Laminar differences in cortical receptive fields measured by reverse correlation of intracellular recordings

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Introduction

Our knowledge of receptive fields and sensory transformations in rodent barrel cortex (S1) lags behind other sensory systems. Firing rates of neurons in S1 can be low, making reverse correlation of high-dimensional stimuli challenging. Additionally, most researchers rely on simple single-whisker laboratory stimuli for receptive field mapping, which are neither ethological nor capable of revealing spatiotemporal complexity. Here we use a novel multi-whisker stimulator system that moves 9 whiskers independently in arbitrary directions, exploring a vastly larger stimulus space than conventionally examined. By recording intracellularly rather than extracellularly, we can additionally access information available in the subthreshold response to calculate receptive fields even for neurons with little or no spiking activity.

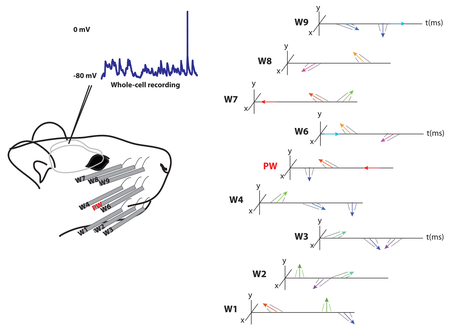
After exploring a number of stimulus-response models, including conventional Linear-Nonlinear models as well as quadratic models, we found that a filtered input nonlinearity model (of the form discussed in Ahrens et al, 2008) provided an effective and parsimonious representation of the responses. In this model, the whisker deflections are mapped through a static nonlinearity that re-represents the whisker movements binned into an 8-directional space, before being temporally filtered, weighted across whiskers, and summed to predict the voltage response. Our model is able to predict neural responses to novel stimuli with a correlation coefficient as high as 0.84. Furthermore, through repeated presentations of identical stimuli, we show that our model captures ~ 90% of the predictable variance (Sahani and Linden 2003), suggesting that the main nonlinearities in stimulus response are spike-threshold rather than network nonlinearities.

Analysis of the spatiotemporal receptive fields across layers and cell-types reveals the emergence of unique spatial and temporal features encoded in the supra- and infragranular layers, and serves as a useful comparison to similar studies from the visual and auditory systems. Because all of our neurons are recovered histologically and registered according to cell-type and sub-circuit identity (barrel vs. septal) we are able to make inferences about the functional roles of specific sub-circuits in sensory processing as well as directionality of functional information flow. Finally, because we are able to calculate receptive fields online and play "optimal" stimuli back to the same neurons, we are well suited to study how specific receptive fields are constructed, as well as what stimuli are likely to drive spiking responses in different layers of S1.

Methods

• Electrophysiolgy: 42 adult (weight 140-340 g, mean 220 g) Wistar rats (Hilltop Laboratories) were head fixed and had craniotomies made over the barrel cortex region. Blind whole-cell recordings were made from neurons spanning all depths of a single barrel column. During recordings the rats were maintained in an unanesthetized, lightly-sedated state using fentanyl.

• Stimulus: Whiskers on the contra-lateral face were trimmed to a length of 10 mm. Nine multi-directional piezoelectric stimulators (Simons, D.J. 1983) were arranged around the face, attempting to keep the PW always at center (defined by extracellular mapping and post-hoc histology). For reverse correlation analysis, we delivered complex sparse noise stimuli to 9 whiskers simultaneously, consisting of high-velocity pulses (peak velocity 2200° / second, 5ms rise-time) in random directions and random times. These velocities approximate those of rats whisking in the natural environment (Ritt, J.T. et al., 2008)

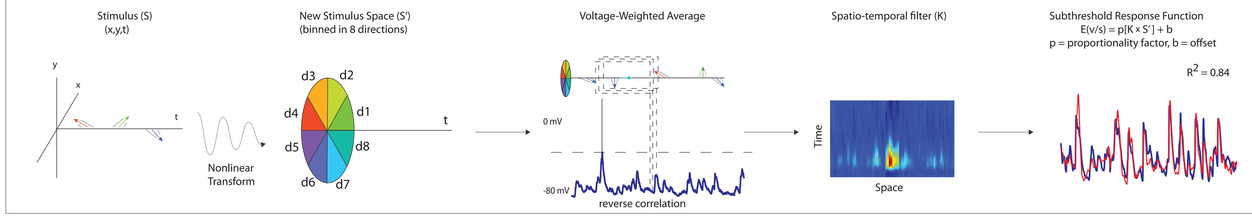


• Histology: Neurons were filled with biocytin and identified histologically post-hoc for morphological analysis. Neurons were registered according to cell type, laminar depth, location within the barrel field, and relation to the barrel vs. septum.

