CRCNS 2021

October 7-9, 2021 @ NYC
New York University

COLLABORATIVE RESEARCH IN COMPUTATIONAL NEUROSCIENCE (CRCNS) 2021 Annual PI Meeting

RENAISSANCE New York Chelsea Hotel
112 West 25th Street, New York, NY 10001

and

WORKSHOP ON MACHINE LEARNING FOR LARGE-SCALE NEUROSCIENCE

Flatiron Institute, Simons Foundation
162 5th Avenue, New York, NY 10010

NYU

NYU NEUROSCIENCE

WELCOME!

We are pleased to welcome you to New York City, for the Collaborative Research in Computational Neuroscience (CRCNS) 2021 Principal Investigator's meeting, hosted by New York University. The CRCNS program is managed by a consortium of research funders in the US (NSF and NIH), France (ANR), Germany (BMBF), Israel (BSF), Spain (ISCIII) and Japan (NICT). The annual meeting brings together principal investigators from grants funded under the program to discuss research progress and future directions of the field. The first two days will be devoted to talks and posters from the CRSNS funded researchers, while the third day will be reserved for a workshop on Machine Learning for Neuroscience, hosted by the Flatiron Institute (Simons Foundation).

Z. Sage Chen, Bijan Pesaran
Organizers

PROGRAM COMMITTEE

Zhe Sage Chen, PhD
Associate Professor
Neuroscience Institute
Dept. Psychiatry
NYU School of Medicine
CRCNS 2021 Co-Chair

Bijan Pesaran, PhD
Professor
Center for Neural Science
New York University
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Jayeeta Basu, PhD
Assistant Professor
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Mitya Chklovskii, PhD
Associate Professor
Computational Neuroscience
Flatiron Institute/NYU

Horacio Rotstein, PhD
Professor
Biological Science
NJIT / NYU

CRCNS 2021 PROGRAM

The program will feature with 2 keynote lectures and 21 oral presentations, plus two panel discussions. (RED: in-person presentation; BLUE: virtual presentation).

THURSDAY, Oct. 7, 2021		
8:00-8:30 *REGISTRATION and BREAKFAST*		
8:30-8:40	Opening Remarks	**Sage Chen & Bijan Pesaran** *NYU*
8:40-	**SESSION 1**	**Chair: Bijan Pesaran**, *NYU*
8:40-9:40	**Keynote lecture**: Rethinking Anesthesia: Systems and Computational Neuroscience	**Emery Brown**, *MIT*
9:40-10:05	*BREAK*	
10:05-	**SESSION 2**	**Chair: Bijan Pesaran**, *NYU*
10:05-10:30	#1. Dynamic visual processing coverage predicts observed differences in natural oculomotor behavior across mammals	**Nicholas Priebe**, *Univ. Texas, Austin*
10:30-10:55	#2 Targeted cortical stimulation reveals some principles of cortical contextual interactions	**Steve Van Hooser**, *Brandeis Univ*
10:55-11:20	#3 Neural encoding of reaches in a linear cortical model	**Sridevi Sarma**, *JHU*
11:20-11:45	#4 Multi-sensory integration in the mouse cortical connectome using a network diffusion model	**Constantine Dovrolis,** *GeogiaTech*
11:45-13:00	*LUNCH*	
13:00-	**SESSION 3**	**Chair: Shy Shoham**, *NYU*
13:00-13:25	#5 Leveraging maximally informative phase-locking of non-REM sleep rhythms to enhance consolidation	**Maxim Bazhenov**, *UCSD*
13:25-13:50	#6 Development of modular patterned activity in visual cortex through intracortical network interactions	**Gordon B. Smith**, *Univ. of Minnesota*
13:50-14:15	#7 Impact of cortical neuromodulation on the efficacy of auditory closed-loop stimulation	**Lisa Marshall**, *Univ of Luebeck*
14:15-15:00	Panel: Promotion of Academic Diversity	**Jayeeta Basu** (moderator) **Catherin Hartley**, *NYU* **Andre Fenton**, *NYU* **Cristina Savin**, *NYU* **Aniruddha Das,** *Columbia* **Xiaosi Gu,** *MSSM*
15:00-15:30	*BREAK*	
15:30-	**SESSION 4**	**Chair: Cristina Savin**, *NYU*
15:30-15:55	#8 Studying complex planning in non-human primates	**Wei Ji Ma**, *NYU*
15:55-16:20	#9 Building a closed-loop BMI for the study and treatment of pain	**Jing Wang**, *NYU*
16:20-16:55	#10 Suboptimal human inference inverts the bias-variance trade-off for decisions with asymmetric evidence	**Tahra Eissa,** *Univ. Colorado Boulder*

16:55-17:20	#11 Olfactory input to cortex encoded on low-dimensional periphery-correlated manifolds	**Woodrow Shew,** Univ. Arkansas, Fayetteville
17:30-20:00	*RECEPTION and POSTER SESSION*	
	FRIDAY, Oct. 8, 2021	
8:30-8:40	Opening Remarks	**Sage Chen & Bijan Pesaran** *NYU*
8:40-	**SESSION 5**	**Chair: Sage Chen**, *NYU*
8:40-9:40	**Keynote lecture:** Multiple maps for navigation	**Lisa Giocomo**, *Stanford*
9:40-10:05	*BREAK*	
10:05-	**SESSION 6**	**Chair: Jayeeta Basu**, *NYU*
10:05-10:30	#12 Time as a continuous dimension in natural and artificial networks	**Marc Howard**, *Boston Univ*
10:30-10:55	#13 Mapping cortico-basal ganglia-thalamic circuitry to decision policies	**Timothy Verstynen**, *CMU*
10:55-11:20	#14 Neural Sequences as an Optimal Dynamical Regime for the Readout of Time	**Sotiris Masmanidis**, *UCLA*
11:20-11:45	#15 Inverse rational control	**Xaq Pitkow,** *Rice Univ.*
11:45-13:00	*LUNCH*	
13:00-	**SESSION 7**	**Chair: Mitya Chklovskii,** *Flatiron Institute*
13:00-13:25	#16 REvealing SPONtaneous Speech Processes in Electrocorticography (RESPONSE)	**Dean Krusienski,** *Virginia Commonwealth Univ*
13:25-13:50	#17 Understanding Cortical Networks Related to Speech Using Deep Learning on ECOG Data	**Yao Wang**, *NYU*
13:50-14:15	#18 Avian Model for the Development of Neural Activity Driven Speech and Vocalization Prostheses	**Vikash Gilja,** *UCSD*
14:15-14:45	Funding Q&A	NSF/NIH/DOE/BSF program officers
14:45-15:15	*BREAK*	
15:15-	**SESSION 8**	**Chair: Horacio Rotstein,** *NJIT*
15:15-15:40	#19 Using brain-optimized deep neural networks to investigate hierarchical computation in human visual areas V1-V4	**Thomas Naselaris,** *Univ. Minnesota*
15:40-16:05	#20 Feedforward and feedback processes in visual recognition	**Thomas Serre**, *Brown Univ.*
16:05-16:30	#21 Measuring animal behavior in social contexts using deep learning approaches	**Sena Agezo**, *Emory University*

WORKSHOP: Machine Learning for Large-Scale Neuroscience: Looking into the Future

Date: SATURDAY, Oct. 9, 2021
Location: Flatiron Institute, Simons Foundation (162 Fifth Avenue, New York, NY)

All presentations will be in-person. Virtual participation will be not possible.

Tentative schedule (subject to change)

SATURDAY, Oct. 9, 2021		
9:00-9:30 Coffee & Breakfast		
9:30-9:50	Opening	**Eero Simoncelli,** *Simons/NYU*
9:50-10:30	TBA	**Scott Linderman**, *Stanford*
10:30-11:10	TBA	**Eva Dyer**, *Georgia Tech*
11:10-11:50	TBA	**Thomas Serre**, *Brown Univ.*
11:50-13:30	*LUNCH*	
13:30-14:10	Flexible identification of cognitive computations from spikes	**Tatiana Engel**, *Cold Spring Harbor Laboratory*
14:10-14:50	TBA	**Xue-Xin Wei**, *Univ. Texas, Austin*
14:50-15:20	*BREAK*	
15:20-16:00	TBA	**Memming Park**, *Stony Brook Univ*
16:00-16:40	TBA	**Cristina Savin**, *NYU*
15:40-16:05	PANEL DISCUSSION	

ABSTRACTS

#1 Breaking the neural code of a cnidarian

Rafael Yuste * and Adrienne Fairhall
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Columbia University

The small freshwater cnidarian Hydra vulgaris has one of the simplest nervous systems in the animal kingdom [1], yet exhibits surprisingly complex behaviors, like somersaulting [2]. Due to its transparency, its complete neural [3] and muscle activity [4] can be effectively imaged. Our goal to take advantage of this experimental angle to "break the neural code" of Hydra: to understand the complete set of transformations from neural activity to muscle activation to behavior.

1. Bosch, T.C., et al., Back to the Basics: Cnidarians Start to Fire. Trends Neurosci, 2017. 40(2): 92-105.
2. Han, S., et al., Comprehensive machine learning analysis of Hydra behavior reveals a stable basal behavioral repertoire. Elife, 2018. 7.
3. Dupre, C. and R. Yuste, Non-overlapping Neural Networks in Hydra vulgaris. Curr Biol, 2017. 4. Szymanski, J.R. and R. Yuste, Mapping the Whole-Body Muscle Activity of Hydra vulgaris. Curr Biol, 2019. 29(11): 1807-1817

2 Computational bases of rheotaxis

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For animals that can be displaced by currents, visual signals are the most salient sensory cues to evaluate self-motion relative to an external reference frame. Yet, in the absence of visual information fishes can orient to the direction of water currents, an innate behavior called rheotaxis. Here we use behavioral data from larval zebrafish to construct a parsimonious computational model that explains how individuals use local cues to determine water-flow direction. Our findings indicate that rheotaxis occurs via peripheral vectorial fractionation of mechanical signals, sensory updating by recurrent yaw rotations, and central integration of bilateral sensory information.

3 Olfactory input to cortex encoded on low-dimensional periphery-correlated manifolds

Andrea K Barreiro, Cheng Ly, Shree Hari Gautam, Woodrow L Shew*
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Olfactory sensory information is processed by complex, dynamic interactions among neurons in the olfactory bulb (OB) and piriform cortex (PC). However, OB and PC do not interact exclusively with each other, resulting in a noisy channel for olfactory signals. How do OB and PC reliably encode olfactory signals in the presence of noise and other signals that do not directly relate to olfactory sensory input? Here we show that projection of high-dimensional population activity onto low-dimensional manifolds in OB and PC can dramatically improve coding of olfactory signals. We revealed these improved coding manifolds using canonical correlation analysis to select specific dimensions of PC that are most correlated with specific dimensions of OB. We demonstrate this phenomenon in the context of odor discrimination and coding of orthonasal versus retronasal stimuli in anesthetized rats and awake mice. Our results suggest that the olfactory system may separate signals from noise by isolating them in distinct low dimensional manifolds.

 # 4 Odor-evoked Increases in Olfactory Bulb Mitral Cell Spiking Variability

Cheng Ly*, Andrea Barreiro, Shree Hari Gautam, Woodrow Shew
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Virginia Commonwealth University

At the onset of sensory stimulation, the variability and co-variability of spiking activity is widely reported to decrease, especially in cortex. Considering the potential benefits of such decreased variability for coding, it has been suggested that this could be a general principle governing all sensory systems. Here we show that this is not so. We recorded mitral cells in olfactory bulb (OB) of anesthetized rats and found increased variability and co-variability of spiking at the onset of olfactory stimulation. Using models and analysis, we predicted that these increases arise due to network interactions within OB, without increasing variability of input from the nose. We tested and confirmed this prediction in awake animals with direct optogenetic stimulation of OB to circumvent the pathway through the nose. Our results establish increases in spiking variability at stimulus onset as a viable alternative coding strategy to the more commonly observed decreases in variability in many cortical systems.

