

Olfactory object recognition, segmentation, adaptation, target seeking, and discrimination by the network of the olfactory bulb and cortex: computational model and experimental data

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Published in *Current Opinion in Behavioral Sciences*, Volume 11, Pages 30–39, 2016

Abstract:

Mammals are poor at individuating the separate components that comprise odor mixtures, but not when components enter environment serially and when there is top-down expectation. Li proposed in 1990 an odor segmentation mechanism using the centrifugal feedback from the olfactory cortex to the olfactory bulb. This feedback suppresses the bulbar responses to the ongoing and already recognized odors so that a subsequent addition of a foreground odor can be singled out for recognition. Additionally, the feedback can depend on context so as to, e.g., enhance sensitivity to a target odor or improve discrimination between similar odors. I review experimental data that have since emerged in relation to the computational predictions and implications, and suggest experiments to test the model further.

Highlights

- A proposal about the role of feedback from the olfactory cortex to the bulb.
- Feedback aids adaptation to background odors so a foreground odor can be segmented.
- Feedback could also serve to enhance sensitivity to target odors.
- Feedback could be context-dependent, and should be odor-specific.
- Neural and behavioral data in human and rodents are consistent with model predictions.

Introduction

The olfactory system contains mainly the odor receptors, olfactory bulb, and olfactory cortex. Each type of odor receptor neuron responds to many types of odor molecules. Hence, an odor object, which (e.g., the smell of a cat) can comprise many types of molecules in fixed proportions, activates a population response across types of receptor neurons, and the populations for different odor objects usually overlap substantially[1••, 2]. The mitral/tufted (M/T) cells in the olfactory bulb receive the receptor inputs via glomeruli, interact with the inhibitory granule cells, and project to the olfactory (mainly piriform) cortex. Their responses to odor are modulated by respiration, and additionally, they often exhibit coherent oscillations (typically in the gamma range) which emerge during inhalation and cease during exhalation. In this paper, we will refer to activity variations at the time scales of breathing or higher-frequency (typically gamma) oscillations as respiratory or high-frequency, respectively. The pattern of the oscillation amplitudes across the bulbar neurons is specific to the input odor[3•]. The cortex is a network of excitatory (pyramidal) cells and inhibitory interneurons, and the spatial range of the excitatory connections is much longer than that in the bulb, making it suitable for the function of associative recognition and memory for odors[4, 5, 6].

The bulbar neural oscillations can exist without the cortex, while the cortex relies on the oscillations in the bulb to respond with oscillations in the same frequency range[7]. Centrifugal feedback from the cortex to the bulb mostly targets the granule cells, and cooling the cortex increases the intensity of the bulbar oscillations[8•]. The olfactory cortex is reciprocally and extensively connected with some higher-order areas including prefrontal, amygdaloid, perirhinal and entorhinal cortices[9, 2]. If multiple objects are well mixed and presented simultaneously, humans and rodents typically enjoy a holistic perception from which it is difficult to identify individual object components[10•, 11••, 12].

So far, most computational models focus on the biophysics in the olfactory system, or study representations of odor information leading to odor detection or recognition. For example, there are models of the cellular biophysics in the bulb intended to explain local field potentials[13], of the way that representation of odor information is dynamically transformed from receptor responses to M/T activities[3•, 14••], of the relationship between neural representations of odor mixtures and odor components[15], of how inhibition in the bulbar circuit could make odor representation sparser[16], of how the timing of the M/T responses within a cycle of the neural oscillations[14••, 17••, 18], or within a sniff cycle[19], could code for odor identity, of how response properties of receptors predict sensitivities in odor detection and discrimination[17••, 20], of how the cortical circuit could learn, through synaptic plasticity, to recognize and form memories of odor identities from bulbar responses[4, 21, 5, 6, 22••], and of how centrifugal feedback on the granule cells might be useful for recognizing odors over multiple sniffs[21]. Using numerical simulations of a system of ordinary differential equations, Freeman[23•] stated that coupling the olfactory bulb, anterior olfactory nucleus (which receives bulbar outputs and sends feedback to glomeruli and granule cells in the bulb), and the olfactory cortex is sufficient to produce chaotic patterns of neural activities, including the respiratory and high-frequency neural oscillations associated with odor discrimination.

However, the most important computational tasks in olfaction must include odor segmentation, which is essential for odor recognition since environments often contain mixtures of odor objects. Li[24••] was the first to formulate the odor segmentation problem. Noting that independent odor objects typically do not enter environment simultaneously when forming mixtures, she proposed that centrifugal feedback to the granule cells can make bulbar responses adapt to the pre-existing background odors so as to single out a newly-arrived odor object for recognition. Subsequently, Hopfield proposed temporal decorrelation of input signals to extract odor components from mixtures[25], perhaps for insects which sample odors on a finer temporal scale than mammals with their coarse sniffing[26]. One may also infer limits on odor segmentation performance from glomerular properties[17••, 20].

