AREADNE 2006

Research in Encoding and Decoding of Neural Ensembles Nomikos Conference Centre, Santorini, Greece 22–25 June 2006



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WELCOME

Welcome to AREADNE 2006, the first 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 give 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 for the first time 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 technologies 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. A secondary goal of the conference is to provide an informal yet spectacular setting on Santorini in which conference attendees can discuss and share ideas outside of the presentations at the conference center. Third, this conference is the kick-off event for our long term project to form a systems neuroscience research institute within Greece. This institute will 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 2006 conference was organized by Nicholas Hatsopoulos (Co-Chair) and John Pezaris (Co-Chair), Dora Angelaki, Thanos Siapas, Catherine Ojakangas, Apostolos Georgopoulos, and Nikos Logothetis.

Local Organizers

Local organization effort has been provided by Nike Makres and Fani Metaxa.

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: (1) To understand how information is coded by large populations of neurons. This involves collaborative efforts between neuroscientists, mathematicians, statisticians, and computer scientists. (2) 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. (3) 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. (4) To use neuroimaging technologies to understand how cognitive behaviors are coded in the human brain. (5) 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

lliovassilema, 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 $+30\mathchar`-22860\mathchar`-22792$, Kondohori, near Fira

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

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

Monastery of Profitis Ilias

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 sand can get extremely hot in the sun. SCUBA diving is also 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 is 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, afternoons 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 21 _____

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

_____ THURSDAY, JUNE 22 _____

- 08:00–08:30 registration opens
- 08:30-09:00 opening remarks

MORNING SESSION John Pezaris, moderator

- 09:00–09:45 **Apostolos Georgopoulos** (University of Minnesota) *Encoding and decoding by neural ensembles: From movement parameters to serial order*
- 09:45–10:30 Andreas Tolias (Max Plank Institute for Biological Cybernetics) Network mechanisms of perception
- 10:30-11:00 coffee break
- 11:00–11:45 **Stephen Lisberger** (University of California San Fransisco) *Signal, noise, and variation in sensory-motor transformations*
- 11:45–12:30 **Greg DeAngelis** (Washington University in St. Louis) *Neural mechanisms of heading perception: Sensory integration and population coding*
- 12:30-14:00 lunch

AFTERNOON SESSION Thanos Siapas, moderator

- 17:00–17:45 Markus Meister (Harvard University) Retinal processing of natural motion
- 17:45–18:15 coffee and light snacks
- 18:15–19:00 **Phil Ulinski** (University of Chicago) *Propagating waves in turtle visual cortex contain information about visual stimuli*
- 19:00–19:45 **Barry Richmond** (NIH) *Memory mechanisms and population codes in sequentially connected temporal lobe brain regions*
- 20:00-21:30 posters

Charles Anderson (WUSTL School of Medicine) Population coding of wavelets in V1

Andreas Bartels (Max Plank Institute for Biological Cybernetics) *Natural movie stimuli* allow mapping of retinotopy and tonotopy in anesthetized monkey cortex

Markus Baumann (Institute of Neuroinformatics) *Coding and decoding of hand grasping signals in the primate parietal and premotor cortex*

Philipp Berens (Max Plank Institute for Biological Cybernetics) *Spikes are phase locked* to the gamma band of the local field potential oscillations in the primary visual cortex of the macaque

Melanie Bernard (Vanderbilt University) Synchrony in cat visual cortex is more selective for natural images than average firing rate

Ali-Reza Boloori (Harvard University) *How does joint activity across a population of neurons influence the precision of coding in the cortex*

Markus Bongard (UMH) Distributed coding in retinal ganglion cell populations

Catherine Chang (Stanford University) *Independent component analysis of 'real' music reveals brain modes selective for parsing event boundaries*

Ben Engelhard (Hebrew University, Jerusalem) *Analysis of movement direction estimation from motor cortices using simple models*

Tomer Fekete (The Weizmann Institute of Science) Representational systems

Christopher Fetsch (WUSTL School of Medicine) *Reference frames of visual and vestibular signals in Area MSTd: Comparison of neural data with model simulations*

David Field (University of Reading) *The neural correlates of path perception and steering investigated using fMRI*

Jozsef Fiser (Brandeis University) *The role of ongoing neural activity in the primary visual cortex of the awake ferret*

Alexander Gail (Caltech) *Dynamics of context-specific movement goal representations in posterior parietal cortex of monkeys*

Jozien Goense (MPI Biological Cybernetics) *fMRI of V1 microarchitecture in the macaque at 4.7T*

Diego Gutnisky (University of Texas Medical School) *Adaptation changes the structure of correlations in primary visual cortex*

Kenneth D. Harris (Rutgers University) *Stereotyped activity flow in auditory neocortical microcircuits*

Linda Hermer-Vazquez (University of Florida) *Information flow through task-related sensory and motor circuits as rats perform a sensory-guided decision-making task*

_ FRIDAY, JUNE 23 __

MORNING SESSION Dora Angelaki, moderator

- 09:00–09:45 **Michael Shadlen** (University of Washington) *Decision variables, time and log odds in parietal cortex*
- 09:45–10:30 Richard Andersen (Caltech) Decision and action in parietal-frontal circuits
- 10:30-11:00 coffee break
- 11:00–11:45 Dan Margoliash (University of Chicago) Restructuring the brain during sleep
- 11:45–12:30 Michale Fee (MIT) Neuronal clocks and noisemakers in the songbird
- 12:30-14:00 lunch

AFTERNOON SESSION Catherine Ojakangas, moderator

- 17:00–17:45 György Buzsáki (Rutgers University) Oscillations organize cell ensembles
- 17:45–18:15 coffee and light snacks
- 18:15–19:00 **Carol Barnes** (University of Arizona) *Alterations in hippocampal population coding during aging*
- 19:00–19:45 Thanos Siapas (Caltech) Decoupling through synchrony
- 20:00-21:30 posters

Raymond Hermer-Vazquez (University of Florida) *Large-scale coordination mechanisms coupling sensory and motor areas prior to skilled movement*

Dorrit Inbar (Hebrew University, Jerusalem) *Correlated neuronal activity in primary and pre-motor cortices of monkeys during performance of different visuomotor association tasks*

Karim Jerbi (CNRS) Coherent neural representation of hand speed in humans

Christoph Kayser (Max Plank Institute for Biological Cybernetics) *Integration of sensory information in auditory cortex*

Georgios Keliris (Max Plank Institute for Biological Cybernetics) *Perceptual suppression in Area V1 of the macaque*

Vasileios Kokkinos (University of Patras) *Robust time-relationships between sharp waves, ripples, and single unit firing in rat ventral hippocampal slices*

Nedialko Krouchev (Université de Montréal) *Seamless encoding and decoding of forward and inverse motor commands by dynamically interacting neural populations*

Hagai Lalazar (Hebrew University, Jerusalem) *Modeling the ongoing cortical dynamics inherent in the local field potential*

Eunjeong Lee (University of Amsterdam) *Neural activities in the medial prefrontal cortex of the rat with multimodal discrimination task*

Yael Mandelblat (Hebrew University, Jerusalem) *The expression of local field potential gamma oscillations in primary motor cortex during reaching movements of an awake behaving monkey*

Maria Markaki (University of Crete) *Extracting speech relevant spectro-temporal modulations using the information bottleneck method*

Eirini Mavritsaki (University of Birmingham) *A neurocomputational analysis of preview* search

Ron Meir (Technion) *Optimal control theory predicts complex patterns of neural activity observed in the primary motor cortex*

Konstantinos Moutoussis (University College London) 'Seeing' invisible motion: Responses of Area V5 neurons in the awake-behaving macaque

Christina Moutsiana (University of Reading) *Contextual influences of surround motion on BOLD activity evoked by a central moving stimulus*

Stefano Panzeri (University of Manchester) *Population coding of natural video stimuli in macaque V1*

Costas Papatheodoropoulos (University of Patras Medical School) *Sedative/amnesic drugs interfere with hippocampal sharp wave/ripple activity*

Tobias Pistohl (Bernstein Center for Computational Neuroscience) *Movement trajectories inferred from human neuronal population signals (ECoG)*

SATURDAY, JUNE 24 _____

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

AFTERNOON SESSION Nicholas Hatsopoulos, moderator

17:00–17:45 **Eilon Vaadia** (Hebrew University, Jerusalem) *Dynamics of learning-related activity of* single cells and neuronal population in motor cortex of monkeys – implications for development of a brain machine interface

17:45–18:15 coffee and light snacks

- 18:15–19:00 **Gerhard Friehs** (NeuroSurgery Foundation) *Experience with a multi-unit brain recording system in human*
- 19:00–19:45 John Pezaris (Harvard Medical School) Proof of concept for a thalamic visual prosthesis
- 20:00-21:30 posters

Richard E. Poppele (University of Minnesota) *Distribution of step-related activity in cat cerebellar cortex during passive hindlimb stepping on a treadmill*

Gita Prabhu (University College London) *Object and grasp related activity in F5 neurones during visually guided grasp*

Gregor Rainer (Max Plank Institute for Biological Cybernetics) *Inferior temporal cortex during real world vision*

Jacob Reimer (University of Chicago) *Oscillations and ensemble activity in motor cortex: Medium and message?*

Sebastien Roux (CNRS) *Precise spike synchronization in monkey motor cortex: From time estimation processes to the selection of movement direction*

Eric Schmidlin (Princeton University) *Cortico-cortical interactions in macaque motor cortex investigated with intracortical microstimulation (ICMS) and transient inactivation with muscimol*

Elad Schneidman (UCL Institute of Neurology) *Weak pairwise correlations imply strongly correlated network state in a neural population code*

Rachael D. Seidler (University of Michigan) *Neural correlates of intermanual transfer of sensorimotor adaptation*

Peggy Seriès (UCL Gatsby Institute) *Fisher information, multiplicative noise and nonlinear decoding*

Soon-Lim Shin (University of Antwerp) *Dynamic synchronization of Purkinje cell simple spikes*

John Soechting (University of Minnesota) *The role of prediction in ocular tracking of targets moving in two dimensions*

Ben Townsend (UCL Institute of Neurology) *Simultaneous recording from two types of identified output neuron in M1*

David Vaillancourt (University of Illinois at Chicago) *Motor selection and sequencing: Role of the basal ganglia and frontal cortex in humans*

Matthijs van der Meer (University of Edinburgh) *Anticipation in a population-coding system: a model of the inputs to rodent head direction cells*

Angela Yu (Princeton University) *To spike or not to spike: Computational optimality, reward, and attention*

Neta Zach (Hebrew University, Jerusalem) *Emergence of context specific responses in M1 and PM cortices*

Margarita Zachariou (University of Nottingham) *The role of cannabinoids in the neurobiology of sensory gating: A firing rate model study*

Zhiyi Zhou (Vanderbilt University) *Spatial coherence of visual stimuli modulates synchronized activity in cat visual cortex*

_ SUNDAY, JUNE 25 _____

MORNING SESSION Nikos Logothetis, moderator

- 09:00–09:45 Gilles Laurent (Caltech) Building pattern classifiers: Tips from olfaction
- 09:45–10:30 Leslie Kay (University of Chicago) Manipulating fast and slow neural synchrony in olfactory processing
- 10:30-11:00 coffee break
- 11:00–11:45 **Roger Lemon** (University College London) *Interaction between ensembles of ventral premotor and motor cortex neurons encoding grasp*
- 11:45–12:30 Nicholas Hatsopoulos (University of Chicago) A language of action in the motor cortex
- 12:30-14:00 lunch

AFTERNOON SESSION Phil Ulinski, moderator

- 17:00–17:45 Miguel Nicolelis (Duke University) The search for principles of neural ensemble coding
- 17:45–18:15 coffee and light snacks
- 18:15–19:00 Alexa Riehle (CNRS) While waiting to move: What is coded by local field potentials in monkey motor cortex?
- 19:00–19:15 closing remarks
- 21:00-24:00 banquet dinner at Selene Restaurant

SPEAKER ABSTRACTS (in alphabetical order by speaker)

Decision and Action in Parietal-Frontal Circuits

Richard Andersen (Caltech)

Parietal and frontal cortical areas form the core of the system responsible for sensory-motor integration. I will describe recent experiments examining this circuit.

One function of this circuit is to transform sensory information into motor coordinates for action. We find that the parietal reach region (PRR) represents targets for reaching in visual (eye) coordinates. The dorsal premotor cortex (PMd) on the other hand uses a relative position encoding. The hand, eye, and target are all represented with respect to one another. This difference coding to our knowledge has not been previously observed in the brain, although it is used in algorithms for robotic control. This relative position coding may be useful for movements that require the coordination of multiple body parts such as hand-eye coordination.

Activity of cells in this core parietal-frontal system is related to decision making. We find that PRR neurons encode expected value including the magnitude, type and probability of expected rewards. Using a new technique for examining the degree of communication between cortical areas we observed greater activity between PRR and PMd when monkeys are free to choose a movement compared to when they are instructed. This increased deliberation and communication is bidirectional and, within the resolution of the technique, simultaneous.

Motor control models typically postulate a "forward model" for predicting movement trajectories in order to remove delays in feedback systems. Lesions to the posterior parietal cortex produce deficits in error correction during reaching, suggesting that it may be a substrate for such a forward model. In recordings from PRR we find that the cells predict the trajectory of a movement in real time, consistent with their representing a forward model for reaching.

The above new findings were incorporated into a "brain-control" task in which the monkeys' intended movements, decoded from PRR and PMd neural activity, were used to control a cursor on a computer screen. The monkeys' intended goals and trajectories, as well as expected value, could all be decoded without the monkeys performing reach movements. These results provide a proof-of-concept that higher-order cognitive signals related to actions and decisions can be decoded and used for neural prosthetic applications. In these applications it is envisioned that the recorded cortical activity of paralyzed patients be used to control assistive devices such as computers, robots or vehicles.

Alterations in Hippocampal Population Coding During Aging

Carol Barnes (University of Arizona)

Aging is associated with specific impairments of learning and memory, some of which are similar to those caused by hippocampal damage. Anatomical and electrophysiological studies indicate that the hippocampus of the aged rat sustains a loss of synapses in the dentate gyrus, and a loss of functional synapses in area CA1. Such changes may contribute to the observed age-related impairments of synaptic plasticity, which include deficits in the induction and maintenance of long-term potentiation (LTP) and lower thresholds for depotentiation and long-term depression (LTD). This shift in the balance of LTP and LTD could, in turn, impair the encoding of memories and enhance the erasure of memories. Studies will be reviewed that link deficits in these plasticity mechanisms with altered hippocampal network dynamics. For example, altered plasticity may affect network encoding by impairing the binding of cues to the hippocampal map, leading to the retrieval of inappropriate maps, or impaired use of external cues to guide navigation. Furthermore, the experience-dependent place-field expansion effect that occurs robustly in young hippocampal pyramidal cells, and requires NMDA receptor activation, is impaired in old hippocampal place cells, and may decrease both the spatial information content of the hippocampal map and the ability of the network to store sequences of locations. Recent studies suggest that pharmacological attenuation of some of these age-related deficits may be possible.

Supported by AG03376, AG12609.

Oscillations Organize Cell Ensembles

György Buzsáki (Rutgers University)

How does the brain orchestrate perceptions, thoughts and actions from the spiking activity of its neurons? Previous single neuron recording research has regarded spike pattern variability as noise that should be averaged out to reveal the brains representation of invariant input. The alternatively view is that variability of spikes is centrally coordinated and that this brain-generated ensemble pattern in cortical structures is a potential source of cognition. Large-scale recordings from neuronal ensembles now offer opportunities for challenging and testing these competing theoretical frames. A postulated signature of the cell assembly is that its participants show a higher probability of spiking together than with members of other assemblies, even in the absence of external inputs. Interactions among parallel-recorded hippocampal neurons revealed a consistent temporal structure beyond that predicted from the environmental inputs. We find that prediction of spike times of hippocampal pyramidal neurons is improved using the spike times of simultaneously recorded neurons, over prediction from the animals trajectory in space, or a spatially-dependent theta phase modulation. Thus, we suggest that the assembly organization arises from the internal dynamics of neuronal circuits, and reflects the operation of non-sensory cognitive phenomena. Importantly, the time window within which spike times were best predicted from simultaneous peer activity is 10-30ms, suggesting that cell assemblies are synchronized at this timescale. Because this temporal window matches the period of the gamma oscillation and the time window for synaptic plasticity, we suggest that cooperative activity at this timescale is optimal for information transmission and storage in cortical circuits. Altering synaptic weights within the hippocampal network by LTP, assembly membership could be altered. We suggest that assembly-based approach provides an insight into centrally-organized (cognitive) events without reference to introspection.

Harris, K. D., Csicsvari, J., Hirase, H., Dragoi, G.. and Buzski, G. Organization of cell assemblies in the hippocampus. Nature 424:552-556, 2003.

Dragoi G, Harris KD, Buzsaki G. Place representation within hippocampal networks is modified by long-term potentiation. Neuron 39:843-853, 2003.

Buzsaki, G. and Draguhn, A. Neuronal oscillations in cortical networks. Science 304: 1926-1929, 2004.

Neural Mechanisms of Heading Perception: Sensory Integration and Population Coding Greg DeAngelis, Yong Gu, and Dora Angelaki (Washington University in St. Louis)

Accurately sensing one's direction of self-motion through the environment is a fundamental task for the nervous system to solve. Visual motion (optic flow) provides a powerful cue to one's direction of heading, but optic flow alone is not always reliable as it is confounded by eye movements, head movements, and object motion. Linear acceleration signals from the otolith organs of the vestibular system provide complementary information. This talk will describe experiments in which we have recorded from neurons in area MSTd during performance of a multi-modal (visual-vestibular) heading discrimination task. Psychophysical results show that monkeys combine visual and vestibular cues near-optimally to judge heading. Simultaneous single-unit recordings reveal that a subset of MSTd neurons with congruent heading preferences for visual and vestibular stimuli may account for the cue integration effects seen psychophysically. In contrast, another subset of MSTd neurons have near-opposite heading preferences for visual and vestibular stimuli, and these neurons do not show improved sensitivity under cue combination. By analyzing the relationships between neuronal responses and perceptual decisions (choice probabilities), we further show that these two subsets of MSTd neurons contribute differently to judgments of heading. If MSTd neurons are critical for heading perception, then the population response should account for the fact that heading discrimination is much more precise around straight ahead than around an eccentric reference. We addressed this issue by using Fisher information to calculate the optimal discrimination performance that could be achieved by decoding the activity of a large population of MSTd neurons. We developed a model to describe the 3D heading tuning functions of MSTd neurons. Fits of this model to our experimental data, along with fits to the variance-mean relationship for each neuron, allowed us to predict how heading discrimination performance should vary with the eccentricity of the heading reference. The predicted heading thresholds from the MSTd population show a dependence on heading eccentricity that is quite similar to that seen in human psychophysical studies (Crowell and Banks 1993). The improved discrimination performance around straight ahead arises not from an over-representation of neurons that prefer radial flow, but rather from an overabundance of neurons that prefer lateral motion and have broad tuning curves with steep slopes around straight ahead. This analysis supports the notion that population activity in MSTd limits discrimination of heading based on optic flow.

