# Neural Circuits for goal-directed Sensorimotor Transformation

## *Voltage-sensitive Dye Imaging of Sensorimotor Cortex during Tactile Detection*


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### Abstract

Sensory information from the external world is integrated in the somatosensory cortex to produce a sensory percept. Somatosensory input is often the result of self-generated movement during the active touch of objects and conversely, sensory information is used to refine motor control. Thus there is an active pathway between the sensory and motor cortical networks which we investigate in the mice whisker sensorimotor system using the *Voltage sensitive dye imaging (VSDI)*. We trained the mice to detect a brief stimulus given to the whisker and report the perceived stimulus by licking the reward spout. During the task, voltage sensitive dye was applied to the mouse neocortex to image the membrane potential dynamics with subcolumnar spatial and millisecond temporal resolutions. Apart from VSDI, the whisker movement was also imaged using a CMOS detector. A brief deflection of whisker evokes an early (<100ms) high depolarization in primary somatosensory barrel cortex and later excites the motor cortex. Our data reveal an active signaling pathway between sensory response encoding stimulus and motor response encoding the lick and the whisk. A late depolarization (100-300ms) was enhanced in hit trials over misses.


## Introduction

Tactile stimulus evokes an action potential firing in the primary somatosensory cortex which then depolarizes the motor cortex through signaling pathways [1]. Therefore it is very important to understand how the sensory-motor loop works. For this we designed a behavioral task where a water deprived mouse is trained to detect brief deflections of the C2 whisker and report the stimulus by licking the spout to drink water [2]. The mouse is placed on a magnetic coil with head restrained support to avoid any motion artifacts (Fig. 1a).

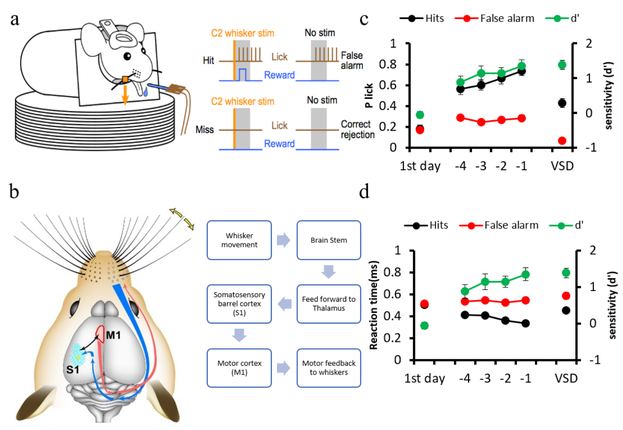


**Figure 1: Experimental Approach.** (a) The head restrained mouse setup to avoid any motion artifacts. Classification of trials into hit, miss, false alarm & correct rejection. (b) Sensory motor pathway in mouse brain. A flow chart of signal states involved in our behavioral task. (c) The probability of lick [P lick] increases to indicate the mouse reaching a stable psychometric performance state. Conversely false alarm rate decreases. (d) Reaction time of hit trials decreases with training.

Sensorimotor signaling pathways forms the basis for sensation and movement (Fig. 1b). In a mouse, brief stimulation of a whisker causes glutamatergic excitation of the brain stem. The signal is fed forward into thalamus before reaching the somatosensory barrel cortex (S1) corresponding to the whisker. Motor cortex is then excited resulting in whisker movement to explore the environment [1]. When the mouse identifies the stimulus and licks the spout within the reward window (<1s), we classify that as a hit trail. If it doesn't lick the spout, we consider it as a miss (Fig. 1a).Mouse learned the task rapidly, reaching stable psychometric performance after a few daily training sessions (Fig. 1c & Fig. 1d).

## Main Objective

To analyse the data from the C2 somatosensory barrel cortex of a head restrained mouse while performing a behavioral task. Data analysis to be done on MATLAB.

## Results

We delivered strong and reliable whisker deflection at 2.5 seconds after shutter cue by a 1ms magnetic impulse acting on iron particles attached to the C2 whisker (Fig. 1a). Catch trials without stimulus were randomly interspersed, and a 2-s no lick period was imposed before both the stimulus and catch trials. VSD images are acquired for 2 seconds after stimulus.

