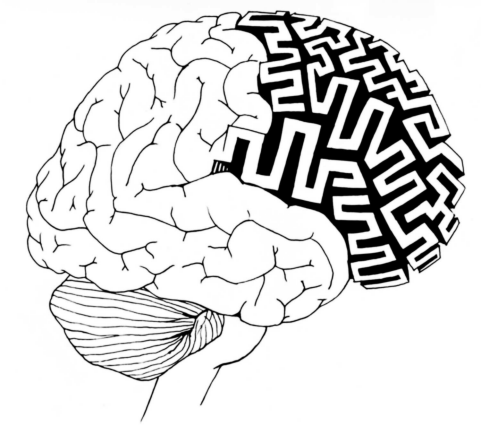
AREADNE 2008

Research in Encoding and Decoding of Neural Ensembles
Nomikos Conference Centre, Santorini, Greece
26–29 June 2008



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AREADNE 2008
Research in Encoding and Decoding of Neural Ensembles
Nomikos Conference Centre, Santorini, Greece, 26–29 June 2008
J. S. Pezaris and N. G. Hatsopoulos, editors

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WELCOME

Welcome

Welcome to AREADNE 2008, the second AREADNE Conference on Research in Encoding and Decoding of Neural Ensembles.

One of the fundamental problems in neuroscience today is to understand how the activation of large populations of neurons gives rise to the higher order functions of the brain including learning, memory, cognition, perception, action and ultimately conscious awareness. Electrophysiological recordings in behaving animals over the past forty years have revealed considerable information about what the firing patterns of single neurons encode in isolation, but it remains largely a mystery how collections of neurons interact to perform these functions.

Recent technological advances have provided a glimpse into the global functioning of the brain. These technologies include functional magnetic resonance imaging, optical imaging methods including intrinsic, voltage-sensitive dye, and two-photon imaging, high-density electroencephalography and magnetoencephalography, and multi-microelectrode array electrophysiology. These tools and techniques have expanded our knowledge of brain functioning beyond the single neuron level.

At the same time, our understanding of how neuronal ensembles carry information has allowed the development of brain-machine interfaces (BMI) to enhance the capabilities of patients with sensory and motor deficits. Knowledge of how neuronal ensembles encode sensory stimuli has made it possible to develop perceptual BMIs for the hearing and visually impaired. Likewise, research in how neuronal ensembles decode motor intentions has resulted in motor BMIs by which people with severe motor disabilities can control external devices.

Conference Mission Statement

There are three major goals of this conference. First and foremost, this conference is intended to bring scientific leaders from around the world to present their recent findings on the functioning of neuronal ensembles. Second, the meeting will provide an informal yet spectacular setting on Santorini in which attendees can discuss and share ideas outside of the presentations at the conference center. Third, this conference continues our long term project to form a systems neuroscience research institute within Greece to conduct state-of-the-art research, offer meetings and courses, and provide a center for visiting scientists from around the world to interact with Greek researchers and students.

Organizing Committee

The AREADNE 2008 conference was organized by Nicholas Hatsopoulos (Co-Chair) and John Pezaris (Co-Chair), Dora Angelaki, Catherine Ojakangas, Thanos Siapas, and Andreas Tolias.

Local Organizers

Local organization effort has been provided by Nike Makris with assistance from Erika Berry and Josh Markey.

Sponsors

Our conference is being sponsored by The University of Chicago's Center for Integrative Neuroscience and Neuroengineering Research (CINNR) with the help of a generous gift from Dr. and Mrs. George Hatsopoulos. We have included a statement from CINNR below:

CINNR is proud to support the AREADNE Conference on Research in Neural Encoding and Decoding of Neural Ensembles. At CINNR, our mission is to foster research in systems and behavioral neuroscience

at the University of Chicago and neural engineering at Illinois Institute of Technology. Work in the Center proceeds from basic science and clinical efforts and emphasizes interdisciplinary approaches to understanding the nervous system. Research in the Center involves a wide range of projects, but five research goals are currently emphasized: (A) To understand how information is coded by large populations of neurons. This involves collaborative efforts between neuroscientists, mathematicians, statisticians, and computer scientists. (B) To use developing knowledge about neural codes to design and implement neural prosthetic devices (or brain machine interfaces) that can be implanted in the retina or visual centers of the central nervous system. Such devices can ameliorate the loss of vision, and can be implanted in the motor cortex and used to control movements in paralyzed patients. (C) To increase our understanding of the basic causes of epilepsy, to develop new technologies that allow the prediction of epileptic seizures and the location of epileptic tissue in the brain, and to use brain machine interfaces to control seizures. (D) To use neuroimaging technologies to understand how cognitive behaviors are coded in the human brain. (E) To use methods from molecular biology to understand how events at the molecular level are related to normal behaviors and to disease states such as Alzheimer's disease, drug or alcohol abuse or psychiatric disorders.

Additional information about CINNR, its members and events can be found at www.cinnresearch.org.

The Myth of Ariadne

The conference name AREADNE is a combination of the conference title, Research in Encoding and Decoding of Neural Ensembles, and the name of the mythological figure Ariadne. Our brain-to-maze logo was inspired by the central role Ariadne played in the myth of Theseus and the Labyrinth.

Ariadne was the daughter of Minos, king of Crete. King Minos built a large, intricate maze called the Labyrinth to house the Minotaur, a fearsome creature that was half bull, half human. Any who attempted to face the Minotaur perished, either by becoming lost in the maze or from the Minotaur's vicious attack. When the hero Theseus came from Athens to slay the Minotaur, Ariadne gave him a sword and a ball of silk thread. Theseus tied one end of the thread at the Labyrinth entrance and unwound it as he went along, so that after he had found and slain the Minotaur, he could escape from the maze by following the thread back out.

LOCAL INFORMATION

We have assembled a bit of local information on Fira and the island of Thera. For additional information, we recommend selecting one of the many guidebooks that have been written on island travel in Greece.

Restaurant Information

Greeks normally eat their evening meal quite late, with restaurants being busiest between 10pm and midnight. The largest meal of the day is often lunch, leading quite naturally to the habitual afternoon nap. Tipping at restaurants is not expected, as the cost of service is normally included in the price of the meal.

Restaurants in Fira

Ambelos, tel +30-22860-22544, caldera view, wine restaurant, about EUR 20 per person

Archipelagos, tel +30-22860-23673, caldera view, Santorini cuisine, about EUR 30 per person

Koukoumavlos, tel +30-22860-22510, caldera view, nouvelle cuisine, about EUR 40 per person

Nikolas, tel +30-22860-24550, Greek cuisine, next to the Town Club, about EUR 15 per person

Poldo, tel +30-22860-24004, souvlaki stand, near the National bank, about EUR 5 per person

Restaurants in Firostefani

Vanilia, tel +30-22860-25631, local cuisine, about EUR 35 per person

Cantuccio, tel +30-22860-22082, Italian cuisine, about EUR 20 per person

Restaurants in Oia

Iliovassilema, tel +30-22860-71614, fresh fish, about EUR 20 per person

Thalami, tel +30-22860-71009, ouzo bar, about EUR 15 per person

1800, tel +30-22860-71485, nouvelle cuisine, about EUR 40 per person

Restaurants in Perivolos-Vlychada

Vlychada, tel +30-22860-82819, Greek taverna by the beach, about EUR 20 per person

The Net, tel +30-22860-82818, fish tavern by the sea, local cuisine, about EUR 40 per person

Recommended Activities

In addition to sweeping vistas, Santorini boasts excellent nightlife, a respectable wine industry, beaches with white, black, or red sand, excavations of ancient civilizations, and some of the best sunsets around.

We are planning optional guided excursions to the archaeological site of Ancient Thera and to the volcano island and sulfur springs at the center of the caldera. These events may not be able to accommodate everyone.

Beyond these two tours (which can be taken privately as well, although without the benefit of our invited experts), there are plenty of other activities on the island. A few suggestions to scratch the surface are listed below.

Archaeological Museum at Fira
open 08.30–15.00 (closed Mondays), tel +30-22860-22217, Ypapantis Street, Fira

Museum of Prehistoric Thera
open 08.30–15.00 (closed Mondays), tel +30-22860-23217, Mitropoleos Street, Fira

Folk Art Museum
open 10.00–14.00 and 18.00–20.00, tel +30-22860-22792, Kondohori, near Fira

Wine Museum
open daily 12.00–20.00, tel +30-22860-31322, located in Vothonas village

Oia at sunset
sunset is at approximately 8pm in late June; once you get to Oia, follow the crowds westward

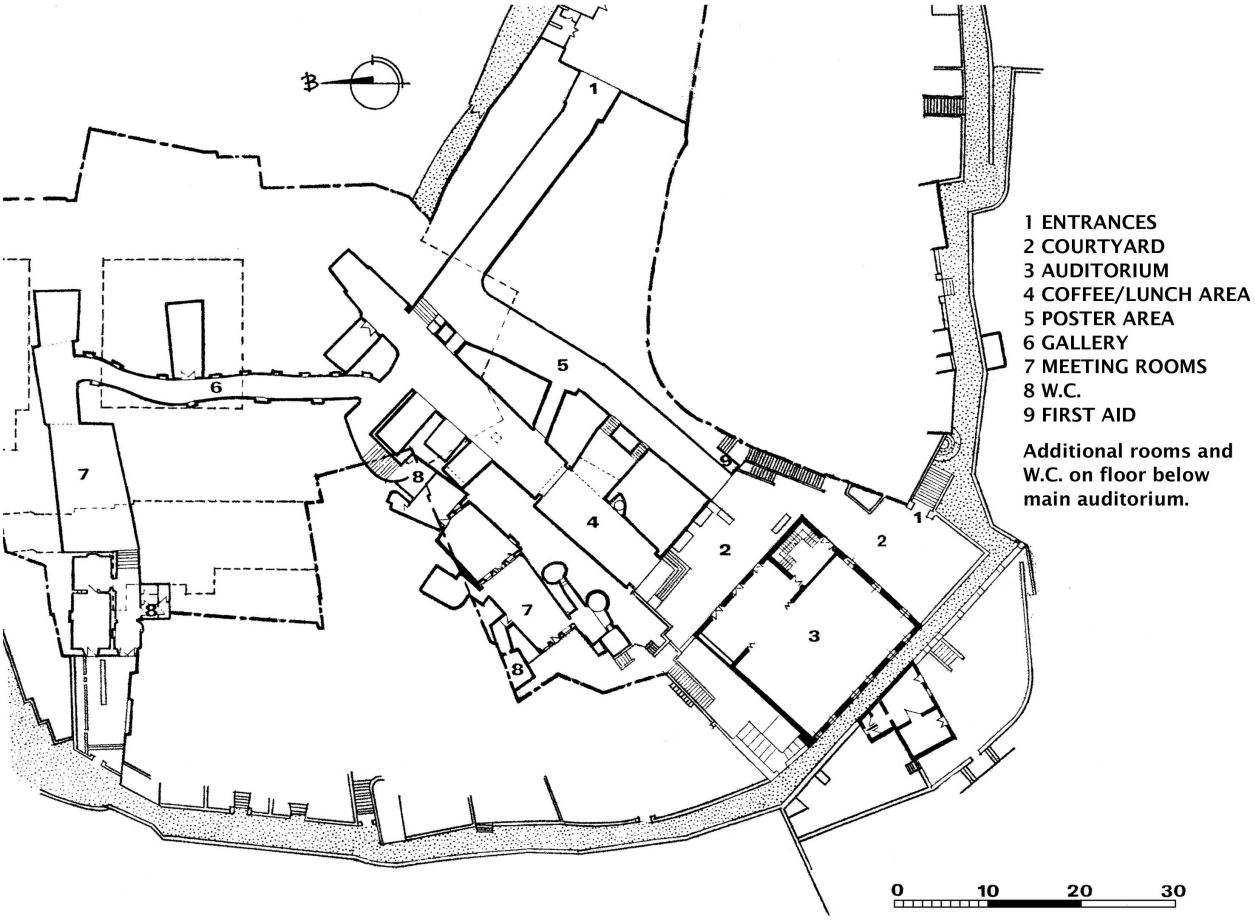
Monastery of Profitis Ilias
in Pyrgos, at the peak of the highest mountain on the island; has a nice ecclesiastic museum

Main Beaches

The beaches on Santorini are beautiful and varied, with white, red, and black sand depending on location. However, swimming must be done with some care as the water gets deep very quickly and rip currents are not uncommon. Flip-flops are a must as the dark sand can get extremely hot in the sun. SCUBA diving is available with trips to wrecks, the volcano, and the underwater caldera face. Beaches are at Perivolos (13 km from Fira), Perissa (13 km), Vlychada (12 km), and Kamari (10 km).

Conference Centre Map

Oral presentations will be held in the main auditorium of the Centre. Coffee breaks will be held in the reception area and courtyard. Posters will be hung on the walls of the passage from the courtyard to the gallery. A first aid station will be available. Please refer to the map below for more details.



DAILY SCHEDULE AND PROGRAM

Overall Schedule

The schedule for the four-day conference follows the Greek lifestyle of having a long lunch, with the afternoon free for siestas or swimming, and a late dinner.

Wednesday

19:00–21:00	welcome reception

Thursday

08:00–08:30	registration
08:30–09:00	opening remarks
09:00–12:30	lectures and coffee break
12:30–14:00	lunch
17:00–21:30	lectures, coffee break and posters

Friday

09:00–12:30	lectures and coffee break
12:30–14:00	lunch
17:00–21:30	lectures, coffee break and posters

Saturday

09:00–12:00	optional excursions (no lunch provided)
17:00–21:30	lectures, coffee break and posters

Sunday

09:00–12:30	lectures and coffee break
12:30–14:00	lunch
17:00–19:00	lectures and coffee break
19:00–19:30	closing remarks
21:00–24:00	banquet dinner

WEDNESDAY, JUNE 25

19:00–21:00 welcome reception at Nomikos Centre

THURSDAY, JUNE 26

08:00–08:30 registration

08:30–09:00 opening remarks

MORNING SESSION Ken Blum, moderator

09:00–09:45 **Gilles Laurent** (California Institute of Technology) *Odor mixture segmentation in an olfactory system*, 26

09:45–10:30 **Larry Abbott** (Columbia University) *Encoding and transformation in the olfactory system of the fly*, 20

10:30–11:00 coffee break

11:00–11:45 **Dora Angelaki** (Washington University in St. Louis) *Functional links between cortical visual and vestibular neurons and multisensory perception*, 21

11:45–12:30 **William Newsome** (HHMI and Stanford University) *To stay or to switch? Neural correlates of choice strategy in simple foraging tasks*, 32

12:30–14:00 lunch

AFTERNOON SESSION Nicholas Hatsopoulos, moderator

17:00–17:45 **Jason MacLean** (University of Chicago) *Up states render neocortical networks insensitive to thalamic inputs*, 28

17:45–18:15 coffee and light snacks

18:15–19:00 **Krishna Shenoy** (Stanford University) *Extracting dynamical structure embedded in premotor cortical activity*, 37

19:00–19:45 **Alexandre Pouget** (University of Rochester) *Neuronal variability: Noise or incompetence?*, 35

20:00–21:30 posters, presenting author

Nikolaos Aggelopoulos (MPI Biological Cybernetics) *The sparseness of stimulus encoding by single neurons and by populations of neurons in the inferior temporal cortex*, 42

Francois Grimbert (INRIA Sophia Antipolis) *A neural field model of VSDOI signals*, 59

Chloe Huetz (BCCN Freiburg) *Discriminating sounds from human electrocorticograms (ECoG)*, 60

Georgios Keliris (MPI Biological Cybernetics) *The role of primary visual cortex in perceptual awareness*, 61

Bjørg Elisabeth Kilavik (INCM-CNRS) *Frequency and amplitude modulations of motor cortical local field potentials during temporal attention and movement preparation*, 62

FRIDAY, JUNE 27

MORNING SESSION John Pezaris, moderator

09:00–09:45 **J. Anthony Movshon** (New York University) *Optimal inference from population responses in visual cortex*, 31

09:45–10:30 **Tatiana Pasternak** (University of Rochester) *Bottom-up and top-down cortical signals during motion discrimination tasks*, 33

10:30–11:00 coffee break

11:00–11:45 **Lynne Kiorpes** (New York University) *What does MT contribute to the perception of visual motion: lessons from development and amblyopia*, 26

11:45–12:30 **Lee Miller** (Northwestern University) *In vivo, spike-timing dependent changes in network functional connectivity revealed by changes in spiking statistics*, 30

12:30–14:00 lunch

AFTERNOON SESSION Catherine Ojakangas, moderator

17:00–17:45 **Thanos Siapas** (California Institute of Technology) *Cortico-hippocampal network dynamics and associative learning*, 38

17:45–18:15 coffee and light snacks

18:15–19:00 **Erin Schuman** (HHMI and California Institute of Technology) *Learning and representation of declarative memories by single neurons in the human hippocampus and amygdala*, 36

19:00–19:20 **Desmond Patterson** (Patterson Instruments) *Big hill him go bang: A condensed explanation of volcanic eruptions*, 34

19:20–19:40 **Andronike Makris** (Hellenic Education and Research Center) *Ancient Thera*, 29

20:00–21:30 posters, presenting author

Fritzie Arce (Hebrew University) *Reaching between lines: rectilinear versus curvilinear trajectories during adaptations to force fields and visuomotor rotations*, 44

Eliana Klier (WUSTL School of Medicine) *Visuospatial updating after passive rotations and translations in three-dimensional space*, 63

Vasileios Kokkinos (University of Patras) *The K-complex initially blocks fast spindles and afterwards evokes faster spindles during stage II of human NREM sleep*, 64

Apostolis Konstantinopoulos (University of Patras) *Eye artifact rejection in EEG data using second order statistics (SOBI method)*, 65

Dimitrios Kourtis (University of Birmingham) *Steady-state somatosensory evoked potentials as a means of probing somatosensory cortex excitability*, 66

Shih-pi Ku (MPI Biological Cybernetics) *Analysis of pattern recognition methods in classifying BOLD signals in monkeys at 7 Tesla*, 67

Aurel Lazar (Columbia University) *Encoding, processing and decoding of sensory stimuli with a spiking neural population*, 68

Nicholas Lesica (LMU Munich) *Enhanced coding of interaural time differences at successive stages in the ascending auditory pathway*, 69

Stefanie Liebe (MPI Biological Cybernetics) *Prediction of behavioral choice and reaction time from local field potential in macaque prefrontal cortex*, 70

Matthieu Louis (Ctr. for Genomic Regulation) *Chemotaxis in drosophila larvae: coding the way forward*, 72

Jakob Macke (MPI Biological Cybernetics) *The role of stimulus correlations for population decoding in the retina*, 73

Keeran Maharajh (U. Colorado, Denver) *Coupling neuronal ensemble mesostate probabilities with information from global activity: a formulation and application to magentoencephalography*, 74

Yael Mandelblat-Cerf (Hebrew University) *How far in time and space do we generalize? Patterns of generalization and its decay while adapting to a novel motor task*, 75

Sotiris Masmanidis (Caltech) *Modular silicon probes for dense mapping of neuronal ensemble activity*, 76

Tomislav Milekovic (BCCN Freiburg) *Control- and performance-error signals in the human electrocorticogram (ECoG)*, 77

Gabriela Mochol (Nencki Inst. of Exp. Biology) *Different cell populations in the superior colliculus use different coding schemes*, 78

Julien Modolo (IMS UMR CNRS 5218) *Mechanism of deep brain stimulation: exploring resonance and simulation-induced decoupling*, 79

Theofanis Panagiotaropoulos (MPI Biological Cybernetics) *Single units reflect visual awareness in the macaque prefrontal cortex*, 80

Panos Pardalos (University of Florida) *Automatic detection of epileptic seizures based on spatiotemporal dynamics of scalp EEG signals*, 86

Laurent Perrinet (DyVA-INCM/CNRS) *Decoding the population dynamics underlying ocular following response using a probabilistic framework*, 81

Tobias Pistohl (BCCN Freiburg) *Decoding natural grasps from human ECoG*, 82

Adrian Ponce Alvarez (INCM CNRS) *Dynamic sequences of states in ensembles of motor cortical neurons*, 83

SATURDAY, JUNE 28

09:00–13:00 optional excursions (no lunch provided)

AFTERNOON SESSION Andreas Tolias, moderator

17:00–17:45 **John Donoghue** (Brown University) *Neural activity in the motor cortex of humans with tetraplegia*, 22

17:45–18:15 coffee and light snacks

18:15–19:00 **George Kostopoulos** (University of Patras) *Neuronal assemblies supporting brain rhythms transformations in sleep and epilepsy*, 25

19:00–19:45 **Panayiota Poirazi** (Institute of Molecular Biology and Biotechnology) *Information processing in single cells and small networks: Insights from compartmental models*, 35

20:00–21:30 posters, presenting author

John Reppas (Stanford University) *Ensemble recordings of neural activity in the prefrontal cortex during oculomotor choice behavior*, 84

Gerard Rinkus (Brandeis University) *Population coding using familiarity-contingent noise*, 85

Maryam Saleh (University of Chicago) *Simultaneous encoding of reach and grasp kinematics in MI and PMv*, 87

Peggy Series (University of Edinburgh) *Shannon versus Fisher information in large populations of neurons*, 88

SUNDAY, JUNE 29

MORNING SESSION Stelios Smirnakis, moderator

09:00–09:45 **Jennifer Groh** (Duke University) *Visual signals in the early auditory pathway (inferior colliculus)*, 23

09:45–10:30 **Sara Solla** (Northwestern University) *Laminar organization of the excitatory network in motor cortex*, 39

10:30–11:00 coffee break

11:00–11:45 **John Dani** (Baylor College of Medicine) *Dopaminergic and nicotinic cholinergic mechanisms alter transfer of information in the CNS*, 22

11:45–12:30 **Michelle Basso** (University of Wisconsin) *A Bayesian readout of superior colliculus populations predicts movement decisions*, 27

12:30–14:00 lunch

AFTERNOON SESSION John Pezaris, moderator

17:00–17:45 **Naoum Issa** (University of Chicago) *Encoding complex images in the population activity of the early visual system*, 24

17:45–18:15 coffee and light snacks

18:15–19:00 **S. Murray Sherman** (University of Chicago) *The role of thalamus: Relay functions and more*, 38

19:00–19:30 closing remarks

21:00–24:00 banquet dinner at Selene Restaurant

SPEAKER ABSTRACTS

(in alphabetical order by speaker)

ENCODING AND TRANSFORMATION IN THE OLFACTORY SYSTEM OF THE FLY

Larry Abbott (Columbia University)

As information passes from olfactory receptor neurons, through the antennal lobe projection neurons and on to third-order neurons in the protocerebrum and mushroom body of the fly brain, it undergoes a series of transformations. I will discuss how encoding of odorant identity is transformed along this pathway leading to a sparse representation of essentially unique odors.

FUNCTIONAL LINKS BETWEEN CORTICAL VISUAL AND VESTIBULAR NEURONS AND MULTISENSORY PERCEPTION

Dora E. Angelaki[1], *Yong Gu*[1], *Greg C. DeAngelis*[2] ([1]Washington University in St. Louis, [2]University of Rochester)

Human observes combine sensory cues according to a statically optimal scheme derived from Bayesian probability theory, but little is known about the underlying neuronal mechanisms. Here we explore multisensory cue integration for self-motion (heading) perception using both visual (optic flow) and vestibular (linear acceleration) signals. Monkeys were trained to perform a fine heading discrimination task where heading stimuli cues were delivered in three ways: (a) inertial motion only (vestibular condition); (b) optic flow only (visual condition); (c) congruent combination of inertial motion and optic flow (combined condition). Trained monkeys, like humans, behaviorally combine visual and vestibular cues to improve heading perception.

We recorded from single neurons in the dorsal medial superior temporal area (MSTd) while the monkeys performed the heading discrimination task. Area MSTd is thought to be involved in heading perception, as neurons in this area are sensitive to global patterns of optic flow as well as translation in darkness. Under bimodal stimulation, MSTd neurons combine visual and vestibular cues linearly but sub-additively. Neurons with congruent heading preferences for visual and vestibular stimuli show improved sensitivity and lower neuronal thresholds under cue combination. In contrast, neurons with opposite preferences show diminished sensitivity under cue combination.

We further show that in the vestibular condition MSTd responses are significantly correlated with the monkeys' perceptual decisions (*choice probabilities*, CPs), independent of visual/vestibular congruency. In contrast, CPs in the visual condition depended strongly on congruency. Whereas for congruent cells, the average visual CP (0.59) is substantially greater than chance, indicating that these neurons fire more strongly when the monkey reports moving toward their preferred heading, opposite cells have an average visual CP (0.45) that is significantly less than 0.5, indicating that they tend to fire more strongly when the monkey reports their non-preferred sign of heading. This suggests that both congruent and opposite cells may contribute to purely visual judgments of heading, but that their activities are read out, or decoded, differently. In the combined condition, we also find that congruent cells have an average CP (0.58) that is substantially greater than chance, whereas opposite cells do not (0.48). Thus, congruent cells are more strongly linked to perceptual decisions during bimodal stimulation. In contrast, opposite neurons may be given less weight during cue integration because they carry less reliable heading information.

These differences in CP with congruency could be explained by differences in correlated activity among neurons. In pairs of neurons recorded simultaneously, however, we found no dependence of noise correlations on visual/vestibular congruency or stimulus condition. Rather, the observed differences in correlation of neuronal activity with perception are consistent with the notion that they might be related to population decoding for multisensory perception. These findings provide the first behavioral demonstration of cue integration in non-human primates and identify a population of neurons that may form its neural basis.

Supported by NIH grants EY017866 and DC04260.

