Abstract

Local field potential (LFP) oscillations are often accompanied by synchronization of activity within a widespread cerebral area. Thus, the LFP and neuronal coherence appear to be the result of a common mechanism that underlies neuronal assembly formation. We used the olfactory bulb as a model to investigate: (1) the extent to which unitary dynamics and LFP oscillations can be correlated and (2) the precision with which a model of the hypothesized underlying mechanisms can accurately explain the experimental data. For this purpose, we analyzed simultaneous recordings of mitral cell (MC) activity and LFPs in anesthetized and freely breathing rats in response to odorant stimulation. Spike trains were found to be phase-locked to the gamma oscillation at specific firing rates and to form odor-specific temporal patterns. The use of a conductance-based MC model driven by an approximately balanced excitatory-inhibitory input conductance that oscillated at the gamma frequency allowed us to provide one explanation of the experimental data via a mode-locking mechanism. This work sheds light on the way network and intrinsic MC properties participate in the locking of MCs to the gamma oscillation in a realistic physiological context and may result in a particular time-locked assembly. Finally, we discuss how a self-synchronization process with such entrainment properties can explain, under experimental conditions: (1) why the gamma bursts emerge transiently with a maximal amplitude position relative to the stimulus time course; (2) why the oscillations are prominent at a specific gamma frequency; and (3) why the oscillation amplitude depends on specific stimulus properties. We also discuss information processing and functional consequences derived from this mechanism.
spiking of an MC population and gamma oscillations in anesthetized, freely-breathing rats in response to odorant stimulation and [2] to build a biophysical model of MC activity under the same in vivo conditions to explain the data. Our data showed that during the transient periods of gamma oscillation, a specific subset of MCs exhibited specific periodic firing phase patterns that could be grouped in a small number of types. Furthermore, the pattern types exhibited by a particular MC are qualitatively related to the nature of the odorant stimulus. These different types of patterns constitute the signature of an entrainment of these cells by an input oscillation [20,21], whose origin can be attributed to the inhibitory granular input [17]. In the model, we verify that this scenario of entrainment effectively reproduces the experimental observations. We further explored the model’s dependence on MC input activity and intrinsic properties, showing that our model robustly exhibited an optimum of entrainment when the oscillation frequency was within the gamma range. Overall, these results provide a detailed quantitative description of the complex MC firing activity at the population level and, at the same time, a theoretical explanation of the links between MC spike trains and gamma LFP oscillations evoked under freely breathing conditions in the OB. Furthermore, these results constitute an important underlying mechanism if future research shows that such a firing activity can support odor coding in behaving conditions.

Results

Part I: experimental data analysis

**Gamma LFP oscillations are recurrent and stable, and the firing rate is highly variable.** Under our anesthetized conditions, odorant stimulation elicited LFP oscillations in the whole OB and spiking activity in the MC layer. Respiratory modulation appeared as a slow, large-amplitude oscillation (~2 Hz) that was visible on the raw trace (Fig. 1A). Although slower than under waking conditions, this respiratory modulation could be associated with theta range frequencies (4–10 Hz). The time-frequency representation (TFR) (Fig. 1B) led to the observation of two other oscillatory frequencies, namely beta oscillations in the 15–35 Hz range and gamma oscillations in the 40–80 Hz range. Gamma bursts occurred at each respiratory cycle around the inspiration/expiration (I/E) transition [8] (Fig. 1B) and were nearly independent of the odorant stimulus. In contrast, the characteristics of the beta bursts depended on the molecular features of the odor [9]. The gamma oscillation positions during the respiratory cycles were remarkably stable between odors, always starting at the I/E transition. The distribution of gamma

**Figure 1. Unit activities and LFP gamma oscillation frequencies had the same mean but very different variability.**

A) Raw signal recorded in the MC layer during odorant stimulation. Vertical continuous lines: I/E transitions; vertical dashed lines: E/I transitions. B) Time frequency representation extracted from the raw signal and based upon a wavelet transformation. The signal energy at each time-frequency point is in a colorscale. C) Top) Distribution of LFP gamma-burst mean frequencies with a normal function fit, which is shown as a black trace. Bottom) Distribution of LFP cycle instantaneous frequency, which is defined as the inverse of the period between two max of the oscillation, and which is normalized to the average frequency of the gamma burst to which the cycle belongs. D) Instantaneous frequencies along one respiratory cycle (six colors for six cells). + are spike positions for which gamma LFP oscillations are present. E) Interspike interval distribution (ISI) for spike trains occurring during gamma oscillations (bin 0.05 cycle, black line, gamma function distribution with the same mean ISI as the experimentally found (see methods)). Contour histogram is the distribution of the mean ISIs that was calculated for each spike train. All units are given in “cycle”.

doi:10.1371/journal.pcbi.1000551.g001
burst mean frequencies was fitted with a narrow Gaussian distribution with a mean of 60.7 Hz (standard deviation: 0.3 Hz, see Fig. 1C, top). Inside each gamma burst, the cycle to cycle frequency was even more stable. Indeed when the frequency of each cycle (the inverse of its length) was normalized relative to the mean frequency of its gamma bursts, the resulting distribution could be fitted with a Gaussian distribution with a standard deviation that was lower than 0.1, which indicated low variability (Fig. 1C, bottom).

In contrast, the MC instantaneous frequencies were highly variable (i) within the same cell, between different epochs of the respiratory cycle, (ii) within the same cell, between odors, and (iii) between simultaneously recorded units. An example is given in Fig. 1D, which shows the course of instantaneous frequencies over the period of a respiratory cycle for six cells that responded to the same odor. These examples show that the MC activities are highly modulated and variable during the respiratory cycles, as previously described [22–24].

Due to the bulbar-specific origins of gamma oscillations and to the regular occurrence of these oscillations across the bulbar surface, we focused our measurements on neuron discharges during LFP gamma bursts. To simplify the comparison between bursts of different frequencies, the interspike intervals (ISI) will always be expressed in fractions of their gamma burst average period (the Cycle unit), and similarly, the MC spike rates will be expressed in spikes per cycle (SpC). The ISI distribution that was observed during these gamma bursts was plotted in Fig. 1E (grey bars). We compared these distributions with a gamma distribution (black line) that reflected the usual random discharge of a neuron with a similar refractory period (0.18 cycles (=3 ms)) and the same mean ISI (1.18 cycles) as the experimental distribution. We observed two major deviations of the experimental ISI distribution from the gamma distribution. One appears around 0.1–0.2 cycles and corresponds to the numerous spike doublets (or high frequency bursts) that can be observed in MC discharges [23]. The second deviation is an excess of the experimental ISI around 0.9–1 cycles. About 25% of the ISIs are between 0.8 and 1.2 cycles, compared to 18% for the gamma distribution. The latter result suggests that during gamma bursts, a large fraction of the MCs tend to fire at a rate close to the oscillation frequency.

The contrast between the regularity of oscillation frequency and the variability of spike discharge led us to the idea that the coupling between both activities could be dependent on neuronal frequency. This hypothesis was investigated further in the following analyses.

**Spike phase distribution during LFP gamma oscillations depends on the MC firing rate.** When an LFP gamma oscillation was evoked in OB slices, the distribution of GABA_\(A\) (Gamma Amino Butyric Acid) event times relative to the LFP oscillation was phased [17] (see Fig. 4G in ref. 21). According to these observations, the MCs should receive, on average, an oscillating conductance locked to the LFP gamma oscillation. Therefore, we expected the MC firing activity to correlate with the phase of the LFP gamma oscillation. For the whole population of MCs, the spike phase distribution was peaked (Fig. 2A), with a maximum around phase 0.5 (circular deviation = 1.67; p < 0.001, Rayleigh non-uniformity test). However, when the cells are segregated by their average firing rates, we observe that cells with firing rates below 1.2 SpC were better phased (Fig. 2B). We thus wondered what the difference was in the relationship between LFP fast oscillations and cells spiking at low and high firing rates.

Looking at individual spike trains on the raw signal (Fig. 2C), we noticed some particular configurations of spike-LFP phase coupling. Spike trains with ≤1 SpC (Fig. 2C, upper panel) were often stable in phase and occurred preferentially during the trough of the oscillation. On the other hand, we observed that some spike trains with >1 SpC exhibited multiple but similar phases across several oscillation cycles (Fig. 2C, lower panel). This relationship between spike phase-locking and MC firing rate raised the possibility that MC populations might be segregated according to their firing rate. We thus decided to examine systematically the relationship between phase trains and LFP oscillations while taking this observation into account.

**Specific phase-locking and spike rate control by gamma LFP oscillation.** An inspection of the spike phases (represented by grey sticks in Fig. 3A and 3B) revealed that a large number of spike trains contained spikes that had phases that were reproducible across cycles. Therefore, we automatically detected and classified the phase-locked patterns according to six qpp types,
A Pattern Classification. Q:P (Q cycles : P spikes )

B Phase-locked pattern examples

C Pattern Distribution

D Distance distribution

E Jitter distribution

Figure 3. Types of phase-locking. A) Classification principles. Spike phases (x-axis) are represented by grey ticks along the successive gamma cycles (y-axis) of a LFP burst. If the spike train has a regular number of spike at each cycle (here, 1 spike at each cycle, see Methods for details), and if the phase jitter is small enough (<0.5) (left panel) in comparison to the mean phase (black boxes), it is classified as a phase-locked pattern (here, a 1:1 pattern). Otherwise (right panel), the spike train is classified as residual. B) Six examples of phase-locked spike trains. Along the top of each plot is indicated the type of pattern (q:p) and its phase jitter. Phase-locked patterns account for 31% of all spike trains. B) Six examples of phase-locked spike trains. Along the top of each plot is indicated the type of pattern (q:p) and its phase jitter. Phase-locked patterns account for 31% of all spike trains. C) Distributions of experimentally found (grey) and randomly generated (black contours) phase-locked pattern types. The majority of the patterns were 1:1 in both distributions. D) Distribution of relative distances (see Methods) from spike train phases to the closest pattern for the experimentally found (grey) and randomly generated (black contours) spike trains. Dashed line is the strict distance limit (0.33) under which the spike train can be considered for phase locking. Note the good agreement between experimentally found and randomly generated distance distributions. E) Distribution of phase jitter for experimentally found (grey) and randomly generated (black contours) spike trains for the respective phase-locked pattern type. The dashed line is the limit (0.5) under which the spike train is considered phase locked. Note that the area of experimentally found distributions under the limit was often larger than those of the randomly generated distributions, especially for the 1:1 patterns (* indicate significant global statistical differences between both distributions, Kolmogorov-Smirnov test, p<0.05).