### HIT versus MISS trials

1. A hit trail has an early strong depolarization in primary somatosensory barrel cortex (S1) corresponding to C2 whisker. Mouse licks the spout to drink water as reward (Fig. 2a).
2. A miss trail has an early depolarization in primary somatosensory barrel cortex (S1) corresponding to C2 whisker. But the mouse doesn't lick the spout (Fig. 2a).
3. It is observed that there is a late depolarization happening in hit trials, which maybe the cause for licking (Fig. 2b).

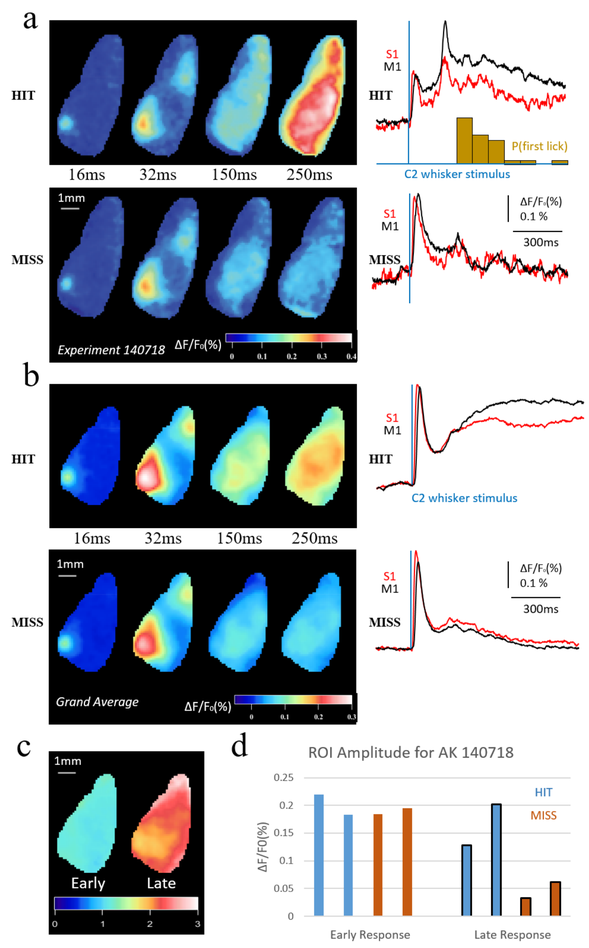


**Figure 2: HIT versus MISS trials** (a) Voltage-sensitive dye (VSD) images of example experiment AK 140718 taken at early phase (16ms & 32ms) and late phase (150ms & 250ms) post stimulus. Region of interest (ROI) curves for primary somatosensory cortex (S1) and Motor cortex (M1). (b) VSD images of grand average (n = 21 mice). ROI curves indicate a clear late depolarization in S1 region for hit trails. (c) Ratio of hit vs miss trials in early (10ms to 50ms) and late (100ms to 300ms) phase (n = 21 mice). (d) Amplitude of ROI (S1 & M1) for hit/miss trials in early (avg. of peak and neighbouring values) and late (avg. of 100ms - 300ms) phases for AK140718.

### Pre-stimulus Quiet versus Whisking

1. A mouse is considered to be quiet if its whisker movement is almost negligible (<5 degrees) over a window of 500ms pre-stimulus. It is Whisking otherwise (Fig. 3c & 3d).
2. Most of the trials indicate higher hit activity (Hit Rate) for pre-stimulus Quiet animals over Whisking ones (Fig. 3a).
3. Animals exhibit a cue in whisker behavior before stimulus is delivered (Fig. 3b).