Neuronal Clocks and Noisemakers in the Songbird

Michale Fee (MIT)

The ability of the brain to recognize and execute precise temporal sequences underlies much of our sensory experiences and behavioral output. Whether we are speaking, swimming, or playing the piano, we are crucially dependent on our brain's capacity to reliably step through a learned sequence of states. Songbirds provide a marvelous animal model in which to study these phenomena. Using newly developed technology for monitoring the activity of single neurons in the brain of singing bird, we have identified circuits in the songbird brain that perform key functions of vocal production and learning. One of these circuits produces a precise representation of temporal order in the brain — essentially a clock. Another circuit produces highly variable output that drives large fluctuations in the songs of juvenile birds, allowing them to explore different vocal patterns. I will combine these observations to propose a model for vocal control and learning based on ideas of reinforcement learning.

Experience with a Multi-Unit Brain Recording System in Humans

Gerhard Friehs, Vasilios Zerris[†], Michael Park, Marc Goldman, Leigh Hochberg[‡], John Donoghue (NeuroSurgery Foundation, [†]Tufts University, [‡]Harvard Medical School)

It is hoped that intracortically-based brain-computer interfaces, by harnessing the natural substrate for movement commands (signals from MI), will provide new assistive technologies for persons with paralysis. We report on our initial experience with BRAINGATE, a long-term multi-electrode recording system implanted in the human brain. The core of the system is a chip measuring 4×4 mm with 100 electrodes which is implanted into the dominant primary motor cortex arm area. It is connected to an external signal processing system which allows for amplification of the extracellular signals, spike detection and sorting, and decoding of the multi-unit recording into a control signal which can be used to operate various output devices.

Our preliminary results indicate that neuronal activity in MI is preserved after spinal cord injury, that it can be modulated voluntarily, and that this neuronal ensemble spiking activity can be decoded into to useful signals. There were no adverse events and the array was explanted successfully after 14 months. The decoded ensemble recordings have been used to control a computer cursor, to drive a robotic arm or move a motorized hand prosthesis. These results suggest that continued efforts on neural decoding will lead to clinical useful devices.

The following authors declare a conflict of interest: Gerhard Friehs, John Donoghue are co-founders and shareholders in CKI. Dr. Hochberg has a clinical trial agreement with Cyberkinetics.

Encoding and Decoding by Neural Ensembles: From Movement Parameters to Serial Order *Apostolos Georgopoulos* (University of Minnesota)

In this lecture I will review methods, issues, and applications of neural coding and computation during the past two decades. Approaches and studies in behaving primates, human subjects, and artificial neural networks will be discussed and selected results illustrated. Finally, the potential for noninvasive neuroprosthetic control, using MEG and EEG, will be assessed.

A Language of Action in the Motor Cortex

Nicho Hatsopoulos (University of Chicago)

Almost 100 years ago, it was postulated that the motor cortex should be viewed as a synthetic organ for complex motor actions such that elementary movements represented by individual motor cortical neurons could be combined in an almost infinite number of ways to generate the rich variety of complex motor actions that are ubiquitous in every day life. This view implies that motor cortex constitutes a sort of language of motor actions where individual motor cortical neurons encode the movement primitives of the language and the manner in which these neurons combine their activities to generate more complex motor actions constitute the grammar of action. Here we show that single motor cortical neurons encode time-dependent movement trajectories and not simply time-independent movement parameters. Moreover, we demonstrate that these movement trajectories can be combined using a simple addition rule when neurons fire simultaneously but independently. Finally, neurons that engage in significant synchronization combine their movement primitives through addition but with an additional gain factor which suggests that a functional role for synchronization may be to increase tuning sensitivity. Our findings are particularly topical given the recent excitement that has been generated by several studies demonstrating that electrical stimulation of motor cortex can elicit complex, time-evolving movements even at the single neuron level (Graziano et al., 2002; Brecht et al, 2004).

Manipulating Fast and Slow Neural Synchrony in Olfactory Processing

Leslie M. Kay (University of Chicago)

One of the most striking features of olfactory system physiology is odor evoked fast oscillations, which represent varying degrees of underlying neural synchrony. Recent studies have shown that artificial ablation (in insects) of fast synchrony impairs and artificial enhancement (in mice) of this synchrony enhances discrimination of similar odorants. The test of whether fast synchrony plays a functional role in odor discrimination depends on whether individuals manipulate the level of synchrony online in a task dependent fashion. We show that rats do this such that fast synchrony is significantly enhanced in difficult odor discrimination tasks, while it is unaffected in easy discrimination tasks. At the other end of the frequency spectrum is theta band olfactory bulb activity associated with inhalation and afferent input to mitral cells. This slow synchrony among principal neurons is disrupted when rats sniff at higher frequencies. However, during fast sniffing in odor investigation significant coherence at high theta frequency is found between the olfactory bulb and hippocampus in a performance-dependent fashion. These two sets of results suggest that fast and slow synchrony can operate simultaneously to serve different purposes, fast synchrony facilitating formation and recall of neural assemblies within a sensory area and slow synchrony facilitating interregional cooperation in sensorimotor or other types of integration.

Building Pattern Classifiers: Tips From Olfaction

Gilles Laurent (Caltech)

Most odors are complex chemical objects, containing tens to hundreds of chemical components (fresh ground coffee, for example, produces two to three hundred volatile analytes). Yet, odor perception is singular: perceptual segmentation of odors in humans fails for mixtures of more than three components. The olfactory system thus offers a good opportunity to study some of the brain's solutions to the very general problems of pattern encoding, learning and recognition. Using recent data collected from insects and fish, I will describe our latest results on the rules and mechanisms at work in this system, focusing in particular on circuits dynamics, connectivity and capacity.

Interaction Between Ensembles of Ventral Premotor And Motor Cortex Neurons Encoding Grasp

Roger Lemon, Thomas Brochier, Alessandra Umilta, Rachel Spinks, Gita Prabhu and Eric Schmidlin (University College London, Institute of Neurology)

This talk will address some of the issues related to how transformations occur between neuronal representations of the physical properties of objects and the motor commands that are needed to grasp them. We have made simultaneous recordings from macaque monkey ventral premotor cortex (area F5) and from primary motor cortex (M1), sampling both single neurons and LFPs in a task in which monkeys were trained to observe randomly-presented objects and then reach, grasp and hold them. We have addressed the question of how these two areas represent the preparation and grasp of differently-shaped objects. We have found that discharge rates in assemblies of area F5 neurones unambiguously represent different sets of objects, and that these neurones are already tuned to different objects and grasps before the monkey grasps the object, which is not the case for PTNs in M1 or for other, unidentified M1 neurones. We have also examined how the pattern of activity in these neuronal assemblies predicts the pattern of EMG activity recorded simultaneously from up to 12 different digit, hand and arm muscles.

A key issue is how premotor representations of the motor plan for grasp of a given object is transmitted to the motoneurons and muscles that generate the hand shape appropriate for that object. We consider that the interaction between F5 and M1 is a key mechanism in generating the motor command, and that the integrity of M1 is essential for motor effects generated by ICMS in F5. We have demonstrated interactions between F5 and M1 at the level of single neurons and LFPs and have shown that activation of F5 can modulate motor outputs to particular muscles from M1 that is specific to preparation and execution of grasp of particular objects.

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Signal, Noise, and Variation in Sensory-Motor Transformations

Stephen G. Lisberger (Howard Hughes Medical Institute & UCSF)

We are evaluating neural coding and decoding by tracing variation from the origin of the sensory drive for smooth pursuit eye movements, in the middle temporal area of the extrastriate visual cortex (MT), to the motor output. The variation of pursuit behavior itself is low-dimensional, with over 90% of the variation accountable in terms of errors in estimating the direction, speed, and time of onset of target motion. Precision in estimating direction and speed of eye movement are in good agreement with perceptual estimates of the same parameters: within 100 ms after the onset of the pursuit response, pursuit is able to resolve 2.3 degrees of target direction and 15–20% of target speed. The good agreement in the direction and speed precision of pursuit and perception suggests that precision in both behaviors is limited by a single, sensory, noise source. Recordings from Purkinje cells in the floccular complex of the cerebellum are consistent with the idea of a sensory noise source. During the first 100 ms of pursuit, we observe strong trial-by-trial co-variation between the instantaneous firing rate of Purkinje cells and the individual traces of eye movement. These correlations imply a high degree of correlation between the responses of different Purkinje cells, and imply that much of the variation in pursuit arises before signals are subjected to final motor processing in the cerebellum and brainstem.

Restructuring the Brain During Sleep

Dan Margoliash (University of Chicago)

There is an increasing body of evidence that so-called "spontaneous" activity outside periods of overt behavior is important for CNS function. A paradigmatic example of this is functional neuronal activity during sleep, which has been strongly linked to various forms of memory consolidation following episodes of cognitive, sensory and sensorimotor learning. The phenomena of neuronal "replay" during sleep has been identified as a central feature of sleep-mediated memory consolidation. Vocal learning in songbirds is an excellent and well-established model system for learning and memory, and it has been shown at both behavioral and physiological levels that sleep contributes to the vocal learning phenomenon. Interestingly, sleep may serve to inject structured noise into songbird vocal learning. We have demonstrated that physiological properties of certain forebrain "song system" neurons analogous to primary motor cortex neurons are biased to change functional properties during periods of sleep, and in specific fashion. The specificity in the change during sleep of the neurons' bursting properties could serve as a source of structured noise. This introduces the concept of "preplay", activity during sleep that predicts functional (in this case motor) activity the following day. To date, however, our analysis of sleep preplay has largely been limited to sequential recordings from single neurons. The central question we wish to address here is to describe the dynamics of populations of song system neurons during sleep, and to relate these dynamics to the state changes observed at the single neuron and behavioral levels.

Retinal Processing of Natural Motion

Markus Meister (Harvard University)

The visual image of the outside world moves incessantly across the retina, owing to deliberate or random movements of the animal, head, and eye. Yet the visual system can rapidly detect objects within the scene that move relative to the background. We have identified a population of retinal ganglion cells involved in this process. Such a neuron remains silent when the entire retinal image moves coherently, but fires when a small image patch moves differently from the surroundings. I will discuss the neural circuitry that implements this computation, tracing the signals through all the relevant interneurons and their synapses. The retina's choice of algorithm for differential motion detection is quite unusual, yet found to be robust under the conditions of natural vision.

The Search for Principles of Neural Ensemble Coding Miguel Nicolelis (Duke University Medical Center)

No abstract provided.

Perceptions Created Through Microstimulation of the Primate LGN: Proof of Concept for a Thalamic Visual Prosthesis

John S. Pezaris (Harvard University Medical School)

The field of visual prosthetics has concentrated primarily on two targets for stimulation, the retina and the primary visual cortex. The lateral geniculate nucleus of the thalamus, the relay station between these two areas, has been largely ignored because of the difficulty of surgical approach. The development of deep brain stimulation techniques for addressing pathologies of the midbrain has opened surgical access to the thalamus, and motivates a reconsideration of targets for visual prosthetics.

With this background, we have performed a series of experiments in an animal model to demonstrate a proof of concept for a visual prosthesis based on thalamic microstimualtion. To assess the characteristics of electrically-evoked percepts, we performed a study of electrical stimulation of LGN through fine wire electrodes in awake behaving macaques, using a behavioral report to read out percept size and location. We used a simple center-out visually guided saccade paradigm where animals were required to foveate a central point and then saccade to briefly presented target stimuli.

While most targets (and all fixation points) were presented on a computer screen, some targets were presented via electrical stimulation applied to fine wire electrodes placed in the LGN. Trials where the target appeared on the screen were used as a control baseline to compare against trials where the target was presented through electrical stimulation.

Data were collected from two macaques. Each animal immediately generalized to the electrical targets, consistently saccading to a point in space which corresponded to the location of the previously mapped receptive field of cells at the electrode tip. Saccade latencies and accuracies to electrical targets were consistent with those to screen targets, suggestive of a perceptual rather than motor effect. This was verified through a small number of double-saccade experiments.

We conclude that the LGN presents a target for a visual prosthesis with substantial potential for additional investigation.

Memory Mechanisms and Population Codes in Sequentially Connected Temporal Lobe Brain Regions

Barry J. Richmond (NIMH/NIH/DHHS)

We have been studying two sequentially connected brain regions, area TE and perirhinal cortex, related to visual pattern recognition. We find, as has been shown before, that the neurons in area TE show strong pattern selectivity. In addition, however, we find a rapidly adapting signal related to short term or working memory for stimulus pattern. This signal appears as correlation in the noise over time and suggest that a specific ensemble code is present. In contrast, the responses in perirhinal neurons show a different type of plasticity, coding instead for the reward contingent meaning of a stimulus.

When monkeys are performing a sequential delayed match-to-sample task, the correlation in noise stronger between sample and match responses than between sample and nonmatch responses, even when a nonmatch stimulus appears between the sample and match pattern. This characteristic, where the noise when a match is presented is dependent on the noise that was present at the time of sample, implies that a snapshot of the neural response was stored, that is, remembered. This stored signal is then read at the time of the match. We show that correlation in noise is a signature for an adaptive matched filter mechanism in which each neuron adapts to its inputs at the time of the sample and act as a correlator at the time of subsequent inputs. Under this scenario each member of the ensemble would act as a different weight in a matched filter, and when the stored pattern reappeared, a recognition would be registered when the summed output of the filter crosses a threshold. These results show that area TE has characteristics that make it a strong candidate to hold working memory signals. We show how all steps of the memory system, encoding, storage, recall, and identification would be implemented in the ensemble.

The memory mechanisms in perirhinal cortex, a direct target of area TE inputs, are very different. Here the correlations described above are not present. Instead, however, when monkeys perform a visually cued reward schedule task, the neurons have responses that adapt to the reward contingency associated with the visual cues, i.e., they are selective for what the cue means. We show, using a genetically based antisense generating vector injected into perirhinal cortex, that this neuronal plasticity depends on the dopamine D2 receptor. Thus, there is a double dissociation of memory mechanisms in these two directly and reciprocally connected cortical regions. This raises the question about how such neural encoding arises, and what it implies for relations between even apparently heavily connected brain regions.

While Waiting to Move: What is Coded by Local Field Potentials in Monkey Motor Cortex? Alexa Riehle and Sébastien Roux (CNRS & Mediterranean University)

Many features of motor cortical single neuron activity are not strictly related to the motor signal, i.e. movement generation. Instead they are more closely tied to preparation for movement, sensorimotor transformation, or temporal aspects of movement planning. For example, some activity has been described as "preprocessing" [1], i.e. early processing of prior information about features of the forth-coming movement. Furthermore, the transient synchronization of two or more neurons at the end of an estimated time interval can reflect instants of signal expectancy [2]. Such properties are linked to the temporal prediction of forthcoming events, which is essential for optimizing motor performance. Indeed, prior information about when a GO signal will occur significantly shortens reaction time [2]. If these processes arise in a sufficiently large population of neurons, they should also be manifested in the local field potential (LFP), possibly indicating the degree of coherent network activity. LFPs can be recorded from the same electrode as the spikes of a single neuron, by simply low-pass filtering the signal. The LFP is a spatially averaged signal from a small volume, assumed to reflect mainly the synaptic input received by the neurons within the observed volume.

Multi-electrode recordings of both LFPs and single neuron activities were made in motor cortex as monkeys performed two different delayed pointing tasks, in which accurate estimation of two time intervals was essential for correct performance [3]. When a motor cortical LFP is aligned to movement onset, generally three components can be detected: a positive component (P1) directly before movement onset, then a negative (N1), followed by a positive component (P2) after movement onset. The premovement positivity P1 is commonly interpreted as being strongly motor-related and assumed to be linked to the generation of the descending motor volley. Surprisingly however, we observed a large context-related modulation of P1 [4]. (i) Its amplitude was much smaller when removing uncertainty. (ii) It was more closely associated with the processing of movement-related information than with the ultimate motor command. (iii) Its timing did not bear a fixed relationship with movement onset, but differed in relation to reaction time. (iv) And finally, its frequency of occurrence in each monkey varied in parallel with each animal's overall performance and the percentage of context-related "preprocessing" neurons encountered. Interestingly, later LFP components (N1 and P2, after movement onset) did not exhibit these properties. Furthermore, the estimation of a fixed delay period was associated with a single cycle slow wave of the LFP which was modulated in relation to the duration to estimate. Also LFP oscillations in the beta range were observed during the delay, whose frequency increased toward its end but ceased at the time of movement onset. Moreover, synchronization of LFPs recorded a few hundred microns from one another increased strongly during moments of signal expectancy.

LFPs faithfully monitor many of the same aspects of motor cortical operation, such as preprocessing, and expectancy-related synchronization, as seen in single neuron spiking activity. In addition, however, they complement unit recording by revealing "hidden" features, such as event-related slow waves and preparatory, non event-related 15 Hz oscillations, that are not otherwise observable.

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Decision Variables, Time and Log Odds in Parietal Cortex

Michael Shadlen (Howard Hughes Medical Institute & University of Washington)

With little sophistication, the spike rates from sensory neurons can be used to approximate useful statistics for decision making. In the context of deciding between two sensory hypotheses, a simple difference in spike rate between sensory neurons with opposite selectivity is proportional to the log likelihood ratio in favor of one sensory interpretation over another. I will describe neural recording and stimulation experiments from the alert monkey that demonstrate that the brain uses such a difference to make decisions about the direction of motion in a 2-alternative direction discrimination task. The accumulation of this difference to threshold explains the speed and accuracy of simple decisions. A new probabilistic classification task, similar to the weather prediction task reveals a direct representation of log probability in parietal cortex. And, if time permits, I will explain how the brain uses elapsed time to decode such probability. I will do my best to relate these observations to a more general computational framework for the encoding and read out of information by neurons in neocortex.

