Oscillatory Simulation of Mitral and Granule Cell Behavior in the Olfactory Bulb

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Abstract - *This paper presents an oscillatory model of the olfactory bulb. The model involves the two main types of cells in the olfactory bulb, the mitral and granule cells. They are arranged in an array of coupled non-linear oscillators. We simulated the behavior of the bulb in response to different odors as well as to an artificial impulse. This impulse corresponds to a direct stimulation of single glomeruli in the bulb. The model exhibits distinct patterns of oscillation, which are unique for each odor. The observed results resemble experimental observations of the real bulb. In addition we provide a detailed overview of the anatomy of the olfactory bulb and we give reasons why an oscillatory modeling of the olfactory bulb is appropriate.*

Keywords: olfactory bulb, oscillatory neural networks, brain modeling

1. Introduction

What happens, when we experience the variety of scents while wandering through a meadow full of flowers? The sense of smell is one of the richest and most interesting of the human senses.

The olfactory system is close to the periphery of the brain. This vicinity to the environment made it a popular target for many studies on the information processing in the brain. The olfactory system is phylogenetically very old and occupies a large part of the brain in species like e.g. the rat or the tiger salamander. This indicates that it may have served as a precursor for higher parts of the brain. Therefore understanding the behavior of the olfactory system might even help us to understand how other parts of the brain work.

Our intention is to model and simulate the dynamic behavior of an important part of the olfactory system, the olfactory bulb. Many studies on the process of transduction in the olfactory sensory neurons or on the properties of the different cells in the bulb and their connections (e.g. the reciprocal dendrodentritic synapses between the mitral and granule cells) gave us insights into the excitatory and inhibitory mechanisms of odor processing. However it is still a major task to create a mathematical model of the dynamics in the olfactory bulb. Olfactory EEG and other methods have revealed that oscillation and chaos play important roles in the processing of olfactory information [1]. Our model therefore consists of an array of coupled nonlinear oscillators, which resemble groups of mitral and

granule cells in the bulb. The purpose is to simulate the dynamic behavior of the olfactory bulb in a biologically plausible way.

2. Biological facts

The main parts of the mammalian olfactory pathway are the epithelium, the main olfactory bulbs, one for each side, and the olfactory cortex. The olfactory bulb (*bulbus olfactorius*) appears to be structured in a laminar way. The most important distinguishable layers in this architecture are called olfactory nerve layer, glomerular layer, external plexiform layer, mitral cell layer, internal plexiform layer, granule cell layer and the olfactory lateral tract [2].

The sensory neurons (~5 millions in humans) are located in the epithelium, which can be found in the upper part of the nasal cavity [3]. The odor molecules cause the receptor neurons to depolarize, which increases their firing rate. This process is called transduction. Several different theories exist about how that process works in detail [4]. Although each receptor neuron expresses only one type of receptor, it responds to a range of different odor molecules [5]. This implies a vector coding of odors. There are four areas of receptor gene expression on the epithelium [6]. This organization constitutes a so-called odotope map. Even though the expression of receptors is restricted to these areas, neurons expressing a particular type of receptor can be found randomly within these areas. Each sensory neuron projects an unmyelinated axon to the main olfactory bulb. Those axons compose the olfactory nerve layer (*nervus olfactorius*).

The axons of receptor neurons expressing the same kind of receptor type exhibit a strong convergence onto one (or only a few) glomerulus in the glomerular layer of the olfactory bulb [7]. This convergence is retained in spite of the continuous turnover of the sensory neurons. Located in the glomerular layer are about 3000 spherical shaped glomeruli. There, the sensory axons make excitatory synapses with mitral/tufted cells and periglomerular cells. The cell bodies (*somae*) of the mitral cells are located in the mitral cell layer, whereas those of the tufted cells mostly reside in the external plexiform layer. The mitral and tufted cells are also called principal cells, because they are the only cells, which project axons to areas outside the olfactory bulb. Each of these principal cells projects one primary dendrite to a single glomerulus. There are about 26 mitral/tufted cells per glomerulus. The periglomerular cells are supposed to be interneurons, which provide a lateral inhibition between the mitral/tufted cells. The mitral/tufted cells also have secondary dendrites, which extend parallel to the bulbar surface into the external plexiform layer, where they make dendrodentritic reciprocal synapses with anaxonic cells, called granule cells. The somae of those granule cells reside in the granule cell layer. The number of granule cells is much higher than that of the mitral/tufted cells (about 200 granule cells per mitral/tufted cells). The mitral/tufted-to-granule-cell part of the synapse is excitatory, whereas the granule-to-mitral/tufted-cell part of the synapse is inhibitory. Therefore the granule cells are like the periglomerular cells supposed to be local interneurons, which are responsible for the lateral inhibition of mitral/tufted cells, which correspond to neighboring glomeruli. Granule cells are also capable of gradual excitation, that means that only parts of their dendritic trees can be excited, thus defining subsets of closely located mitral/tufted cells [2].

