The Eighteenth Annual Barrels meeting will be hosted by the Department of Anatomy & Neurobiology & the Program in Neuroscience at the University of Maryland School of Medicine in Baltimore, Maryland.

**Program:** Includes sessions with invited speakers and short talks open to the audience. A poster session is also scheduled. Sessions focus on:

* Plasticity and Development
* Motor Control
* Encoding of Behaviorally Relevant Stimuli
* Lemniscal & Paralemniscal Pathways

**Invited speakers**:

Laszlo Acsady

MarkAndermann

Scott Chandler

Nathan Cramer

Alev Erisir

Dirk Feldmeyer Anirvan Ghosh

Mark Jacquin

Steve Leiser

Zach Mainen

Cornelius Schwarz

Dirk Schubert

Murray Sherman

Garrett Stanley

**Hotels**: The conference hotel is the Radisson Plaza Lord Baltimore (<http://www.radisson.com/barrels2005>), and rooms can be reserved at that site. The hotel is 0.6 miles from the conference facilities at the university. Additional local hotels that offer discounts to university guests are listed at: <http://www.fincsvc.umaryland.edu/travel/hotels.cfm>.

Some of the closest hotels are:

Marriott Inner Harbor: 0.4 miles; Brookshire Hotel: 0.5 miles; Day's Inn Harbor: 0.6 miles; Holiday Inn Inner Harbor: 0.5 miles; Wyndham Inner Harbor: 0.6 miles.

**Transportation**: Frequent train and bus services serve Baltimore. Baltimore Washington International (BWI) airport serves numerous USA and international destinations, is 15 minutes from the hotel, and is the recommended airport.

**WELCOME TO Barrels XVIII - 2005!**

**Thursday, November 10, 2005**

**Morning**

**8:15 - 8:30 Welcome
8:30 - 9:00 INVITED TALKS on PLASTICITY AND DEVELOPMENT**

**Moderator: Mary Blue – Kennedy Krieger Institute**

**8:30 – 9:00 - Mark Jacquin, Washington University**

**Molecular mechanisms of trigeminal development**

 In our never-ending search for the Holy Grail (gene(s) and/or molecule(s) that pattern the developing CNS), the issues that will be raised in the context of the trigeminal whisker-barrel model system are: 1) signaling mechanisms via neurotrophins, 2) target specification via transcriptional regulators and 3) mechanisms by which promising genes/molecules pattern the developing whisker-barrel neuraxis. These questions are not new ones, but, we offer new approaches based on our ability to manipulate the mouse genome. And, since mice are walking whiskers, there remain low-lying cherries to pick. NIH Program Project grant with especially vital contributions from Drs. Zhou-Feng Gen and Tom Woolsey, of Washington University, and Reha Erzurumlu, of Louisiana State University.

 To date, a relatively small number of molecules have been shown to be necessary for normal patterning of the developing whisker-barrel neuraxis. These are NGF, serotonin, GAP-43, the NR1 NMDA receptor, FGF8, adenylyl cyclase type 1, a subset of ephrins and Eph receptors, and the transcription factor Drg11. All but the first and last of these apply to the developing cerebral cortex. NGF and Drg11 act upon the developing trigeminal brainstem nuclear complex, in particular, the nucleus principalis (PrV), which is the requisite brainstem structure for higher-order thalamic and cortical patterning. And, they are the 2 molecules that our group has revealed as possible PrV pattern makers. Data will be presented on the actions of NGF and Drg11, and related molecules, in the embryonic development of the PrV, its inputs and outputs. Transgenic, pharmacologic and anatomical methods were employed in *in vivo* and *in vitro* preparations.

 It will be shown that exogenous augmentation of NGF or NT-3 levels produces robust and reliable changes in developing V primary afferent projections to the brainstem (elongation and arborization, respectively). However, transgenic deletion of the NGF or NT-3 genes, with or without associated ganglion cell death via additional deletion of the bax gene, fails to alter barrelette formation. Thus, NGF and NT-3 may be sufficient for pattern formation, but they are not necessary. On the other hand, Drg11 and associated upstream transcriptional regulators, such as Lmx1b, are necessary for PrV pattern formation. Concomitant V ganglion cell death in Drg11 and Lmx1b mutants does not appear to be the mechanism by which PrV patterns fail to develop insofar as Drg11/bax or Lmx1b/bax double mutants also fail to develop patterns.
 **“Open Questions” for extensive discussion include: 1) mechanisms by which neurotrophins impact upon pattern formation, 2) mechanisms by which transcriptional regulators impact pattern formation, 3) additional molecules and genes that the audience members now believe are promising players in our search for the Holy Grail, and 4) the extent to which similar mechanisms operate in the development of other CNS structures.**

**9:00 – 9:30 - Anirvan Ghosh, UCSD**

**Regulation of thalamocortical patterning and synaptic maturation by NeuroD2**

 We have been investigating the role of activity-dependent transcription in patterning of connections in barrel cortex. Using a screen to clone calcium-regulated transcription factors (Aizawa et al., 2004) we identified the basic helix loop helix (bHLH) transcription factor Neurogenic Differentiation 2 (NeuroD2) as a factor required for the proper development of thalamocortical connections in barrel cortex. In *neuroD2* null mice, thalamocortical axon terminals fail to segregate in the somatosensory cortex and the postsynaptic barrel organization is disrupted. Additionally, synaptic transmission is defective in thalamocortical synapses in *neuroD2* null mice. Total excitatory synaptic currents are reduced in layer IV in *neuroD2* null mice, and the relative contribution of AMPA receptor and NMDA receptor-mediated currents is altered. The role of NeuroD2 in both the anatomical development and physiological maturation of thalamocortical connections in barrel cortex suggests that it plays a critical regulatory role in the assembly of cortical circuits.

 **Open questions: Is the AMPA:NMDA ratio at a synapse predictive of the potential plasticity at a synapse? Could one ectopically express NeuroD2 to alter the AMPA:NMDA ratio at synapses and shift critical periods? How do other signaling molecules implicated in barrel formation, such as adenylate cyclase and phospholipase, influence NeuroD2-mediated transcription?**

 **9:30 – 10:00 - Alev Erisir, University of Virginia**

**Developmental plasticity of thalamocortical axons in barrel and visual cortices: how**

**similar are they?**

 The critical period plasticity of thalamocortical axons has been most intensely studied in two sensory systems: barrel cortex of the rodents and the visual cortex of several species, including primates, cats, ferrets and rodents. The plasticities of these two model systems are similar in that they both occur shortly after segregation of thalamocortical axons into whisker specific barrels or ocular dominance columns, and that they are marked by robust changes in their primary input connectivity. Their similarities suggest that a common mechanism may mediate the state of vulnerability of developing axons to the changes in sensory stimuli. On the other hand, unique features of the two models in terms of the length of developmental stages, the deprivation paradigms that are used, and the varying ease of accessibility for electrophysiological and anatomical characterizations make it difficult to confirm the presence of analogous mechanisms.
 I will present findings from my lab, describing morphological properties of developing visual thalamocortical terminals during and after the critical period of layer IV plasticity in the ferret. Ferret visual cortex provides a particularly adventitious system to study visual development due to its delayed maturation. Using quantitative immuno-electron microscopy, we have studied thalamocortical terminals during and after the critical period for layer IV plasticity, and identified several morphological parameters that acquired adult-like properties by the end of critical period. These included thalamocortical terminal size, frequency of synapse formation, interactions with dendritic spinules, and the selectivity for interneuron targets. Our data provides anatomical evidence that, as suggested by the slice experiments in barrel cortex, thalamocortical axons preferentially target parvalbumin containing, presumably fast-spiking, cells. Furthermore, the inputs to GABAergic targets constitute a larger portion of thalamocortical input during the critical period of plasticity, suggesting that thalamocortical-driven inhibitory circuitry may mediate the competitive interactions between deprived and nondeprived inputs during the critical period. Similarly, as is the case in barrel cortex, the differences in the changing patterns of NR2 subunits of NMDA receptors in layers IV and II/III suggest a more direct role for NR2B in maintaining plasticity during the critical period. In order to differentiate activity dependent changes that recover in parallel with the effect of sensory deprivation on critical period, we have used a dark-rearing/recovery paradigm. These experiments revealed that while morphological development of thalamocortical terminals was not activity dependent, their connectivity on postsynaptic cells was affected. Recovery of synapsing frequency of thalamocortical terminals, their preference for GABAergic targets, spinule fraction (a possible measure of postsynaptic spine motility), and the reduction of NR2B subunits in layer IV were delayed about 2-3 weeks, the presumed duration of the critical period. In contrast, the surge of NR2A subunit was delayed, yet recovered acutely after 2 days of light exposure. A similar reduction in synaptic receptors, and recovery were observed in adult animals after light deprivation, suggesting that synaptic NR2A subunits are regulated by a mechanism that is dependent on activity but independent of the critical period.
 In light of these findings I would like to **discuss whether layer IV plasticity in barrel and visual cortices might share a common mechanism. As seems to be the case in visual cortex, might neonatal barrel cortex critical period for plasticity foster three independent yet temporally overlapping phenomena: an activity-independent elaboration of segregated thalamic axons, an activity-dependent life-long modulation of synaptic NMDAR, and an activity-dependent vulnerability to sensory deprivation**.

**10:00 – 10:45 Coffee Break segues into discussion:**

**Moderator: Mary Blue – Kennedy Krieger Institute**

**10:45 – 11:45 - Six topical (10 min) talks**

**Eugene F Civillico and Diego Contreras**

**Integration of whisker responses in supragranular barrel cortex studied with optical recordings *in vivo*.**

Department of Neuroscience, University of Pennsylvania School of Medicine

 To study input integration in cortical layer 2/3, we obtained optical recordings (4 ms time step) of responses to paired whisker stimuli in the anesthetized mouse in vivo using the voltage-sensitive dyes (VSD) RH795 and RH1692. We recorded multiunit activity (MUA) and local field potentials (LFP) in barrel cortex from arrays of tungsten bipolar electrodes simultaneously with optical recordings. Post-hoc superposition of barrel boundaries from cytochrome oxidase histology onto optical recordings allowed binning of pixels into signals corresponding to average activity within barrel columns. Single whisker responses had onset latencies of 16-28 ms in the main barrel, with activity spreading over > 80% of the visible barrels by 32-60 ms post-stimulus. For paired stimuli, interstimulus intervals ranged from 0-200 ms. At ISIs of 0, 5, and 20 ms, the VSD, LFP, and MUA responses to paired stimuli consisted of a single transient, often larger in amplitude and integral than either response alone, but never greater than the linear sum of the two. At 50-100 ms ISI, transient responses to both stimuli could be observed, depending on stimulus strength and barrel map location; however, responses to the second stimulus were decreased relative to control and spatially limited to the area overlying the second stimulated whisker’s barrel. Between 100 and 200 ms, the response to the second stimulus recovered to at least its control amplitude and spatial extent. Electrical stimuli delivered to the cortex did not evoke similar ISI-dependent suppression, but summed linearly with subsequent whisker input.

 **\*Andreas Frick, $Dirk Feldmeyer, \*Moritz Helmstaedter and \*Bert Sakmann
Development and short-term plasticity of monosynaptic connections in the cortical L5A network**

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Layer 5A pyramidal neurons represent an important node within the neocortical networks of the rodent barrel cortex: they integrate sensory information arriving via the lemniscal and paralemniscal pathways of the thalamus and, in turn, project to numerous other cortical and subcortical areas. We studied the properties of monosynaptic connections between layer 5A pyramidal neurons during development by performing dual recordings in acute brain slices taken from 14 to 32 day-old animals. The recorded neurons were then reconstructed to determine their morphology and to compute their innervation domains with reference to the corresponding barrels. We found that the properties of this neocortical connection undergo development-dependent alterations. In young animals (P14-16), the reliability of the monosynaptic connection in response to single presynaptic action potentials is high and few failures occur (<5 %). Synaptic efficacy is in the range of 1.1 mV and depresses in response to repetitive presynaptic firing activity (paired-pulse ratio at 10 Hz ~0.7). During maturation of the cortex (P24-P28), the efficacy and reliability of this connection drop considerably. Furthermore, the short-term modification of unitary EPSPs switches from a depressing to a mostly facilitating one. This switch depends on changes in presynaptic mechanisms and can be reversed using the slow Ca2+ buffer EGTA (10 mM). Modulation of the short-term dynamics will strongly affect the information transfer within cortical circuits.

(Supported by Max-Planck Society).

**R. Blythe Towal1 and Mitra J. Hartmann1,2**

**Bilateral Asymmetries in Whisking Patterns of Freely Behaving Rats**

(1) Department of Biomedical Engineering, (2) Department of Mechanical Engineering,

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 During exploratory behaviors, rats typically "whisk" at frequencies of 5 -15 Hz. Several recent studies have reported that macrovibrissal whisking movements are bilaterally symmetric about the snout: right and left whiskers protract and retract simultaneously. Most of these studies were performed in the head-fixed animal, or as the animal was focused on a task that kept the head pointing in line with the animal's body. In a preliminary study, however, we observed that whisking was not bilaterally symmetric about the snout during head rotations. This observation led to the hypothesis that whisking asymmetry compensated for head rotation in order to preserve symmetry in world-centered coordinates. In the present study we investigated this hypothesis using high-speed, infrared video to record whisking behavior during head rotations in the horizontal plane. Consistent with our previous results, we found asymmetric whisking patterns during every episode of head rotation. In all of these episodes the whiskers "led," both spatially and temporally, on the side towards which the head was turning. The amount by which the whiskers led was correlated with the head velocity. We also found dramatic whisking asymmetries even when there was no head rotation. We discuss possible explanations for these exploratory strategies, including the relationship of whisking asymmetry to central pattern generation. Specifically, we propose a coupled oscillator network between the left and right sides, similar to that proposed for control of intrinsic and extrinsic muscles. We suggest that one function of the asymmetric whisking is to allow the rat to "look ahead" with its whiskers on the side towards which the head is turning by an amount equal to the distance that the head will turn during a whisk.

 **PA McRae, MM Rocco, JC Brumberg, and RT Matthews**

**Activity Dependent Regulation of the Extra Cellular Matrix**

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 Activity plays a critical role in the development of mature synaptic connections that ultimately define the functional cortical network in a variety of sensory systems. Previous work in the visual system has shown that certain extracellular matrix molecules (ECM) may play a particularly important role in this process. Here we investigated the activity-dependent expression of the perineuronal net (PN), a component of the ECM, in the mouse barrel cortex. The development of the PN has been shown to be activity dependent in the visual system and is hypothesized to play a role in synaptic stabilization. Preliminary work showed that PNs detected by the antibody Cat-315, which recognizes a glycoform of aggrecan, were particularly enriched in layers IV and VI of the mouse barrel cortex and that the timing of expression of this molecule coincided with the end of the critical period. To determine if expression of the Cat-315 epitope in the barrel cortex was dependent on sensory experience, whiskers were unilaterally clipped every other day from the right whisker pad commencing at birth through postnatal day 30. Nissl staining of the barrel cortex illustrated that the development of the barrels was not altered by this manipulation. However, there was a significant decrease in Cat-315 expression particularly in layer IV of the contralateral barrel cortex of the experimental group when compared to the ipsilateral hemisphere and control animals. The ipsilateral hemisphere also displayed a decrease in Cat-315 with a level of expression that was intermediate to the contralateral hemisphere and the control animals. There was no change in PN development in other areas of the cortex that were studied. These data suggest that the expression of aggrecan and PNs in the barrel cortex are activity-dependent and suggest an important role for the ECM in regulating plasticity in the somatosensory cortex. This research was supported by NIMH grant T32 MH18882 and PSC-CUNY.

**Michael J. Higley and Diego Contreras**

**Cellular Mechanisms of Cross-Whisker Suppression**

University of Pennsylvania, School of Medicine

 Suppression of sensory-evoked responses by stimuli presented to neighboring regions of the receptive field is a ubiquitous phenomenon in the nervous system. Within the rat barrel cortex, the response to principal whisker (PW) deflection is suppressed by prior deflection of an adjacent whisker (AW), although the mechanisms underlying this effect are unclear. The hypothesis that suppression relies on intracortical inhibition is not consistent with intracellular studies revealing that the magnitude of inhibition does not correlate with the amount of suppression observed. In the present study, we used current source density analysis to quantify suppression before and after cortical inactivation by the GABA agonist, muscimol. Surface-applied muscimol completely blocked intracortical activity, leaving thalamic responses intact. However, the magnitude of cross-whisker suppression was unchanged, demonstrating that suppression cannot be explained via intracortical mechanisms. Extracellular thalamic recordings revealed suppression similar in magnitude to that observed in the cortex. However, intracellular recordings did not reveal strong whisker-evoked inhibition in the thalamus. Instead, PW-evoked PSPs, presumably originating from trigeminal inputs, exhibited a reduction in magnitude following AW deflection, consistent with previous reports of trigemino-thalamic synaptic depression. We suggest that cross-whisker suppression originates largely from trigemino-thalamic depression occurring at synapses shared by AW and PW pathways.

