Prediction of Odor Perception Characteristics from Glomerular Activity Patterns Using a Neural Network Model of the Olfactory System

Zu Soh, Toshio Tsuji, Noboru Takiguchi, Hisao Ohtake *

Abstract—**Recently, the importance of odors and methods for their evaluation have seen increased emphasis, especially in the fragrance and food industries. Although odors can be characterized by their odorant components, their chemical information cannot be directly related to odor qualities. Biological research has revealed that neural activity evoked on the glomeruli (which form part of the olfactory system) is closely connected to odor qualities. In this paper, we report on a neural network model of the olfactory system that can predict glomerular activity and odor qualities from odorant molecule structures. We also report on the learning and prediction abilities of the proposed model.**

Keywords: glomerular activity prediction, odor qualities, olfactory system, neural network model

1 Introduction

Recent research has revealed that odors affect human memory and emotion [1] in addition to enriching our lives. This places increased importance on the process of odor sensory evaluation employed in the fragrance, food and beverage industries. As odors are complex mixtures composed of hundreds of odorants, the main purpose of the sensory evaluation process is to find key odorant molecules in the target odor. The approach proposed by Grosch [2] allows efficient performance of this task by introducing a gas-chromatography system in the sensory evaluation process. This system decomposes the odorants in an odor into time space and sends the decomposed results in real time to a human panel, which then judges the odor qualities of each odorant as well as its impact. However, any sensory evaluation method carries problems related not only to consistency across human panels but also to unstable factors within such panels, including sensory fatigue or variations in health condition. These factors make the sensory evaluation protocol complex and time-consuming. A prospective solution for this problem would be to build a model of the olfactory system based on biological insight to serve as a tool for the simulation of information processing in the olfactory system that allows the prediction of odor qualities.

The most important information directly related to odor qualities is considered to be neural activity on glomeruli that are distributed over the surface of the olfactory bulb, which forms part of the olfactory system [3]. Because the evoked activity is odor-specific, it is considered that odor qualities can be predicted from glomerular activity [4].

In this paper, we report on a neural network model of the olfactory system designed to enable prediction of glomerular activity from the structure of odorant molecules. The model consists of two parts: the glomerular activity prediction part predicts neural activity evoked on the glomeruli, while the olfactory bulb part predicts the perceptual characteristics of odors by simulating the function of the olfactory bulb. Since glomerular activity data on humans are not available, the model described in this paper focused on predicting those of rats. The database used can be found online [5], and provides glomerular activity patterns measured from more than 300 different odorants. Although glomerular activity in humans and rats is different, the structure of the proposed model is irrelevant to such differences. Accordingly, it can be applied to the prediction of human activity once a dataset is provided.

To validate the model, we compared the simulation results with those of odor discrimination experimentation involving mice. Although the measurement results revealed differences in glomerular activity patterns between mice and rats [6], it is expected that these differences can be absorbed by the parameter settings of the model.

2 Biological Facts

This section briefly explains basic biological facts regarding the olfactory system, and outlines the odor discrimination experiment involving mice.

*This work was partially supported by a Grant-in-Aid for Scientific Research (21-9124) from the Research Fellow-ships of the Japan Society for the Promotion of Science (JSPS) for Young Scientists, and Grant-in-Aid for Scientific Research on Innovative Areas (20115010). The authors thank Dr.Kashima for providing the calculation program of graph kernel function. The date of the manuscript submission: 6th Nov. Zu Soh and Toshio Tsuji are with the Graduate School of Engineering, Hiroshima University, Japan. Noboru Takiguchi is with the Graduate School of Natural Science and Technology, Kanazawa University, Ishikawa, Japan. Hisao Ohtake is with the Graduate School of Engineering, Osaka University, Osaka, Japan.

ISBN: 978-988-17012-8-2
ISSN: 2078-0958 (Print); ISSN: 2078-0966 (Online)

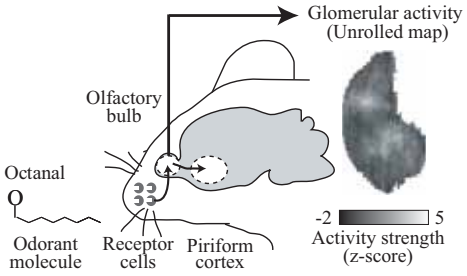


Figure 1: The olfactory system.

