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Corresponding author: JOSHUA C. BRUMBERG

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Barrels by the sea: Barrels XX meeting report

RADDY L. RAMOS, & JOSHUA C. BRUMBERG

5 *Department of Psychology, Queens College, CUNY, New York, USA*

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Abstract

10 The 20th annual Barrels meeting brought together researchers who utilize behavioral, physiological, anatomical, and molecular techniques to understand the structure and function of the barrel system. Barrels XX featured talks on the role inhibition has in shaping cortical responses within the barrel system, the molecular cues that influence the development of the whisker-to-barrel system, and the synaptic plasticity that can shape responses within the system. The meeting highlighted why the whisker-to-barrel system is an ideal model to investigate the development of cortical circuitry and how its functioning can influence behavioral responses.

Keywords: *Barrel, whisker, vibrissa, cortical circuits*

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On the first two days of November 2007, the 20th annual Barrels meeting was convened by the sea in the Sherwood Auditorium of the Museum of Contemporary Art San Diego, La Jolla campus. Barrels XX like all previous meetings brought together researchers who utilize the whisker-to-barrel system as a model to understand neural development, plasticity, physiology, and anatomy.

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The first session on the role of cortical inhibitory circuits was moderated by **Randy Bruno** (Columbia University) who defined some of the important issues surrounding how inhibitory circuits are defined anatomically/physiologically and how they are engaged by sensory stimulation. Dr Bruno highlighted the differences in action potential waveforms between excitatory and one class of inhibitory neurons within the barrel and how these cell types have different response properties. For example, the inhibitory fast spiking units having poorer angular tuning and more multi-whisker receptive fields which are correlated with differences in the number and locations of the thalamic inputs on to these phenotypes. **Diego Contreras** (University of Pennsylvania) highlighted several different roles that inhibition has in the barrel circuit. He emphasized the role inhibition has in determining over what time

period a neuron integrates afferent information, demonstrating that neurons within thalamic recipient zones such as the barrel have much shorter windows than neurons residing in the supragranular layers. Interestingly, intracellular recording studies *in vivo* revealed that increasing the velocity of whisker deflection increases the magnitude of the evoked excitatory postsynaptic potentials (EPSPs) and inhibitory postsynaptic potentials (IPSPs), but does not affect the timecourse of the EPSP/IPSP sequence. In other words, there is no change in the window of opportunity during which EPSPs can exert their influence before they are damped down by disinaptic inhibition after 5–7 ms. Dr Contreras studies argued that whisker-evoked IPSPs have little to do with the finding that when recording from the columnar whisker, prior deflection of an adjacent whisker decreases the columnar whisker response. Next, **Edward Callaway** (Salk Institute for Biological Sciences) emphasized that there are many different types of inhibitory interneurons each with their own characteristic synaptic inputs and axonal targets. Using laser uncaging of glutamate, Dr Callaway demonstrated that interneurons found within a specific cortical lamina received inputs from some, but not all the other cortical laminae and their axons

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Correspondence: J. C. Brumberg, Department of Psychology, Queens College, CUNY, 65–30 Kissena Boulevard, Flushing, NY 11367, USA. Tel: +1 718 997 3541. Fax: +1 718 997 3257. E-mail: Joshua.brumberg@qc.cuny.edu

might only target specific laminae/sub-laminae. For example, using transgenic mice expressing GFP (green fluorescent protein) specifically in interneuron subtypes, it was revealed that Martinotti cells and bipolar cells receive the majority of their excitatory inputs from layers 2/3. His results argued for a dramatic amount of specificity of the connections made onto and originating from cortical interneurons. Finally, **Anna Devor** (University of California San Diego) focused on the mechanisms driving the hemodynamic response in the barrel following whisker deflections. Using physiological and hemodynamic measures, Dr Devor demonstrated that the greatest change in arteriole diameters was centered on the area of greatest cortical activation. In contrast, the surrounding blood vessels constricted. Surprisingly, the hemodynamic response was uncorrelated with simultaneously recorded local field potentials. Imaging techniques indicated that there was a large response observed contralateral to the whisker deflection followed by responses seen in the ipsilateral cortex delayed by approximately 20 ms which was characterized by a constriction of the blood vessels. She concluded that the hemodynamic response was due to the release of vasoactive peptides by interneurons not due to a metabolic demand or increases in multi-unit activity/local field potentials. The morning's session emphasized the diverse roles inhibition has in shaping the responses of neurons and the associated blood flow to the barrel.