 **Peter W. Land and Susan L. Erickson**

**Sub-barrel domains in rat S1: fact or fantasy?**

Department of Neurobiology and Center for Neuroscience, University of Pittsburgh, School of Medicine, Pittsburgh, PA 15261

 Barrel hollows in rat Posteromedial Barrel Subfield (PMBSF) encompass a variety of functional domains, containing for example multiple minicolumns of neurons preferring the same angular deflection of the principal whisker. Using cytochrome oxidase (CO) histochemistry in conjunction with other histological and immunochemical methods we found that rat PMBSF barrels also are structurally heterogeneous. Individual barrels can be composed of two or three, discrete sub-barrel-sized domains. Detailed analysis reveals that sub-barrel domains are relatively consistent in size, having average dimensions that approximate those of large barrels in mouse S1. Sub-barrels are organized into several distinct, repeated patterns. Barrel hollows in rat Anterolateral Barrel Subfield and all barrel hollows in mouse S1 appear to consist of single CO domains. Sub-barrels revealed by CO are columnar entities that correspond with cyto- and myeloarchitectonic inhomogeneities within the barrels. Immunostaining for VGLUT2 and 5-HTT shows that sub-barrels demarcate regions densely innervated by thalamocortical (TC) terminals. Unexpectedly, whereas TC terminals are plainly clustered into barrel rows and arcs from P-4 onwards, sub-barrels are not discernable with probes for TC terminals or with CO until after P-8. The coincident emergence of sub-barrels and patterned TC inputs suggests the intriguing possibility that their development may be causally linked.

**11:45 – 12:15 Discussion
12:15 – 1:30 Business meeting and lunch**

**Thursday, November 10, 2005**

**Afternoon**

**1:30 – 3:30 INVITED TALKS on MOTOR CONTROL**

**Moderator: David Kleinfeld, UCSD**

**1:30 – 2:00 Nathan Cramer, University of Maryland Medical School**

**Cortical Control of a Whisking Central Pattern Generator**

 Our current investigations examine the role of the vibrissae motor cortex (vMCx) in modulating the output of a whisking central pattern generator (CPG) and the contributions of recruited motor units to the production of vibrissae movements. Additionally, we investigate the contributions of putative serotonergic CPG components likely to play a critical role in generating rhythmic whisking. During intracortical microstimulation (ICMS) evoked movements, motor units were typically recruited in a stereotypical order such that the amplitude of whisker movements was positively correlated with the number of active motor units. Additionally, active motor units often increased their firing rates as movement amplitudes increased. Thus, vMUs use a combination of motor unit recruitment and rate coding to generate vibrissae protractions. ICMS of the vMCx evoked rhythmic vibrissae movements at frequencies distinct from the stimulation frequency. Larger stimulation intensities were associated with higher frequency of evoked movements and a reduction in the latency to movement onset. Variations in the stimulation frequency had less of an effect on evoked movement kinematics. As was previously observed in voluntary whisking, infusion of the 5HT2 antagonist metergoline into the lateral facial nucleus reversibly degraded ICMS evoked movements. These results support the hypothesis that rhythmic whisking is produced by a whisking CPG, with a prominent serotonergic component, under modulatory control of the vMCx.

 **Open questions include: (1) Vibrissa motoneurons receive inputs from numerous subcortical structures, as well as the motor cortex. The diversity of inputs appears to exceed the network necessary for producing the relatively simple kinematics associated with whisking. What might be the function of having such a range of inputs to vibrissa motoneurons? (2) Mammals that use mystacial vibrissae to gather information about their environment show varying levels of control over vibrissal movements. Rodents, such as the mouse and rat, actively move their vibrissae to palpate objects while vibrissae in other mammals, such as the cat, are more passive in nature. What advantages might be gained by having active control over vibrissae movements?**

 **2:00 – 2:30 Scott Chandler, UCLA**

**Factors controlling rhythmical burst discharge in oral-motor circuits**

The cellular and network processes controlling oral-motor related rhythmical behaviors such as mastication, suckling, and swallowing, are just beginning to be understood. Recently, information on the localization of the most basic rhythmogenic circuits underlying oral-motor activity has been obtained. Yet, the precise synaptic connectivity which allows for the emergence of this activity is not well understood. A hallmark signature of rhythmical oral-motor activity is rhythmical burst discharge in certain trigeminal sensory and motoneurons, as well as interneurons. Although our knowledge of the precise synaptic connectivity within the pattern generating circuits is not known, we are starting to understand the cellular processes responsible for burst pattern generation. Clearly, the seamless integration of the various intrinsic membrane conductances with activation of synaptic ion channel activity in neurons within the associated oral-motor circuits is a critical process that must occur for production of the appropriate neuronal discharge patterns. Recent data suggest that a subpopulation of sensory and interneurons near the trigeminal motor nucleus posses intrinsic conditional burst generating properties that may form the kernel for oral-motor rhythm generation. In this presentation, I will discuss the cellular mechanisms underlying rhythmical burst discharge in those neurons. **An open question for discussion is: What -- if anything -- can we learn from studies of the masticatory CPG about the likely nature of the vibrissal CPG.**

 **2:30 – 3:00 Cornelius Schwarz, Hertie Institute for Clinical Brain Research, University of Tubingen**

**Role of Movement Related Central Signals for Active Touch**

 Animals actively explore their environment in varied ways to optimize sensory input. Actively collected sensory information has the advantage that it is tailored to serve best the behavioral purposes of the animal. But in exchange, this kind of data has to be carefully weighted and interpreted with reference to the explorative strategy used. We use the rat’s vibrissal system as a model system to study adjustment of tactile signals by signals related to explorative movement. Experiments with head-fixed rats trained to whisk toward a moving object and precise whisker tracking allowed us to disentangle sensory and motor aspects of active touch. Recordings in barrel cortex revealed a movement dependent excitatory signal that was correlated with a reduction of the tactile response and its cortical spread. The non-rhythmic nature of the modulatory signal indicated a central origin, a notion confirmed by its intactness and its continued modulatory role after deafferentation. General states of vigilance were unlikely to be at the base of the observed modulation as suggested by spectral analysis of field potentials prior to active and passive touch. The association to movement, on the other hand, was found to be temporally precise such that movement initiation or cessation would switch between active and passive touch within 100-125 ms.

 Pursuing the working hypothesis that the non-rhythmic modulatory signals might stem from the motor system we investigated vibrissal motor cortex which is upstream of presumed rhythm generating circuits in the brainstem. We localized a small sub-region of vibrissal motor cortex (RW) that, indeed, generates natural-like rhythmic whisking at frequencies around 7 Hz when electrically stimulated with long stimulus trains at high frequencies. At the time of writing this abstract we had looked at first preliminary unit recordings within RW during self-initiated whisker movements tentatively confirming its non-rhythmic nature. Combined stimulation of RW and barrel cortex in awake animals showed that RW activation mimics effects of self-initiated active touch in barrel cortex.
 In summary we have established model system that allows us to study central modulation of tactile processing for active perception in rat’s vibrissal system. **Open questions are waiting to be answered on the structural as well as the behavioral level. Structurally, it will be important to figure out the origins and pathways involved in the interference and whether the modulation found can be taken as a general model of cortical inter-areal signal processing. Behaviorally, it will be important to investigate the detailed perceptual benefit of the central modulation found.**

 **3:00 – 3:30 Zach Mainen, CSHL**

**Sniffing patterns in rats performing an olfactory behavioral task**

 Olfaction depends critically on an active motor process, sniffing, to draw air through the nasal epithelium. Sniffing is proximally controlled by a central pattern generator (CPG) in the brainstem, but little is known about the central regulation of the respiratory rhythm during behavior. To understand how sniffing pattern is controlled we recorded sniffing in rats performing an olfactory discrimination task. Rats were trained to discriminate two odors in binary mixtures. Upon entry into the odor-port a computer-controlled olfactometer directed odor flow into the port. The odor with the higher concentration instructed the response to the left / right choice ports and correct decisions were rewarded with water. Rats were implanted with a thermocouple in one nostril to measure the temperature changes between inspired and expired air. This allowed us to register sniffing on a cycle-by-cycle basis. Respiration frequency varied over a wide range (<2 Hz to >12 Hz) during the course of a behavioral session, systematically changing in relation to significant behavioral events such as entry into the odor sampling or reward ports. Rather than a continuous distribution of frequencies, discrete frequency modes were observed. Rats switched to a theta frequency mode (7-10 Hz) shortly before (self-initiated) odor port entry and remained tightly locked to this frequency mode throughout odor presentation. We also observed another, higher frequency (9-12Hz) sniffing mode during reward anticipation, starting before entry into the choice ports and ending when water was received. The switch between different modes occurred very rapidly, almost always within a single respiration cycle. The timing of respiration was related not only to the sensory demands of odor sampling but also to other motor processes. In particular, the timing of head retractions from the odor and choice ports was precisely coordinated with the respiratory cycle. These findings document how task requirements actively direct olfactory sampling and demonstrate that respiratory rhythms interact tightly with reward and locomotor systems. Although we did not monitor whisking in these experiments, previously studies have documented rhythmic coupling between sniffing and whisking, suggesting strong commonalities between the motoric aspects of these modalities.

 **Questions for discussion include: (1) What is the significance of particular frequencies of rhythmic sampling to the extraction of sensory information? (2) Are specific frequencies dictated by the intrinsic physical or neural constraints of individual sensory systems? (3) Does rhythmic coupling of multiple sensory-motor systems reflect constraints of the underlying CPGs? (4) How might inter-modality coupling facilitate neural integration across sensory and motor systems?**

**3:30 – 4:15 Coffee break segues into discussion**

**Moderator: David Kleinfeld**

**4:15 - 5:45 Eight topical (10 minute) talks (and one special video)**

**MM. Rocco, A. Barczak, S. Dave, D. Micic, JC. Brumberg**

**Anatomy and physiology of the interactions within the sensorimotor system**

Department of Psychology, Queens College; Neuropsychology PhD Subprogram, The Graduate Center, CUNY

 Interactions between the primary motor (M1) and somatosensory (S1) cortices are crucial to an animal’s ability to constantly update its motor plans in response to changes in the sensory environment. Within both M1 and S1 there are maps of the body surface such that stimulation in specific motor areas results in stereotyped movements and stimulation of the sensory periphery results in neuronal firing in S1. Using the mouse as a model system we have explored the anatomical basis and the physiological interactions of the sensorimotor system. We stereotaxically targeted injections of either rhodamine labeled microspheres, biotinylated dextran amine, fluoro-emerald or fluoro-ruby into the whisker representation of either S1 or M1 cortex. Results indicate that the majority of S1 neurons that project to M1 reside in layer V and have a stereotyped morphology and are reciprocal in their connectivity. M1 projecting cells in S1 appear to be localized to the barrel periphery and septa while avoiding the barrels themselves. Preliminary data suggests these projections are preferentially organized across barrel rows. In vivo recordings in anesthetized mice (ketamine/xylazine) reveal that electrical stimulation of M1 evokes contralateral whisker movement and neuronal activity in S1. The strength of the feedback connection from M1 to S1 is stimulation frequency dependent. Low frequency stimulation of M1 evokes reliable activity in S1 whereas higher frequency stimulation results in less activity. To further study this connection we have developed an in vitro slice preparation that maintains the synaptic connectivity between S1 and M1. Stimulation in one area results in activity in the reciprocal area that is blocked by the glutamatergic antagonists CNQX and APV. We are utilizing this novel preparation to study the interactions between these two distinct cortical areas. Our results suggest that S1 and M1 in the mouse are strongly interconnected and that the strength of this connection is sensitive to the firing frequency of the projecting neurons. The plasticity of the sensory-motor connection may allow the animal to constantly adapt its motor program to new sensory challenges.

**George Fraser, Jed Hartings and Daniel Simons**

**Adaptation in the trigeminal ganglion**

Dept. Neurobiology, University of Pittsburgh School of Medicine

Pittsburgh, PA

 Studies of central neurons in the whisker-to-barrel pathway have consistently described adaptation effects produced by repetitive stimulation. Adaptation to periodic stimuli, typically thought of as a circuit phenomenon, is in fact also present in recordings in the trigeminal ganglion. Trigeminal responses can adapt as much as 20% during a 1 sec, 40 Hz train of brief pulsatile deflections. This finding led us to develop a theory of trigeminal adaptation based on tissue compliance. We believe that the whisker follicle, following the first few deflections, moves out of its resting position to a deflected position. Subsequent deflections provide less relative displacement to the out-of-position follicle. In order to test this idea, we used neuromuscular paralysis as a manipulator of facial tissue compliance. In accordance with our theory, trigeminal responses to periodic deflections adapted more quickly in paralyzed animals. Visualization of tissue displacement around the base of the hair confirmed that the whisker pad undergoes a lateral translation in the direction of whisker deflection during repeated stimulation. These findings underscore the importance of taking into account the firing properties of primary afferent neurons when interpreting data from central neurons.

**B. Mitchinson**

**Whisking control in the freely behaving rat**

Adaptive Behaviour Research Group, University of Sheffield, UK.

 Experiments using high-speed video recording indicate that both inter- and intra-whisk parameters of whisking patterns in freely behaving rats are affected by contact of the whiskers with the environment (Prescott et al., SFN 2005). These effects tend both to minimise impingement of the whiskers on the environment during protraction, and to maximise the number of whiskers that make contact with a stimulus. Here, we investigate bilateral whisking control in freely behaving dystrophic RCS rats, relating whisking power on each side to the location of obstructions in the vicinity of the head. Semi-automatic video tracking is used to locate the animal in a rectangular arena, and a skull-mounted radio transmitter relays bilateral mystacial EMG. We find that unilateral caudal obstruction generally elicits a reduction in ipsilateral activity, whilst more rostral unilateral obstruction elicits increased bilateral activity.

**Randy Bruno, Heinz Horstmann, Bert Sakmann & Winfried Denk**

**Number and location of synapses made by a single thalamocortical axon onto a cortical neuron**

Max Planck Institute for Medical Research

 Most of our knowledge about synaptic physiology and anatomy has been derived from *in vitro* slice experiments. A connected pair of thalamic and cortical neurons has, however, proven exceedingly difficult to capture in a single slice due to the long tortuous path that thalamocortical axons travel. Here, we combine two techniques, juxtasomal filling and serial block-face scanning electron microscopy (SBFSEM), to precisely determine both the number and locations of all the contacts made by a single thalamocortical axon onto a post-synaptic partner. A single neuron or bulk population in the thalamic ventroposterior medial nucleus (VPM) of young (P28-35) Wistar rats is filled *in vivo*, and a cortical layer 4 neuron in the corresponding somatotopically-aligned barrel is subsequently labeled. Receptive fields of these cells are mapped by controlled deflection of the facial whiskers. After fixation, a SBFSEM is used to generate with ultrastructural resolution (50 nm3 voxels) a 3-dimensional reconstruction of the entire cortical neuron. We are presently comparing the numbers and distributions of synapses onto excitatory and inhibitory cortical cells as well as testing the hypothesis that anatomical synapses are made almost entirely between thalamic and cortical cells having matching receptive fields. Supported by the Max Planck Society

**V.Khatri and D.J.Simons**

**Adapted responses of barrel neurons receive distinct contributions from thalamic and intracortical inputs**

Dept. of Neurobiology, Univ. of Pittsburgh, Pittsburgh, PA, USA 2. Center for the Neural Basis of Cognition, Pittsburgh, PA, USA

 Previously, we demonstrated that in barrel RSUs (regular-spike units) or putative excitatory cells, angularly-nonspecific suppression is accompanied by a relatively small but significant angularly-specific component (Khatri and Simons, 2004). In the present study, we test the following hypotheses: 1) angularly-specific suppression is mediated by thalamocortical inputs and/or the short-term depression of thalamocortical synapses and 2) angularly-nonspecific suppression is produced by angularly-nonspecific intracortical interactions (broadly-tuned inhibition and/or synaptic depression among RSUs with dissimilar angular tuning). To dissociate contributions of thalamocortical and intracortical interactions, adapting whisker deflections were delivered and thalamic neurons were adapted while suppressing cortical activity with electrical stimulation. Prior to presenting adapting stimuli, the angular tuning of single and multi-unit barrel activity (n = 22) was characterized to determine preferred and anti-preferred angles of whisker movement. Subsequently, adapting stimuli and electrical stimulation were presented together or alone prior to test deflections in the preferred direction. Despite electrical stimulation alone strongly suppressing barrel neuron responses to whisker deflections (mean amount of suppression = 60%, range = 0 to 100%), the amount of angularly-specific suppression remained the same regardless of whether or not cortical activity was strongly suppressed. The responses evoked by the test deflection were ~30% smaller when preceded by preferred versus anti-preferred adapting angles irrespective of the magnitude of electrically-evoked cortical suppression. Thus in barrel RSUs, these findings suggest that thalamocortical inputs and/or their short-term depression produce angularly-specific suppression whereas intracortical interactions are a source of angularly-nonspecific suppression. SUPPORTED BY NIH NS19950.