 # 5 Time as a continuous dimension in natural and artificial networks

Marc Howard
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Boston University

Neural representations of time are central to our understanding of the world around us. I review cognitive, neurophysiological and theoretical work that converges on three simple ideas. First, the time of past events is remembered via a population of neurons with a continuum of functional time constants. Second, these time constants evenly tile the time axis with a logarithmic mapping. This results in a neural Weber-Fechner scale for time. Third, these populations appear as dual pairs---one type of population contains cells that change firing rate monotonically over time and a second type of population that has circumscribed temporal receptive fields. Each of these populations represent what happened when in the past, but with different temporal basis functions and can be identified with the real Laplace transform of the past and an approximate inverse of that transform respectively. I review recent work showing that these ideas can be used to build artificial neural networks that have novel properties. Of particular interest, a convolutional neural network built using these principles can generalize to arbitrary rescaling of its inputs. That is, after learning to perform a classification task on a time series presented at one speed, it successfully classifies stimuli presented slowed down or sped up; the range of scales the network can generalize over goes up exponentially with memory and is independent of the number of weights. In addition to providing a foundation for many empirical results, these ideas can be used to develop useful technologies in the near term.

 # 6 Characterizing neuronal synaptic transmission using stochastic hybrid systems

Zahra Vahdat, Abhyudai Singh*, Eck Friauf
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Action potential-triggered release of neurotransmitters at chemical synapses forms the key basis of communication between two neurons. To quantify the stochastic dynamics of the number of neurotransmitters released, we investigate a model where neurotransmitter-filled vesicles attach to a finite number of docking sites in the axon terminal, and are subsequently released when the action potential arrives. We formulate the model as a Stochastic Hybrid System (SHS) that combines three key noise mechanisms: random arrival of action potentials, stochastic refilling of docking sites, and probabilistic release of docked vesicles. This SHS representation is used to derive exact analytical formulas for the mean and noise (as quantified by Fano factor) in the number of vesicles released per action potential. Interestingly, results show that in relevant parameter regimes, noise in the number of vesicles released is sub-Poissonian at low frequencies, super-Poissonian at intermediate frequencies, and approaches a Poisson limit at high frequencies. In contrast, noise in the number of neurotransmitters in the synaptic cleft is always super-Poissonian, but is lowest at intermediate frequencies. We further investigate changes in these noise properties for non-Poissonian arrival of action potentials, and when the probability of release is frequency dependent. In summary, these results provide the first glimpse into synaptic parameters not only determining the mean synaptic strength, but also shaping its stochastic dynamics that is critical for information transfer between neurons.

 # 7 Feedforward and feedback processes in visual recognition

Thomas Serre

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Progress in deep learning has spawned great successes in many engineering applications. As a prime example, convolutional neural networks, a type of feedforward neural networks, are now approaching – and sometimes even surpassing – human accuracy on a variety of visual recognition tasks. In this talk, however, I will show that these neural networks and their recent extensions exhibit a limited ability to solve seemingly simple visual reasoning problems involving incremental grouping, similarity, and spatial relation judgments. Our group has developed a recurrent network model of classical and extra-classical receptive field circuits that is constrained by the anatomy and physiology of the visual cortex. The model was shown to account for diverse visual illusions providing computational evidence for a novel canonical circuit that is shared across visual modalities. I will show that this computational neuroscience model can be turned into a modern end-to-end trainable deep recurrent network architecture that addresses some of the shortcomings exhibited by state-of-the-art feedforward networks for solving complex visual reasoning tasks. This suggests that neuroscience may contribute powerful new ideas and approaches to computer science and artificial intelligence.

 # 8 Mapping cortico-basal ganglia-thalamic circuitry to decision policies

C. Vich, M. Clapp, E. Yttri, Jonathan Rubin*, T.Verstynen

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Mammals exhibit a high level of flexibility when selecting their actions. This decision process is adapted to allow for situations where a desirable result is known (exploitation) and for situations of risk, where outcomes are less certain (exploration). The circuit-level architecture underlying the cortico-basal ganglia-thalamic (CBGT) pathways is ideally suited for flexibly adapting decision policies via dopaminergic plasticity mechanisms. This plasticity modulates the rate of evidence accumulation when evaluating sensory evidence for actions and adjusts the threshold for evidence needed to gate a decision. To understand the mapping between specific CBGT configurations (weight schemes) and parameters of information accumulation during decisions, we applied a strategic sampling approach to explore how CBGT network properties map to parameters of a normative drift diffusion model (DDM), using Canonical Correlation Analysis (CCA). Different configurations of the decision parameters (weights) within the network produce many variants, or phenotypes, of decision policies, based on performance of the network in a 2-armed bandit task. The CCA analysis revealed that the relationship between CBGT synaptic connections and parameters of the DDM fall into 3 low-dimensional clusters. First, overall cortico-thalamic and, to some degree, direct pathway striatal firing rates are associated with the time of onset of evidence accumulation. Second, overall activity in the indirect pathway, including striatal and GPe neurons, are associated with boundary height (i.e., the level of information necessary to gate a decision). Finally, channel differences in both direct and indirect pathway firing rates are associated with variation in drift rate (i.e., the rate of evidence accumulation). Put together, these analyses highlight how different parameters of the decision process may be regulated by different sub-pathways of the CBGT circuits. Thus, we obtain mechanistic predictions about the roles of components of the CBGT network in selecting decision policies and modulating between exploitative and exploratory behaviors.

 # 9 Ventral Tegmental Area Stimulation Induces Hippocampal Remapping

Dorgham Khatib , Gilad Tocker , Jonathan Gross , Genela Morris , Dori Derdikman*
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The hippocampus and associated structures are related to perception of space, learning and memory. Another structure which has been heavily implicated with learning and memory is the Ventral Tegmental Area (VTA) in the midbrain. According to a dominant theory, dopaminergic projections from the VTA to the hippocampal formation are related to the signaling of novelty. However, direct projections from the VTA to the hippocampus are mostly not dopaminergic. Our results demonstrate that stimulation of the glutamatergic neurons but not the dopaminergic ones induce hippocampal remapping. These newly formed maps seem to persist and are stable on the next day, after the stimulation in TH-Cre and DAT-Cre mice, but not in Vglut2-Cre mice. These findings might shed some light on the differential role of the sub-populations of the VTA on formation and stablization of memories.

 # 10 Multi-scale Modeling of Morphologically Realistic Neurons Under Transcranial Magnetic Stimulation

S. Shirinpour, N. Hananeia, J. Rosado, H. Tran, C. Galanis, A. Vlachos, P. Jedlicka, G. Queisser, Alexander Opitz *
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Transcranial Magnetic Stimulation (TMS) of the dorsolateral prefrontal cortex is currently utilized as a non-invasive neuromodulation tool for the treatment of depression. Nevertheless, the basic mechanisms underlying TMS effects at the neuronal level are largely unknown. Since the recording of single-unit activity in vivo during TMS is challenging in animals, and typically not possible for humans, modeling is an important tool to investigate the neuronal response to TMS. Here, we develop a new multi-scale pipeline (NeMo-TMS) for modeling TMS effects across spatial scales.

On the macro-scale, we generate a realistic head model from MRI that includes multiple tissue types (white matter, grey matter, cerebrospinal fluid, skull, and scalp) and use the SimNIBS software to simulate the electric field induced in the brain for a given TMS coil position and orientation using Finite Element Method (FEM). Afterward, simulated electric fields from the previous step are coupled with morphologically realistic neuronal models. These models are solved by discretizing the neuronal branches into small compartments and by numerically solving the cable equation and channel dynamics in the NEURON environment. These neuron-scale simulations allow investigating membrane voltage (depolarization/hyperpolarization), action potential initiation and propagation, field intensity, and orientation necessary for modulating neuron response, etc. Then, we incorporate the membrane voltage data to simulate the calcium concentration induced by voltage-gated calcium-channels at the subcellular scale by solving the calcium dynamics equations. This step is important for understanding neural plasticity due to rTMS protocols. In this study, we also provide results to demonstrate how different neuron types behave distinctly for the same external electric field and therefore make a case for the importance of such multi-scale realistic modeling of neurons. Our pipeline can facilitate research as a tool for hypothesis testing and prediction technique for experiments. Additionally, modeling has the potential to be used for calculating the dose needed for efficient treatment in clinical applications.

 # 11 Neural Sequences as an Optimal Dynamical Regime for the Readout of Time

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Converging evidence suggests that the brain encodes time through dynamically changing patterns of neural activity, including neural sequences, ramping activity, and complex spatiotemporal dynamics. However, the potential computational significance and advantage of these different regimes have remained unaddressed. We combined large-scale recordings and modeling to compare population dynamics between premotor cortex and striatum in mice performing a two-interval timing task. Conventional decoders revealed that the dynamics within each area encoded time equally well; however, the dynamics in striatum exhibited a higher degree of sequentiality. Analysis of premotor and striatal dynamics, together with a large set of simulated prototypical dynamical regimes, revealed that regimes with higher sequentiality allowed a biologically constrained artificial downstream network to better read out time. These results suggest that, although different strategies exist for encoding time in the brain, neural sequences represent an ideal and flexible dynamical regime for enabling downstream areas to read out this information.

 # 12 Calcium modeling of spine apparatus containing human dendritic spines demonstrates all-or-nothing communication switch between the spine head and dendrite

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Dendritic spines are highly dynamic neuronal compartments that control the synaptic transmission between neurons. Spines form ultrastructural units, coupling synaptic contact sites with the dendritic shaft and often harbor a spine apparatus organelle, composed of smooth endoplasmic reticulum and responsible for calcium sequestration and release into the spine head and neck. The spine apparatus has been recently linked to synaptic plasticity in adult human cortical neurons. While the morphological heterogeneity of spines and their intracellular organization has been extensively demonstrated in animal models, the influence of spine apparatus organelles on critical signaling pathways, such as calcium-mediated dynamics, is less known for human dendritic spines. In this study detailed anatomical reconstructions of 9 human cortical spines, using serial transmission electron microscopy, were carried out to quantify and analyze the architectural plan of spines and to incorporate these reconstructions in detailed modeling and simulation of calcium dynamics between spine and dendrite. The anatomical study of reconstructed human dendritic spines revealed that the size of the postsynaptic density correlates with spine head volume and that the spine apparatus volume increases alongside the spine volume. Using a newly developed simulation pipeline these findings were linked to spine-to-dendrite calcium communication. While the absence of a spine apparatus or presence of a purely passive spine apparatus did not enable any of the reconstructed spines to relay a calcium signal to the dendritic shaft, the calcium induced calcium release from this intracellular organelle allows for finely tuned all-or-nothing spine-to-dendrite calcium coupling; controlled by spine morphology, neck plasticity, and ryanodine-receptors. These results demonstrate the strategic position of spine apparatus organelles in the neck of human dendritic spines and their potential relevance in maintaining and regulating spine-to-dendrite calcium communication.

 # 13 Understanding Cortical Networks Related to Speech Using Deep Learning on ECOG Data

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Despite significant advances in neural science, the dynamics by which neural activity propagates across cortex while we think of a word and produce it remains poorly understood. This proposal will develop novel, data-driven approaches for understanding functions and interactions of various brain regions by leveraging rare neural recordings obtained with electrocorticography (ECoG) sensors while neurosurgical patients participate in tasks involving language perception, semantic access and word production. The project consists of multiple core thrusts, including developing neural decoders for language processing as well as developing directed connectivity models.

Towards the first thrust, we have developed a novel neural speech decoding architecture to map the neural signals to either stimulus (perceived) speech or produced speech during various tasks. It consists of an ECoG encoder that maps the neural signals to a compact set of interpretable speech parameters, and a speech synthesizer that converts the speech parameters to a speech spectrogram. Critically, the architecture can be configured to use different causality structures: use only the past (up to the current) neural signals (causal model), use only current and future neural (the anti-causal model), or both the past and future signals (the non-causal model). All three models can produce natural speech with quantitative metrics exceeding the state-of-the-art, however the use of past or present causal structures allows us to interpret cortical structures that are predicting future motor commands or processing reafferent feedback from the patient’s own speech. While a majority of previous report models are non-causal (dipping into the future), our causal model has only a slightly degraded performance in terms of quantitative metrics, promising potential real-time speech prosthesis applications. An analysis of the causal and anti-causal models provided evidence of a mixed cortical organization where pre-frontal regions, classically involved in motor planning and execution were engaged in both predicting future motor actions (causal model) as well as processing the perceived feedback from speech (anti-causal model). Similarly, portions of the superior temporal gyrus which is classically involved in speech perception showed evidence of anterior regions which were predicting future speech (causal) and more posterior regions that were processing reafferent speech feedback (anti-causal). Our findings are the first to systematically disentangle the dynamics of feed forward and feedback processing during speech and provide evidence for a surprisingly mixed cortical architecture within temporal and frontal cortices. Our approach provides a promising new avenue for using deep neural networks in neuroscience studies of complex dynamic behaviors.