In order to test the significance of these results, we compared our experimentally recorded patterns to patterns that were expected by chance when the phase-locked pattern detection was applied to a randomly generated spike train family with the same firing rate distribution (see Methods for details and other alternatives for random spike train generation when the ISI distribution or the phase reference are imposed). We observed that the proportion of phase-locked spike trains among all spike trains was reduced (15% in the random distribution) compared to the experimental results (31%). As detailed in the Methods section, the classification of a spike train as a pattern is a two step process. The first step of this classification relies on a “relative distance” measure. The “relative distance” between each experimental (or random) spike train and theoretical patterns was computed, which indicates how close they were in terms of spike count. The “relative distance” distribution (Fig. 3D) was similar between the experimental and randomly generated spike trains, which attests to the similarity of the spike counts of the random and experimental spike train distributions. Thus, the differences between experimental and random data must be due to the second step of the classification process, which estimates a “jitter” that measures the reproducibility of spike phases across cycles. Indeed when comparing the distribution of jitter for experimental and random spike trains, the jitter values that fell below the jitter threshold (i.e., 0.5 dashed lines in Fig. 3E) were more numerous for the experimental spike trains than those expected by chance. Additionally, experimental and random phase distributions showed significant differences for the 3:1, 2:1, 1:1, and 1:2 patterns (Kolmogorov-Smirnov test, p<0.05) (Fig. 3E). Significance was not reached for the 2:3 and 1:3 patterns due to the small number of experimental observations of these patterns (N = 21 and N = 8). In addition, the relative proportions of the different type of phase-locked patterns were similar (45% and 36% for the 1:1 and 2:1 patterns) under the experimental and random conditions. It was noticeable, however, that the proportion of the 1:1 pattern in comparison to other patterns was significantly higher under the experimental conditions than under random conditions (Chi-square test, 70, p<0.01). Overall, these results showed that a significant population of MCs can be locked to the oscillation for various individual MC firing rates, which suggested that multiple patterns can co-exist across different cells. This finding raises the question, which we will address later, of the nature of the
underlying mechanism that controls train structure in relation to the LFP.

To further characterize the relationship between cell discharge and LFP oscillation, we observed how the discharge of cells that exhibited a phase-locked pattern during a gamma oscillation evolved before, during, and after the oscillation. First, for all cells exhibiting the same type of pattern, the cell instantaneous frequency was plotted at each spike time (see Fig. 4 Ai to 4Avi for the different types of patterns, where time 0, in all cases, denotes the onset of gamma oscillations). The instantaneous frequency was measured at each spike time and was defined as the inverse of the ISI preceding the spike. The ISI unit was a cycle of LFP gamma oscillation. When the ISI fell out of the LFP gamma burst, the time reference was the mean cycle of the LFP gamma burst. This representation showed that the 3:1, 2:1, and 1:1 experimental patterns (Fig. 4Ai–Aiii) were characterized by stable instantaneous frequencies during gamma episodes, whereas highly variable discharges could be observed before and after the gamma episodes. Hence, the regular discharges observed for these patterns seemed to be due to a specific process that occurred during gamma oscillations and not due to previous stability. On the other hand, the instantaneous frequency of the 2:3, 1:2, and 1:3 experimental patterns (Fig. 4Av – Avi) exhibited a smaller decrease in variability between the “before” and “during” gamma oscillations, which suggested that the regularity detected there was more intrinsic to MC discharge and less due to the oscillation. Finally, these results were compared across the different q:p patterns the mean (Fig. 4Bi), and the standard deviation (Fig. 4Bii) of the firing rate was estimated using a 50-ms time bin. Interestingly, phase-locked cells adopted a pattern with an average firing rate that was close to their own average firing rate before the oscillation (except for a small mismatch between the 2:3 and 1:2 patterns). For all types of patterns, the standard deviation of the instantaneous frequency decreased immediately after the onset of the gamma oscillation. Overall, this suggests that gamma oscillations could regularize the discharge of MCs while segregating them according to their intrinsic firing rates (i.e., cell firing rates if oscillatory input is absent). However this result does not unequivocally imply the dominance of the network oscillation on the mitral discharge, since both appeared to be intricately connected.

![Figure 4](https://www.ploscompbiol.org/file/10.1371/journal.pcbi.1000551.g004)

**Figure 4. Firing rate control during gamma episodes.** A) Instantaneous frequencies (1/ISI) were plotted from 200 ms before the gamma burst to 300 ms after. t = 0 at the beginning of the gamma burst, which is shown as a grey zone and by the symbolic oscillation atop of each graph. For each pattern type (Ai-vi), black dots are instantaneous frequencies (y-axes) as a function of their time position (x-axes) relative to the beginning of the LFP gamma burst. The mean instantaneous frequency (bold line) ± its standard deviation (thin lines) is estimated by averaging instantaneous frequencies over time bins of 50 ms. B) Mean firing rate averaged over 50-ms time bins (Bii) and its standard deviation (Bii) for spike trains expressing one type of phase-locked pattern (see legend for symbol-pattern correspondence). Compared to A, cells that do not fire during a bin are also taken into account in the average. Bii clearly shows that the firing rate standard deviation decreases for all patterns immediately after the gamma oscillation begins.

DOI:10.1371/journal.pcbi.1000551.g004
Relation between pattern types and odors. Given that pattern formation is observed during gamma bursts, we aimed to evaluate the correlation of pattern presence with odor specificity and physiological relevance. We compared the reproducibility of the pattern formation of the neuronal response during stimulation with the same odor and a different odor.

The probability of finding the same pattern in an MC response was significantly higher for responses to the same odor than for responses to different odors (probability of finding the same pattern in response to the same odor: 0.049, to different odors: 0.015, p-value < 0.05, paired t-test, n = 98, see the distribution of these probability differences computed for each cell in methods). This test was performed on 98 cells among 143 cells. We selected the cells for which there were at least two recorded responses for at least two different odors. If only phase-locked patterns were considered (that is we did not take into account non-pattern spike train in opposition to the preceding analysis), then probabilities of finding the same pattern were enhanced to 0.60 and 0.49 for responses to the same odor and to different odors respectively (Kolmogorov-Smirnov test, p-value = 0.07, n = 48). Further investigations of our data at this point do not fully determine the role of locking. Nonetheless, this result reinforces the possible significance of patterns for encoding information about the nature of the odor and could help with the decoding of other structures. Although further analysis with additional data would be necessary to obtain a more quantitative understanding of the patterns’ physiological function, these patterns were found to be qualitatively related to odors. The reliability (60%) of getting one pattern in response to one odor remains relative.

Part II: modeling study

The relationships between unit activity and gamma LFP oscillations during phase-locking raise the question of whether reciprocal entrainment mechanisms exist between MC and LFP oscillations. We addressed one part of this question using a biophysical model 1) to investigate the modalities of entrainment of MC activities by granule cell activities and 2) to explain the spike train structures measured experimentally. The use of a model allowed us to perform studies that are not currently feasible with animal studies.

Model MCs can be differentially phase locked by an oscillation of their inhibitory input. Before presenting our results, we must characterize the physiological conditions of locking. The existence of a correlation between LFP oscillations and spiking patterns presupposes neither the cause-effect relationship between the two activities nor the biophysical mechanisms of interactions in the bulbular network to explain the phase-locked patterns. In vitro experimental results by Lagier et al. (2004) [17] (see their Fig. 4G) showed that, during LFP gamma oscillation, MCs can receive an average level of inhibition due to tonic activation of GABA_A receptors, along with a superimposed phasic inhibition that occurs at gamma frequency. From the synaptic connectivity and the individual synaptic strength, we were able to estimate the average level of tonic inhibitory conductance (called gI) to be on the order of 20 S/m^2 and the amplitude of the oscillation (i.e., the phasic inhibitory conductance, called gIo) to be up to 30% of the average level (see Methods for details about the MC model and all of the parameter estimations). We tested how the response to sensory inputs, which was mimicked by a constant and tonic excitatory conductance (called gE), and was influenced by the inhibitory sinusoidal conductance (gI + gIo) oscillating at a frequency (fIo) in the gamma range (Fig. 5A). This inhibitory conductance oscillating at 60 Hz was set to 0%, 10%, or 30% of the average inhibitory conductance gI (i.e., gIo = 0, 2, or 6 S/m^2, respectively). As shown by the different plateaus on the curves of the cell response (Fig. 5Ai), the occurrence of such an inhibitory conductance stabilized the firing rate. The frequencies at which the firing rate was stabilized corresponded to the fIo patterns that occurred around frequencies given by p/q multiplied by the frequency of the imposed oscillation (60 Hz). Throughout this analysis, q and p are distinct integers chosen among {1, 2, 3}. These frequencies corresponded to frequencies in the experimental phase-locked patterns. The larger the oscillation amplitude, the wider the stabilized plateau (see the curves from blue to green in Fig. 5Ai). Interestingly, the inhibitory oscillation was able to increase the firing rate (the plateau for 1:1 lies above the curve with gIo = 0) and could evoke firing in a silent cell (Fig. 5Ai). Under noisy conditions (Fig. 5Ai), the conductance-frequency response was partially preserved, but the smallest plateaus (for 2:1, 2:3, and 1:3) disappeared. Figure 5Bi shows, in the noiseless case, phase diagrams of trains that were extracted from each of the plateaus mentioned in Fig. 5Ai (referred as “a”–“e”). The relatively good agreement with experimental observations [e.g., compare the experimental spike trains in Fig. 3B with the simulated trains in Fig. 5Bi] suggests that MCs can be driven effectively by an oscillatory input during gamma oscillations. Additional spike trains that were extracted from the non-plateau portions of the firing rate response curve (referred as “i”–“j”) in Fig. 5Ai are shown in f through j of Fig. 5Bi. These results indicate that MCs are entrained by an oscillatory inhibitory conductance mainly when the neuron fires at the same frequency as the imposed 60 Hz oscillation, and that this entrainment can also explain the patterns that are observed in our experiments. This result is partly specific to the model, since other intrinsic properties for other neurons would not lead to a 1:1 entrainment. Indeed, all cochlear neurons have dissimilar entrainment properties with regard to the frequency of entrainment [25].