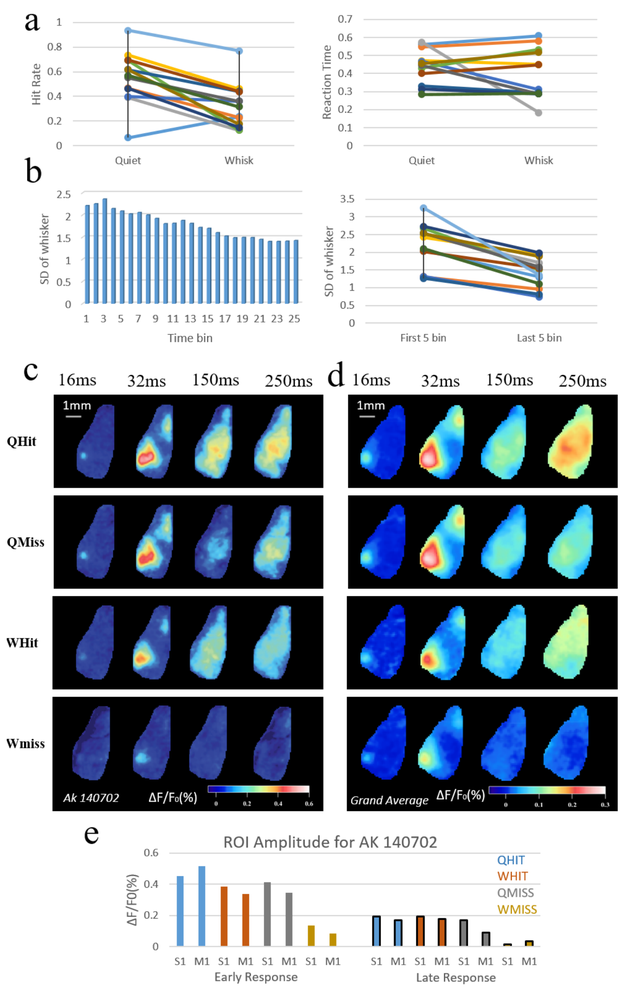


**Figure 3: Pre-stimulus Quiet versus Whisking** (a)Hit rate and Reaction time of Quiet versus Whisking trials (n = 13 mice). (b) Standard deviation (SD) of whisker movement pre-stimulus with time bins of 100ms. To the right is the average of first 5 and last 5 bins of SD trace. (c) VSD images of example experiment AK 140702 taken at early phase (16ms & 32ms) and late phase (150ms & 250ms). They are classified into Quiet HIT/MISS, Whisking HIT/MISS trials. (d) VSD grand images for n = 13 mice. (e) Amplitude of ROI (S1 & M1) for Qhit, Qmiss, Whit, Wmiss trials in early and late phases for AK140702.

### Pre-stimulus Quiet: Post-stimulus Quiet vs Whisking

Quiet hit post stimulus whisking (PSTW) & Quiet miss PSTW has similar dynamics, but different end result (Fig. 4a & 4b).