**Carl Petersen, Sylvain Crochet and Isabelle Ferezou**

**Whole-cell recordings and voltage-sensitive dye imaging in the barrel cortex of awake mice.**

Laboratory of Sensory Processing, Brain Mind Institute, Ecole Polytechnique Federale de Lausanne, Switzerland.

 Little is known about the synaptic events underlying brain states, sensory processing and perception in awake mice. In order to begin exploring these complex issues, we have correlated membrane potential changes with mouse behaviour. Whole-cell recordings measured the membrane potential of individual neurons in the somatosensory barrel cortex of awake head-fixed mice. Voltage-sensitive dye imaging measured ensemble membrane potential changes across the whisker map of the barrel cortex in awake freely moving mice. Mouse behaviour was quantified by high speed tracking of whisker movements. Slow and large-amplitude membrane potential changes and propagating waves of activity occurred spontaneously during quiet behaviour. During whisking membrane potential changes were smaller, more rapid and correlated with whisker movement in some neurons. Passive whisker stimulation during quiet behaviour evoked large-amplitude postsynaptic potentials (PSPs) compared to the smaller amplitude PSPs evoked by passive stimuli during whisking periods. However, large PSPs were evoked during whisking as a mouse actively touched an object. Therefore sensory processing in mice during quiet behaviour is highly sensitive to passive stimulation, whereas during whisking the sensory cortex responds well to whisker-guided object detection.

**Hui-Chen Lu, Daniel A. Butts, Pascal S. Kaeser, Wei-Chi She, Roger Janz, and Michael C. Crair**

**Barrel map development relies on efficient neurotransmitter release**

Department of Neuroscience, Program in Developmental Biology, Baylor College of Medicine

Cortical maps are characterized by remarkable precision with organized arrays of thalamocortical afferents (TCAs) that project into distinct neuronal modules. Here we present evidence that efficient neurotransmitter release is crucial for mouse barrel map development using *barrelless* mice, a loss-of-function mutant of calcium/calmodulin-activated adenylyl cyclase I (AC1). We demonstrate that release efficacy is substantially decreased in *barrelless* TCAs. We identify RIMs, active zone proteins that regulate neurotransmitter release, as important AC1 targets in the presynaptic terminal. We further show that RIM1α mutant mice have cortical barrel pattern and TCA neurotransmitter release deficits, reinforcing the role of RIM proteins in mediating AC1 signaling in barrel map development. Finally, we present a model to show how inadequacies in presynaptic function will interfere with activity-dependent processes in neuronal circuit formation. These results demonstrate that the development of cortical barrel maps relies on efficient synaptic transmission that is mediated byAC1 function.

**Kevin D. Alloway, Li Lou, Fidel Nwabueze-Ogbo, Shubhodeep Chakrabarti**

**Origin of SI Barrel Cortex Projections to MI, SII, and the Neostriatum**

Penn State University Hershey Medical Center

 We recently reported that SI projections to MI originate primarily from neurons located above and below the layer IV septal region [J Comp Neurol 480:299, 2004]. While it is known that SI also projects to SII and the neostriatum, the origin of these projections has not been determined with respect to the septal and barrel regions. To address this issue, we injected retrograde tracers (cholera toxin subunit B, Fluoro-Gold, True Blue) into SII or into the neostriatum, and then we reconstructed the labeled SI neurons with respect to the barrel and septal compartments of layer IV. After injecting SII, labeled neurons were found in the extragranular layers of SI barrel cortex and were uniformly distributed with respect to the septal and barrel regions. After injecting the neostriatum, labeled neurons appeared primarily in cortical layer V, and these were uniformly distributed with respect to the barrel and septal regions of layer IV. In summary, MI receives selective information mainly from neurons associated with the septal regions, but the information sent to the neostriatum and SII is less selective and originates from both the septal and barrel compartments.

**5:45 -- 6:15 Discussion
6:15 onwards -- Dinner, discussion, and posters**

**Friday, November 11, 2005**

**Morning**

**8:30 – 10:00 INVITED TALKS on ENCODING OF BEHAVIORALLY-RELEVANT STIMULI**

**Moderator: Ehud Ahissar**

**8:30 - 9:00 Mark Andermann, MIT**

**Systematic Mapping of Frequency, Somatotopy and Direction in Rat SI**

 Most mammals have high-resolution visual perception, with primary visual cortices that contain fine-scale, inter-related representations of multiple features (e.g., ocular dominance and orientation). Rodents lack precise vision, but their vibrissa sensory system provides a high-resolution tactile modality. An understanding of the organization of feature maps in barrel cortex could provide important clues to the computational strategies employed during tactile perception. Previously, we described a resonance-related map of high frequency stimuli across arcs of barrel columns. Here, we examined the hypothesis that systematic sub-barrel organization exists for multiple representations. Using a novel, omni-directional stimulator and multi-tetrode recordings, we delineated somatotopic and directional receptive fields from 9 vibrissae simultaneously at multiple cortical locations. We found precise somatotopy within a vibrissa column, resolved at a scale of ~50mm. A direction preference map was systematically linked to this somatotopic gradient along the rostral-caudal axis, such that neurons were tuned for motion towards their preferred surround vibrissa. This sub-barrel direction map was present in layers IV and II/III, and demonstrated an emergent refinement in the supragranular layers. These data show that multiple feature properties are somatotopically organized within a barrel, and suggest that systematic maps are a common property of high-resolution sensory systems across multiple spatial scales **Open questions include: (1) What is the utility (if any) of feature maps in barrel cortex for perception? (2) Does the high resolution of the vibrissa sensory system dictate that multiple features must be represented on the primary sensory sheet, as already observed in primary visual and to some extent primary auditory cortices?**

**9:00 – 9:30 Steve Leiser, Children’s Hospital of Philadelphia**

**Responses of Trigeminal Ganglion Neurons during Natural Whisking in the Awake Rat**

Rats use their mystacial whiskers to locate and discriminate tactile features of their environment. Surrounding each whisker follicle are mechanoreceptors that transduce movements and deflections of that whisker into electrical impulses that are transmitted to the brain via primary afferent neurons whose somata are located in the trigeminal ganglion (Vg). Extracellular recordings in the Vg have classified two distinct types of cells by their response to ramp-and-hold whisker stimulation, rapidly-adapting (RA) and slowly-adapting (SA). The activity of these cells in the awake rat is unknown.
Therefore, we developed a method to chronically record Vg neurons in the awake rat to identify their firing patterns under natural whisking behaviors. Our findings show that all cells recorded had (1) no activity when the whiskers were not in motion, (2) significant activity when the rat was whisking in air – well correlated with whisk frequency and (3) a further increase in activity when the whiskers contacted an object. These results suggest all cells provide information about the movement of whiskers in air and are capable of encoding information regarding contact with an object.

 Furthermore our data also suggest that there may be some differences in the precise nature of the information encoded between RA and SA cell populations. During whisking in air SA cells fired an average of 3.5 spikes per whisk while RA cells fired less than one spike per whisk. However, individually, SA cells demonstrated a broader range of spikes per whisk than RA. When comparing their responses to contact, RA cells increased their activity more than SA cells. While these results can not explicitly delineate what properties of the stimulus RA and SA cells encode because the animals were allowed to freely move within the recording chamber, they do suggest that the classical RA and SA division of cell types in the Vg has relevance for understanding how cells in the Vg encode somatosensory stimuli and require further study.

 **Open Questions: Are the differences we see in RA and SA cell activity relevant for encoding sensory information? If so, what do RA and SA cells encode? If not, why have RA and SA cell types?**

 **9:30—10:00 Garrett Stanley, Harvard University**

**Neural Representations of Tactile Patterns**

 (Speaker's note: experiments were conducted by Roxanna M. Webber and Alireza S. Boloori)The vibrissa pathway transforms features of the tactile world into neuronal representations which ultimately form the animal’s perception of surfaces and objects in the outside world. Understanding the relationship between the sensory stimulus and the corresponding neural representation is a crucial step in identifying the ethologically relevant elements of the neural code. We have previously shown that the cortical response to tactile patterns can be well predicted from the observed response characteristics for paired vibrissa deflections. Specifically, the cortical response to complex patterns of relatively low frequency (< 40Hz) vibrissa deflections is largely predictable from a nonlinear combination of underlying constituent elements. These constituent elements reflect the time-course of post-excitatory response suppression revealed through a paired-deflection “condition/test” stimulus paradigm. More recently, we have shown that the cortical representation of even more complex spatiotemporal patterns is similarly predictable from the simple paired-vibrissa interactions, and that the relative phase of periodic stimuli across vibrissa strongly influences the cortical response. Taken together, these nonlinear neuronal interactions 1) shape the transient and steady-state adaptation response, 2) predict the response heterogeneity observed experimentally across cortical cells, and 3) set theoretical limits on discriminability based on a simple ideal observer of cortical activity.

 **Open Questions: What are the relevant frequencies, and how do we resolve low frequency and high frequency findings? How are these response properties modulated by behavioral state? What is the functional role of adaptation?**

**10:00 – 10:45 Coffee break leads directly into discussion**

**Moderator: Ehud Ahissar**

**10:45 – 11:45 Six topical (10 minute) talks**

**John Curtis and David Kleinfeld
Cortical neurons that code vibrissa contact in face-centered coordinates**

UCSD
 We address the nature of contact -induced spiking in vibrissa primary sensory (S1) cortex of rat. In our paradigm, rats are trained to perch while whisking and to contact a sensor with one or more vibrissa in return for a liquid reward. We record single-unit spikes from vibrissa S1 cortex, along with the electromyogram of the mystacial pad as a surrogate for vibrissa position and the time and extent of vibrissa contact. We observe two classes of units in which the contact-induced response in S1 cortex is conditional on the phase (or position) of the vibrissa within the whisk cycle. In essence, these units report contact in face-centered coordinates. In one class, contact leads to a transient increase (~ 20 ms) in spiking over a small range of the whisk cycle. In a second class, contact leads to a sustained (~ 200 ms) increase in spiking. This response acts as a short-term memory of contact. Finally, a third class of response is the sustained inactivation of units upon contact. The computational consequences of all three signals for motor control will be discussed.

 **Susan L. Erickson and Peter W. Land**

**Inhibitory interneurons and cortical columnar organization**

University of Pittsburgh School of Medicine Dept. Neurobiology

 Different classes of inhibitory neurons are postulated to participate in inter- versus intracolumnar information processing in the cortex. In tangential slices through rat S1 we found four morphologically distinct subtypes of interneurons, each bearing a unique relationship to the columnar modules of the local barrel and sub-barrel architecture. Large basket cells (LBCs) have broad axonal arbors that extend into the surrounding septum and often into neighboring barrels. Within their home barrels, LBC axons innervate all sub-barrel compartments. In contrast, small (SBC) and nest basket cells (NBCs) axons are typically limited to a single sub-barrel compartment. All basket cells have simple dendritic arbors that are smaller than the axon. Finally, dendrite-targeting neurogliaform cells (NGCs) have very small axonal arbors that are coextensive with their dendritic domains, and approximate the dimensions of physiologically defined cortical minicolumns. The axons of all four cell types commonly distribute anisotropically with respect to the cell soma. Interestingly, for SBCs and NGCs, sub-barrel borders and barrel sides both appear to constrain the distribution of processes. These data provide evidence that different classes of inhibitory neurons serve to coordinate activity 1) between barrel columns, 2) within sub-barrels, or 3) at the minicolumn scale.

 **Jason Ritt and Chris Moore**

**High-speed videography of rats exploring textured surfaces**

MIT McGovern Institute

Elasticity dominates vibrissa motion in many contexts, as exemplified bymechanical resonance. In anesthetized animals, peripheral and cortical units are frequency-tuned consistent with principal vibrissa resonance. In recent work we explored other mechanical components, notably stick-slip due to friction, and found motions that are not predicted by surface profile alone. It is unclear what contribution these mechanical properties make, if any, to sensory behavior in the awake rat, or if rats actively manipulate the expression of vibrissa mechanics by adapting whisking motions to sensory context. Specifically, the extent to which resonance and related phenomena occur during behavior is unknown. We have initiated high resolution videography of vibrissa motions in awake rats freely exploring precision milled textures. As expected from our previous work and consistent with data from other labs, we observe elastic oscillations of vibrissae as rats whisk the textures. Oscillation frequencies appear to be vibrissa dependent, while the occurrence of oscillations depends on the whisking context. We have begun quantifying fast transients due to interactions with the surface (e.g. displacements and velocities). Relating task performance to mechanical responses, and

their modulation by sampling strategy, is ongoing.

 **Lu Li and Ford F. Ebner**

**Barrel cortex actively redefines the tuning maps in rat thalamus.**

Department of Psychology Vanderbilt University Nashville, TN 37203 USA

 Computational maps within neural structures are thought to include mechanisms for optimizing the representation of behaviorally relevant information. We investigated the role of cortical feedback on dynamic adjustments in one such map: whisker angular tuning in the thalamus of the rats¡¯ vibrissa system. Single VPM neurons were mapped for their principal whisker and angular tuning preference at low intensity (2X threshold). Another microelectrode was advanced into layer VI of the ipsilateral homologous barrel column and the angular tuning properties of cortical neurons along the penetration were also mapped. Then, the upper section of layer VI of the appropriate barrel column was stimulated electrically for 30 minutes. Comparing the angular tuning properties of the same VPM relay neuron before and after cortical microstimulation identified a profound impact on angular tuning. When the stimulated layer VI neurons in the appropriate barrel were tuned to the same preferred direction of whisker movement as the thalamic neurons, stimulation of layer VI sharpened the angular tuning curve the VPM cell by increasing the response to the ¡°preferred¡± direction. In contrast, when the stimulated layer VI neurons in the appropriate barrel were tuned to non-preferred directions of the thalamic neuron, stimulation of layer VI either broadened the angular tuning curve by reducing the response to the “preferred” direction, or shifted the angular tuning preference of the thalamic neuron towards the preferred direction of the cortical neuron. We conclude that cortical inputs continually influence many properties of thalamic VPM neurons, one way being to bias the thalamic relay neurons to be most sensitive to the most frequent direction of whisker stimulation. (Supported by grant NS 25907)

 **de Kock CPJ, Bruno RM, Spors H and Sakmann B
Laminar comparison of suprathreshold receptive fields in rat barrel cortex using *in vivo* juxtasomal recordings**.

Max-Planck Institute for Medical Research Jahnstrasse 29 D-69120 Heidelberg Germany

 Sensory inputs could be encoded in the brain by fewer neurons firing a smaller number of action potentials (APs) than previously thought. This is known as “sparse coding” and has been suggested for many cortices including the barrel cortex. The barrel cortex of rodents processes information arriving from the facial whiskers and projects to second order brain areas where animal behavior is ultimately determined. To understand how information from the whiskers is translated into behavior it is therefore crucial to know how sensory input is coded in the barrel cortex. We used juxtasomal recordings to characterize AP firing and receptive field (RF) size in response to controlled mechanical deflection of individual whiskers. This technique is not invasive to the cell but still allows for morphological identification of the recorded cell (Pinault, JNeurosci Methods 1996). Recordings were made in the major input layer (L4) and output layers (L2/3, L5A and L5B) of the barrel cortex of urethane-anaesthetized Wistar rats (P25-30). Subsequently, the recorded cell was filled with biocytin for morphological identification and 3D reconstruction. Septal-related and inhibitory neurons were excluded from the analysis. Our results suggest that L5B cells dominate the output of the barrel cortex. Nevertheless, evoked firing rates across layers were low, supporting the idea of sparse coding in barrel cortex.

