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The olfactory glomerulus: A cortical module with specific functions

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Abstract

The axons of many olfactory receptor cells converge on an individual glomerulus in the olfactory bulb, where they make contacts with the distal dendrites of mitral and tufted cells. Each glomerulus is targeted by olfactory receptor neurons expressing a single type of olfactory receptor protein. The glomerulus provides a unique model in which the function of a cortical module can be unambiguously established. Here we review the increasing evidence that a key functional operation of the glomerulus is to act as a signal-to-noise enhancing device in the processing of sensory input and that this function is critical across vertebrate and invertebrate species for the ability to detect specific odor stimuli within "noisy" odor environments and to carry out discriminations between odor molecules that are structurally closely related.

Introduction

In this post-genomic era great strides are being made in analyzing the structural, molecular, and physiological properties of the olfactory pathway, in both invertebrates and vertebrates. It is becoming apparent that many of the properties are conserved throughout phylogeny (Hildebrand & Shepherd, 1997). Among these, none is more characteristic and fundamental than the olfactory glomerulus.

The classical histologists established that the glomerulus receives converging axons from many olfactory receptor cells, where they make contacts with the distal dendrites of neurons in the olfactory bulb (Cajal, 1911). In different species a glomerulus varies in size from a diameter of a few tens of microns up to 200 μm or more. In some species it is indistinct, particularly in locusts, fish and some amphibians, in others it is sharply demarcated by the cell bodies of surrounding neurons. The equivalence of these modules in invertebrates and vertebrates was suggested by Hanström (1928) and firmly established around 1980 (Boeckh *et al*., 1977; Chambille *et al*., 1980; Masson & Mustaparta, 1990; Matsumoto & Hildebrand, 1981; Shepherd, 1981). In its modular multicellular character the glomerulus is similar to barrels in rodent somatosensory cortex (Woolsey & Van der Loos, 1970), cortical columns (Hubel & Wiesel, 1962; Mountcastle, 1957), and striasomes (Goldman & Nauta, 1977). Anatomically, it is the most distinct multicellular modular unit in a cortical structure in the brain.

What is the functional significance of this anatomical unit, for olfactory processing and as a model for cortical modules? With regard to cortical modules, this is not a trivial question. Horton & Adams (2005) have recently carried out an exhaustive review of nearly 50 years of literature on the cortical column since the pioneering report of Mountcastle (1957). They conclude that there is no evidence that cortical columns and cortical barrels have any fundamental function to contribute to cortical processing. The olfactory glomerulus could therefore provide a unique model in which the function of a cortical module can be unambiguously established. Like the cortical column, a glomerular unit defines a population of functionally-related neurons that extends across multiple layers. Unlike the cortical barrel, its function is not in relation to a defined anatomical structure but rather in relation to the encoding of complex sensory stimuli.

Current evidence in mammals suggests that each glomerulus is targeted by olfactory receptor neurons (ORNs) expressing a single type of olfactory receptor (OR) protein (Ressler *et al*., 1994; Vassar *et al*., 1994; reviewed in Mombaerts, 2004). But what are the functional properties that are involved in processing this information? Physiological analysis has been difficult

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Table 1. Glomerular properties contributing to signal-to-noise enhancement

Inputs
Massive convergence of sensory input to a glomerulus.
All sensory input to a glomerulus is unimodal.
Ephaptic synchronization of olfactory receptor cell axons.
Input synapses
Monosynaptic connections to mitral/tufted/periglomerular cell dendrites.
AMPA/kainate and NMDA EPSP components (see text).
Dendrodendritic synapses
Autoreceptors for spillover glutamate.
Synchronization by spillover glutamate.
Synchronization by mitral-to-mitral cell gap junctions between glomerular tufts.
Synchronization by periglomerular cell axonal and dendrodendritic inhibition.
Disinhibitory dendrodendritic microcircuits.
Intrinsic properties
Active properties of M/T dendrites.
All-or-nothing response of glomerulus at threshold.
Modulation by centrifugal systems and neuropeptides.

because glomeruli are meeting places of axon terminals and dendritic branches, far from the cell bodies of most of the participating neurons. However, evidence has accumulated over a number of years that suggest several hypotheses.

For the purposes of this review, we will focus on the hypothesis that one of the key functional operations of the glomerulus is to act as a signal-to-noise enhancing device in the processing of sensory input. We will see that various lines of evidence support this role, which appears to be critical, across all species, for the ability to detect specific odor stimuli within "noisy" odor environments and to carry out discriminations between odor molecules that are structurally closely related.