The mitral/tufted cells provide the only output of the main olfactory bulb. Their axons form the olfactory lateral tract (*tractus olfactorius*), which extends to the olfactory cortex (piriform or prepyriform cortex). The axons of the mitral/tufted cells also develop collaterals at the level of the granule cell layer [2]. Those side-branches terminate at granule cells, thereby providing another excitatory input for the granule cells.

The olfactory bulb receives not only input from the sensory neurons, but also from higher parts of the brain through centrifugal afferent pathways. Those pathways initiate in the olfactory cortex and the anterior commissure [2] and terminate mostly on the granule cells. The granule cells are therefore believed to have a modulatory effect on the whole bulb.

3. Simulation consideration

Models of information processing in the olfactory bulb should be simple enough to be analyzed mathematically, but should also be as close as possible to the biological findings. The

main task is to bridge this gap. Besides several models of single neurons in the olfactory pathway [8][9] and models of microcircuits in the olfactory bulb [10], there exist a few models, which focus on modeling the behavior of the bulb on a higher level. Some of them also include the olfactory cortex.

Our object of research is a modification of the model of Li and Hopfield [11]. This model involves the two main types of neurons in the olfactory bulb: the mitral and granule cells. The glomerular layer is neglected. The input of the model consists of a vector, whose components are composed of the background activity of the sensory neurons, the odor input and gaussian noise. The odor input varies in time according to the sniff cycle. Only the excitatory mitral cells receive this sensory input. They are connected to inhibitory granule cells within a circular architecture, which is an abstraction of the spherical architecture in the real bulb. The granule cells are capable of lateral inhibition of the mitral cells. The mitral and granule cells form an array of non-linear coupled oscillators. The granule cells also receive input from the centrifugal afferent pathway, which can modulate the oscillations in the bulb. The bulb exhibits oscillations, which are coherent over the entire bulb, but vary in amplitude and phase dependent on the actual input of the sensory neurons [11].

4. Oscillatory arguments

The olfactory system was one of the first parts of the brain, in which rhythmic activity of populations of neurons was studied. The olfactory bulb exhibits oscillations, which are coherent over the entire bulb, but can vary in amplitude and phase at different locations. These oscillations are coupled to the respiratory or sniff cycle of the animal [12]. There is a tendency towards increased amplitudes and frequency, while an odor is perceived at the inhalation phase. This burst of activity can last until shortly after the exhalation phase has started. Simultaneous EEG recordings at different parts of the olfactory bulb in rabbits [12] have shown that a distinct pattern of amplitude is characteristic for each odor. Freeman also discovered the chaotic character of these oscillations. Activity becomes more ordered, while odor input is present. This leads to the suggestion that odors may be represented

in the olfactory bulb by limit cycle attractors of neural activity.

The model we consider involves excitatory mitral and inhibitory granule cells, which together form a non-linear oscillator. Several of these oscillators are coupled within a biologically plausible architecture. The system is therefore able to exhibit complex oscillatory behavior, which resembles the behavior of the real olfactory bulb.