 **J. Alex Birdwell2, R. Blythe Towal1, Joseph H Solomon2, and Mitra J. Hartmann1,2**

**A role for dynamics in the extraction of 3-dimensional object features during whisking**

(1) Department of Biomedical Engineering, (2) Department of Mechanical Engineering, Northwestern University, Evanston, IL, USA, 60208

 Studies of the rodent vibrissal-trigeminal pathway typically examine neural responses to kinematic variables such as angular position, velocity, and acceleration, but neglect whisker dynamics (forces and torques). Using a micromechanical force tester, we measured forces at the base of isolated whiskers as they were deflected into objects placed at different radial distances. Digital photographs were taken to characterize the whisker shape at each displacement step. Our results show that torque information at the whisker base is directly related to whisker curvature, and is sufficient to extract information about radial object distance. In addition, the shape of the whisker during bending was found to be consistent with predicted deflections based on a cantilever beam model. Using a hardware (robotic) whisker array, we then demonstrated that three variables – angular position, velocity, and torque, are sufficient for the complete 3-dimensional extraction of object features. We conclude that torque is likely to be important parameter during whisking behavior, and provide preliminary evidence for the presence of torque-sensitive cells in the trigeminal ganglion.

**Friday, November 11, 2005**

**Afternoon**

**1:15 – 3:15 INVITED talks on LEMNISCAL and PARALEMNISCAL PATHWAYS Moderator: Martin Deschenes – Laval University**

**1:15 – 1:45 Laszlo Acsady, Institute of Experimental Medicine**

**Selective GABAergic control of the paralemniscal pathway in the thalamus**

  The response properties of the lemniscal and paralemniscal pathways greatly differ at the level of thalamus. Activity of the lemniscal axons, which originate in the principal trigeminal nucleus reliably evokes action potentials in the ventral posteromedial nucleus (VPM). In contrast neurons of the n. posterior (Po) which receive paralemniscal inputs from the interpolaris nucleus of the trigeminal complex respond poorly to whisker deflection.

 In this study first I demonstrate that the sluggish responses of Po neurons are not the consequence of weak peripheral drive. Axons originating in the interpolaris nucleus were found to establish large excitatory terminals on the proximal dendrites of relay cells via multiple release sites. These ultrastructural features are compatible with peripheral excitatory driver afferents. Po neurons, however, were found to be contacted also by peculiar large GABAergic terminals. These GABAergic boutons differed qualitatively from the well-known GABAergic input arising from the reticular nucleus. Indeed, anterograde and retrograde tract-tracing studies disclosed that these GABAergic axons arise from extrareticular sources i.e. from the zona incerta (ZI) and the anterior pretectal nucleus (APT), two diencephalic nuclei located ventrally and caudally to the thalamus. APT and ZI terminals preferentially innervated the proximal dendrites of relay cells in Po via multiple (up to 13) release sites.

 This synaptic arrangement strongly suggested a powerful inhibitory control of the paralemniscal pathway, which we tested in in vitro and in vivo conditions Stimulation of the APT in vitro evoked GABA-A receptor mediated current in Po neurons, which showed weak paired pulse depression. In current clamp configuration, stimulation of a presumed single fiber was able to induce low threshold burst in the relay cell. Chemical activation of APT in vivo inhibited Po cell activity and shifted its preferred phase of firing relative to the slow cortical oscillation. APT-thalamic cells were found to fire high frequency bursts in urethane anesthetized rats, whereas incerto-thalamic neurons maintained tonic high frequency firing during light ketamin anesthesia. These data indicated strong tonic extrareticular GABAergic inhibition over Po neurons. Indeed, intracellular in vivo experiments disclosed a tonic bombardment of IPSPs in Po neurons but not in VPM cells. ZI lesion abolished the high frequency inhibitory input in many Po cells.

 Extrareticular inhibition was also found to be involved in evoked activity. On their way to the thalamus interpolaris axons emit collaterals both in the APT and in the ZI, where they form contacts on the GABAergic cells of ZI by establishing several synapses, a rare condition in excitatory to inhibitory connections. ZI neurons responded to whisker stimulation with a short latency. Intracellular recordings of Po neurons revealed that the first synaptic event following whisker deflection is a prominent inhibition. Whisker-evoked excitatory postsynaptic potentials with fast rise time and longer onset latency were unveiled only after lesioning the zona incerta. Excitation survived barrel cortex lesion, demonstrating its peripheral origin
 These data demonstrate that a novel type of inhibitory afferent system is a major contributor in shaping the response properties of Po neurons. Unlike the lemniscal pathway the paralemniscal input is under a strong feed forward inhibitory control at the level of thalamus. Thus, the information triggered by passive whisker deflections is blocked in the thalamus, and hitherto unidentified disinhibitory mechanisms have to operate to open the thalamic gate of the paralemniscal pathway.
 **The ultimate question is how lemniscal and paralemniscal information is integrated in the cortex. To understand it we have to reveal how the paralemniscal signal is generated at the level of thalamus. Po receives not only peripheral but cortical driver input as well. Thus, the question is how top-down layer V driver inputs interact with bottom-up peripheral driver signals in the thalamus and how these two major excitatory pathways are controlled by the highly efficient GABAergic extrareticular system.**

**1:45 – 2:15 Dirk Schubert, C&O Vogt Inst. F. Brain Research**

**Intracortical functional connectivity of pyramidal neurons in layer Va suggests a possible function as a cortical interface between the paralemniscal and lemniscal pathway**

In primary somatosensory cortex layer Va is thought to be one major cortical entry point for tactile sensory information transmitted through thalamocortical afferences of the paralemniscal pathway. We investigated layer Va pyramidal neurons, one likely target of these afferences, in terms of their possible integrative capabilities and function in intracortical networks. For this we combined detailed electrophysiological and morphological characterization with mapping of intracortical origins for excitatory and inhibitory synaptic inputs onto single pyramidal neurons by caged glutamate photolysis of rat barrel cortex in vitro. Though being electrophysiologically heterogeneous, layer Va pyramidal neurons displayed uniform morphological properties and comparable functional input connectivity patterns. We found all layer Va pyramidal neurons possessing numerous horizontal bouton-laden axonal profiles within their own layer, reaching well into the neighboring barrel associated cortical column. From the same innervated region they also received the bulk of their excitatory and most robustly inhibitory inputs. Layer Va pyramidal neurons furthermore projected extensively to granular- and supragranular layers, with the granular layer being the second prominent source for their intracortical synaptic inputs. Layer Va pyramidal neurons thus may effectively integrate information intralaminarly as well as from neurons in layer IV, the main processors of sensory information of the lemniscal pathway. This gives direct evidence for the notion of layer Va pyramidal neurons functioning as an early cortical interface between the paralemniscal and the lemniscal pathways. **An open question is: What other cortical layers are wired in a way to promote exchange of information between these two sensory pathways?**

**2:15 – 2:45 Dirk Feldmeyer, Research Centre Jülich**

[**Monosynaptic connections between spiny stellate cells in layer 4 and pyramidal cells in layer 5A indicate early convergence of lemniscal and paralemniscal afferent pathways.**](http://www.neurobio.pitt.edu/barrels/BarrelsSchedule.html#Dirk_Feldmeyer:_Monosynaptic_connections#Dirk_Feldmeyer:_Monosynaptic_connections)

 Monosynaptic interlaminar connections between spiny stellate cells in layer 4 (L4), the main cortical recipient layer for thalamic projections and pyramidal cells in layer 5A (L5A), one of the main cortical output layers, were examined anatomically and functionally by paired recordings in acute brain slices. The somata of pairs forming interlaminar L4-to-L5A connections were located predominantly close to or directly under the barrel-septum wall in layer 4. Superposition of spiny stellate axon arbours and L5A pyramidal cell dendritic arbours suggested a blob-like innervation domain underneath a L4 barrel wall. Synaptic connections between L4 spiny neurones and L5A pyramidal cells were of high reliability and relatively low efficacy with a unitary EPSP amplitude of 0.6 mV; their connectivity was moderately high (1 in 7 pairs tested was connected). Following repetitive stimulation (10 Hz), the EPSP amplitude exhibited weak paired pulse depression (PPR  0.8). This suggests that the L4-to-L5A connection has a relatively high release probability and is comparable to other connections established by L4 spiny neurones.

 The existence of monosynaptic L4-to-L5A connections indicates that the specific “lemniscal” thalamic input from the ventrobasal nucleus of the thalamus (VPM) to the cortex and the more unspecific “paralemniscal” afferent thalamic projections from the posterior medial nucleus of the thalamus (POm) merge already at an initial stage of cortical signal processing. These connections establish a monosynaptic coupling of the input to the cortex and its output, thereby effectively by-passing the supragranular layers. How this pathway affects cortical signalling or is involved in its control remains to be elucidated. **Open Questions: How does the 'short circuit' between layer 4 spiny neurons and layer 5A pyramidal cells affect proposed models for the parallel sensory signal processing of the lemniscal and paralemniscal pathways? Are layer 4 spiny neurons involved in the feed-back control of excitatory signal flow in the neocortex?**

**2:45 – 3:15 Murray Sherman, University of Chicago**

[**The Role of Thalamus in the Flow of Information to Cortex**](http://www.neurobio.pitt.edu/barrels/BarrelsSchedule.html#Murray_Sherman_#Murray_Sherman_)

 The prevailing view of thalamocortical functioning is that information is relayed to cortex via primary sensory thalamic nuclei and then is processed via direct corticocortical connections. We suggest another view: that primary thalamic relays represent a first relay of a type of information (e.g., visual or somatosensory; these are first order relays) and that much corticocortical communication has a thalamic link via higher order relays. Examples of first and higher order relays, respectively, for vision are the lateral geniculate nucleus and most or all of the pulvinar, and for somatosensation, are the ventral posterior and most or all of the posterior medial nuclei. It is important in this schema to distinguish between corticothalamic projections emanating from layer 6 and those from layer 5. All thalamic relays receive a layer 6 input, which is modulatory in function and mostly feedback; it does not represent significant information flow. Only higher order relay receive, in addition, an input from layer 5, which does carry the information to be relayed to the next cortical area and thus is feedforward. The idea is that these layer 5 inputs have the same properties and function for higher order relays as do retinal and medial lemniscal inputs to the lateral geniculate and ventral posterior nuclei. The implication for somatosensory processing is that the ventral posterior nucleus (and probably some of the posterior medial nucleus) acts as a first order relay to S1 and that much information is then carried from S1 and beyond in cortex via relays through the posterior medial nucleus. This view challenges and extends the conventional view that corticocortical communication is based mainly on direct corticocortical connections. In this sense, any new information reaching a cortical area, whether from a subcortical source or another cortical area, benefits from a thalamic relay. Thus the thalamus not only provides a behaviorally relevant, dynamic control over the nature of information relayed, it also plays a key role in basic corticocortical communication. Evidence to support this hypothesis will be presented. **Open questions include (1) What is the functional significance of higher order thalamic relays, such as much or most of the posterior medial nucleus? (2) Where is non-barrel cortex (e.g., "septal" or "disgranular" cortex) of S1 in the hierarchy of information processing? And finally, as a speculative question, (3) What is the role of the thalamus, or, why do we have one?**

**3:15 – 4:00 Coffee break leads directly info discussion**

**Moderator – Martin Deschenes**

**4:00 – 5:30 Eight topical (10 minute) talks**

**Malgorzata Kossut and Anita Cybulska-Klosowicz**

**In the beginning of learning, communication between the barrel field is enhanced**

Laoratory of Neuroplasticity, Nencki Institute, 3 Pasteur Str., 02-093 Warsaw, Poland

In the vibirssal system, inputs from two whisker pads are transmitted separately to interhemispheric connections. These interactions depend on the behavioral requirements of the animal and its level of arousal. We mapped the brains of mice with [14C]2-deoxyglucose (2DG) autoradiography during the first and the third session of classical conditioning training, involving whiskers stimulation on one side of the muzzle paired with aversive or appetitive unconditioned stimulus. We have previously found that such sensory pairing produces associative learning-dependent modifications of vibrissal representation in the contralateral barrel cortex. In the present experiment, during the first pairing session, an increased 2DG uptake was seen in the barrel cortex in both hemispheres. The observed effect was the same independently of the applied unconditioned stimulus. In the third session of the sensory pairing, activation of the barrel cortex was unilateral, as expected after unilateral whisker stimulation. Thus we have shown that sensory stimulation directed to one cerebral hemisphere in the initial stage of learning activates the primary sensory area in both hemispheres. The results suggest that during the early phase of conditioning, when alertness presumably is the strongest, the interhemispheric interactions are enhanced.

**Marie Pohl and Asaf Keller**

**Response to vibrissal stimulation in rat superior colliculus**

University of Maryland

 The superior colliculus is important for multi-modal sensorimotor processing, and is involved in both vibrissal sensation and in controlling whisker movements. Furthermore, the superior colliculus interacts reciprocally with the zona incerta, which we have recently shown to be critical for gating sensory input. This places the superior colliculus as a possible center involved in attention and consciousness. However, the responses of collicular neurons to controlled vibrissal inputs, and the modulation of these responses by behavioral states remain unknown. To address these issues we recorded extracellularly from superior colliculus units in halothane-anesthetized rats. In many collicular neurons, vibrissal stimuli evoked responses with short latencies (≤ 10 msec) and large magnitudes (>> 1 spike/stim). Responsive cells had a low spontaneous firing rate, and their PSTHs often presented multiple peaks. Increasing arousal by tail pinch resulted in an increase in response magnitude and reliability. Thus, collicular responses are more rapid and robust compared to other trigeminal stations that receive similar vibrissal sensory input and zona incerta inhibition.

**Tony J. Prescott, Ben Mitchinson, Chris Melhuish, Peter Redgrave**

**Three-dimensional reconstruction of whisking patterns in freely moving rats.**

Adaptive Behaviour Research Group, University of Sheffield, UK.

 The whisking behaviour of sighted and dystrophic RCS rats was recorded using a high-speed video camera while the animals moved freely in a walled arena. With the camera positioned vertically we recorded top-down and side-on (via a front-silvered mirror) views of rat whisking within a 15x15x8cm volume. This data was then used to compute 3-d reconstructions of whisker-tip trajectories. Rats moving across a smooth, horizontal surface display a characteristic whisking pattern. The head is tilted downwards such that at the beginning of each whisk the vibrissae are raised and swept back and during protraction they move forwards and downwards bringing the rostral macrovibrissae into light contact with the floor. Animals observed rearing-up to explore walls show a similar pattern of "dabbing" against surfaces. These results indicate that (i) rats use the whisker tips for some forms of exploratory behaviour; (ii) positioning of the macro- and micro-vibrissae is synchronised; and(iii) whisker movement is under feedback control that tends to maximise the number of whiskers contacting nearby surfaces, whilst minimising the extent to which the whiskers "impinge" upon those surfaces. We also present a control-theoretic model of whisking pattern generation showing how sensory feedback may mediate some of the observed behavioural effects.

**P. W. Hickmott**

**Effects of a representational border on inhibitory synaptic potentials in adult rat primary somatosensory cortex (S1).**

Dept. of Psychology & Interdepartmental Neuroscience Pgm.

 In rat S1, stimulation of connections that stay within a representation (NCB) yields inhibitory responses (IPSPs) that are larger than those evoked by stimulation of connections that cross into an adjacent representation (CB; Hickmott & Merzenich, 1997). Such differences may reflect the fact that there are fewer axons that cross a representational border than project within a representation (Mason et al, SFN Abstr. 2003). In this abstract we investigated whether inhibitory synapses have different properties between NCB connections and CB connections. The border between the forepaw and lower jaw representations was mapped in adult rats (>P90) using in vivo recording and marked with DiI. Coronal slices were taken from the marked region and maintained in vitro. Whole-cell recordings were obtained from layer 2/3 neurons close to the border. Filling solution with a high concentration of chloride (100 mM) was used to enhance IPSP amplitude. Horizontal connections within layer 2/3 were electrically stimulated; stimuli were either at a site that was across the border from the neuron (CB) or at an equivalent site within the representation (NCB). IPSPs were isolated by bath application of 10 µM CNQX plus 100 µM APV. The synaptic efficacies of IPSPs were estimated by using minimal stimulation of CB and NCB connections. The mean minimal IPSP amplitudes (n=5) were .53±.11 mV for CB and .55±.15 mV for NCB. The short-term dynamics of IPSPs were also examined by stimulating CB and NCB connections with short trains of stimuli at various frequencies (5-20 Hz). IPSPs from CB and NCB stimulation exhibited different falling time dynamics and steady-state amplitudes during these trains (n=3). These data suggest that the synaptic efficacies IPSPs are similar between CB and NCB connections, but that there are differences in their short-term dynamics. Thus, a representational border can affect the properties of inhibitory synapses. Supported by NINDS NS42241.

