Chem. Senses 30 (suppl 1): i283–i284, 2005
doi:10.1093/chemse/bjh225

Making Scents Out of Spatial and Temporal Codes in Specialist and Generalist Olfactory Networks

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Key words: lateral inhibition, odor coding, olfactory glomeruli, oscillations, synchronization

Introduction

The first-order olfactory centers in the brains of vertebrates and invertebrates are characterized by arrays of morphologically discrete glomeruli, and cross-phyletic comparisons have repeatedly found striking similarities in glomerular organization across evolutionarily remote animals. A growing list of studies shows that the vertebrate olfactory bulb (OB) and insect antennal lobe (AL) are organized chemotopically, and an individual glomerulus reflects the odor-response profile of the olfactory receptor neurons (ORNs) that converge on it (Bozza and Kauer, 1998; Belluscio *et al.*, 2002; Ng *et al.*, 2002; Wang *et al.*, 2003). While these different studies using a wide range of methods have supported glomerular chemotopy in diverse species, many fundamental questions about the neural circuitry underlying these activity patterns remain. Evidence is increasing, in fact, that the molecular receptive range (MRR) or 'odor tuning' of a glomerulus is also shaped by interglomerular—and particularly inhibitory—interactions (Christensen *et al.*, 1998; Lei *et al.*, 2002; Sachse and Galizia, 2003; Aungst *et al.*, 2003; Nagayama *et al.*, 2004), but the cellular and synaptic mechanisms underlying this modulation remain poorly understood.

Heterogeneity in glomerular output

While uniglomerular projection neurons (PNs) associated with a given glomerulus have similar MRRs, mitral and tufted (M/T) cells in mammals (Nagayama *et al.*, 2004) and the diverse PNs that innervate the same glomerulus in insects (Vickers *et al.*, 1998; Sadek *et al.*, 2002) have been shown to differ in their physiological responses to odors. These findings emphasize that glomeruli are not isolated 'islands' of neuropil or simple relay elements, and an increasing number of studies, many in insects, show that the MRR and/or dynamics of a PN's odor-evoked response are influenced by interactions with other glomeruli. For instance, interglomerular AL circuitry in both honey bees (Sachse and Galizia, 2003) and moths (Vickers *et al.*, 1998; Lei *et al.*, 2002) can modify the relatively narrow tuning of the ORNs that provide input to a glomerulus, resulting in a modification of PN responses. This is especially evident when the blend of odors that selectively activates several identified glomeruli simultaneously is used as a stimulus (Christensen *et al.*, 2000; Christensen and Hildebrand, 2002). The same may not be true, however, for glomeruli in the fruit fly *Drosophila*. In a recent study using electrophysiological recordings, it was proposed that network mechanisms can transform the odor tuning of glomerular outputs (Wilson *et al.*, 2004), while two other studies using activity labeling failed to find any such signal transformation (Ng *et al.*, 2002; Wang *et al.*, 2003). Reasons for such divergent results remain unclear, emphasizing the need to learn more about the complex synaptic circuitry in the glomerular neuropil.

'Specialists' versus 'generalists'

Recent studies in a variety of insect species have provided compelling evidence that receptor cells previously identified as 'generalists' (e.g. responding to multiple plant-derived volatiles) exhibit much greater selectivity and sensitivity when stimulated with the appropriate odor ligand (Ignell and Hansson, 2004; Skiri *et al.*, 2004). This is true also at the central level. We recently found glomeruli that are very selective for enantiomers of a plant monoterpene (Reisenman *et al.*, 2004) and another that is extremely sensitive to CO_2 (Guerenstein *et al.*, 2004). It seems, therefore, that the sometimes false characterization of olfactory receptors and central neurons as 'broadly tuned' may be due to the lack of a well-defined key stimulus and/or the use of unnaturally elevated odor concentrations (Christensen and Hildebrand, 2002; Ignell and Hansson, 2004). Since odor selectivity and sensitivity are inextricably linked, care should be exercised in characterizing any olfactory cells or networks as 'specialists' or 'generalists' unless a sufficient number of odors are tested using a physiologically appropriate range of concentrations.

Synchrony with and without oscillations

The brain's information coding strategies have been debated for many years, and this discussion has included the mechanisms by which odors are discriminated. Since the 1940s, when Adrian first recorded from the OB, a number of investigators have found evidence for a possible functional role of oscillatory activity in odor coding (Adrian, 1942; Gelperin *et al.*, 1996; Kashiwadani *et al.*, 1999; Laurent *et al.*, 2001; Friedrich, 2002), but this remains an area of active debate, at both the physiological and behavioral levels. In the locust and honeybee, for example, studies suggest that network oscillations may be important for encoding olfactory information (reviewed in Laurent *et al.*, 2001), whereas studies in moths have not been able to substantiate these findings (Christensen *et al.*, 1998, 2000, 2003; Heinbockel *et al.*, 1998; Vickers *et al.*, 1998, 2001; Daly *et al.*, 2004a). Aside from species differences, such divergent findings may also result from our lack of detailed knowledge about the synaptic circuitry that encodes olfactory information in the OB and AL. Another possibility is that most published experimental-stimulus protocols have not addressed whether oscillatory patterning is maintained under conditions that mimic natural odor plumes (Vickers *et al.*, 2001; Ditzen *et al.*, 2003; Uchida and Mainen, 2003). Yet another possible source of disagreement may reflect the fundamental ability of sensory circuits in the brain to be modulated by experience, as we recently demonstrated in *Manduca* (Daly *et al.*, 2004b). In sum, recent findings challenge the idea that specific, slow temporal patterns of activity encode different odors. Instead, they support numerous studies in both invertebrates and vertebrates arguing that much of the information encoded in spiking patterns in sensory systems is associated with stimulus dynamics (Buraças and Albright, 1999) and that these patterns can be modified by learning (Wilson and Stevenson, 2003). Future studies that seek to understand olfactory coding from the animal's perspective will no doubt lead to new revelations about the functional significance of temporally patterned neural activity as it relates to the natural dynamics of odor plumes.

Acknowledgements

Many thanks to the talented folks in John Hildebrand's lab who have contributed to this work, especially Andrew Dacks, Pablo Guerenstein, Hong Lei, Vince Pawlowski, Carolina Reisenman and Heather Stein. This work is supported by National Institute on Deafness and Other Communication Disorders Grants DC-05652 to T.A.C. and DC-02751 to J.G.H.

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