

Odor representations in the mammalian olfactory bulb

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A first key step in studying a sensory modality is to define how the brain represents the features of the sensory stimulus. This has proven to be a challenge in olfaction, where even the stimulus features have been a matter of considerable debate. In this review, we focus on olfactory representations in the first stage of the olfactory pathway, the olfactory bulb (OB). We examine the diverging viewpoints on spatially organized versus distributed representations. We then consider how odor sampling through respiration is a key part of the odorant code. Finally, we ask how the bulb handles the challenging task of representing mixtures. We suggest that current evidence points toward a representation that is spatially organized at the inputs but later distributed, with the spatial organization not being used for much computation. Nevertheless, this is a simple representation that effectively represents multiple individual odorants, as well as odor mixtures. © 2010 John Wiley & Sons, Inc. *WIREs Syst Biol Med*

We approach the issue of odor representations in the olfactory bulb (OB) of mammals by asking the question: what are the essential variables of the stimulus that the OB needs to represent? We consider two key variables: odor identity and intensity. We make a special mention of representation of odor mixtures, as mixtures have a particularly interesting role in olfaction. We will discuss how the OB appears to represent this information using spatial and temporal coding. We shall focus on mammalian systems and will not discuss in detail work done on non-mammalian vertebrates¹ and insects.²

In its broadest definition, spatial coding can be thought of as the rule that the location of a cell (or synapse) determines what it means to downstream cells, so neural activity in a specific region or groups of regions will describe a stimulus. Similarly, temporal coding can be thought of as the rule that the pattern of spiking of a cell over time is what is important to downstream cells. Though the two are often combined to give *spatiotemporal* coding, the spatial and temporal aspects can often be described separately.

We propose that the apparent strong spatial coding in the OB is primarily a feature of input

representations, is dispensed with in subsequent stages, and may not be a computational feature of the OB. We also suggest that the OB has made a virtue of the physiological necessity of intermittent sampling coupled to respiration and utilizes respiration phase as a key attribute in feature encoding. In our view, a key challenge for the field is to condense these diverse aspects of representation at the input and output stages of the OB into a compact model of olfactory feature encoding and its transformation. The outlines of such a model are beginning to form and stand in sharp counterpoint to the pervasive topographic and rate-coding view of sensory coding that has come from the visual system.

SPATIAL MAPS OF ODOR IDENTITY AND INTENSITY

The first stage of odor identity coding in the OB rides on the back of the spectacularly well-organized projections from distinct olfactory receptor neuron subtypes in the olfactory epithelium to the OB (Figure 1).³ There is a nearly ideal one-to-two mapping between ~1200 olfactory receptor neuron subtypes, each expressing a molecularly distinct receptor protein, to the ~2400 glomeruli in the rat or mouse. The confounding factor in this elegant picture is that receptor neurons have a broad selectivity which is often difficult to predict.⁴ Nevertheless, this precise map leads to spatial organization in bulbar input

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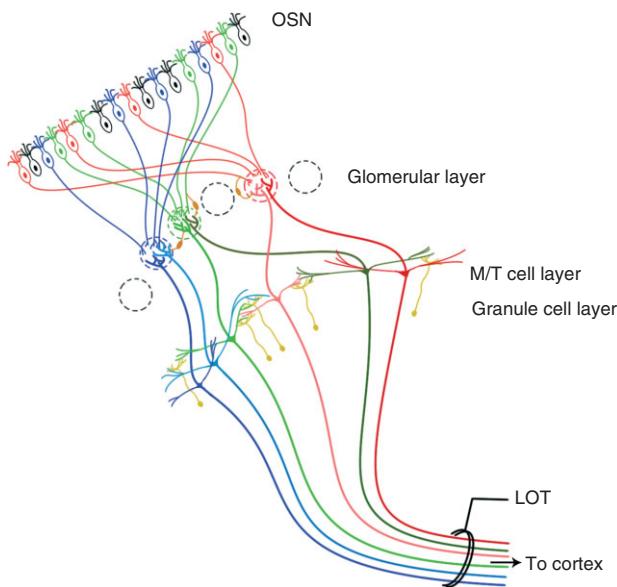


FIGURE 1 | Schematic of the circuitry of the olfactory bulb and its inputs. Olfactory sensory neurons expressing the same receptor type converge onto one or two distinct glomeruli with a convergence ratio exceeding 5000:1. Mitral/tufted (M/T) cells, which are the principal output neurons of the bulb, send a primary dendrite to one glomerulus. M/T cells excite granule cells and receive reciprocal inhibition, through dendrodendritic synapses on their secondary dendrites. The axons of M/T cells project to other brain regions through the lateral olfactory tract.

(glomerular) responses, which have been studied for several decades.

Conversely, at the M/T cell layer, there have been fewer studies looking at the spatial maps and a much larger number looking at temporal aspects of coding.