**Verena C. Wimmer(1), Randy M. Bruno(2), Christiaan P.J. deKock(3), Thomas Kuner(4), Matthew J. During(5) and Bert Sakmann(6)**

**Columnar organization of VPM- and POm-axons throughout the whole cortex**

(1)-(4), (6) Max-Planck-Institute for Medical Research, Department of Cellphysiology, Heidelberg, Germany (5) Department of Molecular Medicine and Pathology, Functional Genomics and Translational Neuroscience Laboratory, University of Auckland, Auckland, New Zealand

 Thalamocortical projections are divided into two anatomically separate pathways. VPM cells give rise to the lemniscal projection whereas POm neurons give rise to the paralemniscal projection. We investigated thalamocortical projections into the different cortical layers using stereotaxic injection of recombinant viruses expressing hrGFP or Synaptophysin-EGFP. Highly efficient infection of thalamic relay nuclei revealed that axons from the VPM innervate the barrels in layer 4, a band which overlaps lower layer 5B and upper layer 6, and also layers 2/3. POm axons terminate in layer 5A, the septa, and layer 1. Surprisingly, in all layers except layer 1 the separation between barrel- and septum-related axon bundles is still apparent. Between the VPM- and POm-innervated areas of layer 5 there is a gap which does not receive significant input from either of the two nuclei. Quantification of synaptophysin-labeled presynaptic boutons demonstrated that, in contrast to previous findings, layers 2 and 3 receive substantial direct input from VPM. These results suggest an unexpected degree of anatomical separation between VPM- and POm-projections throughout the whole depth of the cortex, and underline the impact of direct thalamic input to nongranular layers.

**Soo-Hyun Lee, Peter W. Land and Daniel J. Simons**

**Layer-specific effects of neonatal whisker trimming adult rat barrel cortex** Department of Neurobiology, Univ.of Pittsburgh Schl. Med., Pittsburgh, PA 15261, USA In the rodent somatosensory system, neonatal whisker deprivation affects functional organization within layer 4 barrel circuits, with effects persisting even after months of whisker regrowth during adulthood. Previous studies comparing deprived vs. non-deprived barrel neurons showed that whisker trimming from the day of birth results in higher spontaneous firing rates, more robust responses to deflections of principal and adjacent whiskers, and weaker inhibitory interactions between neighboring whiskers. We examined whether these changes in layer 4 barrels are reflected in the responses of layer 2/3 neurons. Extracellular unit recordings were obtained from adult rats whose whiskers had been trimmed for 30 days from the day of birth and allowed to regrow > 30 days. Similar to previous studies, layer 4 regular-spike units (RSUs) showed significantly increased spontaneous and stimulus-evoked firing rates and broadened angular tuning in trimmed animals. Increases were disproportionately greater for normally weaker responses, e.g., those evoked by whisker deflection offsets vs onsets or by adjacent vs principal whiskers. In contrast to RSUs, presumed excitatory neurons, layer 4 fast-spike units (FSUs), presumed inhibitory neurons, were significantly less responsive to whisker stimulation, despite their elevated spontaneous activity. Surprisingly, firing rates of layer 2/3 RSUs and FSUs in trimmed rats were similar to the control group, despite the increased excitability of the underlying layer 4 barrel. However, as in layer 4, receptive field size of layer 2/3 neurons become larger. These findings demonstrate that neonatal whisker trimming followed by whisker regrowth leads to layer-specific effects within the cortical column. Control-level responsiveness in layer 2/3 may reflect a decrease in excitatory synaptic strength from abnormally active layer 4 barrel. Supported NIH NS19950 and NS41428.

**John Isaac**

**Rapid, activity-dependent plasticity in timing precision in neonatal barrel cortex**

NINDS, NIH, 35 Convent Drive, Bethesda, MD 20892

 During development neuronal networks acquire the ability to precisely time events. This is a critical developmental step since precise timing is required for information processing and plasticity in the adult brain. Despite this it is not known what process drives this maturation in timing. I will present recent work from my laboratory showing that long-term potentiation (LTP) induced at thalamocortical synapses in neonatal layer IV barrel cortex produces a rapid and dramatic improvement in input and output timing precision. LTP reduces the latency and variability of synaptically-evoked action potentials and reduces co-incidence detection for synaptic input. In contrast, LTP has only a small and variable effect on synaptic efficacy. This improvement in timing occurs during development, suggesting this process occurs in vivo in the developing barrel cortex. Thus, rather than increasing synaptic efficacy, the primary role of this form of neonatal LTP is to enable neurons to precisely time events.

**Manuel Castro-Alamancos and Yoshie Tawara-Hirata**

**Area-specific resonance of excitatory networks in neocortex: a substrate for cortical myoclonus**

Dept. Neurobiology and Anatomy Drexel University College of Medicine

 In slices, isolated excitatory networks (i.e., devoid of inhibition) of the motor cortex but not of the barrel cortex produce spontaneous ~10 Hz oscillations. Current source density analysis (CSD)in combination with fluorescent imaging revealed the location of current sinks and sources associated with these activities. In behaving rodents, the ~10 Hz oscillations of the excitatory motor cortex network produce movements that resemble a myoclonus.

**5:30 – 6:00 Discussion segues into dinner and small groups.**

**Small groups sign-ups will be organized in real time as the discussion draws to a close. We hope that each small group will choose a particular topic of interest and go to dinner to talk about it.**

**POSTERS**

**Hajnalka Bokor1 and Martin Deschênes2**

# A third pathway to the barrel cortex

**1Institute of Experimental Medicine, National Academy of Science, Budapest, Hungary 2CRULRG, Laval University, Québec City, Canada**

Traditionally vibrissal information reaching the barrel cortex has been divided into two major pathways; lemniscal and paralemniscal, with relays in the VPM and in Po nuclei respectively. Here we describe a pathway independent from the above two routes involving a specific relay cell population in the ventrolateral part of the VPM (VPMvl). Anterograde and retrograde track tracing studies confirmed that a population of neurons located in the posterior part of the interpolar subdivision of the spinal trigeminal nucleus gives rise to a projection to the VPMvl. This projection is different from the one targeting Po. Whisker stimulation revealed VPMvl cells with robust short latency responses, to several (5-12) whiskers. Whisker evoked responses survived lesion of the principal trigeminal nucleus, whereas VPM barreloid neurons were rendered unresponsive after the lesion. Recording in the thalamic reticular nucleus revealed a specific subpopulation of reticular cells that also showed multiwhisker responses. Neurobiotin labeling revealed that these neurons selectively project to the VPMvl. Taken together with the distinct projection pattern of VPMvl cells into the barrel cortex (Pierret et al., 2000), the present data demonstrate the existence of a third pathway in the trigeminal system. The functional significance of this pathway remains to be examined.

**Ali-Reza Boloori and Garrett B. Stanley**

**Spatiotemporal interactions influence precision of coding by single- and multiple neurons in the rat barrel cortex**

**Division of Engineering & Applied Sciences, Harvard University**

Response integration across the spatiotemporal receptive field (RF) is a general feature of sensory coding, and has an important role in shaping responses to naturalistic stimuli. Coding of spatiotemporally distributed stimuli by the primary somatosensory cortex (SI) of the rat vibrissa pathway is strongly influenced by such integration across the vibrissa array. Motivated by the high capacity of the vibrissa pathway for transmission and processing of textural information, the goal of this study is to quantify the effect of response integration on the precision with which spatiotemporally distributed deflections are encoded. Using a spatiotemporal paired-pulse paradigm, it is shown that, in addition to attenuating the magnitude of the single-cell firing-rate response to a subsequent vibrissa deflection, post-stimulus suppression also increases the delay of the associated response by as much as a factor of two. Moreover, preliminary data show that the temporal spread of the response positively correlates with the degree of firing-rate attenuation. These results demonstrate that, by evoking varying amounts of cortical suppression, spatiotemporal interactions can influence the coding precision of single neurons. Temporal precision of coding may also 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 significantly larger than that due to the common stimulus across trials. There is evidence that this extra degree of time-locking decreases as the level of response suppression increases. These findings indicate that spatiotemporal interactions constrain the textural information carried by groups of neurons in a way likely to be important in the natural setting.

**Eric C Chen1, Daniel Tam2, Alex Pinhas2, & Joshua C Brumberg12**

**Neuronal morphology of mouse barrel cortex layer VI: Effect of sensory deprivation. 1 Neuropsychology PhD Subprogram, The Graduate Center, CUNY, NY, NY 2 Department of Psychology, Queens College, CUNY, Flushing, NY, NY**

The mouse somatosensory cortex is organized into neuronal clusters called barrels that represent in a one-to-one fashion the whiskers on the contralateral mystacial pad. Layer six of the cerebral cortex is the most morphologically diverse layer, and can be subdivided further into VIa and VIb. Layer six receives thalamic afferent inputs as well as local and distant cortical sources, and gives rise to the feedback corticothalamic projection and also cortico-cortical, corticoclaustral, and commissural fibers. The development of the somatosensory cortex is experience-dependent, and to look at the role activity plays in the development of layer VI we trimmed from birth (for the first post-natal month) the mystacial whiskers. Utilizing the Golgi staining technique we labeled neurons in a nonbiased fashion and with the aid of the Neurolucida system reconstructed their morphologies. Data indicate that there are distinct classes of neurons within layer VI based on their somatic and dendritic morphologies. The preliminary data on effects of sensory deprivation suggest that sensory-deprived mice (trimmed group) have larger somal body, more numbers dendritic nodes, and longer total dendrites when analyzed comparatively to that of control group mice (untrimmed group). The additional factor of developmental age and its relationship to the trimming paradigm and neuronal morphology is currently under analysis. Characterizing the neuronal elements within layer VI is an important step towards understanding the constituents and their role in the processing of sensory information.

**Nathan Cramer and Asaf Keller**

**Cortical Control of a Whisking Central Pattern Generator**

**Program in Neuroscience, Dept. of Anatomy & Neurobiology, University of Maryland School of Medicine, Baltimore, MD.**

Our current investigations examine the role of the vibrissae motor cortex (vMCx) in modulating the output of a whisking central pattern generator (CPG) and the contributions of recruited motor units to the production of vibrissae movements. Additionally, we investigate the contributions of putative serotonergic CPG components likely to play a critical role in generating rhythmic whisking. During intracortical microstimulation (ICMS) evoked movements, motor units were typically recruited in a stereotypical order such that the amplitude of whisker movements was positively correlated with the number of active motor units. Additionally, active motor units often increased their firing rates as movement amplitudes increased. Thus, vMUs use a combination of motor unit recruitment and rate coding to generate vibrissae protractions. ICMS of the vMCx evoked rhythmic vibrissae movements at frequencies distinct from the stimulation frequency. Larger stimulation intensities were associated with higher frequency of evoked movements and a reduction in the latency to movement onset. Variations in the stimulation frequency had less of an effect on evoked movement kinematics. As was previously observed in voluntary whisking, infusion of the 5HT2 antagonist metergoline into the lateral facial nucleus reversibly degraded ICMS evoked movements. These results support the hypothesis that rhythmic whisking is produced by a whisking CPG, with a prominent serotonergic component, under modulatory control of the vMCx. Supported by PHS grant NS35360 (AK).

**R. Blythe Towal1 and Mitra J. Hartmann1,2**

**Bilateral Asymmetries in Whisking Patterns of Freely Behaving Rats**

**(1) Department of Biomedical Engineering, (2) Department of Mechanical Engineering, Northwestern University, Evanston, IL, USA, 60208**

 During exploratory behaviors, rats typically "whisk" at frequencies of 5 -15 Hz. Several recent studies have reported that macrovibrissal whisking movements are bilaterally symmetric about the snout: right and left whiskers protract and retract simultaneously. Most of these studies were performed in the head-fixed animal, or as the animal was focused on a task that kept the head pointing in line with the animal's body. In a preliminary study, however, we observed that whisking was not bilaterally symmetric about the snout during head rotations. This observation led to the hypothesis that whisking asymmetry compensated for head rotation in order to preserve symmetry in world-centered coordinates. In the present study we investigated this hypothesis using high-speed, infrared video to record whisking behavior during head rotations in the horizontal plane. Consistent with our previous results, we found asymmetric whisking patterns during every episode of head rotation. In all of these episodes the whiskers "led," both spatially and temporally, on the side towards which the head was turning. The amount by which the whiskers led was correlated with the head velocity. We also found dramatic whisking asymmetries even when there was no head rotation. We discuss possible explanations for these exploratory strategies, including the relationship of whisking asymmetry to central pattern generation. Specifically, we propose a coupled oscillator network between the left and right sides, similar to that proposed for control of intrinsic and extrinsic muscles. We suggest that one function of the asymmetric whisking is to allow the rat to "look ahead" with its whiskers on the side towards which the head is turning by an amount equal to the distance that the head will turn during a whisk.

 **A. Darbar, R.T. Stevens, B.R. Krauss, A.H. Siddiqui and C.J. Hodge, Jr**

**Opposing Effects of Dilantin and Amphetamine in Post-lesion Functional Recovery of Rat Barrel Cortex.**

**Dept. of Neurosurgery, SUNY Upstate Medical University, Syracuse, NY 13210.**

To maximize the benefits of current neurological treatment and to minimize the impact of injury, we examined the ability of commonly administered drugs, amphetamine and Dilantin (DPH) to positively or negatively affect the functional recovery of cerebral cortex following excitotoxic injury. In the present study, maps of whisker functional representation (WFR) in rat barrel cortex were obtained using Intrinsic Optical Imaging before and 9 days after kainic acid (KA) lesions. During the post-lesion survival period animals were either treated with DPH, amphetamine, saline or received no treatment. Following the survival period, WFR were again measured and compared with pre-lesion measurements for each treatment group. These data suggest KA lesions cause increases in WFR areas when compared to control (P < 0.05). Treatment with amphetamine further increases the WFR area (although statistically non significant) while DPH showed significant (P < 0.016) decreases in WFR areas. Significance (P < 0.0006) was also seen between amphetamine and Dilantin groups. Two commonly used drugs, amphetamine and Dilantin have opposite affects in the functional recovery/plasticity of injured cerebral cortex. These results emphasize the complex nature of the cortical response to injury and may have implications on the effects of different medications on eventual functional recovery.

**Ming-Chieh Ding\* 1,2, Emiri Tejima3, Eng H. Lo3, and Garrett B. Stanley2**

**Electrophysiology of the rat barrel cortex following traumatic brain**

**1Harvard-MIT Division of Health Sciences & Technology, Cambridge, MA 02138 2Division of Engineering and Applied Sciences, Harvard University, Cambridge, MA 02138 3Neuroprotection Research Lab, Departments of Radiology and Neurology, Massachusetts General Hospital, Charlestown, MA 02129**

Neuronal injury resulting from direct mechanical impact activates secondary processes of cytotoxicity (excitotoxicity, oxidative stress, and apoptosis), which continue to evolve over hours/days. Following injury, the electrical activity of neuronal populations within relevant brain structures has not been widely studied at the single- or multi-unit level, and the role that the electrical activity may play in the recovery process is only beginning to be addressed. In this study, Long-Evans rats were subjected to traumatic brain injury (TBI) in the barrel cortex through the use of a controlled cortical impactor (CCI) device. With the use of a paired-pulse and 3-pulse whisker deflection paradigm, TBI at the electrophysiological (single/multi-unit and EEG) and histological levels in the barrel cortex of the rat somatosensory system were monitored and evaluated at various time points following recovery. Post-stimulus time histograms (PSTH) seem to indicate that periods of enhanced excitation and cortical suppression exist following induction of injury. Excitotoxicity and cortical spreading depression (CSD) are often reported following traumatic brain injury and the resulting changes in PSTH amplitudes at multiple time points after TBI induction. The results suggest a possible perturbation in the balance of inhibitory and excitatory neuronal activity in the cortex following injury. These data provide possible insight into the time course of the development of injury and could potentially serve as indicators of outcome. Controlled modulation of inhibitory and excitatory activity at critical time points could lead to more effective interventions for enhancing recovery following TBI. This work was supported by the Whitehall Foundation (GBS, MD) and National Institutes of Health Grants NIH R01-NS40529 and NIH R01-NS48422 (EHL, ET).