We next analyzed the influence of the oscillation amplitude on spike phase-locking. For this purpose, a color map was used to plot the phase jitter, which was defined in the same way as it is used to classify spike trains as a phase-locked pattern or not, as a function of the amplitude of the oscillating inhibitory conductance, from 0 to 30% of the average of the inhibitory conductance (y-axis) and the amplitude of the MC excitatory input conductance (Fig. 5Gi). The so-called “Arnold tongue” for 1:1 [20] (zero jitter, which would occur in perfectly locked spikes, in black and noted directly on graph) was the widest, while the tongue for 1:2 was the second widest. The higher the oscillation amplitude, the wider the tongues for 1:1 and 1:2. These tongues were partly preserved under noisy conditions (Fig. 5Gi), but tended to shrink and disappear at low levels of oscillatory inhibition. As a consequence, as the oscillation amplitude tends to increase, a higher proportion of cells may be entrained by the oscillation, even if the cells’ intrinsic firing rate is far from the frequency that is imposed by the entrainment (see the doubled y-axis, below). Therefore, a larger MC population can be recruited when the oscillation amplitude increases.

The next step was to understand the origins of the inter- and intra-pattern phase variability. For this purpose, we represented the spike phase variations according to the driving excitatory conductance gE for two levels of inhibitory conductance, namely 10% (Fig. 6Ai) and 30% (Fig. 6Aii). Under these noiseless conditions, the 1:1 tongue (arrows) had phases that varied continuously from 0.5 to 0.2, as the excitatory conductance increased. We noticed that the range of possible phases for each tongue was not greatly affected by the oscillation amplitude, whereas the conductance range (the gIo band indicated) over which the MC was entrained increased with the oscillation amplitude (compare Fig. 6Aii to 6Ai). Phase-locking was robust to noise, and the phase distribution persisted, although less sharply, for high
levels of noise (Fig. 6Aiii). The model supported the experimental observation that MCs can be phase-locked at various frequencies and under noisy conditions. Finally, comparing the model prediction to our experimental results at the population level is impossible because of the lack of data on the distribution of the input excitatory conductance $g_E$ in the MC population. Thus, in Fig. 6B we present only side-by-side comparisons of those spike phases that can be predicted by the model (left column) for each
type of pattern and their experimental counterparts (right column).

The phases of the spikes of the model come from the patterns that are detected under quiet conditions (contour) (corresponding to Fig. 5Ci) and noisy conditions (grey) (corresponding to Fig. 5Cii). For a better fit, we used only the patterns evoked when $g_{Io} = 4 S/m^2$. We observed agreement between theoretical and experimental data especially under noisy conditions. Indeed, whereas without noise in the model, some differences are observed between the mean phase predicted by the model for the 3:1, 2:1 and 1:1 patterns and those observed in the data, introducing some noise tends to decrease these differences in the mean phase between the model and the experiments. The spike phases of patterns with high

Figure 6. Model phase distribution and comparison with experimental phases in phase locked patterns. A) Model spike phase (y-axis) distribution is plotted like a phase map (see grey scale bar) as a function of $g_E$ (x-axis). For a 10% oscillatory inhibition ($g_{Io} = 2 S/m^2$, $g_I = 20 S/m^2$), the MC model exhibited clear preferential phases (dark spots; arrows indicate tongue q:p). Aii) Increasing the inhibitory amplitude to 30% ($g_{Io} = 6 S/m^2$) value for $g_{Io}$ led to an increased $g_E$ band (see the horizontal double arrow), for which the phases were locked. Aiii) Noisy conditions, which were the same levels of inhibition as in (Aii), caused the phases to scatter around the tongue phases. B) Comparison of model (left panels) and experimental (right panels) phase distribution for spike trains classified as phase locked patterns (one row for each type of pattern). The pattern spike phases are extracted from Fig. 5Ci for the noise free conditions (black contour) and from Fig. 5Cii for the noisy conditions (grey bars) under the synaptic conditions $g_{Io}<4 S/m^2$, $g_E<15 S/m^2$ and $g_I = 20 S/m^2$.

doi:10.1371/journal.pcbi.1000551.g006
firing rates, that is, 2:3, 1:2 and 1:3, seem less sensitive to noise. In addition, the difference of the phase distribution width between the model and experiments could be explained by the measure variability of the gamma phase that was recorded from different depths and that will be further discussed later.

**Synaptic input parameters governing the entrainment.** Having shown that our model can reproduce our experimental results well, we further used it to explore how MC entrainment should depend on network parameters or MC intrinsic parameters.

First, we studied the influence of the excitatory-inhibitory balance. The level of inhibition received by an MC is not known, and it is difficult to infer using standard experimental approaches (see estimation in Methods). It may vary within a range depending on the level of recurrent, lateral, and centrifugal inhibition that are present in the OB network, and these networks are highly variable and modulated in their nature and function. To explore the consequences of the average inhibition for the entrainment, under noiseless conditions, we set the level of background inhibition to different values ($g_I = 6, 20, 100$ S/m$^2$). This range of values corresponds to the range of influence, ranging from a small effect to a complete shunting effect on the spiking activity. We then measured the entrainment for the 1:1 tongue by representing the entrainment diagrams as a function of MC excitatory input and the inhibitory oscillation amplitude (see Fig. 7A). The 1:1 tongue grew wider as the average level of inhibition increased. The tongue width was measured by the $g_E$ band (Fig. 7A), and computed with an oscillation amplitude of 2 S/m$^2$ that increased with the average inhibition level (Fig. 7B, full black line, left y-axis). Alternatively, a given set of conductances ($g_E,g_I$) corresponds to a given MC firing rate, and thus the $g_E$ band can be converted into a f-band that describes the range of firing rates (in the absence of oscillation) at which the MC are entrained by the inhibitory oscillation in a 1:1 pattern. Again, the width of this f-band increases with the average inhibition level (Fig. 7B, full grey line, right y-axis). These results were robust under noisy conditions (see dashed lines in Fig. 7B). Taken together, these findings reveal that a higher level of background inhibition of MCs makes them more capable of being entrained.

Second, we showed that an oscillation frequency in the gamma range is optimal for entrainment. Experimental data showed frequency stability in the LFP oscillation around 60.7 Hz (Fig. 1D). Since the frequency of gamma oscillations varied little under our experimental conditions, as well as under other conditions [10,18], we wondered why the frequencies had these particular values. We tested how the model reacted to other imposed frequencies ($f_{osc}$) of the inhibitory conductance ranging from 5 to 120 Hz and then computed with $f_{E\text{-}threshold\:1:1}$, which corresponds to the level of excitatory threshold for locking.

The last step was to explore how the intrinsic properties of the MC model were potentially responsible for the 60 Hz preference. For that purpose, we varied the time constant of the slow potassium channel, which was responsible of the MC model...
subthreshold resonant properties, from 7 ms to 13 ms. We observed that the peak of maximal entrainment could drift from lower to higher frequencies when this time constant was decreased from 13 to 7 ms (Fig. 8). As a comparison, there is not such a peak of maximal entrainment with an integrate and fire model; the profile of the curve there is only decreasing. We concluded that the intrinsic properties of the MC model may be responsible for the gamma-range frequency preference for entrainment. Although it is not currently possible to alter the intrinsic properties of the neuron experimentally, the model that we used in this study demonstrates that the intrinsic properties of the MCs can interact with network properties, thereby leading to specific entrainment of MCs, the consequences of which will be discussed in the Discussion section.

Discussion

We found that specific MCs produced spike trains that were locked to the gamma LFP oscillations in specific pattern types. Such phase-locked cells exhibited particular firing rates that were stabilized by the occurrence of gamma oscillation. In most cases, the firing rate was one spike per cycle (SpC).

Using a MC model with in vivo-like conditions that receives a small inhibitory 60 Hz sinusoidal conductance, we showed that these observations were characteristic of an entrainment process. The model exhibited similar phase-locked patterns of entrainment, with maximal entrainment for one SpC patterns. The spike phase distributions were similar in the model and the experimental data, and corresponded to the minimum inhibitory conductance associated with the LFP oscillation. This model suggests that there is an efficient process of entrainment in the OB that can make MC activity coherent across various OB areas during gamma oscillations. The relevance of such a mechanism is in the possibility of using it to ensure an underlying basis for neuronal assembly formation that can be used more generally by the nervous system [26].