Recent decades saw an abundance of new experimental data, some seemingly unrelated with each other, and it is instructive to organize and interpret them in a computational framework. This paper uses the framework in Li's model[24••] for this purpose since the model includes both the segmentation and recognition tasks, its proposed route of centrifugal control was also shown[24••] to allow context- or task-dependent behavior such as target seeking, and there is currently no other model that encompasses the experimental data reviewed here.

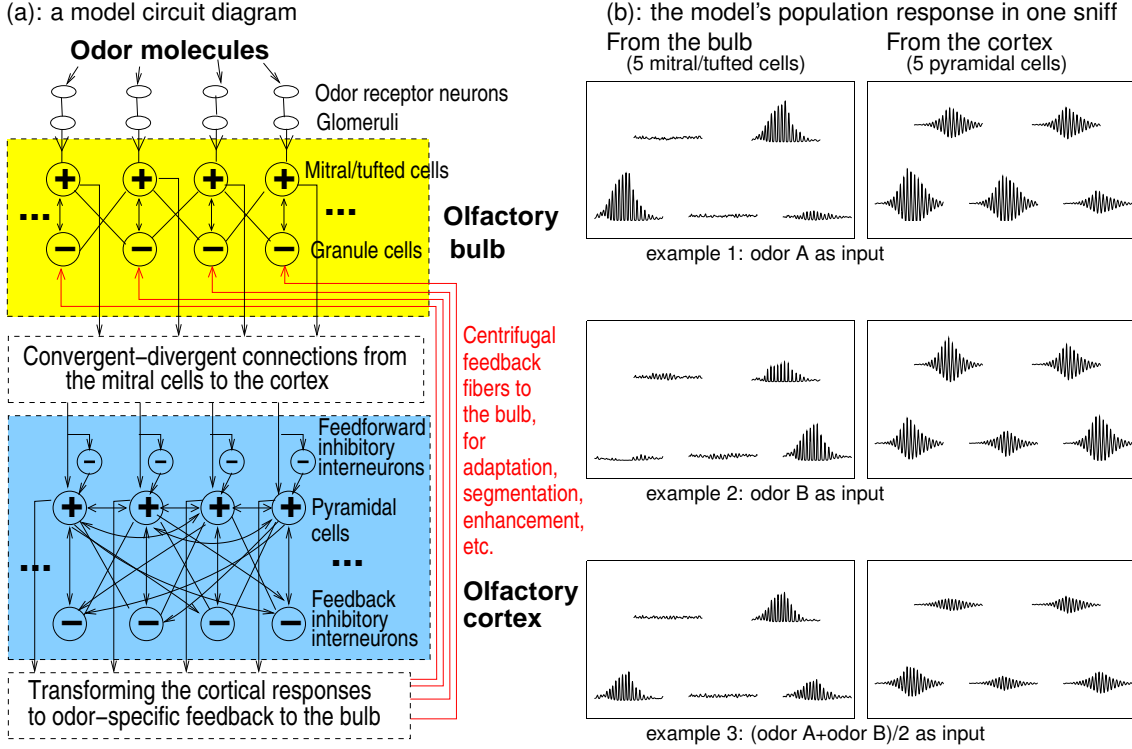


Figure 1: A network model[24^{••}, 22^{••}] of coupled olfactory bulb and cortex for odor recognition, segmentation, and sensitivity enhancement. a: the circuit diagram based on neural anatomy. b: neural responses in one sniff cycle to example odor inputs. Each box encloses the population response pattern (in terms of the temporal traces of activities of five selected neurons) to one particular odor input: odor A, odor B, or the mixture of odors A and B as in[22^{••}]. The bulbar/cortical responses are shown in the left/right column. Each neuron's response contains both the respiratory (the breathing rhythm) and high-frequency (typically in the gamma range) components. The dissimilarity between the response to the mixture and the average of the responses to the odor components is more apparent in the patterns of the phases of high-frequency oscillations.

A network model of olfactory bulb and cortex for odor segmentation and recognition

Briefly, the model is as follows (see [14^{••}, 24^{••}] and Fig. 1). Let i^{th} M/T cell have deviation x_i from resting potential, firing rate $g_x(x_i) \geq 0$ (a sigmoid-like function of x_i), and external sensory input I_i . Analogously, y_i and $g_y(y_i)$ are for the i^{th} granule cell, which receive centrifugal input $I_{c,i}$. Then[14^{••}], $x = (x_1, x_2, \dots)$ and $y = (y_1, y_2, \dots)$ evolve with time t by

$$\begin{aligned} dx_i/dt &= -\alpha x_i - \sum_j H_{ij}^0 g_y(y_j) + I_i, \\ dy_i/dt &= -\alpha y_i + \sum_j W_{ij}^0 g_x(x_j) + I_{c,i}, \end{aligned} \quad (1)$$