In a second thrust focusing on connectivity and cortical interactions we have developed a toolbox of algorithms enabling us to investigate the dynamic directed connectivity between different brain regions. A set of multivariate autoregressive (MVAR) models were implemented to represent how a signal from one electrode influences and predicts others in a data-driven manner. The developed toolbox allows for investigation of different signal processing techniques and their directed connectivity measures (Granger causality, Partial Directed Coherence, etc.). Furthermore, we provide approaches to quantify and report the effect of hyper parameters which typically vary greatly or are difficult to ascertain in the literature. For example, we employ an automatic electrode selection algorithm, which eliminates the need to manually select electrodes (which is a common hindrance in the literature due to MVAR) and allows for investigating the connectivity in a more efficient. Based on the fitted MVAR model coefficients we calculate and analyze connectivity measures of partial coherence and apply orthogonal non-negative matrix factorization to cluster the connectivity dynamics between different electrodes. Our results provide evidence for several prototypical connectivity clusters, some of which follow previously reported dynamics. A major cluster, replicated across tasks and patients, shows directed connectivity from motor cortex onto temporal cortex prior to and at the onset of speech. This result provides the first clear marker, in humans, for a widely theorized corollary discharge which presumably communicated the upcoming speech plan to temporal cortex. We also observe a causal connectivity patterns in inferior frontal cortex during speech which replicate findings from the first thrust.

14 CONSTRAINED HARMONIZATION ALGORITHM FOR POOLING MULTI-SITE DATASETS

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Background: Pooling datasets from multiple studies can significantly improve statistical power: larger sample sizes can enable the identification of otherwise weak disease-specific patterns. When modern learning methods are utilized (e.g., for predicting progression to dementia), differences in data acquisition-methods / scanner-protocols can enable the model to “cheat”, i.e. utilizes site-specific artifacts rather than disease-specific features. In this study, we develop a method to harmonize the performance of DNN classifiers across scanners/sites, via so-called fairness constraints, thereby encouraging consistent behavior while controlling for site-specific nuisance variables.

Methods: We conducted two studies: (a) to demonstrate feasibility of pooling across sites (Site-Pooling) and (b) to pool data across scanners (Scanner-Pooling). For Site-Pooling, our analysis included summaries from Freesurfer processed T1-weighted images of the Wisconsin Alzheimer's Disease Research Center (ADRC) and German Center for Neurodegenerative Diseases (DZNE). The Freesurfer summaries were used to train a two layer neural network classifier and five-fold cross-validation performance was assessed. For Scanner-Pooling experiments, Freesurfer processed MR images from the Alzheimer's Disease Neuroimaging Initiative (ADNI) were used to train a deep 3D convolutional network. Performance average on a held-out test dataset was evaluated. In both cases, a constraint to equalize the performance of the trained classifier across the domains (sites/scanners) was incorporated during training.

Results: Table 1 shows the results of AD/MCI classification for site-pooling analysis. Our proposed method is compared against a naive pooling approach which does not incorporate the “harmonization constraint”. As shown, the proposed method improves the “difference of errors” measure by 8% / 7% and with only a small drop in overall error rates. Figure 1 illustrates the results from our scanner-pooling analysis. The performance across the three scanners, GE, Siemens and Philips, is evaluated pair-wise. A consistent improvement in harmonization is observed and only ~2% drop in overall error rate is seen.

Conclusions: We provide a harmonization constraint based algorithm to mitigate site specific differences when performing analysis of pooled brain imaging datasets in AD studies. In contrast to a method which modifies the data, we achieve harmonization by constraining the classifier to perform similarly across sites/groups/scanners, improving reproducibility.

#15 Two breathing rhythms from one oscillator network

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Rhythms are ubiquitous in the brain; unraveling their cellular mechanisms provides general insights into brain function. The preBötzinger Complex (preBötC) of the lower brainstem generates two breathing-related rhythms simultaneously: one that drives inspiratory breaths on a timescale of seconds and another that produces much larger amplitude sigh breaths on the order of minutes. We know from studies of breathing in rodents, and rodent breathing models in vitro, that these two essential rhythms arise from cell populations derived from Dbx1-expressing progenitor cells (neurons or glia) in the preBötC; however, the underlying mechanisms are incompletely understood. Using the aforementioned breathing model in vitro, we find the inspiratory rhythm depends on baseline excitability in the preBötC (i.e., it is voltage dependent), consistent with the orthodoxy that the inspiratory rhythm depends on recurrent excitatory network activity among Dbx1-derived preBötC neurons. In contrast, the frequency of the sigh rhythm is more robust to changing network excitability (i.e., it is much less voltage dependent). Rhythmic sighs persist even when inspiratory activity has ceased. The lack of voltage dependence, and apparent independence of the sigh rhythm, could indicate a non-neural origin, for example rhythmic glia. We tested that idea by perturbing gliotransmission, specifically via a broad spectrum blockade of purinergic signaling, and we measured inspiratory and sigh rhythms via multiphoton imaging of Dbx1-derived preBötC neurons and motor output in vitro, but we found no effect on the frequency or amplitude of sigh rhythm. Thus, we propose a framework for inspiratory and sigh rhythmogenesis whereby a recurrent excitatory network generates inspiratory rhythm while an intracellular biochemical calcium oscillator drives sigh-related network bursts and sets their frequency. We formalize these mechanisms in a mathematical model of Dbx1-derived preBötC neurons that recaps both the inspiratory and sigh rhythms. We test nontrivial predictions of the model in vitro: blocking either calcium release mediated by inositol 1,4,5-trisphosphate receptors, or endoplasmic reticulum calcium uptake by SERCA-type ATPase pumps, we diminish, and in some cases abolish, the sigh rhythm. This work reveals that inspiratory and sigh rhythms emanate from a single genetically well defined population of brainstem neurons, and elucidates how these distinct neural rhythms interact with one another on cellular and network levels. Ultimately, this work explains how one brain region can generate two unique and physiologically significant rhythms.

#16 A Biologically Interpretable Graph Convolutional Network to Link Genetic Risk Propagations and Imaging Biomarkers of Disease

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We propose a novel deep neural network for whole-genome imaging-genetics. Our genetics module uses hierarchical graph convolution and pooling operations that mimic the organization of a well-established gene ontology to embed subject-level data into a latent space. The ontology implicitly tracks the convergence of genetic risk across biological pathways, and an attention mechanism automatically identifies the salient edges in our network. We couple the imaging and genetics data using an autoencoder and predictor, which couples the latent embeddings learned for each modality. The predictor uses these embeddings for disease diagnosis, while the decoder regularizes the model. For interpretability, we implement a Bayesian feature selection strategy to extract the discriminative biomarkers of each modality. We evaluate our framework on a population

study of schizophrenia that includes two functional MRI (fMRI) paradigms and gene scores derived from Single Nucleotide Polymorphism (SNP) data. Using 10-fold cross-validation, we show that our model achieves better classification performance than the baselines. In an exploratory analysis, we further show that the biomarkers identified by our model are reproducible and closely associated with deficits in schizophrenia.

#17 **Suboptimal human inference inverts the bias-variance trade-off for decisions with asymmetric evidence**

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Solutions to challenging inference problems are often subject to a fundamental trade-off between bias (being systematically wrong) that is minimized with complex inference strategies and variance (being oversensitive to uncertain observations) that is minimized with simple inference strategies. However, managing this trade-off requires using the optimal strategy for a given complexity, giving it unclear relevance to the many conditions in which inference strategies are suboptimal. We examined inference problems involving rare, asymmetrically available evidence, which human subjects solved using a variety of strategies that were suboptimal relative to the Bayesian ideal observer. These suboptimal strategies reflected an inversion of the classic bias-variance trade-off: subjects who used more complex, but imperfect, Bayesian-like strategies tended to have lower variance but excessive biases because of incorrect tuning to latent task features, whereas subjects who used simpler heuristic strategies tended to have higher variance because they operated more directly on the observed samples but lower, near-normative biases. The results yield new insights into the principles that govern individual differences in behavior that depends on rare-event inference and more generally about the information-processing trade-offs that are sensitive to not just the complexity but also the optimality of the inference process.

#18 **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 demyelination-related 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.

#19 Building a closed-loop brain machine interface for the study and treatment of pain

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Pain has both sensory and affective components, making accurate detection and prompt therapeutic intervention difficult. To address this challenge, we have designed a closed-loop neural interface combining pain detection with treatment in real time. Pain is detected by an unsupervised learning model using either neural spikes or local field potential (LFP) recordings from the anterior cingulate cortex, a prominent region that encodes pain affect. Meanwhile, optogenetic or electrical stimulation of the prefrontal cortex is used to deliver nociceptive control. Our neural interface that combines cortical sensing with neuromodulation accurately detects and relieves both evoked and tonic pain in freely-behaving rats. When we combine neural signals from the anterior cingulate cortex with signals from the primary somatosensory cortex, a region that encodes the sensory pain information, we achieved even higher decoding accuracy and greater therapeutic specificity Furthermore, LFP-based pain decoding remains consistent over months. Thus, a closed-loop brain-machine interface, especially a multi-region neural interface, will greatly facilitate pain research in animal models and has the potential for therapeutic translation.

#20 Studying complex planning in non-human primates

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As AlphaZero has revolutionized the AI of planning when the number of possible futures is combinatorially large, our lack of understanding of how biological brains plan in such situations has come into stark contrast. Most neuroscientists favor planning tasks that don't require much thinking ahead. We will show that it is possible to study planning in non-human primates in a task of intermediate complexity while maintaining experimental tractability and computational modelability. Our paradigm is four-in-a-row -- a variant of tic-tac-toe and Go Moku. In this task, which has a state space of size ~10^16, people think ahead but also make use of retrospective information. We will describe human in-lab data, mobile platform data, and initial results of non-human primate training. We will also describe a computational model of decisions in this game.

#21 Multiplicative computation in face-selective neurons

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A recent theoretical study on primate face-selective neurons (Hosoya and Hyvärinen, 2017) has predicted that a crucial computational component of those neurons may be multiplication between two units: facial feature detection (eye, mouth, etc.) and facial category detection (face or non-face). Since such operation is not typical in alternative models like sparse coding or deep learning models, it can be crucial for identifying the underlying computational principle in the face-processing system. In this study, to validate this prediction, we conduct a monkey experiment aiming at revealing multiplicative structure in responses of face-selective neurons. To do so, we present a large number of face images added with Gabor-shape noise and estimate a form of multiplicative model, which starts with a simple basis model mimicking the early visual processing and then performs a multiplicative operation on the outputs of two parametrized linear filters with different nonlinearities. In our preliminary results, a population of neurons in an anterior face patch (AM) showed significantly better prediction performance for held-out test data, in comparison to a non-multiplicative case with a single filter. Moreover, for those neurons, one filter often had a pattern like facial parts and outline, whereas the other showed prominently strong suppression when the input face image was heavily corrupted by Gabor-shape noise and thus does not look like a face. These results are consistent with our theoretical prediction of a multiplicative computation between a facial feature detector and a category detector, which thus encourages further experiment in this direction.