DOPAMINERGIC AND NICOTINIC CHOLINERGIC MECHANISMS ALTER TRANSFER OF INFORMATION IN THE CNS

John A. Dani, Daoyun Ji, Lifen Zhang, Tiangxiang Zhang, Fu-Ming Zhou (Baylor College of Medicine)

To pass along the information contained in action potentials, spikes usually have to be translated into neurotransmitter release at synapses. Many mechanisms are known to modulate this information transfer process. Data will be presented focusing on the neurotransmitter systems for dopamine and acetylcholine. The following mechanisms will be considered: (A) Induction of synaptic plasticity is modulated by nicotinic acetylcholine receptors. The synaptic modulation is dependent on the location and timing of the nicotinic activity. (B) Unit recordings from freely-moving rats revealed that nicotine increases the burst firing of dopamine neurons throughout the midbrain. However, the frequency dependence for dopamine release varies within different terminal fields. Consequently, nicotine increases the general dopamine concentration mainly in only one target area. (C) During antidepressant treatment with selective serotonin reuptake inhibitors, dopamine terminals begin to release both dopamine and serotonin (5-HT). In this case, when dopamine neurons fire, they also send a 5-HT signal, altering the temporal and spatial relationship between dopamine and 5-HT signaling.

NEURAL ACTIVITY IN THE MOTOR CORTEX OF HUMANS WITH TETRAPLEGIA

John Donoghue, J. Simeral, M. Black, S-P. Kim, W. Truccolo, L. Hochberg (Brown University)

Neural interface systems (NIS) are being designed to help restore communication and control to humans with tetraplegia. The advent of NIS clinical trials using implanted microelectrode arrays has provided a unique opportunity to examine spiking of a population of neurons and local field potentials (LFP) in conscious humans. In our pilot clinical trial we have recorded signals in the motor cortex of four humans: two with spinal cord injury, one with ALS and one with a brainstem stroke. We have found that motor cortex in these participants share many features of its homologue in able bodied non-human primates, including velocity and position tuning, and somatic sensory receptive fields. In addition, we found that neurons are activated by imagined (?) or attempted action in the absence of movement. Neurons related to various imagined arm and hand actions are intermingled within a small (4×4 mm) patch of motor cortex. Using a Bayesian decoding method, humans with tetraplegia can carry out point and click cursor actions and control robotic devices using the spiking of small populations of neurons. I will discuss the features of the motor cortical neurons in human participants and the potential for humans to use cortical activity to achieve direct control of assistive devices using a NIS.

Support: VA, NIH NINDS Javits Award, NICHD, NIBIB, ONR

VISUAL SIGNALS IN THE EARLY AUDITORY PATHWAY (INFERIOR COLLICULUS)

Jennifer M. Groh[1], *David A. Bulkin*[1], *Kristin K. Porter*[2] ([1]Duke University, [2]University of Alabama School of Medicine)

The textbook view of sensory processing is that each individual sensory system has its own dedicated pathway for processing the physical attributes of the stimulus, and that interactions between sensory processing do not occur until signals reach higher-order cortical structures known as association cortex. An important test of this view is to investigate early, supposedly unimodal brain regions for evidence of input from other sensory modalities.

The inferior colliculus (IC) is intriguing in this regard because it is situated early in the auditory processing stream—before auditory signals reach thalamus or cortex—and yet it has been implicated in visually-guided calibration of auditory space in barn owls. We have previously found evidence for eye position sensitivity in the primate IC. This suggests that the IC may play a role in mediating visual and auditory interactions.

Do IC neurons respond to visual stimuli? We found that a majority of IC neurons (64 percent of 180 neurons) in awake monkeys carried visual and/or saccade-related signals in addition to their auditory responses. The response patterns included excitatory and inhibitory visual responses, increased activity time-locked to the saccade, and slow rises in activity time-locked to the onset of the visual stimulus.

Which IC neurons respond to visual stimuli? Based on several previous studies in species other than primates, it has been suggested that the ICX plays a role in multisensory processing but the ICC (central nucleus) does not. To see if this was true for visual signals, we conducted a series of mapping experiments in which assessed multiunit activity at regular intervals throughout the IC. We found visual responses in both putative ICX and putative ICC, in approximately equal proportions. This suggests that in the primate, both of these subregions of the IC play a role in integrating visual and auditory information. More broadly, our results show that interactions between sensory pathways can occur at very early points in sensory processing streams. This in turn implies that multisensory integration may be a low-level rather than an exclusively high-level process.

ENCODING COMPLEX IMAGES IN THE POPULATION ACTIVITY OF THE EARLY VISUAL SYSTEM

Naoum Issa (University of Chicago)

Visual scenes are encoded throughout the visual system by the distributed activity of neurons with a variety of response properties, some linear, some not. The linear representation of scenes across primary visual cortex can be predicted to a large extent from high-resolution maps of spatiotemporal tuning properties including orientation, spatial frequency and temporal frequency preferences and bandwidths. For example, population responses change with image drift speed in a predictable way that depends on the combination of all the tuning properties. Early visual cortical areas also have nonlinear representations of scenes, and it is typically thought that these nonlinear representations derive from intra-cortical processing. In particular, second-order image features—features that cannot be detected by linear filtering mechanisms and therefore are not predicted by maps of spatiotemporal tuning properties—are often argued to be first synthesized in V2 by combining the outputs of V1. We show, however, that this nonlinear representation is already present in a subset of LGN neurons and that these responses account for many of the cortical tuning properties to second-order stimuli. We suggest that in the earliest cortical stages there are two parallel, orientation selective streams built from fundamentally different inputs, one responsive to Fourier energy in the stimulus (the linear stream) and the other responsive to second-order image features (a non-linear stream).

NEURONAL ASSEMBLIES SUPPORTING BRAIN RHYTHMS TRANSFORMATIONS IN SLEEP AND EPILEPSY

George K. Kostopoulos (University of Patras)

Recent electrophysiological studies of brain rhythmical activities open a window to the highly integrated nature of its functioning across time and space scales. Area-specific relatively higher frequency oscillations are increasingly shown to be nested in and modulated by more widely synchronized slow rhythms. The respective phase and power relationships determine the rhythms' impact on very important brain functions like input gating, binding and synaptic plasticity modulation. Some changes in brain function and indeed some brain malfunctions seem to involve transformations of such rhythm patterns based on mechanisms of short or long term synaptic plasticity. Evidence supporting and qualifying these notions will be reviewed from work in our laboratory at the University of Patras, as well as older work at the Montreal Neurological Institute and our recent collaboration with the Human Brain Dynamic Laboratory, RIKEN, Japan.

(A) Animal experiments partly supported by clinical EEG studies have shown that spike and wave discharges (SWD) characterizing absence seizures may develop in the same cortico-thalamo-cortical circuits which elaborate normal sleep spindles (13–15 Hz). The transformation of the latter rhythm to SWD (3 Hz) appears to demand mild but hypersynchronous across cortex hyperexcitability (possibly spear-headed by focal cortical events), which by exciting thalamic reticular neurons forces the thalamic pace-maker to multiply the duration of its inhibitory period. The result is loss of consciousness.

(B) The appearance of the characteristics of the second stage of non-REM sleep K-Complexes and spindles depends on cortical and thalamic pacing respectively. We show that when the two overlap, K-complexes stop completely the running spindle rhythm, but immediately after they trigger spindles always faster by about 1 Hz. This rhythm resetting is most likely again a cortical influence on thalamic pacing mechanisms.

(C) Hippocampal circuits elaborate sleep related sharp-wave-ripples (SWR) in an area specific way: we observed $in\ vitro$ synchronous activity resembling SWR in slices from ventral but not dorsal hippocampus. The fact that the ventral part of hippocampus is much more epileptogenenic than the dorsal one may be related to our observation that NMDA-receptor dependent epileptogenesis in these slices was characterized by long-term potentiation of high-frequency oscillations.

(D) MEG whole sleep recordings at RIKEN analyzed with Magnetic Field Tomography (Ioannides, 2006) revealed an area in left dorsal medial frontal cortex, which during deep slow wave sleep displays gamma band activity higher than active wake condition. Since subcortical afferents to thalamocortical circuits are not conducive to gamma band activation at this stage, while delta wave related inhibition is maximal in the wider area, we propose gamma activation may arise from intracortical lateral disinhibition.

Examples (A) and (B) are instances of rather slower rhythm transformations at the brain's major hub, the thalamus, while examples (C) and (D) suggest that (archi- and neo-) cortex can also sustain circuit interactions leading to the development of strong, fast rhythms. The possibility of transformations and resetting of rhythms suggest that what appears as a large number of brain rhythms may be supported by relatively few pacing mechanisms, which however are highly interacting and exceptionally sensitive to a plethora of conditions.

WHAT DOES MT CONTRIBUTE TO THE PERCEPTION OF VISUAL MOTION: LESSONS FROM DEVELOPMENT AND AMBLYOPIA

Lynne Kiorpes, J. Anthony Movshon (New York University)

Neurons in macaque monkey MT/V5 are known to be selective for motion speed and direction. Previous research has shown a close correspondence between psychophysically measured motion sensitivity of adult monkeys and the response properties of MT neurons. Hence, it is widely assumed that MT represents an important neural substrate for perception of visual motion. Sensitivity to visual motion is immature in primate infants and develops over a long, slow time course that continues over the first 3 years after birth in monkeys and up to age 10 in humans. This developmental process is compromised by abnormal visual experience during an early critical period. Using a population analysis, we evaluated the relationship between neuronal motion signaling and behaviorally measured motion sensitivity during normal development and following abnormal visual experience.

We used random dot kinematograms (RDKs) as stimuli for psychophysics and physiology; in both cases, the displays were optimized for best performance/response. Behavioral data showed poor coherence sensitivity in young monkeys and better sensitivity to fast speeds compared to slow speeds. In animals with poor vision resulting from abnormal visual experience during development (amblyopia), the deprived eyes showed reduced coherence sensitivity that was especially pronounced at slow speeds. The physiological data reflected some, but not all, of the abnormal patterns seen in the behavioral data. Many basic response properties of MT neurons were adult-like in 1-week-old monkeys. Most neurons were selective for direction and speed but coherence sensitivity was weak. Similarly, in adult amblyopic monkeys, basic properties of MT neurons were normal but coherence sensitivity of neurons driven by the deprived eye was poor and the distributions of preferred speed were shifted toward faster speeds for amblyopic eye cells.

To compare psychophysics and physiology we used a simple pooling model to construct neurometric functions for discrimination of preferred vs. anti-preferred direction as a function of coherence for cells recorded from infants at each age and for each eye of amblyopes. For the infants, the change in behavioral threshold parallels neuronal threshold change up to 16 weeks but not thereafter. For amblyopes, neurometric functions for the amblyopic eye were all shifted to higher coherence levels compared to the fellow eye but in only 1 of 4 cases was the shift greater than would be expected by chance. Additional psychophysical and oculomotor data from our lab also suggest a mismatch between motion perception and the properties of MT neurons. These results suggest that mechanisms downstream from MT actually limit motion sensitivity.

ODOR MIXTURE SEGMENTATION IN AN OLFACTORY SYSTEM

Gilles Laurent (California Institute of Technology)

The olfactory system is an interesting sensory system with which to study general issues of sensory coding and plasticity. It accomplishes simpler tasks than visual or auditory systems do, and solves in very few steps. I will describe a Hebbian homeostatic mechanism involved in the regulation of spike timing in the third layer of this system, and the possible consequences that this property might have for learning and memorization of odors.

A BAYESIAN READOUT OF SUPERIOR COLLUCULUS POPULATIONS PREDICTS MOVEMENT DECISIONS

Michelle A. Basso, Byounghoon Kim (University of Wisconsin)

How perceptions, thoughts, decisions and actions arise from the activity of populations of neurons is arguably the most vexing question in cognitive neuroscience. A number of lines of evidence from experimental work in monkeys reveal that perceptual decisions evolve within eye movement (saccade) centers of the brain such as the lateral intraparietal area (LIP), frontal eye fields (FEF) and the midbrain superior colliculus (SC).

Simultaneous recordings from multiple neurons within the monkey SC made during performance of a task in which one, differently-colored target appears in an array with three, samecolored stimuli, reveal that when the discriminability between the level of target and distractor neuronal activity is high, saccade choices are likely to be accurate. In contrast, when the discriminability between the level of activity of target and distractor neurons is reduced, saccade choice performance is likely to be poor. Indeed, ROC analysis showed that ROC area (and d, a measure of discriminability) scaled approximately linearly with the choice performance of monkeys. The results overall were consistent with the suggestion that SC neuronal activity signals an eye movement decision. Multiple neuron recording results also reveal that the choice of the particular saccade depends upon the combined activity of neurons representing targets and distractors.

A critical, unresolved issue is how the activity of SC neurons signaling targets and distractors is pooled to contribute to the saccade choice and then, how the pooled activity is read-out to result in a saccade. In other words, a key question remains unknown; what is the decision rule that underlies movement choice? To explore this latter question, we implemented and compared three decoding schemes using the simultaneously recorded SC neuronal data population vector average (PVA), winner-takes-all (WTA) and a Bayesian decoder, maximum a posterior estimate (MAP).

We recorded from four SC neurons simultaneously while monkeys made a choice of one saccade from among four possible. When choice performance ranged between 60–99% accurate, both the WTA and the PVA predicted saccade choices correctly on about 70% of the trials. On the subset of trials when performance was 100% accurate, the PVA still predicted saccade choices correctly for only about 70% of the trials, whereas WTA predicted saccade choices correctly on 80% of trials. Thus, the accuracy of the PVA and WTA decoding schemes varied with performance accuracy and PVA predicted saccade choices maximally on only about 70% of the trials. The Bayesian decoder in contrast, predicted saccade choices very well (80%) for each level of choice performance. Based on these results we conclude that probabilistic decoding schemes are likely to hold the key to understanding how populations of neurons are combined and read-out to result in goal-directed saccade behavior.

UP STATES RENDER NEOCORTICAL NETWORKS INSENSITIVE TO THALAMIC INPUTS

Jason MacLean (University of Chicago)

Patterned neuronal activations, produced by network connectivity, have been postulated for decades to be the potential neuronal scheme for informational representation. Critical to this model, multineuronal patterned activations in cerebral cortex arise during UP states—prolonged neuronal depolarizations—occurring simultaneously across many cells. UP states are found in the cerebral cortex both *in vitro* and *in vivo* and are particularly prominent during slow wave sleep (SWS). Recently it has been shown that UP states repeatably involve a particular population of neurons activating in a particular sequence. These network events are statistically indistinguishable in the numbers, identities and sequences of cells activated from UP state to UP state activation suggesting that these sequences are representative of highly favored network states and are likely enabled by structured cortical network connectivity. While cortical UP states can be robustly triggered by thalamic input, our data suggest that spontaneous cortical UP states actually originate in the cortex and not the thalamus. While previous studies have probed the responsivity of single neurons during UP states the responsivity of an active network of hundreds of neurons at once has not been evaluated. This is a critical consideration when attempting to evaluate the potential function of these patterns of activation—are the patterns dynamic facilitating online dynamical data processing?—or are the patterned activations carrying out a fixed function as would be implied by the hypothesis that they are integral to the process of memory consolidation? Experiments at the level of the network are essential for answering this question, because studies in which single or even a few cells are monitored at once fundamentally miss the emergent network-level properties of groups of cells.

Here we examine how stable network states, characterized by stereotyped multineuronal spatiotemporal dynamics behave in response to new inputs arriving as they are ongoing. We find that although thalamic input during the DOWN state is capable of triggering multicellular patterns of activity in layer 4 the same input during UP states does not perturb these patterns. Correspondingly, the large majority of neurons in layer 4 are insensitive to thalamic input if they are in an UP state. The insensitivity occurs regardless of the timing of the input and the electrophysiological and morphological class of neuron. Finally, we analyze the mechanisms responsible for this cortical insensitivity, finding that both thalamocortical and corticocortical EPSPs are greatly attenuated in excitatory neurons during UP states and that this attenuation is likely the result of a major decrease in input resistance that always accompanies the UP state. Our data indicate that DOWN states appear to make the cortex especially sensitive to thalamic inputs while UP states render the neocortex insensitive to impinging thalamic input—perhaps playing a role in repetitively burning in sequences of multineuronal firing corresponding to activity occurring during waking behavior.

ANCIENT THERA

Andronike Makris (Hellenic Education and Research Center)

The city of Ancient Thera was a Spartan colony located on a high rocky point (Mesa Vouno) overlooking the beaches of Kamari to the north and Perissa to the south. The steep, inaccessible slopes of Mesa Vouno offer natural fortification for the site which overlooks the sea and so was uniquely suitable for the surveillance and control of the south-east Aegean. From the 9th century B.C. until the spread of Christianity, the city where Ancient Thera was located was the only urban center on the island. The town plan of the city today is that which was created in the Hellenistic times. The two sandy beaches of Kamari and Perissa, constituted ideal anchorages for the boats of the period.

Ancient Thera has an Agora, a central public space or market square which was the hub of public life. A number of important sanctuaries are extant including that of Apollo Karneios (a particularly dorian Apollo) where dances of nude boys were held in honor of this god. Particularly distinct is the Gymnasium of the Ephebes at the south-east limit of the city, next to the grotto of Heracles, of the 2nd century.

Even though Thera was among the first places in Greece to adopt the Phoenician alphabet for writing the Greek language (at the end of the 9th or beginning of the 8th century B.C.) it does not appear to have played an important role in the promotion of literature.

However the Theran society was organised, there must have been a class of noble (perhaps wealthy land-owners). The tombs of these nobles were more elaborate and had wealthy grave goods. Quite often statues or elegant grave stelae were set up on these tombs.

IN VIVO, SPIKE-TIMING DEPENDENT CHANGES IN NETWORK FUNCTIONAL CONNECTIVITY REVEALED BY CHANGES IN SPIKING STATISTICS

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([1]Northwestern University, [2]Rehabilitation Institute of Chicago)

Learning is thought to result from remapped neural wiring and changes in network functional properties. Spike-timing dependent processes may play a major role by effecting Hebbian-like changes in synaptic strength. These mechanisms have been studied at some length in highly reduced preparations, but they are much more difficult to study in the intact animal because of the highly interconnected networks of neurons that underlie normal behavior. We have recently developed a novel Bayesian algorithm that quantifies changes in functional connectivity through the spiking statistics of such a network (Stevenson et al. 2008). This algorithm combines a generalized linear model (GLM) framework with priors over the connection strengths. In the model, connections are represented by short duration (ca. 100 ms) spatiotemporal kernels. A sparseness prior constrains the number of connections made by each neuron, and a second prior favors connections that vary smoothly in time. We have demonstrated the ability of the algorithm to identify and track changes in connectivity within an artificial network of neurons in which the population of observed neurons is a vanishingly small fraction of the entire network.

Recently it has been shown that spike-timing dependent stimulation protocols can induce stable changes in the stimulus-triggered functional properties of motor cortical cells (Jackson, Mavoori, Fetz, 2006). We have used similar methods to produce changes in the functional connectivity among neurons recorded from the awake, behaving rat. We paired the spiking of a trigger neuron with stimulation at 5–10 ms latency for periods ranging 9–72 hours. Using the Bayesian algorithm, we have demonstrated potentiation of the functional connection between pairs of neurons consistent with spike-timing mechanisms. The potentiation was dependent on the stimulation timing; at large latencies (500 ms), no potentiation occurred. We demonstrate the ability to cause and detect robust changes in the spiking statistics of motor cortical neurons through spike-timing dependent mechanisms. The techniques demonstrated here may provide a powerful means of studying the neural bases of learning. Additionally, creating and altering connections in the brain could be a valuable tool in rehabilitative and brain-machine interface applications.

OPTIMAL INFERENCE FROM POPULATION RESPONSES IN VISUAL CORTEX

J. Anthony Movshon (New York University)

Inferring the state of the world from the responses of sensory neurons is a central problem in neural computation. To explore the best method for extracting information from neural population activity, we used the activity of populations of 40–70 simultaneously recorded neurons from macaque V1 to estimate and discriminate stimulus orientation with four different decoding strategies.

A population vector method, in which each neurons votes for its preferred orientation in proportion to its response, yielded relatively inaccurate estimates and relatively high discrimination thresholds. We obtained somewhat better performance by optimizing the weights in the population vector calculation to minimize the squared error of the estimates. These direct methods estimate orientation without creating an intermediate representation, but the theory of Bayesian statistics suggests that performance could be improved by introducing an intermediate representation of sensory activity to encode the likelihood that each orientation gave rise to the pattern of activity observed. We therefore studied the performance of decoders that explicitly represent this likelihood function. The simple form of this decoder assumes that neuronal spike counts are statistically independent and Poisson distributed. This decoder, like the population vector, can be built directly from measured tuning properties, and yielded better performance than the direct decoders; taking advantage of the probabilistic nature of the neural response can therefore improve performance. Finally, we optimized this decoder by empirically deriving its parameters from the neuronal data using statistical learning theory. This empirical decoder does not assume either Poisson variability or independence, and uses the structure of the data to increase accuracy. The performance of this empirical decoder was the best of the four, and the main reason for its superiority lay in its ability to adjust parameters to take advantage of interneuronal correlations.

Our results suggest that inference from neuronal populations is best achieved by using an intermediate representation of stimulus likelihood that is empirically constructed from a weighted sum of neuronal responses. The computation of likelihood functions to approximate Bayesian optimal inference may be an important reason for the hierarchical pattern of connections among the visual areas of the extrastriate cortex.

TO STAY OR TO SWITCH? NEURAL CORRELATES OF CHOICE STRATEGY IN SIMPLE FORAGING TASKS

William Newsome, John Reppas, Daniel Kimmel, Jessica Powell, Leo Sugrue, Greg Corrado (HHMI and Stanford University)

When presented with alternative choices in simple foraging games, animals develop strategies that can be characterized as decisions to continue foraging – or *stay* – on the current option, or to *switch* in order to forage on the alternative option. The statistics of stays vs. switches are sensitive to the reward probabilities associated with the two options, and in some cases may comprise a near-optimal reward harvesting strategy. We have observed neural signals related specifically to switch decisions in two simple foraging tasks: a dynamic matching task that has been studied extensively in this lab, and an alternating task in which the optimal strategy is win-stay-lose-switch. We studied switch-related signals using single electrodes in the cingulate cortex and using a multi-electrode array in prefrontal cortex. The amplitude, dynamics and frequency of these signals will be compared between the two areas. Our data are consistent with the notion that a decision to switch from one foraging alternative to the other is explicitly coded by neural circuits within these cortices.

BOTTOM-UP AND TOP-DOWN CORTICAL SIGNALS DURING MOTION DISCRIMINATION TASKS

Tatiana Pasternak (University of Rochester)

Perceptual decisions during visual discrimination tasks often require subjects to compare two or more sequentially presented stimuli. During such tasks the stimuli not only have to be processed, but also retained in memory and the comparison between the remembered and the current stimulus has to be performed. We were interested in characterizing the cortical circuitry sub-serving successful execution of such discrimination task. We focused on speed and direction of visual motion and compared the behavior of neurons during such tasks in two interconnected cortical regions, motion processing area MT and a region associated with executive control and working memory, prefrontal cortex (PFC). During these tasks, the monkeys compared either directions or speeds of two moving random-dot stimuli, sample and test, separated by a brief memory delay. During direction discrimination task, many PFC neurons showed robust direction selectivity (DS) in response to the sample and the test, and these responses were modulated by motion coherence in a way reminiscent of neurons in area MT. During a task requiring discriminating stimulus speed and ignoring its direction, the same PFC neurons showed tuning for stimulus speed, resembling speed selectivity in MT. The nature and the temporal dynamics of these motion selective PFC responses supported their bottom-up origins. This response selectivity was task-driven and DS was reduced on trials when the monkey's attention was redirected to stimulus speed or during passive fixation. The nature of task-related changes in response selectivity was also indicative of their access to low-level motion signals. During the memory delay, both MT and PFC neurons carried reliable DS signals during direction discrimination task, although in individual neurons such signals were largely transient and were rare late in the delay. Similarly, speed selective delay signals in PFC during speed discrimination were also largely transient. The transient nature of delay activity suggests that the contribution of PFC neurons to stimulus maintenance, if any, could only be accomplished at the population level. During the comparison phase, responses to the test in both areas were modulated by the remembered stimulus, reflecting access to the remembered sample. During the direction task, comparison-related signals were in the form response suppression on match trials, which appeared in MT about 100 ms earlier than in PFC, making MT is a more likely source of comparison signals. However, during the test, only responses in PFC, not in MT, were predictive of the monkey's decision. During speed discrimination, comparison-related speed signals were also present in PFC, although they were in the form of match enhancement. This effect depended on the difference between the comparison stimuli, strengthening the notion that modulation of test responses by the preceding sample reflects sensory comparisons required by the task.

In summary, these data provide evidence that during motion discrimination tasks, neurons in areas MT and PFC make unique contributions to different task components and are likely to be functionally linked. MT neurons process visual motion and pass this information as bottom-up signals to PFC. PFC, in turn, faithfully represents this sensory information but only when it is behaviorally relevant, pointing to PFC neurons' active participation in processing of sensory signals, perhaps, by supplying top-down signals to visual neurons about the rules governing the use of sensory stimuli. These neurons also carry decision signals likely to be based on sensory comparison signals most likely supplied by area MT.

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BIG HILL HIM GO BANG: A CONDENSED EXPLANATION OF VOLCANIC ERUPTIONS

Desmond Patterson (Patterson Instruments)

Geologically fascinating and visually stunning, the island of Santorini ranks amongst the worlds classic volcanoes. Santorini is the result of two volcanic processes occurring repeatedly over the past 400,000 years: the accumulation of volcanic material from numerous eruptions, and the collapse of the central region to form the present day caldera with soaring cliffs and spectacular harbor. As a preliminary to the mid-conference field trip to the Kameni Islands (the result of historical eruptions over the last 2000 years) this presentation will address one of the questions most commonly asked of volcanologists—"Why do volcanoes erupt the way they do?"

The underlying control on the nature of an eruption is the composition of the source magma beneath (or within) the volcano. Specifically, on the interplay of two composition-dependent parameters: the volatile content and the viscosity. Put more simply: how much gas is dissolved in the magma, and how rapidly can that gas escape? Gas-rich high viscosity magmas produce catastrophically violent explosive eruptions. Gas-poor and/or low viscosity magmas typically produce gentler eruptions.

As magma ascends, the associated decrease in pressure allows dissolved gases (primarily CO_2 and H_2O) to form bubbles within the magma. In the lowest viscosity magmas (such as the basalts of Hawaii and Iceland), these bubbles buoyantly migrate upwards through the magma towards the surface. The typical result is a relatively gentle eruption characterized by a bubbling (actively out-gassing) lava lake and the gentle effusion of runny and now "flat" lava. The upper regions the underlying magma chamber may comprise up to 90% gas in a foam-like structure, and it is the complex formation and collapse of this foam (in a process showing characteristics of self-organized criticality) that determines the specific nature of the surface eruption.