The use of a robust biophysical model allowed us to predict the optimal conditions for an entrainment occurrence if

(i) the chemical features of the odor belong to the chemoreceptive field of an MC, such that its excitatory response will be strong enough to elicit spiking;
(ii) strong tonic network inhibitory interactions that are intrinsic to the bulb and/or generated by the cortex feedback are generated, such that they will balance this excitation and, therefore, provide what is called a level of background inhibition; and
(iii) the distribution of the IPSCs that are received by the MC is sufficiently well phased, which leads to a sufficiently large oscillating conductance, then a single MC has a good probability to be entrained and locked into the oscillation. As a result, its spike phases become tightly controlled by the oscillation.

Contribution of our work to existing experimental data

Our work provides converging arguments in favor of a MC entrainment, suggesting that they receive an oscillatory input in vivo. Although several groups have focused on the temporal relationship between spikes and LFP, the exploration of this entrainment phenomenon has only been partly addressed. The analysis of Eeckman and Freeman [16] differed due to the multi-unit nature of their signal. Kashyadani et al. [18] focused more on a coding hypothesis rather than a dynamic hypothesis and used an artificial sniff, which likely affected the bulb dynamics. One in vitro study has explored the spike/LFP relationship [17]. The network connectivity and dynamic conditions, however, could be very different from those in vivo, and it is difficult to compare in vitro oscillations to those under in vivo conditions.

One potential criticism of our work is the usefulness of such a mechanism under some behavioral conditions, such as where odor presentation induces a decrease in gamma oscillations [14]. The fact that the amplitude of gamma oscillations decreases under particular conditions does not indicate that gamma oscillations are unnecessary for the system. Indeed, the amplitude decreases under particular conditions; however, beta oscillations are simultaneously enhanced, which suggests that the olfactory bulb and cortex together work in a different manner [27,28]. There are other behavioral conditions in which gamma oscillations do not decrease but rather increase with odor presentation [10]. Experimental conditions vary widely depending on the employed paradigm, which can induce different sniffing strategies [29] or different neuromodulatory control of the MC/GC loop [30]. These different conditions are certainly responsible for the variation in the expression of gamma and beta oscillations. The aim of our study was to explore how spikes and oscillation can be phase-locked in the more general situations in which gamma oscillations are present. It would be an interesting second step to perform the same study for beta oscillations and to look for another mechanism that could be responsible for the observed spike/beta oscillation synchronization [31].

Basis of the model and neuronal mechanisms

Our MC model was fitted to reproduce the quantitative and dynamic properties of MCs, based upon recent findings on MC membrane activity. It is consistent with experimental data [17,32–34] and includes essential features of existing models [35–37]. In our model, entrainment was produced by a relatively weak oscillatory inhibitory conductance. When the cell has an input well above the threshold, it fires regularly and even periodically in response to a constant input. Under these conditions, and when the oscillatory input is sufficiently weak, the neuronal response can be predicted from the phase response...
curve (PRC) \[38,39\], which can also predict some characteristics of the tongues \[40\]. Since the PRC of our MC model agrees with the experimental one \[41\], it is likely that our model can accurately predict the MC response to such synaptic inputs. The synaptic mechanisms hypothesized in our model are based on observations made by Lagier et al. (2004) \[17\], who reported that a fraction of the IPSPs received by the MCs were phase-locked relative to gamma oscillations. Other possible mechanisms that could affect the MC membrane potential during gamma oscillations have been proposed: (1) a synchronous inhibition resulting from GABA release from astrocytes \[42\], (2) a synchronous excitation of the MCs by glutamate spillover onto lateral dendrites \[43,44\], and (3) a direct influence of the LFP on membrane voltage \[45,46\]. Of these possible explanations, the functional and dynamic relevance of the interactions between MCs and GCs \[47\] are the most likely processes to occur during gamma oscillations.

Aside from this observation, an important characteristic of our model is that the time constant of the single inhibitory inputs does not play a role because it is the frequency of the oscillatory modulation of the whole inhibitory input that imposes the locking frequency.

It is important to insert this mechanism into a more realistic model in order to take into consideration the spatial distribution of the physiological mechanism in dendrites. The presence of high frequency bursts of spikes in MCs is probably not due solely to the excitatory drive from the sensory input, but also to additional conductance levels beyond those present in the model. For example, the activation of an intrinsic conductance, such as T channels, would facilitate the emergence of high frequency bursts like those in our recordings.

Explanation of model predictions and experimental recordings

Neuronal phase-locking and pattern formation have already been described both theoretically \[20,21,48\] and experimentally \[26,49\]. Our study, performed in the context of the OB with a resonant neuron, however, sheds light on important aspects that are specific to this system.

First, the simulation results provide some precise explanations regarding electrophysiological properties that are not directly accessible by experimentation. The phase of the MC spikes relative to LFP oscillations is precisely distributed in the \(\frac{1}{4}\) to \(\frac{1}{2}\) part of the LFP cycle due to their level of synaptic drive. The phase distributions extracted from simulated data (Fig. 6A) are more precise and go beyond the data that was obtained in the OB \[14,17,18\], as well as our own experimental results. We wish to point out, however, that our experimental measurement of gamma phase was not totally reliable from one particular depth to another, and could have up to \(\frac{1}{4}\) of a cycle of phase shift. Indeed, gamma oscillations are generated by membrane currents flowing on either side of the MC layer, and the simultaneous recording of a gamma oscillation constantly shows a \(\frac{1}{4}\) cycle phase shift when it is recorded up to 100 \(\mu\)m from the MC layer (Fourcaud-Trocme and Buonviso, personal communication). In our recordings, we could not control the exact position of each electrode relative to the MC layer. As a consequence, these recording constraints, as well as the noise level, are likely to be the source of the larger spread of phases during the phase-locked experimental pattern when compared to the model prediction (see Fig. 6B). This can also explain the small discrepancies with recordings from other studies in which the LFP recording position relative to the mitral cell layer was different or more precisely controlled \[16–18\]. In all cases, however, our results are still qualitatively comparable.

Second, lower levels of excitatory conductance in the model were predicted to induce a slight phase lag (corresponding to \(\approx 5\) ms) between the neurons, as shown in Fig. 6A. This phase difference is observed in the cross-correlograms that were presented by Kashiwadani et al. (1999) \[18\] (their Fig. 5A), and it may be achieved by differential activation of the glomerulus \[18,50,51\]. Our predictions are able to explain the result of this previous study.

The model predicts that phase-locked or residual spike trains may depend on the degree of detuning (i.e., the difference between the neuronal intrinsic firing rate and the external network frequency), the strength of coupling, and the level of noise. The continuity between the locked and residual spike trains suggests that entrainment of MCs may be fine-tuned during the gamma oscillation, and may corroborate the locking that was observed in the fish OB \[13\]. However, only simple phase-locking has been found in these species.

Finally, in our model, increasing the global level of excitatory-inhibitory conductance favors entrainment (see Fig. 7A–B). Under anesthetized conditions, the maximal conductance should be directly related to the maximal activity of the peripheral excitation \[51,52\] and to the maximum of synaptic inhibition \[53\], which corresponds to the inspiration/expiration transition. Taken together, these data imply that entrainment should be the strongest at this transition, which is what was observed with the gamma wave appearing around this point (Fig. 1). Interestingly, odors that elicit low theta activity (respiratory modulation), which potentially reflects weak OB activation (e.g., low-concentration odors), generally failed to elicit gamma oscillation \[9\], suggesting that the theta oscillation could gate gamma activity.

Implications on the origin of the gamma oscillation

In the OB, MCs are directly interconnected only within glomerulus \[54–57\] and not across bulbar areas. Instead, MC spikes induce a depolarization of some GC spines, which propagates through parts of the cell to other spines and triggers both synchronous \[58–62\] and asynchronous \[36,55,63–65\] GABA release from granule dendrodendritic synapses onto other MCs. This peak of GABA release is about \(\frac{1}{4}\) of the gamma cycle \((\approx 12\) ms) after the peak of spiking (according to the spike (Fig. 4E) and IPSP (Fig. 4G) phase distributions in \[17\]). The slow component of inhibition \[55,64–66\] may contribute to the global tonic inhibition level that is present in the OB. This synaptic activity suggests that the effective interaction between MCs is inhibition, and that the OB could be approximately modeled as a network of inhibitory coupled MCs.

Our results raise the question of the origin of gamma oscillatory activity in the OB. Do entrained MCs participate in the creation of this rhythm? If so, how? Two models have been recently proposed \[35,36\]. In \[35\], a network of inhibitory coupled MCs is applied to in vitro recordings, in which the gamma oscillation is continuous and evoked by single stimulation. In \[36\], the particular tendency of MCs to synchronize their firing when their stochastic inputs become correlated was studied. Neither of these models, however, has been shown to induce the spiking activity that we report here. This is also the case for the general mechanisms that have been proposed for oscillation generation in inhibitory \[67–69\] and excitatory-inhibitory networks \[69–71\]. It has to be noted that, in these studies, a large heterogeneity in the population intrinsic firing rates usually prevents the formation of an oscillation, and that the case of a resonant neuron is not considered.

Our results, however, suggest the following two hypotheses. First, if MCs behave like oscillators, a possible mechanism for the emergence of the oscillation may be provided by the transition
towards synchrony, a phenomenon that is generally observed in a network of coupled heterogeneous oscillators [20,72]. Second, the model predicts that intrinsic MC properties (according to Fig. 7D and 0) lead to a maximal entrainment in the gamma frequency range. Indeed, a non resonant neuron (i.e. an integrate-and-fire model) does not exhibit this behavior (data not shown). From this, it can be seen that among the MC population that exhibits quite heterogeneous frequencies (see Fig. 4), MCs firing with intrinsic firing rate in the range of 40–70 Hz are better entrained than MCs firing at lower or higher frequencies. The rhythm could be created when this entrained MC population becomes sufficiently large.