where W^0 and H^0 are neural connection matrices and $1/\alpha$ is the membrane time constant (taken as identical across neurons for simplicity). $I \equiv (I_1, I_2, \dots) \equiv I_{\text{background}} + I_{\text{odor}}$ includes a static background $I_{\text{background}}$ and a respiratory odor input $I_{\text{odor}} \equiv P_{\text{odor}} R(t)$ with spatial pattern vector P_{odor} and respiratory modulation $R(t)$. Similarly, $I_c \equiv (I_{c,1}, I_{c,2}, \dots) \equiv I_{c,\text{background}} + I_{c,\text{control}}$ includes background $I_{c,\text{background}}$ and active control $I_{c,\text{control}}$. Response $(x, y) \equiv (\bar{x}, \bar{y}) + (x', y')$ includes respiratory (\bar{x}, \bar{y}) and high-frequency (x', y') parts. Here, (\bar{x}, \bar{y}) is the value of (x, y) that

makes $dx/dt = dy/dt = 0$, hence it adiabatically follows the sensory I (especially when I_c is static). High-frequency (x', y') emerge when the equilibrium (\bar{x}, \bar{y}) is unstable. Approximately,

$$\begin{aligned} dx'/dt &= -\alpha x' - Hy', \\ dy'/dt &= -\alpha y' + Wx', \end{aligned} \quad (2)$$

where matrices H and W have elements $H_{ij} \equiv H_{ij}^0 g'_y(\bar{y}_j)$ and $W_{ij} \equiv W_{ij}^0 g'_x(\bar{x}_j)$ which depend on (\bar{x}, \bar{y}) . Let matrix $A \equiv HW$ have k^{th} eigenvector X_k and eigenvalue λ_k for various k , then [14**] approximately $x'(t) \propto X_1 \exp[-\alpha t \pm i\sqrt{\lambda_1}t]$ (here $i \equiv \sqrt{-1}$) is dominated by the mode $k = 1$ which has the largest $|\text{Im}(\sqrt{\lambda_k})|$ ($\text{Im}(\cdot)$ means imaginary part). Hence, when input I , which determines (\bar{x}, \bar{y}) and thus X_k and λ_k , is such that $|\text{Im}(\sqrt{\lambda_1})| > \alpha$, common high-frequency oscillations (x', y') emerge across the bulb with a spatial pattern of amplitudes and phases dictated by the complex vector X_1 . Since

$$(\text{odor } I, \text{ centrifugal } I_c) \xrightarrow{\text{determines}} \text{respiratory response } (\bar{x}, \bar{y}) \xrightarrow{\text{controls}} \text{high-frequency response } x', \quad (3)$$

odor input I (particularly when $I_{c,\text{control}} = 0$) is coded in both the respiratory \bar{x} and the high-frequency x' , which emerge during inhalation if I has the strength and pattern P_{odor} to make $|\text{Im}(\sqrt{\lambda_1})| > \alpha$. In particular, across the M/T cells, both firing rates and response phases, within a long sniff cycle and a short high-frequency oscillation cycle, should carry odor information [3*, 19].

The left column in Fig. 1b shows three model bulbar response patterns $O \equiv (g_x(x_1), g_x(x_2), \dots)$ using five example M/T cells. The first two patterns are to single odor objects A and B, respectively. The third one, to the mixture of odor A and B, resembles neither the response to odor A or odor B alone, nor the average of the two component response patterns (see also Fig. 2). This is unsurprising given the nonlinear transform from input I to responses \bar{x} and x' . Such mixture behavior is observed physiologically, even when (as is in Li's model [24**]) complex interaction between odor components at the level of the glomerulus is negligible [27*, 28]. These response properties partly underlie the difficulty in identifying the components in a mixture [15].

By equation (3), for any odor input $I_{\text{odor}} = I - I_{\text{background}}$, one can make a centrifugal control $I_{c,\text{control}} = I_c - I_{c,\text{background}}$ to cancel the effect of I_{odor} on the respiratory response \bar{x} , such that \bar{x} behaves as if $I_{\text{odor}} = 0$ and consequently quenches the high-frequency response x' [24**]. This cancelling feedback depends nonlinearly on the bulbar circuit but is specific to the odor input I_{odor} . In model simulations [24**], a linear approximation $I_{c,\text{control}} \propto H^{-1}I_{\text{odor}}$ is effective. Consider the following sequence of events. First, odor A arrives, evoking initial bulbar responses $x = \bar{x} + x'$ (Fig. 2a). Second, the cortex, upon recognizing odor A, sends the cancelling feedback $I_{c,\text{control}}$ (which could be learned by the cortex [22**]) in subsequent sniffs, suppressing the bulb responses to odor A (Fig. 2d) and manifesting odor adaptation. Third, if odor B arrives later, superposed on the pre-existing odor A, the bulb's full adaptation to odor A should make it respond as if odor B is presented alone, achieving effective foreground segmentation. The resemblance between the response to odor B alone and that to the foreground odor B (compare Fig. 2b with Fig. 2e) applies not only to the pattern of response amplitudes, but also to the pattern of high-frequency oscillation phases. Accordingly, odor adaptation is not fatigue, but an active strategy that enables segmentation. In particular, the bulb remains sensitive to newly arrived odors — this would be difficult if adaptation were merely by reducing the sensitivities of the activated bulbar neurons, as new inputs are likely to involve at least a subset of these neurons. In a special case, adaptation makes the bulb respond to an increase in the input strength of the adapted odor as if the increased amount is presented alone without adaptation. The cancelling feedback is a realization of what has become known as predictive coding [29].