2.1 Olfactory System

Figure 1 shows the basic structure of the olfactory system of mice, which consists of three parts: receptor neurons, the olfactory bulb and the piriform cortex. Receptor neurons are distributed on the surface of the nasal chamber, expressing single receptor protein from among thousands of different varieties [7]; each neuron is activated by a specific group of odorants and send signals to the olfactory bulb.

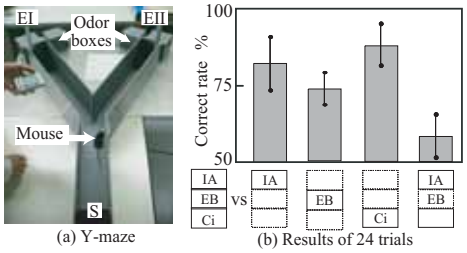
The olfactory bulb mainly consists of glomeruli, mitral cells and granular cells. The glomerulus, which is distributed over the surface of the olfactory bulb, is a round cluster of axon terminals accumulated from receptor neurons. The activity patterns evoked on glomeruli are odor-specific [3] and related to odor qualities [4]. These activity patterns have been revealed only recently, and a database on them is provided online [5].

A mitral cell is an excitatory neuron that receives the output from a glomerulus. These cells are interconnected by excitatory synapses and also excite granular cells, which are inhibitory neurons that then send inhibitory signals back to the mitral cells. Although mitral cells and granular cells appear to form complex connections, recent research has suggested that they form a center on-off surround circuit in which neighboring mitral cells excite each other but distant ones inhibit each other [8].

2.2 Odor Discrimination Experiment on Mice

Nakamura *et al.* conducted a series of odor discrimination experiments involving mice [9]. Since similarities between target odors raise the difficulty of discrimination, the discrimination rate obtained from this experiment can be used as a metric for perception characteristics.

The experiment is started by placing a mouse at point S and training it to select a reward odor that emanates either from end E1 or E2 as shown in Fig. 2 (a). Here, the reward odor was composed of three types of odorants such as [IA EB Ci]. The trained mice are then required to discriminate the reward odor from other odors that share common odorants with it. Figure 2 (b) illustrates the results of an odor discrimination experiment involving ten mice; it shows a perceptual characteristic whereby most of the mice had difficulty in discriminating [IA EB] from [IA EB Ci], suggesting that both odors are very similar.



(a) Y-maze (b) Results of 24 trials

Figure 2: Odor discrimination experiments involving mice.

3 The Proposed Model

The proposed neural network model consists of a glomerular activity prediction part and an olfactory bulb part, as shown in Fig. 3. Input data for the model is provided by a graphical molecular structure. Each odorant molecule included in an odor is converted into a glomerular activity pattern by the glomerular activity prediction part. The olfactory bulb part then mixes the predicted activity patterns and performs generalization and feature extraction. Finally, the differences between the activity patterns of the olfactory bulb are calculated, and the calculated differences are considered as a metric for the perceptual characteristics. This section describes the structure of the model and the proposed learning algorithm for parameter determination.

3.1 Model Structure

3.1.1 The Glomerular Activity Prediction Part

We assumed that glomerular activity could be expressed by a summation of Gaussian functions whose parameters were modulated by molecular structure. Under this assumption, a Gaussian mixture function model for glomerular activity prediction is proposed. The glomerular activity prediction part consists of a receptor layer, two hidden layers, a Gaussian layer and an activity pattern layer. Here, we describe the processes in each layer.

Receptor layer

The receptor layer consists of M units of receptor models described by graph kernel functions [10]. The graph kernel method provides metrics of similarity between two labeled graphs by calculating the probability of correspondence for partial structures. Because actual receptor neurons are considered to selectively respond to structurally similar odorants, a representative odorant is defined as a pseudo receptor. Consequently, the graph kernel function with a representative odorant assigned serves as a receptor model. The strength of the receptor model's response depends on the graph kernel value as calculated using the following equation:

$$K(\tilde{G}_m, G_q) = \sum_{h_m \in V_m} \sum_{h_q \in h_q} p(h_m|\tilde{G}_m) p(h_q|G_q) K_L(b(h_m), b(h_q)), \quad (1)$$

where $\tilde{G}_m$ and G_q are the representative odorant and the input odorant in the labeled graph representation, $p(h_m|\tilde{G}_m)$ and $p(h_q|G_q)$ are the probabilities of occur-