In contrast, higher viscosity magmas (such as fed the major Santorini eruption of about 3600 years ago) hinder such upward migration and gas loss. Instead, the magma reaches near surface levels with much (if not most) the original inventory of volatiles. When the constraining pressure drops below a critical value, the gas rich magma ruptures to the surface and explosively liberates the entrapped gases. The violence of this process is such to completely fragment the magma resulting in airborne volcanic ashes. The eruption ceases or diminishes as the source magma goes flat. Commonly, the centre of the volcano will collapse downwards into the emptying upper magma chamber resulting in a large caldera structure such as the harbour of Santorini.

A common final stage for this style of eruption is for slow, gentle, toothpaste-like extrusion of the residual high viscosity but relatively gas-poor magma to form small lava domes and flows in the floor of the volcanic crater or caldera—it is this process that is responsible for the young Kameni islands of Santorini that we will be visiting.

INFORMATION PROCESSING IN SINGLE CELLS AND SMALL NETWORKS: INSIGHTS FROM COMPARTMENTAL MODELS

Panayiota Poirazi (Institute of Molecular Biology and Biotechnology)

The goal of this presentation is to provide a set of predictions generated by detailed compartmental models regarding the ways in which information may be encoded by single cells and neural assemblies. Towards this goal, I will present modelling studies from our lab that investigate how single pyramidal neurons and small neural networks in different brain regions process incoming signals that are associated with learning and memory. I will first discuss the computational capabilities of individual pyramidal neurons in the hippocampus [1–3] and how these properties may allow a single cell to discriminate between familiar versus novel memories [4]. I will then present biophysical models of prefrontal layer V neurons and small networks that exhibit sustained activity under realistic synaptic stimulation and discuss their potential role in working memory [5].

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NEURONAL VARIABILITY: NOISE OR INCOMPETENCE?

Alexandre Pouget (University of Rochester)

Neuronal responses exhibit a large amount of variability, whether in spike counts or spike timing. This variability is thought to arise from two main sources: stochastic fluctuations, often called noise, and fluctuations in variables internal to the brain, such as the level of attention. We will argue that there is in fact a third source of variability, which we call incompetence. We use the term *incompetence* to refer to deterministic computations that are suboptimal due to incomplete knowledge of the statistics of incoming spikes. This source is likely to be an important source of variability, if not the most important one, in the sense that it has a very large impact on behavioral performance. Incompetence also explains several puzzling results, and in particular the fact that variability in the brain depends on task difficulty and does not appear to be uniform throughout cortex.

LEARNING AND REPRESENTATION OF DECLARATIVE MEMORIES BY SINGLE NEURONS IN THE HUMAN HIPPOCAMPUS AND AMYGDALA

Ueli Rutishauser[1,3], *Adam Mamelak*[2], *Erin M. Schuman*[3] ([1]Caltech, [2]Cedars Sinai Hospital and Huntington Memorial Hospital, [3]HHMI and Caltech)

Episodic memories allow us to remember not only that we have seen an item before but also where and when we have seen it (context). Neurons in the medial temporal lobe (MTL) are critically involved in the acquisition of such memories. Successful detection of novelty is necessary for many types of learning. During retrieval, we can sometimes confidently report that we have seen something (familiarity) but can not recollect where or when it was seen. Thus episodic memories have several components that can be dissociated. We recorded single neurons in the human hippocampus and amygdala while human subjects remembered, and later retrieved, the identity and location of pictures shown. We discovered two classes of neurons that exhibit single trial learning: novelty and familiarity detectors, which show a selective increase in firing for new and old stimuli, respectively. The neurons retain memory for the stimulus for 24 hr. During retrieval, these neurons distinguish stimuli that will be successfully recollected from stimuli that will not be recollected. Similarly, they distinguish between failed and successful recognition. Pictures that were forgotten by the patient still evoked a non-zero response. Remarkably, a simple decoder that has access to the spikes emitted by a few neurons can outperform the patient (i.e. it forgets fewer pictures). These data support a continuous strength of memory model of MTL function: the stronger the neuronal response, the better the memory. We are also investigating whether there are neural signatures during learning that predict whether plasticity was successful or not (measured by whether the stimulus will later be remembered). Remarkably, there are single neurons as well as specific signatures of the LFP that can be used to predict whether a stimulus will be remembered later.

EXTRACTING DYNAMICAL STRUCTURE EMBEDDED IN PREMOTOR CORTICAL ACTIVITY

Krishna V. Shenoy[1], *Byron M. Yu*[1,2], *Afsheen Afshar*[1], *John P. Cunningham*[1], *Mark M. Churchland*[1], *Gopal Santhanam*[1], *Stephen I. Ryu*[1], *and Maneesh Sahani*[2] ([1]Stanford University, [2]Gatsby Computational Neuroscience Unit, University College London)

Our seemingly effortless ability to reach out and swat a fly or grab a cup belies the sophisticated neural computations at work in our nervous system. It has long been recognized that, before moving, we somehow prepare neural activity such that, when called upon, the desired movement unfolds. But the goals of movement preparation and the underlying neural mechanisms remain poorly understood. I will describe some of our recent electrophysiological investigations of how premotor cortex prepares and helps execute movements. Our results suggest that the brain is attempting to optimize preparatory neural activity [1] and can delay movement until this activity is sufficiently accurate [2]. We note that the spiking activity during motor preparation exhibits dynamics beyond that driven by external stimulation, presumably reflecting the extensive recurrence of neural circuitry. We have been developing analysis methods for capturing the dynamics from (96 channel) simultaneous PMd neural recordings while monkeys perform delayed reaching tasks, and I will present recent work that examines the trial-by-trial dynamical trajectories during movement preparation and generation and their relationship with behavior [3–5]. Characterizing these dynamics may reveal important features of neural computation, and may be useful for further increasing the performance of neural prostheses [6,7].

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THE ROLE OF THALAMUS: RELAY FUNCTIONS AND MORE

S. Murray Sherman (University of Chicago)

The LGN and pulvinar (a massive but generally mysterious and ignored thalamic relay) are examples of two different types of relay: the LGN is a first order relay, transmitting information from a subcortical source (retina), while the pulvinar is mostly a higher order relay, transmitting information from layer 5 of one cortical area to another area. First and higher order thalamic relays can also be recognized for the somatosensory and auditory thalamic systems, and this division of thalamic relays can also be extended beyond sensory systems. Thus the first and higher order thalamic equivalents of the somatosensory and auditory systems are, respectively, the ventral posterior nucleus and the posterior medial nucleus (somatosensory), and the ventral versus dorsal portion of the medial geniculate nucleus (auditory). Other thalamic nuclei have also been placed into this framework, and so the medial dorsal nucleus is mostly higher order, while the ventral anterior and ventral lateral nuclei seem to be a mosaic of first and higher order relays. It now seems clear that most of thalamus is comprised of higher order relays. Higher order relays seem especially important to general corticocortical communication, and this challenges and extends the conventional view that such communication is based on direct corticocortical connections. Recent in vitro data from our laboratory using thalamocortical slice preparations and novel imaging techniques provides further data consistent with this hypothesis. We thus conclude that the thalamus is not just a simple relay responsible for getting peripheral information to cortex: instead it both provides a behaviorally relevant, dynamic control over the nature of information relayed, and it also plays a key role in basic corticocortical communication.

CORTICO-HIPPOCAMPAL NETWORK DYNAMICS AND ASSOCIATIVE LEARNING

Thanos Siapas (California Institute of Technology)

Many lines of evidence have shown that the hippocampus is critical for the formation of long-term memories, and that this hippocampal involvement is time-limited. The current predominant conjecture is that memories are encoded in the hippocampus during awake behavior and are gradually consolidated across neocortical circuits under the influence of hippocampal activity during sleep. However, the organization of cortico-hippocampal interactions at the level of networks of neurons remains poorly understood. In this talk I will characterize the timing relationships between hippocampal and neocortical activity, during associative learning tasks as well as during sleep. In addition, I will discuss the evolution of cortico-hippocampal interactions across time, and the consequences of these interactions for the process of memory formation.

LAMINAR ORGANIZATION OF THE EXCITATORY NETWORK IN MOTOR CORTEX

Nicholas Weiler[1,2], Lydia Wood[1], Jianing Yu[1], Gordon M. G. Shepherd[1], Sara A. Solla[1] ([1]Northwestern University, [2]Stanford University)

Cortical layering is a hallmark of the mammalian neocortex and a major determinant of local synaptic circuit organization in sensory systems. In motor cortex, the laminar organization of cortical circuits has not been resolved, although their input-output operations are crucial for motor control. Local circuits in M1 are critically involved in mediating motor-based behavior, as they receive and integrate convergent inputs from sensory and motor systems, and their collective and coordinated output carries the corticofugal signals that generate movement. The neural operations carried out in M1 are accomplished not by corticospinal neurons acting alone, but through an active local network of projection neurons connecting and interacting in highly specific ways. Determining the local circuit organization of motor cortex is therefore an essential step toward a detailed understanding of the cortical mechanisms underlying motor control.

We have used laser-scanning photostimulation based on glutamate uncaging to map the layer-specific connectivity of the circuits in the mouse motor cortex. From these data we computed a laminar presynaptic-postsynaptic connectivity matrix $W_{\text{post,pre}}$ that characterizes the functional layout of the pyramidal neuron network across layers and reveals a complement of stereotypic pathways dominated by layer 2 outflow to deeper layers. An analysis of the network dynamics associated with the experimentally obtained connectivity matrix $W_{\text{post,pre}}$ predicts that stimuli targeting upper but not lower cortical layers should effectively evoke network-wide events. This prediction has been confirmed in experiments with disinhibited slices. Thus, in motor cortex, descending excitation from a preamplifier-like network of upper-layer neurons drives output neurons in lower layers. These results provide a quantitative wiring-diagram framework for further investigation of the excitatory networks mediating cortical mechanisms of motor control.

POSTER ABSTRACTS

(in alphabetical order by first author)

THE SPARSENESS OF STIMULUS ENCODING BY SINGLE NEURONS AND BY POPULATIONS OF NEURONS IN THE INFERIOR TEMPORAL CORTEX

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Sparseness is a measure of the selectivity of neuronal responses. High sparseness indicates low stimulus selectivity with a sparseness of 1.0 indicating a neuron that is non-selective to the set of stimuli. The sparseness of the encoding of stimuli by single neurons and by populations of neurons is fundamental to understanding the efficiency and capacity of representations in the brain.

The sparseness of the responses of single neurons in the primate inferior temporal visual cortex (the single neuron sparseness a^s) was measured to a set of 20 visual stimuli including objects and faces in macaques performing a visual fixation task. Neurons included for analysis had significant firing rate increases from baseline in response to some of the stimuli. The firing rate distribution of 36% of the neurons was exponential. Twenty-nine percent of the neurons had too few low rates to be fitted by an exponential distribution, and were fitted by a gamma distribution. The sparseness a^s of the representation of the set of 20 stimuli provided by each of these neurons had an average across all neurons of 0.77, indicating a rather distributed representation.

The sparseness of the representation of a given stimulus by the whole population of neurons (the population sparseness a^p) also had an average value of 0.77. Ergodicity is the ability to predict the distribution of the responses of the system at any one time (the population level) from the distribution of the responses of a component of the system across time. Considering this in neuronal terms, for the average sparseness of a population of neurons over multiple stimulus inputs to be ergodic, it must equal the average sparseness to the stimuli of the single neurons within the population, provided that the responses of the neurons are uncorrelated (Foldiak 2003). As there is little or no correlation in the response profiles of inferior temporal cortex neurons (Rolls et al, 2004), the similarity of the average single neuron sparseness a^s and population sparseness for any one stimulus taken at any one time a^p shows that the neural representation of visual stimuli such as objects and faces is essentially ergodic.

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ACTION IN MOTION VERSUS ACTION PLANNING: NEURONAL CORRELATES OF ADAPTATIONS TO FORCE FIELDS WITH AND WITHOUT VISUAL FEEDBACK IN THE MOTOR CORTEX

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We have recently shown that prior knowledge and state estimates based on vision and proprioception differentially influence the choice of a trajectory plan when humans adapt to dynamic force fields and visuomotor rotations. Here we use the same experimental design in monkeys to examine the neuronal activity in the motor cortex before, during, and after adaptations to curl force fields with or without visual feedback (VFB).

Each recording session was composed of three blocks of trials: (1) pre-learning standard, (2) force field with or without VFB, and (3) post-learning standard. For the behavioral analysis, we measured trajectory and endpoint deviations. We examined the activity of each cell during two different epochs of a trial: preparatory activity (PA) covers activity during a hold period after target onset (600 ms), and movement-related activity (MRA) during 600 ms after go-signal. Only cells that were stable during recording, with an average firing rate of >1 Hz, and directionally tuned (bootstrap, $p<0.05$) were included in the analysis. Directional tuning of neuronal activity was fitted with the circular von Mises distribution.

The monkeys adapted to both types of force field, showing significant aftereffects in *catch trials* interspersed throughout the learning block. As in humans, adapted trajectories were straight with VFB but were curved without it. Neuronal activity during force field adaptation was found significantly different from the activity during the pre-learning standard reaches, suggesting modulation by force field. Further, such modulation was found to be different between the two feedback conditions. With VFB, cells whose PD was in the range of the required muscle vector (45-90^{o} away from the learned direction) showed the highest activity than the rest of the cells (ANOVA, $p<0.0001$; post-hoc LSD $p<0.01$) in both preparatory and movement-related epochs. The opposite was observed in the without VFB condition; cells whose PD was opposite to the required muscle vector showed the highest PA but the lowest MRA (ANOVA, $p<0.0001$; post-hoc LSD $p<0.01$). Comparison of tuning curves of single units between pre- and post-learning standard blocks showed significant shifts in PD and changes in tuning width in both epochs and feedback conditions (Permutation test, $p<0.05$). At the population level, we found significant PD shift in the same direction as the force field (Sign Rank, $p=0.001$) and narrowing of the tuning curve during preparation for movement in the with VFB condition. No significant tuning curve changes were found in MRA and in the without VFB condition.

The findings indicate differential modulation of activity in the motor cortex associated with adaptations to force field with and without VFB. Our results suggest that while feedback modalities do not differentially influence activity during movement, action planning in the two feedback conditions represent different movement plans.

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REACHING BETWEEN LINES: RECTILINEAR VERSUS CURVILINEAR TRAJECTORIES DURING ADAPTATIONS TO FORCE FIELDS AND VISUOMOTOR ROTATIONS

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When reaching to an object, estimating the hand position is not as certain when we cannot see the hand as when we can see it. This uncertainty can lead to errors in sensory estimates and consequently to movement variability. Optimal estimation of the state of the body and the environment is all the more critical when reaching in novel environments. In such conditions, humans may compensate for errors by combining sensory information with the knowledge gained from previous experience. Here we demonstrate that prior knowledge and state estimates based on vision and proprioception differentially influence the choice of a trajectory plan during adaptations to dynamic force fields and visuomotor rotations.

Separate subjects (n=28) adapted to force fields with or without concurrent visual feedback of their hand trajectory and were retested after 24 hours. Additional groups learned visuomotor rotation immediately after force field to assess interactions between them. We found that comparable levels of endpoint accuracy were achieved in two ways: with visual feedback, the adapted trajectories in force fields were straight whereas without it, the trajectories remained curved. Further, the straight or curved trajectories were carried over to a subsequent adaptation to visuomotor rotation. The transfer of curved trajectories to a different task and feedback condition indicates conclusively that the initial segment of the trajectory in force field without visual feedback does not only reflect deviations imposed by the perturbation but a new trajectory plan with its own inverse and forward models.

Our finding that endpoint accuracy and precision can improve while trajectories remain curved explicitly contradicts the notion that straight trajectories follow from minimizing endpoint variance . The curved trajectories seem to obey a minimum intervention principle in which deviations are not corrected unless they interfere with task performance and that newly acquired control policies (i.e. trajectory plan) are used in subsequent adaptations if they continue to produce successful performance. The dissociated effects on trajectory and endpoint support the notion of separate controllers governing them . Overall, we show evidence that hand path rectilinearity is not an obligatory feature either of adaptation to dynamic curl fields or of processes that act to minimize terminal errors and that visual feedback may only in some cases facilitate the development of rectilinearity.

Supported by: Binational Science foundation (BSF), Israel Science foundation, Johnson&Johnson Fund for Innovative Science, Rosetrees Trust, and Ida Baruch fund

NEURAL SPATIO-TEMPORAL ACTIVITY TO SUBLIMINAL PERCEPTION OF FEARFUL FACE REVEALED BY MAGNETOENCEPHALOGRAPHY

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fMRI studies have recently highlighted the neural correlates of fearful face perception [1], while electrophysiological research has demonstrated that this process can occur before 130 ms [2]. However, it remains difficult to link this data to specify the spatio-temporal dynamics following a fearful face presentation. Combining high temporal (ms) and spatial resolution, magnetoencephalography (MEG) has revealed that the first responses to fear appear in the amygdala and the frontal lobe [3]. Using this technique we investigated the spatio-temporal processing of subliminal and supraliminal fearful face perception.

Subliminal prime stimuli consisted of fearful or neutral faces presented in the central or peripheral visual field for 32 ms. A mask followed this stimulus to avoid a supraliminal perception. After a variable delay (300 to 400 ms), a target was presented for 150ms, consisting of a neutral, fearful or happy face presented centrally or in the periphery of the visual field. Subjects were asked to respond to the happy face target. We recorded the neuromagnetic signal continuously at 625Hz for 12 subjects using a CTF Omega 275 channel whole head system (VSM MedTech, Ltd.) Sensor analysis and beamforming source location analysis were performed on prime and target stimuli.

Sensor analysis demonstrated a difference between fearful and neutral prime stimuli, occurring between 130 and 200 ms in bilateral temporal sensors, when subliminal faces were presented centrally. Source analysis showed that, in the first 200ms, prime fearful face activated the right amygdala. For the target stimuli, differences were observed in bilateral temporal and parietal sensors. Further source analysis will be done to compare source location to subliminal and supraliminal fear perception.

Our findings confirm the hypothesis that right amygdala is implicated in fearful perception in the first 200 ms, reinforcing the hypothesis of a sub-cortical fast visual pathway sensitive to emotional stimuli [4]. Studying subliminal fear perception in MEG for the first time, we demonstrate, here that consciousness of the stimuli is not necessary to activate this fast neural response.

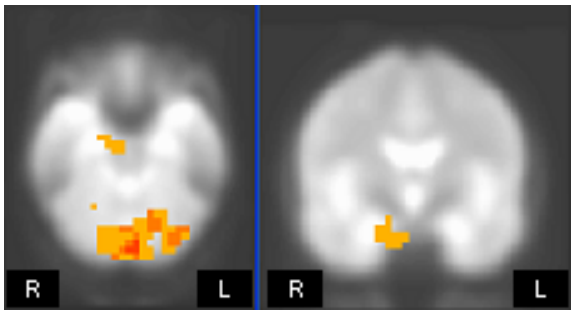

Figure: in contrast with neutral faces, subliminal fearful faces activated right amygdala during the first 200ms.

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PAIRWISE CORRELATIONS AND MULTINEURONAL FIRING PATTERNS IN PRIMARY VISUAL CORTEX OF THE AWAKE, BEHAVING MACAQUE

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Understanding the structure of multi-neuronal firing patterns has been a central quest and major challenge for systems neuroscience. In particular, how do pairwise interactions between neurons shape the firing patterns of neuronal ensembles in the cortex? To study this question, we recorded simultaneously from multiple single neurons in the primary visual cortex of an awake, behaving macaque using an array of chronically implanted tetrodes[1]. High contrast flashed and moving bars were used for stimulation, while the monkey was required to maintain fixation.

In a similar vein to recent studies of *in vitro* preparations[2,3,5], we applied maximum entropy analysis for the first time to the binary spiking patterns of populations of cortical neurons recorded *in vivo* from the awake macaque. We employed the Dichotomized Gaussian distribution, which can be seen as a close approximation to the pairwise maximum-entropy model for binary data[4]. Surprisingly, we find that even pairs of neurons with nearby receptive fields (receptive field center distance < 0.15°) have only weak correlations between their binary responses computed in bins of 10 ms (median absolute correlation coefficient: 0.014, 0.010-0.019, 95% confidence intervals, N=95 pairs; positive correlations: 0.015, N=59; negative correlations: -0.013, N=36). Accordingly, the distribution of spiking patterns of groups of 10 neurons is described well with a model that assumes independence between individual neurons (Jensen-Shannon-Divergence: 1.06×10^{-2} independent model, 0.96×10^{-2} approximate second-order maximum-entropy model[4]; $H/H_1=0.992$). These results suggest that the distribution of firing patterns of small cortical networks in the awake animal is predominantly determined by the mean activity of the participating cells, not by their interactions.

Meaningful computations, however, are performed by neuronal populations much larger than 10 neurons. Therefore, we investigated how weak pairwise correlations affect the firing patterns of artificial populations[4] of up to 1000 cells with the same correlation structure as experimentally measured. We find that in neuronal ensembles of this size firing patterns with many active or silent neurons occur considerably more often than expected from a fully independent population (e.g. 130 or more out of 1000 neurons are active simultaneously roughly every 300 ms in the correlated model and only once every 3-4 seconds in the independent model). These results suggest that the firing patterns of cortical networks comparable in size to several minicolumns exhibit a rich structure, even if most pairs appear relatively independent when studying small subgroups thereof.

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THE ROLE OF CORRELATIONS AND HETEROGENEITY IN THE POPULATION CODE

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Neural population codes across the brain often share many similar features – they have sparsely firing neurons, extreme functional heterogeneity, and distributed patterns of weak and mostly positive pairwise correlations. These qualitative features have been described in the retina, sensory cortex, and hippocampus; they may also be present in other brain regions.

Here we employ simple models to study how heterogeneity and correlation impact the fidelity of the population code. For a two-alternative forced choice discrimination, we calculate the discrimination error for models with a single pool of functionally identical neurons and compare to the case of multiple pools of functionally diverse neurons having the same average firing rate for both stimuli. We find that heterogeneous populations always outperform homogeneous populations, often by large factors. We perform a similar analysis on a population of 111 retinal ganglion cells, finding that the real neurons outperform a matched homogeneous population by as much as ~100-fold in the error rate.

Next, we construct models with weak, positive, pairwise correlations. As previously observed, positive correlations reduce the coding fidelity for a homogeneous pool of neurons, causing its performance to saturate at small population sizes. But if the population has two pools of cells with different firing rates, correlations can dramatically reduce the error. For 100 neurons with average correlation coefficient $C \sim 0.05$, this reduction can exceed a factor of 10^{20} in the error rate. For groups as small as 10 neurons, a similar reduction can be found with average correlation $C \sim 0.3$. We describe the pattern of pairwise correlations that produces this low error code, estimate the network capacity with this coding scheme, and discuss the relationship to experimentally observed pairwise correlations.

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FLEXIBLE MODELS FOR POPULATION SPIKE TRAINS

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In order to understand how neural systems perform computations and process sensory information, we need to understand the structure of firing patterns in large populations of neurons. Spike trains recorded from populations of neurons can exhibit substantial pair wise correlations between neurons and rich temporal structure. Thus, efficient methods for generating artificial spike trains with specified correlation structure are essential for the realistic simulation and analysis of neural systems.

Here we show how correlated binary spike trains can be modeled by means of a latent multivariate Gaussian model. Sampling from our model is computationally very efficient, and in particular, feasible even for large populations of neurons. We show empirically that the spike trains generated with this method have entropy close to the theoretical maximum. They are therefore consistent with specified pair-wise correlations without exhibiting systematic higher-order correlations. We compare our model to alternative approaches and discuss its limitations and advantages. In addition, we demonstrate its use for modeling temporal correlations in a neuron recorded in macaque primary visual cortex.

Neural activity is often summarized by discarding the exact timing of spikes, and only counting the total number of spikes that a neuron (or population) fires in a given time window. In modeling studies, these spike counts have often been assumed to be Poisson distributed and neurons to be independent. However, correlations between spike counts have been reported in various visual areas. We show how both temporal and inter-neuron correlations shape the structure of spike counts, and how our model can be used to generate spike counts with arbitrary marginal distributions and correlation structure. We demonstrate its capabilities by modeling a population of simultaneously recorded neurons from the primary visual cortex of a macaque, and we show how a model with correlations accounts for the data far better than a model that assumes independence.

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REGULATION OF CIRCUITRY SUBSERVING PREPULSE INHIBITION OF THE STARTLE REFLEX BY THE MAJOR HISTOCOMPATIBILITY COMPLEX, CLASS I (MHCI)

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The ability to filter out extraneous sensory information, known as sensorimotor gating, is impaired in patients with schizophrenia. Sensorimotor gating can be measured in both humans and rodents through tests of prepulse inhibition (PPI), an inhibition of the startle response to a strong acoustic stimulus when it is preceded by a brief, nonstartling stimulus. PPI is thought to reflect the intrinsic processing properties of a circuit that includes limbic cortex, striatum, pallidum and pontine tegmentum. Deficits in sensorimotor gating may contribute to core symptoms of schizophrenia, including distractibility, sensory bombardment, and cognitive fragmentation.

Maternal viral infection significantly increases the risk of schizophrenia in the offspring, and recent studies in animal models demonstrate it is the maternal immune response, and not the virus itself, that disrupts fetal brain development, although the underlying mechanisms remain unknown. Here we report that changes in the levels of specific immune proteins, members of the major histocompatibility complex, class I (MHCI), are sufficient to disrupt sensorimotor gating in rodents. In animals genetically deficient for cell surface MHCI, startle responses to strong acoustic stimuli are normal, but PPI is strikingly reduced across a range of interstimulus intervals. Studies in transgenics lacking classical, peptide-presenting MHCI proteins suggest that it is instead the so-called “nonclassical” MHCI proteins—many of which have no known immune role, but are expressed in neurons—that may be required for normal functional outputs from sensorimotor gating circuitry. Preliminary pharmacological and behavioral experiments in mice over-or under-expressing MHCI are consistent with a model in which MHCI affects PPI through modulation of cholinergic pathways.