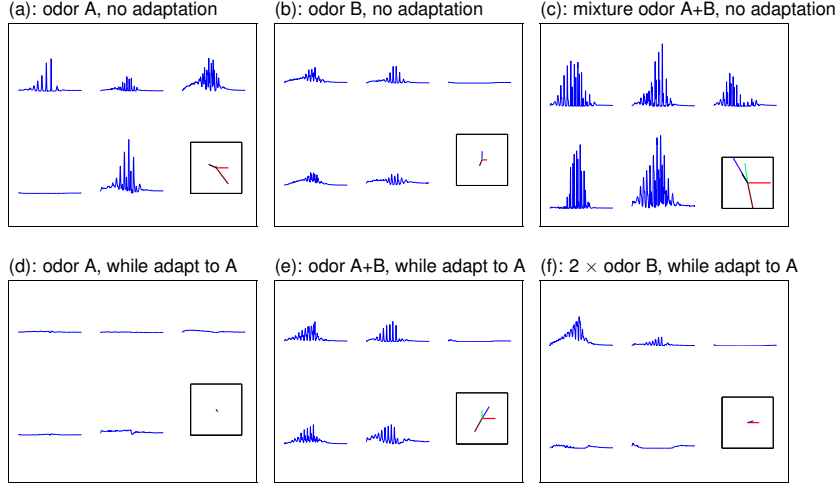


Figure 2: Model bulbar responses in odor segmentation and adaptation. The format of each panel is as in the left column of Fig. 1b, but a plot is added in a box at the lower right of each panel to visualize the amplitude and (relative) phase of each neuron’s high-frequency oscillation (at the dominant frequency coherent across cells) by a vector (color coded for individual neurons) of that amplitude and phase angle. a–c: bulbar responses without odor adaptation, i.e., during the first sniff in exposure to odor input, odor A, odor B, and the mixture odor A and odor B. d–f: bulbar responses to odor A (d), the mixture of odor A and B (e), and double-strength odor B (f) while being fully adapted to odor A (i.e., $I_{c,\text{control}} \propto H^{-1}I_{\text{odor}}(A)$ with $I_{\text{odor}}(A)$ as the I_{odor} for odor A). d, e, and f demonstrate self-adaptation, segmentation, and cross-adaptation, respectively. The bulbar model for this figure is from [24]. Responses from only five (cells 1, 2, 4, 6, and 8) out of ten of the model M/T model cells are shown. Odor A has input $I_{\text{odor}} \propto P_{\text{odor}} = 0.0049 \cdot (1, 1, 1, 1, 1, 1, 1, 1, 1, 1)$, odor B has $P_{\text{odor}} = 0.001 \cdot (5.3, 4.1, 4.4, 2.2, 4.7, 3.9, 5.3, 2.9, 5.2, 3.8)$.

Li and Hertz [22] extended the model to the cortex. With bulbar output O , the net effective bulbar input to the cortical pyramidal cells is $I_{\text{bulb}} = L(O)$, where $L(\cdot)$ is an approximately linear transform including (1) a spatial transform by the lateral olfactory tract to enable each M/T cell project to many cortical locations and (2) a temporal high-pass filtering using the feedforward inhibitory interneurons (Fig. 1a). Due to the high-pass filtering, I_{bulb} is more sensitive to the high-frequency rather than the respiratory part of the bulbar output O . The cortical pyramidal cells and feedback interneurons are analogous to the bulbar M/T and granule cells, respectively, hence we can analyze their dynamics like we did for the bulbar dynamics, replacing (x, y) for the M/T and granule cells by (u, v) for the pyramidal and (feedback) interneurons and replacing sensory input I by the effective bulbar output I_{bulb} . Let \bar{I}_{bulb} and I'_{bulb} , respectively, be the respiratory and high-frequency parts of $I_{\text{bulb}} \equiv \bar{I}_{\text{bulb}} + I'_{\text{bulb}}$, and analogously let $(u, v) \equiv (\bar{u}, \bar{v}) + (u', v')$ (here, (\bar{u}, \bar{v}) is the value of (u, v) that makes $du/dt = dv/dt = 0$ when high-frequency $I'_{\text{bulb}} = 0$). The cortex and bulb differ additionally as follows. First, the pyramidal cells project long-range-wise to each other and to the feedback interneurons [4]. Second, the recurrent connections are such that the cortex does not oscillate spontaneously (i.e., (\bar{u}, \bar{v}) is always stable when $I'_{\text{bulb}} = 0$) [7]. Third, the cortex learns, i.e., stores in its recurrent connections through neural plasticity, the patterns of the bulbar high-frequency drive associated with some odor objects (i.e., the stored patterns are the eigenvectors analogous to X_k for the bulb near equation (2)), the long-range nature of the recurrent connections makes this learning easy [22]. Fourth, pyramidal activities resonate with a bulbar drive I_{bulb} when I_{bulb} (particularly its high-frequency pattern) sufficiently resembles a stored pattern,

