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海 外 特 別 研 究 員 最 終 報 告 書

独立行政法人日本学術振興会 理事長　殿

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海外特別研究員としての派遣期間を終了しましたので、下記のとおり報告いたします。
なお、下記及び別紙記載の内容については相違ありません。

記

1. 用務地（派遣先国名）用務地：サンフランシスコ，CA，（米国）

2. 研究課題名（和文）※研究課題名は申請時のものと違わないように記載すること。
音の聞き分けに着目した聴覚皮質・視床における情報処理機構の解明

3. 派遣期間：令和　1　年　8　月　1　日　～　令和　3　年　7　月　31　日

4. 受入機関名及び部局名
受入機関名：　カリフォルニア大学サンフランシスコ校
部局名：Center for Integrative Neuroscience, Coleman Memorial Laboratory

5. 所期の目的の遂行状況及び成果…書式任意　**書式任意（A4 判相当 3 ページ以上、英語で記入も可）**
（研究・調査実施状況及びその成果の発表・関係学会への参加状況等）
（注）「6. 研究発表」以降については様式 10－別紙 1～4 に記入の上、併せて提出すること。

Introduction

Our brain has a remarkable ability to adapt to the sensory environment. For example, in the cocktail party problem, we can pick up voices in front of us while ignoring other conversations as background noise. In our everyday life, we both consciously and subconsciously select what we hear from the multitude of sounds in any environment and segregate them into meaningful foreground sounds and unimportant background noise. If we pay attention, however, we can listen to other conversations that were initially considered in the background.

Thalamus is the last subcortical station and receives dense feedback projections from the cortex. Auditory cortex and thalamus are thought to extract sound information independent from background noise and to play a key role in transforming sound information to a more robust representation that is less dependent on details of the acoustic stimulus and the background conditions. The relationship of such a sound representation to adaptation and attention is, however, not yet well understood.

In this project, I examined neural activities in two rat core auditory cortical fields, primary auditory cortex (A1) and ventral auditory field (VAF), which receive distinct thalamic inputs. Then, I developed an experimental setup to measure neural activities in behaving animal to study the attentional modulation in signal-in-noise processing.

Method and Result

Estimation of multi-dimensional receptive fields

The structure of receptive fields for the neurons in lower-level stage of the auditory system tend to show simple linear receptive fields, while higher-level neurons have increasingly nonlinear receptive fields due to the increasing assembly of several filters and rectification of inputs at the cellular level. For auditory responses, spectrotemporal receptive fields (STRFs) have typically been estimated as a single filter, which is the average of stimulus envelopes that preceded a spike (stimulus triggered average, STA, Fig. 1A). Capturing the complex aspects of central sound processing, however, requires an expansion from traditional single filter measurements of STRFs to more complex, multi-filter STRFs (mSTRFs). Use of a multi-filter linear-nonlinear approach is essential for better neural systems analysis. I obtained two STRFs per neuron (the first and second maximally informative dimensions, MID1 and MID2, Fig. 1B-C), using mutual information, a quantitative metric to estimate the dependence of a response on the evoking stimulus, based on information theory [3,6].

Functional differences of two cortical fields

I investigated temporal and spectral modulation properties and the cooperativity of multidimensional filters in two core rat auditory cortical fields, A1 and VAF, which are the two first cortical fields receiving thalamic inputs in parallel along the posterior-to-anterior dimension (Fig. 1D). I showed that the spike information conveyed by the first STRF (MID1) was higher in VAF than in A1 and the additional second STRF (MID2) contribution and nonlinear cooperativity of these two filters (MID1 and MID2) were larger for A1 (Fig. 1E). Those findings support that there are potential biological meaningful differences of sound encoding in the two cortical fields, however, it remains elusive what is the exact role of the second STRF.