Glomerular layer

From a functional viewpoint, the most critical piece of information that the OB represents is simply odor identity. Intensity and mixture identification may, in fact, be considered as variations on this primary function. The mapping of odor identity into spatial patterns of activity on the glomerular layer of the rodent OB began to be uncovered by early electrophysiological work by Leveau and MacLeod. They proposed ‘the hypothesis that the 100-million-point olfactory pattern in the mucosa is converted to a homologous pattern of only 2000 points at the glomerular level, which is the real base for central integration.’⁵ Direct data on this hypothesis came when these patterns of activity were directly imaged, initially using metabolic labeling in the form of the 2-deoxyglucose (2-DG) method.

These early 2-DG studies^{6–9} established the most essential facts regarding these glomerular maps (Figure 2):

1. An odor elicits activity in a specific group of glomeruli across the surface of the bulb, forming a punctate pattern.
2. Different odors evoke different patterns.
3. These patterns are bilaterally symmetric and very similar across animals for any given odor.
4. Increasing the concentration of an odor increases the intensity of activation of glomeruli and also recruits more glomeruli which were not active at lower concentrations.

Since these early studies, this region has been studied in great detail with a wide variety of other imaging techniques. These have utilized intrinsic signals,^{10–14} Ca^{2+} sensitive dyes,^{15,16} high resolution functional Magnetic Resonance Imaging,¹⁷ voltage-sensitive dyes (VSDs),^{18,19} immediate early gene expression,^{20–22} phosphorylated extracellular signal-related kinase expression,²³ and pH sensitive genetically encoded dyes.²⁴ Despite this explosion of techniques to study spatial patterns of bulbar activity, they have largely served to reinforce the original facts established by the early 2-DG work.

These spatial recordings have posed a still unresolved question about glomerular coding for odor intensity: Is recruitment of additional glomeruli²⁵ the result of nonspecific response or a strategy to code intensity, or both? Psychophysical studies report that at very high concentrations, a few odors change their quality²⁶ but most of them remain unchanged.²⁷ We speculate that part of the role of the OB is to preserve odor identity codes at the output mitral/tufted (M/T) cell level, despite these changes in the inputs. How this is achieved is an interesting question addressed by a few studies in rats^{27,28} and insects.²⁹

There are two further critical aspects of odor representations in the glomerular layer that the 2-DG studies were inherently incapable of addressing: first, the question of the range of responses of any given glomerulus across stimuli, and second, the temporal dynamics of the responses of glomeruli. We discuss the first here and the latter in the section on Temporal Representations of Odor Identity and Intensity.

Chemotopy

The issue of the molecular receptive range (MRR) of glomeruli leads to a key coding issue: are glomeruli arranged chemotopically, i.e., do similar odorants activate glomeruli that are spatially clustered in the

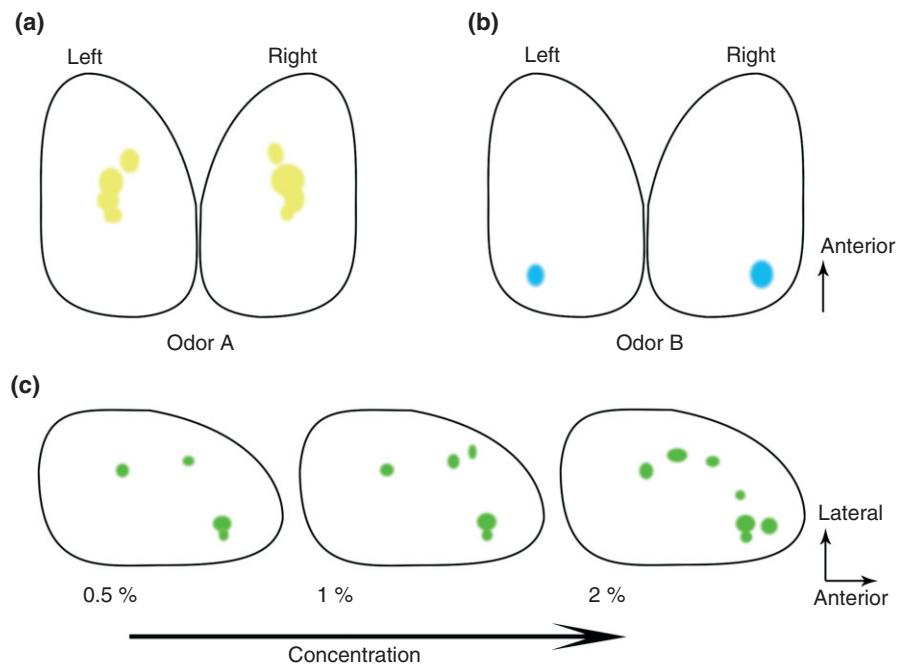


FIGURE 2 | Basic properties of glomerular spatial maps. Schematic of dorsal surface views of the olfactory bulb and glomerular activation. (a) and (b) Odorant stimuli activate bilaterally symmetric patterns of glomerular activity, which are spatially distinct for different odors. (c) Increasing odor concentration recruits more glomeruli. Schematic representation of results from Ref. 46.