Coding implications

Other studies in anesthetized rats have shown that MCs can be segregated into two populations according to whether they phase-lock to gamma oscillations or to beta oscillations, which is likely due to their position relative to the receptive field of the odor [31]. Here, we show that, among MCs that lock to the gamma oscillation, locking is finely tuned depending on the various conditions that control MC entrainment, one of them being the nature of the odor. A subset of the MC population can therefore be entrained and phase-locked at gamma frequencies with patterns depending on the intrinsic firing rate of the MC, which is similar to the previously described rate-specific synchrony [26]. The resulting phase-locked activity map may overlap with the glomerular activity map. This is suggested by our results, which show that pattern types are partially reproducible for the same cell and the same odor. The glomerular map is likely forwarded to MCs as a “rate code” map that is readable by downstream structures. The phase-locked activity map, however, appears to be more elaborate than the simple glomerular map. In particular, the main characteristic of the phase-locked activity map is that it can be modulated by various parameters: such as the conductance level (Fig. 7), the MC intrinsic firing rate (Figs. 4 and 5), and/or the degree of GC-MC coupling (Fig. 5C). It is therefore likely that this phase-locked activity map is modifiable by plasticity mechanisms and central control [10]. Based on the adjustment of the spike phases, the mechanisms described here would result in population activity that is readable by decoding structures which function as coincidence detectors. Pyramidal cells of the piriform cortex have such detection properties [73]. In addition, synaptic integration by pyramidal dendrites is more sensitive to pattern-like inputs, as shown in other sensory systems [74,75]. Thus, our model of a phase-locked map of MC activity across the OB supports the idea developed by Zou and Buck [76] that pyramidal cells could integrate odorant features using a combination of coincident MC inputs (as argued also in [77]) in a way similar to the mushroom bodies of insects [78,79].

Methods

Ethics Statement

All experiments were performed in accordance with the guidelines of the European Communities Council.

Preparation and recording

Male Wistar rats (150–350 g) obtained from Charles River Labs (L’Arbresle) were anesthetized with urethane (i.p. 1.5 mg/kg, with additional supplements as needed) and placed in a stereotaxic apparatus. The dorsal region of the OB was exposed. Bulbar activity was recorded as a broadband signal (0.1–5 kHz) using 16-channel silicon probes (NeuroNexus Technologies, Ann Arbor, MI) with a homemade, 16-channel DC amplifier. The data were digitally sampled at 10 kHz and acquired on a PC using the IOtech acquisition system (Wavebook, IOtech, Cleveland, OH). Probes were placed in the lateral or medial part of the OB at a depth that maximized the number of channels located in the mitral cell layer (MCL). The respiration signal was recorded using a homemade airflowmeter based on a fast response time thermodilution airflow sensor. Odors were delivered through a dilution olfactometer (440 mL/min). The recording protocol was as follows: 5 s of spontaneous activity, 5 s of odor-evoked activity, and 5 s of post-stimulus activity. Each sampling included stimulation by simple linear aliphatic compounds. The varying features of odorants were either the number of carbons in the main chain (chain length: 5, 6, 7 and 10 C) or the functional group associated with the chain (alcohol, ester, aldehyde or ketone). Additional odors have been used, including isomyl acetate, p-cymene, and eugenol. All odors were delivered in front of the animal’s nose at a fraction of 18,10^-2 of the saturated vapor pressure. The time delay between each odor presentation was at least one minute.

Data processing

Respiratory signal. The signal was processed as previously described [80]. Briefly, respiratory cycles were extracted, and, for each one, the time was converted into a phase that had a value that varied as [−π, 0] for inspiration and as [0, π] for expiration. The transition point between inspiration and expiration (I/E) corresponded to the 0 phase, which was detected as the point where the signal crossed the 0 value and which corresponded to the point where there was no variation in pressure.

LFPs. LFPs were obtained by band-passing the recorded signal at 5–200 Hz. To preserve both time and frequency information, we used a time-frequency representation (TFR) that was based upon continuous wavelet transformations, as previously described [81]. Briefly, the LFP signal was convoluted by complex Morlet’s wavelets [82] with a time resolution of 5 ms and a frequency resolution of 1 Hz. Using a wavelet ridge extraction method coupled with a high time-resolution TFR, each gamma oscillatory epoch of the LFP was extracted using an energy threshold to detect its beginning and end. This procedure allowed a reasonable estimation of the phasic, temporal, and frequency features of these oscillations. The TFRs were normalized to the energy measured during the spontaneous activity in the 5 s before odor presentation.

Spikes. Signals from individual electrodes were amplified (gain 1,000×) and filtered from 300 to 5000 Hz. Multunit activity consisted of a few neurons on each electrode. Spikes were clustered off-line using a semi-manual routine. We chose to use only the units that showed a signal/noise ratio ≥5 and to sort cells according to their spike amplitude. Consequently, the number of units that were retained for analysis was restricted to 1–3 per electrode. This conservative procedure resulted in the analysis of a relatively limited number of units but provided high quality data. Additional details of the method are given in Cenier et al. [31]. Moreover, autocorrelograms of spike trains that belonged to presumed single units confirmed that a refractory period exists and precluded the possibility to have multunit recordings included in our single unit ones. The ISI histogram in Fig. 1E shows this refractory period at the population level.

Spike phases. To study relationships between spike and LFP, these were always recorded from the same electrode, we converted spike times into phases that were computed in cycle units (i.e., the phase increased by one at each cycle) during each LFP gamma oscillation epoch. This change in the time axis allowed the interspike interval (ISI) (respective firing rate) to be measured in cycle units (respective spike per cycle [SpC]). Using
phases instead of time allowed us to discard temporal or frequency irregularities across oscillatory epochs.

Statistics

Phases. For a given ensemble of spikes (N) with relative phases \( \{ \phi_n \}_{n=1...N} \), the phase distribution was represented as a histogram (bin size: 0.02 cycle). To analyze this distribution, we used circular statistics [83]. The mean phase \( \bar{\phi} \) is defined by:

\[
\bar{\phi} = \frac{1}{N} \sum_{n=1}^{N} e^{2\pi i \phi_n}.
\]

The circular standard deviation uses the modulus (\( r \)) of this sum and is given by:

\[
s = \sqrt{-2 \log r}.
\]

The value of \( r \) increases from 0 to 1 as the phase distribution changes from being uniform to sharply peaked.

A Rayleigh uniformity test was used to calculate the probability that the data were uniformly distributed (null hypothesis). Using \( p = e^{-Z} \left(1 + (Z^2 - 1) / 4N - (27Z^4 - 24Z^2 + 76) / 288N^2\right) \), with \( Z = N \cdot s^2 / 3 \), the level of significance for non-uniformity is set at a p-value < 0.001 [83].

Interspike Intervals. The interspike interval (ISI) distribution was compared to the distribution of a random variable process following a gamma distribution that was reconstructed in order to have the same mean and a random refractory period (with a Gaussian distribution that had a mean of 3 ms and the standard deviation at 1 ms), such that the refractory period is sorted each time the sorted ISI falls below the refractory period [84]. In addition, we considered both the instantaneous frequency, which was defined for each spike time as the inverse of the ISI, and the mean firing rate, which was given by the average number of spikes that fell within a time bin of 50 ms. The ISI unit was a cycle of LFP gamma oscillation. When the ISI fell out of the LFP gamma burst, the time reference was the mean cycle of the LFP gamma burst.

Detection and classification of phase patterns

Summary of pattern definition. In this study, our aim was to quantify the different proportions of “phase-locked spike trains” in our experimental data. Therefore, we quantified each category of q:p patterns, where q is number of oscillation cycles and p is number of spikes. For this purpose, we used an automatic detection method to determine the limits that defined a q:p pattern. A scheme of this method is presented in Fig. 9. Briefly, the method consisted of measuring the closeness between experimental spike trains and perfectly phase-locked theoretical q:p patterns. In measuring this closeness, the method took into account two parameters:

1. the relative distance, which was based only on the difference in the number of spikes between the experimental and theoretical spike trains during each oscillation cycle;

2. the phase jitter, which measured how well the experimental spikes were phase-locked (based on their position in the q:p pattern).

An experimental spike train had to fall within strict limits for these two parameters to qualify it as a “q:p phase-locked” pattern (see the next section for additional details about those measures). This method of detection was also used for trains produced by the simulations in Fig. 5. In this case, to optimize pattern detection and minimize random noise in the jitter, we used phase trains lasting 50 cycles (cases without noise) or 100 cycles (cases with noise) in Figs. 7 A–B, while 10-second spike trains were used in Fig. 7C–D and in Fig. 8A simplified and stricter constraint on the distance was set by measuring the firing rate, if this did not exceed 2% of the firing rate of the pattern, and a simplified constraint for jitters was set if the standard deviation of phases of all first spikes of each cycle did not exceed 0.05 cycle, which allowed us to more rapidly detect the edges between locked and unlocked zones.

Details of the method for pattern detection. Each spike train [observed both in the experimental results and model (described later)] was represented as a sequence of spike phases (step 1, Fig. 9). From experimental observations, six types of patterns were described for the q:p categories, which were the p spikes per q cycles (q and p are prime numbers between each other and are chosen among [1 2 3]; 3:1, 2:1, 1:1, 2:3, 1:2, and 1:3. In these patterns, the phases were stable from one period to the next. Each spike train was compared with all the different types of q:p patterns to find the closest one. This comparison occurred in two steps:

First, the distance between the spike train and a theoretical pattern was measured (step 2 Fig. 9). The absolute distance is the number of cycles that differ in the number of spikes. For theoretical patterns with multiple spikes per cycle, the first and last cycles could be cut to best match the experimental spike train. This absolute distance was then normalized by the number of cycles over which the spike train spread to obtain the relative distance, which was comparable across spike trains. Mathematically, this relative distance can be written as:

\[
d = \frac{\sum_{c=1}^{C} (N_{PAexp(c)} - N_{PApat(c)})}{C},
\]

where \( C \) is the total number of oscillation cycles, \( N_{PAexp(c)} \) and \( N_{PApat(c)} \) are the number of spikes during the cycle \( c \) in the experimental and theoretical patterns respectively, and \( \delta \) is the dirac function that equals 1 when both indices are equal.