Our results suggest that changes in MHCI levels could mechanistically link maternal immune challenge, a risk factor for schizophrenia, with impaired prepulse inhibition, a fundamental symptom of this disorder. These data also provide a framework for the development of theoretical models describing how alterations in information processing, caused by changes in MHCI, may contribute to sensorimotor disruption in schizophrenia.

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FLEXIBLE SENSORIMOTOR MAPPING: THE PROANTI TASK IN RATS.

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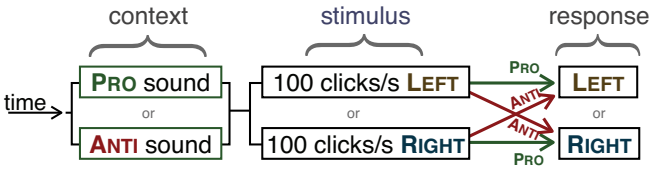
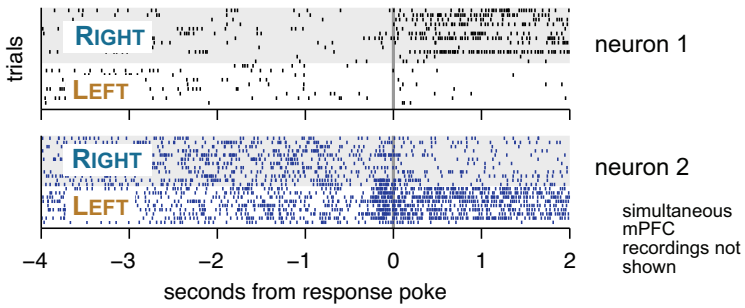
In a complex world, the appropriate response to a given sensory stimulus may vary, depending on the context in which this stimulus is presented. How do ensembles of neurons support context-dependent flexibility of sensorimotor rules? We have recently trained rats in a trial-by-trial sensorimotor rule-switching task. To our knowledge, we are the first group to successfully train rats in such a task; previously, rapid rule-switching could be studied only in primates. In each trial of our task, two types of stimuli are presented. The first is a context sound, and can be either a "Pro" sound (4 KHz FM pure tone) or an "Anti" sound (16 KHz FM tone). The second, later, stimulus is a sound that comes either from a speaker to the left of the rat (100 clicks/sec, Left), or from a speaker to the right of the rat (100 clicks/sec, Right). We call this second stimulus the "localized sound." In Pro trials, the rat must orient *towards* the localized sound to obtain a water reward; in Anti trials, the rat must orient *away* from the localized sound to obtain its reward. To successfully complete both types of trials, the rat must be able to store both sensorimotor mapping rules, and flexibly switch between them as it switches from Pro to Anti trials and viceversa. I will describe the automated training methods we are using to successfully train rats in this difficult rule-switching task.

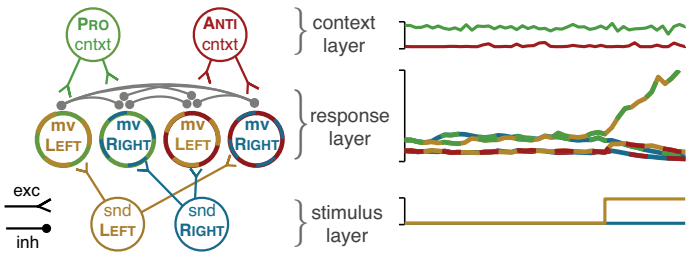


Once our animals are trained, we are using tetrodes to record simultaneously from ensembles of single neurons in both areas mPFC (medial prefrontal cortex; 4 tetrodes here) and rat FEF (frontal eye fields, associated with head orientation movements in the rat; 4 tetrodes here), while rats perform the task.



Spike rasters of two neurons recorded simultaneously from rat FEF. Responses are aligned to the time of the animal's response, and have been sorted according to response direction.

In the literature, one finds several different models of how such flexible sensorimotor mapping could be achieved. We are implementing these models, in addition to one we have ourselves developed, as ensembles of interconnected, conductance-based spiking model neurons. The different models have different connectivities, and these lead to different spike train cross-correlogram signatures. We are comparing neuronal response properties and correlograms found experimentally to the predictions of different models, so as to distinguish between the models.



Schematic diagram of the groups of neurons in our model implementing ProAnti. The right panel shows traces from the different groups of model neurons in a single "Pro, Go Left" trial of the task.

DECODING NEURONAL ENSEMBLE ACTIVITY FROM FMRI DATA

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The ubiquitous functional MR brain imaging studies based on blood oxygenation level dependent (BOLD) signal are conducted at spatial resolution (e.g. 3x3x3 mm) that pools hemodynamic effects induced by neuronal responses of a large neuronal population (of order 10^5-10^6) and has been assumed to average out the selectivity of cortical columns for various feature values. Recent applications of multivariate machine pattern recognition methods to fMRI data, however, have revealed an unexpected richness of information available in the detailed response patterns of voxel ensembles. This information has been used to detect both perceived stimulus patterns and discriminate among multiple mental states. Indeed, the multivariate approach has been shown to be superior to the traditional univariate data analysis for discrimination among activation patterns when voxel sets carry consistent activation pattern associated with various stimuli (e.g. Kriegeskorte & Bandettini, 2007). However, when a neuronal population encodes a given feature by means of a monotonic tuning, the traditional univariate analysis with a preceding spatial smoothing step is a preferable data analysis method.

We explore these multivariate and univariate data analysis approaches in the context of numerosity encoding in the superior temporal cortex. Brain imaging studies demonstrate that human intraparietal sulcus (IPS) responds to numerosity, i.e. abstract numerical magnitude regardless of whether it is represented by the set size of a visual array or symbolically by digits (Brannon, 2006; Dehaene et al, 2004). Macaque neurons in the fundus of IPS have been shown to be selective for a range of numerosity values. Specifically, numerosity tuning curves show a range of selectivity profiles: monotonically decreasing with magnitude, monotonically increasing with magnitude, and narrowly tuned (Nieder & Miller, 2004). We hypothesized that similar properties exist in human IPS. We tested this hypothesis using an event-related fMRI. Digits were presented visually, aurally, or simultaneously in both modalities, and subjects were cued to attend to one modality and respond with the key-press matching the attended digit. During baseline trials, subjects passively fixated on a central cross. Each subject completed one scanning session on a 3T GE scanner consisting of 3 EPI scans. Data were analyzed with a design matrix that modeled the attended stimulus modality and digit magnitude. As expected, visual cortex was significantly activated when the attended modality was visual, and auditory cortex was activated when the attended modality was auditory. The z-map produced by the reference function modeling digit magnitude revealed activation in IPS, among other areas. This is in accord with previous studies that employed digits to represent numerosity. Whereas previous studies show that IPS is selective for numerosity as opposed to other stimulus attributes (such as letter, color, element shape and size), our preliminary results suggest that IPS activation actually covaries with digit magnitude, irrespective of modality. The novel aspect of our result is that IPS activation covaries with digit value, and thus contributes to the evidence that neurons in human IPS are tuned to numerosity as represented by digits, and this representation is supramodal.

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THALAMIC NETWORK RESPONSE TO OSCILLATORY ACTIVITY ASSOCIATED WITH PARKINSON'S DISEASE AND DEEP BRAIN STIMULATION

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Parkinson's disease (PD) is a neurodegenerative disorder which results in enhanced synchronized oscillatory activity in theta and beta bands (3-30 Hz) in the Basal Ganglia (BG) nuclei. Synchronized oscillatory activity observed in the BG nuclei is believed to interfere with the normal functioning of the motor system and lead to Parkinson's disease motor symptoms. In the advanced stages of the disease, Parkinson's disease motor symptoms are managed by surgical methods such as Deep Brain Stimulation (DBS) (Benabid 2003).

DBS is a reversible surgical treatment method which involves delivery of high frequency electrical pulses (120-180 Hz stimulation frequency, 0-5 V pulse amplitude, and 0.06-0.2 ms pulse duration) to specific BG nuclei, such as subthalamic nucleus (STN) or globus pallidus internum (GPi). Despite high clinical efficacy of DBS, the mechanism through which Parkinson's disease motor symptoms are suppressed, remains unknown (Benabid 2003).

While synchronous oscillatory activity in theta and beta ranges is widely associated with pathophysiology of Parkinson's disease, high frequency activity induced in the BG network during DBS is correlated with the suppression of Parkinson's disease motor symptoms. It still remains unknown what makes certain frequencies induced in the BG network "bad" and what makes the others "good"?

In order to address this question, we have extended our previous study on the frequency selective response of thalamocortical cells and we have implemented a bio-physical thalamic network model which included thalamic relay and reticular neurons (Mayer et al. 2006, Destexhe et al. 1998). Thalamus plays a fundamental role in the motor system by closing the cortico-BG loop. Thalamus receives glutamergic projections from the pre-motor cortex and gabaergic projections from the BG output nucleus and projects back to pre-motor cortex. P Brown et al. (2003) have proposed that low frequency oscillations observed in BG nuclei are transferred to cortex by thalamus; resulting in anti-kinetic oscillations in the pre-motor cortex. Effects of low frequency oscillatory BG activity and high frequency DBS induced activity on thalamic processing of cortical inputs could clarify why some frequencies induced in the BG network are associated with pathophysiology while others are associated with treatment. Our model has also been used in order to investigate if the thalamic network processes different cortical firing patterns and frequencies in a different way when the BG input is in the low frequency oscillatory state.

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THE RELATION BETWEEN VISUAL CODING AND STATISTICAL REDUNDANCY FOR CONTOUR CURVATURE IN NATURAL IMAGES

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An important goal of the early visual system is to achieve an efficient code by eliminating redundancy from the incoming signal (see, e.g., Attneave, 1954; Barlow, 1961). We analysed contour curvature in natural images using a measure of curvature redundancy. Curved contours were found in natural images, and local curvature was modeled as the change in tangent for fixed-distance steps along the contour. Curves with a constant angle of curvature, defined as four successive steps with the same tangent (ranging from 0° to 60°), were found in natural images, and we measured the orientation of projections that naturally extend from these curves. The results show that, for angles of curvature between 0° and 30°, the contour extends in the direction of curvature, and the orientation of the extension is proportional to the angle of curvature. However, this natural image property is less obvious with larger curvature angles, and for angles of greater than 50°, there is no preferred extension orientation.

We followed the above analysis with the question: is the visual system sensitive to this "constant curvature" property of contours of natural images? We used a contour-detection task (see Field, Hayes, & Hess 1993) to examine human sensitivity to curved contours that were similar to those extracted by the above analysis. Observers were required to detect a Gabor-element-defined contour that was embedded in a field of randomly oriented Gabor-elements. The contour consisted of four elements that were arranged with a constant angle of curvature (0° to 40°) with, at each end, another aligned Gabor-element, but these end elements were orientated independently of the curve's orientation, with orientations ranging from -30° to 60°. Pairs of stimuli, one containing the contour embedded in a field of randomly oriented and quasi-randomly positioned background Gabor-elements, and the other consisting only of randomly oriented and positioned Gabor-elements, were presented to observers using a two-alternative forced-choice paradigm, and the task of the observer was to indicate which interval contained the contour. Each contour curvature and extension orientation permutation was presented at least 50 times. An estimate of sensitivity to a particular stimulus configuration was indicated by the proportion of times observers identified the correct interval.

Our results show that the visual system is most sensitive to contours with extensions oriented in the direction of contour curvature. This relationship between curvature angle and the orientation of the extension is evident for curvatures of between 0° and 30°, and the orientation relationship is very similar to that observed in natural images (see Figure 1). This similarity between the pattern of curved contours found in natural images and sensitivity of the human visual system supports the assertion of a close relationship between natural image curvature statistics and the encoding of visual information.

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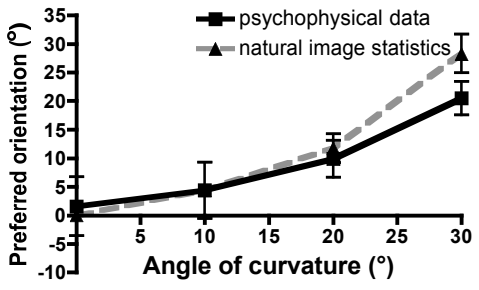

Figure 1. Preferred orientation of contour extension in natural images and for human detection, as a function of the angle of curvature.

BIOPHYSICAL CORTICAL COLUMN MODEL FOR OPTICAL SIGNAL ANALYSIS

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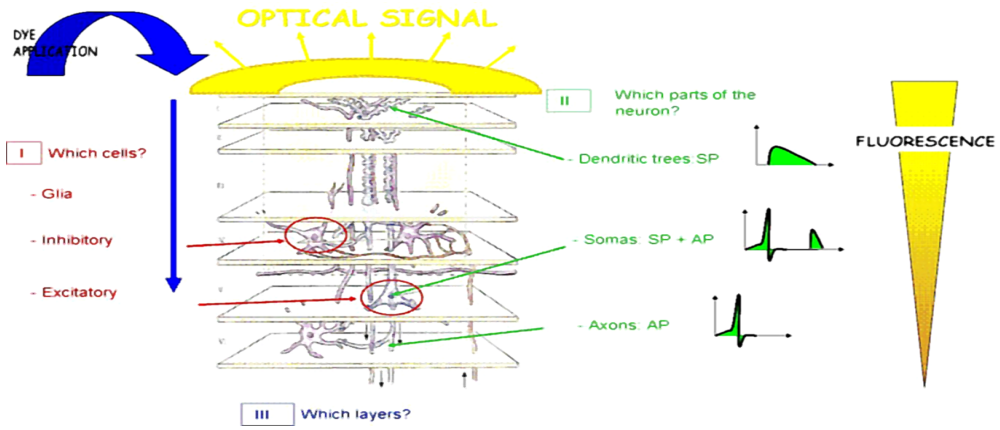
We propose a biological cortical column model, at a mesoscopic scale, in order to better understand and start to interpret biological sources of voltage-sensitive dye imaging (VSDI) signal [1] [2]. The mesoscopic scale, corresponding to a micro-column, is about 50 µm.
We choose a family of models based on a cortical microcircuit, whose synaptic connections are made only between six specific populations of neurons: two populations (excitatory and inhibitory) for three main layers (2/3, 4, 5/6), following [3] and [4]. For each neuron, we use a compartmental description with a conductance-based Hodgkin-Huxley neuron model and we verify that their intrinsic behaviors are in accordance with those shown in [5] by intracellular recordings.

This model confirms and quantifies the fact that the optical imaging signal is the result of an average from multiple components (figure 1) whose proportion changes with levels of activity, but shows surprisingly that inhibitory cells, spiking activity and deep layers may likely participate more to the signal than initially thought.

Method

We use the NEURON software to implement our cortical column model of about 200 neurons and run simulations. The visualization is done thanks to the NEUROCONSTRUCT software.

Figure 1



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A CA1 HETEROASSOCIATIVE MICROCIRCUIT MODEL OF THE HIPPOCAMPUS

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Associative memory is one of the oldest artificial neural network (ANN) paradigms. Input patterns are encoded as the activity patterns across a network of computing units, or neurons. Patterns are stored in the memory by Hebbian modification of the connections between the computing units. A memory is recalled when an activity pattern that is a partial or noisy version of a stored pattern is instantiated in the network. Network activity then evolves to the complete stored pattern as appropriate units are recruited to the activity pattern, and noisy units are removed, by threshold-setting of unit activity. Memory capacity for accurate recall is strongly dependent on the form of patterns to be stored and the Hebbian learning rule employed.

The hippocampus, one of the most widely studied of brain regions, has been associated with the intermediate storage of declarative memories (Andersen et al., 2007). The hippocampal regions CA3 and CA1 have been proposed to be auto- and heteroassociative memories, respectively (Treves and Rolls, 1994). Recent years have witnessed a dramatic accumulation of knowledge about the morphological, physiological and molecular characteristics, as well as the connectivity and synaptic properties of hippocampal neurons (Andersen et al., 2007). Despite these advances, however, only limited insight was gained into the computational function of the neurons; in particular, the role of the various types of interneurons remains elusive.

We advance a CA1 microcircuit model in order to investigate the biophysical mechanisms by which hetero-association of spatio-temporal input patterns is achieved in the hippocampus. The model incorporates the major cell types including pyramidal (P) cells and four types of inhibitory interneurons: basket (B) cells, axo-axonic (AA) cells, bistratified (BS) cells and oriens lacunosum-molecurale (OLM) cells. Inputs to the network come from the entorhinal cortex (EC), the CA3 Schaffer collaterals and medial septum (MS). The EC input provides the sensory information, whereas all other inputs provide context and timing information. The MS input paces the network theta rhythm activity. Storage and recall of memories are separated into different functional theta half-cycles (Hasselmo et al., 2002). Storage is accomplished via an STDP mediated hetero-association of the EC input pattern, and the CA3 input pattern on the pyramidal cell target synapses. The model simulates the timing of firing of different hippocampal cell types relative to the theta rhythm in anaesthetized animals (Klausberger et al., 2003, 2004) and proposes functional roles for the different classes of inhibitory interneurons in the storage and recall cycles of input patterns. We also investigate how the temporal patterning of the inputs interacts with STDP learning to either promote or inhibit pattern storage and hence ultimately pattern recall.

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NEGATIVE SERIAL DEPENDENCE BETWEEN SPIKING INTERVALS IMPROVE RATE ESTIMATION IN POST-SYNAPTIC CORTICAL ENSEMBLE

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We report here that cortical neurons $in\ vivo$, when measured under stationary conditions, exhibit a pattern of negative correlation of adjacent inter-spike intervals. This statistical property has been largely overlooked in the cortex but is known from several other types of spiking neurons. We introduce a new family of non-renewal point processes to model serial interval correlation. By means of analytic calculus and in numeric simulations we show that negative serial correlation reduces the variability of rate signals in single neuron spike trains as well as in the population signal of a large ensemble of neurons. Our theoretic result could be confirmed in experimental $in\ vivo$ single neuron recordings from rat neocortex. We suggest that this reduction in the variability of a given ensemble of neurons will enhance the reliable transmission and decoding of information across successive stages of neuronal ensembles.

We made $in\ vivo$ intracellular recordings from neurons in the somatosensory cortex of anaesthetized rats. For our statistical analyses we chose only recordings devoid of up-/down states that are typically observed under anaesthesia. Testing for serial dependencies of inter-spike intervals is usually impaired by modulations in the firing rate. We therefore applied a novel test strategy to identify stationary parts of the recording. Our results show that most neurons exhibit a significant and negative serial rank-order correlation (approx. -0.2) of neighbouring intervals while higher order correlations were non-significant and close to zero [1]. We give an overview of previous reports on this phenomenon in other types of spiking neurons, including our own findings in mushroom body neurons of the honey bee.

In order to study the potential effect of serial correlation on information processing, we propose a class of autoregressive point process models that incorporate serial correlation of inter-spike intervals for arbitrary lags. Our model describes the marginal inter-event intervals distribution by the family of gamma distributions which includes as special cases the log-normal, the gamma, the exponential and the Weibull distribution. We derive the maximum likelihood estimators for the relevant model paramters and apply them to experimental data sets. It is known that negative serial correlation reduces the Fano Factor (FF) and noise in the low frequency rate regime [2,1]. We analytically calculated the FF in dependence on observation time. For small times the Fano factor always tends to unity, independent of the correlation structure. However, for increasing observation windows a negative serial correlation results in a reduced FF. A window that comprises on average 2 intervals leads to a considerable reduction by up to 50%. We show in numeric smulations and pseudo-poulations of experimentally recorded neurons that this holds true also for the populations signal. Thus, on the systemic level, negative interval correlation can considerably reduces the neuronal variability and thus may enhance information transfer in a rate code.

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MOVEMENT-GOAL REPRESENTATIONS IN THE FRONTOPARIETAL REACH NETWORK

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When planning goal-directed arm movements the sensorimotor system needs to integrate the current behavioral context with given spatial constraints to define and maintain motor-goals. We are interested in how this integration is achieved within the sensorimotor network of reach-related parietal and premotor cortical areas.

We used a memory-guided anti-reach paradigm with partial movement pre-cuing to test the respective roles of the dorsal premotor cortex (PMd) and the parietal reach region (PRR) in the posterior parietal cortex in defining and planning context-specific reach goals. Two cues, one spatial and one contextual, were given to the subjects either simultaneously or at different points in time. The contextual cue instructed the subject to make a move towards (pro) or to the opposite (anti) of the spatial cue. We recorded simultaneously from PRR and PMd with multiple microelectrodes in each area, while monkeys performed the anti-reach task.

Single cell directional tuning during the instructed delay, when either spatial, contextual or both information was available, was used to classify cells in terms of their motor-goal characteristics. Additional to cells that encoded only definite motor goals or potential motor goals, we also found many cells in both areas that encoded specifically only anti-reach motor-goals. They were directionally tuned in anti- but not in pro-trials, when both the spatial cue and the context was shown, and tuned in the same direction, when only the spatial cue was shown but the context was yet undefined. We hypothesize that these ‘anti-goal’ cells represent definite or potential motor goals which are not explicitly predetermined by spatial sensory cues, but rather have to be actively constructed based on spatial sensory information.

Since both areas, PRR and PMd, encode motor-goal location in similar fashion during an instructed delay, we tested which area forms the motor goal first by integrating spatial information about an object location with a currently valid behavioral context. Multi-channel population decoding was used to compare the precise timing of motor-goal formation in both areas. We found that the motor goal is represented earlier in PMd than in PRR. The latency difference was larger in conditions with instructed delay compared to those conditions where the monkey had to respond immediately. Explicit information about the context is represented earlier and stronger in PMd than PRR.

Our results suggest an integration of context and spatial information in PMd to form motor goals for reaches. Motor-goal representations in PRR, in this view, could be the result of feedback projections from PMd, potentially to facilitate the formation of predictions about the sensory consequences of the planned movement.

OPTICAL CONTROL OF CORRELATED ACTIVITY PATTERNS IN LARGE POPULATIONS OF NEURONS

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Spatiotemporal patterns of activity carried across large populations of neurons are the fundamental representation of information within the nervous system. Moreover, emerging evidence indicates that information processing as well as learning and memory processes in both the network and single-neuron levels are highly dependent on the correlation structure of multiple spike trains. Examples include a diverse set of observations and models of correlated network states and correlation-based information encoding, correlation-dependent nonlinearities in dendritic integration, and the phenomenon of spike-timing-dependent plasticity.

We present two methodological breakthroughs aimed at allowing controlled experimental emulation of correlated network activity patterns.

First, we introduce a general new computational strategy for generating multiple spike trains with *exactly* controlled mean firing rates and pair-wise correlation structure (defined in terms of auto- and cross-correlation functions). This approach can be used to generate stationary or non-stationary correlated point processes, and allows the generation of network activity patterns with predictable spatio-temporal correlations.

Next, we demonstrate the direct control of spiking activity in large populations of retinal ganglion cells using an approach generally termed patterned photo-stimulation. We have recently developed several generations of patterned photo-stimulation systems with hundreds of thousands of pixels. Our primary goal in this work is the development of a retinal neuroprosthetic device that will address blindness resulting from degenerative diseases of the outer retina by bypassing the degenerated photoreceptor layer, and interfacing directly with the largely viable Retinal Ganglion Cells (RGCs).

The combination of patterned photo-stimulation and the ability to generate multi-correlated spike trains, leads to a method capable of physically generating complex neural activity patterns with a predefined correlation structure. This new method can be used to experimentally gain a better understanding of neural information representation and processing, and medically in the development of neuro-prosthetic interfaces.

A NEURAL FIELD MODEL OF VSDOI SIGNALS

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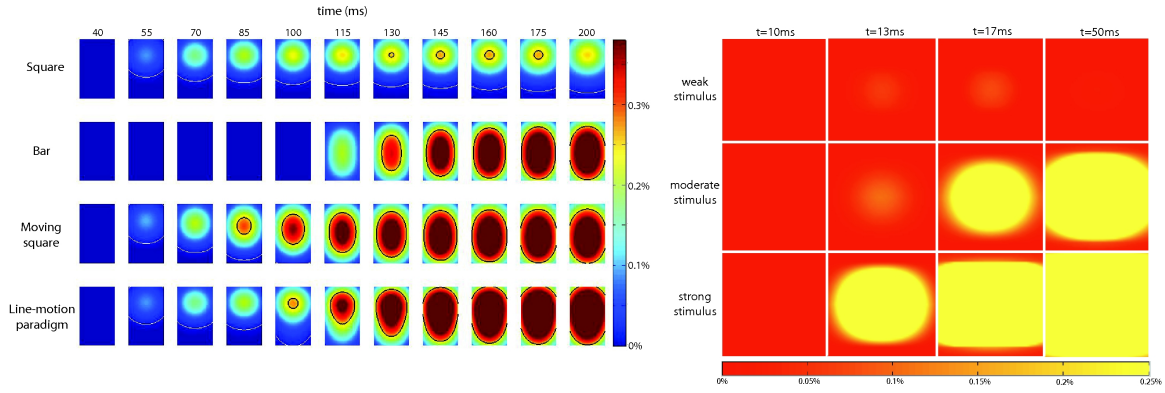
In this poster we present a mesoscale model of voltage sensitive dye optical imaging (VSDOI) signals. We model a cortical area as a two-dimensional neural field with multiple layers. The dynamics of the field are described by a classical integro-differential equation of the Wilson-Cowan type

$$\dot{\mathbf{A}}(\mathbf{r},t) = -\mathbf{L}\mathbf{A}(\mathbf{r},t) + \mathbf{S}\left(\int_\Omega \mathbf{W}(\mathbf{r},\mathbf{r}')\mathbf{A}(\mathbf{r}',t)\,d\mathbf{r}' + \mathbf{I}_{\text{ext}}(\mathbf{r},t)\right).$$

$\mathbf{A}$ is the activity vector of the different types of neurons represented at a given point of the field. $\mathbf{L}$ is a diagonal matrix containing the different synaptic time constants of the field, $\mathbf{S}$ a sigmoidal transform and $\mathbf{I}_{\text{ext}}$, the input to the field arising from other cortical areas or the thalamus. In this equation, the connectivity kernel $\mathbf{W}$ plays a central role. It can be set to account for various cortical structures such as patchy connectivities in the visual cortex or the barrel structure of the rat's sensory cortex. Based on a fine description of the repartition of VSD molecules in the different layers of the field we derive a formula for the direct problem of VSDOI. It takes the form of a compact operator applied to the state vector at each time instant

$$OI(\mathbf{r},t) = \int_\Omega \tilde{w}(\mathbf{r},\mathbf{r}') \cdot \mathbf{A}(\mathbf{r}',t)\,d\mathbf{r}',$$

where $\tilde{w}$ depends on several biophysical parameters, including the kernel $\mathbf{W}$. The validity of the approach is supported by the simulation of two very different, well-known optical imaging experimental setups: the line-motion illusion in the visual cortex of mammals (see figure, left) and the spread of activity in the rat barrel cortex (see figure, right).