bulb? Many studies have demonstrated chemotopy with large, loosely defined domains.^{11,12,30} However, a recent study¹⁴ which uses a larger odor set with no *a priori* assumptions about structures in odor stimulus space has shown that most of these domains are much less well defined than believed, with only two chemical groups showing the majority of clustering. When analyzed from the glomerular MRR point of view, there is only a weak trace of loose chemotopy, and certainly no fine scale chemotopy; nearby glomeruli are as different as far away ones. There is a suggestion that the loose chemotopy that is observed might be a side product of the developmental strategy used by the OB while forming and arranging glomeruli.³¹

M/T cell layer

There are far fewer studies regarding spatial aspects of coding in the M/T cell layer. Anatomical tracing studies have suggested the continuation of glomerular structure to this layer,³² and slice recordings show that M/T cells connected to the same glomerulus are more synchronous.³³ Single unit recordings in awake³⁴ and anesthetized rats³⁵ had suggested that neighboring mitral cells (which are on average more likely connected to the same glomerulus) were more likely to have similar responses than distant cells. Furthermore, there are conflicting reports on whether the glomerular odor-specific activity maps continue through to deeper cell layers. One study using 2-DG³⁶ suggests that mitral cell maps do exist, another using c-fos mapping shows patterns in the

granule cell layer that are much broader than the glomerular maps,²¹ and yet another study shows that c-Jun expression is homogenous throughout the M/T and granule cell layers, regardless of the odor.²²

However, there is one study which has used single unit recordings (thus high spatial resolution), well controlled odor stimuli and has also analyzed responses in the context of their temporal patterns.³⁷ This study shows that neighboring M/T cells are very dissimilar in their responses to the same odors and show no signs of any chemotopic map.

Interestingly, a recent study using calcium imaging at single cell resolution has shown that even in the piriform cortex, there is no indication of spatial organization of odorant responses or chemotopy.³⁸

In summary, the information available so far suggests that the striking anatomical organization of glomerular projections is already diluted when it comes to activity-based chemotopic maps, and the spatial patterns that are observed at the inputs seem to be discarded by the time the information leaves the OB. A spatial code exists in the simplest sense of distinct spatial activation for different odors but without any further topographic organization (however, for a contrasting viewpoint see Ref 30). Thus, the elaborate spatial organization of the anatomy and physiology of the inputs to the OB may primarily serve the purpose of convergence and amplification of olfactory sensory neuron signals.³⁹ In this scenario, interglomerular circuitry still plays an important role, but it may be used for computations such as nonspecific gain control⁴⁰ instead of feature sharpening.⁴¹