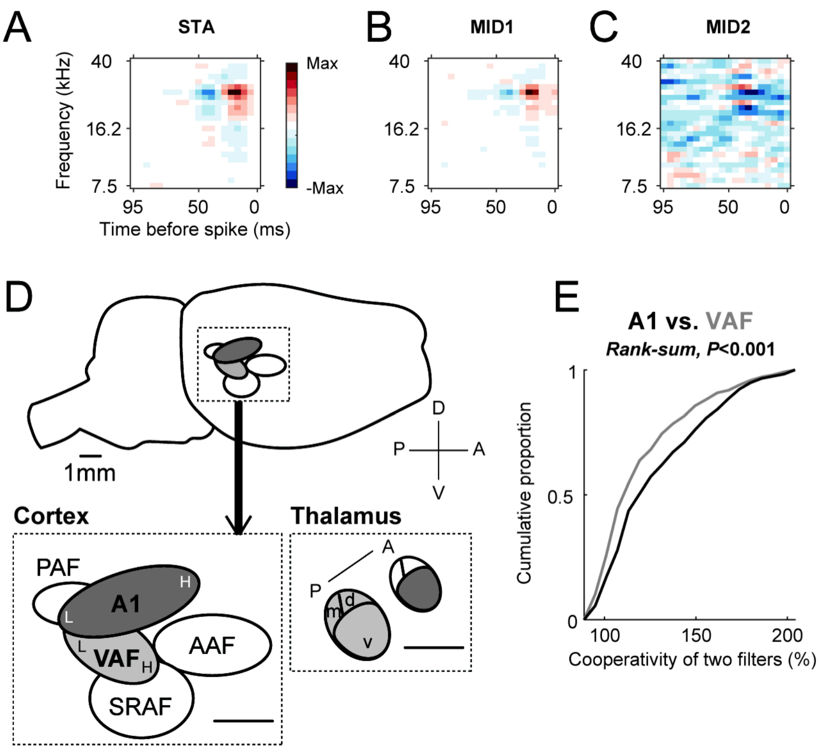

Figure 1. Nonlinear cooperativity of two-dimensional STRFs was larger for A1 than for VAF. (A-C) Example of STRFs for STA (A) or MID analysis (B and C) for a single unit of A1 neuron. (D) Schematic of rat brain. The positions of five auditory fields are indicated on the auditory cortex. The magnified windows show the reversal of frequency gradient at the border of A1 and VAF for the auditory cortex and the corresponding projection sources for A1 (dark grey) and VAF (light grey) in the auditory thalamus. Scale bars: 1 mm. (E) A1 neurons showed larger cooperative gain of the two filters, than VAF neurons. Adopted from Homma et al., 2021.

Developmental plasticity effect on multi-dimensional RFs

In order to investigate how the environmental sound statistics affects STRF development, I raised rat pups in a moderately-noisy spectrotemporal modulated noise during their auditory critical period [1,5,7]. I showed that the spectrotemporal modulation preferences of the STA and MID1 of cortical neurons can be altered by the noise exposure and shifted away from the noise statistics to increase signal-in-noise ratio (SNR). In other words, the shift reduces neural responses to noise and thus enables animals to more effectively extract foreground sound from background noise as proposed in the efficient coding principles. Here I further demonstrated that the spectrotemporal modulation preferences of MID2 can be shifted away from the exposed noise parameters in both of the cortical fields, A1 and VAF, and in a similar direction as STA or MID1 (Fig. 2) [3,6]. In addition, the information values captured by MID2 and the nonlinear cooperativity of the two-filter model decreased particularly in A1 by the noise exposure. These suggest that the second STRF (MID2) may contribute to signal-in-noise-processing but potentially loses effectiveness in processing contextual stimulus effects.

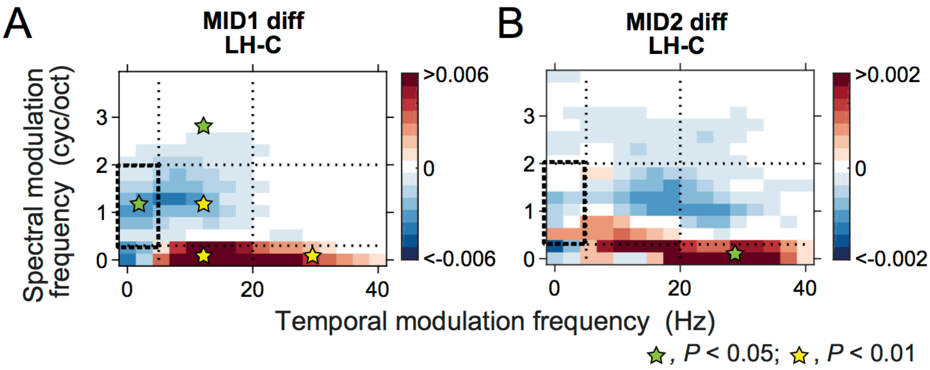

Figure 2. Noise-exposure modified ripple transfer function preferences of MID1 and MID2.
In this example, population ripple transfer functions for MID1 and MID2 were obtained for VAF neurons of Control (C) and noise-exposed (LH) groups, respectively. Then, the differences of the population ripple transfer functions between LH and C groups were computed for MID1 (**A**) and MID2 (**B**). Bold dashed boxes indicate the dominant modulation ranges of the exposure noises. Color bar indicates the values of differences. Adopted from Homma et al., 2021.