We finally analyze these propagation results by discussing the linear and nonlinear mechanisms that led to their generation.

DISCRIMINATING SOUNDS FROM HUMAN ELECTROCORTICOGRAMS (ECoG)

Chloe Huetz[1,2,*], *Tomislav Milekovic*[1,2], *Tonio Ball*[1,3], *Andreas Schulze-Bonhage*[1,3], *Ad Aertsen*[1,4], *Carsten Mehring*[1,2]

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Identifying stimuli from human brain activity constitutes a major challenge in computational neuroscience and receives growing attention since neurophysiological recording techniques and computational analysis methods are continuously improving (Kay et al., 2008). Within these techniques, electrocorticography (ECoG) which records subdural neuronal signals from the brain´s surface of epilepsy patients provides a powerful tool to investigate the neuronal correlates of human perception. This technique appears to be especially suited to study auditory perception since it provides a high temporal resolution and a better spatial resolution and larger frequency range coverage than scalp EEG (Crone et al., 2001).

Here we investigated the neuronal correlates of auditory perception and auditory imagination using ECoG recordings in epilepsy patients. In the first part of the study, we recorded brain activity from the temporal lobe of two epilepsy patients during the presentation of six different auditory stimuli. These stimuli consisted of four artificial stimuli - two frequency modulated (FM) tones (rising and falling) and two “moving” tones (moving from right to left or from left to right) - and two natural stimuli - bird song and speech. Our results show that (1) all stimuli evoked strong high-frequency gamma activity (50Hz-120Hz) on electrodes that were located on the superior temporal lobe, (2) on some individual electrodes, the evoked gamma response was significantly different for different stimuli and (3) the spatial distribution of gamma activity was dependent on the auditory stimulus. Different responses were even found for pairs of artificial stimuli that share the same spectral content like the rising and falling FM tones.
In the second part of this experiment, patients were asked to imagine hearing the same stimuli that were previously presented. As during auditory perception, the auditory imagination also evoked a significant increase of high-frequency gamma band activity, though this increase was in general substantially smaller than for perception.

In summary, our results show that it is possible to discriminate perceived sounds from human ECoG signals recorded on the superior temporal lobe, and that imagination of sounds produces significant increases in the high-frequency range. These findings may also be interesting for alternative approaches to brain-machine interfaces using neuronal activity from the temporal cortex and auditory imagination to control external actuators.

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THE ROLE OF PRIMARY VISUAL CORTEX IN PERCEPTUAL AWARENESS

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Under certain stimulus conditions a single interpretation of the external world cannot be unambiguously designated. When the brain is presented with such stimuli typically only one possible interpretation is perceived and after a few seconds the percept switches abruptly to another. Notably such perceptual alternations happen while the sensory input is kept constant, offering thus a clear dissociation of sensory stimulation and subjective awareness.

A celebrated example of such a perceptual phenomenon is binocular rivalry (BR). It involves alternations of visual perception between two different images presented dichoptically at corresponding retinal locations. Based on many psychophysical studies over decades the primary visual cortex (V1) was implicated as an important candidate for the site of perceptual suppression. However, the first neurophysiological evidence performed in monkeys did not corroborate this but instead found only a small percentage of neurons modulating their activity with the subjective awareness reported by the animals. On the contrary, studies using human functional magnetic resonance imaging (fMRI), have found V1 to be modulating to a large extent, creating an apparent controversy. Therefore, the role of primary visual cortex (V1) in subjective perception remains controversial.

In this study, we studied the effects of perceptual suppression on neural activity in V1 of the macaque. We have used the binocular flash suppression (BFS) paradigm, a variant of BR which ensures excellent control over the subject's perceptual state. We have recorded the spiking activity of a large number of well isolated single units (SUA) and acquired simultaneous local field potentials (LFPs) during the dichoptic presentation of orthogonal orientation gratings. Our design enabled us to determine a) which neurons and LFP bands are correlated with the percept and b) how this is related to their orientation and ocularity preferences.

We find that only a small minority of about 20% of the single units modulate in consonance with the perceptual suppression. Furthermore, the magnitude of the perceptual effect was small (~15%) in comparison to the sensory preference of the neurons. Results of the LFPs were very similar to the single units showing a similar percentage of sites modulating with perception. Analysis of the orientation and ocularity preference of neurons did not show a particular class of cells to be having a greater probability to show perceptual modulations.

This work was supported by the Max-Planck Society.

FREQUENCY AND AMPLITUDE MODULATIONS OF MOTOR CORTICAL LOCAL FIELD POTENTIALS DURING TEMPORAL ATTENTION AND MOVEMENT PREPARATION

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The local field potential (LFP) is thought to mainly reflect local synaptic activity. LFPs tend to oscillate and the typically observed oscillation frequency in pre-central cortex is within the beta range (e.g. 15-30 Hz). Beta range oscillations were associated with various phenomena, from reflecting a 'resting' motor cortex or supporting postural maintenance to rather reflecting attention, sensorimotor binding and movement planning. In this context, amplitude modulations of oscillations were extensively studied. Evidence for modulations of oscillation frequency in relation to sensorimotor integration or motor planning is scarce.

We developed a behavioral task to study motor cortical activity during two contextually different delays introduced in a pre-cued center-out task. Each trial started with a time cue (TC), indicating the delay durations (short or long) in the current trial. The first delay (time delay; TD) demanded temporal attention, in order to be ready for the brief presentation of the spatial cue (SC) at the end of TD. During the second delay (preparatory delay; PD; same duration as TD) the movement direction indicated by SC had to be prepared.

While the monkeys performed the task, multi-electrode LFP recordings were made in primary motor cortex. In the average LFP, typically a visual evoked potential (VEP) could be seen after SC, often directionally selective and larger on short trials. When aligning to movement onset, a movement-related potential (MRP) was clearly visible. The MRP was also directionally selective and larger in amplitude in the long trials. This demonstrates that task timing modulates motor cortical activity, in addition to other movement parameters.

LFP beta range oscillations were observed during both delays, disappearing for several hundred milliseconds following SC (see example in Fig. 1). The oscillations were different in the two delays, with lower oscillation frequency and higher amplitude during temporal attention, when the animal was waiting for the spatial cue, than during movement preparation. In addition, the frequency and the amplitude of the oscillations were directionally tuned during movement preparation. Both the frequency and the amplitude of the oscillations were highest in the movement direction with shortest reaction times. We suggest that beta range oscillations observed in the different cognitive and behavioral contexts reflect the activity of different neuronal networks, some being more related to attention in the absence of precise motor plans, and others more explicitly to movement preparation.

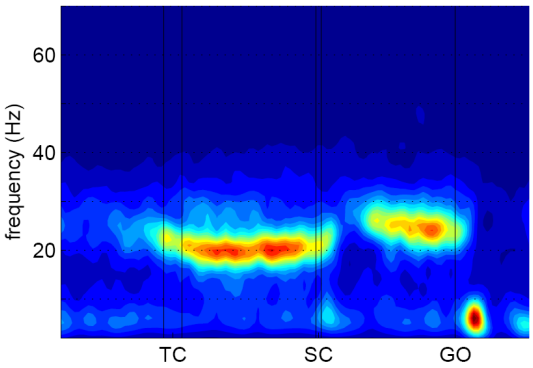

Fig. 1. Time-frequency analysis of one LFP for all long trials. There are strong beta oscillations during the two delays, but the oscillations stop temporarily after SC. The main oscillation frequency was about 20 Hz during TD and 24 Hz during the final part of PD.

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VISUOSPATIAL UPDATING AFTER PASSIVE ROTATIONS AND TRANSLATIONS IN THREE-DIMENSIONAL SPACE

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Visuospatial updating allows us to maintain a stable representation of visual space despite the fact that we are constantly moving. Without such a mechanism for spatial constancy, the world around us would seem to be constantly in motion and we would be incapable of interacting with it. In order for spatial updating to be successful it must combine retinal information about the location of an object with non-retinal information about our own movements. These movements can be both active (e.g., eye movements while watching a tennis match) and passive (e.g., whole-body motion while riding in a train).

Over the last several years, we have undertaken a number of passive, spatial updating experiments to help us answer the following questions: (1) Are efference copy signals of the outgoing, voluntary motor command necessary for spatial updating? (2) Are gravito-inertial signals taken into account during spatial updating? (3) Can the brain take into account the complexities of the non-commutativity of rotations (i.e., $a \times b \neq b \times a$) for spatial updating? (4) Can we update equally well for rotations and translations in three-dimensional space? To answer these questions we used two motion platforms capable of passively moving human subjects in all three degrees of freedom for rotations (yaw, pitch and roll) and translations (fore-aft, lateral and vertical). In all these studies, subjects were first briefly shown a target at a randomly chosen spatial location and were then passively rotated or translated to a new body orientation (during this intervening motion, the subjects fixated a central target so that the vestibuloocular reflex was cancelled). At the end of the induced motion, the subjects waited for the central target to be extinguished, which was their cue to make a saccadic eye movement to the remembered location of the flashed target.

We found that: (1) Efference copy signals of the self-initiated, motor command are not necessary for accurate target localization after intervening whole-body rotations. Other signals, like those from the vestibular system and/or proprioceptive cues, can also be used to maintain spatial constancy. (2) Gravity signals are vital for spatial updating about axes that normally move the body relative to gravity (e.g., roll), but are not as important for updating about axes that do not change the gravity vector (e.g., yaw). (3) The brain does take into account the non-commutative properties of rotations, generating different saccade trajectories depending on the order of the whole-body rotations. (4) Accurate spatial updating was found for fore, aft, rightward, leftward and upward translations, with poorer performance for downward translations.

Taken together, we find that the brain has developed a robust system to handle the intricacies of visuospatial updating. It can make use of both rotational and translational sensory signals to gauge the amplitude and direction of intervening movements, and it can also use gravitational signals when necessary. It can handle the extra computations associated with updating after rotations about the roll axis and after non-commutative rotations. Future research on this remarkable mechanism will focus on the pathways for vestibular/proprioceptive cues from the brainstem to the cortical regions that exhibit spatial updating at the neuronal level, and how movement information from various sources are integrated to provide a unified measure of the intervening motion.

THE K-COMPLEX INITIALLY BLOCKS FAST SPINDLES AND AFTERWARDS EVOKES FASTER SPINDLES DURING STAGE II OF HUMAN NREM SLEEP

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The 2nd stage of non-REM (NREM) sleep is characterized by K-complexes (very large negative or negative-positive EEG waves of >500ms, predominant over frontal areas) and spindles (generalized rhythmical waxing-and-waning sequences of ~0.5-3sec waves at ~11-15Hz), the latter being further subdivided in slow (<13Hz, most prominent frontally) and fast ones (>13Hz, most prominent over centroparietal areas). It is hypothesized that K-complexes are born out of a slow intra-cortical oscillation (<1Hz) and that its negative-positive phases correspond to a sequence of a hyperpolarization-depolarization. The role of the K-complex is considered to be both a building stone of the slow-wave sleep and a reactive response against endo- or exogenous stimuli associated with transient homeostatic responses. The rhythm of spindles is generated in the thalamic reticular nucleus and spindles are further widely synchronized by corticothalamic projections. Their main role is postulated to be the inhibition of sensory input to the cortex, inducing plastic changes at the same time, which involves them in memory consolidation. K-complexes and spindles do coincide but their mechanisms are suggested by several studies to be independent. Here, we present evidence of a clear interaction between the two.

We recorded whole night's sleep from seven adult subjects (6 females, one male, mean age 28y) with regular sleep habits. 64-channel EEG was used along with standard EOG and EMG, and sleep staging was performed according to the established standards. By visual inspection, we identified singular spontaneous generalized K-complexes (more than 200 from every subject) and marked the occurrence of both their negative peak and the peak of their positive phase, the latter where applicable. We also identified slow and fast spindles (more than 300 from every subject) and marked their middle negative peaks. We used FFT-based event-related time-frequency analysis in order to extract the spectral features of our samples. We selected the central Cz electrode in order to study the effect of the spontaneous singular generalized K-complex on fast spindles. In all subjects and in all cases we observed that when K-complexes occurred during the course of fast spindles they invariably blocked them. In their place and during the rising negative phase of the K-complex, we observed slower rhythms in the range of ~7-11 Hz. After the negative K-complex peak and over the positive phase, spindles progressively resumed but at a higher spectral frequency than before (increased by ~1-2Hz). The same increase in spindle frequency was observed in samples where K-complexes directly evoked spindles, that is, without the K-complex being preceded by a spindle. The spindle frequency elevation and the intra-K-complex slower rhythm frequency did not correlate to either the amplitude of the negative K-complex peak or the amplitude of the positive phase or the existence of the positive phase. They were also not dependent on whether the samples were taken from the descending NREM stage II (where slow-wave sleep follows) or the ascending (where REM sleep follows). Phase synchronization analysis of K-complexes coinciding with fast spindles showed that the K-complex did not change the already high inter-hemispheric synchronization of fast spindles over the central areas.

This study shows that K-complexes, regardless of their characteristics and the type of stage II met, block coincidentally running fast spindles and evoke a new sequence of higher frequency spindles without changing the inter-hemispheric synchronization.

EYE ARTIFACT REJECTION IN EEG DATA USING SECOND ORDER STATISTICS (SOBI METHOD)

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Eye movement artifacts represent a critical issue for electroencephalographic (EEG) series analysis and a number of signal processing techniques approaches have been proposed to reduce their contribution in EEG recordings, especially when aiming in an online analysis in the frame of a brain computer interface system. The aim of the present work is the application of a Blind Source Separation algorithm (BSS) in eye artifact rejection of EEG datasets. BSS decomposes the signal in Independent Component Analysis (ICA) components based on spatial patterns of sources/generators. We have seen that the BSS algorithm is able to distinguish components from simulated data that are generated from different and spatially separated sources, superior with respect to methodological artifact suppression to those of FastICA algorithm. Especially we apply the SOBI (Second-order blind identification) that is based on the second order statistics. The criterion of rejection is the temporal correlation between the Independent Components and the artifact–waveform. SOBI decomposes the signal into multiple sources. Based on that an Artifact Rejection EEG toolbox (ARES) was developed. The real EEG data on which this was applied is a finger tapping motor task and a subsequent imagination of the same motor task. About 100 trials of each session were used, of 1500 msec duration each (sampling rate 1000 Hz). The data imported to the algorithm were unfiltered and the algorithm was applied where the eye artifact was detected. Time and frequency results indicated that SOBI algorithm preserved and recovered the brain activity. These results on real data also demonstrate that the method is able to suppress blinking and saccade artifacts in a semi-automated way. Finally, we concluded that second-order BSS-based algorithms (SOBI) provided an effective technique for eye movement removal even when EOG recordings were not available or when data length was short. Future work will be the online implementation of such methods for artifact rejection of a Brain Computer Interface system.

STEADY-STATE SOMATOSENSORY EVOKED POTENTIALS AS A MEANS OF PROBING SOMATOSENSORY CORTEX EXCITABILITY

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This study explored the use of steady-state somatosensory evoked potentials (ssSEPs) as a continuous probe on the excitability of the sensorimotor cortex during the foreperiod and the response time of a cued choice reaction time task. ssSEPs were elicited by bilateral, repetitive (22.2 Hz) median nerve electrical stimulation applied at the wrist. Scalp-recorded ssSEPs were analyzed by means of dipole source analysis to achieve optimal separation of left and right hemisphere ssSEPs. The ssSEPs were generated by two symmetrical dipole sources located in the primary somatosensory cortex. The source waveforms were sinusoidal signals oscillating at the frequency of the driving stimuli. Continuous Wavelet Transform using complex Morlet wavelets was applied in order to extract the time course of ssSEP modulation. In addition to the extraction of ssSEPs, the analysis included a derivation of lateralized attention and movement-related potentials, *i.e.* ADAN and LRP. The time course of ssSEP modulation, remarkably similar to the time course of ADAN and LRP, was characterized by a reduction of ssSEP amplitude at latencies just following the latency of the ADAN (~ 400 ms) and the latency of the LRP (~1200 ms). This reduction was greater for contralateral than for ipsilateral movements. In addition, a significant bilateral reduction of ssSEP amplitude was recorded during movement execution. This reduction was also stronger for contralateral movements. The study demonstrates that ssSEP methodology represents a feasible approach to the measurement of movement-related changes in cortical excitability, which may be used to resolve ambiguities in the interpretation of lateralized event-related brain potentials.

ANALYSIS OF PATTERN RECOGNITION METHODS IN CLASSIFYING BOLD SIGNALS IN MONKEYS AT 7-TESLA

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Pattern recognition methods have shown that fMRI data can reveal significant information about brain activity. For example, in the debate of how object-categories are represented in the brain, multivariate analysis has been used to provide evidence of distributed encoding schemes. Many follow-up studies have employed different methods to analyze human fMRI data with varying degrees of success. In this study we compare four popular pattern recognition methods: correlation analysis, support-vector machines (SVM), linear discriminant analysis and Gaussian naïve Bayes (GNB), using data collected at high field (7T) with higher resolution than usual fMRI studies. We investigate prediction performance on single trials and for averages across varying numbers of stimulus presentations. The performance of the various algorithms depends on the nature of the brain activity being categorized: for several tasks, many of the methods work well, whereas for others, no methods perform above chance level. An important factor in overall classification performance is careful preprocessing of the data, including dimensionality reduction, voxel selection, and outlier elimination.

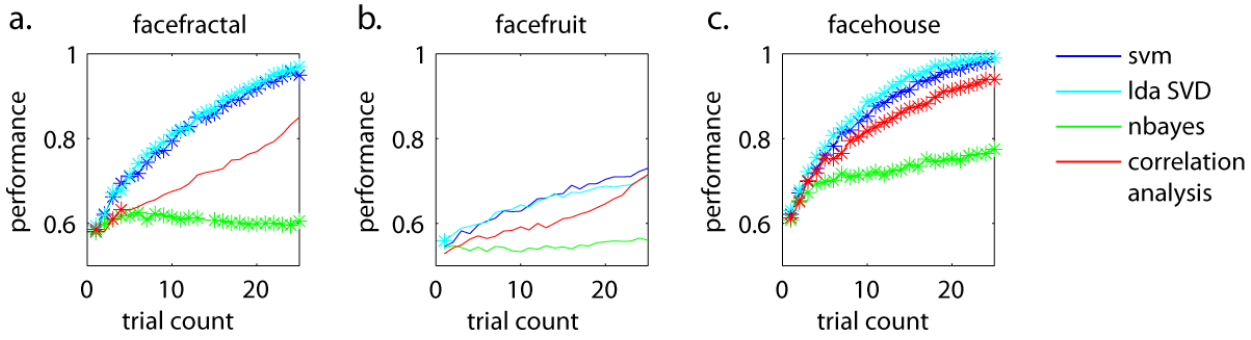

Figure 1: Performance of different multivariate classification methods, when discriminating faces against other object categories (house, fruit, fractal). The x axis represents the number of trials over which we average to test the classifiers (from single trial analysis to averages over 25 trials); the y axis is the average percentage classification error. Classifiers performing significantly above chance (as determined by a permutation test) are indicated by stars. LDA and SVM perform almost identically, followed by correlation and then GNB. Finally, we remark that apparently high rates of correct classification are no guarantee of above-chance performance.

ENCODING, PROCESSING AND DECODING OF SENSORY STIMULI WITH A SPIKING NEURAL POPULATION

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We investigate an architecture for the encoding, processing and decoding of visual stimuli such as natural and synthetic video streams (movies, animation). The stimuli are encoded with a population of spiking neurons, processed in the spike domain and finally decoded (see Figure 1). The population of spiking neurons includes level crossing as well as integrate-and-fire neuron models of ganglion cells with feedback. A number of spike domain processing algorithms are demonstrated including faithful stimulus recovery, as well as simple operations on the original visual stimulus such as translations, rotations and zooming. All these operations are executed in the spike domain. Finally, the processed spike trains are decoded for the faithful recovery of the stimulus and its transformations.

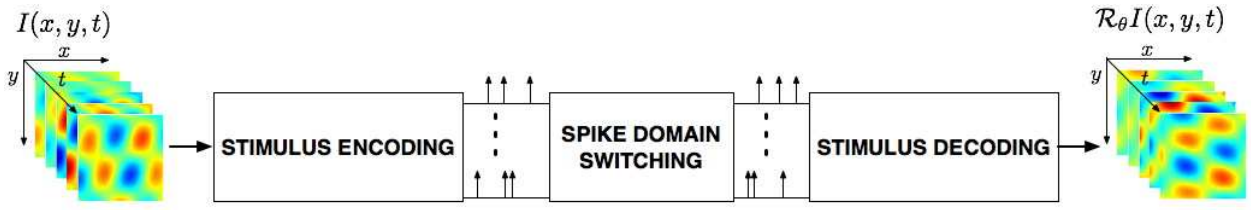

Figure 1: Block diagram representation of the spike processing architecture.

We show that the class of linear operations described above can easily be realized with the same basic stimulus decoding algorithm. What changes in the architecture, however, is the switching matrix (i.e., the input/output "wiring") of the spike domain switching building block (see Figure 1). For example, for a particular setting of the switching matrix, the original stimulus is faithfully recovered. For other settings, translations, rotations and zooming of the original video stream are obtained (see Figure 2).

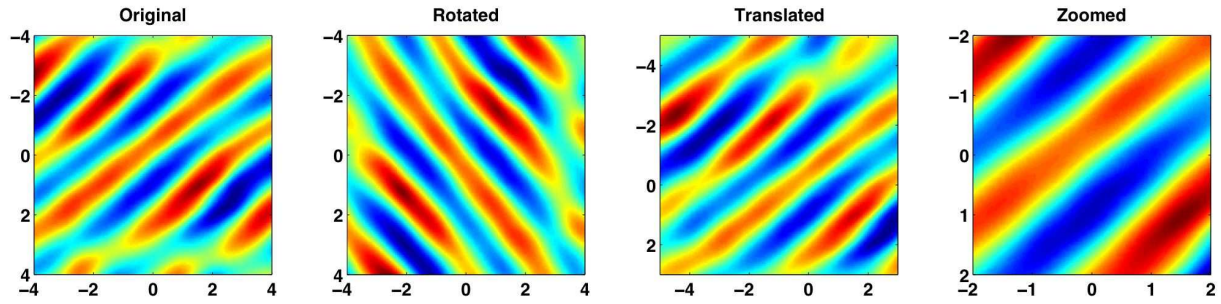

Figure 2: Switching in the spike domain leads to the faithful recovery of the original, rotated, translated and zoomed video stream. Each spiking neuron is preceded by a spatial Gabor filter.

Acknowledgements
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ENHANCED CODING OF INTERAURAL TIME DIFFERENCES AT SUCCESSIVE STAGES IN THE ASCENDING AUDITORY PATHWAY

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We examined the coding of interaural time differences (ITDs) across a wide range of sound levels at successive stages in the ascending auditory pathway, the medial superior olive (MSO) and dorsal nucleus of the lateral lemniscus (DNLL). We made single-unit recordings from MSO and DNLL neurons with low best frequencies (<1500 Hz) in anesthetized gerbils and measured ITD tuning curves as spike counts in response to pure tone stimuli at different ITDs and intensities (from 30 to 70 dB SPL). We found that the intensity-dependence of ITD tuning curves in the MSO and DNLL were strikingly different. In the MSO, the peak of the tuning curve typically increased with increasing intensity, as did the trough and the spike count variability. In the DNLL, where spike counts were typically much higher than in the MSO, the peak of the tuning curve also increased with increasing intensity (before saturating at high intensities), but the trough decreased and spike count variability remained relatively constant. In MSO, both the best ITD (that which corresponded to the tuning curve peak) and the half width of the tuning curve remained relatively constant with increasing intensity. In the DNLL, the best ITD was also relatively constant with increasing intensity, while the half width of the tuning curve decreased.

To examine the functional consequences of these differences in ITD tuning curves in the MSO and DNLL, we computed the mutual information between the spike counts and the stimulus. We found that both the maximum information about any one ITD (the quantity relevant for a labeled-line code) and the mean information across all ITDs (the quantity relevant for a population code) were significantly higher in the DNLL across a wide range of intensities. To understand how different tuning curve parameters influence the mutual information in the spike counts, we created model MSO and DNLL tuning curves and measured the change in information following a change in each parameter. We found that in both the MSO and DNLL, the increase in the peak of the tuning curve with increasing intensity resulted in an increase in both maximum and mean information. However, in the MSO, this increase in information was offset by the decrease in information caused by the increase in the trough and spike count variability. In the DNLL, the increase in information is maintained, as changes in other parameters with increasing intensity have little effect. We also compared the experimentally observed values of best ITD and half width to those that maximized the maximum and mean information in the model spike counts. In both the MSO and DNLL, we found that the observed values are close to those that maximize mean information, but not maximum information. Taken together, these results suggest that ITDs are represented in the auditory brainstem in a population code such that the mean information about all ITDs in the response of individual neurons in maximized. Furthermore, this code is enhanced from the MSO to the DNLL through an increased robustness to changes in intensity, allowing an increase in the peak of the ITD tuning curve without corresponding increases in the trough or spike count variability.