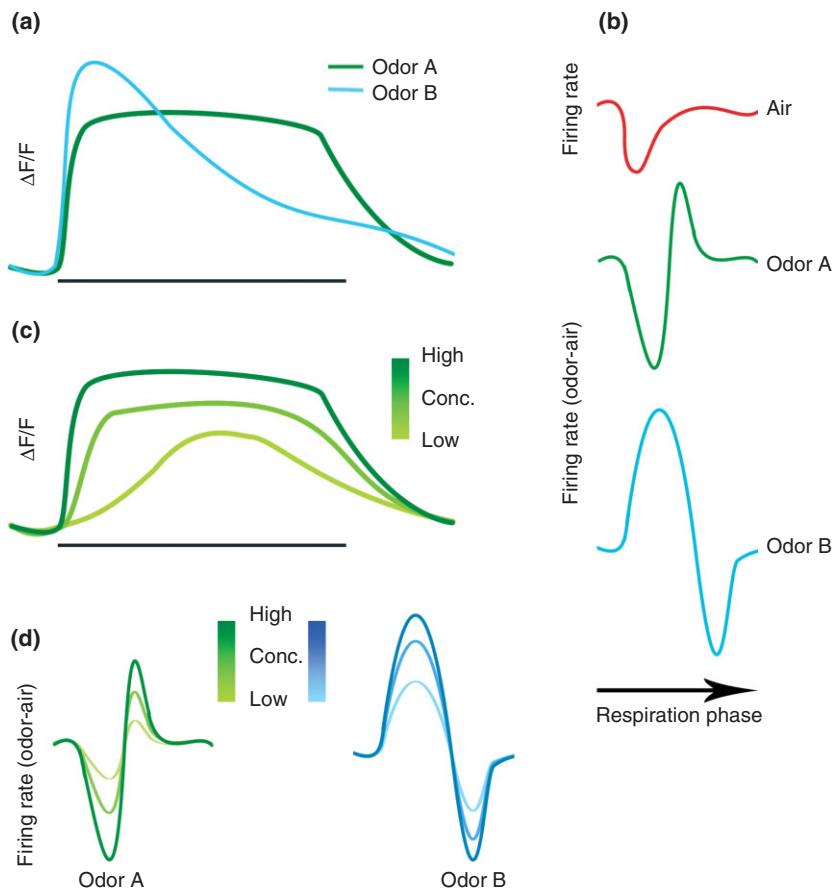


FIGURE 3 | Temporal properties of glomerular and M/T cell responses. (a) The same glomerulus can respond differently to different odors (blue and green) (b) A mitral cell responds to air alone with some respiration tuning patterns and the same M/T cell can respond with different respiration tuning patterns for different odors. (c) Increasing the odor concentration can change glomerular responses by decreasing latency and increasing amplitude of responses. (d) M/T cells respond to increases in odor concentration by increasing only the amplitude of the respiration tuning curve after subtracting the air tuning. Black horizontal bars represent 5-s odor stimuli. ((a) and (c) adapted with permission from Ref 53. Copyright 2004 PNAS. (b) and (d) adapted with permission from Ref 57. Copyright 2008 Neuron).

TEMPORAL REPRESENTATIONS OF ODOR IDENTITY AND INTENSITY

We now turn to aspects of temporal coding of odor features. Though there are many studies of local field potentials in the OB,^{42,43} we shall only discuss temporal studies of glomerular responses and studies which have recorded spiking of individual neurons. We also do not discuss the vast literature on temporal coding in insects and zebra fish but instead direct the reader to the following reviews.^{2,44}

One key observation is that rodents can perform odor-based tasks in only a single sniff. This implies that natural odor processing can be complete in under 150 ms.^{45–48} Most anesthetized studies fail to resolve events on these timescales, and this is a concern in interpreting their findings. The details of the differences between anesthetized and awake temporal dynamics are only partially understood⁴⁹ and will be valuable for a better understanding of coding in these regions.

Glomerular layer

High-temporal resolution VSD recordings were first carried out in the salamander.¹⁹ The earliest studies in

rodents also used VSDs.^{18,50} Later, calcium dyes were used to image these dynamics in awake animals.⁵¹ These studies showed that spatiotemporal patterns emerge on the timescale of tens of milliseconds, and that there is a variety of temporal properties in the glomerular responses to different odors. These include differences across glomeruli in modulation of latency, rise time, and modulation by sniffing across different stimuli. The effect of increasing concentration is to decrease the rise times and latency in anesthetized rodents,¹⁸ and it has a modest effect in awake rats.⁵² Not surprisingly, in all studies with sufficient temporal resolution, glomerular activity was found to be coupled to the respiratory rhythm.^{18,51,52}

Heterogeneity of temporal properties is not the same as the presence of a temporal code. These temporal properties should vary systematically, different for different odors and concentrations. A study in anesthetized mice which observed responses of single glomeruli to different odors at varying concentrations found that an individual glomerulus responds with different temporal properties across stimuli (Figure 3).⁵³ It thus appears that there are indeed indications of a temporal code in the glomerular layer.

M/T cell layer

Right from the early studies of spiking patterns of M/T cells in mammals,^{54,55} it has been recognized that these cells may use a temporal code. M/T cells respond to odors with a time varying and reproducible firing rate profile, which is usually patterned over the respiration cycle. Interestingly, the baseline response to air alone is also patterned at both glomerular^{18,52} and M/T cell level,^{34,56–58} and it is often this patterning over a respiration cycle, or ‘respiration tuning’, that changes on presentation of an odor, without necessarily a change in average firing rate (Figure 3).^{34,57,58} Furthermore, even at the population level, ensembles of M/T cells have been shown to contain information at multiple timescales.⁵⁸

Odor intensity has been observed to have a graded effect on mitral cell temporal activity.^{55,59} However, the natures of the changes reported have differed widely, from changing drastically⁵⁵ to changing modestly⁵⁹ to remaining largely stable across concentrations.⁶⁰ Some of these differences may be explained by the differences in preparations (tracheotomized versus freely breathing, and different anesthetics used), odor concentration regimes used, and the inherently problematic nature of analyzing amplitudes of a temporally patterned signal.⁵⁴ However, a unified model described below incorporates much of this variety of responses into a single explanation.⁵⁷

ODOR MIXTURES

Odor mixtures pose a strong test for theories of odor representation. In principle, the system must simultaneously encode multiple odor identities as well as the proportions in which odor components are present. Many natural olfaction tasks are based on analyzing mixtures in a certain context. Two broad types of mixture processing tasks exist. First, *odor segmentation*, i.e., breaking a complex odorant into its components, or determining that a specific odor is present in a mixture. Second, *odor synthesis*, i.e., grouping different odors which occur together into a unitary percept. Another aspect of the same property is performing *odor generalization* or pattern completion, i.e., classifying two similar odor mixtures as the same despite a difference. To address these questions, one must ask: what is the representation of an odor mixture in relation to the representation of its components? Surprisingly, both at a spatial and at a temporal level, there is evidence that the representation of a mixture in the OB is simply the sum of its components.