Decoupling Through Synchrony

Thanos Siapas (Caltech)

Synchronization is a key property of many biological, physical, and engineering systems. The level of synchronization in distributed systems is often controlled by the strength of the interactions between individual elements. In brain circuits the connection strengths between neurons are constantly modified under the influence of spike-timing-dependent plasticity rules (STDP). However, the consequences of these local rules for the global dynamics of brain networks are not fully understood. In this talk, I will show that when recurrent networks exhibit population bursts STDP rules exert a strong decoupling force that desynchronizes activity. I will discuss the implications of this counterintuitive result for the transfer of information in cortico-hippocampal networks during memory formation, and the therapeutic effects of deep brain stimulation for Parkinson's disease and epilepsy.

Network Mechanisms of Perception

Andreas Tolias (Max Plank Institute for Biological Cybernetics)

Despite recent progress in systems neuroscience, basic properties of the neural code still remain obscure. For instance, the responses of single neurons are both highly variable and ambiguous (similar responses can be elicited by different types of stimuli). This variability/ambiguity has to be resolved by considering the joint pattern of firing of multiple single units responding simultaneously to a stimulus. Therefore, in order to understand the underlying principles of the neural code it is important to characterize the correlations between neurons and the impact that these correlations have on the amount of information that can be encoded by populations of neurons. Here we applied the technique of chronically implanted, multiple tetrodes to record simultaneously from a number of neurons in the primary visual cortex (V1) of the awake behaving macaque, and to measure the correlations). We find that, contrary to widespread belief, noise correlations in V1 are very small (around 0.01) and do not change systematically neither as a function of cortical distance (up to 600 μ m) nor as a function of the similarity in stimulus preference between the neurons (uniform correlation structure). Interestingly, a uniform correlation structure is predicted by theory to increase the achievable encoding accuracy of a neuronal population and may reflect a universal principle for population coding throughout the cortex.

Propagating Waves in Turtle Visual Cortex Contain Information About Visual Stimuli Philip S. Ulinski (University of Chicago)

Visual stimuli elict waves of activity that propagate across the visual cortex of freshwater turtles. These waves can be studied using either multielectrode arrays or voltage sensitive dyes. Waves that have been imaged using voltage sensitive dyes can be represented as movies. They typically originate near the rostral pole of the cortex and propagate in a relatively stereotyped manner from rostral to caudal across the cortex, sometimes leading to the formation of a secondary wave that moves across the cortex in the opposite direction. Short duration visual stimuli elicit waves that last for more than two seconds. Propagating waves can be simulated using a large-scale model of turtle visual cortex that consists of approximately 1,000 biophysically realistic compartmental models. Waves of this kind are expected to occur in any sheet of neurons that are connected by excitatory synapses and could, consequently, be only an epiphenomenon of cortical organization. This presentation will summarize evidence that the waves in turtle visual cortex contain information about the position and speed of objects moving in visual space. Movies of waves evoked by either flashes of diffuse light, spots of light or moving spots were studied using an in vitro eye-brain preparation of turtle visual system and the large-scale model. Movies of the waves were analyzed using a variant of principal component analysis, the Karhunen-Loeve (KL) decomposition. Waves could be accurately represented as a sum of three spatial eigenfunctions weighted by time-dependent coefficients. An individual wave could then be represented as a trajectory in a three dimensional phase space, A-space, spanned by the coefficients, $a_1(t)$, $a_2(t)$ and $a_3(t)$. A second KL-decomposition was applied to a trajectory in A-space to produce a point in a second phase space, B-space, that was spanned by three spatial coefficients, $b_1(x,y)$, $b_2(x,y)$ and $b_3(x,y)$. Spots of light presented at different points in visual space produced different points in B-space, suggesting that position in visual space is represented in the spatiotemporal dynamics of the waves. Initial analyses used the full 1,500 ms of the wave. However, double KL-decompositions were also carried out using time windows of increasing duration. This analysis produced a sequence of points, or a *b-strand*, in B-space. Analyses of the b-strands produced by different stimuli suggested that the information content of the waves reaches a peak by about 180 ms after stimulus presentation, and then declines.

This work was done in collaboration with Bijoy Ghosh at Washington University and Kay Robbins and David Senseman at the University of Texas at San Antonio. It was supported by a grant from the CRCNS program at the National Science Foundation.
Dynamics of Learning-Related Activity of Single Cells and Neuronal Population in Motor Cortex of Monkeys – Implications for Development of Brain Machine Interface

Eilon Vaadia (Hebrew University, Jerusalem)

We studied generation and modifications of neuronal representations of purposeful arm movements during sensorimotor learning. The basic behavior consisted standard reaching movements. Once the animals learned this task, we recorded neuronal activity while they learned visuomotor rotation and/or arbitrary associations. In parallel, the above experiments are used to develop improved algorithms for brain machine interface.

We show that; (1) Both local field potentials and single units can be used to infer the movement direction (2) Learning induces specific improvement in encoding and decoding of the learned parameters; the learned direction and learned color. (3) Learning induced changes in neuronal activity during one learning session, occurred early in the learning in SMA and only later in MI, suggesting that MI, at the lower level of the system, adjusts its representations only after the higher level enabled acquisition of the task. (4) The improved representation after learning enables a more accurate inference of movement direction from neuronal populations.

These results indicate that simple learning tasks can enhance performance of brain machine interfaces. To further improve movement reconstruction on the basis of neuronal activity, we developed a kernel method of prediction of movements with two main features: (1) Using non-parametric approach that does not assume cell independence, imposes relatively little assumptions on the tuning properties, and allows representation of behavior not only in average rate but also in highly specific neural temporal patterns; and (2) Taking into account the nature of kinematics of arm movement. This algorithm outperforms linear regression and other Kalman-filter algorithms.

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POSTER ABSTRACTS (in alphabetical order by presenter)

Population Coding of Wavelets in V1

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With population codes, the signal to noise ratio (SNR) of each degree of freedom is proportional to the number of neurons allocated to represent them [1]. Following this hypothesis, one can use the measured distribution of the preferred spatial frequencies (SF) of simple cells (SC) in V1 to obtain a measure of the SF dependence of the SNR conveyed by the retinal/LGN ganglion cells. This work describes the results of such an analysis on several hundred monkey SCs, as well as complex cells (CC), measured by J. Cavanaugh and W. Bair [2] in the Movshon lab. The results quantitatitely demonstrate that ganglion cells and cortical cells in V1 utilize highly redundant codes to represent image data.

As an overview of the central issue, we start with the common assumption SCs represent the coefficients of a wavelet like decomposition of the image. The number of wavelet coefficients as a function of $\log_2(SF)$ scales as the square of the central SF, which is sharply peaked at the Nyquist limit of the image. If the number of SCs at each SF is allocated proportionally to the wavelet density, then one would expect the preferred SF of almost all SCs to be at the highest possible SF. In contrast, the histogram of the $\log_2(SF)$ of SCs and CCs measured at a given eccentricity has a unimodal shape with the peak about 3 octaves below the highest SF. Our analysis shows the reason for the large number of cells at low SF's is to represent the low SF wavelet coefficients at a high SNR level. The source of the high SNR at low SF's is a consquence of the $1/SF^2$ power spectrum of natural images being conveyed, largely unwhitened, by the retinal ganglion cells as a population code.

A brief summary of the analysis follows: (1) The spatial frequencies are renormalized by an estimate of the local Nyquist sampling frequency in the retina at the eccentricity at which the cell was measured. The histograms of the normalized SF's η are largely independent of eccentricity. (2) The histogram $H(\log_2(\eta))$ is modeled as being proportional to the number of SC's per wavelet $N(\eta)$ times the wavelet density η^2 . The number of neurons per wavelet $N(\eta)$ is assumed to be proportional to a model of the SNR based upon a modified $1/\text{SF}^2$ power spectrum of natural images divided by a flat noise power spectrum, which arises from assuming the noise is dominated by statistically independent noise in the ganglion cells.

$$N(\eta) \propto SNR(\eta) \propto \exp(-\beta \eta^2)/(\eta^2 + \eta_0^2)$$

The retinal lowpass filter $\exp(-\beta\eta^2)$, identified with the P cell center receptive fields (RF), drives the power to near zero at the Nyquist limit. The low SF cutoff η_0 is associated with the maximize size of horizontal connections that limit the size of RFs in V1 [2]. Fits of the model histogram $N(\eta)\eta^2$ to the SC data results in $\beta \approx 6$ and $\eta_0 \approx 0.04$. The analysis of complex cell data produces $\beta = 4$ and $\eta_0 = 0.08$. A value of $\beta = 4 - 6$ corresponds to a spatial filter twice the diameter of P cell RF centers, and $\eta_0 = 0.04 - 0.08$ is consistent with the large 3-4mm horizontal connections found in V1. The consistency of the fit parameters with these independent measures helps to validate the analysis. Under the assumption there is one SC per wavelet at the highest SF's leads to ≈ 1000 SCs per wavelet for SF's at the mode of the distribution, a highly redundant population code. Integrating the density gives $\approx 25-50$ SCs and 10 - 25 CCs per retinal input; providing the first quantitative explanation for why there are more than 100 cortical cells per retinal input in V1.

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Natural movie stimuli allow mapping of retinotopy and tonotopy in anesthetized monkey cortex.

A. Bartels, M. Augath, K. Moutoussis, S. Zeki, N. K. Logothetis Max Planck Institute for Biological Cybernetics, Tuebingen, Germany and University College London, UK.

In traditional functional magnetic resonance imaging (fMRI) carefully controlled stimuli are used to reveal cortical regions that are differentially responsive to distinct stimuli. In human fMRI studies we have shown that the varying intensity of features, such as faces or color, seen in a movie, can be used to map feature selective regions, such as the human V4 complex for color or superior temporal regions (STS) and lateral fusiform cortex (FFA) for faces (Bartels & Zeki, 2004). Here we applied the same paradigm in the anesthetized monkey to identify regions involved in processing various low- and highlevel features. The advantage of this approach is that effects of attention or eye-movements can be excluded. In early visual cortex (V1-V3) we found that the BOLD signal was predicted by both, changes in frame-by-frame pixel intensities (luminance changes) as well as by image contrast. These two measures were not correlated with each other in our movie stimulus. Early visual cortex thus seems to code for two independent stimulus dimensions. Responses to each were so specific that we were able to obtain retinotopic maps by correlating voxel-time series with time series of either of these stimulus dimensions as a function of their spatial location in the movie display. In contrast, color and face variations correlated most with BOLD signal changes in V4 and in the STS. In auditory cortex, we were able to obtain tonotopic maps based on the movie soundtrack, by correlating sound intensities at different frequencies with BOLD signal of every voxel. Our results illustrate that, in monkey as in man, movies - even though uncontrolled - allow surprisingly specific mapping of high- as well as low-level features, down to retinotopy and tonotopy.

Movie-based retinotopy :





Figure: Retinotopic maps from BOLD signals obtained during a movie display. A: Section through a monkey brain. Coloured voxels correlated (p<0.001) with luminance changes over time during the movie. B: 'Receptive field maps' of the two voxels at the arrow's origin: colour-coded correlation coefficients of this voxels BOLD signal with luminance changes at every location during the movie. C: Scene-shot (with location grid) and colour map for best-correlating location, used for the angle map on the right.

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Coding and decoding of hand grasping signals in the primate parietal and premotor cortex

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Hand manipulations are crucial for human and non-human primate behavior. Recently, hand grasping signals in the premotor (area F5) and anterior parietal cortex (AIP) have been shown to play a central role for the high-level planning of hand grasping movements. To investigate these neural representations quantitatively, we developed a behavioral control system and recorded single-unit activity while animals performed power and precision grips in various wrist orientations.

The control system consists of a custom-built object with a handle that can be positioned in several orientations by a stepper motor. Sensors on the handle detect if it is grasped with a power grip (as when grasping a hammer) or a precision grip (as when grasping a pin). Two touch sensors in front of the animal define initial left and right hand positions while several LED lights indicate the task instructions. An optical eye tracker (ISCAN) allows monitoring the eye position. Real time LabView is used to control the system and the monkey's behavior online. Animals are trained to perform a delayed grasping task, in which they first place both hands on the resting positions and look at a fixation light. Then, the grasp target (handle) is presented in one of five different, randomly selected orientations and colored LEDs indicate the required type of grasp (power or precision). After a delay period of about one second, the fixation light goes off and the animal is required to grasp and pull the handle in order to be rewarded with a small amount of juice.

Preliminary single-unit recordings in one animal using movable microelectrodes indicate that neural activity in the parietal cortex (AIP) is modulated by the delayed grasping task: A first group of neurons fires specifically for a certain grip type (power vs. precision grip), while a second group shows specificity for wrist orientation, and a third one is modulated by both parameters. One fraction of cells shows this tuning only during motor execution, while the others are activated also during motor planning. These results suggest that neural activity of these areas can be used to decode hand-grasping movements, e.g., as needed to control neural prosthetic devices.

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Spikes are phase locked to the gamma-band of the local field potential oscillations in the primary visual cortex of the macaque

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Oscillations in the local field potential (LFP) are abundant across species and brain regions. The possible role of these oscillations in information processing in the primary visual cortex (V1) of the macaque still remains largely elusive despite that V1 is one of the most extensively studied brain areas. To this end, we used chronically implanted, multiple tetrodes and recorded the spiking activity of single neurons and LFPs from area V1 of the awake, behaving macaque. Moving and static gratings of different orientations were used for visual stimulation.

In agreement with previous reports we find that the increase of the LFP gamma-band power is a function of the orientation of the stimulus. Surprisingly though, there is only a weak correlation between the peak of the multi-unit spiking activity orientation tuning functions and the peak of the orientation tuning function of the gamma-band power of the LFP. There is however a different kind of relationship between spikes and LFP. Namely, the timing of the spikes is not randomly distributed in time but instead is locked to the phase of the gamma-band of the LFP. Specifically, the spikes of 60 out of 151 well-isolated single units showed significant phase locking to the LFP (P<0.05, circular Rayleigh test). On average, the spikes occurred on the downward slope of the LFP oscillation. In contrast to the presence of phase precession reported in the rat hippocampus, the phase tuning in V1 is stable over time. Specifically, the preferred phase of the spikes does not seem to change over time during the presentation of the stimulus. Moreover, the preferred phase is not significantly modulated as a function of the orientation of the stimulus (Figure A).

This temporal structuring of the spiking activity of neurons in V1 could allow coding of information in the temporal regime (Panzeri & Schultz, 2001). In addition it could also potentially synchronize populations of neurons (Fries 2005). We are currently investigating these conjectures.



Figure A. Example of an orientation (lower panel) as well as phase (left panel) tuned neuron. The middle panel shows the joint spike histogram of phase and orientation. There is no apparent relationship between preferred phase and orientation of the stimulus. The right panel shows one oscillation cycle centered on 0 radians.

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Synchrony in Cat Visual Cortex is More Selective for Natural Images than Average Firing Rate

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Our brains process and interpret sensory information in order to generate perceptions of the environment or motivate behavior. However, the underlying mechanisms by which salient stimulus features are represented in neuronal responses remain unresolved. We have previously shown that synchrony between cell pairs can represent co-circular contours, suggesting that synchrony may also be involved in encoding more complex contours. To investigate the relative merits of encoding by firing rate or cooperation within neural assemblies during natural vision, we compared the selectivity of average firing rate and synchrony of cortical cells exposed to a sequence of 4500 natural images. Using a 10x10 microelectrode array, we recorded from 71 complex cells in the primary visual cortex of two paralyzed and anesthetized cats. We randomly identified (without regard to spatial selectivity or RF location of members) 350 neural assemblies, ranging in size from 2 to 8 cells with 50 assemblies per size group. We used the fourth moment (excess kurtosis) of the response distribution as a measure of selectivity for each assembly. Response distributions with a large kurtosis are more selective in that they have a high probability of a weak response and a low probability of a strong response for any single image in the sequence. Therefore, an assembly whose response distribution is highly leptokurtic (excess kurtosis > 0) will respond strongly to only a few images in the sequence and is thus more selective. We measured the synchrony and average firing rate response distributions for each assembly over the set of images and found that all distributions were leptokurtic, but synchrony response distributions were highly leptokurtic and kurtosis increased nearly exponentially with assembly size. On the other hand, the kurtosis for average firing rate response distributions staved relatively constant across assemblies of different size. Synchrony was 3.9 times more selective than average firing rate for pairs of cells and 302.4 times more selective for assemblies of 8 cells. These results suggest that synchronous activity among neural assemblies is more selective than average firing rate in the context of natural images. Increasing assembly size enhances the ability of synchronous coding to discriminate, but there is no information gain for average firing rate when additional cells are considered. We propose that higher-order features found in natural images (e.g. complex contours) are responsible for the high selectivity of synchrony compared to average firing rate because adequate descriptions of high-order spatial correlations require the coordinated response of multiple cells. This process is cumulative, in that more complex structures require larger neural assemblies for accurate description. [Supported by NIH: RO1 EY014680-03]



<u>Figure 1</u>. The kurtosis (selectivity) of synchrony response distributions (a) increases nearly exponentially with assembly size, but (b) remains constant for firing rate distributions. (c) Example where the receptive fields for a given assembly (N = 4) lie along a complex contour in the image with the best synchrony response, but (d) follow no particular structure in the image with the best average firing rate response (which may be dominated by the response of one or two cells).

How does joint activity across a population of neurons influence the precision of coding in the cortex?

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The rat vibrissa (whisker) pathway has a high capacity for the transmission and processing of textural information. Until now, most studies have only considered how single neurons in the primary somatosensory cortex (SI) of the rat encode vibrissa information. In contrast, even the motion of a single vibrissa is represented by thousands of neurons at the input layer to the cortex (layer 4). Population activity is therefore expected to play an important role in the coding of vibrissa information. It has been shown previously that cortical neurons exhibit response suppression for stimuli with frequencies greater than approximately 4-8Hz. Since the effect of suppression is to lower both the magnitude and precision of the response, it is believed that weaker responses generally degrade the quality of coding by the cortex. Furthermore, mechanisms that confer response precision on single neurons have been identified. What has not been addressed is how joint activity between multiple neurons affects coding accuracy and precision. In this study we ask whether, and how, the precision of single neuron responses, observed over multiple trials, extends to precision across multiple neurons observed in a single trial. Specifically, we studied how the precision of joint coding changed with modulations in single-cell response precision and magnitude. Preliminary data suggest that the temporal precision of coding may be improved through joint observation of multiple cells. For simultaneously recorded pairs of neurons, time-locking of post-stimulus responses to each other within a single trial was on average larger than that due to the common stimulus across trials. There is evidence that this extra degree of time-locking is present for a wide range of single-cell response precision and magnitude. The observed correlations between groups of neurons are likely reflective of a common input process, presumably from the thalamic VPM nucleus. Both experimental and modeling studies of the functional properties of this shared source of noise promise to yield a more comprehensive picture of coding in the SI. Our previous work has shown that discrimination performance improves with increasing response precision of single neurons. It is therefore expected that temporally precise firings across multiple neurons can significantly lower discrimination error, and thus improve coding in SI.