Some of the properties that have been identified that potentially contribute to signal-to-noise enhancement are summarized in Table 1. It is convenient to consider the properties in relation first to the input, then to intrinsic synaptic processing, and finally to the output.

Massive convergence of unimodal sensory input

Quantitative characterization of the sensory input to a glomerulus began in the laboratory of Wilfrid Edward Le Gros Clark, chair of anatomy at Oxford (Le Gros Clark, 1957). Le Gros Clark was one of the great anatomists of the mid-twentieth century who, among his many contributions to the anatomy of the brain, was one of the triumvirate of scientists who exposed the Piltdown Man forgery in the 1950s. His anatomical studies of the regional topographic relation between the olfactory epithelium and the olfactory bulb (Le Gros Clark, 1957) complemented Adrian's physiological evidence for spatial representation of odors in the olfactory bulb during the 1950s (Adrian, 1950).

Allison and Warwick, in Le Gros Clark's laboratory, carried out the first quantitative studies of the elements in the olfactory pathway. From these studies, as summarized in Allison (1952), came the estimates of 50,000,000 olfactory receptor cells on one side in the rabbit, 2,000 olfactory glomeruli, and 24 mitral cells and 54 tufted cells per glomerulus. In the ensuing decades these numbers have been tested at various times in different vertebrate species (see Meisami, 1991). Because there is surprising variation in the estimates, specific numbers for the elements must be treated with caution.

An important constraint arising from studies of olfactory receptor genes is the evidence that the subset of genes expressing a given receptor projects to two glomeruli, implying that the number of glomeruli should be twice the number of functional genes (Ressler *et al*., 1994; Vassar *et al*., 1994). However, there are exceptions to this rule (Hoppe *et al*., 2003). In different insect species, the numbers of glomeruli are smaller (50–300), as are the numbers of olfactory receptor cells (50,000–300,000) (Rospars & Chambille, 1989).

One can conclude that the convergence ratio of ORNs onto glomeruli is overall in the range of 5,000–10,000 : 1 in most vertebrate species. This is a very high value in comparison with convergence ratios of other systems in the brain (summarized in Shepherd, 1979). Although the ratios are lower, perhaps 500–1,000 : 1 in the insect, this is also still a large number. It appears that a high overall convergence ratio of sensory input onto a receiving module (the glomerulus) is a highly conserved feature across all olfactory systems. Our task is to identify what essential operation this feature performs.

Initially there was little insight into what implications this high ratio would have for the kind of information that is processed by a single glomerulus. Le Gros Clark (1957) contributed a thoughtful review of the possibilities but could not distinguish between the possibilities that glomeruli are highly specific or nonspecific.

A personal note by one of us (GMS). I began my electrophysiological studies of the olfactory bulb as a model system for cortical processing in the laboratory of Charles Phillips in Oxford. Charles recommended that we engage Tom Powell, one of Le Gros Clark's faculty in the anatomy department, to collaborate on the anatomical localization of our electrode recordings. Powell had just returned from a sabbatical with Mountcastle where they carried out their classical study correlating the functional with the structural column (Powell & Mountcastle, 1959). Thus I soaked up the traditions of Le Gros Clark's work on the topographical relations of the peripheral olfactory pathway and the quantitative studies of his students along with the earliest concepts of the cortical column. To stimulate the olfactory nerves and record from bulbar cells required testing Le Gros Clark's anatomical evidence for a topographical relation. I was able to demonstrate this by placing a stimulating electrode on the nerve bundles just under the

nasal bone, at a site I called the "dorsal recess'' of the nasal cavity, between the top of the nasal septum and the lateral nasal wall. From there I found that I was able to obtain sharply "on-beam'' responses of mitral cells, periglomerular cells, tufted cells and granule cells to single olfactory nerve (ON) volleys (Shepherd, 1963), reassuring physiological evidence of a topographical relation between that nerve bundle and the recording site in the dorsal olfactory bulb. This is the region of Zone 1 of the olfactory epithelium and its projection to the dorsal olfactory bulb, in today's vocabulary (Ressler *et al*., 1993).