4.1 Spiking neurons

Another possibility to model the olfactory bulb is to use the so-called spiking neuron networks. Several authors have proposed models of spiking neuron networks [13]. These models involve single neurons, which have as output discrete spikes rather than continuous real values. These discrete spikes are then integrated by the post-synaptic neurons over the time. The real valued output of conventional artificial neurons is an abstraction of the firing rate of the biological neurons. The spiking neuron networks were developed to explain certain biological phenomena, which could not be explained within the conventional models. It is proven that they have at least the computational power of the conventional models and are able to perform even better in some cases. However, there are several reasons why we propose an oscillatory model instead of a spiking neuron model of the olfactory bulb. The majority of neurons in the bulb are granule cells, which are anaxonic. Instead of propagating their output via axonic spikes they effect the post-synaptic neurons through gradual excitation. Therefore it seems to be appropriate to model only the mitral/tufted cells with spiking neurons. Furthermore a lot of experience has been gained with the conventional real valued networks, whereas the research on spiking neuron networks is still in development. It is yet unclear how the information should be encoded (e.g. interval between spikes). In addition there is only insufficient experimental data. To validate such a model one needs simultaneous recordings of spike trains, which are accurate enough in terms of time. The oscillatory model on the other hand is sufficient to explain various biological findings and is simple enough to be analyzed mathematically. Future biological results will show if and how it is necessary to increase the

degree of neural detail in order to describe the biological example in a better way.

5. Model architecture and mathematical basis

Single artificial mitral and granule cells in our model are abstractions of populations of corresponding cells in the real bulb. Experiments with masses of olfactory cells have shown [1], that the cell behavior can be approximated by sigmoid functions. We used two different sigmoid functions (f_{mitral} and $f_{granule}$) as output functions for the mitral and the granule cells respectively, according to their different biological properties. Figure 1 shows the non-linear output function for the granule cells.
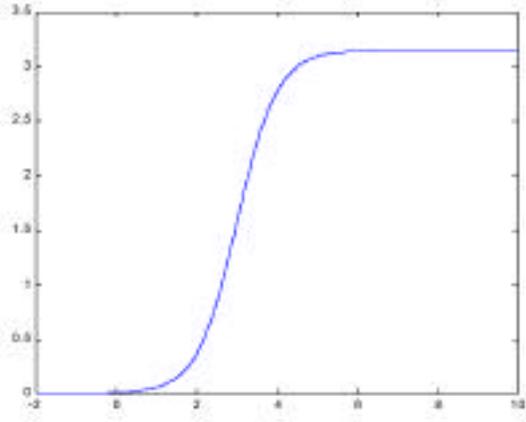

Figure 1 Granule cell output function

The mitral and granule cells are connected within a circular architecture. Each mitral cell is connected to neighboring granule cells, as is each granule cell to neighboring mitral cells. There are no connections between mitral cells or between granule cells. Nevertheless there is a lateral inhibitory effect between mitral cells mediated by the granule cells. The behavior of the mitral and granule cells is determined by the first-order differential equations (Eq.1) [11].

$$\frac{\partial x}{\partial t} = m \times f_{granule}(y) - \alpha_{mitral}x + e(t)$$

$$\frac{\partial y}{\partial t} = g \times f_{mitral}(x) - \alpha_{granule}y + c(t) \tag{1}$$

x and y are the activation vectors of the mitral

and granule cells respectively. g and m denote the connection strengths. α_{mitral} and $\alpha_{granule}$ are time constants of the mitral and granule cells. $e(t)$ and $c(t)$ are the sensory input to the mitral cells and the centrifugal input to the granule cells respectively. Granule cells have an inhibitory effect on mitral cells. Therefore the connection strengths of connections from granule to mitral cells are negative. Those from mitral to granule cells are positive, because of the excitatory character of mitral cells.

An isolated pair of directly neighbored mitral and granule cells represents a damped non-linear oscillator. This non-linear oscillator can be approximated for small amplitudes by a damped sinusoidal oscillator (Eq.2) [11].

$$\frac{\partial x}{\partial t} = m \times f_{granule}(y_0)y - \alpha_{mitral}x$$

$$\frac{\partial y}{\partial t} = g \times f_{mitral}(x_0)x - \alpha_{granule}y \tag{2}$$

The values of x_0 and y_0 are determined by the sensory input and the centrifugal input to the system and represent the oscillation center, around which the linearization has been made. x and y denote now the deviation from x_0 and y_0. The solution becomes (Eq.3) [11].