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DISTRIBUTED CODING IN RETINAL GANGLION CELL POPULATIONS

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We studied the concerted firing patterns of neuronal populations in the vertebrate retina. Participating ganglion cell ensembles were identified and classified, revealing a general distributed coding scheme of the retinal output. Neuronal responses of retinal ganglion cell populations were recorded using the Utah cortical multi-electrode array. The resulting response pattern were sorted into "classical" units and classified according to the temporal course of the individual response.



figure: population member identification

Using a Markov-chain like approach existing firing patterns were extracted, identified and further analyzed to identify performance limits of the identified distributed code.

Based on this approach we are able to identify a possible general distributed coding scheme for a selected set of visual stimuli. The combinatorial firing pattern can be decomposed into sub-ensembles distributing to the code. Sub-ensembles are composed of a temporal firing sequence of a discrete number of of up to 10 neuronal units.

The distributed coding scheme observed inside the retinal ganglion cell populations recorded, gives further evidence that their target neurons in primary visual cortex could act as coincidence detectors. Using a classification scheme based on the temporal response time course of each identified neuronal unit, a general distributed coding scheme in the vertebrate retina could be approximated

Independent Component Analysis of 'real' music reveals brain modes selective for parsing event boundaries

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Introduction. Event segmentation is crucial to understanding incoming streams of information, allowing for the extraction of relevant features as well as meaningful structure. In music, perceptual event boundaries comprise a variety of hierarchical levels and types ranging from fine-grained note-boundaries to coarse-grained phrases and movements. We investigated the neural dynamics of event segmentation for movement transitions using functional neuroimaging (fMRI) and a model-free analysis method.

Methods. Subjects with minimal musical training were scanned at 3T while listening passively to live recordings of classical music. Excerpts from the symphonies of William Boyce (an English baroque composer of the 18th century) were chosen as stimuli because the musical structure in these symphonies contains a number of easily-identifiable transitions. We performed model-free independent component analysis (ICA) of the fMRI data using MELODIC (www.fmrib.ox.ac.uk/fsl/). A heuristic clustering algorithm was employed to identify independent components (ICs) that corresponded across subjects. Spatial ICs in the resulting clusters were entered into a second level random effects analysis to reveal activations common to all subjects. Time-courses of the ICs in each cluster were averaged, linearly detrended and Wiener-filtered to deconvolve the hemodynamic response from the BOLD signal.

Results. ICA generated two non-overlapping spatial modes that showed marked activity at the event boundaries (see figure). These could be clearly distinguished as (1) a bilateral "inferior frontal-cortical"-"posterior temporal" (iFC-pT) mode, and (2) a bilateral "dorso-lateral prefrontal"-"posterior parietal" (dLPFC-pP) mode. Granger causality analysis revealed a causal relationship between the iFC-pT mode and the dLPFC-pP mode (iFC-pT causes dLPFC-pP). Earlier activation of the iFC-pT mode may indicate its involvement in detecting fundamental features of the stimulus, such as perceiving event boundaries; the dLPFC-pP mode, activated later, may be associated with generating abstract representations of the event in working memory.

Conclusion. We conclude that event segmentation of 'real music', an ecologically relevant stimulus, activates a network of brain regions that have meaningful temporal dynamics. To our knowledge, this is the first study to examine event segmentation in 'real' music. Our systems-level approach provides insight into the spatial and temporal dynamics of neural populations involved in the processing of musical event boundaries.

Figure. (Top) Spatial modes. iFC-pT (blue), dLPFC-pP (red). It is apparent that the two spatial modes are non-overlapping. (Bottom) Timecourse of iFC-pT mode (red), event markers for movement transitions (black). It can be seen that the activations faithfully track the event boundaries.





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Analysis of movement direction estimation from motor cortices using simple models

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How well can movement direction be extracted from neuronal activity in motor cortex? We have studied the accuracy of direction estimates from single-trial activities of single units recorded in motor cortex of monkeys performing a center-out task. We have compared three linear models: the Population Vector, Optimal Linear Estimator, and the Cosine OLE – a novel linear estimator which uses the parameters of cosine tuning for the correlation matrices. In our data set the CosOLE outperforms the other linear estimators. We have also examined the degree of improvement gained by using temporally resolved responses as opposed to a simple rate code.

To gain insight into the distributed coding of movement direction in motor cortex, we used our database to construct a statistical model that captures the enormous heterogeneity of response properties observed in cortical neurons. This model accounts for the correlations between various features of the responses, such as mean firing rates, direction selectivity and R^2 values, and will allow a computational study of coding of movement direction in large populations.

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Representational systems

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Representation can be thought of as the embodying of the knowledge (or experience) a system acquires in its activity. If instances of activity are taken as points, one can ask what is the correspondence between the structure of ensuing set of instances, which we refer to as activity space, and the knowledge embodied within the system. Specifically, we hypothesize that the intrinsic properties of a set, mainly its topological structure determines its representational capacity, that is its utility as a vessel of embodying knowledge, .

We present a framework, in which multi-detector measurements of nervous activity, for example, Voltage sensitive dye imaging (VSDI) data can be analyzed. First, data undergoes a standardization, which registers the structure of activity. This is a transformation which registers (spatiotemporal) regions of excitation and inhibition in a given instance of activity.

Next, we proceed to compare ongoing activity data sets obtained from disparate states of vigilance. The reason for this is twofold : 1.) First, at least some states can be thought of embodying more or less content (for example sleep vs. wakefulness), thus we expect the associated activity spaces to differ in their representational capacity 2.) Secondly, as EEG recordings are typical given a state, we posit that the same is true for the underlying distribution of voltage – namely that structure is an invariant of state. Thus, one can utilize structure sensitive functions, that is, functions which classify activity according to state, to help overcome the gross under-sampling of the high dimensional activity spaces imposed by practical constraints, and derive feasible measures in which the structure of these spaces can be probed.

To achieve this, a neighborhood of a data set is taken within some confidence limit ("fattening the data"). Now, one can proceed and obtain the explicit level set of a structure sensitive function of the average (or median) value associated with a state. This allows for the explicit calculation of the Betti numbers associated with the set which are a numeric representation of the homology of the level set (the homology of a set is a topological invariant which measures the "holes" of all dimensions existing in a set. Homology can be considered as a grossly grained measurement of a structure of a set). We present some preliminary results of VSDI data obtained from the primary visual cortex of primates.

Reference frames of visual and vestibular signals in area MSTd: comparison of neural data with model simulations

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The integration of visual and non-visual cues is critical for accurate spatial perception and motor planning. Convergence of signals from different sensory modalities is well documented in several cortical and subcortical areas, but it remains unclear exactly how populations of neurons represent and combine multiple inputs. One important problem concerns the reference frames in which spatial information is encoded in the brain. Visual signals originate in an eye-centered reference frame, while non-visual signals (e.g., auditory or vestibular) are initially encoded in a head-centered frame. Because the eyes can move freely in the head, these two coding schemes are seemingly incompatible, presenting a major obstacle for multisensory integration.

A straightforward solution to this problem might be to represent spatial information in a single, cueinvariant frame of reference. We tested this hypothesis for visual and vestibular signals in extrastriate area MSTd, a region that contains neurons selective for the direction of self-motion (heading) defined either by optic flow or by actual inertial motion. We measured the tuning of single MSTd neurons for heading based on visual and/or vestibular cues, and we varied eye position to determine whether signals were coded in an eye-centered, head-centered, or intermediate frame. Contrary to the hypothesis, the two modalities did not share a common reference frame: tuning for visual cues was found to be predominantly eye-centered, whereas vestibular signals were coded in an intermediate reference frame that was closer to head-centered.

A similar pattern of results has been observed for other areas and modalities, including the superior colliculus (visual and auditory) and intraparietal sulcus (visual, auditory, and tactile). The emerging trend is that the primate brain does not employ a general strategy of representing multiple signals in a common reference frame. Instead, neural populations typically include a continuum of reference frames ranging from eye-centered to head-centered, with a substantial portion of cells showing intermediate frames (e.g., partially shifting receptive fields). In many cases, including our MSTd results, the reference frames of visual and non-visual signals are poorly matched for individual neurons. This property results in a misalignment of spatial tuning for the two modalities, at least for some positions of the eyes in the orbits.

Recently, a family of neural network models has been used to explain these counterintuitive and somewhat puzzling results (Deneve, Latham, and Pouget, *Nat. Neurosci.* 4: 826-31, 2001; Avillac et al., *Nat. Neurosci.* 8: 941-9, 2005). These networks utilize a recurrent framework in which the hidden units combine multiple signals by computing basis functions over the inputs. When trained to produce accurate output in either a head- or eye-centered frame, the hidden units are found to encode stimulus location in a variety of reference frames that are not typically matched for the two cues. In fact, it is suggested that a distributed representation including intermediate reference frames is useful for performing the coordinate transformations required to read out spatial information in any desired frame of reference. We adapted this framework to the case of visual and vestibular signals in MSTd, and found that the model performs well in spite of the observed discrepancy in reference frames. Our findings support the hypothesis that MSTd and other multisensory areas may act as recurrent basis function networks that can compute accurate spatial estimates in the absence of a common reference frame for the two modalities.

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The neural correlates of path perception and steering investigated using fMRI

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Representing direction of self-motion is a key task for the visual system, and other sensory modalities. One of the main visual cues to direction of self motion comes from optic flow, which usually arises from the ground plane across which the animal travels. In macagues, the ventral intraparietal area (VIP) contains flow sensitive neurons that are tuned for heading direction (Bremmer et al., 2002). Initially, we confirmed the similar function of the human VIP homologue in a task where participants made a continuous path judgment while viewing a display simulating sinusoidal locomotion over a ground-plane. The display for this task was like fig 1, but with no visible road edges. We then examined the neural correlates of self-motion in two important new situations. Firstly, we investigate the neural correlates of a cue providing information about future direction of self motion in addition to the current (or instantaneous) information that is available from ground-plane optic flow. We added two visible road edges onto the ground-plane allowing the observer to perceive, for example, that they are currently on a path curving to the right, and that in approximately two seconds time they will be curving to the left provided they stay on the road (see fig 1). This information about future direction of motion is not available from ground-plane flow, but in most ecological settings such information is available. Relative to ground plane flow alone, the road produced a bilateral parietal activation focused on, but more extensive than, the (separately localised) lateral intraparietal area LIP. The LIP contains a topographic map of the salience of objects in the visual field, which is used in the selection of targets for saccades. Other cortical eve fields were not selectively activated by the roadway. We repeated the experiment with fixation in all conditions, producing the same result, thereby ruling out the possibility that differences in explicit eye movements produced the observed activations in and around the LIP region. As a control for activation due to low level features of the road, we produced the stimulus shown in fig 3. The undulating visual motion of the "horizontal road" was not related to path, but matched the road in fig 1 for low-level features. The "horizontal road" activation was comparable to that for ground plane only.



A second aspect of self-motion perception in ecological settings is that perception is not generally divorced from action. Perception of self-motion is normally part of a closed loop control system. To introduce closed-loop control we allowed participants to steer their own course down the sinusoidal road (fig 1 with path judgement was now the baseline). Steering was not perfect and produced a time-varying error signal between current path and desired path, such as that shown in fig 2. We matched the error signal in a control condition where the computer controlled sinusoidal path travelled was out of phase with the road, and participants made path judgements. The anterior portion of the road related parietal activation was considerably more active when an error signal was present, whether due to participant steering or added by the computer during the path judgement task. Further activations for participant steering that were not driven by the error signal were bilateral cerebellum, left dominant dorsal premotor cortex, and supplementary eye fields (SEF) / supplementary motor area (SMA). These areas may be involved in the forward and inverse models necessary to map the steering device we used onto the simulated environment.

The role of ongoing neural activity in the primary visual cortex of the awake ferret.

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There is a discrepancy between the generally accepted role of ongoing activity during visual development, where spontaneous firing is viewed as an important guiding activity indispensable for proper emergence of the visual structure, and during visual perception, where spontaneous neural activity is considered to be unwanted noise. This discrepancy stems from the presently dominant view of cortical information processing, based on anesthetized recordings, which posits that visual information is analyzed in a feedforward signal-processing manner where ongoing activity is accidental and can be neglected.

To study this discrepancy, we analyzed multi-electrode recordings in the primary visual cortex of awake behaving ferrets (N=20) at postnatal day (P) 24-26, P44-45, P71-90 and P131-168. Multi-unit recordings were obtained in three different conditions: in the dark, when the animals watched random noise sequences, and when they saw a natural movie. At all ages there was a significant spatio-temporal structure in the observed neural activity and this structure showed a distinctively evolving pattern across ages. As a consequence, the characteristics of the spatial and temporal statistics of the firing shifted with age and even in the adult animals they were more related to each other across different conditions at a given age than to the statistics of the input. The high spatial correlations across different recording sites during the dark condition ruled out the possibility of averaging out the "noise" correlations and thus questioning the validity of feedforward signal processing models.

An alternative model is based on a generative Bayesian framework where ongoing activity represents momentary perceptual biases of the brain based on previously obtained information and internal states. To test the validity of this framework, the same data was analyzed using a Hidden Markov Model. We found clearly distinct internal states in all conditions defined by approximately stationary firing rates and abrupt transitions between states. The identified HMMs were specific to particular conditions classifying untrained neural activity correctly about 90% of the times. These findings suggest that even in the primary visual cortex neural processing can be best described as a rapid dynamic transition between a large number of states, where the external input modulates the intrinsic dynamics by selectively boosting particular states.

Dynamics of context-specific movement goal representations in posterior parietal cortex of monkeys

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The posterior parietal cortex plays a key role in performing sensorimotor transformations. The parietal reach region (PRR) in the medial intraparietal cortex specifically is involved in visuospatial planning of arm reaches. How do the relative contributions of visual sensory processing and movement planning develop during the preparation of a visually instructed reach movement, i.e., what are the neural dynamics of the visuomotor transformations in PRR?

To dissociate visual sensory from motor-related neural activity monkeys performed a visually cued, memory-guided anti-reach task. Monkeys either had to reach to a memorized peripheral target position (PRO-reach) or to a diametrically opposed position (ANTI) while keeping central ocular fixation. We recorded single unit spiking activity and local field potentials (LFP). We used time-resolved single-channel tuning analysis and population decoding analysis to quantify the dynamics of sensory-to-motor transformations in PRR.

The spatial tuning of PRR spiking activity and LFP mainly depended on the position of the reach goal, and little on the instructing cue. This was true not only late in the memory period, shortly before the movement initiation, but, more remarkably, with short latency after the cue presentation at the beginning of the memory period. Only during the short period of cue visibility a subset of PRR neurons (approx. 10%) encoded sensory information on the cue position. Consequently, during the cue period it was possible to decode the position of the cue based on the short-term spike rates of all recorded single units. It was not possible to decode the cue position based on the LFP signals in any frequency band. This is mostly likely due to the small fraction of PRR neurons that is tuned for the visual cue during the cue period, combined with the fact that in LFP the activity of a large number of neurons is superposed. From the beginning of the memory period both, the spike and the LFP data represented the position of the reach goal. The spatial tuning in the LFP power was restricted to frequencies above ~15Hz; lower frequency LFPs were not spatially selective.

The neural representation of the reach goal in PRR evolves later in the ANTIthan in the PRO-condition. The neural delay corresponds well to reaction times being increased by 40-50ms in the ANTI- as compared to the PRO-reaches, when the monkeys performed a reaction-time task instead of a memory task. This kind of reaction time differences is well known from other experiments with variable stimulus-response compatibility (Simon effect).

Our findings support the hypothesis that PRR immediately translates current sensory information into reach movement plans even in the memory task, rather than storing the memorized cue location. The results also show that PRR represents integrated knowledge on spatial sensory information combined with abstract behavioral rules (PRO/ANTI) to represent the desired movement goal independent of the instruction stimulus, and that this integration process takes longer in case of anti-reaches, maybe due to the necessity of calculating an inversion vector.

FMRI of V1 microarchitecture in the macaque at 4.7T

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For fMRI to be able to provide insight in the cortical circuitry, the spatial resolution and specificity of the fMRI signal need to be sufficient to visualize the microarchitecture of the cortex at the laminar and columnar level. The current spatial resolution of the fMRI signal however is too coarse to be able to reliably visualize the cortical microarchitecture. Cortical columns of ~1 mm have been observed with fMRI, but achieving higher (submillimeter) resolution is problematic, because the specificity of the activation is determined by the hemodynamic properties of the vascular bed. The conventional Gradient-Echo (GE) sequence used for BOLD-fMRI is sensitive to signal from veins and venules, and is strongest at the cortical surface, where draining vessels are located. This has limited the spatial specificity of the conventional fMRI signal to about 1 mm. By using the Spin-Echo (SE) fMRI signal instead, which is more sensitive to the capillary fraction, and less sensitive to veins, the specificity of the fMRI signal can be enhanced. Sequence optimization allowed us to further increase spatial specificity, and to achieve submillimeter spatial resolution. This resolution allows visualization of the cortical laminae, as shown in V1 in the anesthetized macaque (figure). The SE-BOLD signal was localized to layer IV/Duvernoy layer 3, with little activation in the upper cortical layers. The spatial resolution and specificity shown here allows determination of differences in laminar profiles depending on visual input. When motion and flicker stimuli were compared, the unequal laminar distribution of motion-direction selective laminae could be clearly discerned. Our results indicate that the point spread function for SE-fMRI is 0.5 mm or less, and is sufficient to observe differences in functional activation at laminar resolution.



Upper panel: Percent change map of the SE fMRI activation in V1, at a resolution of $333x326 \mu m$. The 2 mm slice was positioned perpendicular to the cortex, to minimize partial volume effects. The stimulus was a full field rotating checkerboard.

Lower panel: High resolution anatomical image of the same slice as above. Spatial resolution $250x250 \ \mu m$, 2 mm slice thickness. The white matter and Gennari-line can be clearly distinguished, and functional activation coincides with the Gennari-line (compare upper panel).

