

**"What unique advantage does the rodent vibrissa sensorimotor system offer that makes it particularly suited for groundbreaking discoveries in neuroscience, and why?"**

## **Feedback and loops**

Thalamocortical loop from Simone Russo: The mouse vibrissae system is an ideal model to investigate feedback interactions between the thalamus and cortex, with minimal interference from other cortical and thalamic regions. The primary somatosensory (vS1) cortex receives strong inputs from a limited subset of thalamic nuclei, including the ventroposterior medial, ventroposterior lateral, and the posterior thalamic nucleus (*Harris, Mihalas et al Nature 2019*). This input is reciprocated by complementary feedback projections from the vS1 cortex to the same thalamic nuclei, forming a prototypical feedback loop. Moreover, the ability to label functional subcircuits encoding information from individual whiskers - through aligned barrels in the cortex and barreloids in the thalamus - enables the identification of neurons and connections that constitute, in a pauci-synaptic circuit, a full recurrent loop. Importantly, the thalamic neurons within the barreloids do not communicate with each other (*Sherman & Guillery, PNAS 1998*) and the cortical subcircuits identified by barrels exhibit minimal cross-communication (*Ebner, JCN 1999*). This isolation makes the vibrissa system a particularly well-suited model for studying cortico-thalamo-cortical loops. In contrast, other systems involve either feedforward interactions with additional cortices or thalamic nuclei, larger polysynaptic loops mediated by other cortical or subcortical structures, or do not permit the functional isolation of specific subcircuits.

Thalamocorticortical loop from Garrett Stanley: Much of what we know about how signals propagate from region to region is inferred from separate recordings done in separate experiments. There is growing expertise and interest in multi-site recordings and specifically in measuring and analyzing direct synaptic connections across brain regions. I argue that the thalamocortical circuit of the whisker pathway is uniquely positioned to address this issue, given the discrete nature of the barreloids/barrels and the chances of recording from connected neurons in-vivo.

Cortico column-to-column loops from Dan Shulz: Because of its unique anatomical structure, barrels in vS1 cortex have been considered as a paradigmatic system to study the 'cortical column'. However, the very specific spatial arrangement of 'barrels' and the cortico-cortical horizontal connectivity in this area, which has been largely overlooked, is particularly well-suited to study center-surround interactions and multi-whisker integration. This provides the opportunity to explore the role of specific spatial properties like somatotopy and map continuity in sensory coding (compared to discontinuities in other parts of the primary somatosensory cortex such as the paw representation). This knowledge of sensory coding in vS1 cortex is invaluable to guide the design of optogenetic stimulation patterns that can be delivered directly onto the mouse cortical surface to provide relevant somatosensory information while bypassing the sensory organs. Such research constitutes a key step forward to develop effective somatosensory feedback strategies to improve motor control in the context of brain-machine interfaces.

From Dan Feldman: We have a great system to study the principles of feedforward/feedback processing across cortical areas, including anatomical/pathway questions (corticothalamocortical loops), computations (predictive coding), and learning.

From Mitra Hartman. It's a great example of a homeoactive sensing system. Very different implications for efference copy than alloactive sensing systems, e.g., vision. Best system to close the sensorimotor loop and to study nested motor control: reflex, oscillation, voluntary.

## Internal models of motor control

Sensorimotor predictions from Farzaneh Najafi: The rodent vibrissa system can be used to study sensory consequences of movements, and test predictive coding theories. This system allows for the study of how sensory predictions inform motor planning and execution, adapting based on past sensory experiences and current contextual cues.

Formation of internal models of body and space ... during early development from Soohyun Lee: Unlike other sensory systems, the somatosensory system is functional from the embryonic stage. This early onset provides a unique opportunity to study how mental representations of the body and surroundings are established during early development. Given that the somatosensory system is inherently sensorimotor, the strong interaction between sensory and motor components in rodents may play a critical role in shaping these internal models, as sensory inputs inform motor adjustments and vice versa. This dynamic interplay is essential for refining body schema and spatial awareness and may offer insights into how integrated sensory-motor experiences contribute to the early development of accurate internal representations.