Correlation between behavioral performance and neural decoding accuracy

I established a vocalization-in-noise detection behavior paradigm using the Go/No-Go paradigm, and I showed that the behavior performance was well reflected by vocalization-in-noise decoding accuracy of auditory cortical neurons in anaesthetized animals as determined by a nearest-neighbor linear decoder (Fig. 3) [1,5,7].

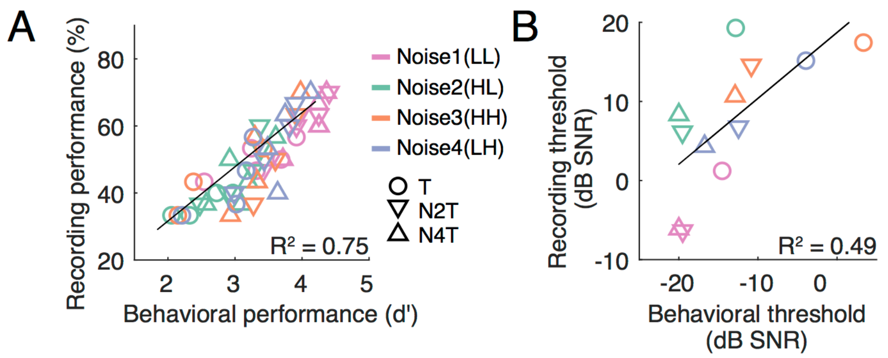

Figure 3. Correlation between behavioral and neuronal vocalization-in-DMR performance.
(A) Behavioral sensitivity for vocalization-in-DMR detection and physiological decoding accuracy for each SNR condition of vocalization-in-DMR task were correlated (Pearson correlation coefficient, $R = 0.78$, $p < 0.0001$). (B) Behavioral and decoding thresholds were highly correlated ($R = 0.70$, $p = 0.01$). Adopted from Homma et al., 2020.

Measuring neural activities in awake behaving animal

Then, to examine top-down effect of attentive listening, I have developed a custom-built behavioral training platform in a soundproof chamber, where a head-posted animal runs on a treadmill listening to sound stimuli while an acute multi-contact electrode is inserted in the brain and spiking activities are monitored (Fig. 4). I prepared four computers for presenting sound stimuli, obtaining neural activities, regulating the behavioral task, and tracking animal's running speed on the treadmill. The four computers are controlled by custom-written Matlab/Python scripts and communicate each other via Internet communicating protocols with very short latency. This was necessary to obtain neural and behavioral data linked to exact stimulus presentation timing. The behavioral task asks animals to detect rat vocalizations from spectrotemporally modulated noise while randomly changing their SNRs.