PREDICTION OF BEHAVIORIAL CHOICE AND REACTION TIME FROM LOCAL FIELD POTENTIAL IN MACAQUE PREFRONTAL CORTEX

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Previous studies have shown that prefrontal cortex (PFC) plays an important role in working memory and decision-making processes. Specifically, in tasks in which a sample stimulus has to be held in memory during a brief delay and then compared to a subsequent test stimulus (delayed-matching to sample paradigm), neurons in PFC show enhanced spiking activity whenever the sample stimulus matches the test stimulus (Miller et al, 1996). This enhancement could encode the match between the test stimuli with the item held in memory and thus mediate the decision to report a match.

We investigated whether the local field potential (LFP) recorded in PFC of rhesus monkeys also carries information about whether the test stimulus matched the sample and whether this signal predicted the behavioral choice.

In a delayed matching to sample paradigm a sample stimulus was presented followed by a probe stimulus after a delay period. The task required the animal to initiate a lever response if the two successively presented stimuli were identical (match). In the other case (non-match), the animal was required to withhold the lever response.

Consistent with previous findings the majority of PF neurons showed enhanced spiking activity in match-trials (70%, Binomialtest, $p<0.02$). This effect was also reflected in the simultaneously recorded LFP, at the majority of the recorded sites the visual evoked response to the test stimulus was stronger in match vs. non-match cases (85%, Binomialtest, $p<0.001$). Furthermore, the magnitude of the evoked response predicted the animal's behavior: In cases in which the animal correctly reported a match, we observed a significantly larger evoked response than in cases in which the animal missed a match (t-test, $t_{39}>4.7$, $p<0.001$).

In addition, we found a significant positive correlation between the latency of the evoked response and the reaction time of the animal. The response of the animal did not follow the evoked response at a fixed latency. Rather, an increase in the latency to the test stimulus resulted in a proportional increase in reaction time. Based on this covariation it was possible to predict the reaction time on a single trial basis (Pearson correlation coefficient between predicted and actual reaction times $r=0.71$, $p<0.001$).

These results show that the LFP in PFC carries performance-related information, which makes it possible to decode the behavioral choice as well as the reaction time in a visual memory task.

STRUCTURE OF BRAIN CONNECTIVITY AND TREATMENT EFFECTS

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To date, basic mechanisms of epileptogenesis remain considerably unclear in the mammalian central nervous system and investigators agree that no single mechanism underlies epileptiform activity. Different forms of epilepsy are probably initiated by a set of different mechanisms. The quantification of interactions among different brain regions has played an important role in further understanding of the epileptogenic phenomena in both humans and animal models.

Clinical observation has been a most common method for evaluating influences of therapeutic interventions in epilepsy and other neurological disorders. Evaluating the efficacy of treatments has traditionally focused on comparing the frequency of seizures during treatment to a finite baseline period. Electroencephalogram (EEG) recordings are used as a supplemental clinical tool in these evaluations. Besides counting the number of seizures as a measure of treatment effects there is currently no reliable tool for evaluating the treatment in the current clinical environment. Subtle differences in interactions among different brain regions hidden at the micro level of the EEG might provide new and valuable information related to therapeutic effects. Recent findings in the field of nonlinear dynamics of EEG recordings have shown the causal activities among various brain regions. Cross Mutual Information (CMI) analysis represents a method for estimating and quantifying both linear and nonlinear statistical dependencies between two EEG time series, and have been shown to have superior performance to the traditional correlation analysis.

In this study, we present a new approach for evaluating treatment effects through modeling and assessing brain connectivity before and after treatments. The first step of the proposed approach is to transform the connectivity behavior into a connected graph. The connectivity for each pair of brain regions is quantified by the CMI, and then the maximum clique algorithm is subsequently applied to find the group of highly connected brain regions that is represented by a clique with a maximum size. Clinical treatment outcome measures and results of connectivity analysis are presented.

CHEMOTAXIS IN *DROSOPHILA* LARVAE: CODING THE WAY FORWARD

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Chemotaxis involves directed navigation toward attractive stimuli and away from aversive stimuli. Although this process is critical for the survival of all motile animals, the mechanisms by which higher organisms with complex nervous systems navigate through chemical gradients remain poorly described. We are studying this problem in *Drosophila* larvae which represent a powerful paradigm to investigate the neurobiological principles of odor coding.

An odorant stimulus can be fully specified by three variables: odor quality, odor intensity and time of occurrence. To chemotax, larvae must perceive and integrate changes relative to these variables. Using high-resolution computerized analysis of animals evolving in stable odorant gradients, we established a quantitative correlation between stimulus conditions and behavioral responses [1]. In particular, we inferred the typical concentration time courses experienced by freely moving animals. We showed that animals possessing only a single olfactory sensory neuron are able of robust chemotaxis.

To reproduce the dynamical nature of ethologically relevant stimuli, we devised a novel olfactometer allowing us to vary odor concentration in real time. On this basis, we have undertaken to characterize how dynamical olfactory stimuli are encoded at the levels of the peripheral olfactory sensory neurons (OSNs) and the projection neurons. As a starting point, we are limiting the input to the larval olfactory system to a single OSN - enough information to support chemotaxis. Combinations of functional OSNs will be considered in the future. Our long-term goal is to develop an integrated model accounting for the sensory and decision-making processes underpinning larval chemotaxis.

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THE ROLE OF STIMULUS CORRELATIONS FOR POPULATION DECODING IN THE RETINA

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All information about the visual world passes through the optic nerve, so with access to the spike trains of a large number of retinal ganglion cells, one should be able to construct a decoding algorithm to discriminate different visual stimuli. Despite the inherent noise in the response of the ganglion cell population, everyday visual experience is highly deterministic. We have designed an experiment to study the nature of the population code of the retina in this "low error" regime.

We presented 36 different black and white shapes, each with the same number of black pixels, to the retina of a tiger salamander while recording retinal ganglion cell responses using a multi-electrode array. Each shape was presented over 100 trials for 0.5 s each and trials were randomly interleaved. Spike trains were recorded from 162 ganglion cells in 13 experiments. As we wanted to focus on the role of correlations induced by the stimulus (signal correlations), we removed noise correlations by shuffling trials.

We designed decoding algorithms for this population response in order to detect each target shape against the distracter set of the 35 other shapes. We constructed binary response vectors using a single 100 ms bin following the presentation of each shape. First, we used a simple decoder that assumes that all neurons are independent. A second decoder, which takes into account correlations between neurons, was constructed by fitting Ising models (Schneidman et al., 2006) to the population response using up to 162 neurons for each model. We also constructed the statistically optimal decoder based on a mixture model, and an optimized linear classifier using logistic regression.

For small population sizes the decoders were almost indistinguishable in performance. However, when using populations of many neurons, the optimal and Ising decoders performed considerably better than the "independent" decoder. For certain shapes, the optimal decoder had 100 times fewer false positives than the independent decoder at 99% hit rate, and, in the median across shapes, the performance enhancement was 8-fold. While the decoder using an Ising model fit to the pairwise correlations did not achieve optimality, it was up to 50 times more accurate than the independent decoder, and 3 times more accurate in the median across shapes.

In a second class of analyses, we used decoders that take spike latencies into account, rather than just the absence or presence of a spike. In some cases, these decoders performed better than the binary decodes described above. However, also for these decoders, taking stimulus correlations into account was necessary for reaching the low-error regime.

Our study suggests that results about population codes obtained using a small number of neurons are not necessarily transferable to large populations, or to decoding tasks that can be performed at very high precision. We find that discrimination with very low error using large populations requires a decoder that models signal correlations.

COUPLING NEURONAL ENSEMBLE MESOSTATE PROBABLITIES WITH INFORMATION FROM GLOBAL ACTIVITY: A FORMULATION AND APPLICATION TO MAGNETOENCEPHALOGRAPHY

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While much is known about the electrophysiology of individual neurons, and many models exist regarding dynamical behavior of several interconnected neurons, a key challenge remains on how the dynamics of large neuronal populations can be modeled? From a bottom-up approach, this is computationally infeasible solely using the electrophysiology of the individual neurons and their interactions with each other, due to the high dimensionality of the problem. Conversely, but potentially related to a solution of the above problem, is how can information be decoded from the collective behavior of a neuronal population macro-state to a finer scale?

Developments within statistical physics and information theory [1,2] over the last half century may help in formulating solutions to these questions. Specifically, Bayesian inference and maximum entropy provide a framework from which a minimally biased probability distribution of the constituents of a given system can be inferred given its global observations and model. Here, we provide mathematical details of the maximum entropy principle illustrating one mechanism of how correlated activity from neuronal populations may be decoded at the local level.

This line of thought is not completely new, as there have been recent studies [3-5] providing evidence that aspects of information encoding, specifically with regards to correlated neuronal network states, can be described using maximum entropy principles. We propose to extend these studies by investigating the applicability of this general principle to an even larger scale, incorporating descriptions of whole brain cortical activity which can be observed using magnetoencephalography (MEG). As a demonstrative example of the technique, we will present a maximum entropy probabilistic solution to the under-constrained linearized inverse problem in MEG, where individual (voxel space) current dipole moments are sought based on measured global magnetic fields. Its relation and comparison to existing inverse solutions will also be presented.

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HOW FAR IN TIME AND SPACE DO WE GENERALIZE? PATTERNS OF GENERALIZATION AND ITS DECAY WHILE ADAPTING TO A NOVEL MOTOR TASK

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We present experiment and analyses designed to investigate generalization of a local adaptation to force field (FF), measured by behavioral performance and neuronal activity. To this end we recorded neuronal activity in M1 while a monkey performed a well known center-out reaching movements ("*standard* ") to 7 out of 8 directions whereas introducing FF in the 8th direction ("*learnt direction*").

Previous studies reported a bimodal narrow generalization function, which drops off towards 45 degrees but moderately rises back by 180 (Donchin 2003). Although our experiment's scheme encourages not generalizing, when checking trials which immediately followed a FF trial, we found a similar generalization function around the learnt direction.

Interestingly, we found that the decay in time of generalization is different across space. Generalization to 180 degrees away from the learnt direction decayed after two trials while generalization to 45 degrees contra to the applied FF direction remained highly significant for over than 7 trials.

We examined neuronal activity along the learning process by tracing cell's preferred direction (PD). Previous studies showed that introducing FF to all movement directions caused PD-shift in the direction of FF (Li 2001). In our case, apparently, the generalization function described above also governs neuronal changes giving rise to only subpopulations of cells that show significant PD shift; cells with PD up to 45 degrees away from learnt direction, and less pronounced - cells with PD about 180 degrees away.

These results show the complexity of generalization. On one hand, the tendency to generalize seems to be highly robust, appearing even when there's no actual need. On the other hand, it partially decays very fast. Further analyses should and will be done to explore the neuronal basis of generalization pattern and dynamics.

MODULAR SILICON PROBES FOR DENSE MAPPING OF NEURONAL ENSEMBLE ACTIVITY

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Mapping single-cell brain activity on a large scale is a crucial challenge on the path to understanding collective neuronal phenomena that give rise to learning, memory, and behavior. Extracellular multielectrode arrays modeled on microelectromechanical systems (MEMS) present a promising method for scaling up the number and density of recorded neurons, with a high level of spatial precision. Already, these devices have begun to provide glimpses of the rich interplay of action potentials and local field potentials across large neuronal populations. However, in spite of significant progress, there appears to be an impasse in the recording capabilities of current technology. Contributing factors include inadequate use of the probe's available surface for recordings, limited ability to sample the brain with multiple electrodes in all three principal directions, and size-related limitations on the number of recording channels. Our aim is to greatly enhance the capabilities of microfabricated probes in order to enable dense 3D mapping of action potential activity across large neuronal populations, with single-cell fidelity. To accomplish this we are developing a modular-architecture neural probe based on ultrathin silicon substrates. We are attempting to combine the following attributes in our devices: (i) twice the ordinary recording density with recording channels added to the back side of the silicon probe; (ii) increased channel capacity with minimal tissue displacement through nanoscale interconnects; and (iii) 3D modularity enabled via assembly into a multilayered structure. This presentation reviews our preliminary progress in this endeavor. Measurements in rats and locusts suggest the devices appear to hold promise in neural recording applications.

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CONTROL- AND PERFORMANCE-ERROR SIGNALS IN THE HUMAN ELECTROCORTICOGRAM (ECoG)

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From previous studies it is known that error-related neuronal signals can be found in human EEG and fMRI. These studies investigated error-related signals using trial-based paradigms with a binary outcome, correct or false. Therefore, the reported error signals provide the information whether the subject performed the whole trial correctly or not.

Here we investigated neuronal error signals in the human ECoG during a continuous control task. We differentiated between signal coding for reduced control (control error) and signal coding for task performance (performance error). To this end, ECoG and EEG signals were recorded from two epilepsy patients playing a video game. Subjects had to control a spaceship in one dimension with a joystick (left-right) to avoid blocks dropping from the top. When the spaceship collided with a block a “life” was lost and the game ended when all (20) “lives” were lost. Collision with a block was, therefore, defined as a performance error. On random occasions movement direction of the spaceship was set to be opposite to the actual joystick movement direction for 500 milliseconds (spaceship moved to the left if the joystick was moved to the right and vice versa). This was defined as a control error. Control errors appeared such that they could only be recognized reliably by simultaneously observing the game and controlling the spaceship and not by observation alone. To verify this, we carried out visual control sessions in which subjects watched a replay of one of their previous gameplay sessions.

We found separate ECoG electrodes and signal components that coded for control errors only, for performance errors only and for both control and performance errors in different brain regions including the motor cortex. The majority of the signals were in the gamma frequency range (40Hz - 128Hz). The observed error-related signals could not be attributed to the movement of the subjects as channels with error-related signals exhibited no or only very weak tuning for movement or velocity. Watching the spaceship collisions during the visual control sessions produced similar neuronal performance error signals but no neuronal control error signals.

In summary, our results show that it is possible to record and differentiate between performance and control error signals in the human ECoG. These error-related neuronal signals may be useful for improving the performance of brain-machine interface algorithms by correcting mistakes online and/or by improving the adaptation of BMI decoding algorithms.

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DIFFERENT CELL POPULATIONS IN THE SUPERIOR COLLUCULUS USE DIFFERENT CODING SCHEMES

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The main retinal input to superficial layers of cat's superior colliculus (SC) comes from two parallel information processing channels, Y and W. The Y channel originates in retinal ganglion cells, which at any eccentricity have large somata, radially symmetric dendritic trees and big caliber axons. Retinal W cells constitute very heterogeneous group with small to medium pericarions and different shapes of dendritic trees. The two classes differ also physiologically and are postulated to play different functional roles in vision. The spatial resolution of both Y and W cells is low but the two groups differ in temporal resolution. The Y neurons are characterized by high temporal resolution, good responsiveness to high stimulus velocities and nonlinear summation within receptive fields. They seem to be involved in the processing of information about fast moving visual stimuli. By contrast, temporal resolution of W cells, which are postulated to play a crucial role in ambient vision, is low. They are activated by slowly moving stimuli and their responsiveness to visual stimuli is "sluggish".

Given the very different properties of the two retinal input channels to the SC it is interesting to find out if there are any differences in variability of responses of the SC cells to visual stimulation since they might suggest different schemes of visual information coding. To check it, we recorded extracellular single unit activity from superficial, retinorecipient layers of the SC of anesthetized and paralyzed cats during visual stimulation by moving light spot. On the basis of the velocity response profiles the recorded cells were separated into group receiving input from Y channel, group receiving input from W channel and mixed class activated by inputs from both channels. Accordingly, the first two groups encompassed cells activated exclusively by either fast or slow moving stimuli. The neurons in the third group responded to stimuli moved within a broad range of velocities. All were excited by slow motion but some were excited while other were suppressed by high velocities.

In experimental data we observed an increase of response variability during slow velocity stimulation which activated W input. On the other hand during responses to high velocities (Y input) augmentation of response reliability was visible. We compared the experimental data to surrogate spike trains derived from two models, Inhomogeneous Poisson Process (IPP) and Inhomogeneous Markov Interval Process (IMI). None of the models could fully account for the observed experimental dependencies, but the IMI model accounted well for the decrease of response variability during activation by fast stimuli. The disagreement of experimental data with the IPP model in all groups of SC cells independent of their velocity preference allows to reject the hypothesis of simple rate coding. The disagreement of IMI model with the response data to low velocity stimuli suggests that more complex temporal dependencies might play a role in processing of information within the W channel. The observed differences in response variability of collicular neurons with different velocity preference suggest different coding schemes for populations of SC neurons related to Y and W visual pathways.

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MECHANISMS OF DEEP BRAIN STIMULATION: EXPLORING RESONANCE AND STIMULATION-INDUCED DECOUPLING

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Recently, deep brain stimulation (DBS) has become a standard symptomatic procedure for Parkinson's disease (PD) and other movement and psychiatric disorders. Despite its success, the effect of this invasive and costly procedure is not completely understood. Indeed, how high-frequency, electrical stimulation of the subthalamic nucleus (STN) in the basal ganglia improves symptoms is not known. Furthermore, DBS raises several interesting paradoxes: it mimics the effects of a lesion, improves symptoms when the frequency is >100 Hz whereas low-frequency DBS has no effect or even worsens symptoms.

In order to reconcile these various paradoxes, we explore the complex formed by the STN and the external segment of the Globus Pallidus (GPe) with a computational model. We investigate the possibility that DBS induces a functional decoupling between STN neurons. First, we develop neuronal models for STN and GPe neurons based on the Izhikevich model. Second, we derive population equations for the STN-GPe complex including connectivity and time delays. Third, we explore the dynamical behaviour of this model under different connectivity patterns. Finally, we apply a DBS current to the STN at different frequencies.

Our simulation results suggest that STN-GPe complex can exhibit two different dynamical states: 1) a stable state, where both nuclei have a low and stable activity (physiological condition), or 2) an oscillatory activity where both nuclei exhibit low-frequency (systematically below 10 Hz) synchronized bursts of activity (pathological condition). Thus, activity at low frequencies appears to be intrinsic to the STN-GPe complex when it becomes disrupted. Consequently, we propose that low-frequency (below 20 Hz) DBS is ineffective, or even enhances pathological activity in the STN-GPe complex, because it resonates with the intrinsic frequency of the STN-GPe complex.

Furthermore, we test the hypothesis that DBS causes a "stimulation-induced decoupling" (SID) between STN neurons, i.e., that individual dynamics of STN neurons become dominant compared to neuronal interactions within the STN. Thus, we simulate the activity of the STN-GPe complex with pathological dynamics, and apply a high-frequency DBS current to the STN. Our results show a high degree of similarity, whether there were recurrent connections in the STN or not. This suggests that DBS "isolates" neurons from one another, and breaks the relay of activity throughout and within the STN. Thus: 1) At the cellular level, high-frequency DBS prevents the generation of synchronized, low-frequency activity within the STN, 2) At the network level, this weakens the impact of cortical feedback to the STN and 3) At the motor feedback loop level (linking functionally cortex, basal ganglia and thalamus), the loop "opens", as in the case of subthalamotomy.

In summary, based on our results, we suggest that the difference in motor improvement between low and high frequency DBS is due to resonance phenomena between DBS current frequency and STN-GPe intrinsic frequency respectively. Furthermore, we suggest that SID is a plausible physiological mechanism for DBS which reconciles the paradox between stimulation and lesion effects and between excitation and/or inhibition of the STN. For the first time, this mechanism proposes a comprehensive multiscale (cellular, network, feedback loop) explanation of the effects of DBS in PD.

SINGLE UNITS REFLECT AWARENESS IN THE MACAQUE PREFRONTAL CORTEX

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Binocular rivalry has been combined successfully with single unit recordings in awake, behaving macaques to study the mechanisms of subjective visual perception. These studies find that a small percentage of neurons in primary visual cortex (V1) are correlated with the animal's subjective percept. A much higher percentage of neurons are tuned to the perceived stimuli in visual areas higher up in the hierarchy (around 40% in areas V4, V5/MT and ~90% in the inferior temporal cortex (IT)). However, the role of neurons in prefrontal cortical areas in subjective perception remains largely unknown. In this study we used binocular flash suppression (BFS) to explore the neuronal correlates of visual awareness in the macaque PFC and specifically in the inferior prefrontal convexity. BFS is a visual stimulation paradigm closely related to binocular rivalry which permits the robust induction of a visual percept under dissimilar visual input conditions. We found that the firing rate of almost 70% of the visually selective neurons closely followed the induced visual percept. The vast majority (95%) of the perceptually modulated neurons fired more when their preferred stimulus was perceptually dominant. Only a tiny fraction of these neurons fired more when the preferred stimulus was perceptually suppressed in agreement with results from IT. Interestingly, we observed that when a preferred stimulus was flashed and thus perceived, the neuronal responses of single units following the perceptual alternation were transient. This is in stark contrast to IT where more sustained responses were observed.

Our findings provide further evidence in support of a role of higher brain areas in processing an explicit perceptual representation during ambiguous visual stimulation. In addition, it points to the existence of a corticocortical neuronal network consisting of perceptually modulated neurons in IT and PFC that process an explicit representation of a visual percept and could thus mediate visual awareness.

DECODING THE POPULATION DYNAMICS UNDERLYING OCULAR FOLLOWING RESPONSE USING A PROBABILISTIC FRAMEWORK.

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The machinery behind the visual perception of motion and the subsequent sensorimotor transformation, such as in Ocular Following Response (OFR), is confronted to uncertainties which are efficiently resolved in the primate's visual system. We may understand this response as an ideal observer in a probabilistic framework by using Bayesian theory (Weiss et al., 2002) which we previously proved to be successfully adapted to model the OFR for different levels of noise with full field gratings or with disk of various sizes and the effect of a flickering surround (Perrinet and Masson, 2007).

More recent experiments of OFR have used disk gratings and bipartite stimuli which are optimized to study the dynamics of center-surround integration. We quantified two main characteristics of the global spatial integration of motion from an intermediate map of possible local translation velocities: (i) a finite optimal stimulus size for driving OFR, surrounded by an antagonistic modulation and (ii) a direction selective suppressive effect of the surround on the contrast gain control of the central stimuli (Barthélemy et al., 2006, 2007).

Herein, we extended in the dynamical domain the ideal observer model to simulate the spatial integration of the different local motion cues within a probabilistic representation. We present analytical results which show that the hypothesis of independence of local measures can describe the initial segment of spatial integration of motion signal. Within this framework, we successfully accounted for the dynamical contrast gain control mechanisms observed in the behavioral data for center-surround stimuli. However, another inhibitory mechanism had to be added to account for suppressive effects of the surround. We explore here an hypothesis where this could be understood as the effect of a recurrent integration of information in the velocity map.

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DECODING NATURAL GRASPS FROM HUMAN ECoG

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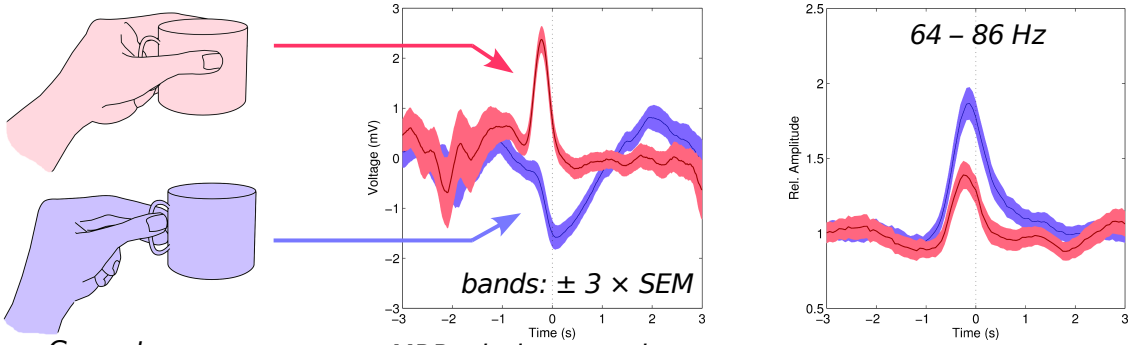
Electrocorticograms (ECoG) - neuro-electric signals measured intracranially and subdurally on the cortical surface - provide information about arm movement. Considering the possible application of movement-related ECoG signals in a brain-controlled motor prosthesis, it would be very useful to also obtain information about intended grasping movements.

We conducted experiments on subjects who had ECoG electrodes implanted over the motor cortex and other brain areas for pre-neurosurgical epilepsy diagnosis. Subjects were instructed to reach for an object (cup), residing on one of four possible positions, grasp it with the hand contra-lateral to the electrode implantation site, and then place it onto another position in an uninterrupted and self-paced manner. For each grasp, subjects decided themselves on whether to use a whole-hand grip or precision grip (see figure). Additionally, the object was switched between a lightweight cup and an identical cup, charged with a heavy weight, in a block-wise manner.

The ECoG signals, recorded simultaneously to the movements, were significantly different for both grasp types. These differences were observed for the low-pass filtered ECoG (reflecting movement-related potentials, MRPs), as well as for the amplitudes in higher frequencies, especially in the high gamma-range (> 60 Hz) (see figure).

Independently of the object weight and position, we could predict the grasp type from signals, measured over hand/arm motor cortex, with up to 99 % accuracy, using regularized linear discriminant analysis, trained and tested on mutually exclusive subsets of the recorded data. While the most accurate information was obtained from low-pass filtered activity, fairly accurate classification of grasp types was also possible from amplitudes of higher-frequency activity, especially from a high gamma-band (64 – 86 Hz).

Our findings suggest, that neuronal population signals, measured on the cortical surface, might be suitable as a basis for multi-modal control of grasping in a brain-machine interface (BMI).



Grasp types | *MRPs during grasping (low-frequency activity)* | *Relative γ-amplitudes during grasping*

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DYNAMIC SEQUENCES OF STATES IN ENSEMBLES OF MOTOR CORTICAL NEURONS

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Changes in neuronal activity are not necessary time-locked to specific sensory or motor events. From trial to trial, network processes may occur both at different moments and speeds. Analysis tools using averages across trials, such as the peri-stimulus time histogram, discard this trial-by-trial variability and, thus, may obscure some features of the neural processes. To account for this, hidden Markov models (HMM) were applied on simultaneously recorded spike trains [1,2]. This probabilistic method makes the assumption that network activity goes through a sequence of discrete states. Here, states are defined as vectors whose components are the firing rate of the neurons. Transitions from one state to another are associated with changes in the firing rate of many neurons. HMM allows one to determine the most likely sequence of states that the ensemble of neurons visited within a trial. This might help to align the data according to internal states and to make statistical analyses in which the trial-by-trial variability is taken into account.