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Adaptation changes the structure of correlations in primary visual cortex

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It is believed that the visual system has evolved to code natural stimuli efficiently. It has been proposed that visual adaptation reduces neural redundancy to increase the effective dynamic range of neurons. Although it is known that adaptation changes the selectivity and preferred orientation of cells in visual cortex the effects on correlation structure has not been explored yet. We studied the correlation between pair of neurons in macaque visual cortex before and after brief adaptation to an oriented bar. The stimulus comprised oriented bars of random orientations presented at 60 Hz. The adaptation block was preceded by a 400 ms oriented bar of fixed orientation. We found that adaptation reduces correlations depending on the relationship of the preferred orientation of each pair of cells and the orientation of the adapting stimulus. The consequences for neural coding were explored by computing the Fisher Information of the correlation structure before and after adaptation. Populations of cells were able to better code orientation for stimulus around the adapting stimulus and for orientations orthogonal to it. In this way, we found that adaptation improves neural coding consistently with psychophysical performance.

Stereotyped activity flow in auditory neocortical microcircuits

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Information is processed in the cortex by the parallel action of large numbers of neurons. To study the structure of ensemble activity during sensory stimulation, we recorded auditory cortical populations (40-100 cells) while presenting simple stimuli (tones, noise, and clicks) in a passive listening paradigm. We observed a diversity of stimulus tuning and temporal response profiles, even amongst neurons recorded on a single electrode. Neural firing rates varied substantially with stimuli; however, differences between the temporal structures of responses evoked by multiple stimuli in a single neuron were small, compared to differences between the temporal structures of multiple cells to a single stimulus.

At the population level, diverse yet reliable onset latencies revealed a stereotyped spread of activation through the recorded population. This activation sequence was similar across stimuli, and also for spontaneously occurring patterns associated with the start of cortical UP states. To investigate the consequences of this temporal structure for stimulus coding, we performed a population vector analysis. Population codes evolved with time, characterized by increasing sparseness and orthogonalization during the first few hundred milliseconds of stimulus presentation. We hypothesize that our observations may reflect the interplay of recurrent network activity and diverse cellular physiologies.

Information flow through task-related sensory and motor circuits as rats perform a sensory-guided decision-making task

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Rats are thought to exhibit executive functioning on a par with primates when tested with olfactory-driven tasks (Slotnick & Schellinck, 2002; Schoenbaum & Setlow, 2001). Olfactory cortex is thought to be the most ancient vertebrate cortex, and its connections with motor cortex and midbrain motor nuclei constitute an ancient sensorimotor interface (Lacalli, 2001; Aboitiz et al., 2003). We therefore have been using rat neural circuitry and behavior as a simplified model (relative to primates) to study large-scale information across sensory, multiple prefrontal, and motor areas during decision making and other executive tasks. Here, using simultaneous recordings of multi-single units and local field potentials, we explored the flow of information between the output layers of the posterior piriform cortex, the forelimb motor cortex, and a midbrain motor site, the magnocellular red nucleus, as rats performed a well-learned, olfactory driven GO/NO-GO task. We employed an analysis technique, partial directed coherence, to the local field potential data to determine whether activity in any area preceded or lagged behind activity in any other area during the task. Strikingly, on 100% of analyzed trials, activity in the piriform and motor cortices preceded that in the red nucleus at all frequencies between 0 and 100 Hz. In contrast, on 40% of analyzed trials, activity in the motor cortex preceded that in the piriform cortex at the onset of target sniffing, an asymmetry that was rapidly followed by classical coherence between the two areas in the low gamma (30-50 Hz) range. During target sniffing on GO trials, a large subpopulation of neurons exhibited a markedly reduced, though transient (<100 ms) firing rate, and the presence of this inhibition strongly predicted trial outcome. We are currently analyzing the spike data to determine whether the relative latencies to inhibition in each area support the hypothesis that sniffingrelated motor activity initially drives olfactory processing. This overall set of analyses is important because few studies have addressed the temporal and frequency-domain relationships across large-scale neural circuitry during awake behavior.

Large-scale coordination mechanisms coupling sensory and motor areas prior to skilled movement

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Despite the existence of electrophysiological techniques for recording from multiple brain areas simultaneously in awake animals, relatively little is known about the nature of the transient coordination between olfactory and motor processing areas during distinct phases of olfactomotor tasks. The aim of our study was to identify the mechanism(s) of coordination among neurons in the output layers of posterior piriform cortex, the forelimb motor cortex, and the midbrain red nucleus during performance of an olfactory-guided, GO/NO-GO reaching task. Recording multi-single units and local field potentials in all three areas, we found highly significant, transient, temporally overlapping (i) inhibition of spike firing rate and (ii) membrane hyperpolarization during odor sampling on GO trials with the real food pellet that was not observed on NO-GO trials with chemically inert, visually identical non-food pellets. Moreover, by examining timefrequency-decomposed local field potentials, we found that during odor sampling on GO trials, a transient increase in high-gamma energy occurred, whereas lowgamma energy was present during odor sampling on both GO and NO-GO trials. All three of the above observed phenomena occurred within half a theta cycle. In concert with studies demonstrating the major role played by the dynamics of inhibitory networks in sculpting neural activity, these findings suggest that the cooccurrence of transient spike rate inhibition, membrane hyperpolarization, and high-gamma oscillations, are part of the mechanism coupling disparate sensory, motivational and motor circuits prior to task execution.

Correlated neuronal activity in Primary and Pre motor cortices of monkeys during performance of different visuomotor association tasks

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It had been shown that patterns of neuronal activity in motor cortices and tuning curves may change during sensorimotor learning (Mitz et al, 1991, Wise et al, 1998, Gandolfo et al, 2000, Paz et al, 2003, and Paz et al 2005). In this study, we examined co-variation of response patterns and temporal cross-correlation to study dynamics of interactions between cells during performance and adaptation to different visuomotor tasks.

Neuronal activity from monkeys' motor cortices was recorded in each session by a multi-microelectrodes array. Each recording session was comprised of the following blocks of trials: 1. *Standard* 8-direction center-out task (a well known task); 2. Adaptation to *visumotor-rotation* (two directions with the same rotation); 3. Adaptation to *arbitrary-association* (two colors associated with two different movement directions). The session ended with repetition of the standard center-out task.

The poster presents patterns of correlation found in these different behavioral states. We demonstrate that correlation patterns between neighboring cells and even distant cells in M1 and Premotor cortices may change in relation to behavior. In particular, pairs of cells with correlated firing patterns during performance of standard task, tend to exhibit different correlation strength or pattern during adaptation.

These results suggest that the cortical network can reorganize during performance of non-standard visoumotor associations to generate correct behavior.

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Coherent neural representation of hand speed in Humans

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Electrophysiological studies of motor control in non-human primates demonstrate correlations between neural discharge in primary motor cortex (MI) and various limb movement parameters including hand velocity^{1,2}. Increasing evidence points towards a distributed encoding of velocity in multiple cortical areas³⁻⁵. In Humans, brain regions involved in speed control can be detected with functional imaging⁶, however, the underlying dynamic neural mechanisms are still poorly understood and their investigation requires millisecond temporal resolution. We used whole-head magnetoencephalography (MEG) and recent imaging solutions⁷ to investigate the putative relationship between ongoing neural activity and time-varying hand speed during continuous visuomotor control in Humans.

We recorded neuromagnetic signals from 15 subjects while they continuously manipulated a track-ball to counter the unpredictable movements of a cube rotating about its center. The visuomotor control task (VM) was alternated with a rest condition (R). The neural activity underlying the data recorded during epochs of VM and R was obtained from the corresponding single-trial MEG source image sequences. The presence of task-related coupling between ongoing brain activity and hand speed was then investigated by evaluating the phase-locking⁸ between the activity at each of approximately 12000 elementary brain location and the subjects' instantaneous hand speed.

Our results demonstrate the presence of significant low-frequency phase-locking between human MI and hand speed during visuomotor control. Furthermore, we also found significant coherence between MI and multiple cortical and subcortical brain regions. The large-scale brain network included: the contralateral dorsal premotor, primary somatosensory, inferior parietal, bilateral secondary motor, superior parietal lobule, left dorsolateral prefrontal cortex, right ventral and orbital prefrontal cortices, ipsilateral anterior cerebellum and subcortical areas including the thalamus. The detection of these areas via their interaction with MI within the frequency range of MI-hand speed coupling suggests that these areas are part of a spatially distributed functional network involved in mediating low-level parameters of motor behavior.

The present MEG source imaging study reveals a direct coupling between neural activity and timevarying hand speed and suggests a possible role for coherent oscillations in mediating spatially distributed neural representations of limb kinematics. Such non-invasive studies of movement-related ongoing neural activity in Humans might have important implications for the investigation of motor encoding within largescale neural networks and thereby the development of new strategies in neural prosthetic devices⁹.

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Integration of sensory information in auditory cortex

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Traditionally it is assumed that information from different senses is integrated only in higher association cortices. Contrasting this belief, we demonstrate multisensory integration in areas proximal to primary sensory areas - in the so called auditory belt.

Using a combination of high-resolution functional magnetic resonance imaging (fMRI) in electrophysiological recordings in macaque monkeys, we quantify the integration of audio-visual and audio-tactile stimulation. Integration of auditory noise with tactile stimulation of the hand is reliably found in anaesthetized animals at the posterior end and along the lateral side of the auditory belt. This integration occurs only for temporally coincident stimuli and obeys the principle of inverse effectiveness: integration is stronger for less effective stimuli. Locations with significant integration responded to auditory alone stimulation but only few to tactile alone. Combining visual and auditory stimulation, robust multisensory integration in auditory cortex was found in alert animals, but only weaker in anaesthetized animals. Similar to audio-tactile integration, the audio-visual interaction was found in areas of the belt. Together our results suggest that touch and vision related activity in auditory cortex arise from a different set of projections. Touch related information arrives as feed-forward input, vision related input arrives in a top-down fashion.

Our findings demonstrate that multisensory integration can occur early in the processing hierarchy - one processing stage above primary auditory cortex. Further, this multisensory integration occurs pre-attentive, as demonstrated in anaesthetized animals. Such early integration might be necessary for quick and consistent interpretation of our world and might explain multisensory illusions where a stimulus perceived by one modality is altered by a stimulus in another modality.



Legend: A) fMRI based delineation of primary auditory cortex (core regions, red color) and regions showing integration of auditory and tactile signals (blue). B) Section through auditory cortex, parallel to the lateral sulcus. The dashed lines delineate core and belt regions. C) Functional organization of auditory cortex. Auditory input from the thalamus comes to A1 and R and from there to higher auditory areas. Integration of auditory and tactile signals occurred mostly in areas CM and CL.

Perceptual Suppression in area V1 of the Macaque

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Under certain stimulus conditions we encounter pronounced perceptual suppression of suprathreshold visual stimuli. The brain mechanisms underlying these phenomena are poorly understood. Binocular rivalry (BR) and Binocular Flash Suppression (BFS) provide us excellent behavioural tools to study this phenomenon. During these paradigms visual stimuli are completely extinguished from our awareness for a substantial amount of time despite being physically present on our retinas. Therefore, we can study the dissociation between the neural responses that underlie a mere sensory representation of the visual input and what is perceived. Primary visual cortex (V1) has been implicated as an important candidate for the site of perceptual suppression. However, interestingly electrophysiological studies in V1 have found only a very small percentage of neurons to be correlated with the percept^[1]. In contrast, human fMRI studies^[2,3] have shown that the BOLD signal during such perceptual alternations modulates almost as much as when the stimuli are non-ambiguously presented separately. These contradicting results led to the speculation that the local field potential (LFP) signals, which have been shown to correlate with the BOLD signal, will also show correlations with perception in agreement with the BOLD results and thus potentially solve the apparent controversy. To this end, a recent study^[4] claimed that low frequency (<30Hz) LFP signals in V1 correlate well with the subjective experience of macaques during BR.

We have used BFS and recorded neural activity from large populations of well-isolated single neurons (SUA) from V1 using chronically implanted and non-chronic tetrodes in awake behaving macaques. In addition to the SUA we also simultaneously recorded multi-unit (MUA) and LFP signals. In agreement with previous electrophysiology experiments we find a very small percentage of single neurons (12%, t-test: p<0.05) as well as MUA sites (15%) to be correlated with the animals¹ percept during the binocular presentation of two gratings of orthogonal orientations. Interestingly, an even smaller percentage (7%) of gamma-band LFP sites show a significant modulation and no other LFP band (e.g. alfa or beta-bands) showed stronger perceptually related modulation. In addition, the amplitude of the normalized population response in all three signals shows a small fractional modulation in comparison with the monocular presentation of the gratings (see figure). We therefore conclude that the activity in V1 is not a good predictor of the perceptual alternations at least using the classical simple measures of firing rate and power modulations of the signals.



Figure 1: Normalized population response for SUA (A,B), MUA (C,D) and gamma-LFP (E,F). Average for all significantly tuned horizontal sites is depicted in the first column (A,C,E) and vertical in the second column (B.D.F). Light grey refers to the case vertical was perceived during the binocular presentation (starting from monocular horizontal) and dark grey when horizontal was perceived **References:** [1] Leopold DA, Logothetis NK. Nature. 1996 Feb 8:379(6565):549-53. [2] Tong F, Engel SA. Nature. 2001 May 10;411(6834):195-9. [3] Polonsky A, Blake R, Braun J, Heeger DJ. Nat. Neurosci. 2000

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Robust Time-Relationships between Sharp Waves, Ripples, and Single Units firing in Rat Ventral Hippocampal Slices

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Ventral hippocampal slices taken from adult rats and perfused in normal medium display synchronous activity resembling in vivo sharp waves (SPW). Recorded extracellularly in CA1 area stratum pyramidale, SPW are mostly positive field potentials crowned by ripples (~100-300) and multi-unit activity (Papatheodoropoulos and Kostopoulos 2002). Their main generators are IPSPs or EPSP-IPSP sequences, which appear to depend on a variety of neurotransmitter systems and synchronization mechanisms. In pursue of understanding these mechanisms, we have studied the shortand long-term correlations between SPW, ripples and several carefully identified units. Custom-made software was developed to discriminate different neuronal single-unit responses and to mark the peaks of SPW and ripples. Some individual neurons tended to fire exclusively (16/90) or preferentially (3/90) during the rising phase of the SPW. Others during its top (2/90 and 1/90) and others during both (14/90 and 13/90). One neuron fired during the falling phase of SPW. 37/90 showed no preference and 4/90 fired exclusively at the intervals of SPW. Ripples appeared larger and most often during SW but some of them were observed in between SPW as well. All units fired preferentially at the negative peaks of ripples and almost none of them during a ripple positive peak. The time relationships between SPW, ripples and single units varied in the different slices but remained remarkably robust in a given recording. It seems likely that ripples represent population events directly related to neuronal excitation. SPW coincide with strengthening and substantial clustering in time of ripples, the casual relationship between the two being still elusive.

Seamless encoding and decoding of forward and inverse motor commands by dynamically interacting neural populations

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A distributed coding scheme developed in the last decade provides for sensory-motor integration and stochastic estimation [1,2,3]. Furthermore, it involves neural processing whose principles and features are highly compatible with key results in experimental neurophysiology. Suggesting a population-level representation, this biologically-inspired class of computations is sufficient to perform the sensory-motor transformations required in skilled control of limb movement. The neural assembly is robust to the stochastic nature of external signal encoding. Its attractor dynamics has been demonstrated to allow rapid output convergence to the unbiased and efficient functions of the input signals.

Here we extend this paradigm to encoding and predicting time-varying signals. We define an extended neural module which performs sensory-motor integration of a set of three signals either one of which can be the output of the computation. We demonstrate a plausible way for the brain to eliminate the need to build and maintain separate forward and inverse models [4]. Finally, an architecture composed of encapsulated standard modules implements the sliding (composite) variable approach [5] to the control of muscles in a planar biomechanical model of the arm in the presence of external dynamic perturbations.

The central nervous system (CNS) cannot provide continuous control signal updates, if only since neural transmission happens at rather finite velocity, limited by inherent neurophysiological factors such as axonal conduction times and synaptic delays. Hence, the simulated model functions essentially in discrete time with controls that are formed by two pathways: A feed-forward component implements the internal model of the limb, which provides for skilled performance especially in the presence of learned external dynamics. A delayed sensory feedback pathway reacts to significant errors of the composite variable by ballistic-like corrections as suggested in [5].

Fast convergence of the model's internal dynamics is essential to match the constantly changing external context. We discuss the transient dynamics and stability properties of the assembly. Although the network never reaches asymptotic steady states, a 'contracting' [6] reduction of the effect of perturbations over time is very desirable, providing exponential convergence rates. The proposed computational organisation has Kalman-filter-like properties, offering a modular representation of the relevant environment.

Future work may include to incorporate adaptive internal model formation, and could also serve as a backbone to reinforcement learning with policy switching in the presence of multiple environment conditions (viz. catch trials).

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Modeling the Ongoing Cortical Dynamics Inherent in the Local Field Potential

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We modeled the dynamics of the spontaneous (ongoing) network states in motor cortex inherent in the local field potentials, from simultaneously recorded multi-electrodes in behaving monkeys. Cortical networks exhibit ongoing dynamics irrespective of directed stimulus or behavioral trials. These ongoing network states carry information, as they have been shown to correlate with the average evoked states during trials (Kenet T, et al, 2003). These states can also account for a large portion of the inter-trial response variability (Arieli A, et al, 1996), and as a result can be used to predict single trial responses. Finally, they have been shown to correlate with behavioral responses (Adrian AD, et al, 1934; Arieli A, unpublished results). We chose the LFP as a measure of the network state, as it is believed to reflect the synaptic activity from a large ensemble of neurons in the vicinity of the microelectrode.

We trained a linear dynamical system with gaussian noise (Kalman Filter) using the EM algorithm. Using the LFP signal as our observations, we learned a model for the hidden network states. This model was then used to predict the evolution of the LFP on untrained data.

The complexity of the network states was examined by finding the optimal size of the hidden state vector. Similarly, the correlation between the LFP at different electrode sites was assessed by testing the effect of adding signals from more electrodes to the observation vector, on the model's predictive power. We further tested the predictive power of the model when trained on limited frequency bands of the LFP signal. Several studies have shown correlations between the activity in certain frequency bands and spiking activity (e.g. Lee H, et al, 2005; Murthy VN, et al, 1992). To examine the relation between the ongoing activity and the activity during single behavioral trials, we tested the model's predictive power on the LFP during experimental trials. Lastly, we show how incorporating the model's output can be used to predict the single trial spike rate responses in single cells, during behavioral trials.

