

Summary

The sense of taste is crucial for life: It enables animals to detect nutrients and potential toxins in ingestible substances. Taste information is detected at the level of taste receptors of taste cells, which are organized in characteristic structures named taste buds. This information is then transmitted via pseudounipolar gustatory sensory neurons to the brainstem and higher brain centers. In the brainstem and higher brain centers, taste information is processed to generate behaviors appropriate to the given signal, such as swallowing nutritious substances or spitting potentially harmful ones.

Many animal species including some fishes possess taste buds only in their oral cavity. However, many fish species have taste buds also on their outer body surface. Topological analysis on a catfish showed a clear segregation between projections from 'inner' and 'outer' taste buds, into the vagal and the facial lobes of the brainstem, respectively. Furthermore, neuronal activity measurements in catfish and zebrafish facial lobe suggested some functional segregation between umami and bitter taste detection. However, to the best of our knowledge, there exist no studies examining taste receptor distribution on body surface and oral cavity in any fish species. Consequently, it is unclear whether the functional segregation in the brainstem is newly generated in these circuits or is faithfully transmitted from a corresponding segregation of taste receptors in the periphery.

Within the brainstem, local reflex circuits generate the first behavioral output (swallow or spit). Such a circuit consists of gustatory sensory neuron axon terminals, an interneuron, and a motor neuron. These circuits were investigated mainly in the goldfish vagal lobe, but a potential segregation between the processing of umami and bitter stimuli was not investigated.

Here we employed the vertebrate model system zebrafish to combine a topological analysis of umami and bitter taste receptor (T1Rs and T2Rs, respectively) expression in the oral cavity with a topological analysis of neuronal responses to umami and bitter stimuli in the vagal lobe, the brain region receiving gustatory input from the oral cavity. T1R and T2R expression was investigated using *in situ* hybridization, and neuronal activity was monitored by calcium imaging.

Our results show an anterior focus of the density of both T1R- and T2R-expressing taste cells in the oral cavity of zebrafish, with no segregation between the distributions of these two receptor groups. In contrast, we observed a clear spatial segregation of responses to umami

and bitter tastes in the vagal lobe. These responses were categorized in five different types and each response category shows a different segregation pattern in the vagal lobe. These results suggest that this segregation of responses first occurs at the level of signal processing in the vagal lobe rather than being simply propagated from a similar segregation in the sensory surface.

While doing the *in situ* hybridization experiments to investigate the topological distribution of T1R- and T2R-expressing taste cells in the oral cavity, we found dense clusters of T1R- and T2R-expressing cells on the nostrils. We did a quantitative analysis of the densities of these cells and compared them to other taste cell-containing tissues of zebrafish. Our results show that the nostrils of zebrafish are about as densely populated with T1R- and T2R-expressing cells as the canonical taste organ lower lip and much more densely populated than the oral cavity. These results suggest that the nostrils may play an important role in the taste system of zebrafish.

Taken together, we established the topology of T1R and T2R taste receptor expression in the oral cavity, revealed the nostril as a new taste organ, identified five different categories of umami and bitter responses in the vagal lobe and established category-specific spatial distributions. These results engender several functional implications discussed in detail in the following three chapters.

Our findings on the nostrils of zebrafish gave rise to our first manuscript “Expression of taste sentinels, T1R, T2R, and PLC β 2, on the passageway for olfactory signals in zebrafish”. This manuscript is in its last revision round in the journal “Chemical Senses” at the moment (23.09.2023). This manuscript is added to the present thesis as the first chapter. The second chapter of the present thesis “Zebrafish gustatory sensory surface topology: Anteroposterior gradient of both umami and bitter taste receptors in the oral cavity, but no segregation between them” focuses on the topological distribution of T1R- and T2R-expressing taste cells in the oral cavity of zebrafish. The third chapter “Functional segregation of taste qualities in the zebrafish brainstem vagal lobe is generated and sharpened locally.” presents our findings on the neuronal responses to umami and bitter tastes in the vagal lobe of zebrafish.

All three chapters of the present thesis are prepared in the form of individual manuscripts. We plan to submit the second chapter of the present thesis as manuscript to the journal “The Journal of Comparative Neurology” and the third chapter to the journal “The Journal of

Neuroscience”. Therefore, we have followed the guidelines of the respective journals for the citation style while preparing these two chapters.