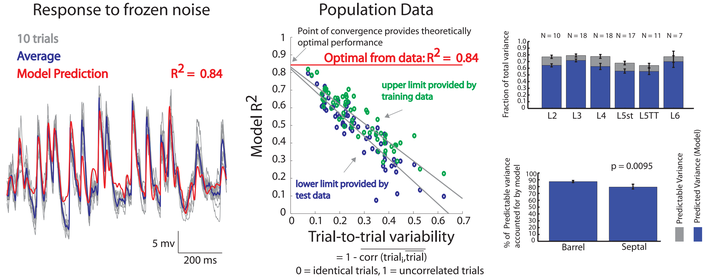
• Analysis: Physiology data was analyzed using custom-written routines in MATLAB. All stimulus-response model predictions were performed on cross-validation data. Laminar identities were defined by the cortical depth of the recovered soma.

1. Modeling the subthreshold response and spatiotemporal receptive fields of neurons in S1.

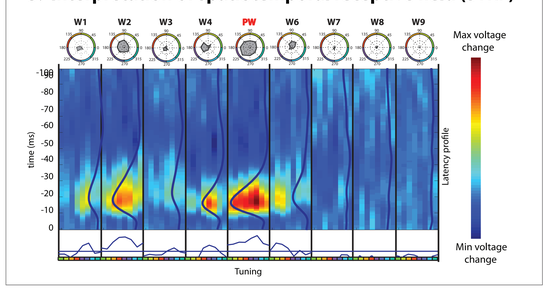
Subthreshold receptive fields and stimulus-response functions are estimated using a voltage-weighted average on a nonlinear stimulus space.



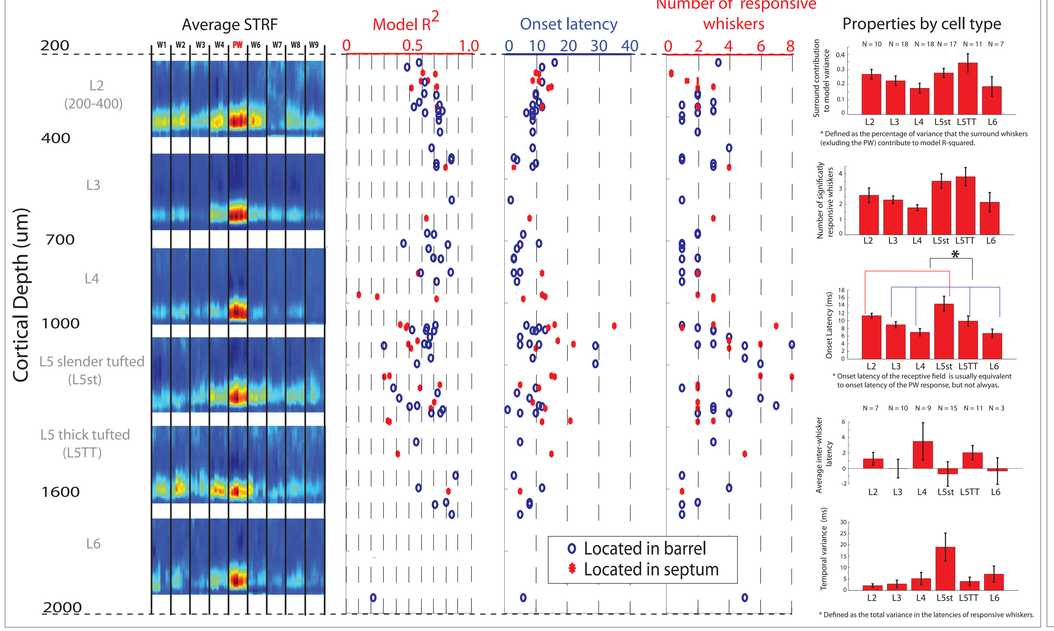
2. Linearized model aproximates nearly optimal performance.