$$x = r_0 e^{-\alpha t}\sin(\omega t + \phi) \tag{3}$$

with

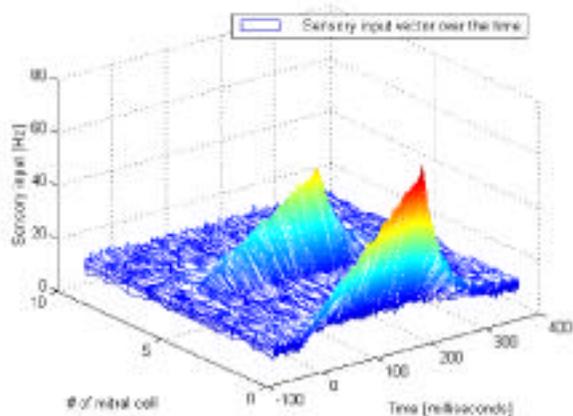$$\alpha = (\alpha_{mitral} + \alpha_{granule})/ 2$$

and

$$\omega = \left[-gmf_{mitral}(x_0)f_{granule}(y_0) + \frac{(\alpha_{mitral} - \alpha_{granule})^2}{4}\right]^{1/2}$$

Several of these single non-linear damped oscillators are coupled in the model. This array of oscillators provides the medium for the patterns of oscillation the model displays in response to simulated odor input.
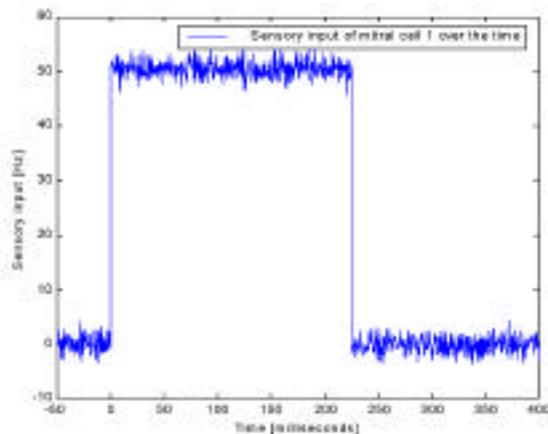
6. Simulation results

We present in this paper the results for two different types of input to the model. The first input corresponds to a whole breath cycle [11]. After the inhalation has started the firing frequency of the sensory neurons, which are sensitive to this odor, increases approximately linearly as does the concentration of odor molecules in the nasal mucous membrane.

During exhalation the frequency drops exponentially, until it reaches the level of spontaneous activity of the sensory neurons (Figure 2.a). The second input corresponds to an artificial impulse (Figure 2.b). Such an input to the mitral cells can be achieved by direct stimulation of single glomeruli or even single mitral cells with electrodes or patch-clamps. Schoppa et al. have investigated how the behavior of the real bulb in response to such impulses is determined by different receptors [14]. All computer simulations were done on a PC with MATLAB® ver. 5.3[1] .

a)

b)

Figure 2 Types of sensory input: a) sensory input vector over one breath cycle; b) direct stimulation of one glomerulus

We added gaussian noise to both types of input. However, computer simulations have shown, that the dynamic behavior of the model

is stable under the influence of noise, e.g. the emerging patterns of oscillation do not change, when different noise is present. The progression of the activation of the mitral and granule cells is different for different inputs. In particular the bulb responses to different odor input with spatio-temporal activation patterns, which are unique for each simulated odor. The bulb can classify different odors. Figure 4 shows the unfiltered signals of activation of the granule cells over the period of a whole breath cycle in response to a particular simulated odor. After inhalation has started a burst of oscillatory activity emerges. The specific pattern of oscillation, which is exhibited by the bulb model, is coherent over the whole bulb.

We calculated a simulated EEG based on the activation vector of the granule cells. The simulated EEG also exhibits a burst of oscillatory activity during inhalation. The oscillation rides on the slow respiratory background wave as can be seen in Figure 3. The shape of the simulated EEG is very similar to experimental results of the real bulb [1].