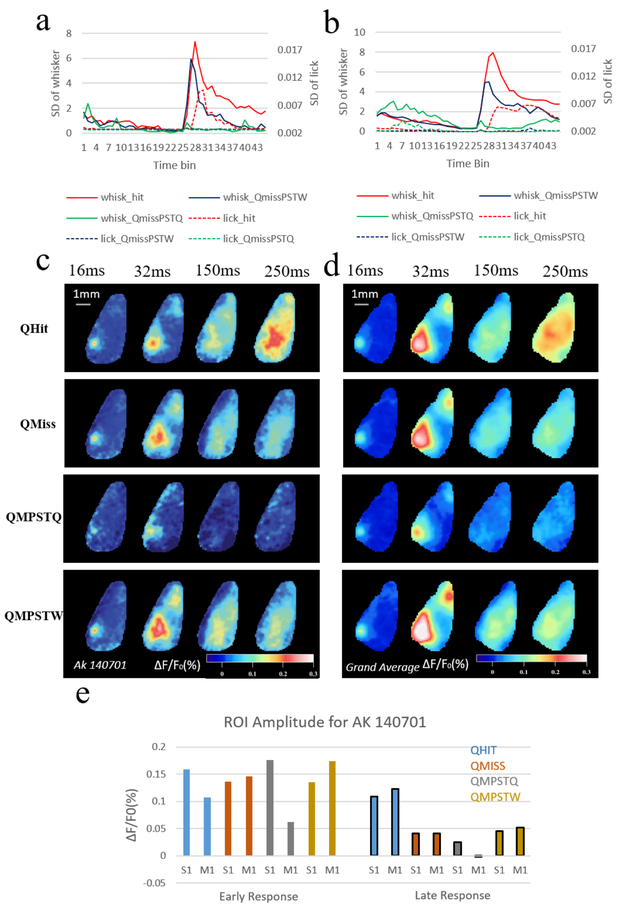


**Figure 4: Pre-stimulus Quiet: Post-stimulus Quiet vs Whisking** (a) SD of whisker and lick trace for experiment AK 140701 for different conditions. (b) Average SD of whisker and lick trace for n = 13 mice. (c) VSD images of experiment AK 140701 taken at early phase (16ms & 32ms) and late phase (150ms & 250ms). They are classified into Quiet HIT/MISS/PSTW/PSTQ. (d) VSD grand images for n = 13 mice. (e) Amplitude of ROI (S1 & M1) for Qhit, Qmiss, QmissPSTW, QmissPSTQ trials in early and late phases.

### Trail to Trail Variability

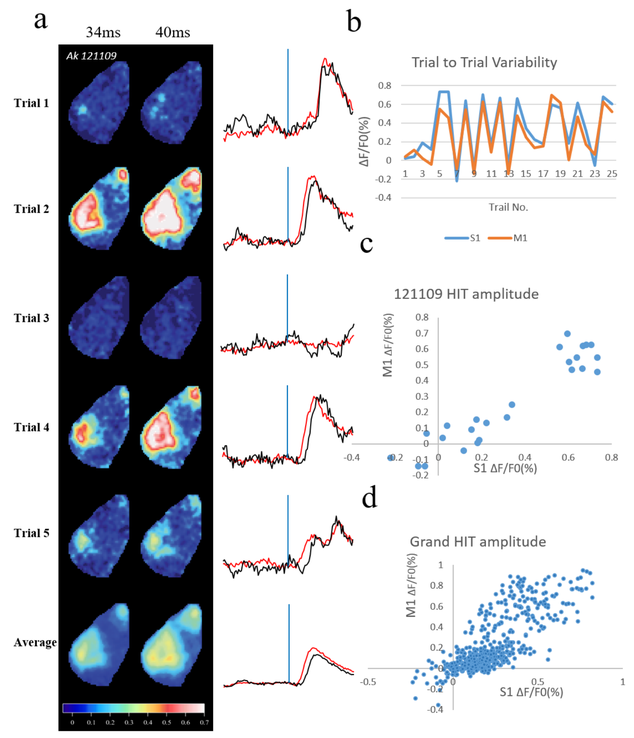


**Figure 5: Trail to Trail Variability** (a) VSD images of experiment AK 121109 taken at early phase (34ms & 40ms) with ROI plots (5 trials). (b) Variability of early peak amplitude in S1 and M1 regions over successive hit trials (25 trials). (c) S1 vs M1 scatter plot for AK 121109 hit trials (25 trials). (d) S1 vs M1 scatter plot for all hit trials (n = 21 mice).

## Forthcoming Research

1. Triangulate the region responsible for late depolarization of hit trials.
2. Assess the role of the entire dorsal cortex during tactile detection using optogenetic tools.

## References


[1] Isabelle Ferezou, Florent Haiss, Luc J. Gentet, Rachel Aronoff, Bruno Weber, and Carl C.H. Petersen. Spatiotemporal dynamics of cortical sensorimotor integration in behaving mice. *Neuron*, 56(5):907 – 923, 2007.

[2] Shankar Sachidhanandam, Varun Sreenivasan, Alexandros Kyriakatos, Yves Kremer, and Carl C. H. Petersen. Membrane potential correlates of sensory perception in mouse barrel cortex. *Nat Neurosci*, 16(11):1671–1677, Nov 2013.