After a brief break there followed a series of short platform talks moderated by **Martin Deschenes** (Laval University). **Kentaroh Takagaki** (Leibniz Institut für Neurobiologie) demonstrated using voltage-sensitive dyes that neuronal activity is highly correlated with recorded EEG and that the overall activity of the neurons imaged does not encode for the direction a whisker is deflected. Whisker stimulation evokes waves of activity that appear to encode the presence but not any characteristic of the stimulus. **Illan Lampl** (Weizmann Institute of Science) focused on how adaptation to whisker stimulation influences the balance of excitatory vs inhibitory inputs onto neurons. Using *in vivo* whole cell recording techniques from layer 2/3 and 4 neurons, it was observed that the incoming PSPs became slower and broader due to greater adaptation of disynaptic IPSPs. Specifically, excitatory inputs were found to initially decrease in magnitude faster but reached a steady state whereas inhibitory inputs adapt throughout the stimulus train. Interestingly, adaptation was found to be greater in layer 2/3 compared to layer 4 neurons. **John Curtis** (University of California San Diego) looked at how whisker kinematics and stimulus contact are reflected in the spike trains of neurons in rat barrel cortex.

Using rats trained to whisk and make contact with a stimulus as well as those trained to whisk in air, most neurons responded to stimulus contact, but a significant population (20%) only responded when the contact occurred at a specific phase of the whisking cycle. This signal may allow the animals to estimate the location of an object in space. A shunting inhibition model with three compartment cells (dendrites, soma, spike generator) was capable of fitting experimental data.

The afternoon session initiated with a series of short talks moderated by **Mitra Hartmann** (Northwestern University). **Cornelius Schwarz** (University of Tübingen) argued that there were two perceptual channels encoding whisker movement: one that is conveyed by slowly adapting receptors and is activated by high amplitude low velocity sweeps and the other is selectively activated by low amplitude high velocity impacts and is conveyed via rapidly adapting receptors. *Ideal observer analysis* revealed that a single spike is capable of reliably encoding the presence of a stimulus but three spikes are required to match psychometric data.

Vivek Khatri (Hunter College) demonstrated that a subpopulation of trigeminal ganglion neurons encode whisker kinematics in head-fixed rats trained to whisk in air. **Christian de Kock** (Erasmus University Medical Center) using juxtacellular recording/labeling techniques in head-fixed rats whisking in air showed that the firing rates of cortical neurons varied as a function of the lamina that the soma was situated. Layer IV neurons showed no correlation with whisking, layer V thick tufted neurons decreased their firing in response to whisking, and layer V thin tufted neurons increased their firing rates with whisking. Most of the responsive neurons fired preferentially during the protraction phase of the whisking cycle. **Ehud Ahissar** (Weizmann Institute of Science) focused on the issue of object encoding in space. He posited that radial coding (distance from the head) was based on a firing rate code since firing rate decreased as a whisker encounters an object close to the base to its tip. Where an object was in the horizontal plane was based on a time code. Finally, vertical coordinates are encoded by a spatial code (which whiskers contacted the object, e.g., A row vs E row). **Tony Prescott** (University of Sheffield) using high-speed videography demonstrated that whisking changes when a rat contacts an object with its whiskers, resulting in decreases in whisk amplitude, decreases in the spread of the whiskers, and increases in the time that it takes to reach maximum protraction. The net result of these adaptations is to maximize sampling of the contacted object. **Hajnalka Bokor** (Institute of Experimental Medicine, Hungary) demonstrated that the local

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field potential in the barrel cortex was more correlated with the activity in the posterior medial nucleus (POm) of the thalamus compared to the ventral posterior nucleus (VPM). Silencing the cortex via initiation of spreading depression resulted in no activity in POm, but VPM was unaffected.

Thursday late afternoon saw the first Barrel data blitz where researchers were given exactly 3 min to present their latest results. This was followed by a poster session and dinner at the La Jolla Women's Club across the street from the Museum.

Friday morning started with a session on the molecular development of the barrel system led and moderated by **Jochen Staiger** (Albert-Ludwigs Universität). Dr Staiger provided an overview of the basic processes underlying neural development including: neural induction, polarity/segmentation, migration, determination/differentiation, axon guidance, target selection, synapse formation, and finally refinement of synaptic connections. **Yashushi Nakagawa** (University of Minnesota) focused on the cues leading to the development of specific thalamic nuclei. Thalamic sensory nuclei are generated in the rostral thalamus and the gene *Olig3* marks the entire thalamic progenitor zone. In contrast, *Mash1* and *NKX2.2* demarcate the rostral zone. The genesis of specific thalamic nuclei and the migration of cells from the progenitor zone to their final resting place is influenced by gradients of *Dbx1* (caudal > rostral) and *Olig2* (rostral > caudal). **Ed Lein** (Allen Institute for Brain Science) provided a detailed description about how the Allen Institute for Brain Science went about the task of screening the mouse brain for all its known gene products as well as preliminary data from a project to do the same for the human brain. The data contained within the generated database is being used to determine the regional expression of specific genes to determine if specific cortical areas, for example, primary somatosensory cortex (S1), have distinct gene profiles. Approximately 3000 genes show heterogeneous expression in S1 when compared to other cortical areas. Among this list, neurons in layer V and VIb have the most specific/restricted gene profiles. Approximately, 155 genes found in this list delineate interneurons. **Peter Kind** (University of Edinburgh) focused on the role that phospholipase C-Beta1 (*PLCB₁*) has on the development of the barrel cortex. The gene is present early in development, but not during later stages and its targeted deletion results in the absence of the barrel pattern using cell makers, despite normal segregation of thalamocortical afferents. Dr Kind went on to demonstrate that many of the key steps of barrel formation (pathfinding by thalamocortical afferents, dendritic orientation, and synapse formation) are all dependent upon glutamate receptors.