We analyzed multiple single neuron data recorded simultaneously in the motor cortex of a monkey who was trained in a pre-cued center-out task. During each trial, two contextually different delays were presented. Each trial started with a time cue (TC), indicating the delay durations (700 or 1500ms) in the current trial. The first delay demanded temporal attention, in order to be ready for the brief presentation of the spatial cue (SC). During the second delay, the movement direction indicated by SC had to be memorized and prepared.

A HMM analysis was performed. Preliminary results revealed that the ensemble activity of simultaneously recorded neurons presents a robust sequence of states related to the behavioral task. Most of the time the ensemble is in a single state that dominates upon the others (Fig.1A). Transitions are abrupt and manifest a concomitant change in the firing rate of the neurons. The pattern of states is relatively stable across all trials within the same experimental condition (Fig.1B).

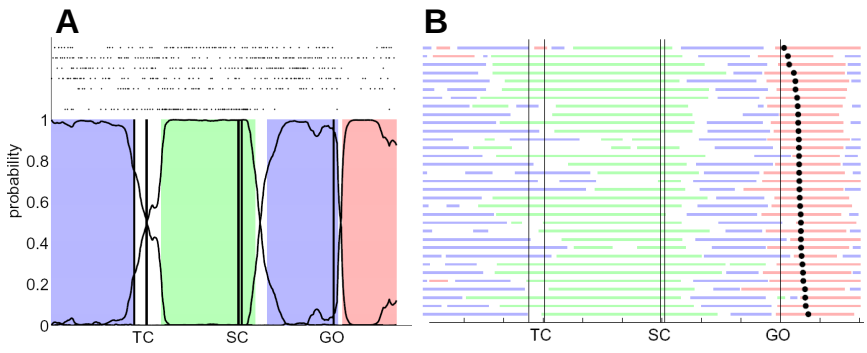

Fig 1: State sequence in an ensemble of six neurons. A) The six rows of dots represent the spike trains recorded during a representative single long trial (delay duration: 1500ms). Black curves in the lower part show the probability of each state in time. If the probability is larger than 0.75, the state is indicated by a specific color attributed to each of the 3 states and we consider that the ensemble is unequivocally in one state. B) Sequence of states for all trials belonging to the same condition. Periods where a single state dominates are colored. White spaces are periods of uncertainty ($p < 0.75$). Trials are arranged according to increasing behavioral reaction times (black dots).

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[2] Jones et al. (2007). *PNAS* 104: 18772-18777

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ENSEMBLE RECORDINGS OF NEURAL ACTIVITY IN THE PREFRONTAL CORTEX DURING OCULOMOTOR CHOICE BEHAVIOR

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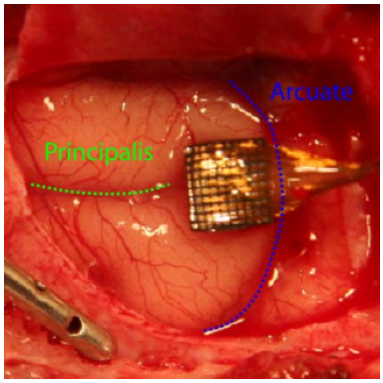

Tasks that require an observer to choose where to look have revealed important insights about how and where brain activity might shape simple decision-making. Recent years have seen a comprehensive effort to understand how the activity of single neurons might reflect the wide range of decision variables that influence oculomotor choice behavior. Here we attempt to extend the reach of these previous studies, by recording decision-related activity from ensembles of neurons in the prefrontal cortex. We implanted a 10-by-10 *Cyberkinetics* recording array into the pre-arcuate gyrus of two macaque monkeys (see figure). High-quality, long-term (> 9 months) recordings were obtained from both animals, as they performed three types of visually guided eye movements.

(1) In the delayed (overlap) saccade task, monkeys made instructed eye movements to a single peripheral target. Spatially-tuned responses during the target-onset period, the delay period and the peri-saccadic interval were consistently obtained on the majority of electrodes. (2) Perceptually-guided decision-making was studied with a two-alternative direction discrimination task. Monkeys viewed a noisy random-dot stimulus, and indicated the direction of perceived motion by making an eye movement to one of two otherwise identical targets. A subset of neurons whose response fields were engaged by either target exhibited choice-predictive behavior during the decision-making interval: soon after the appearance of dot motion, their activity was modulated according to which target was ultimately selected by the monkey. In some experiments, it was possible to extract ensembles of up to 100 such choice-predictive neurons. (3) In the third task, animals engaged in a simple foraging behavior, in which they were asked to choose between a red and a yellow saccade target based on the experienced value (reward rate) of that color on previous trials. In addition to within-trial selectivity for the color and location of the selected target, this experiment revealed between-trial effects - such as reward and choice history signals - that may be related to experience-dependent changes in behavioral strategy.

Our results demonstrate that it is possible to target array recordings to a high-level oculomotor representation in the cerebral cortex. Such recordings make it feasible to study ensemble coding of target selection, motor planning and execution in the saccadic system, in much the same ways that the reach system has previously been investigated. We will present new results that rely uniquely on population activity, such as estimates of single-trial neural dynamics, and discuss their importance for existing behavioral models of oculomotor decision-making.

POPULATION CODING USING FAMILIARITY-CONTINGENT NOISE

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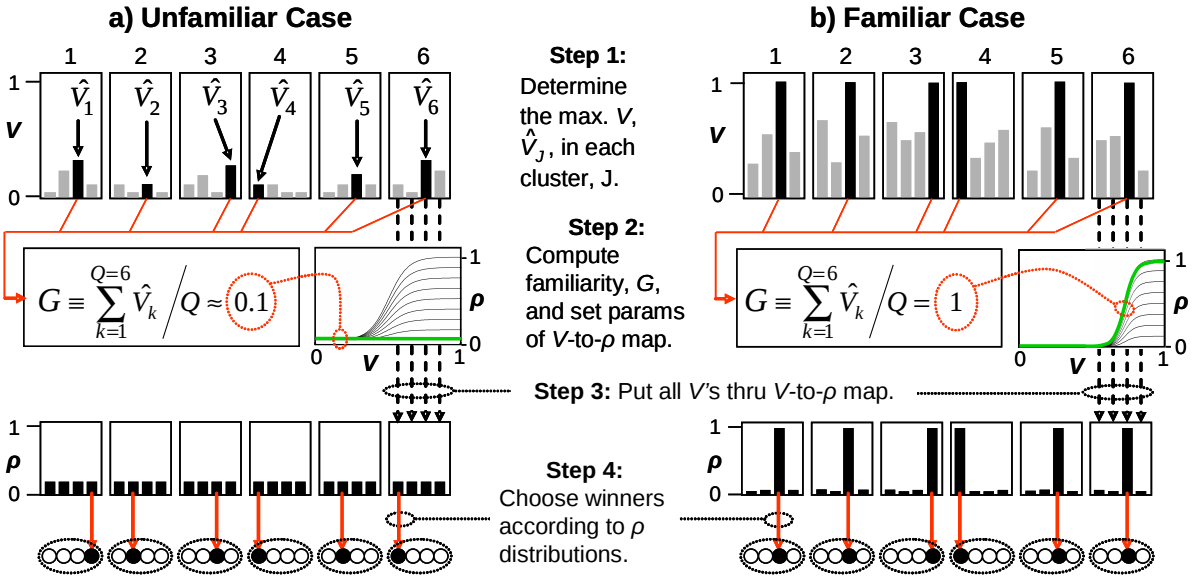
Many prior neural models of decision-making use a global arousal measure, perhaps reflecting norepinephrine levels, to titrate randomness into the choice process. The value (expected reward), V, of each possible choice (hypothesis) is computed. Then the V distribution is converted to a probability distribution, ρ, as a function of arousal level; i.e., higher arousal $\rightarrow$ more randomness added $\rightarrow$ less likely that the highest-V choice wins; lower arousal (i.e., more focused attention) $\rightarrow$ less randomness added $\rightarrow$ more likely that the highest-V choice wins. In the main, these prior models have used localist representations (codes) of choice; i.e., one coding unit per choice, whether that unit be a single cell or a distinct population of cells. Our proposed model departs from earlier work in two ways. 1) Instead of arousal/attention, it uses a global measure of *familiarity*, G, i.e., the degree of match between the expected and actual inputs, to titrate randomness. 2) It uses a sparse distributed code, i.e., each choice's code is a *set* of Q cells and any given cell participates in many codes. Instead of expected reward, we define a cell's V as the degree of match between its receptive field and its current input pattern, i.e., a *local* degree of *evidence*.

The figure's top row shows hypothetical V values over a representational field with 24 cells grouped into six WTA clusters. It contrasts two cases: *unfamiliarity* (all cells have weak local evidence, $V \approx 0$) and *perfectly familiarity* (each cluster has a cell with $V=1$). We call the set of $Q=6$ cells with the maximum V, $\hat{V}$, in the cluster (black bars), the *most favored* code, or $\hat{V}$ code. Note, the $\hat{V}$ code is the same in both cases. But, the average, G, of the $\hat{V}$ code differs greatly, $G \approx 0.1$ for unfamiliar case, $G=1$ for familiar. Normatively, when unfamiliarity is detected, a new code having little overlap with any previously assigned code should be assigned. Our model achieves this by making the V-to-ρ map be a constant function (green line). Choosing six winners from the uniform distributions (bottom left) yields the minimal expected overlap between the final code (bottom row) and the $\hat{V}$ code (code separation). Conversely, when perfect familiarity is detected ($G=1$), the model should reactivate the code that represented the current (familiar) condition in the past, i.e., the $\hat{V}$ code. Thus, the V-to-ρ map is made highly expansive (green sigmoid), yielding the highly peaked distributions (lower right). This maximizes the probability that the $\hat{V}$ cell in each cluster wins, and thus, that the $\hat{V}$ code, as a whole, gets reactivated (code completion). More generally, morphing the V-to-ρ map smoothly as a function of G confers the property that similar inputs map to similar codes.



AUTOMATIC DETECTION OF EPILEPTIC SEIZURES BASED ON SPATIOTEMPORAL DYNAMICS OF SCALP EEG SIGNALS

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Objectives: To study the spatiotemporal dynamics of scalp EEG signals recorded from patients with temporal lobe epilepsy for seizure detection, localization and prediction.

Background, Significance and Rationale: Since its discovery by Hans Berger in 1929, the electroencephalogram (EEG) has been the most utilized signal for assessing brain function clinically. Scalp EEG-video monitoring has been a standard procedure in the pre-surgical evaluation of patients suffering from medically intractable epileptic seizures. Its efficiency depends on the ability to detect seizures. Because EEG is a direct correlate of brain function, an extremely complex system, it is a very complex signal, both in time and in space. Further, it is well known that paroxysmal transients that occur in normal sleep, as well as signal attenuation, poor spatial resolution, and noise or artifacts, greatly reduce the utility of the current automated techniques for EEG analysis. Therefore, to make quantitative analysis for scalp EEG clinically useful, it is essential to first identify signal characteristics that are not only sensitive to seizure activities but also robust to the noise/artifacts in scalp EEG signals.

Methods: Multi-channel scalp EEG recordings obtained from 37 patients (total length ~ 2882 hours = 120 days, with a total of 103 seizures) with history of intractable epileptic seizures were analyzed in this study. Datasets were not pre-selected before the analysis. Signal complexity, frequency and amplitude variation were estimated for each 5.12 non-overlapping epoch in each of the 16 recording channels. Pattern match regularity statistic (PMRS) was used to estimate the signal complexity for the detection of the rhythmic patterns in the ictal EEG. The calculation involved state space reconstruction, search for the pattern matched state vectors, and the estimation of pattern-match probabilities. Signal frequency and amplitude variation were used for automatic rejection of artifacts caused by recording noise, movement/muscle, chewing, electrode failure, and other sources. The same algorithm parameters were used for all patients. We evaluated the performance of the seizure onset detection by estimating the detection sensitivity and the false detection rate per hour. We also checked the identification of seizure onset zones as well as a dynamic pattern before the seizures.

Results: Significant drop of PMRS values at seizure onset was observed. The values stayed low during the entire ictal period and went back to the baseline value postictally. Coupled with noise/artifact rejection rules, more than 90% (93/103) of the seizures were detected with an overall false detection rate of 0.0177 per hour (i.e., 1 false detection per 56.5 hours). By comparison of PMRS values between the recording brain sites, the seizure onset zones were correctly identified and the ictal durations were properly estimated. Furthermore, by examining the PMRS profiles one hour before seizures, we observed that there exists PMRS convergence among brain sites during the pre-seizure periods.

Conclusions: The results from this study suggest that there exist changes of dynamic characteristics in scalp EEG signals that are detectable by quantitative analysis. With sophisticated pattern recognition and classification techniques, it is possible to develop clinically useful applications that can enhance the efficiency of EEG monitoring procedure.

SIMULTANEOUS ENCODING OF REACH AND GRASP KINEMATICS IN MI AND PMv

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Kinematics studies have demonstrated features related to the coordination between the reach and grasp components of prehensile movement. Although neurophysiologic studies have characterized reach components and grasp components independently, they have scarcely demonstrated how neurons may encode them simultaneously. Further, for the grasp component, these studies have only addressed how neurons' firing rates modulate with respect to grasp category, not in terms of the kinematics representing the pre-shaping of the hand during a reach-to-grasp movement. In both fields, it is still a matter of debate whether reaching and grasping are encoded separately in the cortex or as one complex movement. The first aim of our study is to model reaching and grasping in terms of the kinematics of the shoulder, elbow, wrist and finger joints and to identify spatially and/or temporally invariant features shared by reach and grasp-related variables. Such features might be an instantiation of the coordinated action between reach and grasp movements. To this end, we recorded the absolute position of retro-reflective spherical markers with an infra-red camera motion tracking system (Vicon™). These markers were glued onto different segments of the monkeys' arms as to define the shoulder, elbow and wrist as planes and the fingers as segments. Joint angles between the planes and segments were then calculated. The monkeys were trained to reach and grasp 4 different objects that elicit different hand postures. These objects are presented to the monkey by a 6 degree of freedom robot at 6 different locations from the starting position. Preliminary kinematics data support prior kinematics studies' findings by showing a tighter relationship between grasp aperture size vs distance from start position, compared to grasp aperture size vs movement duration (Fig. 1). Grasp aperture size was calculated as the Euclidean distance between the markers on the distal interphalangeal joints of the thumb and index fingers. Since hand distance is a reach-related variable and grasp aperture is a grasp-related variable, this is preliminary evidence that a prehensile movement is invariant for a given target size and location, when it is modeled as a joint trajectory between reach and grasp-related variables.

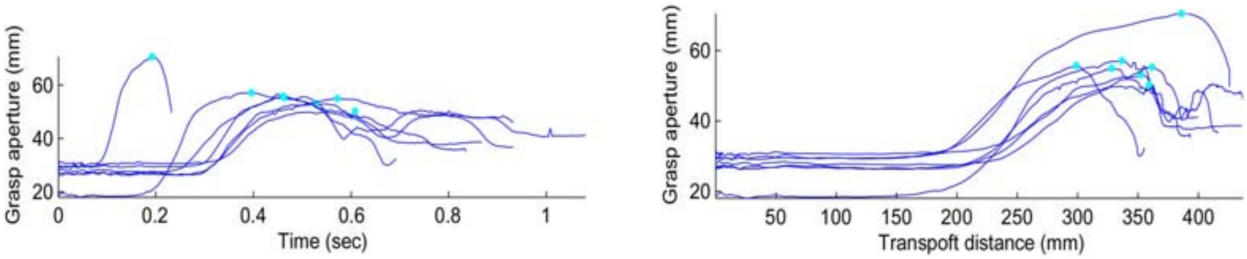

Figure 1. Grasp Aperture vs Movement Duration (left) and Grasp Aperture vs Distance from Start Position (right). The blue dots represent the maximum grasp aperture.

In the next few months, we will analyze the larger set of reach and grasp variables in order to further investigate spatiotemporally invariant features between these movements. Together with the kinematics, we recorded action potentials from neuronal ensembles within ventral premotor cortex (PMv) and motor cortex (MI) using chronically implanted Utah microelectrode arrays, implanted in two rhesus macaques. Our second goal is to assess how much of these neurons' spiking probability may be described by the joint kinematics of reach and grasp related variables.

SHANNON VERSUS FISHER INFORMATION IN LARGE POPULATIONS OF NEURONS

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Understanding how information is represented and transformed by populations of neurons is a major goal of neuroscience research. The accuracy with which information is encoded can be quantified using two types of measures: Shannon information (and derived quantities) and Fisher information (FI). Shannon information is commonly used to quantify the accuracy of single neurons or pairs of neurons. When populations of neurons are studied, however, FI is typically chosen, both in theory and in experiments [1,2]. This is because Shannon information is thought to be computationally intractable for more than a few cells [3]. FI and Shannon information belong to very different statistical fields (information theory vs statistical parameter estimation). While an asymptotic relation between these quantities has been shown [4], it is unclear, however, how they would compare in plausible conditions.

Recently, Butts and Goldman [3] used simple models of neural responses and the stimulus specific information (SSI), a derivative of Shannon information, to investigate how single cells encode stimuli. They showed that whether a neuron best encodes stimuli corresponding to the tuning curve peak, or stimuli falling at the tuning curve's flanks depends on the amount of noise: the best encoded stimulus can transition from high-slope to high-firing rate regions of the tuning curve if response variability increases. Interestingly, these results are in strong contrast with the predictions of FI, which always favors the tuning curves' flanks. However, the SSI was only computed for populations of up to 4 neurons, and it was unclear whether these results would be relevant for larger populations of neurons.

Here, using Monte-Carlo integration, we show that in fact, the SSI can easily be computed for models of much larger neural ensembles (up to 200 independent neurons), allowing a direct comparison between a Shannon-based measure and FI in large populations of neurons. We use this method to re-investigate the results of [3]. We systematically compare how individual neurons participate in population codes by computing the FI and the marginal SSI for increasing population sizes, varying time-windows and different noise levels. We show that the predictions of the SSI and FI converge very rapidly as a function of the number of neurons in the population. In populations of 50 neurons, they are qualitatively similar, even for very small integration windows and high noise. The stimuli that are best encoded are then always those falling at the flanks of the tuning curves. To assess the generality of this observed similarity between the SSI and FI in large populations of neurons, we extend our analysis to different Shannon-based measures (e.g. 'specific surprise'), and situations where specific tasks are explicitly considered (e.g. fine vs broad discrimination, detection).

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BIOPHYSICAL MECHANISMS INVOLVED IN INITIATING AND MAINTAINING PERSISTENT ACTIVITY IN A PFC PYRAMIDAL MODEL NEURON

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Sustained activity of a subset of prefrontal pyramidal neurons throughout the delay period of a working memory task seems to provide the necessary neural processing to establish the behavioural continuity over time. Although persistent activity in the PFC is well described, the underlying biophysical mechanisms have yet to be elucidated. The goal of this work is to delineate the role of a synaptic (NMDA) conductance and intrinsic mechanisms (*i.e.* I_{CAN}) in the initiation and maintenance of persistent activity in a single PFC pyramidal neuron model. The compartment model of a PFC pyramidal neuron was implemented in the NEURON simulation environment, which included detailed structural properties and biophysical mechanisms. Specifically, our model neuron includes modeling equations for 14 types of ionic mechanisms, known to be present in these cells, as well as modeling equations for the regulation of intracellular calcium and potassium concentration. Among these, a model for the calcium activated non-selective cation current (CAN conductance) is included, in order to simulate the experimentally induced Gq-coupled receptor activation in PFC pyramidal neurons and the presence of afterdepolarization. The model neuron was validated for the somatic and dendritic responses of the neuronal model, the afterdepolarization, and the neuronal response to synaptic activation based on experimental results. The validated models were then used to study the hypothesis that both the NMDA and the CAN conductance contribute to the emergence and maintenance of persistent activity. Specifically the presence of the CAN conductance was necessary for initiation of persistent activity, while increasing the NMDA conductance decreased the necessary CAN conductance to induce persistent activity. Furthermore, modulation of the CAN conductance affected the firing frequency of the neuronal response during persistent activity while modulation of the NMDA conductance altered the firing frequency during the stimulus. We suggest the NMDA conductance acts as a boosting mechanism for initiation of persistent activity in a single-neuron model while the CAN conductance has a more regulatory role of the firing frequency during persistent activity. Our next goal is to investigate whether these biophysical mechanisms also contribute to the persistent activity induced in a reverberating pyramidal neuronal circuit.

STEREOTYPY OF SUBMOVEMENTS MAY BE AN EMERGENT FETURE OF INTERACTION ACROSS LONG-LOOP FEEDBACK CONTROL, CEREBELLUM, AND BASAL GANGLIA

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Movement intermittency refers to the commonly observed characteristics of continuous movements to have brief intermittent reductions in speed. Between the local speed minima, the speed profile is typically a smooth roughly bell-shaped curve. This corresponds to the appearance that continuous movements are generated as segments that are blended together. Submovements, which have been identified by non-smooth speed profiles, have been observed over various types of movements both in human and non-human primates. However, although some mechanisms for such intermittencies have been suggested (Craik 1947, Miall et al 1993, Milner 1992, Todorov and Jordan 1998), an biologically feasible mechanism yet remained unclear.

Roitman et al (2004) showed recently that similar intermittency, described in terms of sequential, non-overlapping “speed pulses”, is also present in visually-guided manual tracking of primates. In particular, speed pulse amplitude and duration scaled characteristically with tracking speed. Roitman and Ebner (2005) have also shown this in humans. Certain relationships between speed pulse amplitudes and durations are found in those two studies: 1) Affine relationship between amplitudes and durations at a given target speed, 2) affine slopes increases as the target speed increases, 3) yet the distribution of speed pulse durations is relatively invariant over various target speeds. This may imply a presence of systematic scaling of a movement segments.

However, this does not necessarily imply a rescaling of stereotyped movement templates. In particular, a RIPID cerebro-cerebellar feedback control model (Takahashi 2007) that incorporates switching attributed to the basal ganglia and small amounts of motor control white noise reproduces qualitatively the scaling features described. More quantitative simulations of primate data are in progress. The model implements an error dead-zone within a transcortical feedback loop. As predicted by Miall et al (1993), an inner, faster non-visual loop is an important component of the intermittency mechanism, and the process enhances the stability of long-loop control. The results appear to reconcile stereotypy with the sampled servo view of kinematic intermittency.

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INTERPRETING NEURAL DYNAMICS IN THE BRAIN WITH PARTIAL DIRECTED COHERENCE

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Monosynaptic projections from the hippocampus to medial prefrontal cortex (mPFC) are thought to be involved in regulating working memory. The neural dynamics of this connectivity were compared *in vivo* under control conditions and after kainic acid (KA) administration, using partial directed coherence analysis (PDC).

PDC is a statistical technique based on autoregressive modeling of multivariate time series in conjunction with the concept of Granger Causality and provides clues to directional connectivity and magnitude of information flow between neuronal ensembles. Hippocampal and mPFC local field potentials (LFPs) were recorded in isoflurane-anaesthetised rats with a 16-wire micro-electrode array and an 8-wire micro-electrode bundle respectively. Separate groups of rats were administered KA or received no drug treatment. PDC was applied to LFP data in animals with confirmed dorsal hippocampal and mPFC placements.

In the control group, PDC detected a stronger flow of information from lateral to medial hippocampal sites and from mPFC to the hippocampus. KA disrupted this directionality in the hippocampus, but did not alter directionality between mPFC and the hippocampus. These results suggest that a significant flow of information also occurs in the mPFC-to-hippocampus direction, and that acute-elevated neuronal activity, induced by KA administration, does not disrupt this inter-regional connectivity.

REAL TIME DECODING OF HAND GRASPING SIGNALS FROM MACAQUE PREMOTOR AND PARIETAL CORTEX

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A brain machine interface (BMI) for visually guided grasping would provide significant benefits for paralyzed patients given the crucial role these movements play in our everyday life. We are developing a BMI to decode grasp shape in macaque monkeys online. Neural activity is evaluated using chronically implanted electrodes in the anterior intraparietal cortex (AIP) and ventral premotor cortex (F5), areas known to be involved in the transformation of visual signals into hand grasping instructions. Macaque monkeys were trained in a delayed grasping task, where they first placed their hands at rest and fixated a red LED before a grasping handle was presented in one of 5 different orientations, and the color of an LED instructed the animals to grasp the handle either with a power or precision grip, respectively. After a short delay the fixation LED dimmed instructing the monkey to perform the required grasp. Correct trials were rewarded with a small amount of juice. After successful training 5 floating micro-electrode arrays (FMA; MicroProbe Inc) were implanted in AIP (2) and F5 (3) of 1 animal. Each array comprised 16 platinum-iridium electrodes (length 1.0-4.5mm, spacing 0.5 mm). This configuration was chosen to facilitate the recording of neuronal activity within cortical sulci instead of on the cortical surface.

Neural signals were sampled using a Cerebus (Cyberkinetics Inc, Foxborough, MA) Neural Signal Processor (NSP) and streamed to a dedicated decoding PC via UDP. Spike sorting was conducted manually online by setting time-amplitude discrimination windows. Decoding was implemented using maximum likelihood estimation. We benchmarked decoder performance offline before commencing BMI experiments by using a spike simulator tool capable of creating artificial Poisson-distributed spike trains as well as loading and replaying previous neuronal recordings. Both decoder and simulator were implemented in C++ including the Neuroshare library for reading files, the Cerebus UDP Network Protocol and a graphical user interface.

In the BMI experiment, spiking activity from AIP and F5 was collected initially while the monkey performed the delayed grasping task, to determine the distribution of spike counts for each of the possible grasping combinations. Then in “prosthetic grasping” trials, spike data was sampled online during the planning phase, and the planned grasp was decoded in real time. The decoded grasp was presented to the monkey visually during the grasp phase. If correct the animal received a small juice reward. Initially we decoded grasp type (precision vs. power) with mean accuracy 94%. Following this we simultaneously decoded grasp type and 2 grasp orientations (target tilted to left or right) achieving a mean accuracy of 91%. Finally we were able to decode 6 conditions (grasp type and 3 orientations, target tilted left, target oriented vertically, and target tilted right) with mean accuracy 72%. These results are proof-of-concept for a BMI for visually guided grasping. This BMI could be extended for a larger number of grip types and orientations as needed for prosthetic applications.