Figure 5 shows the activation of a single mitral cell under the influence of a direct stimulation of the glomerulus corresponding to that mitral cell. The activation drops to a low value right after the artificial impulse. This is caused by lateral inhibition mediated trough neighboring granule cells. Then it rises exponentially until it reaches the initial value representing a state of zero odor input. Experiments made with slices of the olfactory bulb of mice have shown a qualitatively similar behavior of the real bulb [14] in response to direct stimulation of single glomeruli.
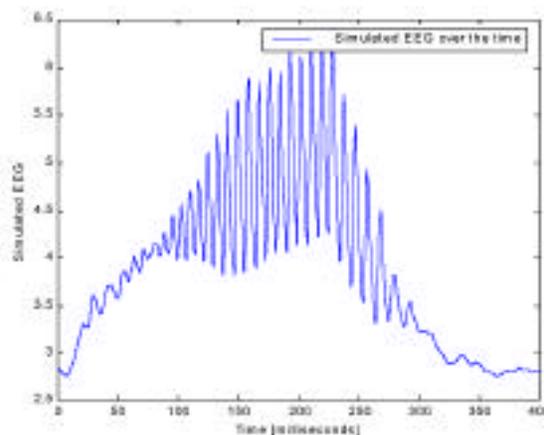

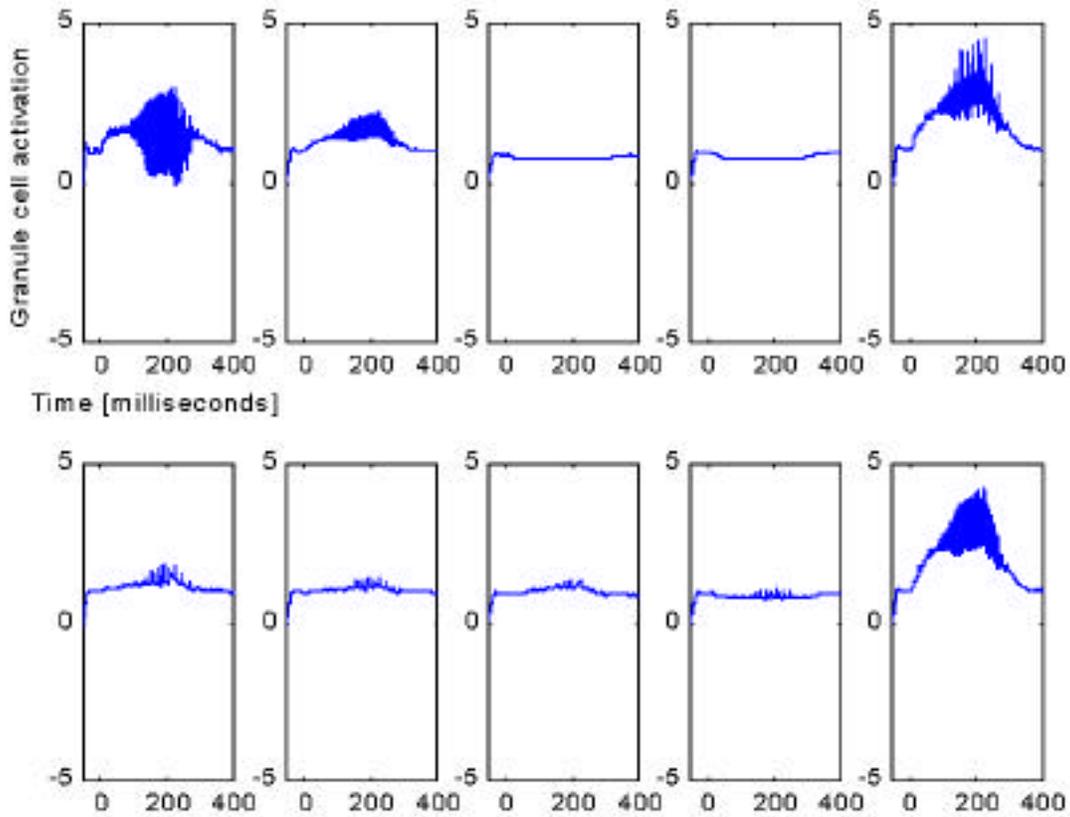Figure 3 Simulated EEG over one breath cycle