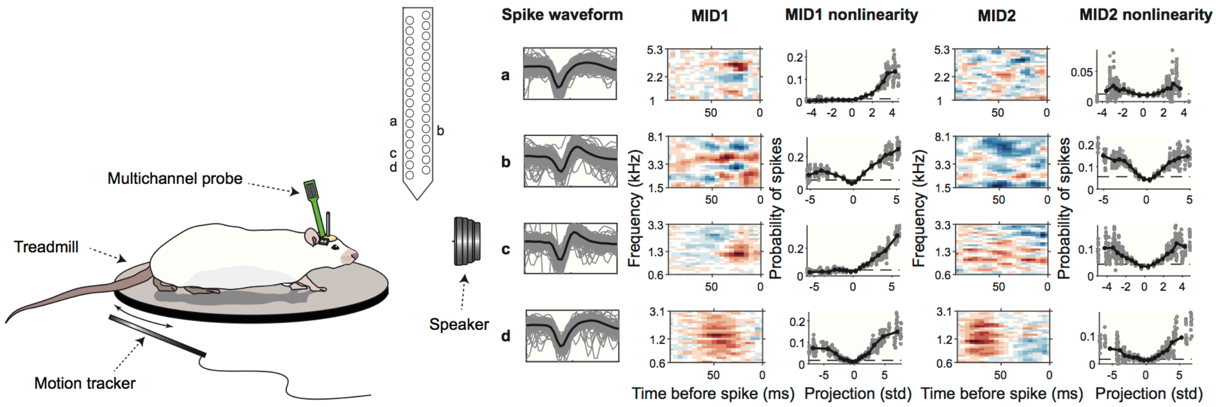

Figure 4. Experimental design and examples of multi-dimensional STRFs in awake rat.
Headposted rat was placed on the treadmill, and sound was played from the speaker mounted 15 cm away from the midpoint of the two ears. An acute multichannel recording probe was inserted in the auditory cortex. The magnified probe view indicates the positions of four example units, a-d. Spike waveforms, filter structures and input-output functions ("nonlinearity") for MID1 and MID2 are shown for each unit. Preliminary data.

Top-down modulation in attentive listening

Auditory scene analysis is achieved by bottom-up and top-down modulations. The bottom-up adaptation allows us to extract information in an efficient coding manner that is guided by a subconscious sensitivity to variations in stimulus statistics. Noise tolerant encoding appears strongest in cortical neurons and is correlated with adaptation to stimulus statistics. Along the auditory pathway, receptive fields shift from encoding simple sound attributes (such as tone frequency, intensity, and sound source location) towards more mean-, contrast-, and noise independent information. On the other hand, top-down modulation enables us to deliberately and intentional select information via attention mechanisms or by inducing task-specific learning adaptation.

Using the experimental setup that I developed to examine neural activities in behaving animal, I am currently working on collecting and analyzing data to understand how cortical activities are modulated by different internal states (e.g. anaesthetized, awake, attentive or moving). I apply the two-filter model based on information theory [3,6] and coordinated neuronal ensembles [2] analyses. These approaches are expected to reveal nonlinear processing and high-order synchronized activities related to active listening.

Concluding remarks

I characterized the functional differences and developmental plasticity changes of A1 and VAF neurons using a two-filter receptive field model [1,3,5-7]. Then, I developed a setup to obtain neural spiking activities in behaving rat and investigate attentional modulations in a challenging hearing condition. In addition, I collaborated in the characterization of coordinate neuronal ensembles in auditory cortex and their relationship to the encoding by individual neurons [2]. I also wrote a review article introducing the anatomy and physiology of descending corticothalamic feedback projections and discussing its potential roles in speech and music processing [4]. After the end of the fellowship, I will stay in the host lab as a postdoctoral fellow to complete these projects.

Acknowledgments

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Publications

1. **Natsumi Y. Homma**, Patrick W. Hullett, Craig A. Atencio and Christoph E. Schreiner. Auditory cortical plasticity dependent on environmental noise statistics. ***Cell Reports*, *2020*,** 30(13), 4445-4458.e5.
2. Jermyn Z. See**, Natsumi Y. Homma**, Craig A. Atencio, Vikaas S. Sohal, and Christoph E. Schreiner. Information diversity in individual auditory cortical neurons is associated with functionally distinct coordinated neuronal ensembles. ***Scientific Reports, 2021***, 11(1), 4064.
3. **Natsumi Y. Homma**, Craig A. Atencio, and Christoph E. Schreiner. Plasticity of Multidimensional receptive fields in core rat auditory cortex directed by sound statistics. ***Neuroscience, 2021***, 467, 150-170.
4. **Natsumi Y. Homma**, and Victoria M. Bajo. Lemniscal corticothalamic feedback for auditory scene analysis. ***Frontiers in Neuroscience, 2021.*** *15:1-23.* Review.

Scientific presentations

5. **Natsumi Homma**, Craig Atencio, Patrick Hullett, and Christoph Schreiner, Noise exposure induced cortical auditory receptive field plasticity and improved signal-in-noise performance dependent on the sound statistics (Poster, selected for the Poster Blitz). ***Association for Research in Otolaryngology 43rd Annual MidWinter Meeting***, San Jose, CA, USA. February 2020
6. **Natsumi Y. Homma**, Craig A. Atencio, and Christoph E. Schreiner, Multidimensional receptive field plasticity to environmental sound statistics in core rat auditory cortex (Poster). ***18th Advances and Perspectives in Auditory Neuroscience (APAN)***, online (web-based). October 2020.
7. **Natsumi Homma**, Craig Atencio, Patrick Hullett, and Christoph Schreiner, Auditory cortical signal-in-noise mechanisms revealed by developmental plasticity (Flash talk). ***The 5th Japan-US Science Forum in Boston***, online (web-based). November 2020.