At the glomerular level, this has been analyzed by intrinsic imaging studies in mice^{10,61} and calcium

imaging in zebra fish.⁶² These studies have shown that both simple binary mixtures and complex natural mixtures are represented as a topographic sum of the responses of the individual components. Thus, it appears that at the level of input to the OB, there are no significant mixture interactions. While this is suggestive, there are as yet no direct studies on topographical summation of mixtures at the M/T level. This would require massively parallel recordings from the M/T layer⁶³ or calcium imaging over large areas.³⁸

The temporal aspects of mixture processing have been studied primarily at the M/T cell level. A number of studies have addressed the question in animals which do not have respiration-based odor sampling.^{62,64,65} These studies either do not find any way to predict the response of a mixture given the responses of the components, or find one or the other component dominating, or simply find cases where components and mixture all have the same responses. We are aware of two studies which address the question in the context of respiration tuning.^{57,66} In the study by Giraudet et al.,⁶⁶ M/T responses to a mixture mostly appeared either identical to one of the two components or were unpredictable. However, Khan et al.⁵⁷ provided evidence for a model that can predict the details of a response to a mixture from the responses to the components.

In this model, an odor response is obtained if one takes the respiration tuning curve (firing rate profile over a respiration cycle) of a cell in response to pure air and subtracts it from the same curve in response to an odor. The resulting tuning curves seem to be the key property representing odor identity. They scale in amplitude with odor concentration. Furthermore, if the tuning curves for two component odors are determined, the response to the mixture is predicted by a concentration-weighted sum of the two odor tuning curves (Figure 4).

This is a phenomenological model and not a mechanistic one. There are many important mechanistic models of the vertebrate OB and insect antennal lobe^{67–73} (for a review see Ref 74). It will be interesting to see how these models incorporate findings from recent studies such as this and others regarding odor mixtures.^{64,75}

CONCLUSION

Unlike vision, the field of olfaction has struggled with defining the representation of this complex, multidimensional sensory modality even at the receptor and first neuronal processing stages. We suggest that the outlines of a general olfactory representation model are now emerging and are surprisingly simple. We propose that odor representations in the bulb are

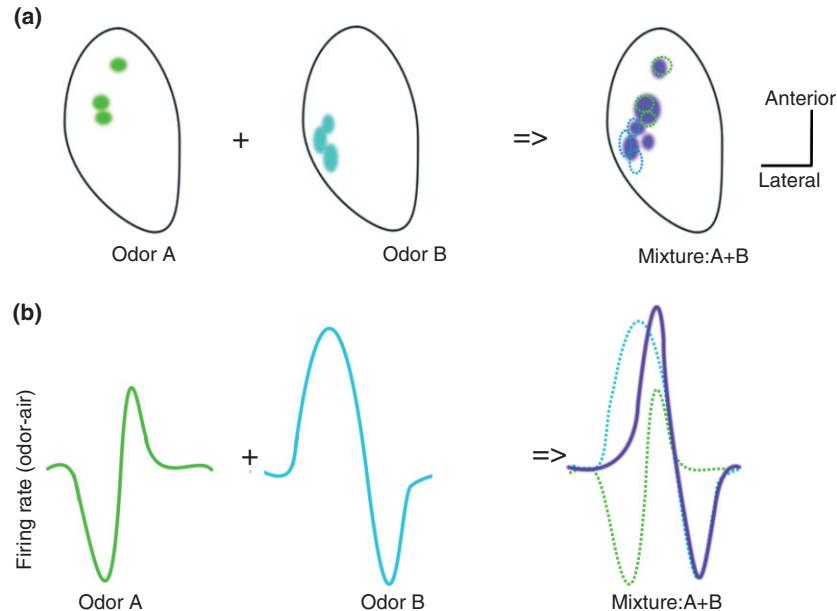


FIGURE 4 | Representation of mixtures.

(a) Schematics of dorsal surface views of glomerular activity for odor A, odor B, and for a mixture of A and B. At the level of glomerular spatial maps, the representation of a mixture is very close to the topographic sum of the representations of the components. (b) M/T cell respiration tuning patterns for two odors sum linearly to give the response of the mixture. The mixture response is shown overlaid with the component responses on the right. ((b) adapted with permission from Ref 57. Copyright 2008 Neuron).

spatially distributed in the output layer, are temporally tuned with respect to respiration, and sum and scale linearly. Such a model raises several interesting further questions for the field. First, what is the exact mechanism of creating these odor representations in the OB? This mechanism should be able to account for the above mentioned effects of changing concentration and mixtures. Second, how might these properties of odor representations feed into later stages of olfactory processing and possibly the higher order computational tasks of stimulus synthesis and segmentation?⁷⁶ Third, how might this linear code work with the issues of receptor turnover and stimulus variability? Fourth, if recordings are done from

large numbers of widely distributed individual cells, will there be patterns which emerge across cells, which provide a further level of encoding?