ISBN: 978-988-17012-8-2
ISSN: 2078-0958 (Print); ISSN: 2078-0966 (Online)

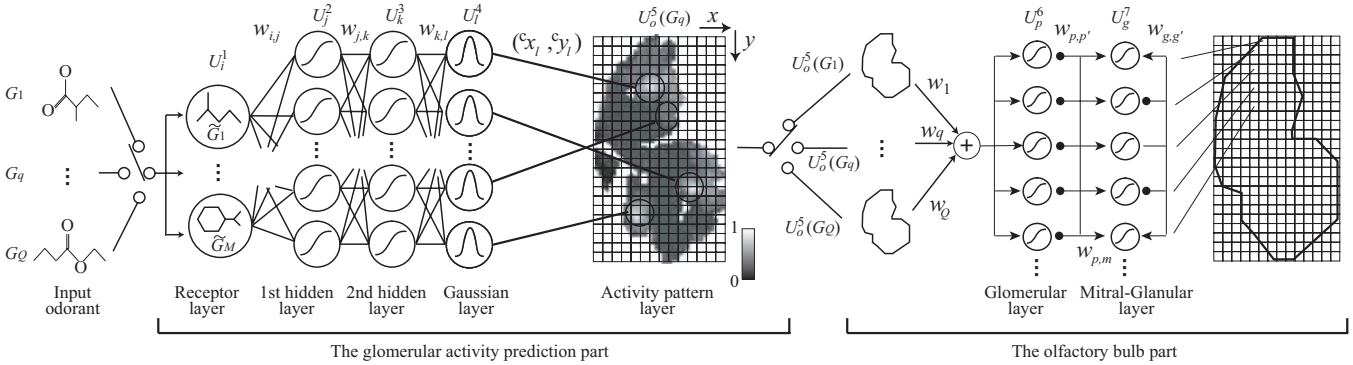


Figure 3: The structure of the proposed olfactory system model.

rence for paths h_m and h_q, and $K_L(b(h_m), b(h_q))$ is a function that calculates the correspondence of the label of h_m and h_i.

The output of the receptor unit U^1_m is a normalized graph kernel value defined as:

$$U^1_m = \frac{K(\tilde{G}_m, G_q)}{\sqrt{K(\tilde{G}_m, \tilde{G}_m)K(G_q, G_q)}}. \quad (2)$$

Hidden layers

The hidden layers are a classical feed-forward neural network model that converts the input from the receptor layer into the strength of the activity at the connected region on the glomerular layer. Each of the two hidden layers consists of MN sigmoidal function units. Here, N is the value of the Gaussian function that is assumed to approximate the major glomerular activity evoked by the representative odorant. The outputs of the hidden layers are given by the following equations:

$$U^h_j = \frac{1}{1 + \exp\{-a(\sum_m w_{mj} U^{h-1}_m - \theta)\}} \quad (h \in 2, 3), \quad (3)$$

where h is the layer number, and a and θ are the gain and threshold constant of the sigmoidal function, respectively.

Gaussian and activity pattern layers

The outputs of the hidden layers are input to the Gaussian layer through connective weights w_{kl}, and generate glomerular activity strength according to the following equation:

$$U^4_{l,(x,y)} = \sum_k w_{ki} U^3_k \exp\{-\alpha(x_{c,l} - x)^2 - \beta(y_{c,l}, y)^2\}, \quad (4)$$

where $(x_{c,l}, y_{c,l})$ denotes the center coordinates on the activity pattern layer to which a Gaussian unit is connected, and the parameters α and β control the width of the Gaussian curve.

The activity pattern layer consists of 1,805 linear function units allocated at each coordinate (x, y). The units add up the input from the Gaussian layer according to the following equation:

$$U^5_{o,(x,y)}(G_q) = \sum_l U^4_{l,(x,y)}. \quad (5)$$

Consequently, the glomerular layer allows prediction of glomerular activity $U^5_{o,(x,y)}(G_q)$ of an input odorant G_q. Although the number of linear units is determined based on the order of the actual number of glomeruli, it should be noted that each linear unit does not correspond to actual glomeruli, and we do not intend to predict the activity of each glomerulus.