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Neural activities in the medial prefrontal cortex of the rat with multimodal discrimination task

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The medial part of the prefrontal cortex is known to contribute to executive functions, including attention and attentional set shifting¹. Attention can be described as selecting, focusing and sustaining on behaviorally relevant stimuli at the cost others, less relevant ones. Switching attention upon changing environmental demands is an essential characteristic of cognitive flexibility, not only in daily life but also in the clinic and in research settings. Not surprisingly, Attentional Set Shifting (ASS) has been found to be impaired in schizophrenia, autism, attention deficit/ hyperactivity disorder (ADHD) and in personality disorders. Attention and ASS might be encoded by medial prefrontal cortex (mPFC) neurons (Brain-lesion study¹) and appear to be dynamic functions of specialized neural networks incorporating mPFC. In order to understand a neural mechanism of attentional shifting, we have investigated ensemble coding strategies of neurons in the prefrontal cortex of freely moving rats by using the multi-electrode (tetrode) recording technique² and a dedicated custom-made behavioral box. We designed a Multimodal Attentional Set Shifting (MASS) task which was set in the box which can present visual, odor and sound stimuli and store all behavioral responses of the rat on a computer. The box equipped with a chamber which has an odor port, a speaker and a visual screen and a reinforcement tray. The learning task required that once the trial onset light turned on, the rat had to put its nose in the port of the chamber, where stimuli were simultaneously presented (odor sample, visual pattern or sound). While performing this procedure, the rat was required to discriminate between different stimuli of the same dimension (i.e. vision, olfactory, sound) in order to get reinforcement, only one dimension being relevant for reward. The rat performed a series of discriminations with simple and compound discrimination within single sessions.

In the conference, we will present initial behavioral and *in vivo* neurophysiological results especially on tasks with odor-visual discrimination under a hypothesis that mPFC neurons encode sensory-specific attributes of stimuli with a dominant representation of relevant sensory dimension and neural correlates pertaining to motor planning and actions.

KEY WORDS: Attentional set shifting, Multimodal, Multi electrode recording, Odor-Visual discrimination, Cognitive neurophysiology

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The expression of local field potential Gamma oscillations In Primary motor cortex during reaching movements Of an awake behaving monkey

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To investigate the expression of gamma oscillations, we recorded local field potential (LFPs) in M1 and compared evoked responses in 89 cortical sites in two task conditions: (1) performance of standard (STD) task and (2) adaptation to visuomotor rotation. Monkeys were over trained on the STD task but had to learn the visuomotor rotation task within a single session (Paz el at 2003).

We hypothesized that the appearance of oscillations may have a relationship to motor planning and performance. We found that oscillations start to emerge after trial initiation and terminate, with low variability, after target appearance (defined as "oscillating period"). Furthermore, quite surprisingly, we found in each task condition a significant linear relationship between mean power of oscillations during oscillating period and motor reaction time (time from go signal to initiation of movement) – a high power implies a relatively long reaction time. When comparing between tasks, standard trials showed reaction time and power of oscillations exceptionally lower than during visuomotor rotation trials.

When examining the dynamics of oscillating period along the recording day, we discovered that both the tendency of oscillations to appear and the mean power of these oscillations gradually increase. Changes are pronounced in the beginning of the standard trials, following stabilization and subsequent changes when switching to visuomotor rotation.

These results strengthen the linkage of gamma oscillations to preparatory functions, alertness and attention. We speculate that strong oscillations may represent the recruitment of learning mechanisms and attention that can cause to a longer reaction time.

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Extracting speech relevant spectro-temporal modulations using the information bottleneck method

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Neural computations performed in early and central stages of auditory processing, have inspired efficient algorithms for speech / non-speech discrimination based on the spectro-temporal modulations present in audio signals (Mesgarani et al, 2005). These multi-dimensional representations can model speech signals particularly well; yet, they are highly redundant across other natural sounds, as well. Auditory neurons of humans and animals seem to solve the problem of discrimination between behaviorally relevant and irrelevant classes of sounds, by tuning to the temporal modulations that differ most across them (Woolley et al, 2005)

In this work, we adopt this approach for speech/non-speech discrimination (music, animal vocalizations, environmental noises). Using the information bottleneck method (Tishby et al, 1999), we obtain a compact representation for each class, which maintains its most relevant features. A simple thresholding classifier is built, and compared to the method of Mesgarani et al, 2005 (which employs a multilinear dimensionality reduction technique along with support vector machines) for speech / nonspeech discrimination, at different SNR conditions. The proposed method could be generalized to the task of speech recognition, or speaker identification.

A neurocomputational analysis of preview search

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It is well known that humans prioritize information in the visual field by using "selection by space" to process information only at certain locations. However, recently it has become apparent that also time can determine the focus of the selection process, e. g., processing of new objects can be prioritized over processing old objects (see Watson et al,2003 for a review). To study properties of "selection by time", Watson and Humphreys (1997) devised a new version of visual search task named preview search. In general, in visual search tasks, participants are asked to find a known target item amongst irrelevant distractor items. The time it takes participants to detect the target is measured (reaction time). It is well-established that the slope of the search function (reaction time as function of the number of items in the display) depends on the features of the target and distractor items. Watson and Humphreys (1997) adapted a standard colour-form conjunction task (blue H target vs blue A and green H distractors), in which half of the distractors were presented in advance (blue As) of other distractors plus the target (when present): preview search. They found that search was more efficient in the preview condition than in the conjunction condition, and it could approach the efficiency found when the new items were presented alone (single feature baseline). Therefore, this finding suggests that participants only search for the new items and supress the old items.

There are a few biological inspired models of visual search but presently no neurocomputational model of visual marking effect. The model presented here contains synaptic connections (NMDA, AMPA and GABA) and a frequency adaptation mechanism based on I_{AHP} . I_{AHP} is not only included for its biological plausibility but also as a suppression mechanism being crucial for possibly simulated the visual marking effect. Moreover, its temporal behaviour is similar to the crucial timing between preview display and target display (Watson and Humphreys,1997). The network architecture was based on a visual search model by Deco and Zihl (2001).

The simulations showed that, even though the frequency adaptation mechanism was essential for simulating the visual marking effect, an additional inhibitory influence during the preview display presentation was needed. As this inhibition is an external input to the model, it could be speculated that it is produced by other brain areas. Intrestingly, this is consistent with findings by Pollman et al. (2003) who identified an area in the superior parietal lobule that played a particular role in preview search, including inhibiting the locations of old items.

Optimal Control Theory Predicts Complex Patterns of Neural Activity Observed in the Primary Motor Cortex

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What determines the specific pattern of activation of primary motor cortex (M1) neurons in the context of a given motor task? Following the introduction of the population vector view by Georgopoulos et al. in 1982, it was shown by Mussa-Ivaldi (1988) that cosine tuning and the population vector do not necessarily imply that M1 encodes movement directions. Rather, this work showed how such phenomena might arise from correlations with specific muscle attributes. The current state of knowledge about the complexity of neural activity in M1 makes it clear why physiological models are required. In particular, dissociation experiments (Crutcher & Alexander, 1990) have clearly shown that some M1 neurons are related to muscle activity. However, Mussa-Ivaldi's muscle coding hypothesis does not determine the identity of the muscle-related variables encoded by neurons in M1. Nor does it specify the physiological elements and the mechanisms involved in executing this muscle plan. In order to address these shortcomings, we present a systems level physiological model describing the transformation from the neural activity in M1, through the muscle control signal, into joint torques and down to endpoint forces and movements. The redundancy of the system is resolved by adding a biologically plausible optimization criterion related to energy consumption and noise. Each trajectory in the space of neural inputs to motor neurons is associated with a cost value, and the selected trajectory is the one for which the cost is minimal. Our model aims at being the 'simplest' physiological model able to predict the complex patterns of M1 neural activity. Such a model offers several advantages. It uses a single free parameter, the robustness to which can be easily determined. Due to model's simplicity and mechanistic form it provides intuition as to the most important properties of the system and a causal explanation of how they determine the overall system behavior. From a computational point of view, the model provides simple analytic results, leading to further insight. Despite its relative simplicity, it captures key features of the spinal cord and the biomechanical system in the context of a series of experiments performed by Kalsaka and co-workers (1997, 1998, 2003, 2005) as well as the experimental results described in (Georgopoulos 2000, Paninski et al. 2004). The model's predictions provide a surprisingly good approximation to a variety of non-trivial experimental results that, to the best of our knowledge, have not been previously explained by a single model in a mechanistically explicit way, and give rise to predictions of neural activity at both the population level, and at the level of single neurons. These results attest to the importance of incorporating essential biomechanical features and constraints in explaining the behavior of M1 neurons. The main features explained by our model are:

- (i) Narrow tuning functions.
- (ii) Diverse control signal PDs, which deviate from the joints' pulling directions.
- (iii) The pulse step response in the isometric task.
- (iv) Movement related phenomena: reversal of PDs during movement, non cosine tuning at welldefined moments during movement.
- (v) Changes of the PD due to different hand locations.

'Seeing' invisible motion: responses of area V5 neurons in the awake-behaving macaque

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We studied the relationship between brain activity and conscious visual experience of motion in area V5, the activity of which correlates directly with perceived motion in monkey and man. We used flash-suppression to dissociate the constant stimulus from the varying percept and showed that neurons in V5 modulate their firing rate according to whether a random-dot motion stimulus is perceived or not. In all cases, these changes reflect the ones produced under physical stimulus alternations, i.e. are higher for the motion compared to the static checkerboard stimulus and also increase in strength with increases in the directional coherence of the perceived dot movies. Over half of these perceptually-modulating neurons showed a further modulation when the strength of the suppressed motion stimulus was varied. These modulations also reflected the ones observed under physical stimulation - an increase in firing rate with an increase in the coherence of the motion stimulus. V5 neurons were thus shown not only to modulate their responses with respect to perceptual modulations under constant stimulation conditions, but also with respect to physical stimulus modulations under constant perceptual conditions. Therefore, characterizing neurons as 'perceptually modulating' or 'stimulus modulating' is not straightforward. Furthermore, activity in V5, which correlates with the perceived motion, also modulates in response to changes in the physical stimulus that never reach perceptual awareness. Our results suggest that there is no clear distinction between purely 'processing' and purely 'perceptual' neurons or areas in the brain. It is rather the activation of the same neuronal assemblies, responsible for the processing of a certain visual feature, that can also lead to its perception.

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Contextual influences of surround motion on BOLD activity evoked by a central moving stimulus.

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Background

In studies of humans viewing static stimuli, Williams et al (*J. Neurophysiology 89*: 525–533, 2003) demonstrated that fMRI could be used to study contextual effects on a population of visual neurons. They showed that static gratings in a surrounding annulus had suppressive or facilitatory effects on the activity level evoked by a static grating in a central area inside the annulus, which depended on the orientation of the surrounding grating. In this study we looked for an effect of the direction of motion of a surrounding annulus on the BOLD activity associated with a moving stimulus inside the annulus.

Method

The stimulus display consisted of a central circular area (diameter 3 deg), and a surrounding annulus (inner diameter 3 deg, outer diameter 9 deg), which could be presented alone or together. Luminancemodulated circular gratings of 48% contrast, which were either moving (expanding/contracting) or stationary, could be presented in the centre and/or surround. When the gratings were in motion, their direction of motion reversed every 0.66 sec. Spatial frequency and velocity were linearly increased with eccentricity (M-scaled), in order to make the salience of the motion the same across the whole stimulus. Direction of surround motion could be either the same as or opposite to that of the centre. Regions of interest (ROI) were initially defined by the contrast moving centre > static centre, and in a second step voxels were excluded if their activity was significant in the contrast moving surround – static surround. The aim was to isolate voxels where the direct retinotopic activation was from the moving centre only.

Results

Two contrasts were run in the ROI. They compared the activation in the ROI clusters when the surround and central motion (presented simultaneously) had the same or the opposite direction with the activation when only the moving central area was presented. The moving centre condition used in the t tests was independent of that used to define the ROI. 28 out of the 48 ROI clusters activated among all 6 participants showed significant increase in fMRI activation when the direction of the surround was opposite to that of the centre, demonstrating a facilitatory effect. When the direction of motion in the surround was the same as the centre, activity in 18 of the 48 clusters was significantly reduced, indicating suppression due to the surround.

Conclusions

The ROI are anatomically located in MT+ and other extrastriate motion areas. Half of the neurons in MT+ are known to have antagonistic centre-surround organisation (Allman et al., *Perception* 14(2):105–26, 1985). Our data suggest that there is a similar antagonistic organisation in human MT+, at least at the population level. We are currently investigating the effect of a gap between centre and surround on the BOLD activity. We are also interested in whether isoluminant motion in the surrounding area will have the same effect.
Population coding of natural video stimuli in macaque V1

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Although it is widely accepted that neurons in cortex encode information about the external world at the population level, little is still known on the structure of neuronal population codes under natural stimulation conditions. In particular, it is not known whether correlations between neurons are important for encoding information. To characterize the cortical population code underlying visual function, we recorded extracellularly the simultaneous activity of neuronal populations in primary visual cortex (V1) of an anaesthetized macaque, while the animal was viewing a video of monkeys behaving in their cages. Neuronal activity was recorded with an electrode array with approx. 1.5 mm spacing. We could record action potentials from a small cluster of neurons at each of 6 different electrodes. We computed, from 30 repeated presentations of the same video, the probability of each neuron firing in response to each part of the video. From this probability distribution of spike patterns at different times of the video, we computed the amount of Shannon's Mutual Information / that each neuronal cluster conveyed about the sequence of visual stimuli (methods similar to that of de Ruyter et al. Science 1997). We found that each individual cluster conveyed on average 6 bits/sec of information. In addition, to understand how information from different cells is combined together, we computed the information about the video that can be extracted by observing the simultaneous activity over a small population of neural clusters. The size of the population was varied from 2 to 4, and we took the average of the information conveyed by each subpopulation with a given size. We found that the average information increased linearly with the population size. This suggests that information is conveyed at the population level, and that each neuronal cluster carries fully independent information about the visual stimuli. Then, we addressed whether correlations are an important part of the neural population code. If this was the case, we would expect that a downstream neural system decoding the V1 population activity would lose a large amount of information when not paying attention to cross-correlations between neurons. The importance of correlations in decoding can be formalized in information theoretic terms by computing ΔI , the amount of information that is lost by ignoring information when decoding the population activity (Latham and Nirenberg, J. *Neurosci.* 2005). We found that ΔI was very small, of the order of 1% for population size in the range 2-4. Thus cross-correlations between cortical neurons were not important for transmitting information about natural stimuli.

In conclusion, the above results suggest that V1 represents natural visual stimuli through a distributed population code that combines independent information coming from different neurons without relying on correlations.

Sedative/amnesic drugs interfere with hippocampal sharp wave/ripple activity.

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Sharp wave/Ripple (SPW/Ripple) complexes are one of the prominent collective activities of the hippocampal network characterizing certain behavioral states. SPW/Ripples have been proposed as a neural substrate for information transfer between hippocampal and cortical circuits participating in the process of memory consolidation.

Several sedative agents including barbiturates and benzodiazepines induce memory impairment through unknown mechanisms.

In this study, employing a recently developed in vitro model of SPW/Ripples, in rat ventral hippocampal slices, we examined the effects of several sedative drugs with varying impact in memory impairment.

The barbiturate thiopental, known to induce anterograde amnesia, significantly slowed down the rate of SPW/Ripples at a concentration-dependent manner, destroyed SPW rhythmicity and reduced network synchronization along the CA1 region. Thiopental although significantly prolonged single SPW at the concentrations of 50-200 μ M it shortened the associated ripple episodes at all concentrations from 25 to 100 μ M and decreased the ripple frequency (at 50-100 μ M). Thus, thiopental had an overall decreasing effect on both SPW and ripples. On the other hand phenobarbital, another barbiturate, at clinically relevant concentrations not inducing amnesia (25-100 μ M) did not change the ripple frequency although it significantly accelerated SPW.

Diazepam and midazolam, two classical benzodiazepines producing amnesia, selectively affected ripple activity. Specifically, diazepam (0.5-1 μ M) significantly decreased the ripple frequency without consistently affecting SPW, although a trend in increasing their rate was observed. Midazolam, although did not significantly affect SPW characteristics, it decreased the ripple frequency at concentrations likely to induce amnesia (1 μ M). The results indicate that various sedative drugs distinctly interfere with the mechanisms underlying network organization into SPW/Ripple activity. Furthermore, they reveal a correlation between drugs or drug concentrations reported to induce memory impairment and decrease of several features of ripple activity. The findings are consistent with in vivo data relating SPW/Ripples to memory processes and may represent a mechanism underlying the amnesic effects of certain sedative substances.

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Movement trajectories inferred from human neuronal population signals (ECoG).

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Considerable efforts are being made towards implantable brain-machine interfaces (BMIs), recording and decoding neuronal activity from the human brain. The electrocorticogram (ECoG) recorded directly from the surface of the human brain may provide an attractive neuronal control signal for BMIs, as it does not require electrodes penetrating intact brain tissue. Recently, it has been demonstrated that subjects can control the power of different ECoG frequency ranges to move a computer cursor on a screen [1]. To operate an external actuator with multiple degrees of freedom it would be desirable to directly extract complete movement trajectories from the measured ECoG potentials. Here we address this question by investigating whether both movement direction speed (magnitude of the velocity vector) can be directly decoded from the human ECoG. To this end, subjects performed center-out arm reaching movements in four and eight directions, and a continuous motion task, moving between nine different targets, both in a horizontal plane. ECoG activity was recorded with a dense electrode array (64 electrode contacts, 10mm spacing) subdurally implanted in epilepsy patients. We decoded movement related ECoG activity on a single-trial basis and obtained the following results: (1) The direction of arm reaching movements in the center-out task could be accurately classified. (2) Movement speed could be inferred continuously during arm movement, with considerable accuracy (see Figure).



Speed Profiles: Section of curves for both, measured (black dashed line) and decoded (gray solid line) arm speed. Decoding was based on a linear regression model, trained on about 16 minutes of neuronal and movement data, recorded prior to the test data. The speed profile reconstructed from neuronal test data was significantly correlated with the measured profile (CC: correlation coefficient). CC=0.697 for the whole test set. CC=0.821 for the section displayed.

Our results provide further evidence [1,2] that the ECoG recorded from the human frontal cortex with densely spaced subdural electrodes constitutes an attractive control signal for neuronal motor prostheses without the need for measurement of spiking activity.

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Distribution of step-related activity in cat cerebellar cortex during passive hindlimb stepping on a treadmill. ²Valle, MS, ³Bosco, G, ¹Eian, J and ¹Poppele, RE

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In this study we examine the responses of cerebellar cortical neurons to passive hindlimb stepping. Previously our lab showed that activity recorded from precerebellar neurons in the spinal cord under the same conditions could be accounted for by a relationship to the global kinematics of the hindlimb axis. In fact, regression analyses that included the limb axis length and orientation as predictors of neural activity accounted for over 80% of the response variance in a large population of neurons. However, because of the irregular firing of cerebellar cortical neurons in decerebrate animals, correlation techniques may not be as sensitive in detecting step-related changes in neural activity. Thus we examined various alternative analytical approaches to find a more objective assessment of cell responsiveness.