i.e., $u' \approx s \cdot I'_{\text{bulb}}$ with a sensitivity $|s|$ that increases with the similarity (in patterns of amplitudes and phases) between the bulbar drive and any stored memory (this resonance is a generalization of a pendulum's resonance to external drive when the driving frequency matches the intrinsic frequency). The right column in Fig. 1b shows the cortical responses to odor A, B, and their mixture. The model cortex had stored memories of A and B but not the mixture, so that the cortical response to the mixture is weaker. Finally, the pyramidal responses are transformed to a desired centrifugal control pattern $I_{c,\text{control}}$ [22••].

For Li's proposed centrifugal adaptation, the cortex simply transforms bulbar responses to the corresponding $I_{c,\text{control}}$, so the detail of the cortical model to implement this transform is not critical. We should however note the following. First, the cortex has to have the odor information, e.g., by recognizing the bulbar output, in order to provide an odor-specific $I_{c,\text{control}}$ for adaptation. Li and Hertz modelled non-recognition as weak cortical responses[22••]; whether this is the case physiologically is unclear, as non-recognition could involve learning, attention, and their associated neuromodulators and response properties[6]. What matters is a lack of (a sufficiently) effective $I_{c,\text{control}}$ under non-recognition. Second, the high-pass filtering of bulbar inputs to the cortex suggests that the cortex prioritizes the odor information in the high-frequency rather than the respiratory part of the bulbar output. Behaviorally, adaptation, or recovery from it, takes from seconds to minutes, this could be implemented in our model but is inessential. With stationary odor input, feedforward and feedback between the bulb and cortex should reach an equilibrium with residual responses in both structures[22••].

Experimental data in relation to the predictions and implications of the model

Helped by modern experimental technology[30, 31], much data pertaining to Li's model have since emerged. Some of them were predicted originally[24••], others are natural extensions.

Figure-ground segmentation in bulbar responses

Using a design analogous to Fig. 2a–e, Kadohisa and Wilson[32••] showed in anaesthetized rats that odor adaptation, and neural response levels that may reflect figure-ground segmentation, occurred only in the cortex but not in the bulb. However, on awake mice, Vinograd et al 2015 (abstract in *Soc. Neurosci Abstr* 2015, Program No. 561.10) found that population responses in the bulb to a foreground odor superposed on an adapted background resembles the response to the foreground odor alone, and that bulbar responses adapt to exposed odor (bulbar adaptation had also been observed by Chaput and Panhuber[33•]). Also, Vinograd et al found that adaptation and figure-ground segmentation to be stronger in the awake than anaesthetized mice, perhaps explaining the apparent contradiction with Kadohisa and Wilson's findings. The necessity of the awake state to facilitate adaptation and figure-ground segmentation is consistent with the proposal that centrifugal feedback is the underlying mechanism, and that odor-specific adaptation is a computational strategy rather than fatigue. Recent imaging data in mice also indicate that the centrifugal feedback[34••] and bulbar activities[35, 36] depend on whether the animal is awake or anaesthetized, and the granule cells which convey the feedback to the M/T cells are more active when the animals are awake[36, 37].

Odor object component in a mixture is better identified after smelling a mixture of the other components

A natural prediction from the model is that it should be easier to identify an odor object component in a mixture (mixture X) if observers are first adapted to another mixture (mixture Y) composed of the other components in the first mixture. This is simply because mixture Y corresponds to the background odor entity in our model while mixture X corresponds to the superposition of the foreground odor and the background odor. This has indeed been observed recently in human observers[38••, 39]. Similar findings were observed in rats trained to react only to a particular target odor and not to a mixture of this target odor with another odor; however, after pre-exposure to the other odor, the rats reacted to the mixture as if it were the target odor alone[40•].