3.1.2 The Olfactory Bulb Part

The olfactory bulb part consists of the glomerular layer and the mitral-granular layer. This part predicts odor similarities from the activity patterns evoked on the mitral-granular layer. The predicted odor similarity can be considered as the counterpart of the discrimination rate obtained from the odor discrimination experiments.

Input to the glomerular layer

The input of the glomerular layer is a weighted summation of the glomerular activities evoked by all odorants contained in an inputted odor. Each activity is predicted separately using the glomerular activity prediction part. Supposing an odor which is composed of odorants $[G_1, \cdots, G_q, \cdots, G_Q]$, the input is described as the following equation:

$$u^6_p = \sum_q w_q U^5_{o,(x,y)}(G_q), \quad (6)$$

where $U^5_{o,(x,y)}(G_q)$ is the activity pattern evoked by the odorant G_q.

The glomerular layer

The glomerular layer includes P Grossberg's neuron models described by the following equation [11]:

$$\frac{dU^6_p}{dt} = \tau U^6_p + (\zeta - U^6_p)u^6_p - U^6_p \sum_{p'(p \neq p')} w_{p,p'} u^6_{p'}, \quad (7)$$

where τ is the time constant, ζ is the saturation constant, and $w_{p,p'} < 0$ represents the inhibitory connective weights in the glomerular layer. If the neuron models are fully connected to each other with the same strength

ISBN: 978-988-17012-8-2
ISSN: 2078-0958 (Print); ISSN: 2078-0966 (Online)

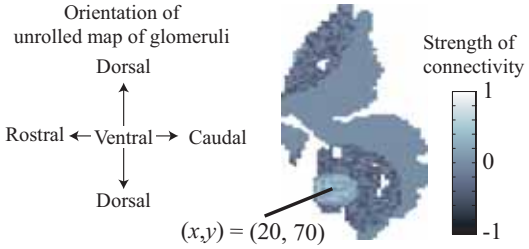


Figure 4: Connective weights $W_{g,g'}$ distribution originated from $(x, y) = (20, 70)$.

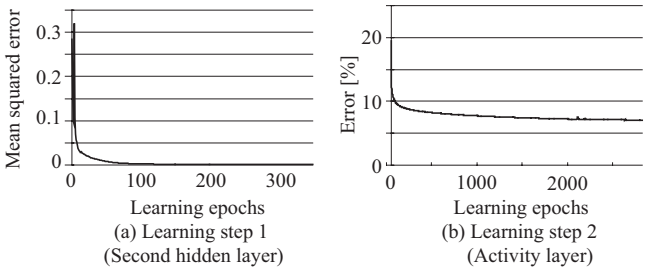


Figure 5: The learning curves.

(except to themselves), then the output of this layer will converge to the following state [11]:

$$U_p^6 = \frac{\zeta u_p^6}{\tau + \sum_{p'(p \neq p')} w_{p,p'} u_{p'}^6}. \tag{8}$$

When ζ is 1 and τ is small enough, the output of a neuron model becomes the division of input to the pth neuron and the sum of inputs to all neurons, i.e., the input to each neuron is normalized by the total strength of inputs to the glomerular layer.

The mitral-granular layer

The mitral-granular layer consists of sigmoidal neuron models. The neuron models in this layer have mutual connections in a center on-off surround manner: nearby neurons connect with excitatory connections ($w_{gg'} > 0$), and distant ones connect with inhibitory connections ($w_{gg'} < 0$). The neuron model is defined by:

$$\frac{du_g^7}{dt} = \tau u_g^7 + U_p^6 + \sum_{g'} w_{gg'} u_{g'}^7, \tag{9}$$

$$U_g^7 = \frac{1}{1 + \exp\{-a(u_g^7 - \theta)\}}, \tag{10}$$

where u_g^7 is an internal state, U_g^7 is the output of the neuron model, and U_p^6 is the input from a Grossberg's neuron model in the glomerular layer. In this model, $w_{gg'}$ is determined based on the following equation proposed by Osuna *et al.*[12]:

$$w_{(x,y),(x',y')} = \begin{cases} [0,1], & d < D_e \\ [-1,0], & D_e < d < D_i \\ 0, & d > D_i \end{cases}, \tag{11}$$

where D_e and D_i are distance constants and d is the Euclidean distance.

