Summary

Olfactory receptor neurons (ORNs) provide an animal with information about odors in its environment. In mammals and insects, individual ORNs mostly express a single olfactory receptor (OR). ORNs expressing the same OR gene form subpopulations, converging on one or a few spatially invariant glomeruli. Glomeruli are spherical subunits of the olfactory bulb (vertebrates) or antennal lobe (AL, insects), the first olfactory processing center in the brain. Within a glomerulus ORNs make synaptic contacts with inhibitory GABAergic neurons local to the OB/AL and 2^{nd} order neurons relaying the olfactory information to higher brain centers. The basis for understanding how odors are coded within olfactory systems is knowledge about its input. In order to describe the input to olfactory systems we need to know the odors activating or inactivating all subpopulations of ORNs, defined as their molecular receptive ranges (MRR).

To this end I characterized the MRR of an exemplary ORN subpopulation in great detail using the model organism *Drosophila melanogaster*. Employing the UAS-Gal4 system, I expressed Cameleon2.1, a Ca^{2+} sensitive fluorescent dye, under control of the OR gene promotor Or22a. This allowed me to monitor selectively the odor-evoked responses of the ORNs expressing this OR *in vivo* by using optical imaging. I tested a panel of 104 odors from a variety of chemical classes. Odor evoked responses were measured from the primary dendrites and somata of the ORNs on the antenna and from their axonal terminals in the glomeruli of the AL. The results showed graded responses to 39 stimuli for which I subsequently established dose-response curves. The most potent odors were ethyl and methyl hexanoate. These odor molecules elicited responses at dilutions as low as 1:100,000,000, thereby showing that Or22a has a broad yet selective MRR challenging the distinction between specialist and generalist ORNs. By systematically testing another 15 structurally very similar odors I was able to determine some molecular determinants of the MRR. These observations were corroborated by a modeling approach in collaboration with Daniel Baum from the Zuse Institute Berlin (ZIB) who developed an algorithm for semi-flexible superpositioning of 3D molecular structures.

Comparing the MRR measured in the dendrites and somata on the antenna with the MRR obtained at the axonal endings within the AL, showed that both were identical. This finding further substantiated the notion that the MRR of a glomerulus reflects the odor specificity of the OR expressed in the ORNs innervating it. However, a detailed analysis of antennal and AL response kinetics revealed differences e.g. in fall time and response duration. In order to test whether these temporal differences were due to a shaping role of inhibitory AL local neurons, I applied the ionotropic GABA agonist muscimol and the Cl^- channel blocker picrotoxin. I found evidence for odor-specific presynaptic inhibition of ORN responses. While presynaptic inhibition changed the amplitude of the responses, fall time and response duration remained stable. Thus the differences in kinetics of antennal and AL responses could be attributed to different Ca^{2+} sources contributing to either signal.

Finally, I started the characterization of another OR, namely Or47b. This OR is in many regards different from Or22a and of special interest because to date hardly anything is known about the physiology of ORNs expressing Or47b. I identified several ligands the majority of which was inactivating. These results show the coding complexity of the olfactory system already at the input level.

This study represents a further step towards understanding odor coding in the periphery of the *Drosophila* olfactory system. Furthermore, it provides a sound basis for further exploring the role of the AL network.