#22 The Natural Scenes Dataset (NSD): A massive 7T fMRI dataset to bridge cognitive neuroscience and artificial intelligence

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Developing accurate, generalizable models of sensory representation requires extensive stimulus sampling due to the vast dimensionality of sensory inputs. Here we designed, collected, and pre-processed a massive, high-quality fMRI dataset that can be used to advance our understanding of how vision is achieved in the human brain. Using ultra-high-field fMRI (7T, whole-brain, T2*-weighted gradient-echo EPI, 1.8-mm resolution, 1.6-s TR), we measured BOLD responses while each of 8 participants viewed 9,000–10,000 distinct, color natural scenes (22,500–30,000 trials) in 30–40 weekly scan sessions over the course of a year. As participants fixated a central point, they performed a long-term continuous recognition task in which they judged whether they had seen each image at any time during the experiment, either in the current scan session or any previous scan session. Data collection also included substantial additional measures including resting-state data, retinotopy, category localizers, anatomical data (T1, T2, diffusion, venogram, angiogram), physiological data (pulse, respiration), eye-tracking data, and additional behavioral assessments outside the scanner. We show that the data are of exceptional quality, with participants having nearly perfect response rates, high task performance, and low head motion, and with brain images having high contrast-to-noise ratio and spatial stability across scan sessions. Both the raw and pre-processed data will be made publicly available to the scientific community. Given its unprecedented scale, quality, and breadth, NSD can be used to explore diverse neuroscientific questions with high power at the level of individual subjects, and opens new avenues of inquiry in cognitive neuroscience and artificial intelligence.

#23 A fast and flexible method for modeling peripheral vision

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In recent years, vision science has made great strides towards understanding the encoding in peripheral vision, and in particular in understanding visual crowding. Testing models of peripheral vision has relied heavily on the ability to generate members of the equivalence class of the model, a process that is often slow. Here we present an efficient dataflow model that, while not a neural network, utilizes the high-performance optimization machinery of modern deep learning to find members of the equivalence class orders of magnitude faster. Importantly, this framework affords greater freedom to experiment with different model statistics and flexibly change the underlying filters. We demonstrate this by adding explicit end stopping to the previous model, and testing it on a texture metamer task.

#24 Leveraging voxel-level data for construction of regional brain connectivity networks

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Functional brain connectivity networks of single subjects are key to provide insights into the diseased or injured brain. These networks are often constructed from functional Magnetic Resonance Imaging (fMRI) data, and connect together inter-correlated brain regions, which consist in groups of dependent voxels. Previous works have focused on aggregating variables within predefined groups. However, such approaches suffer from loss of relevant information and can lead to incorrectly identifying edges. We present two novel frameworks that directly use information at the voxel level to infer connectivity networks. In the first, inter-correlation density estimation is followed by a thresholding step, based on correlation screening, to reliably detect non-zero correlations between regions while accounting for dependence between pairs of voxels in the same region. This framework was applied to a real-world dataset from resting-state fMRI data acquired on rats. Second, a novel spatiotemporal random effects model is proposed for fMRI signals at the voxel level. Compared to existing approaches, the proposed model is more flexible in that it does not require stationarity of the mean or variance across time. Rather, the correlation between regions, which is commonly used to quantify connectivity, is assumed to be constant in time. Estimators are implemented under the assumption of a Gaussian likelihood function, and their performance is illustrated on simulated data.

#25 Targeted cortical stimulation reveals some principles of cortical contextual interactions

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Cross-orientation suppression is a form of contextual normalization in visual cortex, but whether cortical circuits participate in this normalization is unclear. We used intrinsic signal imaging to visualize orientation maps of ferrets and patterned optogenetic stimulation to activate sets of columns that either matched or were orthogonal to the preferred visual orientation of neurons recorded with electrodes. Optogenetic stimulation of particular orientation columns caused activity that spread to orthogonal orientation columns via synaptic connections in the network. Integration of visual and optogenetic signals was linear at low firing rates but became sublinear at higher firing

rates. When visual or optogenetic stimulation of columns preferring one orientation was combined with optogenetic stimulation of columns preferring the orthogonal orientation, we observed suppression but much less than would be expected if cortical circuits provided a large fraction of visual cross-orientation suppression, suggesting that properties of pre-cortical inputs primarily underlie cross-orientation suppression, consistent with previous studies.

 # 26 Neural Encoding of Reaches in a Linear Cortical Model

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A major open question of motor control research is how connectivity among populations of neurons is tuned in such a way as to give rise to temporal patterns of muscle activation that produce efficient trajectories for reach targets regardless of the orientation of the arm, its position in space, or the intended direction of movement. One possibility is that these connections were formed through an evolutionary process that sought to optimize arm reaching performance subject to energy constraints. To test this idea, we develop a linear dynamical model of the motor cortex with feedback coupled to a two joint, physics-based model of the macaque arm with six muscles. We optimize the connections between neuronal populations and between these populations and muscles with respect to an objective function that penalizes reach error across a training set, as well as neural and muscular energy use. We find that, to produce accurate and efficient reaches across a wide range of movement directions and regions of space, it is necessary to represent target-related inputs that activate the neurons and feedback from muscles back to neurons in a combination of rectangular and joint angle coordinates, suggesting that the motor cortex may use multiple coordinate systems when encoding reaches. In addition, we show that certain properties of motor cortical neurons which have been observed in experiments, such as shifts in tuning curves that occur when the workspace changes, along with muscle synergies that tend to span multiple joints, arise naturally as a result of optimizing movement efficiency and accuracy.

#27 Measuring animal behavior in social contexts using deep learning approaches

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Understanding animal behavior in a social context requires tracking and quantifying their behaviors as they interact with each other. Recently, there has been notable progress in developing deep learning algorithms and software to track multiple animals in social paradigms. Some of these algorithms only track animal identities, which has been shown to be robust. Other algorithms detect key points on the animals' bodies to estimate poses, which can be reasonably successful when the animals are some distance apart or have brief close contact with each other. However, these algorithms exhibit poor tracking accuracy when the animals spend more time with each other, performing key social behaviors such as huddling, mutual-grooming, and mating. To help improve the tracking of animals within social contexts, when the animals are close for long periods, we implemented a pipeline that combines multiple deep-learning-based tracking methods to obtain detailed and high-accuracy postural trajectories of multiple animals. Tested on a data set of prairie voles - a model organism for the study of social interactions - our pipeline robustly maintains animal identities and increases the accuracy of the posture tracking over applying convolutional neural network methods by themselves. With this improved tracking accuracy, we can build a better representation of the behaviors of animals in a social context, isolating behaviors that are key for

understanding the dynamics of social interactions. This work is supported by NIMH grants 1R01MH115831 and P50MH100023.

28 CRCNS US-Japan Research Proposal: A computational neuroscience approach to skill learning and transfer from visuo-haptic VR to the real-world

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This project aims to develop a neurobehavioral model of complex skill learning by integrating information from both brain activity and body movement in real time as participants learn real-world activities. Together with an NICT funded team, we will also study the use of novel visuo-haptic VR to provide a slow-tempo method for training tasks that are impossible to slow, such as the juggling of balls, a task requiring precise inter-limb timing and visuospatial processing and motor execution. There has been relatively little study of such a complex motor act, and we have developed methods to jointly analyze movement and brain activity to do so. We present results from the analysis of (pre-covid) pilot dataset of juggling individuals. First, we demonstrate that it is possible to reliably extract spatially localized brain activity related to visual processing, spatial attention, multi-sensory integration and motor execution despite movement. Methods used spectro-temporal and connectivity analysis of source-resolved analysis of high-density EEG together with timing events extracted from videos of ball trajectories. In parietal cortex, known to be involved in spatial processing, we found robust alpha-band signatures at the moment the thrown ball reached its apex, a time thought to be critical for trajectory estimation required for the planning of the timing and location of the next catch. Motor regions had activity correlated to contralateral hand movements, with broad-band increases around the time of catch. A highly notable finding is narrow-band response between 70-80 Hz that shows sustained activity, but sharp transitions at the time of catching for both hands, signaling a possible role in intra-hand coordination. We are currently analyzing performance and brain activity in terms of three components of juggling skill: throw accuracy, ball trajectory prediction, and timing stability. We plan in the next year to conduct experiments in proficient jugglers with LCD shutter glasses to blank visual tracking of ball trajectory at different points to test neural dynamics in response to perturbation of input. With the NICT team, we will collect and analyze EEG with the slow-motion juggling platform, validating similar behavior and neural responses for full-speed juggling, then taking advantage of the slow-motion juggling to more deeply parse the temporal dynamics of brain activity during complex motor execution.

29 A computational study of cortico-thalamic synaptic input effects within a thalamocortical network for slow oscillations

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Slow wave sleep consists of two major EEG rhythms, cortical slow oscillations (SOs) and thalamo-cortical sleep spindles. Both oscillatory rhythms play important roles in memory formation and synaptic plasticity. Interactions within the thalamocortical system are relevant for synchronizing SOs and concurrent sleep spindles. To investigate the role of synaptic inputs for these two oscillatory rhythms, we developed a thalamocortical network model [1]. The thalamic component of this network model contains two cell layers, one with thalamocortical (TC) cells and one with reticular (RE) cells. The cortical network model component also consists of two layers, a pyramidal (PY) cell layer and an interneuron (IN) layer. The intrinsic currents of all cells are simulated by

Hudgkin-Huxely kinetics, whereas for synaptic currents first order kinetic schemes are used for AMPA, NMDA, and GABAA receptors [2]. GABAB receptors are simulated by a high order kinetic scheme. The SO up state is initiated through synaptic miniature currents and terminated by short-term synaptic depression. Synaptic conductances between the thalamic and cortical network are altered through AMPA receptor weights. The simulation results show that increased cortico-thalamic synaptic input reduces spindle activity in the thalamic network. Due to weak thalamic activity, the cortical network receives weaker thalamic synaptic input with a longer time delay (~450 ms after up state initiation), leaning toward the end of the up state. Strong cortical excitatory synaptic inputs to the thalamic network seem to decrease spindle activity and also disturb the temporal coordination between SOs and spindles in the thalamocortical network. Together, the model is able to generate EEG rhythms of slow-wave sleep, and some interdependencies.

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#30 Compositionality and dimension reduction methods for kinematically redundant upper limb movements

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For multi-limb movements of the lower extremity, it has been shown convincingly that the kinematics as well as the muscle activity during multi-segment coordination can be modeled successfully by the flexible combination of a limited number of components, or source functions, which can be interpreted as movement primitives. Different ways to extract such components have been proposed, and it is still being investigated how such components map onto control units of the motor system, and how they depend on the choice of different coordinate frames to describe the kinematics of complex motor patterns. We investigated these questions for upper limb movements, combining the recording of kinematics and EMG signals with different methods from machine learning for such compositional representations.

First, we investigated multi-segment coordination strategies and the nature of the mapping from end-effector to joint motions during simple curved 3D arm movements, such as elliptical and figure eight drawings. We represented the kinematically analyzed movements as the composition of time-dependent basis functions (sources), using the FADA algorithm (Chiovetto, et al. 2016), an anechoic demixing method (Omlor and Giese, 2011). It was used to infer the underlying time-based sources for both the joint rotations and the 3D end-effector trajectories. Using this algorithm, we inferred the time shifts between different sources and the coefficients by which the sources are weighted. Our analysis showed that three sources are sufficient to approximate the joint and end-effector trajectories successfully. We derived the time-dependent sources and found that the sources for Cartesian coordinate hand trajectories are strikingly similar to those for the arm joint trajectories. However, this phenomenon was found to only hold true when the joint space movements were represented in an extrinsic reference frame: using absolute coordinates (a. elevation angles with respect to gravity and b. azimuth angles) relative to an axis parallel to the body frontal plane, as opposed to intrinsic relative anatomical coordinates. This observation was validated through several statistical methods. These findings suggest that similar time-shifted sources may serve as mediators between the upper limb end-effector and joint space for the kinematically redundant human arm. In particular, expressing joint trajectories in terms of extrinsic coordinates could allow a linear mapping between upper limb end-effector and joint trajectories, thus helping to resolve the existing kinematic redundancy.