Figure 4 shows an example of connection strength distribution originated from $(x, y) = (20, 70)$. Here, the upper left side (rostral dorsal part) of the glomeruli in Figure 4 is affected by the inhibitory input, because the neuron models at the edge of the unrolled map are connected based on the original location [5] on the olfactory bulb.

The perceptual difference between two arbitrary odors is then defined using the mean error value between the evoked activities in the mitral-granular layer. The calculated error is considered to correspond to the discrimination rate of the odor discrimination experiment described in Section 2.2. This is because mitral cells send information to the piriform cortex for odor recognition in the actual olfactory system.

3.2 Learning Algorithm

The proposed learning algorithm consists of three steps; steps 1 and 2 adjust the glomerular activity prediction part, and step 3 adjusts the olfactory bulb part.

Before learning, an arbitrary odorant dataset that contains L odorants and corresponding glomerular activities is obtained from the database website [5]. The dataset is then divided into three parts according to the average cross correlations between glomerular activities: odorants with average cross correlations lower than C_1 fall into learning dataset 1, those larger than C_1 and lower than C_2 to learning dataset 2, and those larger than C_2 to the validation dataset.

Step 1

Using learning dataset 1, Step 1 adjusts the connective weights $w_{i,j}$ and $w_{j,k}$ by providing teaching signals to the second hidden layer of the activity prediction part shown in the left side of Figure 3. The learning algorithm employed is a back-propagation algorithm called RPROP [13]. First, the odorants in learning dataset 1 are assigned to the receptor units as representative odorants. As the glomerular activity patterns evoked by the odorants in dataset 1 have the lowest average cross correlations, we assume that the activity patterns are close to orthogonal. Under this assumption, the teaching signal provided to the k-th sigmoidal function unit in the second hidden layer $t_{i,k}$ is determined by the following equation:

$$t_{i,k} = \begin{cases} T_H, & (i-1)N < k < iN \\ T_L, & \text{otherwise} \end{cases} \tag{12}$$

where T_H and T_L are constants in the range of (T_L, 1] and (0, T_H).

Step 2

Step 2 adjusts the connective weights $w_{k,l}$ from the second hidden layer to the Gaussian layer shown in the left

ISBN: 978-988-17012-8-2
ISSN: 2078-0958 (Print); ISSN: 2078-0966 (Online)

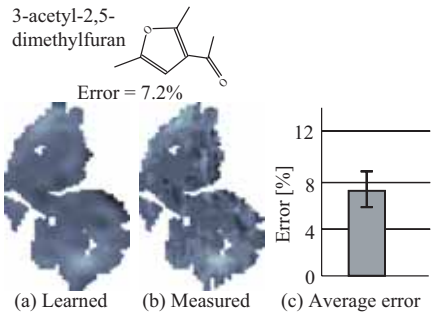


Figure 6: The activities evoked by the odorants in the learning datasets.

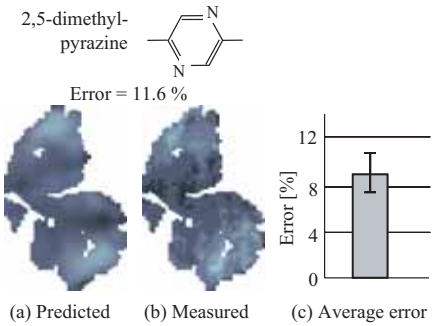


Figure 7: The activities evoked by the odorants in the validation datasets.

side of Figure 3 as well as the parameters included in each Gaussian unit in Equation (4) using learning datasets 1 and 2. In this step, the steepest-gradient method is employed to minimize the sum of mean squared errors between the outputs of the glomerular layer and the measured glomerular activities.

Step 3
This step adjusts the weights w_q included in the Equation (6). First, parts of the odors used in the odor discrimination experiment are chosen as teaching odors. w_q is then manually adjusted to maximize the correlation between the discrimination rates of the teaching odors and the mean error value of the activity patterns evoked on the mitral-granular layer. Other parameters such as D_e and D_i which determines the bounds of the excitatory and inhibitory connection as shown in Figure 4 and Equation 11 are preliminary set as constants.