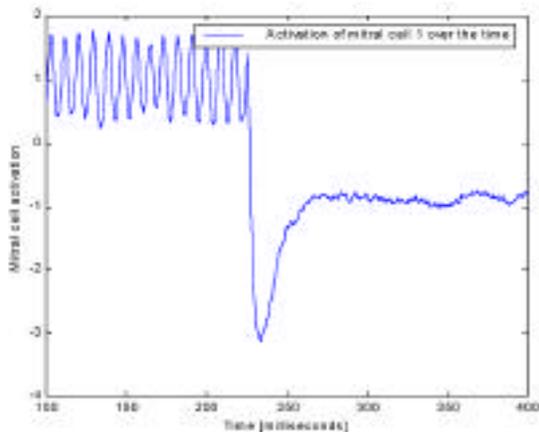Figure 4 Granule cell activation over one respiratory cycle

Figure 5 Single mitral cell activation in response to a direct stimulation of a single glomerulus

7. Conclusions

We simulated the dynamic behavior of the olfactory bulb with an oscillatory model, which is a modification of the model in [11]. We present several reasons why we think that an oscillatory modeling of the olfactory bulb is appropriate. The model involves the two main types of cells in the olfactory bulb, the mitral and granule cells. They together compose an array of coupled non-linear oscillators. The model exhibits a behavior, which is stable under the influence of noise. A distinct spatio-temporal pattern of activation emerges for each simulated odor. The observed results resemble experimental results very closely. In addition we simulated an impulse to the system, which corresponds to a direct stimulation of single glomeruli with electrodes. The behavior of the simulated bulb in response to that input was qualitatively similar to observations of the real bulb. Even though the oscillatory model we used operates on a high level of abstraction and various neural details are neglected it can display dynamic behavior resembling experimental results. As a point of future development incorporating more biological details can

enhance the model, so that its results can be compared to experimental results taken from separate cells with e.g. patch-clamp methods.

8. References

[1] Freeman W.J.: Simulation of chaotic EEG patterns with a dynamic model of the olfactory system. Biol. Cybern., Vol. 56, pp. 139-150, 1987

[2] Mori K.: Membrane and synaptic properties of identified neurons in the olfactory bulb. Progress in Neurobiology, Vol. 29, pp. 275-320, 1987

[3] Schmidt R.F.: Neuro- und Sinnesphysiologie. Springer-Verlag Berlin Heidelberg, 1998

[4] Jacob T.: Olfaction and mind. http://www.cf.ac.uk/uwcc/momed/jacob/research/olfmind1.html

[5] Mori K.: Relation of chemical structure to specificity of response in olfactory glomeruli. Current Opinion in Neurobiology, Vol. 5, pp. 467-474, 1995

[6] Chao S. K.: Review: Molecular analysis of sensory processing in the olfactory system. P&S Medical Review, Vol. 3, No.1, December 1995

[7] Keverne E.B.: Olfactory learning. Current Opinion in Neurobiology, Vol. 5, pp. 482-488, 1995

[8] Bhalla U.S. and Bower J.M.: Exploring parameter space in detailed single neuron models: Simulations of the mitral and granule cells of the olfactory bulb. Journal of Neurophysiology, Vol. 69, pp. 1948-1965, 1993

[9] Woolf T.B., Shepherd G.M. and Greer C.A.: Local information processing in dendritic trees: Subsets of Spines in granule cells of the mammalian olfactory bulb. The Journal of Neuroscience 11(6), pp. 1837-1854, June 1991

[10] Aradi I. and Erdi P.: Multicompartmental modeling of neural circuits in the olfactory bulb. Int. J. Neural Systems, 7 (519-527), 1996

[11] Li Z. and Hopfield J.J.: Modeling the olfactory bulb and its neural oscillatory processings. Biol. Cybern., Vol. 61, pp. 379-392, 1989

[12] Freeman W.J.: The physiology of perception. Scientific American, Vol. 264, (2) pp. 78-85, 1991

[13] Maass W.: Networks of spiking neurons: The third generation of neural networks. Neural Networks, Vol. 10, No. 9, pp. 1659-1671, 1997

[14] Schoppa N.E., Kinzie J.M., Sahara Y., Segerson T.P. and Westbrook G.L.: Dendrodentritic inhibition in the olfactory bulb is driven by NMDA receptors. The Journal of Neuroscience 18(17), pp. 6790-68, September 1998