**R. Galvez1; K. Szymanek2; W.T. Greenough2\***

**Fmr1 cortical barrel expression in a mouse model of the Fragile X Mental Retardation Syndrome**

**Northwestern University, Chicago, IL, USA 2. University of Illinois, Champaign, IL, USA**

The following analysis took advantage of the well characterized somatosensory whisker barrel cortex to examine fmr1 expression, the gene that codes for FMRP (Fragile X Mental Retardation Protein) during dendritic development. Analysis of fmr1 expression in layer IV of the somatosensory cortex of fmr1 knockout mice (FraX mice) revealed a peak in expression at postnatal day 15 in males. During normal cortical barrel development at approximately postnatal day 15, spiny stellate cells in the inner 1/3 of the barrel wall extend dendritic processes into the barrel hollow while retracting dendrites oriented towards the wall. Prior analysis of dendritic properties in the barrel cortex of adult male FraX mice demonstrated an excess of improperly oriented dendrites. These analyses strongly suggest that FMRP plays a critical role in dendritic development. Analysis of fmr1 expression in females, however; demonstrated that expression did not fluctuate over the entire developmental period analyzed. Re-analysis of dendritic properties in adult female FraX mice revealed while they exhibited more improperly oriented dendritic material than in female WT mice, they had significantly less improperly oriented dendritic material than male FraX mice. These analyses strongly suggest that FMRP is differentially modulated depending upon the sex of the subject, and that this modulation has a direct result on neuronal properties. Transcriptional silencing of FMRP in humans has been shown to cause the leading form of inherited mental retardation, the fragile X mental retardation syndrome (FXS). Individuals with FXS have various behavioral abnormalities such as reduced intellect, poor eye contact, hand flapping and / or hand biting, cluttered speech, hyper-activity, impulsivity, and social anxiety. In general, these symptoms are milder in females than in males, an observation that has been attributed to the mosaic pattern of suppression of expression of genes on the two X chromosomes in human females. The most prominent neuronal abnormality associated with FXS has been an excess of long immature appearing spines. These neuronal analyses, however, have all been conducted in males. The current findings strongly suggest that an absence of FMRP can and does differentially modulate neuronal properties depending upon the sex of the subject in FraX mice, where both X chromosomes carry the knocked out Fmr1 gene, thus further suggesting that the affects of FMRP on neuronal development are modulated by sex hormones. Current analyses of the syndrome and FMRP’s role during normal development have neglected this possibility. We feel these findings not only change the way that we think of this syndrome and the molecular players that interact with FMRP, but in so doing, bring us one step closer to understanding how to treat patients suffering from this syndrome. Support Contributed By: NIMH (SFN-MNFP-NIMH-1T32MH20069), NICHD (HD37175), and FRAXA.

**Anirvan Ghosh, Gulayse Ince, and Ben Hall**

**Regulation of thalamocortical patterning and synaptic maturation by NeuroD2**

**Division of Biology, UCSD, La Jolla CA 92093**

We have been investigating the role of activity-dependent transcription in patterning of connections in barrel cortex. Using a screen to clone calcium-regulated transcription factors (Aizawa et al., 2004) we identified the basic helix loop helix (bHLH) transcription factor Neurogenic Differentiation 2 (NeuroD2) as a factor required for the proper development of thalamocortical connections in barrel cortex. In neuroD2 null mice, thalamocortical axon terminals fail to segregate in the somatosensory cortex and the postsynaptic barrel organization is disrupted. Additionally, synaptic transmission is defective in thalamocortical synapses in neuroD2 null mice. Total excitatory synaptic currents are reduced in layer IV in neuroD2 null mice, and the relative contribution of AMPA receptor and NMDA receptor-mediated currents is altered. The role of NeuroD2 in both the anatomical development and physiological maturation of thalamocortical connections in barrel cortex suggests that it plays a critical regulatory role in the assembly of cortical circuits.

**Florent Haiss and Cornelius Schwarz**

**Activation of RW a sub-region in whisker motor cortex switches tactile processing in rats’ barrel cortex.**

**Hertie-Institute for Clinical Brain Research, Department of Cognitive Neurology, University Tübingen, Germany**

Rhythmic whisker movements of rats, typically employed to palpate objects, are controlled by a small sub-region of whisker motor cortex (RW, ‘rhythmic whisking’, Haiss and Schwarz, 2005, J. Neurosci. 25:1579). As it is well established that processing of tactile information in the barrel cortex is modulated by movement we set out to study the possible contribution of RW to this interference. Intracortical microstimulation in RW in conjunction with electrical stimulation of the infraorbital nerve (ION) was applied to study the influence of RW signals on signal processing in barrel cortex in awake rats. ION stimulation alone led to a short latency negative deflection in barrel cortex local field potentials (LFP) followed by a longer lasting positive deflection. We observed that RW activation attenuated the negative deflection of evoked LFPs, but only if the stimulations were precisely timed such that both types of signals arrived in barrel cortex within a few milliseconds. The ensuing positive deflection of the LFP, lasting for about 100 ms (presumably related to an inhibitory phase), was attenuated to a larger degree and was susceptible to a much wider range of intervals between RW and ION stimulation. These results, first, support the notion that motor signals may play a role in the modulation of tactile processing for active vs. passive touch. Second, the stronger effect on long latency portions of tactile signals, point to the possibility that RW mediated modulation may be used to change characteristics of temporal integration in barrel cortex.

**INFLUENCE OF DENDRITIC MORPHOLOGY ON FIRING PATTERNS IN L2/3 INTERNEURONS**

**Moritz Helmstaedter Dirk Feldmeyer Bert Sakmann**

**Max-Planck-Institut f. med. Research Jahnstr. 29 D-69120 Heidelberg Germany**

Dendritic shape and AP firing properties are widely used as criteria to define interneuron subtypes. It is however unclear to which extent variability in dendritic morphology is causal for variability in firing patterns of interneurons. Here, we report the correlation between morphological parameters (the number of primary dendrites and dendritic polarity) and AP firing properties (the AP frequency adaptation ratio) in a set of 45 interneurons from L2/3 of rat barrel cortex (r=0.3). We investigated the causal proportion of this correlation by performing computer simulations in all of the interneurons with a constant set of voltage-gated conductances, thus leaving dendritic morphology as the remaining source of variability. The AP frequency adaptation ratio in the simulated AP firing patterns was still significantly correlated to the number of primary dendrites (r=0.14). Thus, the variability in dendritic morphology can causally account for up to 50% of the measured correlation to AP firing pattern properties. This study shows the significance of dendritic morphology to the shape of AP firing patterns in realistic morphologies, emphasizing the requirement for functionally independent parameters for the definition of interneuron types in the neocortex.

**Hillen, M.J.P(1), Bryars, M.H.(1), Sengpiel, F.(2), Kind, P.C.(1)**

**Barrelgene.info: A web resource for the developmental neuroscience community Section of Biomedical and Life Sciences, Hugh Robson Building, George Square, Edinburgh University, Edinburgh, EH8 9XD 2. Cardiff School of Biosciences, Biomedical Sciences Building Museum Avenue Cardiff CF10 3US, UK**

In order to achieve a detailed understanding of the mechanisms by which neuronal activity regulates barrel development, we need a detailed understanding of the intracellular pathways activated by NMDA receptors during development. While much is known of the developmental expression patterns of NRC components, information concerning individual proteins is often difficult to find as it often eludes standard data searches, leading to unnecessary replication of already published data. The most prominent tools for data searching are NCBI PubMed and Google Scholar. However, these databases have their limitations; PubMed is restricted to title, author and keyword abstract text, potentially missing desired information. Google Scholar searches all of the text in academic publications, but produces an overwhelming number of results, and significant amounts are not relevant. In terms of expression patterns and profiles of proteins and genes, the Jackson Laboratories MGI suite offers an impressive way of mining the literature for such data, but the content is sparse, relying on author submission and a small library curation team; for example, the only gene present in MGI for postnatal layer IV cerebral cortex is Apc2. We present a fully-curated and easily searchable database that offers gene and protein expression patterns, profiles and sequence information, by restricting the content of the database to genes expressed postnatally, that are NRC components and present in somatosensory cortex. By performing exhaustive literature searches utilising Google Scholar and PubMed, and linking to sequence information elsewhere, we can offer a central point to access such information. We also offer information as to whether a mutant mouse is available and its phenotype, if known, and hope to be a location where unpublished observations of transgenic animals displaying normal barrel formation can be found, again to prevent duplication of experiments. Barrelgenes.info should provide a key resource for any researcher interested in the molecular basis of cortical development.

**Barrel Map Development in PKARIIβ Knockout Mice**

**Melis Inan1,2, Hui-Chen Lu3, Wei-Chi She3, Michael C. Crair1,2**

**(1) Baylor College of Medicine, Developmental Biology Program**

**(2) Baylor College of Medicine, Department of Neuroscience**

**(3) The Cain Foundation Laboratories, Department of Pediatrics**

 The first mutant mouse identified without a barrel map was homozygous for the barrelless (*brl*) mutation, which was mapped to the adenylyl cyclase type I (*Adcy1*) gene. Adcy1 is activated by Ca2+ influx possibly through activation of NMDA receptors. It catalyzes cAMP formation and activates cAMP-dependent protein kinase (PKA). Therefore, reduced cAMP levels, and presumably lower PKA activity disrupts barrel map formation.

 To further elucidate the role of PKA in the development of the barrel map, we analyzed PKA Regulatory subunit IIβ knockout mice (PKARIIβ-/-). We first examined PKA activity in the somatosensory cortex of these mutants, and found it to be reduced by 50% with respect to wild type controls. Analysis of the cortical barrel pattern in these mice shows that TCA clustering was similar to littermate controls, but the organization of layer IV cortical neurons into barrel walls was dramatically disturbed.

 We also analyzed the developmental expression profile of PKARIIβ by staining thalamocortical slices from wild type animals of different ages using a PKARIIβ antibody. At postnatal day 3 (P3), when layer IV is generated, PKARIIβ expression appeared to be high in this layer. It was expressed as a barrel pattern in the cortex at P5 and even after the second postnatal week. Double staining using antibodies for pre- and postsynaptic markers together with PKARIIβ on P5 wild type thalamocortical slices showed that PKARIIβ extensively colocalized with postsynaptic but not with presynaptic markers. Moreover, thalamic barrelloid organization in PKARIIβ-/- mice is similar to wild types at P5. The PKARIIβ expression pattern together with the “barrel” phenotype of PKARIIβ-/- suggests that this phenotype is specific to the cortex.

 Electrophysiological experiments were carried out to characterize the functional properties of the thalamocortical synaptic response in PKARIIβ-/- mice. Field potential recordings indicated no significant difference in the gross synaptic transmission of these mutants with respect to wild types. The AMPA/NMDA ratio was examined using whole-cell patch clamp experiments. Similar to our previous reports, the AMPA/NMDA ratio showed a significant increase with age in wild type littermate controls (P4-P7 mice compared to P9-P11), but not in PKARIIβ-/- mice. Moreover, the AMPA/NMDA ratio remained small in PKARIIβ-/- compared to controls at P9-P11.

 Next, we analyzed if the miniature AMPAR-mediated currents (evoked AMPA minis) were specifically affected in P9-P11 PKARIIβ-/- mice by substituting Ca2+ with Sr2+ in the extracellular ACSF, since Sr2+ leads to the appearance of delayed “miniature” responses due to the persistence of asynchronous quantal release. Evoked AMPA minis were on average smaller in PKARIIβ-/- mice compared to wild type littermate controls. Comparison of the evoked mini EPSC amplitude histograms showed a shift in the peak of distribution with PKARIIβ-/- mice peaking at a smaller amplitude than controls. These electrophysiological results indicate that the number of functional AMPARs at TC synapses is lower on average, leading to smaller AMPAR-mediated currents in PKARIIβ-/- mice.

 We also examined if the phosphorylation of several PKA targets, some of which were reduced in *brl* mice, were affected in the PKARIIβ-/- mice. Western blot analyses of synaptosomes prepared from P11 mice showed that phosphorylation of postsynaptic PKA targets like GluR1, but not presynaptic targets such as Synapsin and Rim were reduced in PKARIIβ-/- compared to wild type littermate controls. These results are consistent with the postsynaptic localization of PKARIIβand postsynaptic phenotype observed in PKARIIβ-/-. Moreover, the reduction in GluR1 phosphorylation is also consistent with our physiology results, as PKA phosphorylation of GluR1 is known to regulate AMPAR trafficking at the synapse.

 Finally, we analyzed map plasticity of TCA clustering in PKARIIβ-/- mice, as TCA pattern formation is intact in these mutants. We found that PKARIIβ-/- mice had a similar degree of plasticity as wild type littermate controls.

With these findings, we show that PKARIIβ-mediated PKA signaling is required for the proper development of the postsynaptic layer IV neuronal barrel organization, and the developmental increase in the number of functional AMPARs at TC synapses, regulated by PKA activity, seems to have an essential role.

**Robert A. Jenks and Garrett B. Stanley**

**Stimulus-driven response dynamics of the whisker/barrel-cortex system in awake behaving rats.**

**Department of Physics and Department of Engineering and Applied Sciences, Harvard University**

Many rodents actively sense the environment using an extensive whisker system on the snout, which has a large somatotopic representation in primary somatosensory cortex. Although many studies have investigated this system in anesthetized rats, there has been a growing recognition of the importance of making electrophysiological recordings in awake behaving animals. We made multiple simultaneous single unit extracellular and multiple field potential recordings from the barrel region of primary somatosensory cortex in adult female Long-Evans rats that were trained to run on a linear track. We placed several piezo-electric films on the side of the track in order to make discrete deflections of the contralateral whiskers with accompanying PSTHs, with varying time separations between each deflection. This paradigm allows us to probe the dynamics of tactile responses in the barrel-cortex network. It has been shown [1] that behavior state modulates tactile responses. We hypothesize that the shallow, short suppression following a stimulus that is characteristic of the awake state optimizes the rat's sensory discrimination ability, while the deep, long suppression characteristic of the quiescent state optimizes the rat's ability to detect the onset of stimuli. Further work will employ a behavioral paradigm that requires the rat to make a choice after a whisker-based detection or discrimination between different piezo spacings, under varying attentional states, in order to test this hypothesis.

**Ofri Levy and Ilan Lampl**

**Amplification of inhibitory inputs mediates spatial suppression of sensory inputs in the barrel cortex**

Sublinear spatial integration in the cortex is believed to be mediated by cortical inhibition. The underlying mechanisms, however, remain unclear. In this intracellular in-vivo study we explored these mechanisms in the barrel cortex. First, we explored the interactions between two pathways activated by neighbouring whiskers. We tested the response of a cortical neuron to stimulation of a given whisker following adaptation caused by repetitive stimulation of a neighbouring whisker. Reduction in the response to test stimulus will indicate synapses common to the two pathways. In most neurons, however, adaptation to one whisker had little effect on the response to another whisker, suggesting that the two pathways share almost no common inputs. Next, we studied changes in the balance between excitation and inhibition evoked by stimulation of two whiskers. Excitation was found to sum almost linearly (~13% less than linearly predicted). Inhibition, however, is substantially amplified (~103% greater than predicted). Amplification is mostly found when inhibition is relatively weak compared to excitation in the individual responses. Reconstruction of the voltage response based on the measured conductances indicates that the non-linear component of the integrated response accounts for large part of the suppression in the integrated response. The shift in balance is accurately predicted by a simple model based on known F-I curves of cortical neurons. Assuming that the firing of inhibitory and excitatory cell populations accounts for the measured synaptic conductance, the model demonstrates that linear summation of excitation is due to activation of excitatory input neurons responding to either one of the whiskers but not to both. Amplification of inhibition is explained by a high threshold and wide receptive fields of inhibitory cells. These rudimentary differences between excitation and inhibition are likely to shape various spatiotemporal cortical neuronal behaviours. Supported by grant 1037/03 from the Israel Science Foundation.