4 Simulation

This section reports on verification of the learning algorithm and the prediction ability of the model for the glomerular activity prediction part and the olfactory bulb part, respectively. The simulation described here is implemented using Matlab numerical computing software.

4.1 Glomerular Activity Prediction Part

$L = 68$ odorants among the 365 provided online with the structure of methyl were chosen as a dataset for the simulation. As the structure of methyl has a minimal influence on odor qualities, this choice is equivalent to a random selection, but facilitates data handling. As a result of learning dataset division, 17 odorants were determined as dataset 1, another 17 as dataset 2, and the rest as the validation dataset.

Considering the comparison of the predicted perceptual characteristics with those obtained from odor discrimination experiments involving mice, isoamyl acetate and ethyl butyrate were added to learning dataset 1. Citral is also an odorant that was used in the experiment involving mice, but its glomerular activity was not provided. Accordingly, we added geraniol instead to learning dataset 1 because it has the largest kernel value for citral among the 365 odorants. This process can minimize errors generated by the glomerular activity prediction part.

In this simulation, the parameter N was set as 15, and T_H and T_L were set as 1.0 and 0.1 respectively. Learning steps 1 and 2 were applied until the average percentage error per linear unit in the activity pattern layer fell below 7%. Figure 5 (a) and (b) show the learning curves of steps 1 and 2, respectively. Figure 6 shows the learned glomerular activity along with its average percentage error with the standard deviation. These figures confirmed that the error of the glomerular activity layer successfully converged to the desired value.

The prediction ability of the model was then tested by inputting the odorants in the validation dataset. Figure 7 shows the predicted glomerular activity with the typical error, and Figure 7 (c) shows the average prediction error and its standard deviation. These figures confirm that the model provides a certain level of prediction ability.

4.2 The Olfactory Bulb Part

Using the olfactory bulb part, we attempted to predict the perceptual characteristics obtained from the odor discrimination experiment involving mice. As mentioned in Section 3.1, the mean error value between the activity patterns on the mitral-granular layer is defined as the metric corresponding to the discrimination rate. In the simulation, we used the discrimination rates of isoamyl acetate, ethyl butyrate and citral for parameter adjustment.

The parameters of inhibitory and excitatory distance in the mitral-glomerular layer were preset as $D_h = 3$ and $D_I = 7$. Following learning step 3, the connective weights w_l were then manually adjusted to maximize the correlation of the discrimination rates with the mean error value of the activity patterns evoked by the three odors described above against odor [IA EB Ci]. As a result, connective weights $w_{IA} = 1.6, w_{EB} = 2.3, w_{Ci} = 0.9$ were found to be the best parameters, with a maximum correlation of 0.92.

ISBN: 978-988-17012-8-2
ISSN: 2078-0958 (Print); ISSN: 2078-0966 (Online)

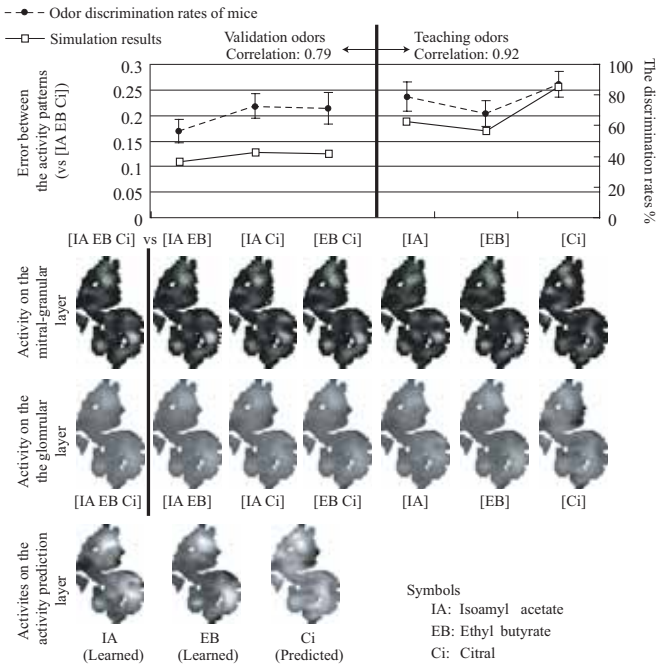


Figure 8: The simulation results.