We applied similar methods also for the modeling of the muscle activity patterns underlying multi-joint coordination during the execution of dexterous reaching movements. Most popular matrix decomposition methods that are used to extract source components or primitives can only identify either spatial or temporal motor modules, but not both types simultaneously. This results typically in overparameterized models that might not reflect accurately how the nervous system simplifies the control problem by combination of a small number of spatio-temporal primitives. Instead, algorithms extracting only spatial or only temporal components typically explain structures in the data by spatial or temporal composition models that are overly complex in the temporal and spatial domain, respectively. This suggests that such models are overall unable to find more simple parameterizations in the class of spatio-temporal models. In order to realize the simultaneous identification of spatial and temporal modules, we propose a decomposition of muscle signals based on the Canonical Polyadic Decomposition (CPD) model (Harshman, 1970). In comparison with classical decomposition models, CPD identifies qualitatively similar spatial and temporal modules, explains a comparable amount of data variance, and requires a lower number of parameters. Furthermore, we show that for variations of parameters in task space, such as reaching direction, the method uncovers latent representations that vary smoothly with the task variables, allowing for the accurate prediction of the muscle patterns for untrained reaching directions. Our results suggest that the proposed space-time decomposition results in more compact models, which might reflect the internal structure of the modular organization of multi-limb coordination more appropriately, and which can be implemented easily by physiologically-realistic circuits using gain modulation.

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31 Responses of both CA1 pyramidal neurons and midbrain dopamine neurons to sustained depolarization are mediated by long-term sodium channel inactivation

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In behaving rodents, CA1 pyramidal neurons receive spatially-tuned depolarizing synaptic input while traversing a specific location within an environment called its place. Midbrain dopamine neurons participate in reinforcement learning, and bursts of action potentials riding a depolarizing wave of synaptic input mediates reward signaling. Slice electrophysiology in vitro shows that both types of cells exhibit a pronounced reduction in firing rate (adaptation) in response to a temporally symmetric current ramp, so that the neuron fires substantially less on the down ramp compared to the up ramp. We show that adaptation in CA1 neurons is more pronounced in the apical dendrite than in the soma. Such adaptation is likely to affect the dependence of the firing rate of CA1 neurons on position within the place field. Our simulations of multicompartmental pyramidal neuron including a five state Markov model of NaV1.6 were calibrated using data from the literature that shows slow inactivation of the sodium current increases with distance along the apical trunk. Our simulations suggest that long-term inactivation of this channel is responsible for adaptation, consistent with our pharmacological experiments. Information on the spatial dependence of long-term inactivation is not available for midbrain dopamine neurons, so we implemented a Markov Model of a different sodium channel, Nav1.2 known to be expressed in these neurons in a single compartment model. Simulations show that the differential contribution of long-term in two subpopulations of midbrain dopamine neurons accounts for their different dynamic range, as assessed by their entry into depolarization block at very different frequencies in response to similar depolarizing ramps. These results suggest long-term inactivation of the sodium channel is a general mechanism for adaptation.

32 Impact of cortical neuromodulation on the efficacy of auditory closed-loop stimulation

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The use of transcranial direct current stimulation (tDCS) has been shown to be effective in modulating membrane potential. Auditory closed-loop stimulation (ACLS) targeting the up-state of ongoing sleep slow oscillation (SO) enhanced endogenous SOs, and thalamocortical spindles, albeit its effect is rather inconsistent on behavior [1,2]. This study aimed to investigate for the potential of tDCS neuromodulation to impact the efficiency of ACLS. Participants went through two nocturnal sleep sessions (ACLS alone and anodal tDCS+ACLS). Learning of two tasks (a non-sense word paired-associate and a figure paired-associate task) took place after sleep and recall the next morning. Encoding performance was additionally assessed by a word paired-associate task. A final session measured cognitive ability. Across all subjects, tDCS+ACLS did not affect behavioral performance. However, there was a highly significant interaction with cognitive ability. tDCS +ACLS on retention ($F(1,15)=15.65$, $p=0.001$, $N=17$). Participants with higher cognitive ability revealed poorer retention performance on the non-sense word paired-associate task in tDCS+ACLS compared to ACLS ($p=0.016$; $n=9$, Wilcoxon rank test), whilst lower cognitive ability participants showed no significant difference ($p=0.80$; $n=8$). In the tDCS+ACLS condition SO-induced fast spindle RMSs was increased at midline frontal, central and parietal sites as compared to ACLS alone. Furthermore, tDCS+ACLS was associated with a larger SO hyperpolarisation down-state amplitude ($p<0.05$, t-Test). In the tDCS+ACLS condition subjects also revealed a decreased sleep quality, longer wake time and shorter REM sleep ($p<0.05$, t-Test). Preliminary results support previous findings on the influence of cognitive ability on the efficacy of non-invasive stimulation. Our study indicates that level of cortical excitability may be linked to differential efficacy of non-invasive stimulation.

33 Auditory closed-loop stimulation during sleep in mice reveals a phase-dependent enhancement of memory consolidation

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In humans, auditory closed-loop stimulation (ACLS) in phase with the endogenous slow oscillation (SO) enhanced SOs and thalamocortical spindles. The effect on sleep-associated memory

consolidation is however less consistent1-3. The present study aims to adapt ACLS to mice to investigate underlying hippocampal and thalamocortical interactions. Mice (C57BL/6) participated in a spatial object place recognition task (OPR). During sleep, within the retention period between the sample and the test phases of the OPR, local field potentials were recorded in the cingulate cortex and dorsal hippocampus by wire arrays. Upon online detection of the hyperpolarization (negative SO half-wave) of non-rapid eye movement sleep in the cortex stimulation (one white noise burst) was delivered, in separate sessions at one of four phases of the SO: close to the SO downstate (DownS), at the down-to-up transition (Down2UpS), at the up-state (UpS) and during the up-to-down transition (Up2DownS). In a fifth session, stimulation was omitted (Sham). The preference for the displaced object in the test phase was above chance levels for ACLS delivered at Down2UpS and UpS only (Down2UpS: $p=0.005$, UpS: $p=0.0051$, one-sample t-test), as previously suggested by the model of the Bazhenov lab. Importantly, performance for stimulation at the UpS was higher than for Up2DownS stimulation ($p=0.0201$, paired t-test, $n=6$). SO-trigger-event correlations of hippocampal sharp-wave ripples and spindles revealed a strong increase at the time of stimulation followed by a significant suppression lasting over 1 second. Event-event correlations of spindles around SOs suggest a stronger modulation of spindle activity for UpS delay relative to sham as compared to all other SO phases. Together, the study reveals a robost effect of single-stimulus ACLS on behavior, yet electrophysiological underpinnings as measured here are rather obscure.

#34 The development of efficient communication in the human connectome

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The development of rapid communication between different brain regions is essential for brain function. Post-mortem studies have shown that the myelination of white matter pathways starts in the late prenatal period and continues in late adolescence. MRI measurements have shown that pathways develop at different rates in different areas, often reaching a plateau around 30-40 years of age. These indirect measurements do not give quantitative information about how the transmission speed develops throughout development. Quantitative neurophysiological measurements of transmission speed in the developing human brain are essential to understand the maturation process of efficient communication that is necessary for brain functions like cognition and behavior.

We collected data in 75 subjects, age 4 to 51 years, who were implanted with intracranial electrodes (electrocorticography - ECoG) to evaluate epilepsy surgery. The electrodes were positioned in MNI space and categorized in either frontal, parietal, temporal or sensorimotor sites. Adjacent electrode pairs were stimulated with ten consecutive pulses (1ms, 4-8mA, 0.2Hz), and we measured cortico-cortical evoked potentials (CCEPs) throughout the other electrodes. These CCEPs expose the underlying physiological networks. We calculated the latency of the initial negative potential deflection (N1-response) that occurs within 100ms after stimulation.

We fitted distributions of latency as a function of age for all 16 combinations of these four brain regions. We found that the latency of the N1 decreased significantly with age, from ~40ms at age 4 years to ~25ms in adulthood. More detailed fits indicated that the transmission delay between cortical areas decreases with 0.23-0.88ms each year, until it plateaus around age 15-29 years old. These increases in speed were observed in both long and short range connections between and within frontal, parietal and temporal areas.

The decreases in the N1 latency reveal that transmission speed in the human brain connectome increases about two-fold from childhood to adulthood. These measurements provide quantitative estimates of the development of efficient communication and can be used in large scale models of the human brain that bridge structural and functional development. With this study, we facilitate the construction of growth curves with velocities in the brain, which could be helpful in diagnosing abnormal development in cognition and behavior.

#35 Locating Deep Brain Stimulation Targets for Major Depressive Disorder using a Network Diffusion Model on the Human Connectome

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Major Depressive Disorder (MDD) is one of the most common mental illnesses and it affects more than 300 million people worldwide. In this study, we investigate how MDD affects information processing in the brain using a network diffusion model on the human connectome. We compare the structural connectivity of 90 MDD patients and 20 control subjects using probabilistic tractography between 396 cortical and subcortical regions. We model the information flow among these regions with an Asynchronous Linear Threshold (ALT) diffusion process. This relatively simple model identifies some significant differences in the activation cascades between control subjects and MDD patients. Our findings provide a justification for certain brain regions that are currently used as Deep Brain Stimulation (DBS) targets -- and the suggest some more possible targets.

#36 Development of modular patterned activity in visual cortex through intracortical network interactions

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Modular (columnar) activity is a fundamental mode of neural activity in the cortex of primates and carnivores and is reflected in distributed functional networks such as that supporting orientation selectivity. Work in ferret visual cortex has shown that already prior to visual experience, early spontaneous activity is modular, revealing millimeter-scale correlations that are predictive of future functional networks and exist in the absence of long-range horizontal projections and patterned feedforward activity. Computational models predict a striking ability of developing cortical circuits to self-organize into modular coordinated patterns of activity, with tightly-coupled excitation and inhibition. Here, we combine widefield epifluorescence calcium imaging with excitatory optogenetics to simultaneously image and stimulate pyramidal neurons in layer 2/3 of developing ferret visual cortex. Optogenetic stimulation with a large (~3 mm) spatially uniform stimulus lead to the rapid emergence of highly non-uniform, modular neural activity. Notably, opto-evoked activity resembled endogenous spontaneous activity in spatial structure, exhibited similar long-range correlations, and resided in a moderately low-dimensional subspace that is indistinguishable from that of spontaneous activity. We further demonstrate that at these early developmental timepoints, intracortical inhibitory activity is already highly organized and tightly coupled to excitation. Together, our results provide strong evidence that modular patterned activity is an emergent property from

intracortical interactions through a self-organizing network, suggesting a potential mechanism for the emergence of distributed functional networks during development.

#37 Encoding Magnitude and Rate of Change of Temperature by Drosophila Noxious-Cold Sensing Neurons

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Reliable sensation of cold temperature and its change is necessary for stimulus-relevant behavioral and physiological responses. Drosophila melanogaster is a model organism providing powerful tools for studying noxious cold sensation. In this study, we combined computational and electrophysiological methods to investigate the neural dynamics of Drosophila larva cold-sensing Class III (CIII) primary afferents. Drosophila CIII larval neurons serve as the primary cold nociceptors and express a suite of thermoTRP channels implicated in noxious cold sensation [1,2]. We found, that CIII neurons responded to a fast temperature decrease with a pronounced peak of firing rate and subsequent spike frequency adaptation towards a steady state. In contrast, they responded with a gradual increase of spiking rate to a slow temperature decrease. Sustained lower temperatures elicited higher steady-state spike frequencies of CIII neuron responses. We quantified this dependence by curve-fitting it to the Boltzmann's function and determined the temperature of half-maximal activation for individual neurons. There was high variability in temperature of half-maximal activation and the pattern spiking activity in CIII neurons. As a population, they can encode both the magnitude of cold temperature and the rate of temperature decrease. We identified two basic cold-evoked patterns of CIII neurons: bursting and spiking. Bursts were more frequently seen within the peak of spiking rate in response to a fast temperature drop. At slow temperature, fewer neurons showed bursts of activity, and the bursting activity did not form a peak of activity. We developed a CIII neuron model based on transcriptomic data from CIII neurons [1] and patch-clamp data on gating characteristics of Drosophila Na+ and K+ channels obtained from the literature [3,4]. It includes phenomenological representation of a TRP current with temperature-dependent activation and Ca2+-dependent inactivation. The model recapitulated the key features of coding of the rate of change and the magnitude of temperature found in electrophysiological experiments. Using the model, we described the mechanisms of two basic CIII cold-evoked activities: spiking and bursting, and phasic and tonic components of their responses, which were determined by basic dynamics of TRP current and its interaction with the voltage-gated Ca2+ current and Ca2+-activated K+ currents.