The relative distance was computed for all types of theoretical patterns, and only the patterns that had a distance \( d < d_{max} \) were further considered in the classification process. For all patterns, \( d_{max} \) was set to 0.33, which corresponded to an allowance of up to less than one-third of the cycles where there could be excess or missing spikes relative to the theoretical pattern.

The selected set of patterns was then submitted to a second round of selection (step 3 and 4 Fig. 9) based on a criterion of phase jitter between the experimental train and each pattern. The estimator of the jitter \( \sigma \) is given in Eqn (4):

\[
\sigma_{jitter} = \sqrt{\frac{1}{(N-K)^{pow}} \sum_{r=1}^{nPA} \left( \frac{\phi_r - \sigma J}{\sigma K} \right)^2},
\]

where \( N \) is the total number of spikes in the train, \( \phi_r \) is the phase of each spike, \( \sigma J \) is the mean phase of the spikes that correspond to position \( J \) in the theoretical pattern cycle (thus it is different for spikes that corresponds to different positions), and \( \sigma K \) is a normalization factor to compensate for patterns with multiple spikes in a single cycle, with \( \sigma K \) equal to the standard deviation of a uniform distribution of a single spike in a 1/K cycle fraction, where \( K \) is the maximal number of spikes in the pattern cycle. The formula is slightly adapted for 2:3 patterns: the denominator N-K...
Figure 9. Method for detection of phase-locked patterns. Step by step description using an example: (1) A spike train taken from experimental recordings is represented with its phases (x-axis, top left) along the successive gamma cycles (y-axis). This train was characterized by the number of spikes in each cycle (left matrix), and we allocated different indexes for spikes in the same cycle in the order in which they appeared in the cycle (right matrix). (2) Independently, a pattern sequence generator created all phase trains that have the same cycle length as the experimental one. In this case, the length was four. Three examples of all these generated pattern sequences are shown as column vectors (theoretical pattern column), each of which is affiliated with a particular pattern (e.g. 1:1, 1:2, 1:3). The absolute distance between experimental spike train and theoretical pattern was measured by summing the result of the equality test over all of the cycles of the train. In terms of spike number, if the spike numbers are identical, then the test result is 0, otherwise it is 1. The relative distance was obtained by dividing the absolute distance by the number of cycles that were covered by the train. At this step, we eliminated the pattern sequences with a relative distance $\geq 0.33$ (e.g. the last line pattern 1:3 example). (3) All of the possible positions were then considered for the spike (index) position of the experimental train in the selected patterns (grid). Single or multiple correspondences are shown for each selected pattern. (4) Based on these positions in the hypothesized pattern, we empirically estimated the mean phase of the pattern from spike positions. For example, in the first plot (top right), the black boxes are the mean phase of spike index 1. A jitter was calculated based on the distance of each spike to the mean phase (distances to the mean phase are marked with arrows in the second plot). This jitter is indicated in the last column. We kept only the pattern with the smallest jitter and considered the original spike train as phase-locked only if this jitter fulfilled the stringent condition ($<0.5$). In this example, the spike train is considered to be a phase-locked 1:1 pattern. (5) We show here some examples of spike trains that were not classified as phase-locked patterns because of their too large distance or too large jitter.

doi:10.1371/journal.pcbi.1000551.g009
takes the value N-3 in order to take into account the degree of liberty that is when phase can vary on 3 different positions and σ₀ changes according to the number of spike in each cycle. The parameter p svc is equal to 1.5 and serves to adjust the formula so that it favors the detection of long trains. The theoretical pattern to be associated with the experimental train was the one with the smallest jitter among those that satisfied the distance constraints given in Eqn (1). If two theoretical patterns showed the same jitter, the one with the smallest distance was selected. The jitter limit was set to 0.5 for the phase-locked patterns. In the presented data, the spike trains that spread over at least three gamma cycles are shown, and the results were similar when spike trains spreading over at least two cycles were also examined. Some examples of residual spike trains are given in the bottom of Fig. 9.

In short, our database consists of 2189 simultaneous recordings of LFP-gamma bursts that are associated with spike trains of various lengths. Other recordings where there were neither spikes nor gamma oscillations were discarded. Among the spike trains, 1210 had strictly more than 1 spike, and 898 spread over at least 3 LFP gamma oscillation cycles. These spike trains were recorded in 143 different mitral cells. Spike train distribution per cell and per odor is provided in Fig. 10A and B, respectively. The pattern study is performed on spike trains that cover at least 3 LFP gamma cycles. Detected pattern distribution over the recorded cell population and tested odor is given in Fig. 10C and D, respectively. Finally, the individual cell contribution to the detected patterns is given in Fig. 10E. The probability of finding the same pattern in an MC response was higher for responses to the same odor than for responses to different odors (see the distribution of these probability differences computed for each cell in Fig. 10F).

Random spike trains. To assess the significance of the phase-locked patterns, we compared our experimentally recorded spike trains to a set of computationally controlled random spike trains. Various methods can be used to draw random spike trains comparable to experimental spike trains. Since we wanted to check the influence of the oscillation on relative spike timings, it was important not to constrain either the interspike intervals nor the spike phase relative to the oscillation, which are some measures that can be influenced by the oscillation. Therefore, we first decided to constrain our model by what appeared to be the measure that was the least contaminated by the oscillation, that is, the mean firing rate of the spike train. For each experimentally observed spike train, we drew and sorted a family of 100 spike trains using a Poisson process with the same mean firing rate but with an imposed minimal interspike interval of 1/4 of an oscillation gamma period, which corresponded to a refractory period of about 4 ms (similar to what is observed experimentally). This refractory period was reset to 0 in the few cases where firing rate of the observed spike train could not allow a refractory period as large as 4 ms. We verified that experimental and random ISI distributions were in good agreement. Each random spike train had the same number of spikes as the experimental one. Finally, the sorting of random spike trains used the same procedure as described for the experimental pattern detection. The number of spike trains generated (100 times the number of experimentally observed spike trains) was sufficient to obtain smooth distributions when compared to experimental ones.

Second, in order to see how the ISI distributions could account for the pattern proportions, instead of sorting random spike trains by the mean firing rate of their equivalent experimental spike trains, we sorted them by their global ISI distribution (see Fig. 1E). This resulted in a pattern proportion of 19%. This suggests that the ISI distribution is part of the formation of patterns. Lastly, we wanted to know whether the phase reference that is imposed by the oscillation could account for the pattern detection. We rephased each random spike train in order to make the mean phase of the spike fall in the trough of the oscillation, as this would happen under experimental conditions. When using the set of spike trains with the same ISI distribution as the experimental spike trains, we detected 25% of patterns instead of the 19% obtained without rephasing. In all cases, the proportion of phase-locked random pattern is below the proportion of experimental ones (31%), which shows that oscillations impose strong constraints on the cell discharges: the ISI distribution, phase preference in the cycle and the order of ISI occurrence.

MC model

The MC model was derived from a previous study [35], which was derived in turn from [35]. The model uses parameters from [86,87]. Its essential features are (1) spiking activity through sodium spikes, (2) bursting activity (Fig. 11A), (3) its current-frequency response (Fig. 11B), (4) resonant properties as revealed...
Figure 11. Methods for comparison of original and reduced MC model. A) Voltage traces of the original 9-variable MC model (left) and the reduced 4-variable MC model (right) are similar in terms of spike timing and subthreshold regime for similar ranges of injected current (in A/m²). B) Subthreshold oscillation frequency (dashed line) and spiking frequency (continuous line) are plotted as a function of the injected current for both 9-variable (grey) and 4-variable (black) models. C) Subthreshold resonance. Resonance frequency extracted from eigenvalues of the system at its resting potential for both 9-variable (grey) and 4-variable (black) models. D) Phase response curve estimated at 40 Hz spiking frequency show that integration properties are similar while both model are spiking (See method for construction). E) Response to oscillatory input. The spike trace (vertical ticks), the oscillatory conductance, and the voltage trace are plotted for the 4-variable without noise (left) and with noise (right)).

doi:10.1371/journal.pcbi.1000551.g011

through sub-threshold oscillations (Fig. 11C), and (5) phase response curve (Fig. 11D). The method to compute the resonance frequency is to linearize the system of dynamical equations around its equilibrium for a given membrane potential and to extract this frequency from the imaginary part of complex eigenvalue $\lambda$ (Imag($\lambda$)/$2\pi$). The method to compute the phase response curve [39] was to impose a small instantaneous voltage deviation along the period of spiking (here equal to 25 ms).