Using these parameters, odors [IA Ci], [IA EB] and [Ci EB] were input to the model, and the correlation was calculated in the same manner. Figure 8 shows the simulation results. The upper row shows the discrimination rates of mice and the error between activity patterns, the second and third row respectively show the activity patterns on the mitral-granular layer and the glomerular layer, and the lower row shows the activity patterns on the activity prediction layer. The figure shows that the predicted error poses the same tendency as the discrimination rate for mice with a correlation of 0.79. This result confirmed the ability of the model to predict perceptual characteristics.

5 Conclusions and Future Work

In this paper, we proposed an olfactory model consisting of two parts. The simulation results confirmed that the glomerular activity prediction part enables glomerular activity prediction when provided with graphical molecular input, and the olfactory bulb part enables prediction of the tendency of error rate obtained from the results of the odor discrimination experiment involving mice.

Since the data set used in the simulation is small compared to the whole odorant space, we intend to expand the range of target odorants and odors in future work. We also plan to establish a parameter-setting algorithm especially for the olfactory bulb part. Odorant concentration is also a critical parameter that we aim to introduce in the near future.

References

[1] Hertz, R., Engen, T., "Odor memory review and analysis," *Psychonomic Bulletin and Review*, V3, N3, pp. 300-313, 2005

[2] Grosh, W., "Evaluation of the key odorants of foods by dilution experiments, aroma models and omission,", *Chemical senses*, V26, pp. 533-545, 2001

[3] Mori, K., Yoshihara, "Y. Molecular recognition and olfactory processing in the mammalian olfactory system." *Progress in Neurobiology*, V45, pp. 585-619., 1995.

[4] Youngentob, S.L., Johnson, B.A., Leon, M., Sheehe, P.R., Kent, P.F., "Predicting Odorant Quality Perceptions from Multi-dimensional Scaling of Olfactory Bulb Glomerular Activity Patterns," *Behavioral Neuroscience*, V120, N6, pp. 337-1,345, 2006.

[5] Leon, M., Johnson, B.A., "Glomerular Response Archive," [online] Available http://gara.bio.uci.edu

[6] Johnson, B.A., Xu, Z., Ali S.S., Leon M., "Spatial representations of odorants in olfactory bulbs of rats and mice: similarities and differences in chemotopic organization," *The Journal of Comparative Neurology*. V514, N6, pp. 658–73, 2009.

[7] Buck, L., Axel, R. "A novel multigene family may encode odorant receptors: a molecular basis for odor recognition." *Cell*, V65, pp. 175–187, 1991.

[8] Aungst, J.L., Heyward, P.M., Puche, A.C., Karnup, S.V., Hayar, A., Szabo, G., Shipley, M.T., "Centre-surround inhibition among olfactory bulb glomeruli," *Nature*, V426 pp. 623–329, 2003.

[9] Okuhara, K., Nakamura, T., "Explore Algorithms in the Olfactory System of Mice," Software Biology, V3, pp.20–25, 2005 (in Japanese.)

[10] Kashima, H., Tsuda, K., Inokuchi, A.,gKernels for Graphs,hin Kernel Methods in Computational Biology, edited by Scholkopf, B., Tsuda, K., Vert, J.P., The MIT Press, pp. 155-170., 2004

[11] Raman, B., Gutierrez-Osuna, R., "Concentration Normalization with a Model of Gain Control in the Olfactory Bulb," *Sensors and Actuators B*, V116, pp. 36–42, 2006.

[12] Yamanaka, T., Gutierrez-Osuna, R., "Contrast Enhancement of Gas Sensor Array Patterns with a Neurodynamics Model of the Olfactory Bulb," Raman, B., *Sensors and Actuators B*, V119, pp. 547–555, 2006.

[13] Riedmiller, M., Braun, H., "A Direct Adaptive Method for Faster Backpropagation Learning: The RPROP Algorithm," *Proceedings of the IEEE International Conference on Neural Networks*, V1 pp. 586-591, 1993.

ISBN: 978-988-17012-8-2
ISSN: 2078-0958 (Print); ISSN: 2078-0966 (Online)