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#38 REvealing SPONtaneous Speech Processes in Electrocorticography (RESPONSE)

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The complex dynamics of brain activity and the fundamental processing units of continuous speech production and perception are largely unknown, and such dynamics make it challenging to investigate these speech processes with traditional neuroimaging techniques. Intracranial EEG (iEEG), such as electrocorticography (ECoG) and stereotactic EEG (sEEG), measure electrical activity directly from the brain and can provide insights about widespread networks for speech production and understanding, while simultaneously providing localized information for decoding nuanced aspects of the underlying speech processes. Thus, iEEG is instrumental for investigating the detailed spatiotemporal dynamics of speech. In pursuit of the ultimate objective of developing a natural speech neuroprosthetic for the severely disabled, the present work investigates real-time synthesis of overt speech directly from brain activity, as well as the neural processes of continuously-spoken overt and imagined speech production. iEEG data have been collected from subjects undergoing clinical monitoring for epilepsy at the Mayo Clinic Florida, Northwestern University, University of California San Diego, and Virginia Commonwealth University Epilepsy Centers. Subjects performed a battery of speech tasks including overt and imagined continuous speech based on phonetically-balanced sentence prompts, as well as spontaneous overt and imagined speech via standard picture description and directed conversation tasks. The high gamma-band power (70-170 Hz) of iEEG, which has been shown to be highly correlated with a variety of cognitive processes, was extracted and analyzed in conjunction with the recorded speech signals. Traditional automatic speech recognition techniques with a customized iEEG frontend were applied to time-align speech with the corresponding phones, thus facilitating the spectral reconstruction in preparation of parametric speech synthesis. Results of offline and real-time speech synthesis of spoken and imagined speech will be presented.

#39 Juggling on the moon: Computational neuroscience of skill acquisition

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This project aims to elucidate the brain mechanism of motor skill acquisition, which is not yet fully understood. By using a more complex juggling task as our research target instead of a simple motor task as traditionally used, we plan to visualize the dynamic brain process of complex skill acquisition in the human brain and develop a more realistic computational model of the mechanisms of complex skill acquisition. We also aim to study the impact of learning tempo and test if a novel method slow-tempo training using visuo-haptic virtual reality (VR) can enhance skill acquisition. In the first year of the project, the NICT funded team has developed a juggling system to realize the training while moving the body slowly (slow-tempo training). Specifically, using VR and haptic devices, we developed a VR system (a juggling system on the moon) that enables slow-tempo training in which juggling is performed in an environment where the ball moves more slowly than normal, as if under the reduced gravity of the moon. In order to record the brain activity during skill acquisition, we also made an adapter to fix the head-mounted display on the head without interfering with the electroencephalography (EEG) electrodes. In the future, we will perform experiments to measure brain activity and behavior with juggling beginners to verify the impact of the slow-tempo training on juggling ability. In addition, we will use the system to better understand complex brain dynamics related to skill acquisition and execution by extracting brain activity related to juggling skills from EEG data using the analysis method we have established with UCSD. Based on these findings, we will work with UCSD to computationally model the brain mechanisms related to juggling skill acquisition.

#40 The Role of Biomechanics in the Neural Control of Balance during Standing and Walking

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Maintaining balance while standing or walking is a challenging task, as evident in the propensity to fall in older people and patients with neurological disorders. Our research has examined the control of balance in healthy individuals with a focus on the relative role of neural and mechanical contributions, including the role of assistive devices. To create challenging conditions for healthy individuals, we examined behavior during standing or walking on a narrow beam. A first study focused on how humans maintain mediolateral balance when standing on a narrow beam, either with bare feet or wearing rigid soles, affecting the critical interface between foot and ground. Our results showed that the altered foot-ground interaction critically influences balancing behavior, suggesting that the mechanics of this interface must be considered to understand the human controller. A simplified model of a double inverted pendulum model including foot-beam interaction could replicate the differences in balance between the two foot contact conditions. Additional analyses revealed anticorrelation between lumped upper- and lower-body angular momentum in both novice and expert subjects. Comparison of different balancing controllers for the inverted pendulum model from the robotics literature showed that a controller that predominantly utilized hip actuation matched human behavior best.

A second study examined foot-ground interactions during walking on the narrow beam, again bare-foot or wearing rigid flat soles. The whole-body angular momentum showed that walking with rigid soles improved balance performance in both expert and novice subjects. However, improvements in balance performance with rigid soles did not persist after removing the flat soles. This absence of any aftereffect suggested that the improved balance performance when constraining the foot joints by a rigid sole was the result of a mechanical effect rather than a change in neural control.

A third study on postural balance focused on the effect of mechanical support via canes. Following numerous studies that highlighted the importance of haptic information, this study examined the mechanical effect of supporting devices. Participants stood on a beam supported by two canes, one in each hand, and applied minimal, preferred, or maximum force onto the canes; canes were positioned in the frontal plane or in a tripod configuration. Ground reaction forces and forces exerted on the canes showed that while canes reduced the variability of center of pressure and center of mass, forces exerted on the canes beyond the preferred level yielded no further benefits, in fact had a destabilizing effect: the displacement of the hand on the cane increased with force, as pushing destabilized the inverted pendulum of the cane. In the preferred condition, participants exploited the altered mechanics by resting their arms on the canes while their sway utilized the larger base of support. Despite the challenge of a statically unstable system, these results show that, in addition to augmenting perceptual information, using canes can provide mechanical benefits. However, while canes improved postural balance, this improvement did not transfer to subsequent performance without canes. As with wearing rigid soles, using canes may have limited scope for rehabilitation of balance ability.

A fourth simulation study examined the role of mechanics on upright posture by analyzing the directions of the foot-ground interaction force vectors. Previous work identified a point of intersection of the force vectors that exhibited consistent frequency-dependent behavior. To test whether this behavior was the signature of neural control or a consequence of biomechanics, this study compared simulated quiet standing with human subject data. The simplest competent model that approximated human standing was again a double inverted pendulum with torque-actuated ankle and hip joints, consistent with earlier results. A linear feedback controller based on position and velocity errors of each joint revealed that the relative cost between state deviation and control effort directly affected where intersection point crossed the vertical position with respect to the center of mass. A similar effect was obtained by varying the relative cost between the ankle and hip control effort. Among the many controller parameter sets considered, the one that best reproduced the human data used minimal control effort and more ankle torque than hip torque. This suggests that the detailed profile of intersection point height variation with frequency is a signature of neural control.

#41 NMDA-dependent serial biases in working memory

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The primate prefrontal cortex, due to its unique anatomical and cellular organization, is thought to play an important role in the maintenance of working memory, the ability to maintain information in mind over a period of seconds. NMDA receptors, which are abundant in the prefrontal cortex, are thought to be critical in that respect because of their ability to maintain neurons at an excited state for an extended period of time and to induce plasticity of synaptic connections. Direct experimental evidence linking their cellular role to working memory behavior has been scant, however. To tease their role, we relied on an "imperfection" of working memory, serial dependence: the contents of memory in a previous trial often affect what is being recalled in a following one. Serial dependences are systematically affected in patients with schizophrenia, and anti-NMDAR encephalitis, suggesting an underlying NMDAR-dependent mechanism. We thus trained monkeys to perform working memory tasks and examined history dependent biases in their responses under control conditions, and under systemic administration of ketamine, an NMDA receptor antagonist. Monkeys exhibited serial biases, which depended on the relative location of successive, remembered stimuli. These were generally reduced by ketamine, in a dose-dependent fashion. Our results provide empirical validation of the role of NMDA and provide an avenue of investigating the underlying NMDA-receptor activity in working memory.

#42 A neuromuscular model of human locomotion that is able to flexibly adapt its gait parameters

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Human locomotion is amazingly flexible. We effortlessly walk with different combinations of step length, cadence and speed and are able to easily adopt different gait patterns. Achieving this level of flexibility requires sophisticated control, particularly to maintain upright balance, as the human body is mechanically unstable during locomotion. Changing the gait pattern, therefore, is a challenge. In the presented work, we present a walking model that can freely select a gait from a wide range of patterns. We define a gait pattern as a combination of the three outcome measures

step length, cadence, and the resulting walking speed. Our approach is based on a recently developed model that allows execution of task-level motor plans. The control model comprises a supraspinal layer that generates an updatable movement plan that is transformed into descending commands using an internal model. In a spinal layer, descending commands are integrated with spinal reflex modules such as the stretch reflex. The biomechanical model comprises 8 DoFs, realistic moment arms, and 22 Hill-type muscles. Here we use the supra-spinal module to modify four control parameters that affect cadence and step length. (i) Target step time is the planned time of the swing leg to heel-strike, (ii) target trunk lean and (iii) target leg angle are the goal angles for the upper body and swing leg in the sagittal plane and (iv) propulsion is a coordinated activation of stance leg muscles that accelerate the body forward. Each control parameter affects multiple outcome measures. Increasing the target step time, for instance, does not only lead to faster steps, but also changes the resulting foot placement and kinetic energy, due to the changed dynamics of the body in order to maintain balance. We use evolutionary optimization to find control parameter sets that achieve different desired values for the outcome measures cadence, step length and the resulting speed. The model is able to flexibly combine a wide range of step lengths, cadences and walking speeds and is able to transition between those during locomotion.

#43 Towards Closed-Loop Speech Synthesis from Stereotactic EEG: A Unit-Selection Approach

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Speech synthesis from neural signals is envisioned to restore natural and intuitive spoken communication to people who have lost the ability to speak due to neurological disease or injury. Invasive measurements of neural activity, such as electrocorticography (ECoG) and stereotactic electroencephalography (sEEG), have proven capable of representing the spatiotemporal dynamics related to speech production processes. Toward the development of a speech neuroprosthesis, we implement a closed-loop system that based on an approach that has been demonstrated to synthesize intelligible single words in offline analyses. This approach utilizes the unit-selection method, which is well established in conventional speech synthesis domains for converting electrophysiological activity such as from electromyography (EMG) directly into audible waveforms. Here, rather than using EMG, sEEG training data is used to populate a codebook with pairs of neural and acoustic data. In the decoding step, the neural activity is compared to each entry to determine the most similar match, from which the associated acoustic segment is concatenated to the prior audio segment selections to form the final output. The ultimate goal is to decode imagined speech processes and we hypothesize that, with a closed-loop setup, a patient can adapt their brain activity accordingly to the continuous audible feedback to improve the quality of the synthesized speech output. Our proposed approach is capable of meeting the real-time requirements of such a setup. To date, we have evaluated system performance retrospectively on a corpus of 5 patients implanted with sEEG electrodes who performed read-aloud experiments while time-aligned neural and acoustic data were recorded. While previous studies primarily focused on cortical activity from cortical areas, we investigate activity originating in deeper brain structures. Our results revealed significant correlations between synthesized and original speech, which is a promising preliminary step toward implementing closed-loop control experiments.

#44 Using brain-optimized deep neural networks to investigate hierarchical computation in human visual areas V1-V4

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Visual areas V1, V2, V3, and V4 are often characterized as instantiating hierarchical computation. It has been hypothesized that the defining feature of this hierarchy is compositional dependence, i.e., each area applies a transformation to the outputs of the preceding area. Recently, task-optimized deep neural networks (DNNs) have been shown to yield impressively accurate predictions of brain activity in V1-V4, and for most networks, V1-V4 align with network layer depth. This result has been construed as evidence that V1-V4 are compositionally dependent. To carefully assess this interpretation, we analyzed the Natural Scenes Dataset, a massive dataset consisting of fMRI measurements of human brain activity (7T, 1.8-mm resolution) in response to up to 30,000 natural scene presentations per subject. We used this dataset to optimize DNNs to predict responses in V1-V4. In such brain-optimized networks, features distribute across layers in any way that improves the prediction of brain activity. This allows us to assess whether the alignment of V1-V4 with layer depth is a general property of DNNs that accurately predict brain activity. We found that when a single DNN is trained to jointly predict activity in V1-V4, alignment emerged in the sense that bottom layers of the DNN were more important for predicting activity in a given area than the areas above it in the hierarchy (e.g., bottom layers were more important for predicting activity in V1 than in V2-V4, and so on). Conversely, top layers were more important for predicting activity in a given area than the areas below it. Interestingly, when four distinct networks were independently trained to predict each of areas V1 through V4, there was no evidence for this type of alignment with layer depth. For example, the bottom layers in the network trained to predict V1 were less important than the bottom layers in the network trained to predict V4. Importantly, jointly and independently trained networks yield equivalent prediction accuracy. From these findings, we conclude that there is considerable flexibility in how to implement stimulus transformations that accurately predict brain activity in V1-V4. Some stimulus transformations are consistent with compositional dependence while others are not. We suspect that compositional dependence--without additional qualification--is too general a property to adequately explain the nature of the visual representations encoded in V1-V4.