In this review, we have taken a strongly model-driven viewpoint of representation: can one quantitatively and concisely map odorant stimuli into activity patterns in the bulb? We argue that many lines of study converge to suggest that such a representation does exist. We assert that a predictive, mechanistic, and quantitative model of olfactory coding will be of great importance in providing a conceptual framework for early olfactory processing and will strengthen the hypotheses one can make about olfactory processing through higher centers.

REFERENCES

1. Kauer JS, White J. Imaging and coding in the olfactory system. *Annu Rev Neurosci* 2001, 24:963–979.
2. Laurent G. Olfactory network dynamics and the coding of multidimensional signals. *Nat Rev Neurosci* 2002, 3:884–895.
3. Mombaerts P, Wang F, Dulac C, Chao SK, Nemes A, et al. Visualizing an olfactory sensory map. *Cell* 1996, 87:675–686.
4. Araneda RC, Kini AD, Firestein S. The molecular receptive range of an odorant receptor. *Nat Neurosci* 2000, 3:1248–1255.
5. Levetau J, MacLeod P. Olfactory discrimination in the rabbit olfactory glomerulus. *Science* 1966, 153:175–176.
6. Jourdan F. Spatial dimension in olfactory coding: a representation of the 2-deoxyglucose patterns of glomerular labeling in the olfactory bulb. *Brain Res* 1982, 240:341–344.
7. Lancet D, Greer CA, Kauer JS, Shepherd GM. Mapping of odor-related neuronal activity in the olfactory bulb by high-resolution 2-deoxyglucose autoradiography. *Proc Natl Acad Sci U S A* 1982, 79:670–674.
8. Sharp FR, Kauer JS, Shepherd GM. Local sites of activity-related glucose metabolism in rat olfactory bulb during olfactory stimulation. *Brain Res* 1975, 98:596–600.
9. Stewart WB, Kauer JS, Shepherd GM. Functional organization of rat olfactory bulb analysed by the