We reduced the number of variables in the model from nine to four by removing each of the variables individually and checking that the simpler model retained the essential features listed above; at the same time, some of the parameters were adjusted as necessary. The main characteristics were preserved as depicted in Fig. 11. The remaining variables were the membrane potential ($V$), the activation ($m_{K_s}$) and the inactivation ($h_{K_s}$) gating variable of the slow potassium current. The dynamics is described in Eqs. 5–8:

\[
C \frac{dV}{dt} = -g_L(V - E_L) - g_{Na}m_{Na}^3 h_{Na}(V - E_{Na}) - g_{K_s}m_{K_s}^2 h_{K_s}(V - E_{K_s}) - g_{K_F}m_{K_F}h_{K_F}(V - E_{K_F}) + I_{syn}
\]

The maximal conductance of the ionic channels was $g_{Na} = 500 \text{ S/m}^2$; $g_{NaP} = 1.1 \text{ S/m}^2$; $g_{K_s} = 310 \text{ e S/m}^2$; $g_{KA} = 100 \text{ S/m}^2$; $g_{K_F} = 100 \text{ S/m}^2$. The leak conductance is $g_L = 0.1 \text{ S/m}^2$. The product $\bar{m}_{K_s} \cdot \bar{h}_{K_F}$ is approximated to 0.004. The reverse ionic potentials are $E_{K} = -70 \text{ mV}$ and $E_{Na} = 45 \text{ mV}$, and the membrane reverse potential is $E_L = -66.5 \text{ mV}$. The membrane capacitance is $0.01 \text{ F/cm}^2$.

Synaptic Inputs

In terms of amplitude, to assess the synaptic inputs that the MCs receive under in vivo conditions, the MC model input resistance was verified to be consistent with the order of magnitude of
synaptic inputs that an MC actually receives. Experimentally, the input resistance of an MC was found to be 115 MΩ [88]. We assumed that a limited part of the total membrane area was responsible for the input resistance and that axial resistance (or intracellular resistivity) was negligible for this neuronal small portion. This portion included the soma and proximal dendrites and corresponded to 10% of the total area or ~13.10^3 μm^2 [98,99] given that, beyond a distance of about 100 μm from the soma on either the primary or secondary dendrite, synaptic inputs are not conveyed to the soma [91]. This experimental “effective” input resistance becomes 1.72 Ω.m^2 when related to the membrane unit area. Our model is consistent with experiments since its input resistance measured at hyperpolarized membrane potential is 1.5 Ω.m^2.

Previous studies have examined the kinetics of signaling to MCs and have found that MCs receive slow [64], fast, and asynchronous or simply fast inhibition from GCs [60]. In [17], it was reported that MCs receive weakly phased inhibition during gamma oscillation. From Fig. 4G of their report, we visually estimated that the amplitude of this phasic inhibition was up to 30%. The preferential phase of this oscillatory inhibition was estimated to be 350±9° of the LFP oscillation, and it showed strong statistical significance (p<10^-8 by the Rayleigh test). Therefore, based on these experimental observations, our model assumes that on average, MCs receive an input current of the form (Eq.9):

$$I_{syn} = (ge + ge(t)\eta(t))(V - E_E) + (gi + gi(t)\eta(t))$$

which is composed of a baseline conductance, including constant excitatory (ge) and inhibitory (gi) conductances, as well as a sinusoidal part, i.e., the oscillating conductance whose amplitude is ge(t) and whose frequency is fi. A white noise component was added to each excitatory and inhibitory component with amplitudes gi and ge(t), respectively, that were chosen to induce noise comparable to what is observed with in vivo intracellular voltage recording [88]. No other source of noise was added. ge(t) and gi are set to zero in Figs. 7 and 8. ge is set to 0.282 S.m^-2.ms^-1/2 in Fig. 7B and 0.141 S.m^-2.ms^-1/2 in Fig. 7D.

The reversal potentials of the excitatory and inhibitory inputs were E_E = 0 mV and E_I = -70 mV, corresponding to the reversal potentials of AMPA/NMDA receptors and GABA_A receptors, respectively.

Inhibitory synaptic inputs can completely stop MC firing activity [30] and reshape the temporal organization of spike trains [60]. It was therefore appropriate for our model to take into account the levels of inhibitory conductance that could have such effects on MC activity. The maximum conductance of a single synaptic input has been estimated to be on the order of 1 nS [92,93]. A single MC has around 10,000 connections with GCs. As mentioned above, only about 10% of these inputs are conveyed to the soma [91], which corresponds to ~1,000 synapses. Such a limited integration of the total synaptic input is consistent with other studies [94,95]. Assuming that an MC receives inhibitory inputs from 1,000 synapses during every gamma cycle (period of ~16 ms) and assuming an exponential time decay of 5 ms for GABA_a [53,60], it can be shown that, during the gamma oscillation, the MC average inhibitory input conductance is given by 1000*1nS*5 ms/16 ms = 312 nS. For the membrane area mentioned above, this represents ge = 20 S/m^2. ge was adapted to reach a frequency up to 200 Hz, as observed in vivo. For example, Fig. 11E shows a voltage trace of the MC model that is forced by the oscillation and that receives tonic excitatory and inhibitory conductances. The amplitude of the oscillatory component gi is discussed in the Results.

Simulations

For a given input, MC activities were measured after at least one second of simulation to avoid transient effects. Euler integration was used with a time step of 0.02 ms. Simulations were performed using Matlab 7.0 (The Mathworks, www.mathworks.com).

Author Contributions

Conceived and designed the experiments: FOD EH NB. Performed the experiments: FOD TC NB. Analyzed the data: FOD EH TC NB. Contributed reagents/materials/analysis tools: FOD EH TC NB. Wrote the paper: FOD EH TC NB.