#45 Cross-lingual semantic representations in the human brain

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Extracting meaning from language is a uniquely human ability. We have previously shown that semantic information from spoken and written English language is represented in a broad network of semantically-selective areas distributed across the human cerebral cortex. However, it is an unresolved question whether these semantic representations are similar across languages. Here we studied how the semantic content of narratives is represented in the brains of bilingual subjects. We used functional magnetic resonance imaging (fMRI) to record brain activity while participants read several hours of the same narrative stories in two linguistically different languages (English and Chinese). We then built voxel-wise encoding models to characterize selectivity for semantic content across the cerebral cortex. We first extracted different semantic features from the stories by projecting each stimulus word into an embedding space that encodes the meaning of words as vectors. Then, for each subject and language, we used regularized regression to estimate a mapping from semantic features to brain responses in each voxel. We used the estimated mapping to predict brain responses to a held-out narrative, and then used prediction accuracy on the held-out narrative to determine whether each voxel represents semantic information in each language. Our preliminary results indicate that, in a variety of regions across temporal, parietal and prefrontal cortices, voxel-wise models estimated from one language (e.g. English) accurately predicted

responses in the other language (e.g. Chinese). These results suggest that semantic representations are independent of the language through which the semantic information is received.

#46 An MCell model of the mouse neuromuscular junction to predict structure-function relationships in the active zone in healthy and diseased states

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We have developed an MCell model to study structure-function relationships at the mouse neuromuscular junction active zone. MCell is a highly accurate stochastic diffusion-reaction simulation tool (www.mcell.org) capable of modeling accurate 3D geometries and allows particle-based stochastic simulations of biochemical systems. We have constrained this model using the measured presynaptic action potential (using a voltage-sensitive dye), active zone structure (using previously published electron micrographs), and electrical measurements of synapse function in healthy and diseased states. In particular, we are focused on the density, distribution, and function of voltage-gated calcium channels, docked synaptic vesicles, synaptotagmin-1 proteins, and synaptotagmin-7 proteins. This approach has illuminated microscopic mechanisms underlying action potential-triggered synaptic vesicle release during single and short trains of activity (including mechanisms for short-term synaptic plasticity). We have compared results using active zone models of healthy synapses, and those that have been perturbed to model the neurological disease Lambert-Eaton myasthenic syndrome.

#47 Triple phase-locking of non-REM sleep rhythms maximizes the effect of hippocampal indexing in mPFC

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Systems Consolidation Theory posits that the hippocampus encodes new information for later cortical consolidation during non-REM sleep. Specifically, the triple phase locking of cortical slow oscillations (SOs) and sleep spindles and hippocampal sharp-wave/ripples (SWRs) is thought to allow the hippocampus to replay recent memories and to index corresponding cortical memory traces to be replayed and learned for long-term storage. Despite the success of Systems Consolidation Theory in explaining many experimental findings regarding how cortex and hippocampus coordinate memory consolidation, many of its central predictions remain untested. To understand the details of this coupling, we analyzed single-unit activity from the medial prefrontal cortex (mPFC) and CA1 of the hippocampus from rats trained to run a spatial sequence memory task and developed a biophysically-realistic thalamocortical network model implementing SWR input and SOs. First, we analyzed the distribution of SWR arrival times and we observed, in agreement with previous studies, that SWRs in vivo exhibit a tendency to occur immediately after the Down-to-Up transition (DUt) of SOs. To investigate the function of this phase preference in hippocampal indexing, we developed a biophysically-realistic thalamocortical network model based on Hodgkin-Huxley neurons and capable of transitioning between awake and sleep states and equipped with a spike-timing-dependent plasticity rule on synapses between pyramidal cells. Applying approaches from statistical field theory and network information theory to both our model and in vivo recordings, we showed that the von Neumann entropy of cortical population activity is a suitable proxy to measure transient sensitivity to external perturbations, while the PC dimension can capture persisting effects of the perturbation throughout a SO. Using these measures, we provide evidence that, although SWRs can transiently bias cortical activity during any phase of the cortical SO, there is an optimal phase during which SWRs can maximally bias persistent activity and robustly drive consolidation. Moreover, we show that the presence of thalamocortical sleep spindles during the Up state of a SO significantly influences the PC dimension of cortical activity, which previous results from our model predict would result in increased sensitivity to external perturbations. These findings provide a functional and computational account for the triple phase locking observed during non-REM sleep, as well as computational techniques which can be applied to interrogate transient and persistent sensitivity to external perturbations in recurrent networks.

#48 Leveraging maximally informative phase-locking of non-REM sleep rhythms to enhance consolidation

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A multitude of studies have supported the hypothesis that phase-locking of cortical slow oscillations (SOs), and hippocampal sharp wave-ripples (SWRs) during non-REM sleep promotes long-term consolidation. However, there has been relatively little attention given to the precise temporal ordering of these events. A few studies in rodents have shown that SWRs tend to occur shortly after the down-to-up state transition (DUt) of SOs in the mPFC. Previous work from the Bazhenov lab has shown that this temporal relationship between SWRs and SOs in the frontal pole also holds in humans, and could be replicated in a biophysical model of the thalamocortical-hippocampal loop (Sanda et al., Cer Cortex, 2021). Moreover, simulations of this model predicted that cortical input to the hippocampus was responsible for setting this bias in the phase preference of SWRs relative to SOs. Here, we employ a closed-loop auditory stimulation paradigm, which uses the LFP to detect the trough of the SO, to better understand how the temporal dynamics of SOs and SWRs impact memory consolidation. This paradigm could bias the distribution of SWR occurrences centered around the trough of the SO to peak just after the onset of auditory stimulation. In other words, this paradigm could be used to evoke SWRs in mice at arbitrary delays from the trough of the SO. Using the model of the thalamocortical-hippocampal network, we found that connections from the thalamus to CA1, such as those known to originate from the nucleus reuniens, are necessary for this SWR inducing effect of auditory stimulation to occur. Given that auditory stimulation could reliably induce SWRs, the simulated results of the model in the control condition were analyzed to determine how the phase of the SO at the time of a SWR affects the mutual information (MI) between the cortex and CA1, under the assumption that increased MI could facilitate increased efficacy of systems consolidation. The model predicted that MI is greater when SWRs occur during the DUt as opposed to during the down or up states. Indeed, behavioral analysis of the mice indicated that this was the case. Thus, the data suggests that properly timed auditory stimulation can enhance consolidation by sharpening the distribution of SWRs around the phase of the SO which results in maximal MI between CA1 and mPFC. Importantly, the model predicts that projections from the nucleus reuniens of the thalamus to CA1 are critical to this phenomenon, as they are necessary for auditory stimulation to reliably induce SWRs with a negligible delay. When considered with the previous research from our lab indicating that cortical input to the hippocampus is responsible for biasing the distribution of SWRs to occur at the DUt, these findings suggest a computational function for this phase relationship. Namely, that cortical input to the hippocampus imposes a bias on the occurrence of SWRs such that the majority occur during a period when cortex is the most receptive to external input.

#49. The Role of Biomechanics in the Neural Control of Balance during Standing and Walking

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Maintaining balance while standing or walking is a challenging task, as evident in the propensity to fall in older people and patients with neurological disorders. Our research has examined the control of balance in healthy individuals with a focus on the relative role of neural and mechanical contributions, including the role of assistive devices. To create challenging conditions for healthy individuals, we examined behavior during standing or walking on a narrow beam. A first study focused on how humans maintain mediolateral balance when standing on a narrow beam, either with bare feet or wearing rigid soles, affecting the critical interface between foot and ground. Our results showed that the altered foot-ground interaction critically influences balancing behavior, suggesting that the mechanics of this interface must be considered to understand the human controller. A simplified model of a double inverted pendulum model including foot-beam interaction could replicate the differences in balance between the two foot contact conditions. Additional analyses revealed anticorrelation between lumped upper- and lower-body angular momentum in both novice and expert subjects. Comparison of different balancing controllers for the inverted pendulum model from the robotics literature showed that a controller that predominantly utilized hip actuation matched human behavior best. A second study examined foot-ground interactions during walking on the narrow beam, again bare-foot or wearing rigid flat soles. The whole-body angular momentum showed that walking with rigid soles improved balance performance in both expert and novice subjects. However, improvements in balance performance with rigid soles did not persist after removing the flat soles. This absence of any aftereffect suggested that the improved balance performance when constraining the foot joints by a rigid sole was the result of a mechanical effect rather than a change in neural control. A third study on postural balance focused on the effect of mechanical support via canes. Following numerous studies that highlighted the importance of haptic information, this study examined the mechanical effect of supporting devices. Participants stood on a beam supported by two canes, one in each hand, and applied minimal, preferred, or maximum force onto the canes; canes were positioned in the frontal plane or in a tripod configuration. Ground reaction forces and forces exerted on the canes showed that while canes reduced the variability of center of pressure and center of mass, forces exerted on the canes beyond the preferred level yielded no further benefits, in fact had a destabilizing effect: the displacement of the hand on the cane increased with force, as pushing destabilized the inverted pendulum of the cane. In the preferred condition, participants exploited the altered mechanics by resting their arms on the canes while their sway utilized the larger base of support. Despite the challenge of a statically unstable system, these results show that, in addition to augmenting perceptual information, using canes can provide mechanical benefits. However, while canes improved postural balance, this improvement did not transfer to subsequent performance without canes. As with wearing rigid soles, using canes may have limited scope for rehabilitation of balance ability. A fourth simulation study examined the role of mechanics on upright posture by analyzing the directions of the foot-ground interaction force vectors. Previous work identified a point of intersection of the force vectors that exhibited consistent frequency-dependent behavior. To test whether this behavior was the signature of neural control or a consequence of biomechanics, this study compared simulated quiet standing with human subject data. The simplest competent model that approximated human standing was again a double inverted pendulum with torque-actuated ankle and hip joints, consistent with earlier results. A linear feedback controller based on position and velocity errors of each joint revealed that the relative cost between state deviation and control effort directly affected where intersection point crossed the vertical position with respect to the center of mass. A similar effect was obtained by varying the relative cost between the ankle and hip control effort. Among the many controller parameter sets considered, the one that best reproduced the human data used minimal control effort and more ankle torque than hip torque.

This suggests that the detailed profile of intersection point height variation with frequency is a signature of neural control.

#50 Inverse Rational Control

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A fundamental question in neuroscience is how the brain creates an internal model of the world to guide actions using sequences of ambiguous sensory information. This is naturally formulated as a reinforcement learning problem under partial observations, where an agent must estimate relevant latent variables in the world from its evidence, anticipate possible future states, and choose actions that optimize total expected reward. This problem can be solved by control theory, which allows us to find the optimal actions for a given system dynamics and objective function. However, animals often appear to behave suboptimally. Why? We hypothesize that animals have their own flawed internal model of the world, and choose actions with the highest expected subjective reward according to that flawed model. We describe this behavior as rational but not optimal. The problem of Inverse Rational Control (IRC) aims to identify which internal model would best explain an agent's actions. Our contribution here generalizes past work on Inverse Rational Control which solved this problem for discrete control in partially observable Markov decision processes. Here we accommodate continuous nonlinear dynamics and continuous actions, and impute sensory observations corrupted by unknown noise that is private to the animal. We first build an optimal Bayesian agent that learns an optimal policy generalized over the entire model space of dynamics and subjective rewards using deep reinforcement learning. Crucially, this allows us to compute a likelihood over models for experimentally observable action trajectories acquired from a suboptimal agent. We then find the model parameters that maximize the likelihood using gradient ascent. Our method successfully recovers the true model of rational agents. This approach provides a foundation for interpreting the behavioral and neural dynamics of animal brains during complex tasks. Finally, we show preliminary analyses from the application of this method to behavioral data from monkeys performing this task.

