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Title: Structured representation of odors in a third-order olfactory area

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Abstract: In the Drosophila brain, dense, combinatorial representations of odor in early olfactory circuits are transformed to a sparse and selective code for odor identity in the Kenyon cells (KCs) of the mushroom body, a major third-order associative olfactory area. The transformation dramatically decorrelates and increases the separability of odor representations, which may be particularly advantageous for the categorization, storage, and recall of information during learning and memory. The functional logic of how individual KC feature selectivity arises, and how the KC population efficiently encodes the full range of odor stimuli important to the fly, are not well understood. To investigate the mechanisms by which odor representations are generated in the mushroom body, we used volumetric two-photon functional imaging of a nuclear-targeted genetically encoded calcium indicator to measure large-scale, population representations of odor at cellular resolution in the mushroom body. Using a chemically diverse panel of ~25 odors, we show that the representation of odors in mushroom body coding space is invariant across individual flies -- the degree of similarity between the representations of two odors is highly predictable from brain to brain. However, the representational distance between specific odors in mushroom body coding is poorly predicted by their distance in peripheral odorant receptor space, given assumptions that KC receptive fields arise from the integration of random subsets of olfactory inputs. This result suggests that structured olfactory input contributes to the formation of KC receptive fields, an idea consistent with the results of recent large-scale EM reconstruction of KC synaptic input. These findings raise the intriguing possibility that, given that the odor space of the natural world is highly structured, the olfactory code may be adapted to the statistics of natural odor space, allowing more efficient encoding with a limited number of neurons. We are building on these findings by investigating the possible developmental mechanisms by which structured input arises in the mushroom body, including testing for a possible role of odor experience in shaping KC odor representations.