We recorded unit activity from widely distributed areas in the medial anterior lobe of the cerebellar cortex in decerebrate cats. The animals were mounted in a frame with hindlimbs suspended and resting on a treadmill. Passive stepping was achieved by manually moving a limb forward and allowing it ride back on the moving treadmill (see Poppele, et al. Exp Brain Res 149:361, 2003) Each recorded cell was localized on a map of the unfolded cortex that included lobules 1 – 5, between 1.5 and 5.5 mm lateral from the cerebellar midline (i.e. zones b and c; see Perciavalle, et al. Eur J Neurosci 10:1975, 1998).

Unit activity was analyzed in several ways to determine a) whether any movement-related activity was consistently present and b) whether the activity was related to hindlimb kinematics; specifically:

- 1. In the frequency domain we determined the fraction of the total signal response power that had the same frequency components as the stimulus.
- 2. We also averaged the response activity over 4 identical stimulus cycles to determine the response variance across cycles and compared the averages from 2 separate 4-cycle periods as a simple measure of response stationarity.
- 3. In the time domain we used a multivariate regression model of global hindlimb kinematics to determine the amount of response variance that could be explained by the limb movement.

The results of each analysis were plotted on the cerebellar map (see figure below, left) and they showed a pattern that was generally consistent with the classical receptive field organization of the anterior lobe. The fraction of stimulus power was generally higher in the responses of cells located in hindlimb areas of zone b than those in zone c, i.e. medial to 3 mm, being highest in lobules 2 and 3. However there was also a significantly high fraction of stimulus power in the responses of cells in lobules 4 and 5, which are classically known to have forelimb receptive fields.

Cells with responses that were significantly explained by the kinematics model ($R^2 > 0.2$) were similarly distributed (right). There were however cells in lobules 1, 4 and 5 with responses having a high fraction of stimulus power that were not well accounted for by the regression model. The signal variability accounted for about 65% of the model R^2 but less than 30% of the variability in the fraction of stimulus power in the responses. We conclude that the regression model is more sensitive to noise and that the fraction of signal power may provide a more sensitive measure of the relationship to the leg movement stimulus. Supported by NIH Grant NS 21143.



Maps of unfolded cerebellar cortex. Anterior lobe lobule number along the ordinate and lateral distance from midline (mm) on abscissa. Shading shows the locations of cells having responses with a significant fraction of response power corresponding to stimulus power (left plot) or locations of cells with responses that were significantly accounted for by the regression model (right plot).

Object and grasp related activity in F5 neurones during visually guided grasp

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The sensorimotor transformation required for visuomotor grasp is thought to be carried out by corticocortical circuit involving connections from the anterior parietal region (AIP) to the ventral premotor cortex (F5) to the primary motor cortex (M1) (Jeannerod et al., 1995). In this model the processing of the threedimensional properties of the objects is carried out in AIP and the selection of an appropriate motor plan for grasp in area F5. Visuomotor neurones in area F5 show discharge during object presentation which can be related to the subsequent grasp, supporting this intermediate role (Rizzolatti and Luppino, 2001; Murata et al., 1997). However, as previous research has associated each object with a particular grip, the early firing of F5 visuomotor neurones may represent a purely visual response. This study addresses whether early firing of F5 visuomotor neurones varies according to the grip to be used or the object presented, by modulating object and grasp independently.

Two purpose-bred macaque monkeys (*Macaca mulatta*) were trained to grasp differently shaped objects with the right hand, using specific hand postures. Two objects, a cube and a ring, could be grasped using either a side grip or a top insertion grip. The required grasp was indicated using a visual marker. At the start of each trial the monkey used both hands to gently press two homepads; this illuminated an object mounted on a shuttle device in front of the monkey and switched on a red/orange LED. The monkey could see the object and the reflection of the LED through a half-mirror. After 1 ± 0.5 s the monkey was cued, by the LED switching to green, to reach, grasp, and pull the object towards it using the trained hand, hold it in a target displacement zone and then release it. During the task, simultaneous recordings were made from single neurones in area F5 in the left hemisphere with 4-6 independently movable electrodes.

Task-related neurones were divided into two categories, visuomotor and 'motor'. Visuomotor neurones showed modulation of activity compared to baseline during the presentation phase, defined as the period from the visual presentation of the object to the 'go' cue. 'Motor' neurones only showed activity different from baseline during the movement phase, from the 'go' cue to object displacement. Approximately half of the visuomotor neurones showed a significant main effect (ANOVA, p<0.05) for object, grasp or both in the presentation phase which increased to three quarters in the movement phase. In the presentation phase, the majority of visuomotor neurones showed a main effect for object, in the movement phase for both object and grasp. During the movement phase visuomotor neurones showed earlier activation compared to the 'motor' neurones.

The results support the hypothesis that when an object is first presented, 'visuomotor' neurones are concerned with visual processing of the physical properties of the objects rather than planning the movement. Later, on receiving the cue to grasp, activation is related to the subsequent action. The earlier peak of activation of the 'visuomotor' neurones compared to the 'motor' neurones suggests that these neurones have a role in an early stage of the visuomotor transformation required for object-orientated grasp.

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Inferior temporal cortex during real world vision

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Much of current visual neuroscience is performed using standardized procedures. Most notably, these generally include stimulus delivery using computer displays, the requirement of fixation, repeated performance of experimental conditions and lengthy conditioning of animals on tasks to allow for behavioral reports. Correlating neural responses with stimulus characteristics and behavior lies at the heart of systems neuroscience. These controlled conditions have many advantages, but at the same time can only represent an approximation of the processes that occur during real world vision.

But how much are we missing under these constraints? Real world vision is characterized by eye movements in three dimensions as observers fixate and track objects in the environment. What are the characteristics of spike trains collected under such conditions and how do they differ from those collected during task performance. How much can be said about neural activity by applying the correlational approach to data acquired under these conditions? Does what we learn about neural activity and selectivity during task performance generalize to real world vision? To begin to address these questions, we have recorded extracellular activity of several inferior temporal cortex neurons simultaneously while monkeys viewed face and object stimuli presented on a computer monitor at the center of gaze during fixation. Then we record activity of the same neurons during interaction with a human experimenter, while measuring the monkeys' eye position and recording the visual input using a camera. We compare about 5 minutes of activity collected during these two conditions. Preliminary results suggest many IT neurons were dynamically modulated during real world vision. Peak firing rates (eg at 200ms binwidth) tended to be greater during real world vision than during task performance. Some IT neurons showed markedly different interspike interval distributions in the two conditions.

Our findings suggest that a dynamic three dimensional visual environment may be a useful tool for elucidating the function of visual neurons.

Precise spike synchronization in monkey motor cortex: from time estimation processes to the selection of movement direction

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It is commonly accepted that perceptually and behaviorally relevant events are reflected in changes in firing rate in widely distributed populations of neurons [1, 2]. Another concept, the temporal coding hypothesis, suggests that not only changes in firing rate but also precise spike timing constitutes an important part of the representational substrate for perception and action, such as spike synchronization or other precise spatio-temporal patterns of spike occurrences among neurons organized in functional groups, commonly called cell assemblies [3, 4].

The accurate estimation of time intervals or the temporal prediction of forthcoming events is essential for optimizing motor performance. During preparation and execution of a planned movement, motor cortical neurons change their activity not only in relation to the features of the forthcoming movement (such as its direction) but also in relation to higher cognitive events linked to time estimation processes [5], e.g. signal expectancy (**SE**). Using a delayed pointing task, it as been shown that, at the moment when a GO signal was expected but did not appear, some neurons changed phasically their activity [5], transient synchronization among two or more neurons occurred [6] and also the correlation between local field potentials increased [7].

To explore spike synchronization patterns in pairs of neurons in relation to **SE** and/or to prior information about movement direction, we recorded simultaneously the activities of multiple neurons in monkey primary motor cortex during the performance of a choice reaction time task requiring correct time estimation [5]. In this task, which involved different degrees of spatial and temporal uncertainty, the choice of movement direction was a function of time. To investigate the dynamics of spike synchrony, the unitary events method [8] and the classical tool of cross correlation analysis were used.

We found (i) consistent patterns of spike synchronizations linked to **SE**, and thus to time estimation processes. Surprisingly, we observed (ii) an effect of learning new durations, with a shift in time of the transient occurrence of synchrony from the old expected signal to a new one. And finally, we found (iii) directionally selective patterns of spike synchronizations during movement preparation which presented reciprocal patterns related to the two opposite movement directions.

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Cortico-cortical interactions in macaque motor cortex investigated with intracortical microstimulation (ICMS) and transient inactivation with muscimol.

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The aim of this study was to investigate whether motor effects in the hand evoked by repetitive trains of intracortical microstimulation (ICMS) from the ventral premotor cortex (area F5) depend upon cortico-cortical connections with the primary motor cortex (M1). A recent study¹ showed that single shocks in the hand area of F5 alone do not elicit EMG activity in hand muscles but strongly facilitate the EMG responses evoked by test stimulation of the M1 hand area.

In two adult macaque monkeys we investigated these interactions by recording the EMG responses to trains of ICMS in both cortical areas before and after microinjection in the hand area of M1 of the GABAergic agonist, muscimol. All work was carried out in accordance with UK Home Office regulations.

The location and topography of M1 and F5 were first identified using MRI. Under aseptic conditions, a plastic grid containing 50 vertical holes was permanently fixed over each area, the holes allowing the implantation of intracortical stimulating electrodes or a microcannula allowing microinjection of muscimol. The monkey was lightly sedated (ketamine/ medetomidine HCI) and EMG responses evoked by trains of ICMS were recorded from intrinsic hand and digit muscles. Responses were recorded before and after the inactivation of M1 using 0.9-1.5 μ L of 0.5% muscimol. Electrodes were also chronically implanted in the pyramidal tract (PT).

Muscimol inactivation of the hand area of M1 resulted in a dramatic decrease of the amplitude and probability of EMG responses evoked not only from M1, but also from F5. This was not observed with control microinjections of saline. Although, after muscimol injections in M1, there was some reduction in the EMG responses to stimulation of the PT this effect was far less dramatic than virtual abolition of responses from F5.

In conclusion, M1 appears to play a major role in the transmission of information from the premotor cortex to the motoneurones of hand muscles, and the classical motor effects elicited from premotor cortex may well be dependent upon the integrity of M1. This situation applies only to acute deactivation, and longer-term plastic changes may well result in a different outcome after permanent lesions e.g. after stroke.

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Weak pairwise correlations imply strongly correlated network states in a neural population code

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Correlated activity of groups of neurons has been observed in many different neural systems, often in relation to specific stimulus features or motor outputs. The functional roles of these correlations and their sources are central to our understanding of the neural code, and have been heavily debated in recent years. Clearly, exhaustive sampling of large groups of neurons is impossible, and so successful analysis depends on simplifying hypotheses. However, experiments on many systems hint that complicated, higher order interactions among large groups of elements play an important role.

To explore the nature of correlations and information coding in large networks of neurons, we recorded the joint activity of dozens of ganglion cells, from the intact salamander and guinea pig retinae. We then studied the network activity patterns in response to natural and artificial movies. We show that weak correlations between pairs of neurons coexist with strongly collective behavior in the responses of ten or more neurons. Surprisingly, we find that this collective behavior is described quantitatively by models that capture the observed pairwise correlations but assume no higher order interactions. These maximum entropy models are equivalent to *Ising* models, and predict that larger networks are completely dominated by correlation effects. This suggests that the neural code has associative or error-correcting properties, and we provide preliminary evidence for such behavior. As a first test for the generality of these ideas, we show that similar results are obtained from networks of cultured cortical neurons.

Finally, we investigate the way groups of cells encode information collectively about the stimulus, focusing on the success of time-dependent maximum entropy models in capturing the variability of the responses of neural populations to repeated stimuli, bounding the information carried by a large group using maximum entropy models of the population, and characterizing the functional similarity of different multi-cell firing patterns.

Neural Correlates of Intermanual Transfer of Sensorimotor Adaptation J. A. Anguera¹, C. A. Russell², D. C. Noll³, & R. D. Seidler^{1,2,4} ¹Division of Kinesiology, ²Dept. of Psychology, ³Depts. of Biomedical Engineering & Radiology, ⁴Neuroscience Program, University of Michigan

The sensorimotor system must be adaptable in order to deal with the changing demands of everyday life. One common way of studying this adaptive capacity is through visuomotor adaptation, where the mapping between visual and motor space is distorted. Neuroimaging studies of visuomotor adaptation in human subjects have revealed that a variety of cortical and subcortical brain regions contribute to early adaptive processes, including the primary motor cortex (M1), prefrontal cortex (PFC), parietal cortex, supplementary motor area (SMA), and cerebellum (cf. Ghilardi et al., 2000; Graydon et al., 2005; Imamizu et al., 2000; Krakauer et al., 2004). In the later stages of learning, researchers have reported weaker but sustained activation in the cerebellum, parietal, and temporal cortex (cf. Graydon et al., 2005; Imamizu et al., 2000; Krakauer et al., 2004). These studies have contributed greatly to our understanding of the mechanisms underlying visuomotor adaptation. What remains unclear, however, is the laterality of the involved brain regions, as these former studies have only tested subjects that performed movements with the right (dominant) hand. The simplest prediction regarding the lateralization of brain regions contributing to sensorimotor adaptation might be that traditionally so-called motor regions would shift their activation to the contralateral homologue when hand of performance switches, while non-motor regions would not. However, it is not so easy to classify brain regions according to motor and nonmotor functions, particularly the parietal and premotor regions described above. Thus, in the current investigation, we tested transfer of adaptation from one hand to the other to allow for assessment of which brain regions contribute to learning in an effector-dependent manner as opposed to those creating a more abstract representation. Two groups of subjects performed a visuomotor adaptation task in which they adapted hand movements to a 30° rotation of the visual display. One group (fMRI group) performed the task in a 3.0 Telsa MRI scanner, while the other group (control) performed an abbreviated version of the task outside of the scanner. The fMRI group performed the adaptation task with the right (dominant) hand and then subsequently transferred to performance with the left hand; the control group performed the adaptation task with their left hand without prior right hand training.

The fMRI subjects showed better performance with the left hand than the control group, demonstrating a transfer of learning effect. Early adaptation processes were associated with bilateral activation at frontal, parietal, and cerebellar regions, among others. Activation became more focal with practice, with activation remaining in the left inferior parietal lobule and the left middle temporal gyrus. At transfer to left hand performance, activation was localized primarily in the right hemisphere, with activation at the precuneus, inferior frontal gyrus, middle temporal gyrus, and superior temporal gyrus. These regions showed no spatial overlap with sites engaged in either early or late learning, suggesting an effector-dependent role for these regions in transfer of learning. In contrast, conjunction analyses revealed that the left superior parietal lobule was equally engaged at both early learning and transfer of learning, implying that this region represents the acquired adaptive state in an abstract fashion. These data demonstrate the utility of transfer designs for parsing out the respective contributions of brain regions to effector-dependent versus abstract levels of learning.

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FISHER INFORMATION, MULTIPLICATIVE NOISE and NONLINEAR DECODING

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How can the brain carry out computations reliably when its building blocks -- neurons -- are notoriously noisy? What part of the population response corresponds to the 'signal'? How can it be extracted and used?

A first step in answering these questions is to analyze simple models of population codes using the framework of Fisher information. In such models, it is often assumed that neither the response variance nor the noise correlations (the covariance matrix) depend on the stimulus. For Gaussian noise, Fisher Information then consists of a single 'linear' term that depends on the covariance matrix and the derivative of the tuning curves, and all information can be extracted using a linear decoding scheme. It is likely, however, that the second order statistics also vary with the stimulus. If so, Fisher Information also includes a second term, which depends on the derivative of the covariance matrix. Importantly, information in that term can increase with the number of neurons, N, in cases where the first term saturates with N. Moreover, this information can not be extracted using a linear decoder, nor by the recurrent network proposed by Deneve et al (1999). Instead, a nonlinear decoding method is required.

Here we explore the significance of this finding. We use a combined linear/quadratic estimator to decode the responses of large populations of neurons. We show that this gives a simple decoding method, one that is locally efficient even when there are stimulus-dependent correlations, and that is greatly superior to linear methods for large populations of neurons and plausible noise models. However, we show that this method is difficult to apply directly to real neuronal data, since satisfactory estimates would require a very large amount of recording trials. We propose however two different methods, or `simplified quadratic decoders', which are slightly suboptimal, but which can be used to estimate Fisher Information and decode the responses in a data-robust way.

Applications to simulated and real data are discussed and compared to previously proposed linear and nonlinear decoding techniques.

Dynamic synchronization of Purkinje cell simple spikes

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Purkinje cells (PC) generate two types of spikes, simple spikes (SSs) and complex spikes (CSs). High frequency SSs are driven by parallel fibers (PFs) originating from diverse brain stem areas and the spinal cord, while complex spikes (CSs) are generated by climbing fibers (CFs) solely originating from the inferior olive¹. Despite the large overlap of PF inputs impinging on PCs lying along the same PF beam², SSs do not show any precise synchronization in PCs separated by more than 500 μ m³. Conversely, precise synchronization of SS spikes has been reported in pairs of close by PCs, either on the same electrode or two electrodes separated less than 100 μ m^{4,5}.

To elucidate the mechanism underlying precise synchronization of SSs, we have analyzed crosscorrelations of nearby PCs in detail. We report here that only SS pauses are precisely synchronized while other spikes show broad correlations as reported previously^{3,5}. Pauses in SS trains can be generated by multiple mechanisms. It has been reported that CSs are always followed by pauses. On the other hand, pauses can also be generated by intrinsic afterhyperpolarization, decreased PF input, and/or increased inhibition from surrounding interneurons. All these pauses would be indistinguishable in spike trains recorded from PC axons contacting downstream neurons in the deep cerebellar nucleus (DCN).