We now know that several bundles carry axons from members of the subset of ORNs expressing a given OR and converge on their target glomeruli. To the extent that this "one cell—one receptor—one glomerulus'' rule holds, it implies that all of the axons converging on the target glomerulus are carrying the same information about the identity of the stimulating molecule. This 100% redundancy in the input is highly unusual in the nervous system. According to signal theory, redundancy is a waste of information channels (see Riecke *et al*., 1997). However, there can be many functions of redundant input channels. One is to protect against loss of channels due to loss of olfactory receptor neurons from noxious agents in the inhaled air. A second one is to increase the probability of activating the many target neurons connected to the glomerulus. A third one is to increase the opportunity for synchronization across numbers of fibers through electrical currents flowing through neighboring axon membranes, called ephaptic interactions; these will increase the simultaneous actions in the glomerulus on the target neurons.

Many of these functions amplify the effect of an input from individual axons to many acting in concert. An analogy is the grouping of muscle cells into a whole muscle that amplifies the weak forces generated by the individual sliding filaments into the large forces of the whole muscle. In the olfactory pathway, the glomerulus allows multiple unimodal inputs to be concentrated on one subset of bulbar neurons. This wiring feature ensures that this subset of bulbar neurons is as sensitive as possible to threshold responses of this subset of ORNs. It also helps those bulbar neurons to respond to increasing odor concentrations in a faithful manner. Some of these properties were demonstrated by Van Drongelen & Døving (1978), who recorded ORN responses to increasing concentrations of odor molecules and inferred that as concentration increases more ORNs are activated.

Properties of input synapses

Within the glomerulus, a key question is the direct synaptic targets of the afferent terminals. Initially there was no evidence on this point. In my (GMS) first physiological recordings of the spike responses of bulbar neurons to a single ON volley, the relatively long latencies due to the slow conduction times and the slight changes in latency with differing stimulus strength meant that one could not apply the usual criteria used in the spinal motoneuron to discriminate between mono- and polysynaptic activation. I therefore had to leave this connection unspecified in the first wiring diagram for the olfactory bulb circuits (Shepherd, 1963). However, the electron microscopic studies of Reese and Brightman (1970), Pinching and Powell (1971) and White (1972) gave clear evidence that the ON terminals in most mammalian species make monosynaptic connections onto the mitral and tufted as well as, in most species, the periglomerular (PG) cell dendrites in the glomerulus. As with the Ia inputs to motoneurons (Capaday & Stein, 1987), this confers maximum specificity and potency on these synapses in activating their dendritic targets. Recent electron microscope (EM) studies have revealed a rich diversity of PG cells in terms of biochemical markers and recipients of mono and polysynaptic afferent input (Kosaka & Kosaka, 2005).

The next question to be answered was the nature of the neurotransmitter at these synapses. Glutamatergic excitatory postsynaptic potentials (EPSPs) in bulbar dendrites, through both alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA)/kainate and N-methyl d-aspartate (NMDA) receptors, was first shown in the isolated turtle olfactory bulb preparation by Berkowicz *et al*. (1994) and by Shipley and colleagues (Ennis *et al*., 1996) and ourselves (Chen & Shepherd, 1997) in the rat olfactory bulb slice. The presence of both components in the response to glutamate means that this synaptic connection can mediate both rapid responses to input from the ORNs as well as slow large amplitude responses that can be large amplitude and reflect activity-dependent plasticity changes.

More recently, there has been increasing interest in the presynaptic modulation of the ON input. Evidence has been obtained for action of gamma-amino butyric acid (GABA) released from the PG cell dendrites back on the ON terminals (Aroniadou-Anderjaska *et al*., 2000), and for dopamine mediating presynaptic inhibition of the axon terminals (Ennis *et al*., 2001). One function of this presynaptic inhibition appears to be to extend the dynamic range of the post-synaptic bulbar neurons. Another one is likely to exert some feedback control over the very strong excitatory drive from the incoming axons, particularly as increasing odor concentrations drive these thousands of cells to higher firing frequencies.

Properties of dendrodendritic interactions within the glomerulus

A critical step forward in understanding the physiological operations within a glomerulus was the EM

evidence showing synapses between the dendrites that were themselves postsynaptic to the terminals of the incoming axons (Pinching & Powell, 1971; Reese & Brightman, 1970; White, 1972). Some dendrites were seen to make Type I (presumably excitatory) synapses onto dendrites that themselves make Type II (presumably inhibitory) synapses onto the dendrites making the Type I synapses. It was inferred that mitral/tufted (M/T) cell dendrites are excitatory onto PG cell dendrites, and PG cell dendrites are inhibitory onto M/T cell dendrites.