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PHASE SPACE STRUCTURE OF SPIKING NEURAL NETWORK WITH LAPLACIAN COUPLING

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Let us consider a Leaky Integrate-and-Fire neural network with discrete time dynamics given by

$$V_i(t+1) = \gamma V_i(t)[1 - Z(V_i(t))] + \sum_j W_{ij} Z(V_j(t)) + I_i \qquad (1)$$

with V_i the membrane potential of neuron i, $\gamma \in [0,1]$ the leak, $Z(x) = 0$ if $x < \theta$ and 1 otherwise, where θ is the threshold. It has been shown in [1] that the attractors of eq.1 are generically periodic orbits, although the period can be arbitrarily long. Moreover, the dynamics is chaotic, namely sensitive to initial conditions and perturbations, in a non generic region of the parameter's space, traditionally called the "edge of chaos". Interpreted in terms of neural outputs (raster plots) as the response to an input current (I_i), one can show that the system either exhibits stable input-output responses with low variability, or a high variability with low stability. The largest variability occurs at the edge of chaos, but what is the structure of this set? In order to investigate its structure we consider here a $1D$ circular network with (discrete) Laplacian coupling, i.e. with a diffusive interaction given by $W_{i\,i\pm1} = \alpha, W_{ii} = -2\alpha$ and 0 otherwise with $\alpha > 0$. In Figure 1(Left), dAS is the maximal amplitude of a perturbation that leaves the orbit stable. The edge of chaos corresponds to $dAS = 0$. Figure 1(center) shows the period of the most sensitive orbit. Figure 1(right) depicts the minimal distance between the input vector and the firing rate vector corresponding to allowed orbits. These results show that even in this simple network structure an input has drastic and non trivial effects on the global dynamics, in the structure of the edge of chaos and also on the response variability to the stimuli.

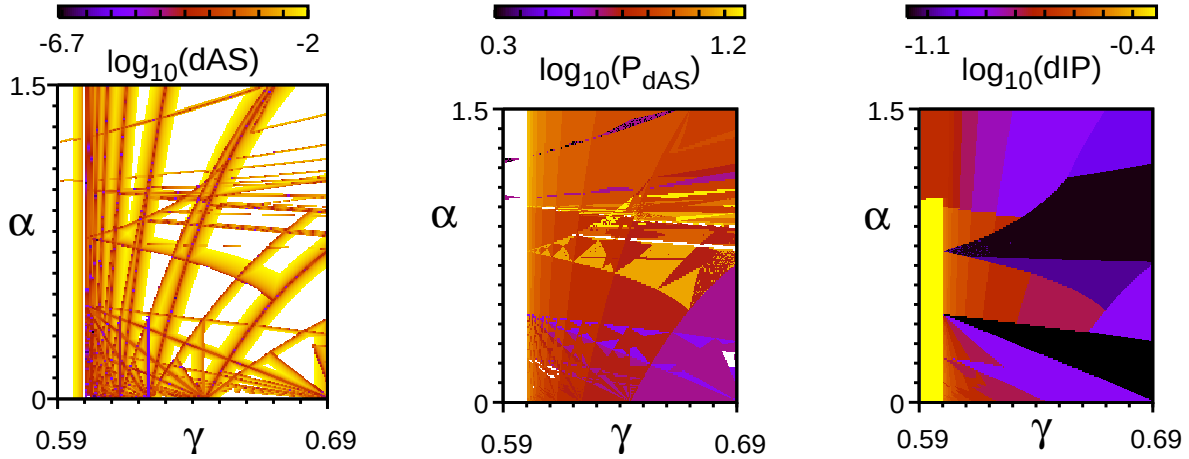

Figure 1. Simulation of 5 Neurons with threshold $\theta = 1.0$ and input intensity $I = 0.4$: **(Left)** $\log(dAS)$, white denotes $dAS < 10^{-7}$ at $\gamma = 0.6$ and $dAS \geq 10^{-2}$ everywhere else in the graphic. **(Center)** $\log(P)$, where P is the period of the orbit that minimizes dAS, white denotes $P = 1$ at $\gamma < 0.6$ and $P > 20$ everywhere else. **(Right)** Minimum distance between the input and the firing rate vector.

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FIRING PATTERNS OF CLUSTERS OF NEURONS IN V1 HAVE HIGH-ORDER, STIMULUS-CONTINGENT CORRELATIONS

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The multineuronal firing patterns of a set of neurons offers important insights into their underlying network structure and the manner in which neural activity represents information. Yet, because the number of potential interactions grows exponentially as the network size increases, a complete characterization can be difficult. The principle of maximum entropy (MaxEnt) may provide a solution to this problem.

MaxEnt models generate canonical multineuronal firing distributions that are consistent with a set of specified constraints but are otherwise maximally unstructured. In recent applications to populations of retinal neurons and neurons in cortical slices and cultures, it has been shown that pairwise interactions account nearly completely for multi-neuronal firing patterns. However, it remains unclear if these findings hold in intact cortex, and how they can be extended to take stimulus-dependence into account. To address this, we implement a similar analysis of multineuronal firing patterns from tetrode recordings in V1 of the anesthetized macaque. We present a pseudorandom binary random checkerboard stimulus and simultaneously record clusters of 3-5 cells from 19 different sites in 6 animals. We test three model classes: an independent model; a model with pairwise constraints; and a "common-input" model, with constraints on the probability that a neuron fires when any ensemble of neurons fires.

As in the retina and *ex vivo* cortical recordings, we find significant deviations from independence. Both the pairwise and the "common input" models capture much of this deviation. However, in contrast to those findings, we find significant deviations of the observed firing patterns from pairwise MaxEnt predictions in many (8/19) clusters. The "common input" model also captures most of the deviation from independence, but its prediction of multineuronal firing patterns is typically worse than that of the pairwise model. Thus, unlike the retina and cortical cultures, multineuronal firing patterns in cortical circuits suggest multineuronal interactions.

To examine the extent to which the observed multineuronal correlations are stimulus-dependent, we construct a hierarchy of MaxEnt models conditioned on one to four of the most informative spatiotemporal pixels. Surprisingly, we find that for a number of sites, this conditioning reveals two regimes of network behavior: for some states of the pixels, the observed firing patterns are captured by an independent model or a pairwise model, while in other states, the deviations from the MaxEnt prediction are increased. This provides statistical evidence that even in response to unstructured spatial stimuli, V1 neuronal activity is dynamically organized into stimulus-dependent multineuronal groups.

DYNAMICS OF DECISION CRITERION SETTING IN VISUAL PERCEPTION

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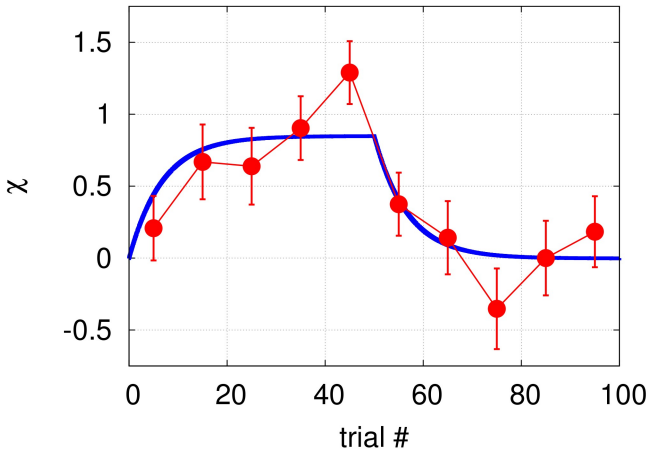
Signal Detection Theory (*SDT*) provides the best known theoretical model to interpret human perception, and particularly when behavioural experiments on discrimination and classification are considered. Two main assumptions of *SDT* are the existence of noise and of a decision criterion. Noise affects the processing of a stimulus, so that a related neural response can be predicted only on a statistical basis; verbal reports in a discrimination task result then from the comparison between neural responses and the criterion, encoded within the neural system. Psychophysical paradigms usually assume the decision criterion to be constant. Indeed, very few works have so far addressed the crucial issue of how criterion changes upon variation of boundary conditions like, for example, prior presentation probabilities.

We present a novel method, as well as its experimental implementation, aiming at assessing the criterion dynamics. In an orientation “yes-no”, one-interval experiment within the visual modality, changes in the criterion are induced by means of a feedback technique. The criterion setting dynamics is investigated using the simplest model for closed-loop systems, *i.e.* a low-pass-filtered amplifier characterized by a time constant τ and an amplitude A. The model has an immediate physical interpretation.

Data have been analyzed on a trial-by-trial basis through both a maximum likelihood estimation and a lock-in, phase-detection technique. Besides experiments, numerical simulations have been carried out in order to test and calibrate the method.

The results robustly confirm the method’s reliability. As an example, the figure reported below shows the criterion dynamics assessed on a single subject. Each data point corresponds to the criterion position, evaluated on a block of 10 trials and using conventional SDT. The solid line corresponds to the model fitted to the experimental data. The fit clearly shows an exponential adaptation of the criterion ($\tau \approx 7$ trials).

Further, promising developments of the method will be discussed. This work was in part supported by the Provincia Autonoma di Trento.



STIMULUS-INDUCED CORRELATION FOR DIFFERENT INTEGRATE-AND-FIRE NEURON MODELS

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Integrate-and-fire (IF) neurons have found widespread applications in computational neuroscience, in particular, in stochastic versions of these models. We present results on the white-noise driven perfect, leaky, and quadratic integrate-and-fire models and focus on the spectral statistics (power spectra, cross spectra, and coherence functions) in different dynamical regimes (noise-induced and deterministic firing regimes with low or moderate noise). We make the models comparable by tuning parameters such that the mean value and the coefficient of variation of the interspike interval agree for all of them. We find that under these conditions the power spectrum under white-noise stimulation is often very similar while the response characteristics (characterized by the cross spectrum between a fraction of the input noise and the output spike train) differs in part drastically. We also investigate how the spike trains of two neurons of the same kind (e.g. two leaky integrate-and-fire neurons) correlate if they share a common noisy synaptic input. We show that depending on the dynamical regime either two quadratic or two leaky IF neurons are more strongly correlated. Our results suggest that, for simulations of large populations of neurons, the details of the chosen IF model have a strong effect on correlation and regularity of the output.

A HIERARCHICAL PREDICTIVE CODING MODEL OF VISUAL PROCESSING

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The traditional view on visual processing is dominated by bottom-up signaling. It postulates that more and more general stimulus features are extracted as the stimulus representation proceeds from lower to higher stages of the visual system, e.g., from V1 to IT. However, well-known phenomena such as the extra-classical receptive field effects found in many visual areas are difficult to explain within the bottom-up paradigm.

On the other hand, the roles of top-down signals in visual processing have been intensively studied experimentally in the last few years and have also been modeled theoretically. In particular, predictive coding, in which feedback from higher cortical areas carries expectations of lower level activity, has been shown to explain the emergence of extra-classical receptive field effects (Rao and Ballard, 1999).

Since top-down predictions cannot be independent of the bottom-up input, the interpretation of a visual scene must be an iterative process in which the initial activation pattern relaxes to a solution matching expectation with sensory experience. However, in models, such as the one of Rao and Ballard, where top-down effects propagate over all layers of the visual hierarchy, the relaxation times are too slow compared to the time scale of visual processing.

Our starting point is the mathematical observation, confirmed by extensive simulations, that in predictive coding relaxation results in each higher layer essentially performing principal component analysis of the activity (firing rates) in the preceding lower layer. We show how this analysis can be done without propagating top-down effects through the entire visual hierarchy. In our model, not only the top-down connectivity, but also the effective resulting feedback is confined to proximal layers, yielding fast relaxation. This suggests a way for the visual system to square the need for fast processing with the integration of top-down clues. Furthermore, we simulate limited receptive fields in a hierarchy of processing stages and show that predictive coding is indeed effective in this biologically plausible context.

We also make it explicit that in a biologically plausible implementation each layer requires both coding for stimulus representation and for the prediction error. This sheds new light on the interpretation of activation patterns observed in V4 which have seemed impossible to reconcile with predictive coding (Rainer, Lee, and Logothetis, 2004).

TUNING OF NEURONAL CABLES WITH VOLTAGE-DEPENDENT K^+ CHANNELS

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In many neurons voltage signals are conducted without action potentials. This graded-potential signalling is the exclusive form in the majority of neurons of the vertebrate retina, the hair cells in the inner ear, and several types of receptor neurons and interneurons in the insect sensory and motor systems. However, graded potential signalling is also important in spiking neurons, where post-synaptic potentials are conventionally conducted along dendrites without action potentials. When the neuronal membrane contains voltage-gated channels, they change the cable properties on the neurons. The subthreshold behaviour of voltage-dependent membrane properties has been investigated experimentally or by modelling (Mauro et al, 1970, J. Gen. Physiol. 55, 497–523; Koch 1999, Biophysics of Computation: Information Processing in Single Neurons, Oxford; Häusser et al., 2000, Science 290: 739-744).

The exact effects of voltage-dependent channels on cable properties of neurons depend on the voltage and time-dependent properties of the channels in question. In some instances creation of resonances induces the cable to prefer certain signalling frequencies (e.g. in hair cells, Fettiplace and Fuchs 1999, Annu Rev Physiol 61: 809–834 ; review by Hutcheon and Yarom, 2000, Trends Neurosci. 23, 216–222), but generally the complex interplay between the voltage-dependent channel properties and the cable geometry results in complex filtering properties. In some cases, e.g. when inactivation of K^+ channels is strongly present already in resting state, we can expect even relative amplification of depolarizing voltage signals (Niven et al., 2003, Nature 421:630-634), which normally would require the action of Na^+ or Ca^{2+} channels.

We present a modelling approach, where the properties of neuronal cables containing different types of voltage-gated K^+ channels (outwardly and inwardly rectifying, non-inactivating and inactivating) are systematically investigated. The simplest model treated is that of an invertebrate sensory neuron (a ball-and-stick model). In addition, we relate coding of synaptic inputs to the voltage-dependent cable properties in a simplistic model mimicking some aspects of vertebrate central neurons, and investigate the changes of the post-synaptic signals in different types of voltage-dependent cables.

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STATE-DEPENDENT SPIKE TIMING RELATIONSHIPS BETWEEN HIPPOCAMPAL AND PREFRONTAL CIRCUITS DURING SLEEP

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Coordinated activity between the neocortex and the hippocampus during sleep is believed to reorganize neural circuits in support of memory consolidation. However, the timing relationships of spiking activity across cortico-hippocampal networks, which are key determinants of synaptic changes, are not well understood. Here we use chronic tetrode recordings in freely behaving rats to show that cells in the prefrontal cortex tend to fire consistently between 0 and 100 ms after hippocampal cells in naturally sleeping animals. This provides evidence at the single cell-pair level for directional interactions between these areas within the window of plasticity. Moreover, we find that these interactions are driven by population bursts during hippocampal sharp-wave/ripple events (SWR), a prominent feature of slow-wave sleep (SWS), and are absent during rapid-eye movement (REM) sleep. Finally, the prefrontal response to SWR bursts is biphasic: a kernel of highly correlated cells is followed 70-100 ms later by a diffuse set of weakly correlated cells. These findings suggest that SWR events serve as an atomic unit of hippocampal-prefrontal information transfer during sleep. In addition, the differences in spike timing relationships between SWS and REM sleep suggest that these brain states may have different consequences for synaptic reorganization at the circuit level.

A WAVELET-VARIANCE BASED ALGORITHM FOR AUTOMATIC EPILEPTIC SPIKE AND WAVE ACTIVITY DETECTION

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Absence seizures were first described by Poupart in 1705. Clarification and delineation of absence seizure types remained elusive until the past 25 years, when systematic neurophysological studies using video-EEG monitoring techniques aided the description of the protean manifestations and clinical syndromes associated with absence seizures . The EEG features of absence seizures have been well documented by multiple authors.

For typical absence seizures there is sudden onset of 3 Hz generalized bilaterally synchronous and symmetrical spike- or multiple spike-and-slow wave complexes. The voltage of the discharge is often maximal in the frontocentral regions. The frequency tends to be faster, about 4Hz, at the onset and slows to 2 Hz toward to end of discharges. The interictal EEG background is generally normal for subjects with typical absence seizures disorder with prompt return of normal preictal background activity immediately after the discharge ends.

Evaluating the efficacy of absence seizure treatments has traditionally focused on comparing the frequency of seizures during treatment to seizure frequency during a finite baseline period. EEG recordings are used to supplement clinical observations of care givers. However there is currently no reliable tool for rapid absence seizure counting which can quickly detect the absence seizure configuration in the current clinical environment. Besides merely counting the number of seizures as a measure of treatment efficacy for absence seizures (defined for this purpose as spike and wave discharges $>$ 3 seconds in duration) may not provide a full explanation of the therapeutic effect.

In this study we present a wavelet variance based algorithm for detecting continoous spike and wave activity. Then this activity in classified in seizure and non seizure activity and the effect of the antiepileptic drug (AED) under investigation is studied. Clinical validation of the method together with analysis of sensitivity and specificity of the algorithm are presented.

FREQUENCY-SELECTIVE CODING OF TRANSLATION AND TILT IN MACAQUE CEREBELLAR NODULUS AND UVULA

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The cerebellar nodulus/uvula (NU) receives inputs from most vestibular primary afferents (both otolith organs and semicircular canals) and also secondary vestibular afferents originating from the vestibular nuclei. To understand the functional significance of this part of the vestibulo-cerebellum, we have characterized Purkinje cell responses during three-dimensional translation, rotation and their combinations across different frequencies. By using a variety of stimuli, we were able to manipulate otolith and canal signals independently and together. We hypothesized that unlike primary afferents (coding net linear acceleration and angular velocity), Purkinje cells in the NU receive spatially and temporally transformed otolith/canal signals, necessary to solve the tilt/translation ambiguity and detect inertial motion. Based on behavior, we also hypothesized that this interaction would be frequency-dependent. The simple spike (SS) activities of 220 Purkinje cells were recorded in the cerebellar nodulus (folium 10) and ventral uvula (folium 9c, d) of the vermis of two rhesus and one fascicularis monkeys.

Most Purkinje cells exhibited strong modulation during translation with little or no modulation during tilt (i.e., rotation that changes head orientation relative to gravity). At the same time, we observed robust SS responses during combinations of translation and tilt (stimulus exclusively activating vertical semicircular canals), similar to those during translation. In contrast, there was no modulation during rotations that do not change head orientation relative to gravity. Preferred directions for both otolith and canal-driven signals were aligned with canal axes. Canal-driven SS modulation encodes angular position, a temporally integrated signal necessary to cancel gravitational acceleration during tilt. But SS responses during translation are also partially integrated, such that they encode combinations of linear velocity and acceleration. As a result of these dynamics, canal-driven and otolith-driven responses are temporally matched for canceling linear accelerations due to gravity only in a narrow frequency range centered around 0.5 Hz. Indeed, tilt velocity gains increase at low frequencies, and many cells modulated during static tilt. Thus, the nodulus/uvula encodes either translation or net linear acceleration in a frequency-selective manner. At frequencies of 0.16 Hz and below, canal-driven angular position signals are insufficient to cancel out the partially integrated otolith drive during tilt. These signals could represent the neural basis of similar frequency dependencies seen in behavior.

POTENTIAL ORIGIN OF ENAHNCED NEURAL ACTIVITY DURING BMI EXPERIMENTS

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During planning and execution of reaching movements, the firing rate of cortical motor neurons is modulated by multiple motor, sensory, and cognitive variables. In particular, neural modulations by movement direction and speed have been characterized extensively during stereotypical reaching movements, and described computationally using tuning curves. Successful decoding of this information from ensemble of cortical neural facilitated the development of brain-machine interfaces (BMIs), which use the decoded velocity or position signal for controlling an external actuator.

Recent BMI experiments demonstrated that the modulations in the firing rate of the recorded neurons increased abruptly when the monkeys started operating the BMI [1]. The enhanced modulations could not be explained solely by movement-related signals, thus suggesting that they are related to computational tasks that become more significant in novel motor contexts. Furthermore, the initial enhancement in firing rate modulations declined gradually with subsequent training. These effects mirrored the initial degradation in behavioral performance, which was followed by gradual improvement during subsequent training.

Here we explore the origin of the enhanced modulations in the context of two motor control strategies, including feedback error correction and optimal control. In the framework of feedback error correction the enhanced modulations are hypothesized to encode execution and prediction errors and thus are expected to correlate with execution errors. According to optimal control, neural activity is expected to relate to the distance from the target and the enhanced neural activity is hypothesized to represent explorative activity.

We first quantify the enhanced neural modulations as the deviation between the overall neural modulations and those attributed to the kinematics of the movement. We then determine the contribution of the execution error and the distance from the target to the modulations of the neural activity; and assess how well each signal can account for the enhanced neural modulations. We conclude that the analysis support the hypothesis that the enhanced neural modulations encode execution errors.

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RECOVERY OF PRIMARY VESTIBULAR AFFERENT ACTIVITY DURING REGENERATION

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The vestibular system provides for compensatory reflexive behaviors such as postural adjustments and oculomotor responses that occur during motion. Aminoglycoside antibiotics are known to produce receptor cell death and afferent damage, both of which regenerate over time in birds. The aim of this study was to determine the functional capacity of a population of vestibular afferents during the regeneration process. Neural recordings from vestibular afferents in both normal birds and those undergoing regenerative recovery for 2 to 52 weeks following initial total loss. Each afferent was characterized as either a semicircular canal or otolith fiber using rotations in different planes, linear motion and OVAR. Once identified, the responses to sinusoidal stimuli at different frequencies were obtained. rotations. Maximum sensitivity vectors were determined using 0.5 Hz rotations and different head rotations. For canal fibers, at 2-12 weeks recovery, the mean spontaneous discharge rates were significantly lower than those of normals. After 2 weeks of recovery, none of the 62 fibers recorded exhibited any response to motion, and at 3 weeks of regeneration, the majority (65/75) still did not respond. After 4 weeks, sensitivity to motion was detected in nearly 30% of the fibers, however they exhibited greatly reduced gains. Fibers at 4-12 weeks recovery exhibited increasing gains at high frequencies, but were greatly reduced at low frequencies. Phase values for these afferents had high variance, but generally were advanced relative to normals. Following 24-52 weeks of regeneration the afferent gain and phase response values to motion were not significantly different from those in normal birds. In terms of sensitivity vectors, at early regeneration time points, vestibular afferents exhibited broader tuning curves that sharpened by 12 weeks recovery.

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IMAGING THE OXYGEN EXTRACTION FRACTION WITH FMRI USING MODERATE HYPERCAPNIA

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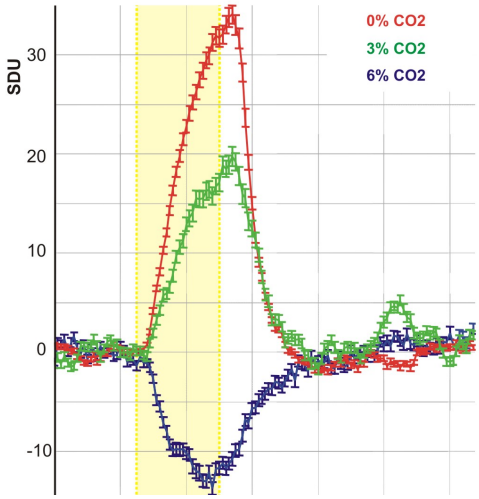
The BOLD signal is an indirect hemodynamic signal which is sensitive to cerebral blood flow (CBF), cerebral blood volume (CBV) and oxygen extraction fraction (OEF). We observe in the anesthetized monkey a vasodilatory ceiling effect during inhalation of 6% CO_2 where CBF or CBV is not further increased by an additional sensory stimulus. We show with simultaneous fMRI and electrophysiology recordings, that the fMRI response during 6% inhaled CO_2 to a sensory stimulus reflects an oxygen extraction weighted signal. With this method, oxygen extraction fraction can be imaged by means of fMRI without injection of an exogenous drug.

Combined electrophysiology and fMRI recording were performed in the primary visual cortex (V1) of 5 anesthetized monkeys in 8 experimental sessions using the techniques described by Logothetis et al in Nature 2001 [1,2]. Hypercapnia was induced by administration of premixed medical gases containing 3% or 6% CO_2 and 21% O_2. Ventilation with 3% and 6% CO_2 increased end-tidal CO_2 by approximately 9mmHg and 20mmHg, respectively. For visual stimulation, a rotating full field checkerboard was presented to both eyes of the monkey (12s on/ 12s off/ 39s on). For analysis of the BOLD data, a region-of-interest (ROI) has been selected at normocapnia restricted to V1 and correlation coefficients larger than 0.15.

During normocapnia, the ROI in V1 contained in average 120±60 voxels with a positive correlation coefficient. During 3% CO_2 the amplitude of the BOLD response decreased and only few voxels (5±5) were negatively correlated to the paradigm. During 6% CO_2 most active voxels within the ROI (72±42) were negatively correlated. For time courses see figure 1. Importantly, the amplitude of the stimulus-induced responses of MUA and LFP responses during stimulation remained stable during both 3% and 6% CO_2 compared to normocapnia. CBF or CBV acquired in different sessions did not respond to stimulation for 6% CO_2. The temporal dynamics of the inverted BOLD response for 6% CO_2 is 1.2±0.9s earlier than that of the BOLD responses for 0% and 3% CO_2.



region (ROI selected under normocapnia) for 0%, 3% and 6% CO_2.

Baseline local field potentials in the gamma and theta range, as well as multi-unit activity, decrease their power by up to 15% under 6% CO_2 inhalation. In contrast, frequency bands higher than 24Hz are still modulated by a sensory stimulus under hypercapnia. Thus, the BOLD signal during 6% hypercapnia can be used to investigate the cerebral metabolic rate of oxygen consumption ($CMRO_2$) without the concomitant changes in CBF and CBV while the electrophysiological responses were preserved.

[1]Logothetis at al. Nature (2001); [2]Logothetis et al. NatNeurosci (1999).

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