**Y.Ma, H.Hu, A.Agmon**

**A novel subtype of layer 4 targeting, quasi-fast spiking, somatostatin containing neocortical interneurons**

**Department of Neurobiology and Anatomy and the Sensory Neuroscience Research Center, West Virginia University, WV 26505**

GABAergic interneurons in the neocortex can be classified into several subtypes, based on their morphological features, electrophysiological properties and neurochemical markers. Somatostatin-containing GABAergic interneurons have been characterized electrophysiologically as “low-threshold spiking” (LTS), and some can be classified morphologically as “Martinotti cells” with dense axonal projections to layer 1, but they have not been further subclassified. To determine if somatostatin-containing GABAergic interneurons segregate into distinct subtypes, we used novel transgenic mice that express GFP in different subsets of somatostatin-containing interneurons. In the line designated X94, GFP-expressing neurons were largely localized to the thalamo-recipient layers 4 and 5b, while in the line designated X98, GFP-expressing neurons were found mostly in layer 6. We also used the previously described GIN line, in which GFP expression is restricted to somatostatin-containing interneurons in the upper cortical layers. We recorded from GFP-expressing neurons, filled them with biocytin, and compared electrophysiological and morphological properties between the 3 lines. X94 neurons exhibited unique electrophysiological features, most prominently their low input resistance, high maximal firing rate and strongly “stuttering” firing pattern, but did not fire low-threshold spikes. Their axons arborized densely in layers 4 and 3, with only sparse projections to layer 1. X98 neurons exhibited very high input resistance, fired low-threshold spikes and sent dense axonal projections to layer 1. GIN neurons had properties intermediate between the two other lines. We propose that X98 interneurons are classical Martinotti cells, while X94 interneurons belong to a novel, quasi-fast spiking interneuronal subtype. The spatial restriction of the X94 interneurons to thalamocortical recipient layers suggests that they may play a unique role in sensory processing.

**Ben Mitchinson**

**A physical model of active whisking and early signal processing in the whisker pathway Details previously submitted by email on 07.20.05**

**B.Mitchinson1\*; T.J.Prescott1; K.Gurney1; M.J.Pearson2; I.Gilhespy2; A.J.Pipe2**

**A computational model of a brainstem loop for whisker pattern generation.**

 **1. Psychology, Univ. of Sheffield, Sheffield, United Kingdom 2. IAS Lab, Univ. of the West of England, Bristol, United Kingdom**

 We present a control-theoretic, computational model of whisking pattern generation in brainstem, and of the positive and negative feedback from sensory signals that may mediate observed behavioural effects. Experiments using high-speed video recording indicate that both inter- and intra-whisk parameters of whisking patterns in freely behaving rats are affected by contact of the whiskers with the environment (Prescott et al., SFN 2005). These effects tend both to minimise impingement of the whiskers on the environment during protraction, and to maximise the number of whiskers that make contact with a stimulus. Here, we describe a model of whisker pattern generation in brainstem, and of an associated closed sensorimotor loop. This loop runs from the pattern generator to the whisker musculature, through the interactions of the whiskers with the environment to the whisker follicles, and back up to the pattern generator. We are developing a set of artificial whiskers to form the sensor array of a mobile autonomous robot (Pipe et al., SFN 2005); here, we construct a simple two-dimensional simulation of the reponse of these whiskers to drive signals, and their interaction with environmental point obstacles. We use the mechanical signals thus generated to drive a previously published electromechanical model of transduction within the whisker follicle (Mitchinson et al., Proc Biol Sci 2004, 271:2509-16). The remainder of the loop we develop here. The simulated 'whisking environment' also supplies useful visual feedback on the operation of the model, which can be fairly directly compared with video recordings of rats. We demonstrate that this model can reproduce the aspects of whisking behaviour described above, and go on to transpose it into 'spiking' neuron network form, again confirming its operation. Finally, we discuss the proposed seat of this system in the rat brain, with reference to previously published anatomical and electrophysiological data.

**A.J.Pipe1; C.Melhuish1; M.J.Pearson1; I.Gilhespy1; B.Mitchinson2; K.Gurney2; T.J.Prescott2\***

**Artificial, active vibrissal array modeling the mechanics and neurology of rat whisking**

**1. School of Electrical & Computer Engineering, Univ. of West of England, Bristol, United Kingdom 2. Psychology, Univ. of Sheffield, Sheffield, United Kingdom**

 We present a 4x natural scale artificial whisker sensory system modeled on the structure and behavior of rat facial macro-vibrissae.

The approach taken is designed specifically to assist the work of biologists by implementing models based on biological data, embedding them onto a mobile robotic platform, and testing them thoroughly in a real-world environment. In the current physical model the characteristics of the artificial vibrissae, such as shape and resonance, have been designed to match real vibrissae by using selected composite materials. The intrinsic muscles of the rodent mystacial pad have been implemented using a fiber-like metal actuator called BioMetalTM which mimics some of the important properties of real muscle with each artificial whisker separately actuated. A spring has been used to represent the elasticity of the skin covering the pad to generate passive retraction.The sensory apparatus of real vibrissae has been modeled using micro-strain gauges and Digital Signal Processors. The follicle sinus complex at the base of each vibrissae, and the primary afferents in the trigeminal ganglion, have been simulated using an electromechanical model based on anatomical and electrophysiological data (Mitchinson et al., 2004, Proc Biol Sci. 271:2509-16) and implemented directly in VLSI electronic hardware using a Field Programmable Gate Array. Whisker assemblies are mounted in arrays on a platform able to move in a manner analogous to natural whisking. The outputs from this system are spike trains similar to those reported from measurements carried out on rats (Szwed et al, 2003, Neuron, 40, 621-630) and are passed to a spiking neuron model of the trigeminal sensory complex for further processing. The complete whisker sensory model will be used to orient a mobile robot in a maze-like arena with the aim of advancing the functional understanding of rat whisking behavior.

**T.J.Prescott1; B.Mitchinson1; P.Redgrave1; C.Melhuish2; P.Dean1\***

**THREE-DIMENSIONAL RECONSTRUCTION OF WHISKING PATTERNS IN FREELY MOVING RATS 1. Psychology, Univ. of Sheffield, Sheffield, United Kingdom 2. IAS Laboratory, Univ. of the West of England, Bristol, United Kingdom**

 The whisking behavior of normally-sighted and dystrophic Royal College of Surgeons rats was recorded using a Photron Fastcam 1024 PCI high-speed digital video camera, while the animals were moving freely in a rectangular, walled arena. With the camera in a vertical position, a mirror slanted at 45 to the floor surface allowed the capture of both top-down and side-on views of rat whisking within a ~12x10x6cm window. Recordings at 250fps were able to discriminate the position of multiple vibrissae and identify whisker tips with good accuracy. Calibration of the camera/mirror setup allowed matching of individual whiskers across views and between frames and thus the 3D reconstruction of whisker trajectories.

 Recordings of rats moving across the arena floor show that the typical whisking pattern of a rat crossing a smooth, horizontal surface is as follows. At the beginning of each whisk cycle the vibrissae are raised and swept back; during the protraction phase of the whisk the vibrassae are then brought forwards and downwards in an arc that brings the rostral macrovibrissae into light contact with the floor surface. These movements occur in phase with a lowering of the head such that the microvibrissae on the chin generally contact the floor at the same time as the macrovibrissal tips. Recordings of animals that are rearing-up to explore walls show a similar pattern of palpitating or dabbing the whisker tips against surfaces of interest. These results suggest that (i) rats prefer to use the tips of their whiskers when engaging in some forms of exploratory behavior; (ii) the synchronized positioning of the macro- and micro- vibrissal tips provides a series of discrete samples of the local environment layout as the animal moves; and (iii) the movement of the whiskers is under feedback control that acts to maximise the number of whiskers contacting nearby surfaces, whilst minimising the extent to which the whiskers impinge upon those surfaces.

**CD Rittenhouse, DJ Pinto**

**The sensitivity of cortical barrel neurons to input timing and magnitude: implications for circuit processing**

**Dept. of Neurobiology and Anatomy Dept. of Biomedical Engineering, University of Rochester School of Medicine, Rochester, NY.**

Previous studies have demonstrated that responses of whisker-barrel circuits are sensitive to rapidly changing thalamocortical input signals. In this study, we examined how this sensitivity depends on the intrinsic properties of individual barrel neurons. We used whole-cell patch recordings in rat brain slices to examine the sensitivity of barrel neurons to input timing and magnitude using injected current and conductance waveforms. Square currents were used to classify cells as regular spiking (RS), fast spiking (FS), or other neuronal subtypes (e.g., low-threshold spiking). Current ramps varied in magnitude and rate of rise were used to assess the sensitivity of each neuron using a relatively standard stimulus. For a more natural stimulus, we used a dynamic clamp to simulate synaptic volleys of thalamic input varied in spike count and temporal distribution. Responses were quantified in terms of firing probability, latency to first spike, and variability. All three measures depended both on input magnitude and timing for all cell types and for both protocols. FS cells required a higher input magnitude than RS cells to reach threshold (50% firing probability). RS cells had longer and more variable latencies than FS cells. Responses to simulated thalamic volleys revealed differences not apparent in responses to current ramps. FS cell response latency decreased linearly with input distribution breadth but varied little with input spike count above threshold. By contrast, RS cell response latency decreased nonlinearly with both input distribution breadth and increased input spike count. These data suggest that the intrinsic response properties of barrel neurons contribute to the sensitivity of the barrel circuit to input timing. Moreover, preliminary modeling results suggest that differences between RS and FS cell responses can enhance the circuit’s overall sensitivity to input timing by means of synaptic interactions. Support provided by: Sloan and Whitaker Foundations.

**Robert N. S. Sachdev, Bilal Haider, Alvaro Duque, Andrea Hasenstaub, Yuguo Yu, David McCormick**

**CORTICAL ACTIVITY MODULATES STIMULUS EVOKED CORTICAL RESPONSES IN PRIMARY SOMATOSENSORY CORTEX OF THE RAT AND PRIMARY VISUAL CORTEX OF THE CAT: A COMPARATIVE STUDY**

**Department of Neurobiology, Kavli Institute for Neuroscience, Yale University School of Medicine New Haven, CT.**

Cortical activity can strongly modulate sensory responses. Exactly how spontaneous cortical activity may influence sensory responses in the neocortex has been investigated recently by examining the interaction of spontaneous Up and Down states with responses to whisker stimulation in the rat somatosensory cortex and with visual stimuli in cat visual cortex. These two systems have yielded apparently conflicting results. In rat S1 cortex, a vibrissal-sensory stimulus delivered during the persistent activity of the Up state results in a smaller depolarizing and spike response than when the same stimulus is delivered during the Down state (Sachdev et al., 2004). In contrast, in cat V1 the ongoing network activity of the Up state dramatically enhances responses to visual stimulation (Hasenstaub et al.). In cat V1, neurons are nearly incapable of being driven to spike by a stimulus that occurs during the Down state. Here, we investigated these differing observations in a comparative study. In the rat S1 optimal stimuli (single whisker deflection) evoked reliable and large barrages of PSPs irrespective of cortical state, while in cat V1 presentation of a single flashed bar within the cell’s RF typically did not evoke large barrages of PSPs in the Down state and evoked action potentials only if the network was in the Up state. Ramp and hold deflection of a single whisker in the rat could evoke the transition from Down to Up, while only strong whole field visual stimulation could evoke this transition in cat V1. We conclude that the manner in which the rat somatosensory cortex and cat V1 respond to sensory stimuli may be fundamentally different, with strong and explosive responses being more easily evoked in the rodent barrel system. These differences explain the apparent discrepancy between previous findings concerning the interaction of spontaneous activity and sensory evoked responses. Funded by NIH and the Kavli Center for Neuroscience.

**Dirk Schubert, Esther Grahl, Rolf Kötter, Jochen F. Staiger**

**Intracortical functional connectivity of pyramidal neurons in layer Va suggests a possible function as a cortical interface between the paralemniscal and lemniscal pathway**

**C.&O. Vogt Institute for Brain Research, Heinrich Heine University Duesseldorf, Germany**

IIn primary somatosensory cortex layer Va is thought to be one major cortical entry point for tactile sensory information transmitted through thalamocortical afferences of the paralemniscal pathway. We investigated layer Va pyramidal neurons, one likely target of these afferences, in terms of their possible integrative capabilities and function in intracortical networks. For this we combined detailed electrophysiological and morphological characterization with mapping of intracortical origins for excitatory and inhibitory synaptic inputs onto single pyramidal neurons by caged glutamate photolysis of rat barrel cortex in vitro. Though being electrophysiologically heterogeneous, layer Va pyramidal neurons displayed uniform morphological properties and comparable functional input connectivity patterns. We found all layer Va pyramidal neurons possessing numerous horizontal bouton-laden axonal profiles within their own layer, reaching well into the neighboring barrel associated cortical column. From the same innervated region they also received the bulk of their excitatory and most robustly inhibitory inputs. Layer Va pyramidal neurons furthermore projected extensively to granular- and supragranular layers, with the granular layer being the second prominent source for their intracortical synaptic inputs. Layer Va pyramidal neurons thus may effectively integrate information intralaminarly as well as from neurons in layer IV, the main processors of sensory information of the lemniscal pathway. This gives direct evidence for the notion of layer Va pyramidal neurons functioning as an early cortical interface between the paralemniscal and the lemniscal pathways. Subsequently one would like to know what other cortical layers are wired in a way to promote exchange of information between these two sensory pathways?

**Cornelius Schwarz, Harald Hentschke, Florent Haiss, Olga Rodriguez-Sierra.**

**Role of Movement Related Central Signals for Active Touch**

**Hertie Institute for Clinical Brain Research, Department for Kognitive Neurology, University Tübingen, Germany**

Animals actively explore their environment in varied ways to optimize sensory input. Actively collected sensory information has the advantage that it is tailored to serve best the behavioral purposes of the animal. But in exchange, this kind of data has to be carefully weighted and interpreted with reference to the explorative strategy used. We use the rat’s vibrissal system as a model system to study adjustment of tactile signals by signals related to explorative movement. Experiments with head-fixed rats trained to whisk toward a moving object and precise whisker tracking allowed us to disentangle sensory and motor aspects of active touch. Recordings in barrel cortex revealed a movement dependent excitatory signal that was correlated with a reduction of the tactile response and its cortical spread. The non-rhythmic nature of the modulatory signal indicated a central origin, a notion confirmed by its intactness and its continued modulatory role after deafferentation. General states of vigilance were unlikely to be at the base of the observed modulation as suggested by spectral analysis of field potentials prior to active and passive touch. The association to movement, on the other hand, was found to be temporally precise such that movement initiation or cessation would switch between active and passive touch within 100-125 ms. Pursuing the working hypothesis that the non-rhythmic modulatory signals might stem from the motor system we investigated vibrissal motor cortex which is upstream of presumed rhythm generating circuits in the brainstem. We localized a small sub-region of vibrissal motor cortex (RW) that, indeed, generates natural-like rhythmic whisking at frequencies around 7 Hz when electrically stimulated with long stimulus trains at high frequencies. At the time of writing this abstract we had looked at first preliminary unit recordings within RW during self-initiated whisker movements tentatively confirming its non-rhythmic nature. Combined stimulation of RW and barrel cortex in awake animals showed that RW activation mimics effects of self-initiated active touch in barrel cortex. In summary we have established model system that allows us to study central modulation of tactile processing for active perception in rat’s vibrissal system. Open questions are waiting to be answered on the structural as well as the behavioral level. Structurally, it will be important to figure out the origins and pathways involved in the interference and whether the modulation found can be taken as a general model of cortical inter-areal signal processing. Behaviorally, it will be important to investigate the detailed perceptual benefit of the central modulation found.

**S. Murray Sherman**

**The Role of Thalamus in the Flow of Information to Cortex**

**Department of Neurobiology, Pharmacology & Physiology, University of Chicago**

The prevailing view of thalamocortical functioning is that information is relayed to cortex via primary sensory thalamic nuclei and then is processed via direct corticocortical connections. We suggest another view: that primary thalamic relays represent a first relay of a type of information (e.g., visual or somatosensory; these are first order relays) and that much corticocortical communication has a thalamic link via higher order relays. Examples of first and higher order relays, respectively, for vision are the lateral geniculate nucleus and most or all of the pulvinar, and for somatosensation, are the ventral posterior and most or all of the posterior medial nuclei. It is important in this schema to distinguish between corticothalamic projections emanating from layer 6 and those from layer 5. All thalamic relays receive a layer 6 input, which is modulatory in function and mostly feedback; it does not represent significant information flow. Only higher order relay receive, in addition, an input from layer 5, which does carry the information to be relayed to the next cortical area and thus is feedforward. The idea is that these layer 5 inputs have the same properties and function for higher order relays as do retinal and medial lemniscal inputs to the lateral geniculate and ventral posterior nuclei. The implication for somatosensory processing is that the ventral posterior nucleus (and probably some of the posterior medial nucleus) acts as a first order relay to S1 and that much information is then carried from S1 and beyond in cortex via relays through the posterior medial nucleus. This view challenges and extends the conventional view that corticocortical communication is based mainly on direct corticocortical connections. In this sense, any new information reaching a cortical area, whether from a subcortical source or another cortical area, benefits from a thalamic relay. Thus the thalamus not only provides a behaviorally relevant, dynamic control over the nature of information relayed, it also plays a key role in basic corticocortical communication. Evidence to support this hypothesis will be presented.