Attempts were made to demonstrate the physiological actions of these dendrodendritic synapses. The strategy was to record spike responses to paired, near-threshold ON volleys in dorsal recess nerve bundles, to test whether PG cells could suppress their own activation. This was in fact seen (Getchell & Shepherd, 1975a, b; Shepherd, 1971). In a typical recording, a cell that was just below threshold for responding to a conditioning volley gave a spike response to a second volley. It was suggested that the enhancement was due to the effects of a slow EPSP over the activation route through the afferent axon synapse onto a M/T cell dendrite and/or the dendrodendritic synapse from the M/T cell dendrite onto the PG cell dendrite. By contrast, when the cell responded with a spike to the first volley, there was typically suppression of the response to the second volley. The suppression was suggested to be due to the spike from the conditioning response back-propagating into the dendrites and increasing inhibitory transmitter release back onto the M/T cell dendrites. The recent evidence that GABA can act back onto the ON terminals (Aroniadou-Anderjaska *et al*., 2000) provides another possible site for this effect. The anatomical arrangement of the glomerulus ruled out a possible inhibitory feedback through the PG axons, because they are directed exclusively to neighboring glomeruli.

The fact that the M/T dendrites generate large-amplitude EPSPs, that are normally under strong inhibitory control, was shown by treating the isolated turtle olfactory bulb with the GABA-receptor blocker bicuculline. Under these conditions, the response of a mitral cell to an ON volley was converted from a brief depolarization to a large and prolonged plateau depolarization, giving rise to paroxysmal impulse discharges from the mitral cell (Nowycky *et al*., 1981). This indicates that the effect of a strong ON volley is to set up a large-amplitude and prolonged EPSP (presumably due to the NMDA component) in the distal dendritic tufts of the glomerulus of mitral and tufted cells (see also Chen & Shepherd, 1997). These experiments provide evidence for both strong excitatory and strong inhibitory synaptic actions controlling the excitability of the dendrites within the glomerulus.

Recently a new property has been revealed in the form of gap junctions. There is both electrophysiological (Schoppa & Westbrook, 2001) and EM (Kosaka & Kosaka, 2005; Kosaka *et al*., 2005) evidence for gap junctions between the dendrites of the participating cells. Mitral to mitral electrotonic junctions were demonstrated electrophysiologically by Schoppa and Westbrook (2001). These electrical connections tend to synchronize activity between the participating cells. This effect would therefore add to the synchronizing effect of ephaptic interactions between the incoming ON axons to enhance the co-incident responses of M/T cells to their unimodal inputs (Christie *et al*., 2005). This synchronizing effect may act on the slow EPSPs within the glomerular dendritic tufts, and/or on the rapid action potentials generated in the mitral/tufted cells. We will discuss further the effects of gap junctions in synchronizing action potentials in the next section.

Other functional properties of the distal dendritic tuft of M/T cells within the glomerulus are autoreceptors to and synchronization by spillover glutamate (Schoppa & Westbrook, 2001). Also contributing to the magnitude of the initial EPSP response is the possibility of disinhibitory effects between PG cells.

Intrinsic properties of mitral/tufted cell dendritic tufts

Until now we have focused on the synaptic properties that underlie glomerular function, in particular those involved in amplifying and synchronizing the responses of the bulbar neurons. We finally take up the active properties of the bulbar dendrites, and how they may contribute to amplifying the synaptic responses.

The generation of action potentials in the M/T cell primary dendrite was first analyzed in dual patch recordings by Chen *et al*. (1997) and simulated by compartmental modeling (Shen *et al*., 1999). At low levels of synaptic activation, the EPSPs are generated in the glomerular tuft and spread through the primary dendrite to activate action potentials first at the axon hillock, with back-propagation through the primary dendrite to the glomerular tuft, as in the classical model. At medium to high levels of synaptic activation, action potential initiation shifts toward the glomerulus, with forward propagation to the axon hillock and into the axon. This can be understood as being determined by the relations between the amount of local depolarization imposed by the EPSP in the glomerular tuft, and the density of Na^+-channels along the neuron, with a low to moderate density in the soma-dendritic compartment and a higher effective density in the initial segment. This means that when the local EPSP in the glomerulus is small, it spreads to the lowest threshold site in the axon hillock-initial segment; as it becomes larger, it is able to reach threshold for activating the lower-density Na^+-channels locally before reaching the higher-density channels.