Internal models from Scott Pluta: My point of view on the “unfair advantage” of the whisker system relates to understanding how the brain builds an internal model of self-motion. Obviously, the internal model is built from both afferent and efferent signals, yet the relative contribution of those signals is difficult to pin down. The advantage of the whisker system in this regard is:

1. Simple movements that are easy to measure and quantify. High-speed imaging of whisker motion and extracting the relevant kinematic features is relatively simple (in the head-fixed context, anyway).
2. Whisker trimming is minimally invasive. You can simply trim off the whiskers, while still monitoring volitional movements, and gain insight on the role of sensory reafference to the representation of self-motion. Trimming off the arms or legs of an animal in the middle of an experiment is less than ideal.
3. Nerve block or bisection [with separate sensory and motor nerves]. You can eliminate sensory reafference by disrupting the infraorbital nerve [without interrupting the facial nerve and movement, or vice versa]

Coordinated sensing from David Kleinfeld. There are a multitude of orofacial motor actions that coordinate by breathing. The vibrissa sensorimotor system is the most prominent, yet licking, head rotation, and sniffing are all coordinated. This presents an opportunity to understand the logic of active sensing and the formation of a common internal model for movement along different sensorimotor streams (touch, taste, smell) that ultimately need to be combined to recognize an object.

## Ethology and perception

Biomechanics from Mitra Hartman. It's the only system for which we can model the full sensory input (minus cross-talk through skin) as well as muscle output. This means we can start to connect the biomechanics to the neural signals in a way that no other system can.

From Dan Feldman. The nature of the high-level tactile representation remains unclear. How does a tactile percept build up over touches? Does it? If not, how is tactile recognition mapped onto visual or more cognitive recognition? Are their tactile 'object cells'?

Low dimension sensing from David Kleinfeld: The vibrissa sensorimotor system learns about the local environment by essentially tapping with sticks. What information is gained per tap? What are the energy costs and data rates? Understanding how rodents navigate in the dark and on uneven terrain may inform robust, low-energy robotics.

From Randy Bruno of the neocortical senses, rodents rely more heavily on whisker-mediated touch than skin-mediated touch, vision, audition, or taste. Neural development reflects this: rat vS1 cortex is as thick as the visual cortex of highly visual animals like cats, whereas rat visual cortex and cat somatosensory cortex are relatively anemic, thinner, and with fewer distinct cell types. As transgenic mice have come to dominate nervous system research, their dominant sense is uniquely advantaged for understanding cortical and thalamic processing in general. Other sensory systems may be better used as models for understanding elements of those specific senses, rather than general principles of cortical circuitry. For instance, mouse vision is closely related to human peripheral vision, not foveal vision, in terms of structure and function.

While whiskers are discrete sensors as opposed to the continuous sheet of the retina, cochlea, and skin, the discretization is not preserved beyond layer 4 barrels. All other cortical layers have cellular and synapse distributions that do not respect barrel borders and are therefore continuous representations as in all other senses. Furthermore, the discretization of the whiskers has enabled mapping of stimuli to small specific neural populations more reliably than is possible in other sensory modalities. Thus, for ethological, architectural, and experimental reasons, the whisker system is uniquely advantaged to understanding cortical and thalamic processing.

From Garrett Stanley: There is significant debate regarding the necessity/sufficiency of primary sensory cortex in sensory signaling. I believe that this is due to two factors: a) that this is likely strongly dependent upon the behavioral challenges posed to the animal, and b) that this likely moves around in response to demands, injury/lesion, learning. The whisker pathway is an excellent pathway to address this complex issue.

**Disease models**

From Garrett Stanley: Many diseases/disorders of the nervous system are associated with a specific deficit. Yet, patients exhibit more of a spectrum of symptoms. Specifically Parkinson's disease is associated with motor deficits, yet patients exhibit symptoms related to sensing and cognition. These are very difficult to disentangle. So, as a grand challenge, I propose that the whisker pathway be a powerful model system for trying to disentangle sensory and motor aspects of signaling/behavior.

From Dan Feldman: We have a great system to study sensory phenotypes in neurodevelopmental and other disorders, because we have such a good baseline understanding of circuits, coding, sensory behavior, etc. and because vS1/vS2 are easily accessible for measurements in transgenic mouse models of disease.

**Back to basics**

Cell types from Dan Feldman: We should be using vS1 much more as a platform to understand the variety of cell types in the cortex, and to what extent their function is conserved across cortical areas. V1 is leading the way, thanks to Allen Brain, but there should be another sensory area used for close comparison to establish generality and differences.

Canonical computation from David Kleinfeld. The vibrissa system offers the most modular form of columnar organization in cortex. Given advances in cell types, connectivity, and multisite recording, it is time to return to the question of what computational advantages - if any - are afforded by a canonical cortical circuit.