- 2-deoxyglucose method. *J Comp Neurol* 1979, 185:715–734.
10. Belluscio L, Katz LC. Symmetry, stereotypy, and topography of odorant representations in mouse olfactory bulb. *J Neurosci* 2001, 21:2113–2122.
 11. Meister M, Bonhoeffer T. Tuning and topography in an odor map on the rat olfactory bulb. *J Neurosci* 2001, 21:1351–1360.
 12. Mori K, Takahashi YK, Igarashi KM, Yamaguchi M. Maps of odorant molecular features in the Mammalian olfactory bulb. *Physiol Rev* 2006, 86:409–433.
 13. Rubin BD, Katz LC. Optical imaging of odorant representations in the mammalian olfactory bulb. *Neuron* 1999, 23:499–511.
 14. Soucy ER, Albeanu DF, Fantana AL, Murthy VN, Meister M. Precision and diversity in an odor map on the olfactory bulb. *Nat Neurosci* 2009, 12:210–220.
 15. Friedrich RW, Korschning SI. Combinatorial and chemotopic odorant coding in the zebrafish olfactory bulb visualized by optical imaging. *Neuron* 1997, 18:737–752.
 16. Wachowiak M, Cohen LB. Representation of odorants by receptor neuron input to the mouse olfactory bulb. *Neuron* 2001, 32:723–735.
 17. Yang X, Renken R, Hyder F, Siddeek M, Greer CA, et al. Dynamic mapping at the laminar level of odor-elicited responses in rat olfactory bulb by functional MRI. *Proc Natl Acad Sci U S A* 1998, 95:7715–7720.
 18. Spors H, Grinvald A. Spatio-temporal dynamics of odor representations in the mammalian olfactory bulb. *Neuron* 2002, 34:301–315.
 19. Kauer JS. Real-time imaging of evoked activity in local circuits of the salamander olfactory bulb. *Nature* 1988, 331:166–168.
 20. Sallaz M, Jourdan F. C-fos expression and 2-deoxyglucose uptake in the olfactory bulb of odour-stimulated awake rats. *Neuroreport* 1993, 4:55–58.
 21. Guthrie KM, Anderson AJ, Leon M, Gall C. Odor-induced increases in c-fos mRNA expression reveal an anatomical “unit” for odor processing in olfactory bulb. *Proc Natl Acad Sci U S A* 1993, 90:3329–3333.
 22. Baba K, Ikeda M, Houtani T, Nakagawa H, Ueyama T, et al. Odor exposure reveals non-uniform expression profiles of c-Jun protein in rat olfactory bulb neurons. *Brain Res* 1997, 774:142–148.
 23. Mirich JM, Illig KR, Brunjes PC. Experience-dependent activation of extracellular signal-related kinase (ERK) in the olfactory bulb. *J Comp Neurol* 2004, 479:234–241.
 24. Bozza T, McGann JP, Mombaerts P, Wachowiak M. In vivo imaging of neuronal activity by targeted expression of a genetically encoded probe in the mouse. *Neuron* 2004, 42:9–21.
 25. Fried HU, Fuss SH, Korschning SI. Selective imaging of presynaptic activity in the mouse olfactory bulb shows concentration and structure dependence of odor responses in identified glomeruli. *Proc Natl Acad Sci U S A* 2002, 99:3222–3227.
 26. Laing DG, Legha PK, Jinks AL, Hutchinson I. Relationship between molecular structure, concentration and odor qualities of oxygenated aliphatic molecules. *Chem Senses* 2003, 28:57–69.
 27. Uchida N, Mainen ZF. Odor concentration invariance by chemical ratio coding. *Front Syst Neurosci* 2007, 1:3.
 28. Cleland TA, Johnson BA, Leon M, Linster C. Relational representation in the olfactory system. *Proc Natl Acad Sci U S A* 2007, 104:1953–1958.
 29. Asahina K, Louis M, Piccinotti S, Vosshall LB. A circuit supporting concentration-invariant odor perception in *Drosophila*. *J Biol* 2009, 8(1):9.
 30. Johnson BA, Leon M. Chemotopic odorant coding in a mammalian olfactory system. *J Comp Neurol* 2007, 503(1):1–34.
 31. Zou DJ, Chesler A, Firestein S. How the olfactory bulb got its glomeruli: a just so story?. *Nat Rev Neurosci* 2009, 10:611–618.
 32. Willhite DC, Nguyen KT, Masurkar AV, Greer CA, Shepherd GM, et al. Viral tracing identifies distributed columnar organization in the olfactory bulb. *Proc Natl Acad Sci U S A* 2006, 103:12592–12597.
 33. Schoppa NE, Westbrook GL. Glomerulus-specific synchronization of mitral cells in the olfactory bulb. *Neuron* 2001, 31:639–651.
 34. Bhalla US, Bower JM. Multiday recordings from olfactory bulb neurons in awake freely moving rats: spatially and temporally organized variability in odorant response properties. *J Comput Neurosci* 1997, 4:221–256.
 35. Buonviso N, Chaput MA. Response similarity to odors in olfactory bulb output cells presumed to be connected to the same glomerulus: electrophysiological study using simultaneous single-unit recordings. *J Neurophysiol* 1990, 63:447–454.
 36. Johnson BA, Woo CC, Hingco EE, Pham KL, Leon M. Multidimensional chemotopic responses to *n*-aliphatic acid odorants in the rat olfactory bulb. *J Comp Neurol* 1999, 409:529–548.
 37. Egana JI, Aylwin ML, Maldonado PE. Odor response properties of neighboring mitral/tufted cells in the rat olfactory bulb. *Neuroscience* 2005, 134:1069–1080.
 38. Stettler DD, Axel R. Representations of odor in the piriform cortex. *Neuron* 2009, 63:854–864.
 39. Wilson RI, Mainen ZF. Early events in olfactory processing. *Annu Rev Neurosci* 2006, 29:163–201.
 40. Poo M, Isaacson JS. Odor representations in olfactory cortex: “sparse” coding, global inhibition, and oscillations. *Neuron* 2009, 62:850–861.
 41. Yokoi M, Mori K, Nakanishi S. Refinement of odor molecule tuning by dendrodendritic synaptic inhibition