Centrifugal feedback: its odor-specificity, time course, and the consequence of turning it off

According to the model, the centrifugal $I_{c,control}$ for adaptation is specific to the adapted input odor. Furthermore, this feedback should last at least until the next sniff. Hence, if the adapted odor I_{odor} is suddenly withdrawn, as in Fig. 2f, the centrifugal $I_{c,control}$ will persist for a period consistent with the time it takes for subjects to recover sensitivity to the adapted odor. Using multiphoton calcium imaging to monitor this feedback in awake mice, Otazu et al[34••] indeed found this feedback to be odor specific, such that the responses of the synaptic boutons on the feedback fibers to the granule cells are selective to odors and influenced by odor concentration. Furthermore, they observed that these feedback responses often outlast stimulus presentation by several seconds.

Otazu et al further reported that silencing the cortical activities, presumably turning off I_c completely including its baseline $I_{c,background}$, enhanced bulbar responses in the M/T cells, confirming the previous observation using cortical cooling[8•].

Functional relevance of the neural oscillations

Whether there is a functional role for high-frequency neural oscillations, particularly in the visual system, has been controversial. Our model asserts that (see equation (3)) the high-frequency bulbar oscillations x' contain odor information and should be useful for odor coding and recognition. Using the GABA_A antagonist picrotoxin to interfere with neural mechanisms underpin high-frequency oscillations, Stopfer et al[41••] demonstrated that eliminating the oscillations in honeybees impaired difficult discriminations between similar odors, but leaving intact simpler discriminations between dissimilar odors. In mice, increasing the power of neural oscillations in the bulb (by disrupting GABA_A receptors in granule cells) makes the animal better at discriminating between closely related monomolecular alcohols or between mixtures of alcohols[42], although the finding was somewhat complex as it depended on the animals' experience with the odor discrimination test. Furthermore, the power of gamma oscillation in the bulb is enhanced in rat when they make finer discriminations between odors[43•]. These findings support the idea that high-frequency neural responses contain odor information and are used for discrimination. In addition, they suggest that odor information contained in the lower frequency responses, \bar{x} , is also used by the animals. This implies that, although the cortex high-pass filters the bulbar drive to prioritize the high-frequency signals, the sensitivity to the low-frequency signals is only relatively reduced rather than completely diminished by this filtering. Li and Hertz[22••] used such a filtering in their cortical model so that the bulbar low-frequency signals influence the cortical low-frequency

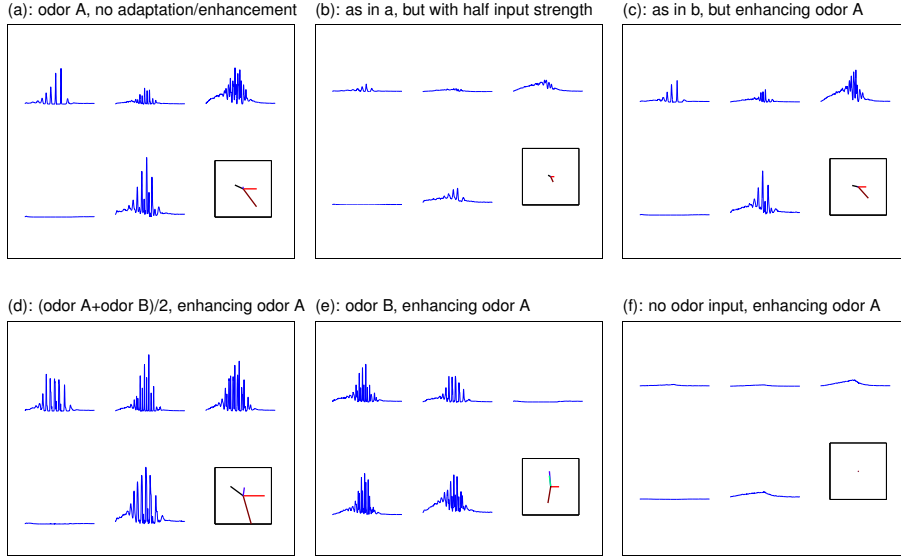


Figure 3: Model bulbar responses without or with odor searching (i.e., enhancement) for a target odor (odor A, i.e., using centrifugal $I_{c,\text{control}} \propto -H^{-1}I_{\text{odor}}(A)$). This figure uses the same model, odors A and B, and plotting format as in Fig. 2. a and b: bulbar responses to odor A at full (a) or half (b) input strength, without odor adaptation or enhancement. c–f: bulbar responses under centrifugal feedback aimed to enhance odor A, with sensory inputs as half strength odor A (c), half strength mixture of odor A and B (d), odor B (e), and no odor input (f), respectively. Note that centrifugal feedback to enhance odor A does not lead to hallucination of odor A when odor A is absent (e and f).

response (\bar{u}, \bar{v}) and place the cortex in a dynamic regime that is receptive to the high-frequency oscillations from the bulb.

Searching for a target odor

Let $I_{c,\text{adapt}}$ denote the centrifugal control $I_{c,\text{control}}$ for adapting to an odor object. Li’s model predicted that[24••] reversing this control signal, i.e., making $I_{c,\text{control}} \propto -I_{c,\text{adapt}}$, should enhance, rather than suppress, the bulbar response to this object. We call $I_{c,\text{control}} \propto I_{c,\text{adapt}}$ and $I_{c,\text{control}} \propto -I_{c,\text{adapt}}$, respectively, adapting and enhancing feedback.

