Non-topographical contrast enhancement enables disambiguation of high-dimensional neural representations

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The topographical mapping of external stimulus spaces is a common principle of neural organization, and contributes to sensory input processing by facilitating contrast enhancement mechanisms such as center-surround lateral inhibition. Because this form of contrast enhancement relies upon mutual inhibition among neurons proportional to the similarity of the information they mediate, the intrinsic topology of the contrast enhancement mechanism must match the underlying topology of the sensory map upon which it acts. For example, the spatial contrast of retinal images is enhanced by lateral inhibitory projections within the two spatial dimensions of the retinal field (Werblin and Dowling, 1969; Cook and McReynolds, 1998), and auditory frequency tuning in the inferior colliculus and medial geniculate body is similarly sharpened along the single dimension of frequency space (Yang et al., 1992; Suga et al., 1997; Lu and Jen, 2001). In the olfactory system, contrast enhancement is believed to sharpen odor quality representations (Yokoi et al., 1995; Mori et al., 1999), which map onto an indeterminate but certainly high-dimensional sensory space that is largely common among conspecifics. However, no mechanism has been proposed in any neural system that is capable of mediating contrast enhancement in more than two dimensions, which is essential to its function in the olfactory modality. We here propose and demonstrate a novel mechanism, non-topographical contrast enhancement (NTCE), enabling arbitrarily high-dimensional contrast enhancement by olfactory bulbar circuitry (Figure 1).

Perceptual similarities among odorants map onto an intrinsically high-dimensional odor quality space. Unlike wavelength or frequency, which define the one-dimensional ordering of visual and auditory qualities respectively, any variation in the molecular structure of an odorant will effect changes in ligand binding affinity and efficacy for each of the olfactory receptors

expressed by a given animal. As olfactory sensory neurons (OSNs) expressing a given odorant receptor converge onto specific glomeruli in the olfactory bulb (Mombaerts et al., 1996), a species with 1000 functional olfactory receptor genes, (and hence 1000 chemotopically distinct glomeruli), as is estimated in mouse (Mombaerts et al., 1996; Mombaerts, 2001), will consequently generate primary odor representations that can be depicted as 1000-dimensional vectors. While consistent interglomerular activity correlations deriving from the statistics of the olfactory environment will compress the theoretical dimensionality of this sensory space to less than this maximum, stimulus representations nevertheless retain a substantially higher dimensionality than the two physical dimensions available in cortical structures.

Representational patterns of arbitrary dimension can be compressed into lower-dimensional spaces by forming discrete maps; that is, maps with embedded discontinuities. Algorithms such

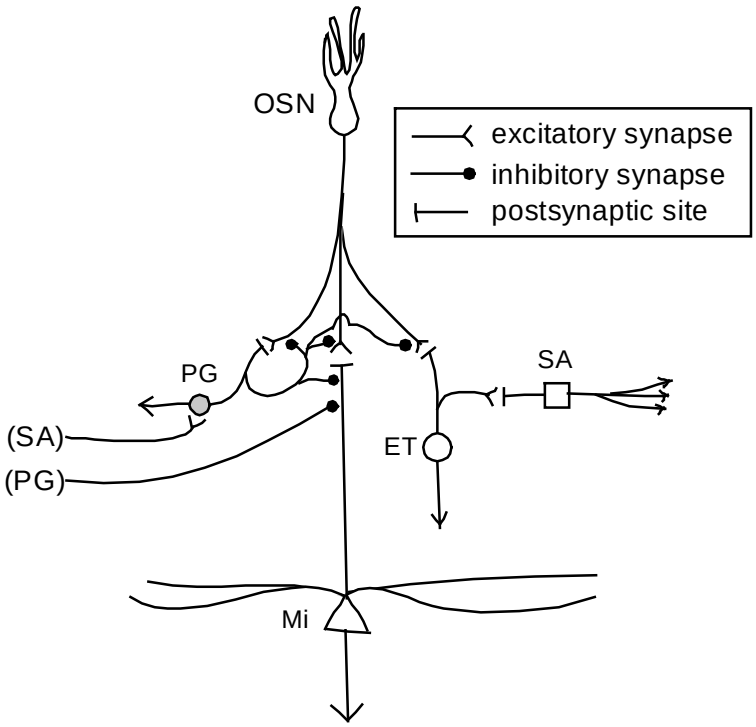

Figure 1: Schematic of olfactory bulb glomerular circuitry. OSN, primary olfactory sensory neuron; Mi, mitral (principal) cell; PG, periglomerular cell, ET, external tufted cell, SA, short axon cell. Arrowheads denote axonal projections to regions not denoted in the figure; parenthetical cell names denote axonal projections from other glomeruli to the glomerulus depicted.

as the self-organizing map (Kohonen, 1982; Haykin, 1999) perform such transformations adaptively, and are able to retain local similarity relationships up to the limits imposed by the intrinsic dimensionality of the input representation, at which point discontinuities are inevitable. However, this compression does not change the intrinsic topology of the odor representation; lateral inhibition in two dimensions remains computationally incapable of mediating effective contrast enhancement in this high-dimensional modality. How, then, can olfactory contrast enhancement be mediated not only high-dimensionally, but with the correct topology, as derived from the unambiguous high-dimensional similarity relationships among the glomeruli (and associated mitral cells) attuned to particular molecular receptive ranges? The NTCE model described herein illustrates how the neural circuitry intrinsic to the olfactory bulb glomerular layer is capable of mediating contrast enhancement and pattern disambiguation among arbitrary and unpredictable odorant stimuli drawn from an arbitrarily high-dimensional olfactory stimulus space, and in several ways appears to be optimized for this task. The underlying principles are first illustrated in a simple circuit model, and then elaborated using a biophysically constrained compartmental model of olfactory glomerular circuitry.