Thus, we defined pauses in this study as all ISIs which are indistinguishable from the pauses following CSs (P, ISI \ge 12 ms) in the spontaneous activity of 38 PCs, recorded in Crus II of anaesthetized rats. Afterwards, a functional difference between spikes surrounding P and the rest, non-pauses (nP), was investigated in 8 pairs of nearby PCs (distance < 100 µm). These PCs showed synchronous correlation in overall SS trains (Z = 8.2 ± 0.9, mean ± SEM, range: 4.6 – 11.5). We found that (1) P (Z = 8.1 ± 1.3) showed similar synchrony as overall spikes do, while nP showed significantly lower synchronization than nP (HW = 70.0 ± 10.6) did, (3) There was no significant difference in synchronicity between spikes relative to the P (starting, ending or surrounded by pauses, p > 0.3, Wilcoxon signed rank test), and (4) there was no change in these results after removing pauses following CS in SS trains. As a possible timing signal in the deep cerebellar nuclei (DCN) is the post-inhibitory rebound spike which strongly depends on the strength and duration of preceding hyperpolarization⁶, we suggest that this dynamic synchronization of PC SSs may serve to control the timely generation of rebound spikes in DCN neurons.

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The Role of Prediction in Ocular Tracking of Targets Moving in Two Dimensions

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We have examined two-dimensional ocular tracking by presenting subjects with targets that initially moved in a straight line, then followed a circular arc, finally reverting to linear motion. The onset of circular motion, the radius of curvature, the arc length and the speed of the target motion were unpredictable from trial to trial. In this experimental condition, the direction of smooth pursuit lagged the direction of the target's motion by about 80 ms, even when the circular motion lasted as long as 2.4 seconds. Since this lag is close to the latency for the initiation of pursuit, we initially took this as evidence for a lack of prediction in the control of pursuit eye movements (Mrotek et al. 2006). In fact, a model in which eye acceleration was related to retinal image velocity (with a time delay of 75 to 90 ms) gave a good fit to the data. In this model, we characterized the motion in local path coordinates, i.e., along directions parallel and perpendicular to the target's path at each point in time. Using this coordinate system, we found that pursuit gain was anisotropic, the gain in the perpendicular direction being about twice as large as the gain in the parallel direction.

Subsequent experiments probed the role of prediction in tracking more directly by temporarily occluding the target's motion. The occlusion consisted of a visible horizontal band on the computer monitor and the target disappeared behind this occlusion. In one experiment, the target did not reappear and subjects were asked to point to the location at which they expected the target to reappear. In this experiment, most subjects pointed (and saccaded) to locations that did not account for the curvature of the target's motion behind the occlusion; the best fit to the data was provided by a linear extrapolation of the target's motion at the time the target disappeared. In a second experiment, the target did reappear and subjects were asked to track the target through the occlusion. In agreement with previous reports, the speed of smooth pursuit decreased markedly when the target was occluded. However, the direction of smooth pursuit angular velocity in the occlusion was statistically indistinguishable from its time course for unoccluded movements. From this experiment, we conclude that subjects did indeed incorporate prediction into their control of smooth pursuit, and that this prediction was not merely a static snapshot of the target parameters extant at the time of occlusion.

In a third experiment, we probed the gain of smooth pursuit under these conditions directly by applying brief (50 ms) perturbations at various points along the trajectory (at the onset of circular motion, and after the target had traversed arc lengths of 45° and 90°). In half the trials, a perturbation was applied in one of 8 directions; in the other half of the trials, there was no perturbation. Following the procedures we used in the other experiments, we characterized the responses in local path coordinates, tangent and perpendicular to the direction of target motion. In the tangential direction, we found that one component of the response was uniform irrespective of the direction of the perturbation. This component consisted of a transient decrease in speed. If this component is subtracted out, the amplitude of the response to perturbations in the parallel and perpendicular directions was approximately equal. This result appears to be at variance with the results from the first experiment in which the apparent gain of pursuit in the two directions differed by a factor of two. In view of the results of the second experiment, we believe that a predictive component, that takes into account the fact that the target's direction changes over time, enhanced the effective retinal image velocity gain in the perpendicular direction.

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Simultaneous recordings from two types of identified output neuron in M1

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There are two parallel pathways by which information from M1 can reach the cerebellum through the pontine nuclei: via collaterals of the corticospinal tract, and through a direct cortico-pontine projection. Therefore the cerebellum receives information from M1 in the form of efference copy of movement commands, as well as communication through a dedicated "private line", respectively. The experiments described here aimed to compare the activity of neurons in M1 that belong to each of these pathways.

Previous single unit work in M1 focussed on its output due to the bias of electrophysiological recordings towards the large layer V pyramidal output neurons (Humphrey and Corrie, 1978). Combining these recordings with antidromic stimulation enables the target structures of these outputs to be identified, allowing insight into the functional significance of neuronal activity that is projected to a particular location. Using this method, previous work has studied cells identified as pyramidal tract neurons (PTNs) which send information through the corticospinal tract (CST). The present experiments extend this by comparing simultaneous recordings from PTNs and those of a separate class of cells potentially projecting to the pontine nuclei but not the PT: so called cortico-pontine neurons (CPNs).The study thus compared M1 outputs to the spinal cord and to the cerebellum during movement.

Simultaneous recordings were made using up to 5 microelectrodes inserted into M1 of 2 macaque monkeys, trained to perform a precision grip task against a range of different spring constants. A total of 93 cells (25 PTNs, 36 CPNs and 32 unidentified units) were analysed.

We asked 2 basic questions. Firstly, do CPNs show the same task-related activity as PTNs? The cerebellum receives information about the features of corticospinal output via CST collaterals to the pons, so CPNs might be expected to communicate different information and might therefore demonstrate different responses to the parameters of the task. We found that PTNs and CPNs showed similar patterns of task-related discharge, discharged at similar latencies relative to movement onset, and showed similar correlations of firing rate with spring force. However, subtle differences were observed: CPNs showed more tonic firing rates on average during the hold period and PTNs showed slightly but significantly greater scaling of activity with force (2-tailed t-test, P<0.05), consistent with their more direct influence on hand muscle motor neurons.

Our second question was: do these CPNs show significant synchronization with other PTNs? Precise synchronisation of spiking activity between neuron pairs was assessed using cross-correlation histograms (CCHs) with 1 ms bins. Spurious synchronisation caused by task related modulation of discharge was corrected using an instantaneous firing rate (IFR) predictor. The significance of peaks and troughs was assessed using 99% limits assuming Poisson distributed bin counts. Overall synchrony between pairs of neurons in M1 was relatively weak, with only 6/158 pairs (4%) demonstrating significant features in the cross correlation histogram around 0ms lag. One significant cross-correlation between a PTN and CPN was observed, suggesting synaptic connectivity between these two cell types in M1. For a clearer measure of synchronisation in the population, CCHs were averaged across individual pairs belonging to each pair type. 99% Poisson significance limits were also applied to these average CCHs. Mean synchrony between PTNs and CPNs (N = 31 pairs) was not significant in contrast with mean synchrony between PTNs and PTNs (N = 12 pairs). Taken together, these results suggest a relative but not absolute segregation of these two output networks within M1.

Overall, our findings demonstrate that the cerebellum can receive similar movement-related information via multiple output pathways from M1, and that neurons which project to these pathways interact within the motor cortex.

Motor Selection and Sequencing: Role of the basal ganglia and frontal cortex in humans

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Playing the piano requires a well learned sequence of movements in which different sound intensities require the selection of different finger forces. The mechanisms of sequence generation were originally addressed by Lashley ¹, and since this time both sequencing and selection processes have been studied at behavioral and neurobiological levels. Our primary interest in this study is the role of the basal ganglia in sequence generation². In particular, the globus pallidus has been implicated in sequence generation ³⁻⁵ and the striatum has been related to both sequencing and selection ^{2, 6, 7}. However, the precise role of each basal ganglia nucleus in sequence generation and selection in humans is unknown. We conducted an fMRI study at 3 Tesla focused on nuclei of the basal ganglia, along with the motor cortex, supplementary motor area (SMA), anterior cingulate cortex (ACC), and dorsolateral prefrontal cortex (DLPFC) in participants performing a precision grip force task. Right-handed participants (n = 10) produced force that was either externally-guided (with visual feedback) or internallyguided (without visual feedback) using their right middle finger, index finger, and thumb during three fMRI scans. The three scans included holding a constant force, performing a sequence of similar force pulses, and selecting a sequence of different force pulses. Hypothesis testing was performed using regions of interest analyses of the basal ganglia and cortical regions. Here we show that the basal ganglia of humans are involved in force selection and sequencing with nucleus specific activation occurring in an anterior and posterior organization. We found that the selection only process was associated with cortical areas such as the DLPFC and ACC, and the caudate nucleus in the basal ganglia. Areas associated with both selection and sequencing of force was found in the pre-SMA, anterior putamen, and external segment of globus pallidus (GPe). These regions of the frontal cortex and basal ganglia were posterior to the areas associated with selection only. Several areas were involved in only sequence generation, including cortical areas such as SMA and primary motor cortex (M1), and the posterior putamen, subthalamic nucleus (STN), and internal segment of globus pallidus (GPi). The areas involved in sequencing, but not selection, were situated posterior compared with the regions associated with the selection of force. Our results demonstrate that specific nuclei of the basal ganglia regulate selection and sequencing processes in an anterior to posterior neural architecture.

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AREADNE 2006 abstract

Anticipation in a population-coding system: a model of the inputs to rodent head direction cells

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The rodent head-direction (HD) system can be seen as one of several brain systems across different modalities and species that display anticipatory or predictive properties. Like the HD system, several of these systems process a continuous quantity like speed, direction or position using population codes: examples include motion perception extrapolation, motor control of hand movements, and hippocampal place cells. The HD system represents a onedimensional variable (direction) so is relatively simple, and as such makes a good model for studying sensory integration and anticipation in a populationcoding system.

Here, we simulate possible mechanisms underlying its anticipatory properties, using a large (~17 hours) corpus of rat tracking data for testing and validation. Previous explanations of HD anticipation have relied on putative offset connections between attractors, for which experimental evidence is so far lacking, and the developmental mechanisms needed to support such connectivity are unclear. We provide an alternative hypothesis based on the properties of the inputs to the HD system: we show that spike rate adaptation (SRA) and post-inhibitory rebound firing (PRF), as found in medial vestibular nucleus neurons *in vitro*, can generate realistic ATIs in a simulated HD attractor network. In the single attractor case, anticipation is always accompanied by an increase in tracking error, although it is small compared to simply increasing the gain of the input. However, when the HD signal is propagated trough several layers, optimal tracking in the final layer is achieved by generating anticipation in the first layer. We suggest experiments to test this idea.

In addition to the main result that input properties could be the source of HD anticipation, there are interesting observations to be made on the anticipatory time intervals (ATIs) of individual simulated cells. ATIs of different cells in the same brain area are known to be highly variable; we show that this appears to require little, if any, biological differences between cells, independent of the method used to generate them. A further source of ATI variability is the HD profile being tracked: different profiles lead to different ATIs for different anticipation models.

To spike or not to spike: computational optimality, reward, and attention

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Why do neurons spike? Clearly, graded outputs can communicate more bits than binary ones: photoreceptors and bipolar neurons in the retina, for instance, release neurotransmitters in a graded fashion. It is generally thought that all-or-none action potentials are required for propagating information over long distances. However, many neurons with short axonal processes, such as local interneurons, also have spiking outputs. Here, we argue that sequential binary outputs may be desirable from a *computational optimality* viewpoint. We can view the spike train of a neuron as a sequence of votes for the presence of a stimulus being present with features that the neuron "cares about" (e.g. certain values of orientation, color, and motion direction for a visual cortical neuron). As such, there is a trade-off between how sensitive the neuron is to changes in its synaptic inputs, and how robust it is against noisy fluctuations. It reflects the fundamental conflict between the *speed* with which the properties of the environment can be detected, and the *accuracy* of this detection process.

These issues can be formalized precisely as examples of stochastic control processes. This mathematical framework readily admits problems in which a decision has to be made about a variable for which repeated indirect observations are available, and there is both temporal and accuracy pressure. It turns out that often the *optimal* policy for deciding that the inputs reflect one kind of stimulus versus another (or the appearance versus continued absence of a stimulus) consists of setting a fixed threshold on a Markov internal variable, which essentially tracks the sufficient statistics of the inputs, and reporting the corresponding decision as soon as that threshold is crossed (and remaining silent otherwise). This is the case whether synaptic inputs are characterized as a Poisson process, as is assumed in some neuronal models, or as a diffusion process, in which each EPSP/IPSP contributes a positive/negative kernel to the membrane potential. From the optimized for the rate at which the external environment can be expected to change (and the internal uncertainty to grow). Also, resetting of the membrane potential after a spike, reflecting a resetting of the information accumulation process, is appropriate if the synaptic inputs carry independent information over time. These arguments form the *computational* motivation for neurons being leaky integrate-and-fire units with reset.

Several recent papers have argued that neurons, and neuronal population, need to encode uncertainty about sensory inputs and internal knowledge either implicitly or explicitly. If neurons are sequential decision-makers, however, the uncertainty in their inputs are encoded and propagated in a very straight-forward fashion. Assuming information independence over time, faster output firing rate directly results from more active inputs, which induce greater confidence about the stimulus having the desired properties. The spiking pattern is also appropriately Poisson/irregular, due to the noisy, fluctuating nature of the inputs (and any additional processing noise). The crux of challenge of this optimal decision-making argument of neuronal processing, is that the synaptic inputs need to be transformed appropriately into the Markov variable encoded in the membrane potential, on which the decision threshold is placed. In particular, if the input statistics change, the transformation into the membrane potential, and potentially the decision threshold itself, should also change correspondingly.

This framework has interesting implications for linking the function and mechanism of neuromodulators. Of the four major neuromodulatory systems in mammals, dopamine and serotonin have been implicated in rewardand punishment-related signals; acetylcholine and norepinephrine have been proposed to signal different kinds of uncertainty. Since reward and informational uncertainty, the two main drivers of attention allocation, are both explicitly represented in the objective function of the sequential decision-making problem, they play a critical role in determining the decisional threshold. This translates into a modulation of the response *sensitivity* of a neuron, much as neuromodulators are known to be capable of from electrophysiological studies.

Finally, as sequential decision-makers, hierarchical neuronal systems no longer face the question of when to stop propagating information and when to start making decisions or initiating responses. In the proposed scheme, neurons propagate information and make decisions at *every* level of processing. The theory also makes the prediction that animals that have slower responses have less of a temporal pressure in single neuron decision-making, and therefore can be expected to have fewer neurons with spiking outputs (and more with graded responses) compared to faster-moving animals.

Emergence of context specific responses in M1 and PM cortices

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How dynamic is cortical representation? Studies of plasticity associated with a profound change in input characteristics (i.e, amputation, sensory deprivation, etc.) suggest that on the time scale of days, the adult cortex is malleable to a certain extent. However, little is known about the dynamics of changes in neural representation within the time scale of seconds.

In order to address this question, we recorded extra cellular activity from 32 electrodes placed in M1 and Premotor cortices of two monkeys while learning a new arbitrary association task. The task involved finding the correct association between target color and movement direction, and was learned for two colors, appearing randomly at one of two locations. Location of the targets was task-irrelevant.

We found that learning induced (1) a change in neuronal sensitivity- as the task progressed more and more neurons became sensitive to the new relevant parameter, e.g. the target color. (2) Emergence of context specific responses, with neurons showing different response profile for different tasks. These results demonstrate that neural activity in M1 and premotor cortices can change their respective response profile within time scales of seconds to accommodate behavioral performance.

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The Role of Cannabinoids in the Neurobiology of Sensory Gating: A firing rate model study

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Abstract

Gating of sensory (e.g. auditory) information has been demonstrated as a reduction in the auditory-evoked potential responses recorded in the brain of both normal animals and human subjects. Auditory gating is perturbed in schizophrenic patients and pharmacologically by drugs such as amphetamine, phencyclidine or ketamine, which precipitate schizophrenic-like symptoms in normal subjects. The neurobiological basis underlying this sensory gating can be investigated using local field potential recordings from single electrodes. In this poster we use such technology to investigate the role of cannabinoids in sensory gating. Cannabinoids represent a fundamentally new class of *retrograde* messengers which are released postsynaptically and bind to presynaptic receptors. In this way they allow fine-tuning of neuronal response, and in particular can lead to so-called *depolarization-induced suppression of inhibition* (DSI). Our experimental results show that application of the exogenous cannabinoid WIN55, 212-2 can abolish sensory gating as measured by the amplitude of local field responses in rat hippocampal region CA3. Importantly we develop a simple firing rate population model of CA3 and show that gating is heavily dependent upon the presence of a slow inhibitory (GABA_B) pathway . Moreover, a simple phenomenological model of cannabinoid dynamics underlying DSI is shown to abolish gating in a manner consistent with our experimental findings.

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Spatial coherence of visual stimuli modulates synchronized activity in cat visual cortex

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Coherent spatial structure such as "good continuity" is proposed as one of the binding rules in Gestalt psychology, though biological mechanisms for detecting continuity are not well understood. We have found that synchrony in the cat visual cortex shows corresponding modulation when the spatial coherence of visual stimuli is systematically deconstructed, which suggests that synchronized responses in the neural population might play an important role in capturing continuity. We used the Bionics 10x10 microelectrode array to record 49 complex cells from areas 17 and 18 in two paralyzed and anesthetized cats. In order to determine whether synchrony contributes to the encoding of spatial coherence, we presented drifting sine wave gratings with or without phase shifts of segments of the gratings. We created the phase shifts by dividing the regular grating into subregions of equal size along bounds orthogonal to its orientation and assigning an arbitrary phase to each subregion. All stimuli were presented at three different orientations, and subregions were pseudo randomly shifted within ranges of ±180°, ±90°, or ±45° in different trials. We studied only cells (N = 28) that had their preferred orientation no more than 10° away from that of any of the presented stimuli. We quantified synchrony strength by using the cross-correlation histogram derived from the joint post-stimulus time histogram (Aertsen et al. 1989), and compensated for changes in firing rate by normalization. A total of 85 cell pairs showed synchronized responses during stimulus presentation. In more than 80 percent of trials, statistical analysis (Wilcoxon signed ranks test for matched pairs) shows that synchrony induced by stimuli with a larger phase shift range (worse continuity) is significantly lower (p < 0.025) than that induced by stimuli with the same subregion size but smaller phase shift range (better continuity). Our result implies that synchrony can encode changes of spatial coherence in the visual stimulus while the temporal coherence of the stimulus is maintained constant. We propose that cells in the early visual pathway can act as contour detectors, implemented through correlated firing in the neural population.



Figure (A). Drifting sine wave grating with phase shift was used as the stimulus. (B). One example of synchrony change for stimuli with different phase shifts. Filled plot: cross-correlogram (CCG) with the central peak value of 0.030 for stimulus with an average phase shift of 53°; unfilled plot: CCG with the central peak value of 0.044 for stimulus with an average phase shift of 13°.

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