Fig. 3abc demonstrate that, in the model, odor enhancement increases the sensitivity to a target odor such that the bulb responds to a weak input of this odor as if the input was stronger. Meanwhile, if the target odor is absent from input, odor enhancement typically does not lead to hallucinations, i.e., the response does not resemble that to the target odor, see Fig. 3ef. With non-linear interaction between bulbar neurons, targeting the centrifugal feedback to the granule, rather than the M/T, cells helps to prevent hallucinations[24••].

In an experiment[44•], human observers were asked if any odor was present without knowing the odor identity. In trials with odor presentation, the observers were faster to reply positively when they were simultaneously shown an image (of, e.g. oranges) suggesting the presented odor compared to the situation when no image, or an image suggesting a different odor object, was shown. However, in trials without odor presentation, seeing the image did not increase their false alarm rate. Enhancing feedback for the odor object suggested by the image may underlie this observation.

Enhancing sensitivity to a target odor object can also be useful for detecting whether this object is a component in a mixture. A recent study[45**] showed that rodents could competently distinguish whether or not a target odor object was present in a mixture made from an unpredictable composition of components selected from 14 possible candidates. The rodents learned to do so after extensive training that started with non-mixture odor presentations and gradually progressed by adding more components in the mixture. This finding is apparently at odds with previous studies[10*, 46, 47] showing that rodents, like humans, find it difficult to identify components in odor mixtures. There is however no inconsistency by noting the following: the previous studies probed whether animals that had only learned to associate a mixture with a reward would react to a component object in this mixture as equally rewarding, however they did not make the animals perform the task of deciding whether a given target odor was present in a mixture. A separate study on humans found that, although humans are unable to name all odor component objects in a mixture when the mixture contains more than three or four components which are individually known to them[11**]; they can still identify whether a target odor is present in a mixture made of up to 12 components[48]. It is possible that to decide whether a target odor is present in a mixture without first adapting to a background made of the complementary components in the mixture, animals use an odor seeking or enhancement strategy by the centrifugal feedback $I_{c,\text{control}} \propto -I_{c,\text{adapt}}$, as suggested by our model. Fig. 3ad demonstrate that, in the model, enhancing sensitivity to a target odor makes the response to a mixture containing this target appear as if the target odor was presented alone.

Task- and context-dependent centrifugal control of bulbar responses

Centrifugal feedback could also help fine discrimination. Let $I_{\text{odor}} = I_{\text{odor}}(a)$ and $I_{\text{odor}}(b)$ be odor inputs for two very similar objects a and b . They evoke respiratory responses $(\bar{x}, \bar{y}) = (\bar{x}(a), \bar{y}(a))$ and $(\bar{x}(b), \bar{y}(b))$, respectively, which in turn determine the respective high-frequency responses $x' = x'(a)$ and $x'(b)$, see equation (3). Let $\bar{I}_{\text{odor}} \equiv [I_{\text{odor}}(a) + I_{\text{odor}}(b)]/2$ and $\delta I \equiv I_{\text{odor}}(a) - I_{\text{odor}}(b)$. A small δI gives a small $(\delta\bar{x}, \delta\bar{y}) \equiv (\bar{x}(a), \bar{y}(a)) - (\bar{x}(b), \bar{y}(b))$, which in turn leads to a small difference between the high-frequency responses to the two odor objects so that it will be difficult to discriminate between them. It can be shown[24**] that $\delta\bar{x} \approx S_x \delta I$ and $\delta\bar{y} \approx S_y \delta I$ with sensitivity matrices $S_x \equiv (\alpha^2 + HW)^{-1}\alpha$ and $S_y \equiv (\alpha^2 + WH)^{-1}W$ which depend on (\bar{x}, \bar{y}) through matrix elements $H_{ij} = H_{ij}^0 g'_y(\bar{y}_j)$ and $W_{ij} = W_{ij}^0 g'_x(\bar{x}_j)$. Meanwhile, (\bar{x}, \bar{y}) depend on both \bar{I}_{odor} and $I_{c,\text{control}}$ (see equation (3)). Hence, given \bar{I}_{odor} (i.e., given a and b), a suitable centrifugal control $I_{c,\text{control}}$ can enhance sensitivities S_x and S_y by reaching a suitable (\bar{x}, \bar{y}) . In other words, a suitable $I_{c,\text{control}}$ increases discrimination sensitivity by a population level gain control. Fig. 4 demonstrates this control, note that this control enhances the high-frequency responses in Fig. 4cf, as seen in animals during finer discrimination[43*].