Irrespective of the topology of a stimulus space, successful contrast enhancement enables the single or few most strongly activated units to yield robust output, while output activity in slightly less-activated units is specifically quenched by inhibition and minimally activated units remain inactive. That is, output activity as a function of input activity will form one half of a Mexican hat on-center/inhibitory-surround function, the signature function of contrast enhancement (*hemihat function*; Figure 2A). As shown in a a simplified illustrative model, NTCE will generate this function independently within each glomerulus by driving parallel excitatory and inhibitory processes with the same sensory input, given that the inhibitory process both is more sensitive to that input than the parallel excitatory process and saturates at a lower activity level (Figure 2B). Under these conditions, each glomerulus will inhibit its own output in scaled

proportion to its sensory input, such that its net output activity exhibits a hemihat function along the axis of input activation level, which in turn derives from a conflation of receptor-ligand affinity and ligand concentration (Cleland and Linster, 1999). This is precisely what the architecture of the olfactory bulb input layer provides. Direct sensory input from OSN axonal arborizations activates both periglomerular neurons and mitral cell primary dendrites; periglomerular cells in turn inhibit mitral cell primary dendrites, providing parallel inhibitory and excitatory determinants of glomerular output. In order to disambiguate ligand concentration from ligand-receptor affinity, the activity of individual glomeruli must be normalized to the sum of

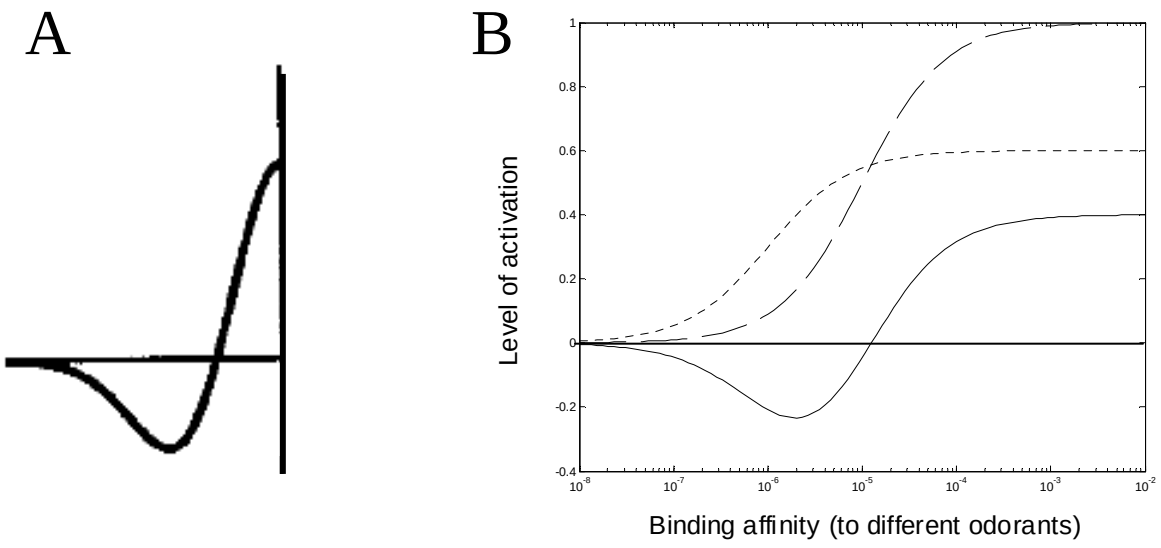

Figure 2: A: "Hemihat" function (one half of an on-center/inhibitory surround Mexican hat function). **B:** Simplified, illustrative model of non-topographical contrast enhancement (NTCE) in a single glomerulus by dendodendritic glomerular circuitry. *Dashed line*: excitatory synaptic input from the olfactory sensory neuron (OSN) ensemble to a model mitral cell as a function of the affinity (tuning) of its affiliated odor receptors for a given odorant species. Greater ligand-receptor affinity is to the right. *Dotted line*: activation of a juxtaglomerular neuron by the same excitatory OSN synaptic input. While it may express the same glutamate receptors as those on the mitral cell apical dendrite, its sensitivity may be substantially greater than that of the mitral cell due to any of a number of factors influencing intracellular gain (cf. Cleland and Linster, 1999). The maximum inhibitory effect of the juxtaglomerular cell on the mitral cell, however, is less than the maximum excitability of the mitral cell. *Solid line*: subtraction of inhibitory (dotted line) from excitatory (dashed line) influences on mitral cell to yields a hemihat function for net mitral cell activation. This mitral cell will be excited only by a narrower range of better-tuned odorants (or higher concentrations of less well-tuned odorants) compared with the same mitral cell in the absence of juxtaglomerular inhibition (this ambiguity between concentration and affinity is resolved by the second stage of the NTCE algorithm). Furthermore, this mitral cell will be actively inhibited by odorants to which it is only moderately well-tuned, enhancing the contrast between those odorants to which it is best-tuned and those to which it is only moderately well-tuned in its contribution to the odor representation.