References

1. Rinberg D, Koulakov A, Gelperin A (2006) Sparse odor coding in awake behaving mice. J Neurosci 26: 8857–8865.
2. Hromadka T, Deweese MR, Zador AM (2008) Sparse representation of sounds in the unanesthetized auditory cortex. PLoS Biol 6: e16.
3. Jacobs AL, Fridman G, Douglas RM, Alam NM, Latham PE, et al. (2009) Ruling out and ruling in neural codes. Proc Natl Acad Sci U S A 106: 5936–5941.
4. Bi GQ, Poo MM (1998) Synaptic modifications in cultured hippocampal neurons: dependence on spike timing, synaptic strength, and postsynaptic cell type. J Neurosci 18: 10464–10472.
5. Cassenaer S, Laurent G (2007) Hebbian STDP in mushroom bodies facilitates learning of odor temporal patterns in the olfactory bulb of the anesthetized rat. Eur J Neurosci 27: 1432–1444.
6. Rodriguez E, George N, Lachaux JP, Martinerie J, Renault B, et al. (1999) Perceiving the phases of the LFP oscillation, and it showed strong statistical significance (p<10^-8 by the Rayleigh test).
7. Fries P, Reynolds JD, Rorie AE, Desimone R (2001) Modulation of oscillatory neuronal synchronization by selective visual attention. Science 291: 1560–1563.
8. Buzsáki G, Czosnyka M,功用 F (2000) Rhythmic sequence through the olfactory bulb layers during the time window of a respiratory cycle. Eur J Neurosci 17: 1811–1819.
9. Czirr T, Amat C, Llado P, Garcia S, Lafaye de Micheaux P, et al. (2008) Odor vapor pressure and quality modulate local field potential oscillatory patterns in the olfactory bulb of the anesthetized rat. Eur J Neurosci 27: 1432–1440.
10. Kay LM (2003) Two species of gamma oscillations in the olfactory bulb: dependence on behavioral state and synaptic interactions. J Integr Neurosci 2: 31–44.
11. Ravel N, Chabaud P, Martin C, Gaveau V, Hugues L, et al. (2003) Oscillatory learning modifies the expression of odor-induced oscillatory responses in the gamma (60–90 Hz) and beta (15–40 Hz) bands in the rat olfactory bulb. Eur J Neurosci 17: 350–358.
12. Wehr M, Laurent G (1996) Odour encoding by temporal sequences of firing in oscillating neural assemblies. Nature 384: 162–166.
13. Friedrich RW, Habermann CJ, Laurent G (2004) Multiplexing using synchrony in the zebrafish olfactory bulb. Nat Neurosci 7: 862–871.
14. Martin C, Gervais R, Hugues E, Messaoudi B, Ravel N (2004) Learning modulation of odor-induced oscillatory responses in the rat olfactory bulb: a correlate of odor recognition? J Neurosci 24: 399–397.
15. Besheh J, Kopell N, Kay LM (2007) Olfactory bulb gamma oscillations are enhanced with task demands. J Neurosci 27: 8358–8365.
16. Eeckman FH, Freeman WF (1990) Correlations between unit firing and EEG in the rabbit olfactory system. Brain Res Rev 15: 159–162.
17. Slaifer S, Carleton A, Ledo PM (2004) Interplay between local GABAergic interneurons and relay neurons generates gamma oscillations in the rat olfactory bulb. J Neurosci 24: 4392–4392.
18. Kashihara H, Sanski YF, Uchida N, Mori K (1999) Synchronized oscillatory discharges of mitral/tufted cells with different molecular receptive ranges in the rabbit olfactory bulb. J Neurophysiol 82: 1786–1792.
19. Kay LM, Besheh J, Brea J, Martin C, Rojas-Libano D, et al. (2009) Olfactory oscillations: the what, how and what for. Trends Neurosci 32: 207–214.
20. Pávko A, Rosenblum M, Kurths J (2001) Synchronization: A Universal Concept in Nonlinear Sciences. Cambridge, MA: Cambridge University Press.
21. Izhikevich E (2007) Dynamical Systems in Neuroscience: The Geometry of Excitability and Bursting; Cambridge, MA: MIT Press, editor.
22. Chaput MA, Buono N, Berthoz A (1999) Temporal Patterns in Spontaneous and Odour-evoked Mitral Cell Discharges Recorded in Anaesthesized Freely Breathing Animals. Eur J Neurosci 4: 813–822.
23. Lesteranne R, Tuckwell HC, Chalazonetou M, Chaput M (1999) Repeating triplets of spikes and oscillations in the mitral cell discharges of freely breathing rats. J Neurosci 11: 3185–3193.
24. Bouvino N, Chaput MA, Berthommier F (1992) Temporal pattern analyses in pairs of neighboring mitral cells. J Neurophysiol 68: 417–424.
25. Rhode WS, Greenberg S (1994) Encoding of amplitude modulation in the cochlear nucleus of the cat. J Neurophysiol 71: 1797–1825.
26. Markowitsa DA, Collman F, Brody CJ, Hopfield JJ, Tank DW (2000) Rate–spike latency patterns: using noisy oscillations to detect equally active neurons. Proc Natl Acad Sci U S A 10: 8422–8427.
27. Neville KR, Haberly LB (2003) Beta and gamma oscillations in the olfactory system of the urethane-anesthetized rat. J Neurophysiol 90: 3921–3930.
28. Martin C, Gervais R, Messascoli B, Ravel N (2006) Learning-induced oscillatory activities correlated to odour recognition: a network approach. Eur J Neurosci 23: 1801–1810.
29. Wesson DW, Donahou TN, Johnson MO, Wachowiak M (2008) Sniffing behavior of mice during performance in odor-guided tasks. Chem Senses 33: 1273–1292.
30. Gire DH, Schoppa NE (2008) Long-term enhancement of synchronized oscillations by adrenergic receptor activation in the olfactory bulb. J Neurophysiol 99: 2021–2025.
31. Genier T, David F, Litaudon P, Garcia S, Amat C, et al. (2009) Respiration-gated formation of gamma and beta neural assemblies in the mammalian olfactory bulb. Eur J Neurosci 29: 921–930.
32. Fourcaud-Trocmé N, Galan RF, Urban NN. Ionic current basis of the typeII transients in inhibitory neurons. J Neurosci 26: 3646–3655.
33. Desmaisons D, Vincent JD, Lledo PM (1999) Control of action potential timing by intrinsic subthreshold oscillations in olfactory bulb output neurons. J Neurosci 19: 10727–10737.
34. Balu R, Larimer P, Strowbridge BW (2004) Phasic stimuli evoke precisely timed spikes in intermitently discharging mitral cells. J Neurophysiol 92: 743–753.
35. Barthélery B, Lagier S, Faure P, Lledo PM (2006) Circuit properties generating gamma oscillations in a network model of the olfactory bulb. J Neurophysiol 95: 2678–2691.
36. Rubin DB, Cleland TA (2006) Dendro-dendritic synaptic signals in olfactory bulb granule cells. J Neurosci 26: 3605–3615.
37. Galan RF, Fourcaud-Trocmé N, Ermentrout GB, Urban NN (2006) Correlation-induced synchronization of oscillations in olfactory bulb neurons. J Neurosci 26: 3600–3604.
38. Brown E, Moehlis J, Holmes P (2004) On the phase reduction and response of a noisy neuron model to subthreshold periodic stimulation. Phys Rev Lett 93: 134101.
39. Magrin C, Gervais R, Messascoli B, Ravel N (2006) The mean discharge frequency locking in the olfactory bulb output neurones of rats. J Physiol 490(Pt 1): 63–77.
40. Parra L, Bikson M (2004) Model of the effect of extracellular fields on spike time resetting curves in real neurons and its significance for neural-network modeling. J Neurophysiol 92: 10647.
41. Galan RF, Ermentrout GB, Urban NN (2005) Efficient estimation of phase–resonance curves in real neurons and its significance for neural-network modeling. Proc Natl Acad Sci U S A 102: 7248–7252.
42. Zou Z, Buck LB (2003) Odor maps in the olfactory cortex. Proc Natl Acad Sci U S A 100: 7274–7279.
43. Bruno RM, Sakmann B (2006) Cortex is driven by weak but synchronously firing neurons with sparse, random connectivity. Neural Comput 15: 509–530.
44. Kuramoto Y (1975) Self-entrainment of a population of coupled non-linear oscillators. IEEE Trans Autom Control 19: 16–22.
45. Borgers C, Kopell N (2003) Synchronization in networks of excitatory and inhibitory spiking neurons. J Comput Neurosci 8: 183–208.
46. Bengio Y (2006) Learning complex patterns with local transformations. J Comput Neurosci 8: 115–130.
47. Wang XJ, Buzsaki G (1996) Gamma oscillation by synaptic inhibition in a model of neurons with recurrent excitation and inhibition. J Neurophysiol 76: 3119–3134.
48. Sompolinsky H, Crisanti A, Galan RF, Torre LA (1998) Dynamics of neural oscillator populations. Neural Comput 10: 1881–1895.
49. Desmaisons D, Vincent JD, Lledo PM (1999) Control of action potential timing by intrinsic subthreshold oscillations in olfactory bulb output neurons. J Neurosci 19: 10727–10737.
50. Coffman AW, McAllister AH, Fries P, Singer W (2005) Can phase precession be a mechanism for rule learning in the hippocampus? Neuron 47: 357–363.
51. Wang XJ, Buzsaki G (1996) Gamma oscillation by synaptic inhibition in a model of neurons with recurrent excitation and inhibition. J Neurophysiol 76: 3119–3134.
52. Zou Z, Buck LB (2003) Combinatorial effects of odorant mixes in olfactory bulb granule cells. J Neurosci 26: 3605–3604.
53. Perez-Orive J, Bazhenov M, Laurent G (2004) Intrinsic and circuit properties of mitral cell ensembles during gamma oscillations in vitro. J Neurosci 24: 6037–6047.
54. Zou Z, Buck LB (2006) Combinatorial effects of odorant mixes in olfactory cortex. Science 311: 1477–1481.
55. Bruno RM, Sakmann B (2006) Cortex is driven by weak but synchronously firing neurons with sparse, random connectivity. Neural Comput 15: 509–530.
56. Kuramoto Y (1975) Self-entrainment of a population of coupled non-linear oscillators. IEEE Trans Autom Control 19: 16–22.
57. Borgers C, Kopell N (2003) Synchronization in networks of excitatory and inhibitory spiking neurons. J Comput Neurosci 8: 183–208.
58. Bengio Y (2006) Learning complex patterns with local transformations. J Comput Neurosci 8: 115–130.
59. Wang XJ, Buzsaki G (1996) Gamma oscillation by synaptic inhibition in a model of neurons with recurrent excitation and inhibition. J Neurophysiol 76: 3119–3134.
60. Sompolinsky H, Crisanti A, Galan RF, Torre LA (1998) Dynamics of neural oscillator populations. Neural Comput 10: 1881–1895.
61. Zou Z, Buck LB (2003) Odor maps in the olfactory cortex. Proc Natl Acad Sci U S A 100: 7274–7279.
62. Bruno RM, Sakmann B (2006) Cortex is driven by weak but synchronously firing neurons with sparse, random connectivity. Neural Comput 15: 509–530.
63. Wang XJ, Buzsaki G (1996) Gamma oscillation by synaptic inhibition in a model of neurons with recurrent excitation and inhibition. J Neurophysiol 76: 3119–3134.
64. Sompolinsky H, Crisanti A, Galan RF, Torre LA (1998) Dynamics of neural oscillator populations. Neural Comput 10: 1881–1895.
65. Zou Z, Buck LB (2003) Combinatorial effects of odorant mixes in olfactory cortex. Science 311: 1477–1481.
66. Franks KM, Isaacson JS (2006) Strong single-fiber sensory inputs to olfactory cortex coding. J Neurophysiol 94: 357–363.
67. Perez-Orive J, Mazor O, Turner GC, Casanova S, Wilson RL, et al. (2002) Oscillations and sparsening of odor representations in the mushroom body. Science 297: 339–363.
68. Brown E, Moehlis J, Holmes P (2004) On the phase reduction and response of a noisy neuron model to subthreshold periodic stimulation. Phys Rev Lett 93: 134101.
69. Zou Z, Buck LB (2006) Combinatorial effects of odorant mixes in olfactory cortex. Science 311: 1477–1481.
70. Franks KM, Isaacson JS (2006) Strong single-fiber sensory inputs to olfactory cortex coding. J Neurophysiol 94: 357–363.
71. Perez-Orive J, Mazor O, Turner GC, Casanova S, Wilson RL, et al. (2002) Oscillations and sparsening of odor representations in the mushroom body. Science 297: 339–363.
72. Perez-Orive J, Mazor O, Turner GC, Casanova S, Wilson RL, et al. (2002) Oscillations and sparsening of odor representations in the mushroom body. Science 297: 339–363.
73. Brown E, Moehlis J, Holmes P (2004) On the phase reduction and response of a noisy neuron model to subthreshold periodic stimulation. Phys Rev Lett 93: 134101.
89. Davison AP, Feng J, Brown D (2000) A reduced compartmental model of the mitral cell for use in network models of the olfactory bulb. Brain Res Bull 51: 393–399.
90. Migliore M, Hines ML, Shepherd GM (2005) The role of distal dendritic gap junctions in synchronization of mitral cell axonal output. J Comput Neurosci 18: 151–161.
91. Lowe G (2002) Inhibition of backpropagating action potentials in mitral cell secondary dendrites. J Neurophysiol 88: 64–85.
92. Isaacson JS (2003) Mechanisms governing dendritic gamma-aminobutyric acid (GABA) release in the rat olfactory bulb. Proc Natl Acad Sci U S A 98: 337–342.
93. Davison AP, Feng J, Brown D (2003) Dendrodendritic inhibition and simulated odor responses in a detailed olfactory bulb network model. J Neurophysiol 90: 1921–1935.
94. Xiong W, Chen WR (2002) Dynamic gating of spike propagation in the mitral cell lateral dendrites. Neuron 34: 115–126.
95. Migliore M, Shepherd GM (2008) Dendritic action potentials connect distributed dendrodendritic microcircuits. J Comput Neurosci 24: 207–221.