Further experimental analysis of the active properties of the glomerular tuft is in progress.

Using Ca^{++}-imaging and two-photon microscopy, it is possible to map the invasion of a back-propagating action potential into successive orders of branching of the tuft (W. R. Chen & W. Xiong, in preparation). The fact that NMDA receptors and intrinsic Ca^{++} is involved in tuft activity suggests that the tuft is sensitive to activity-dependent changes reflecting the exposure of the animal to different types of odors.

Synchronization of the action potentials has been studied using realistic compartmental modeling of two mitral cells joined by gap junctions in their glomerular tufts (Migliore *et al*., 2005). One of the constraints on these realistic models was that they would reproduce the shift in action potential initiation site between soma and distal dendrite with increasing EPSP amplitude. The simulations were further able to reproduce the coupling and synchronization between the mitral cells shown experimentally. In the model the site of coupling had a large effect on the amplitude of the local EPSP within the glomerular tuft but was scarcely detectable at the soma due to the filtering effect of the cable properties of the primary dendrite. This may indicate that an important function of having the afferent input occur in the distal dendritic tuft in the glomerulus is to enable local processing to be carried out at these distal sites without having large effects on the integration at the soma.

An additional function of the long primary dendrite appeared when the primary dendrite was removed and the tuft was collapsed into the soma, making the mitral cell into a single summing node, as in a neural network simulation. Under these conditions, the afferent EPSP and electrical coupling occur in the same node where lateral inhibition through the secondary dendrites occurs. Also, the separate functions of the tuft and the lateral dendrites interfere with each other, and the cell cannot carry out its specific functions (Migliore *et al*., 2005). These results demonstrate the usefulness of the mitral cell as a model for analyzing cortical integration (Carlson *et al*., 2000; Shipley & Ennis, 1996). In cortical pyramidal neurons it is difficult to make the case for a critical function for inputs to distal dendrites, whereas in mitral/tufted cells the distal dendrites are clearly the only sites of specific afferent input. The fact that the initial processing of afferent input and the subsequent processing through lateral inhibition (Aungst *et al*., 2003; Urban & Sakmann, 2002) must take place in separate parts of the dendritic tree provides a strong example for the likelihood of a similar separation of functions in the apical and basal dendrites of cortical pyramidal neurons. Neural network modelers need to take these examples into account in developing more realistic simulations of how neurons actually carry out their operations.

In summary, physiologists studying the neocortex often assume that distal dendrites provide only weak background modulation of soma input-output activity. As has been pointed out here, the arrangement of the olfactory bulb, in which specific sensory input is targeted to the most distal dendritic compartment of the mitral and tufted cells, shows that this assumption cannot be sustained. The properties that boost the responses of the distal dendrites of the mitral/glomerular cells are the underlying properties that boost the overall glomerular responses.

All-or-nothing glomerular responses

Among the properties we have discussed thus far are several that amplify the responses received in a glomerulus from subsets of olfactory receptor neurons. This amplification can function over the range of concentrations of a stimulating odorous substance or odor object. To the extent that the amplification applies to the preferred stimulus for a given olfactory receptor, it can function to enhance that signal in relation to the background "noise" due to random activation of the receptor by any of the odorous substances for which the receptor might have some degree of affinity.

What about responses at or just above threshold for activating the receptors and the subsets that express them? In addition to these properties for graded amplification, what about the possibility that a glomerulus might be able to amplify a small input into an all-or-nothing response?

The first evidence for this property came from the classic study of Leveteau and MacLeod (1966). They inserted a bipolar electrode with tips approximately 200 μm apart, or about the distance across the glomerular layer. They moved this array steadily into the olfactory bulb as they stimulated the rat with an odor. No potential difference was recorded until the electrodes spanned the glomerular layer (as shown by later histological localization). At this depth, they frequently recorded large-amplitude slow potentials in response to the odor. Most interestingly, with repeated stimulation these potentials often were all-or-nothing spikes. The authors suggested that a glomerulus may represent a stimulating type of odor molecule by its all-or-nothing response during odor stimulation.