activity across all glomeruli (backward summation; Coenen et al., 2001). In the olfactory bulb, this function is attributable to the short-axon cell lateral network (Aungst et al., 2003). Short-axon cells are indirectly activated by sensory input, ramify broadly across the olfactory bulb, and form excitatory synapses upon periglomerular cells which in turn inhibit local mitral cells. As short-axon cells are few in number and diverge broadly, they are appropriate mediators of a broad and relatively indiscriminate projection of inhibition upon the mitral cell population.

Using the simulator NEURON (Hines and Carnevale, 1997, 2001), we constructed compartmental models of olfactory glomerular circuitry including olfactory sensory input, mitral cell models adapted from those of Chen and colleagues (Shen et al., 1999; Chen et al., 2002), and periglomerular and short-axon cell models of our own design, constrained to available anatomical and biophysical data and exhibiting appropriate single-cell physiological responses to inputs (Pinching and Powell, 1971; McQuiston and Katz, 2001; Aungst et al., 2003). We describe a robust and physiologically appropriate region of parameter space in which the NTCE mechanism successfully mediates high-dimensional contrast enhancement in odor similarity space, indicating the plausibility of this mechanism for underlying contrast enhancement among odor stimuli in the living olfactory bulb.

References

Aungst JL, Heyward PM, Puche AC, Karnup SV, Hayar A, Szabo G, Shipley MT (2003) Centre-surround inhibition among olfactory bulb glomeruli. Nature 426:623-629.

Chen WR, Shen GY, Shepherd GM, Hines ML, Midtgaard J (2002) Multiple modes of action potential initiation and propagation in mitral cell primary dendrite. J Neurophysiol 88:2755-2764.

Cleland TA, Linster C (1999) Concentration tuning mediated by spare receptor capacity in olfactory sensory neurons: A theoretical study. Neural Comput 11:1673-1690.

Coenen OJ-MD, Sejnowski TJ, Jabri MA (2001) Parallel fiber coding in the cerebellum for life-long learning. Autonomous Robots 11:291-297.

Cook PB, McReynolds JS (1998) Lateral inhibition in the inner retina is important for spatial tuning of ganglion cells. Nat Neurosci 1:714-719.

Haykin S (1999) Neural networks: a comprehensive foundation, 2nd Edition. Upper Saddle River, NJ: Prentice Hall.

Hines ML, Carnevale NT (1997) The NEURON simulation environment. Neural Comput 9:1179-1209.

Hines ML, Carnevale NT (2001) NEURON: a tool for neuroscientists. Neuroscientist 7:123-135.

Kohonen T (1982) Self-organized formation of topology correct feature maps. Biol Cybern 43:59-69.

Lu Y, Jen PH (2001) GABAergic and glycinergic neural inhibition in excitatory frequency tuning of bat inferior collicular neurons. Exp Brain Res 141:331-339.

McQuiston AR, Katz LC (2001) Electrophysiology of interneurons in the glomerular layer of the rat olfactory bulb. J Neurophysiol 86:1899-1907.

Mombaerts P (2001) How smell develops. Nat Neurosci 4 Suppl:1192-1198.

Mombaerts P, Wang F, Dulac C, Chao SK, Nemes A, Mendelsohn M, Edmondson J, Axel R (1996) Visualizing an olfactory sensory map. Cell 87:675-686.

Mori K, Nagao H, Yoshihara Y (1999) The olfactory bulb: coding and processing of odor molecule information. Science 286:711-715.

Pinching AJ, Powell TP (1971) The neuropil of the periglomerular region of the olfactory bulb. J Cell Sci 9:379-409.

Shen GY, Chen WR, Midtgaard J, Shepherd GM, Hines ML (1999) Computational analysis of action potential initiation in mitral cell soma and dendrites based on dual patch recordings. J Neurophysiol 82:3006-3020.

Suga N, Zhang Y, Yan J (1997) Sharpening of frequency tuning by inhibition in the thalamic auditory nucleus of the mustached bat. J Neurophysiol 77:2098-2114.

Werblin FS, Dowling JE (1969) Organization of the retina of the mudpuppy, Necturus maculosus. II. Intracellular recording. J Neurophysiol 32:339-355.

Yang L, Pollak GD, Resler C (1992) GABAergic circuits sharpen tuning curves and modify response properties in the mustache bat inferior colliculus. J Neurophysiol 68:1760-1774.

Yokoi M, Mori K, Nakanishi S (1995) Refinement of odor molecule tuning by dendrodendritic synaptic inhibition in the olfactory bulb. Proc Natl Acad Sci U S A 92:3371-3375.