Gord Fishell (New York University), using genetic and physiologic techniques, was able to elegantly show that different phenotypes of GABAergic interneurons develop in distinct proliferative regions of the embryonic forebrain. For example, double bouquet and neurogliaform cells which both discharge regular spikes derive from the caudal ganglionic eminence whereas those with the fast spiking phenotype (basket, Martinotti, and chandelier cells) originate from the medial ganglionic eminence.

The Friday morning session was concluded with a series of short talks moderated by **Mary Ann Wilson** (Johns Hopkins University). **Amy Nakashima** (University of Calgary) showed that Zn^{2+} expression within the barrel cortex was influenced by the sensory environment. Rats in deprived (C-row trimmed) conditions showed elevated Zn^{2+} levels in the deprived barrels. Interestingly, animals reared in an enriched environment for at least 1 week also showed an increase in Zn^{2+} staining. **Malgorzata Kossut** (Nencki Institute for Experimental Biology), using a conditioning paradigm where whisker stimulation was associated with a tail shock, demonstrated that the 2-deoxyglucose representation in layer IV for the associated barrel expanded. Following the training there was an increase in the number of inhibitory and excitatory synapses in the conditioned barrel. **Raddy Ramos** (Queens College, CUNY) reported that inbred mouse strains have a high incidence of cortical malformations. Surveying 11 inbred strains and the Allen Brain Atlas revealed that approximately 30% of animals possessed gross cortical malformations whereas outbred strains did not.

Friday afternoon began with another series of short talks moderated by **Mary Ann Wilson** (Johns Hopkins University). **Mitra Hartmann** (Northwestern University) focused on the mechanical basis of three-dimensional feature extraction. She argued that animals must integrate across multiple whiskers and that these computations may take place in the Interpolaris division of the Spinal nucleus of V. The animal must account for three angular positions (horizontal and vertical planes) as well as torsion (rotation of the whisker), three moments (twists of the whisker, push of the whisker in the horizontal and vertical planes), and three forces (vertical and horizontal translation of the whisker, axial). **Peter Cahusac** (University of Stirling) highlighted the role that metabotropic glutamate receptors have on processing within the barrel. These receptors are often located extrasynaptically and may play important roles in modulating overall activity within the barrel cortex.

Barrels XX concluded with another data blitz prior to the final session on the synaptic plasticity of the barrel system which was moderated and introduced by **David Kleinfeld** (University of California

San Diego). Dr Kleinfeld highlighted the role that spike timing dependent plasticity has in sensorimotor systems and the role that plasticity has in shaping and maintaining the connections within the barrel system. **Kevin Fox** (Cardiff University) highlighted the role of nitric oxide (NO) in the development and maintenance of synaptic plasticity within the barrel cortex. Blocking the synthesis of NO postsynaptically significantly reduced the induction of long-term potentiation. In addition, mice where NO production has been genetically deleted within the cortex eliminate both pre- and postsynaptic components of potentiation. **Hui Chen Lu** (Baylor University) focused on the anatomy and physiology of mGLUR5 knockout mice that have small barrels and altered staining using cellular (Nissl) and metabolic (cytochrome oxidase) stains. Experiments revealed that these animals had a longer critical period where follicle lesions could still impact barrel formation. Cortical neurons in knockout mice displayed more numerous spines on their dendrites and showed larger amplitude mEPSPs. Finally, **Alison Barth** (Carnegie Mellon University) showed that following one day where just one whisker was preserved on each side of the face, there was an increase in spike output for the neurons in the preserved barrel. Further analysis of these mice

in vitro revealed that the size of the AMPA-mediated response in the supragranular layers following stimulation of layer IV was increased and long-term potentiation could not be evoked in the spared column. Dr Barth argued that the lack of LTP was due to the fact that following the deprivation all the synapses have already been strengthened and thus no further increases in synaptic strength were possible.

The Barrels meeting remains the oldest satellite meeting to the Society for Neuroscience annual meeting. Barrels XX once again highlighted the diversity of research that is conducted in this model system for cortical development, anatomy, physiology, and behavior.

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