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Odor Modulation of Electrical and $[\text{Ca}^{2+}]_i$ Activities in Neurons of the Olfactory Bulb

The olfactory bulb is the first relay stage that processes input from the sensory periphery and relays the information to many high-ordered cortical regions. Despite stimulus activity has been observed in vivo, to study the mechanisms underlying odor-evoked activities is much more difficult using in vivo preparation. In this thesis, we use a nose-olfactory bulb slice preparation of *Xenopus Laevis* tadpoles and focus on characterized odor-induced spiking and $[\text{Ca}^{2+}]_i$ activities of OB neurons in the preparation.

Using loose-seal, on-cell patch-clamp recordings, we first investigate spiking activities in mitral cells (MCs) and granule cells (GCs). Both types of neurons can generate action potentials (APs) spontaneously. While a majority of MCs fire APs in bursts, the firing pattern of most GCs appeared to be random discharge. Upon odorant stimulation, spontaneous spiking activity of MCs can be modulated as inhibition or excitation. Spontaneous spikes were clearly suppressed by odorant stimulation in some MCs while odor elicits a train of spikes in other responding MCs. In contrast to MCs, most GCs generated only a few spikes during odorant stimulation.

To further reveal currents and subthreshold membrane potentials underlying the observed spiking activities, we perform patch clamp recordings in the whole-cell, voltage- and current-clamp configuration. Some MCs show an odor-induced slow inward current and APs superimposed on a subthreshold membrane potential depolarization while others display a slow outward current and an odor-induced hyperpolarization associated with odorant stimuli. In contrast to these slow synaptic currents in MCs, odorant stimulation induced a barrage of fast EPSCs in a majority of responding GCs. These results suggest that electrical responses in MCs are driven by certain slow synaptic inputs whereas odor-evoked excitation in GCs is triggered mainly by fast excitatory inputs.

To characterize the stimulus response distributed in the olfactory bulb, we use calcium imaging to monitor activities of a large population of bulbar neurons. First, we observed prominent ongoing $[\text{Ca}^{2+}]_i$ fluctuations in most MCs and in a majority of GCs. These $[\text{Ca}^{2+}]_i$ fluctuations are dependent on the extracellular calcium influx because they can be blocked by superfusion of calcium-free external solution. Furthermore, these spontaneous fluctuations are suppressed by TTX and cadmium indicating that this $[\text{Ca}^{2+}]_i$ activity is dependent on voltage-activated sodium and calcium channels.

Odorant stimulation can modulate ongoing $[\text{Ca}^{2+}]_i$ activities of MCs as enhancement, suppression, or a combination of both, resulting in various complex $[\text{Ca}^{2+}]_i$ response waveforms in MCs. Conversely, a majority of GCs show single or compound $[\text{Ca}^{2+}]_i$ transients upon odorant stimulation. Prominent inhibitory responses in MCs indicate that MCs are functionally coupled to intrabulbar inhibitory network.

Regarding the spatial pattern of odorant responses to a mixture of amino acids, MCs with similar response properties have certain tendency to be located in a spatial neighborhood but at the same time extensively intermingle with cells of opposite response characteristics.

Finally, combining calcium imaging and on-cell patch clamp recordings, we investigate the relationship between somatic $[\text{Ca}^{2+}]_i$ and action potentials in MCs and GCs. Simultaneous recording reveals a precise correlation between $[\text{Ca}^{2+}]_i$ increases and the occurrence of
spikes during spontaneous and odor-evoked activity in mitral cells. Interestingly, $[\text{Ca}^{2+}]_i$ decreases induced by odorant stimulation coincide with the suppression of the spontaneous firing. Granule cells, however, show much lower correlation between $[\text{Ca}^{2+}]_i$ and APs. In addition to AP-correlated $[\text{Ca}^{2+}]_i$ increases, we also observe substantial numbers of uncorrelated events such as increases of $[\text{Ca}^{2+}]_i$ without the presence of APs or APs without $[\text{Ca}^{2+}]_i$ increases. The results indicate that the relationship between somatic $[\text{Ca}^{2+}]_i$ and APs is different in mitral and granule cells. Thus, one must think of the diversity of neurons when relating $[\text{Ca}^{2+}]_i$ activity to spike activity.