A second independent bit of evidence came from the early use of radiolabeled 2-deoxyglucose as an activity marker to reveal that odors are represented in the olfactory glomerular layer by differential activity patterns. At very low odor concentrations, it was typically the case that only one or two tiny foci, associated with one or a few glomeruli, were activated (Sharp *et al*., 1975; Stewart *et al*., 1979). It was notable, however, that even at threshold the foci were extremely dense; that is, threshold was characterized not by a small increase in the density of one or more glomeruli, but rather by intense foci, as if the associated glomerulus, even when activated at threshold, was activated to a very high degree. It was possible to hypothesize that this represented a

kind of "all-or-nothing'' response, akin to the type that Leveteau and MacLeod (1966) had observed with electrophysiological recordings. For this effect to be significant it is not necessary to suppose that the response is maximal, only that there is a non-linear amplification of the small input into a large response.

What might be the basis for this effect? The fact that M/T cell dendritic tufts support action-potential generation, either in the forward- or back-propagating mode, and that the tufts are in communication through gap junctions, suggests that as soon as a given M/T cell reaches threshold depolarization for action potential initiation it will tend to bring all the tufts toward threshold. To the extent that this happens, it will tend to bring into synchronous action all of the bulbar neurons, called a "glomerular unit'', connected to one glomerulus.

Signal to noise enhancement of a sensory map

The foregoing results indicate that the olfactory glomerulus possesses a set of properties that has the effect of boosting the input and the response, thereby increasing the signal-to-noise ratio in responding to sensory input. This does not rule out other equally important possible functions but serves to focus on the best documented physiological operation carried out by the glomerulus.

What is the functional context within which this specific operation is carried out? Here also in the olfactory bulb, this question can be answered with some clarity. The context is that odor stimulation sets up differential activation of different olfactory receptors and their olfactory neuron subsets, which is transferred to the olfactory bulb as differential activation of different olfactory glomeruli. The many studies of odor mapping are beyond the scope of this review; here we focus only on the consensus (see Xu *et al*., 2000) that odor stimulation produces a spatial pattern, called variously an "odor map" or "odor image". Within this image, a given glomerulus contributes a level of activation that is driven initially by the relative affinity of a given olfactory receptor for one or more moieties ("determinants'', "odotopes'') of the stimulating molecule(s), and reflects ultimately the contributions of the postsynaptic properties we have reviewed above.

Within this context, therefore, the function of the glomerulus is to enhance its particular determinant or set of determinants in order for them to be detected as signal against the background noise of the ambient air. Since an odor object activates many receptors and consequently many glomeruli, the odor image is distributed widely within the glomerular sheet, the activation of each glomerulus precisely reflecting the variable affinities of the different receptors for the different determinants of the many molecules making up the odor object. The precision of this distributed glomerular activity pattern for the specific kinds of odor molecules is seen clearly in the recent comprehensive maps of Mori and his associates (Igarashi & Mori, 2005; Takahashi *et al*., 2004).

A cortical module with a specific and universal function

Olfactory glomeruli have a number of physiological properties which may be assumed to subserve a range of operations on their input signals from the olfactory receptors. Among these operations, signal-to-noise enhancement may be postulated to be one of the most important. This property has its significance in relation to the role of each glomerulus in processing the information from a given olfactory receptor, reflecting its relative affinity for the molecules making up an odor object.

It is of interest to view these conclusions in the light of the argument of Horton and Adams (2005) that, while there is no denying that cortical columns and barrels can be demonstrated structurally, a specific function is still lacking. The results reviewed here suggest that the olfactory glomerulus provides a useful model that should be included for consideration. Here is the clearest anatomical module in a cortical structure. The fact that this cortical structure—the olfactory bulb—develops as an outpocketing of the frontal pole of the neocortex emphasizes its potential relevance to understanding cortical modular function (Leise, 1990). We have reviewed data that provide strong evidence for a general information-processing function of signal-to-noise enhancement in this module. In addition, we have placed this within the context of the specific sensory-processing function of representing the relative affinities of different olfactory receptors for their range of odor ligands.

An important factor in the review of Horton and Adams (2005) was that, although a function can be ascribed to a particular kind of cortical column or barrel in a given species, that function can be found in other species lacking such a column or barrel; therefore, the function is not specific for the structure. That argument has limited relevance to the olfactory glomerulus, which is present in nearly all vertebrates and invertebrates. It therefore appears to carry out a function or functions that are fundamental for the processing of the molecular information carried in odor stimulus molecules in most animal species.

In conclusion, it will be useful to include the olfactory glomerulus in future considerations of the functional significance of cortical modules.

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