- in the olfactory bulb. *Proc Natl Acad Sci U S A* 1995, 92:3371–3375.
42. Adrian ED. Olfactory reactions in the brain of the hedgehog. *J Physiol* 1942, 100:459–473.
 43. Neville KR, Haberly LB. Beta and gamma oscillations in the olfactory system of the urethane-anesthetized rat. *J Neurophysiol* 2003, 90:3921–3930.
 44. Wilson RI. Neural and behavioral mechanisms of olfactory perception. *Curr Opin Neurobiol* 2008, 18:408–412.
 45. Uchida N, Mainen ZF. Speed and accuracy of olfactory discrimination in the rat. *Nat Neurosci* 2003, 6:1224–1229.
 46. Wesson DW, Carey RM, Verhagen JV, Wachowiak M. Rapid encoding and perception of novel odors in the rat. *PLoS Biol* 2008, 6:e82.
 47. Abraham NM, Spors H, Carleton A, Margrie TW, Kuner T, et al. Maintaining accuracy at the expense of speed: stimulus similarity defines odor discrimination time in mice. *Neuron* 2004, 44:865–876.
 48. Rajan R, Clement JP, Bhalla US. Rats smell in stereo. *Science* 2006, 311:666–670.
 49. Rinberg D, Koulakov A, Gelperin A. Sparse odor coding in awake behaving mice. *J Neurosci* 2006, 26:8857–8865.
 50. Spors H, Wachowiak M, Cohen LB, Friedrich RW. Temporal dynamics and latency patterns of receptor neuron input to the olfactory bulb. *J Neurosci* 2006, 26:1247–1259.
 51. Verhagen JV, Wesson DW, Netoff TI, White JA, Wachowiak M. Sniffing controls an adaptive filter of sensory input to the olfactory bulb. *Nat Neurosci* 2007, 10:631–639.
 52. Carey RM, Verhagen JV, Wesson DW, Pirez N, Wachowiak M. Temporal structure of receptor neuron input to the olfactory bulb imaged in behaving rats. *J Neurophysiol* 2009, 101:1073–1088.
 53. Wachowiak M, Denk W, Friedrich RW. Functional organization of sensory input to the olfactory bulb glomerulus analyzed by two-photon calcium imaging. *Proc Natl Acad Sci U S A* 2004, 101:9097–9102.
 54. Meredith M. Patterned response to odor in mammalian olfactory bulb: the influence of intensity. *J Neurophysiol* 1986, 56:572–597.
 55. Harrison TA, Scott JW. Olfactory bulb responses to odor stimulation: analysis of response pattern and intensity relationships. *J Neurophysiol* 1986, 56:1571–1589.
 56. Macrides F, Chorover SL. Olfactory bulb units: activity correlated with inhalation cycles and odor quality. *Science* 1972, 175:84–87.
 57. Khan AG, Thattai M, Bhalla US. Odor representations in the rat olfactory bulb change smoothly with morphing stimuli. *Neuron* 2008, 57:571–585.
 58. Bathellier B, Buhl DL, Accolla R, Carleton A. Dynamic ensemble odor coding in the mammalian olfactory bulb: sensory information at different timescales. *Neuron* 2008, 57:586–598.
 59. Cang J, Isaacson JS. In vivo whole-cell recording of odor-evoked synaptic transmission in the rat olfactory bulb. *J Neurosci* 2003, 23:4108–4116.
 60. Chalansonnet M, Chaput MA. Olfactory bulb output cell temporal response patterns to increasing odor concentrations in freely breathing rats. *Chem Senses* 1998, 23:1–9.
 61. Lin da Y, Shea SD, Katz LC. Representation of natural stimuli in the rodent main olfactory bulb. *Neuron* 2006, 50:937–949.
 62. Tabor R, Yaksi E, Weislogel JM, Friedrich RW. Processing of odor mixtures in the zebrafish olfactory bulb. *J Neurosci* 2004, 24:6611–6620.
 63. Lehmkuhle MJ, Normann RA, Maynard EM. High-resolution analysis of the spatiotemporal activity patterns in rat olfactory bulb evoked by enantiomer odors. *Chem Senses* 2003, 28:499–508.
 64. Broome BM, Jayaraman V, Laurent G. Encoding and decoding of overlapping odor sequences. *Neuron* 2006, 51:467–482.
 65. Kang J, Caprio J. Electrophysiological responses of single olfactory bulb neurons to binary mixtures of amino acids in the channel catfish, *Ictalurus punctatus*. *J Neurophysiol* 1995, 74:1435–1443.
 66. Giraudet P, Berthommier F, Chaput M. Mitral cell temporal response patterns evoked by odor mixtures in the rat olfactory bulb. *J Neurophysiol* 2002, 88:829–838.
 67. Brody CD, Hopfield JJ. Simple networks for spike-timing-based computation, with application to olfactory processing. *Neuron* 2003, 37:843–852.
 68. Bazhenov M, Stopfer M, Rabinovich M, Abarbanel HD, Sejnowski TJ, et al. Model of cellular and network mechanisms for odor-evoked temporal patterning in the locust antennal lobe. *Neuron* 2001, 30:569–581.
 69. Davison AP, Feng J, Brown D. Dendrodendritic inhibition and simulated odor responses in a detailed olfactory bulb network model. *J Neurophysiol* 2003, 90:1921–1935.
 70. Hendin O, Horn D, Tsodyks MV. Associative memory and segmentation in an oscillatory neural model of the olfactory bulb. *J Comput Neurosci* 1998, 5:157–169.
 71. Linster C, Hasselmo M. Modulation of inhibition in a model of olfactory bulb reduces overlap in the neural representation of olfactory stimuli. *Behav Brain Res* 1997, 84:117–127.
 72. Rall W, Shepherd GM. Theoretical reconstruction of field potentials and dendrodendritic synaptic interactions in olfactory bulb. *J Neurophysiol* 1968, 31:884–915.

73. White J, Hamilton KA, Neff SR, Kauer JS. Emergent properties of odor information coding in a representational model of the salamander olfactory bulb. *J Neurosci* 1992, 12:1772–1780.
74. Cleland TA, Linster C. Computation in the olfactory system. *Chem Senses* 2005, 30:801–813.
75. Carlsson MA, Chong KY, Daniels W, Hansson BS, Pearce TC. Component information is preserved in glomerular responses to binary odor mixtures in the moth *Spodoptera littoralis*. *Chem Senses* 2007, 32:433–443.
76. Haberly LB. Parallel-distributed processing in olfactory cortex: new insights from morphological and physiological analysis of neuronal circuitry. *Chem Senses* 2001, 26:551–576.