

## News Release

### Title

**Novel role of synaptic clustering in dendrites**

### Key Points

- **Synaptic clustering at distal dendrites strengthened sublinear integration and expanded the dynamic range of binaural computation.**
- **This dendritic synapse geometry improved the ITD tuning for low-frequency sound.**
- **This study would identify the universal cellular basis of sound source localization.**

### Summary

The research group of Assistant Professor Rei Yamada and Professor Hiroshi Kuba (Department of Cell Physiology) at Nagoya University Graduate School of Medicine (Dean: Kenji Kadomatsu, MD, PhD) found the novel role of synaptic clustering in dendrites.

Synaptic clustering in principle promotes supralinear integration and increases the impact of spatiotemporally correlated inputs. However, we show in avian binaural coincidence detectors for sound localization that clustering of synapses rather promotes the dendritic attenuation but augments the intensity tolerance of the binaural computations.

Auditory coincidence detection is the neuronal basis of encoding interaural time differences (ITDs) for sound source localization and occurs in neurons of nucleus laminaris (NL) of birds. NL neurons change their dendritic morphology according to the tuning-frequency (characteristic frequency: CF), such that those respond to lower frequencies have longer dendrites. However, the functional significance of such morphological arrangement was not clearly understood.

In this study, we analyzed the synaptic distribution along the NL dendrites by local uncaging stimulation using a two-photon laser microscope. We found that synaptic inputs were concentrated distally in the long dendrites of low-CF neurons. This synaptic arrangement enabled the low-CF neurons to attenuate synaptic potentials in an input size-dependent manner and expanded the dynamic range of ITD coding. This ensured binaural spatial hearing for wide intensity ranges, highlighting the importance of coupling of synapse geometry with dendritic morphology in sensory signal processing.

This work was published online in Science Advances on November 24, 2021 (4:00 am on November 25 of Japan time).

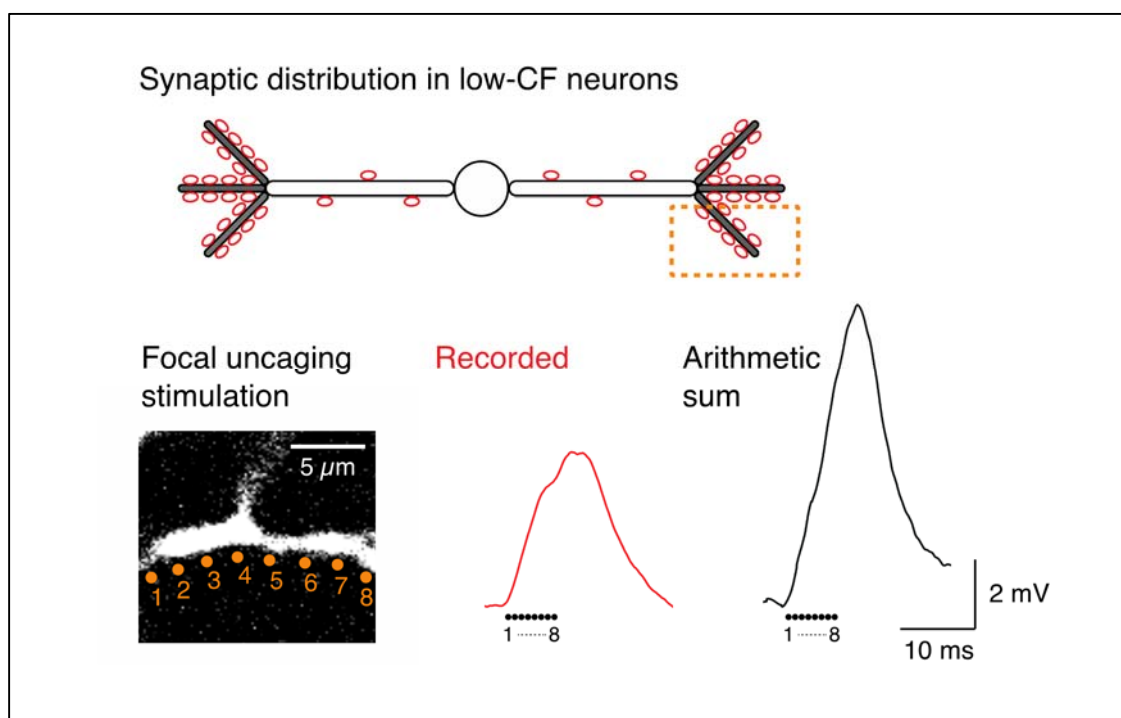
### Research Background

Auditory coincidence detection is the neuronal basis of encoding interaural time differences (ITDs) for sound source localization. In birds, neurons in nucleus laminaris (NL) that receive excitatory inputs from bilateral cochlear nucleus change firing in a manner dependent on ITDs, mediating their well-known coincidence detection. The dendritic morphology of NL neurons is

differentiated along the tonotopic axis, and the length of the dendrites increases with a decrease of characteristic frequency (CF) of neurons. However, the detailed information on the synapse location is lacking and the roles of dendritic computation in the ITD coding remain elusive.

## Research Results

In this study, we analyzed the synaptic distribution along the NL dendrites by local uncaging stimulation of glutamate using a single-photon or two-photon laser microscope and found that synaptic inputs are concentrated distally in the long dendrites of low-CF neurons. We also found that voltage responses at soma were strongly attenuated for those generated at distal dendrites particularly at the strong stimulation. Model study revealed that the clustered inputs at distal dendrite generated



large depolarization at the site, which decreased charge influx through glutamate receptors and increased charge efflux through  $K^+$  channels, then increased the extent of attenuation in an intensity-dependent manner. This sublinear integration prevented unilateral firing and increased the dynamic range of ITD coding. We concluded that the synaptic clustering at distal dendrite would be a cellular basis to accomplish the sound localization for wide intensity ranges of low frequency sound.

## **Research Summary and Future Perspective**

This study not only identifies the cellular basis of sound localization, but also proposes a novel concept that synaptic clustering is a mechanism of expanding dynamic range of neuronal computation by lowering the efficiency of synaptic integration. This finding gives a clue to the variations in synapse geometry and dendritic morphology among cell types and/or brain regions, and facilitates our understanding on computation in the brain.

## **Publication**

Rei Yamada and Hiroshi Kuba

Dendritic synapse geometry optimizes binaural computation in a sound localization circuit.

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