#51 Avian Model for the Development of Neural Activity Driven Speech and Vocalization Prostheses

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Neural prostheses hold the promise of restoring lost function for individuals with motor, speech, and language deficits due to injury and neurodegenerative disease, and to advance our understanding of how the brain controls complex behavior. While limb-based motor prostheses are actively studied and have yielded increasingly high performance, speech, language, and communications prosthesis development, while promising, is more limited. Our work seeks to accelerate speech and communications prosthesis development with an avian model that complements ongoing human studies.

A central aspect of this work is the collection and curation of large-scale datasets that include continuous measurement of vocalization behavior across hours and days along with neural activity from 100s of neurons from multiple brain regions recorded simultaneously, together with information on stimuli delivered and behavior-defining context manipulations. These data enable development and validation of machine learning models that map neural activity to behavior. As a complement to data acquired in human studies, our avian studies facilitate continuous data collection across multiple brain regions in highly controlled settings for larger cohorts of subjects. Thus, data from our studies can enable rapid prototyping of novel neural prosthetic system designs and can be applied to examine the potential for existing designs to generalize across subjects and behavioral contexts.

52 Network resonance can be generated at multiple levels of organization

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In response to oscillatory inputs at multiple frequencies, neuronal networks may exhibit network resonance: spiking activity preferentially occurs at intermediate frequencies. However, the mechanisms underlying network resonance remain poorly understood. In particular, it is not understood how neuronal activity at different levels of neuronal organization contributes to the generation of resonance exhibited by neuronal networks. Here, motivated by experimental findings, we investigate the possible sources of network resonance in a number of representative case studies using biophysically plausible (conductance-based) models and identify the filtering mechanisms that give raise to these phenomena in terms of the participating neuronal components. Using a model of persistent sodium and hyperpolarization-activated currents, we find that subthreshold resonance can be inherited to the spiking domain, which can in turn be inherited to postsynaptic neurons that otherwise do not exhibit resonance. Using a leaky integrate-and-fire model, which exhibits resonance generated directly at the spiking level, in the lack of subthreshold resonance, we show that the suprathreshold resonance can be inherited to postsynaptic neurons. A similar result is obtained using a model with voltage-dependent calcium dynamics. Using a model of short-term synaptic plasticity, we show that the synaptic resonance generated by the combination of synaptic depression and facilitation can be inherited to the spiking domain and to postsynaptic neurons. Finally, we find that resonance can be generated directly at the network level, without subthreshold, spiking, or synaptic resonance. Together, these results show that network resonance can be generated by a combination of low-pass filtering, high-pass filtering, and amplification mechanisms at either the same or different levels of organization. Our results shed light on the multiple circuit mechanisms that can be responsible for the generation of resonance in networks of neurons. Consistent with experimental findings, these scenarios go beyond the standard picture of resonance being generated by negative feedback mechanisms as the result of the interplay of excitatory and inhibitory neuronal populations.

#53 Dynamic visual processing coverage predicts observed differences in natural oculomotor behavior across mammals

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Most vertebrates use saccadic eye movements to quickly change gaze and sample different portions of the environment. Several hypotheses have been proposed to explain saccadic dynamics, from low-level automatic image analysis (e.g. decorrelating receptive field responses) to cognitive scanpaths (e.g. directing gaze towards new objects). The adaptive properties of visual neurons require that saccades should be large enough to sample local information that are uncorrelated with the previous fixation in order to maximize responsiveness. Using this rationale, we previously were able to predict average saccade sizes from the combination of receptive field sizes and natural scene statistics. This prediction applies not only to small fixational saccades, but to all saccades when free viewing natural scenes for both foveate and afoveate mammals. Adaptation recovery times can also explain saccade rate distributions in these different animal species. Here, we examine what general principles would drive the differences for both saccade sizes and rates across three species (mice, marmosets, humans) scanning the same set of natural images. We report that in order to achieve similar coverage over time, animals with larger receptive field sizes require slower rates. For all three animals, saccade rates and sizes decrease with smaller images and over time. Differences in the number of photoreceptors and V1 cells available to process the sampled visual information also appear to play a substantial role in determining saccade rate. We conclude that a diverse set of mammals share a common strategy of maintaining sufficient sampling coverage of their environment over time, under the constraint of conserving energy.

#54 **Short-term sensory memory mediates paradoxical neural-behavioral transformation in C. elegans**

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Habituation is a non-associative learning mechanism in which repeated exposure to the same stimulus results in decreased behavioral responses over time. Neuronal adaptation refers to the associated changes in neural processing that underlie this behavioral decrease in behavioral response. However, adapted (diminished) sensory responses can still elicit robust and non-habituating behavioral responses of uniform magnitude, under certain circumstances, suggesting that prior stimulation can maintain or increase information flow from sensory input to motor output. Our objective is to provide, through experiment and theoretical study, a hypothesis of what leads to neural adaptation and how that translates into behavioral decision making. We begin with a hypothesis that the sensory network attempts to optimize the speed and accuracy of detecting and representing exogenous stimuli. We postulate the network forms representations along two time-scales, one embedding immediate information and one embedding stimulus history (i.e., sensory memory) [1]. Thereafter, through formal mathematical approaches, we identify the optimal neural response strategy under competing different assumptions regarding the contribution of the latter, memory representation. We compare the ensuing neural responses in the model with response patterns as observed in vivo during odor stimulation of the nematode C. elegans using fluorescence microscopy and calcium imaging [2]. The model with explicit memory contributions best predicts experiments both for real-time dynamics and for adaptation levels as they vary with stimulus duty cycle, pulse duration, and inter-trial intervals. Next, we generated corresponding behavioral outputs using a parametric Bayesian decoder architecture which is steered by the latent representations generated by sensory activity. The predictions generated by this model were then validated through experimental observations in presence of odor-elicited behavior stimulus in C. elegans. Interestingly, the model predicted not only the expected regimes

of behavioral invariance (non-habituation) and habituation, but also an unexpected behavioral inversion, in which an appetitive stimulus elicits stimulus valence inverts such as an aversive response to an appetitive stimulus., at long duty cycles and low stimulus concentration. This paradoxical response, predicted for long duty cycles at low stimulus concentration, was indeed observed in C. elegans. Mechanistically, these results indicate that during sensory neural adaptation, the qualitatively inferior immediate stimulus representation can be compensated by secondary dynamical processes downstream of the sensory neurons, via a memory effect. Such dynamics may take the form of interneurons and/or modulatory processes such as neuropeptides, which remain to be studied. However, this compensation appears to may break down with certain stimulation conditions and can even elicit behaviors opposite to expected goal-directed behavior. Overall, our prediction-validation iterative approach provides insights regarding the importance of secondary network effects, beyond immediate sensory neural responses, in mediating sensory detection and behavior.

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#55 **Weak Evidence for Neural Correlates of Task-Switching in Macaque V1**

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A central goal of systems neuroscience is to understand how populations of noisy sensory neurons encode and relay information to the rest of the brain. Three key quantities of interest are (i) how mean neural activity depends on the stimulus (sensitivity), (ii) how neural activity (co)varies around the mean (noise correlations), and (iii) how predictive these variations are of the subject's behavior (choice probability). Previous empirical work is consistent with the idea that both choice probability and noise correlations are affected by task training, with decision-related information fed back to sensory areas and aligned to neural sensitivity on a task-by-task basis. We used Utah arrays to record activity from populations of V1 neurons from two macaque monkeys who were trained to switch between two coarse orientation-discrimination tasks. Surprisingly, we find no evidence for significant trial-by-trial changes in noise covariance between tasks, nor do we find a consistent relationship between neural sensitivity and choice probability, despite recording from well-tuned task-sensitive neurons, many of which were histologically confirmed to be in supragranular V1, and despite behavioral evidence that the monkeys switched their strategy between tasks. Thus our data at best provide weak support for the hypothesis that trial-by-trial task-switching induces changes to noise correlations and choice probabilities in V1.

#56 **Hierarchical statistical models for chronic neural recordings**

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An increasing amount of neural data is being collected using chronic recording techniques. The statistical analyses of such data require statistical tests that account for the day-to-day temporal structure in the collected data. Here we develop a hierarchical regression model for multiunit data collected from Utah arrays. Using ground-truth simulations, and actual data from area V1 during a perceptual decision-making task, we compare the results from our model with simpler alternatives. Those alternatives assume either perfect stationarity, i.e. the same neurons being recorded every day, or complete independence, i.e. different, independently sampled neurons recorded every day. Unsurprisingly, we find that scientific conclusions, e.g. based on the statistical significance of a correlation in the data, can depend critically on making the correct assumption about the data-generating process. We highlight four potential concerns when analyzing chronic array data, and offer concrete solutions to each: (i) accounting for error in both x and y measurements (ii) accounting for repeated measurements from individual electrodes across multiple days, (iii) accounting for variations in which units are picked up by each electrode, and (iv) accounting for day-by-day variations shared across entire arrays.

#57 **A method for detecting variable feedback signals in populations of sensory neurons**

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The activity of sensory neurons is the combined result of feedforward and feedback drives, each of which comprises a mix of meaningful signals and irrelevant signals or noise. Distinguishing between feedforward and feedback signals is important for understanding the nature of response covariability ("noise correlations") and its implications for neural coding. In prior studies, changes in neural covariability between different behavioral contexts ("task-switching") have been used to estimate the influence of feedback signals (Cohen & Newsome 2008, Bondy et al. 2018). Here, we propose a method to estimate a lower bound on the magnitude of task-related feedback without the need for data on a second task by comparing neural variability in the task-relevant direction with the neural variability in equivalent control directions in neural population response space. We observe that this comparison is confounded by the strength of the feedforward signal carried by the limited subset of recorded neurons to be a major confounding factor in this comparison, and show how to correct for the resulting bias. We validate our method using a model of realistic feedforward covariability in primary visual cortex based on Kanitscheider et al. (2015). We extend that model by incorporating heterogenous (learnt) receptive fields as well as variable feedback whose strength acts as ground truth for validating our method. In addition to an analysis of the resulting correlation structure, we perform a power analysis to obtain estimates of how much data is needed to reliably distinguish feedback from feedforward sources of variability.

CRCNS Workshop Attendee List

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4. **Thomas Serre**, *Brown Univ*.
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6. **Xue-Xin Wei**, *Univ. Texas, Austin*
7. **Memming Park**, *Stony Brook Univ*
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11. **Aaron Hsieh**, NYU student volunteer

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14. **Vikash Gilja**

15. **Gordon Berman**

16. **Dean Krusienski**

17. **Christine Constantinople**

18. **John Iversen**

19. **Yao Wang**

20. **Liang Zhan**

21. **Monty Escabi**

22. **Horacio Rotstein**

23. **Johnathan Aljadeff**

24. **Alex Reyes**

25. **Yaroslav Halchenko**

26. **David Lipschutz**

27. Prerana Vaddi

28. Shiva Farashahi, Flatiron

29. Sonat Aksamaz

30. Zach Zeisler, MSSM

31. Jingyang Zhou (Flatiron) -- FREE

32. Pierre-Eienne Fiquet (Flatiron) – FREE

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In-person main meeting registration

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3. **Jonathan D. Gould**, NYU volunteer
4. **Aaron Hsieh**, NYU volunteer
5. Carina Curto, PSU
6. Vikash Gilja, UCSD x 2 in person
7. Gordon Berman x 2 (in person + virtual)
8. Eero Simoncelli, NYU/Simons
9. Dean Krusienski
10. Christopher Del Negro
11. Stephen Van Hooser
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13. Cristina Savin, NYU
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24. Kenneth Whang, NSF
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