new form of plasticity, dubbed Behavioral Time-scale Plasticity (BTSP), which leads to the rapid formation of place fields in previously silent cells, or the shifting of place field location in place cells. BTSP relies on the coincidence of presynaptic firing and a global, dendritic-wide post-synaptic signal consisting of a broad Ca2+ spike, which results in a plasticity window of several seconds or more. These plasticity effects are quantitatively fit by a computational model in which the amplitude and direction of plasticity of a given synapse depends on presynaptic firing, the current state of the synapse and a global signal. However, this model is dynamically complex and is not amenable to analysis, making it difficult to investigate the role of such a plasticity rule in memory formation in large recurrent networks. Here we propose a simple one-dimensional map for synaptic plasticity which qualitatively captures all relevant features of BTSP. Specifically, we can reproduce rapid place-field formation and shifting as well as the dependence of place-field width on the velocity of motion of the animal. Our map can furthermore be straightforwardly extended to recurrent networks, allowing for the analytic derivation of memory capacity for one-shot learning. We find that the weight-dependence of the rule leads to the classical stability-plasticity trade-off in learning by which older memories decay through overwriting.





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