Such feedback control, unnecessary when inputs are easily discriminable and specific for the input objects, may explain the task- and context-dependent neural responses and behavioral performances observed in rodents and humans[49*, 50, 51, 52]. Fig. 4cf uses a hand-picked $I_{c,\text{control}}$ to demonstrate an example of what centrifugal feedback could do. In reality, animals would have to learn the effective feedback through training, i.e., reinforcement learning, and may find alternative feedback signals to improve pattern discrimination. Other forms of feedback could also make response patterns dependent on the reward values of odor inputs, as has been observed in data[49*, 51]. These task- and context-dependent feedback, like that which enables odor seeking (Fig. 3), are akin to top-down attentional control in vision.

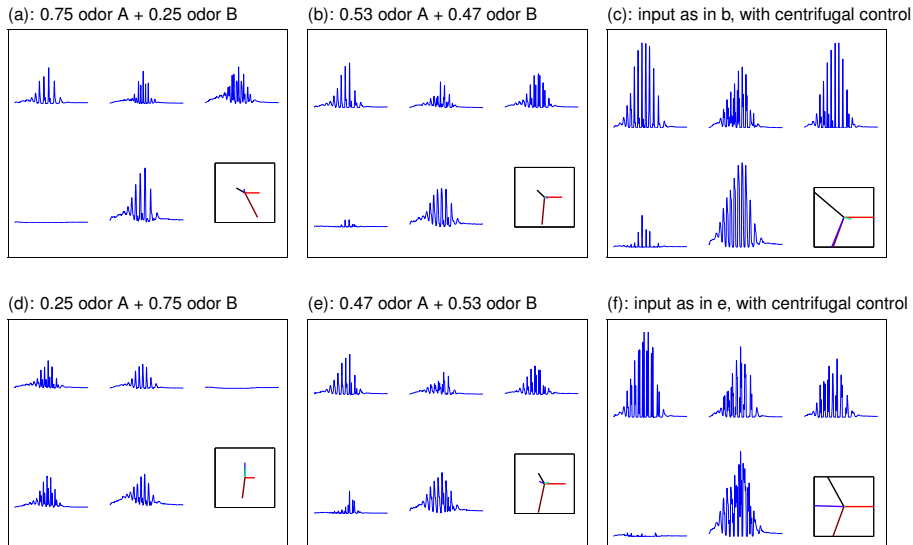


Figure 4: Task-specific centrifugal feedback to aid fine odor discrimination illustrated in six examples (a–f) of model bulbar response patterns: a,b,d, and e without, c and f with, centrifugal control. a and d: easily distinguishable bulbar response patterns to two dissimilar mixtures of odor A and B. b and e: as in a and d but response patterns are now hardly discriminable because the two mixtures have very similar proportions of odor components. c and f: as in b and e, respectively, but centrifugal feedback (same for c and f) is present to enhance sensitivity for both odor A and B. This figure uses the same model, odor input patterns for odor A and B, and plotting format as in Fig. 2.

The effect of odor familiarity

To send an effective, odor-specific, centrifugal feedback $I_{c,adapt}$ for odor adaptation, the central brain must have sufficient information about the adapted odor, e.g., by recognizing the odor in the cortex. The model predicts that[22••], for a novel odor, adaptation should be less effective or take longer to establish, as it takes some time (though this could be brief) before an animal recognizes or becomes familiar with it. Recent data showed that exposure to an odor in previous days decreases bulbar responses to this odor presented for four seconds in each trial[36]. This is consistent with our prediction if the response decrease was due to a faster establishment of adaptation. However, this response decrease was absent under anesthesia even though the animals were awake during previous exposures to the odor[36], consistent with our proposal that adaptation is an active strategy. Hence, odor-specific adaptation can be seen as part of the odor recognition process[22••]. Meanwhile, many other task-dependent controls can also be odor-specific, and hence odor familiarity is also expected to make these controls more effective.

Concluding remarks

We offer our by-now venerable proposal about bulbar processing and centrifugal feedback as a way of understanding and organizing recent exciting data. As discussed, these data agree, to a perhaps disconcerting degree, with the original proposal. More data are needed to settle the discrepancies between different studies concerning the critical prediction of the figure-ground segmentation. While models[14••, 24••, 17••, 18] have argued for odor information in the phases of the high-frequency neural oscillation, data so far have only revealed odor information in the phase of a

respiratory cycle[19, 53].

Few experiments have targetted olfactory cross adaptation at the neuronal level beyond the peripheral receptors. The model predicts[24**] that pre-exposure to one odor should alter bulbar responses to a second odor when the pre-exposed odor is suddenly and unexpectedly replaced by the second odor, as demonstrated in Fig. 2f, and that the centrifugal feedback at the first sniff of the second odor should be specific to the pre-exposed rather than the second odor.

The most pressing questions for future theoretical work include the computational roles of the less abundant centrifugal fibers that target the glomeruli and the many other neural and circuit complexities; some of these involve interactions with other brain areas.

Acknowledgement This work is supported by the Gatsby Charitable Foundation.

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