3. Interpretation of spatiotemporal receptive field (STRF)

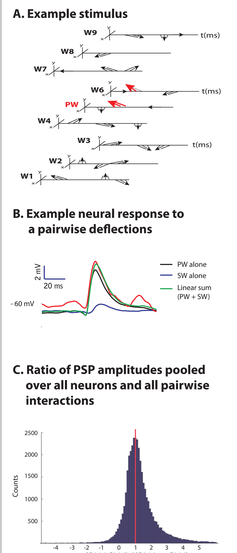


4. Receptive properties by laminar location and cell type

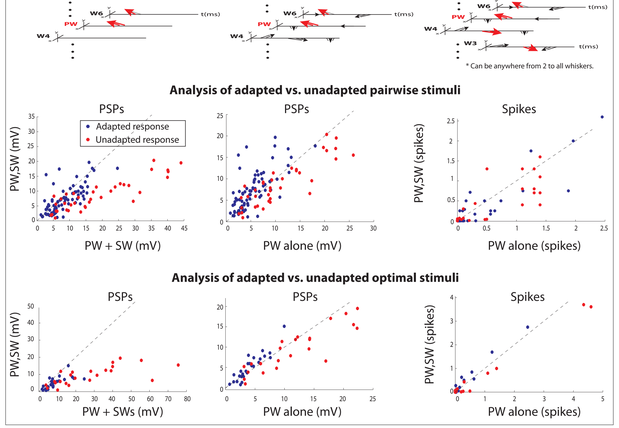


5. Pairwise whisker interactions sum linearly.

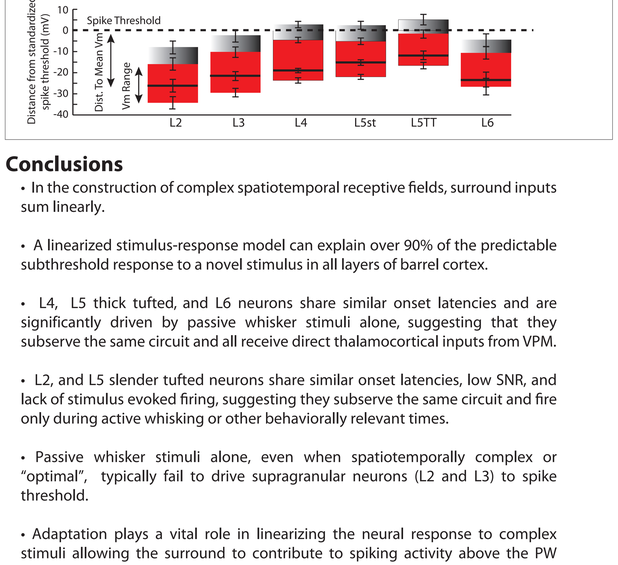
Responses to all possible combinations of whisker deflections were analysed during complex stimulus presentation.



6. Adapted neural response, but not unadapted, is linear in barrel cortex.



7. Thalamorecipient layers, but not others, are driven by passive whisker stimuli.



Conclusions

• In the construction of complex spatiotemporal receptive fields, surround inputs sum linearly.

• A linearized stimulus-response model can explain over 90% of the predictable subthreshold response to a novel stimulus in all layers of barrel cortex.

• L4, L5 thick tufted, and L6 neurons share similar onset latencies and are significantly driven by passive whisker stimuli alone, suggesting that they subserve the same circuit and all receive direct thalamocortical inputs from VPM.

• L2, and L5 slender tufted neurons share similar onset latencies, low SNR, and lack of stimulus evoked firing, suggesting they subserve the same circuit and fire only during active whisking or other behaviorally relevant times.

• Passive whisker stimuli alone, even when spatiotemporally complex or "optimal", typically fail to drive supragranular neurons (L2 and L3) to spike threshold.

• Adaptation plays a vital role in linearizing the neural response to complex stimuli allowing the surround to contribute to spiking activity above the PW alone.

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