**Maik C. Stüttgen & Cornelius Schwarz**

**Impact of kinematic parameters of whisker deflection on detectability in rats Hertie-Institute for Clinical Brain Research, Department of Cognitive Neurology, University of Tübingen, Tübingen**

What determines the detection of a whisker deflection in rats? To elucidate this question, we performed psychophysical experiments in head-fixed rats that were trained to respond to a single whisker stimulus by licking a water reward from a spout in front of their snouts. To separate the contribution of different kinematic parameters on detection, we used whisker deflections based on half period sine waves. By leaving the peak velocity constant, these stimuli allowed us to disentangle the different contributions of peak amplitude and peak acceleration to the detectability of the stimulus. A random sequence of such stimuli was presented to one individual whisker using a piezo bender. The animals’ sensitivity was measured using the method of constant stimuli. The resulting psychometric function appeared bipartite: at low peak accelerations, sensitivity is determined largely by deflection amplitude, while the sensitivity to small-amplitude stimuli follows the peak acceleration of a given stimulus. We have started measuring multielectrode signals from barrel cortex of rats during this task.

**Trigeminal ganglion cell responses to large vibrissal deflections**

**Blythe Towal, Mitra Hartmann, Northwestern University**

As a rat explores the environment with its vibrissae, tactile information must be mechanically transduced back to receptors in the follicle. Mechanical analyses in our laboratory have specifically predicted that torque at the whisker base is a critical variable for determining the radial distance of an object, and that (for point contact) this torque corresponds in a one-to-one fashion with the curvature of the whisker [1]. We have further predicted that a subset of neurons in the trigeminal ganglion (Vg) should encode for torque/curvature [2]. To date, most physiological studies of Vg neurons have evaluated responses only to small whisker deflections (typically less than 6 degrees), and the forces associated with these deflections have not been measured. In the present study, we recorded from anesthetized rats to characterize Vg neuron responses to large (up to 30 degrees) deflections of the vibrissae in varying directions. A sensitive load cell was used to simultaneously measure the imposed forces. Consistent with previous studies, we observed both slowly adapting (SA) and rapidly adapting (RA) cells. In addition, some Vg neurons were found to respond to the radial distance of the applied force, supporting our prediction of torque-sensitivity. Almost all Vg neurons exhibited strong directional sensitivity, but some cells responded only when the whisker was moved towards its resting position, regardless of the direction of motion. This response property contrasts with the global direction sensitivity reported previously and suggests direction sensitivity with reference to the resting position of the whisker. We discuss these results in the context of the encoding properties of Vg cells and subsequent stages of trigeminal processing.

**Jason C. Trageser, Kathryn Burke, Ying Li, Larisa Sellers and Asaf Keller**

**Functional consequences of zona incerta heterogeneity**

**Program in Neuroscience, University of Maryland School of Medicine, Baltimore, MD, USA.**

The zona incerta (ZI) is a predominately GABAergic ventral thalamic nucleus that suppresses whisker-evoked responses in the posterior medial (POm) thalamic nucleus of the rat. Anatomical studies have shown that ZI is comprised of a heterogeneous population of neurons that can be divided into sectors based on immunocytochemical markers. We sought to determine if this anatomical division relates to physiological differences in ZI neurons. Neurons in ventral ZI but not dorsal ZI stain for parvalbumin (Pv). We retrogradely labeled ZI neurons projecting to POm with FluoroGold and immunostained for Pv to define the dorsal/ventral border of ZI. We observed preferential retrograde labeling of ventral ZI neurons co-labeled with Pv. We next obtained in vitro whole cell patch clamp recordings from ZI neurons. Ventral but not dorsal neurons were spontaneously active (median firing rate = 6.0 Hz; 6.7 ± 1.7 Hz). ZI neurons receive cholinergic brainstem inputs and possess muscarinic receptors; we therefore tested the hypothesis that ZI activity is modulated by acetylcholine. Bath application of the cholinergic agonist carbachol to spontaneously active ventral ZI neurons resulted in suppression of their activity (18 of 21). Co-application of the competitive antagonist atropine (30µM) blocked the effects of carbachol (7 of 8). Following recordings, ZI neurons were filled with biocytin for reconstruction. The dendrites of ZI neurons remained confined to the sectors in which their cell bodies were located, rarely projecting across the border into the adjacent sector. We found no significant differences between ZI neurons with respect to soma length (61.5 ± 13.8 µm), soma area (207.7 ± 66.8 µm3), number of dendrites (3.23 ± 1.18) and total dendritic length (990.0 ± 537.7 µm). We propose that ZI is segregated into functionally distinct sectors with spontaneously active ventral ZI neurons preferentially targeting POm. We suggest that brainstem cholinergic activity modulates inhibitory ZI inputs to POm gating sensory transmission.

**Roxanna M. Webber, Alireza S. Boloori, and Garrett B. Stanley**

**Neural Representations of Tactile Patterns**

**RMW is with Harvard-MIT Division of HST; RMW, ASB, GBS are with Div. of Engineering & Applied Sciences, Harvard University**

The vibrissa pathway transforms features of the tactile world into neuronal representations which ultimately form the animal’s perception of surfaces and objects in the outside world. Understanding the relationship between the sensory stimulus and the corresponding neural representation is a crucial step in identifying the ethologically relevant elements of the neural code. We have previously shown that the cortical response to tactile patterns can be well predicted from the observed response characteristics for paired vibrissa deflections. Specifically, the cortical response to complex patterns of relatively low frequency (< 40Hz) vibrissa deflections is largely predictable from a nonlinear combination of underlying constituent elements. These constituent elements reflect the time-course of post-excitatory response suppression revealed through a paired-deflection “condition/test” stimulus paradigm. More recently, we have shown that the cortical representation of even more complex spatiotemporal patterns is similarly predictable from the simple paired-vibrissa interactions, and that the relative phase of periodic stimuli across vibrissa strongly influences the cortical response. Taken together, these nonlinear neuronal interactions 1) shape the transient and steady-state adaptation response, 2) predict the response heterogeneity observed experimentally across cortical cells, and 3) set theoretical limits on discriminability based on a simple ideal observer of cortical activity. Open Questions: What are the relevant frequencies, and how do we resolve low frequency and high frequency findings? How are these response properties modulated by behavioral state? What is the functional role of adaptation?

**Roxanna M. Webber and Garrett B. Stanley**

**Thalamocortical Transformations of Temporal Stimulation Patterns in the Rat Vibrissa System**

**Harvard-MIT Division of Health Sciences and Technology & Division of Engineering and Applied Sciences, Harvard University**

Rats and other rodents use their vibrissae to actively explore the external environment, producing patterns of vibrissa deflections reflecting the interaction between the vibrissa movement and the textural properties of surfaces. The peripheral representations of the stimulus are transformed by the dynamics of the thalamocortical circuitry, producing representations that eventually give rise to the sensory percept. We previously showed that the response of cortical neurons to temporal patterns of vibrissa deflection was predictable from the time course of suppression following an excitatory stimulus. What was not clear, however, was if the observed response patterns were generated through intra-cortical connections or partially inherited from thalamic projections. To address this question, we recorded single unit activity in the ventral posterior medial nucleus (VPM) of the thalamus in anesthetized Sprague-Dawley rats. A subset of VPM neurons increased their response to the third deflection in a three deflection pattern when the first deflection was moved closer in time to the second two deflections, similar to our previous finding of “lifting of suppression” in the cortex. Some VPM neurons also responded to a bi-directional periodic stimulus with a steady-state response that was larger in one direction than the other, consistent with cortical findings. The response of a VPM neuron to the three deflection stimulus was a good indicator of the steady-state response to a periodic stimulus. Taken together, these findings suggest that many of the response properties previously observed in the cortex originate at the level of the thalamus, and thalamocortical transformations further refine them for higher level processing. This work was supported by NIH R01NS48285-01A1 and an NSF graduate research fellowship to R. M. Webber.

**E. L. White**

**Observations on the Shapes of Dendrites**

**Dept. of Morphology Ben Gurion Univ. Sch. of Medicine**

 Dendrites are commonly considered to be cylindrically shaped structures that may have spines whose attachment points bear no particular relationship to dendritic morphology. Analyses of the morphology of spiny stellate cell dendrites reconstructed in 3-D from serial thin sections through mouse barrels indicates that these dendrites are shaped like flattened cylinders; the ratio of the long to short axes in cross-sectioned dendritic profiles is typically 2:1. The flattened shape is maintained along the entire length of the dendrites with essentially no twisting about the central long axis of the process. Planes of flattening are unrelated to the orientation of dendritic segments within the brain, bear no relationship to the plane of section, and are unchanged for various estimates of section thickness. Thus, the flattened shape is due neither to tissue compression, sectioning artifact, or to inaccuracy of the reconstruction method. Spine necks are attached preferentially along the relatively narrow, ridge-like regions of the flattened shafts; the ridges bear two-thirds of the spine attachment points. In cross-section, the dendrites with their attached spines resemble the shapes of bitufted cells most of whose dendrites are attached preferentially to opposite poles of their cell bodies. Thus, both spiny stellate cell dendrites as viewed in cross-section, and bitufted cell bodies are elongated along the poles that give rise to their major projections. These morphological phenomena are suggested to have a common basis: the non-homogeneous distribution of cytoskeletal elements associated with structural stability and/or intracellular transport. Perusal of published work on the apical dendrites of pyramidal cells indicates that they too exhibit the flattened morphology and preferential distribution of spines observed for spiny stellate cell dendrites. The flattened shape may be an artifact of fixation, and if so, could be imagined to result from the shrinking of cell membrane around the cytoskeleton and/or from the collapse of particularly delicate cytoskeletal elements within certain dendritic compartments. Alternatively, the shape reported here may reflect the in vivo condition. Consequences for various aspects of electrical activity within dendrites of the possible compartmentalization of the dendroplasm and of the observed irregular distribution of spines remain to be determined. Supported by Israel Science Foundation grant 52/00-4 ELW.

**Jason H. Wolfe (1), Sohrab Pahlavan (2), Patrick J. Drew(2), Henry D.I. Abarbanel(1), Daniel E. Feldman(2)**

**Whisker resonance measured in the awake behving rat**

1. **Physics Dept., UCSD (2) Division of Biological Sciences, UCSD**

Rats sweep their whiskers across objects to perform high resolution texture discrimination. Whiskers possess intrinsic resonant frequencies, which vary systematically across the whisker pad with whisker diameter and length. The whisker resonance hypothesis posits that as whiskers sweep across a texture, the largest vibrations will be induced in those whiskers whose resonant frequency best matches the frequency spectrum of induced tip vibrations, creating a place code for texture. Although this hypothesis has been tested in the anesthetized animal, it is unclear whether whisker resonance occurs in the awake behaving animal. We investigated the mechanical filtering properties of whiskers in animals trained to whisk freely in air and against textured surfaces. Whisker motion was imaged with high spatial and temporal resolution (4 khz frame rate) using a linear ccd array. High frequency vibrations (>100 hz, mean speed = 6.2 rad/s) were present in whiskers during free whisking in air. Consistent with the resonance hypothesis, vibration spectra were systematically shifted toward higher frequencies in short whiskers relative to longer whiskers within each animal (n=2). As single whiskers (n=4) were trimmed vibration spectra shifted toward higher frequencies and as whiskers (n=2) regrew, vibrations shifted systematically toward lower frequencies. These vibrations were absent in plucked whiskers moved mechanically, but occurred during artificial whisking induced by facial nerve stimulation. These results indicate that vibrations during whisking in air arise from muscle contraction during whisking, filtered by whisker resonance. We hypothesize that these vibrations contribute to spontaneous spiking of whisker afferents.

**Edward Zagha1, Elaine S. Kwon1, Michael Chen1, Alev Erisir2, and Bernardo Rudy1**

**Kv3.3 subunit expression in dendrites of spiny stellate interneurons of barrel cortex**

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K+ channels are ubiquitous in excitable membranes. K+ channels are notably diverse in their voltage-dependence and kinetics of activation/inactivation, and the complement of channels within a neuronal compartment will largely determine the excitability of that compartment. In this study we have focused on the expression, localization and function of a specific voltage-gated K+ channel, Kv3.3, in mouse barrel cortex. Many studies have shown that Kv3 channel expression in the somatic compartment confers the ability of neurons to fire thin spikes at high frequency. In addition to being expressed in the soma and proximal dendrites of a subset of GABAergic interneurons, Kv3.3 immunoreactivity also presents a diffuse pattern under light microscopy. This pattern is isomorphic with the cytochrome oxidase stain of barrel architecture, making Kv3.3 immunoreactivity a useful marker of barrel architecture in double immunofluorescence studies of adolescent mice. Using in situ hybridization and immuno-electron microscopy, we demonstrate that the diffuse barrel stain is likely to emerge from the sub-cellular localization of Kv3.3 subunits in distal dendrites of spiny stellate interneurons. Spiny stellate interneurons are known to receive direct thalamic inputs as well as local cortical inputs, and project glutamatergic terminals to neurons within the same barrel column, contributing significantly to the cortical circuit and likely integral for sensory processing of whisker inputs. Notably, spiny stellate interneurons can not sustain high frequency firing, suggesting a different role for Kv3 channels in excitable membranes when localized to distal dendrites. It is possible that these dendritic Kv3.3 channels influence the propagation and summation of synaptic currents or modulate the dynamics of back-propagating action potentials in spiny stellate interneurons.

**Probing cortical GABAergic interneuron diversity using BAC transgenic mice Edward Zagha1, Ethan M. Goldberg1, Elaine S. Kwon1, Tanya R. Stevens2, Guojun Ma2, Nathaniel Heintz2, and Bernardo Rudy1**

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Cortical GABAergic interneurons exhibit a broad diversity across multiple parameters. Anatomically, these cells display many patterns of dendritic arborization, axonal extent, gap junctional connectivity, and subcellular localization of synaptic contacts onto target cells. Electrophysiologically, these cells display different discharge patterns and short-term synaptic dynamics. Functionally, these cells have been shown to be differentially active with respect to cortical rhythms. There has been a significant effort towards classifying these cells, and identifying molecular markers of the various classes, which will facilitate, among other things, the genetic targeting and manipulation of specific interneuron subsets. Towards this goal, we have identified a number of bacterial artificial chromosome (BAC)-transgenic mice (generated by the NINDS-sponsored GENSAT Project) that label subsets of GABAergic cortical interneurons. Among these, for example, is a 5-HT3A-GFP line, which labels a subset of cortical GABAergic interneurons that are negative for parvalbumin (PV), have a different laminar distribution than PV-containing cells and display either a so-called “regular” or an “irregular spiking” discharge pattern. A novel gene profiling method will be used to identify molecular components that distinguish between functionally different classes of interneurons.

**A physical model of active whisking and early signal processing in the whisker pathway Ben Mitchinson(1), Ian Gilhespy(2), Martin J. Pearson(2), Mokhtar.Nibouche(2), Anthony G. Pipe(2), Chris Melhuish(2), Kevin N. Gurney(1), Peter Redgrave(1), and Tony J. Prescott(1) 1. Department of Psychology, University of Sheffield, UK. 2. Intelligent Autonomous Systems Laboratory, University of the West of England, UK.**

 We describe the development of a physical model of an active whisker and its interface with models of signal processing in the follicle and brainstem. We simulate the whisker shaft using a tapered, composite structure whose design approximates relevant characteristics of real vibrissae. Intrinsic whisking muscles are modelled using 'BioMetal' fibres that mimic some of the properties of real muscle. A spring generates passive retraction. Sensory transduction is modelled using micro-strain gauges, attached to the base of the shaft, whose outputs drive an implementation of our model of electro-mechanical processing in the follicle (Mitchinson et al., 2004, Proc Biol Sci. 271:2509-16) embedded in custom digital hardware. The outputs from the follicle model -spike trains similar to measurements from rat primary afferents (e.g. Szwed et al, 2003, Neuron, 40, 621-630)- are passed to a 'spiking' neuron model of trigeminal sensory complex for further processing. This research is part of the ongoing 'Whiskerbot' project ([www.whiskerbot.org](http://www.whiskerbot.org)) that aims to develop a complete artificial whisker sensory system modelled on the rat macro-vibrissae. In the full model the outputs of the trigeminal complex will drive orienting via a loop through a model superior colliculus, and texture discrimination in a model of barrel cortex. We briefly describe these loops.