A NEURAL NETWORK MODEL OF THE OLFACTORY SYSTEM FOR GLOMERULAR ACTIVITY PREDICTION

Zu Soh, Ryuji Inazawa, Toshio Tsuji

Graduate School of Engineering, Hiroshima University, Hiroshima, Japan
sozu@bsys.hiroshima-u.ac.jp, r_inazawa@bsys.hiroshima-u.ac.jp, tsuji@bsys.hiroshima-u.ac.jp

Noboru Takiguchi

Graduate School of Natural Science and Technology, Kanazawa University, Ishikawa, Japan
ntaki@t.kanazawa-u.ac.jp

Hisao Ohtake

Graduate School of Engineering, Osaka University, Osaka, Japan
hohtake@bio.eng.osaka-u.ac.jp

Abstract: Recently, the importance of odors has begun to be emphasized as well as methods for their evaluation, especially in the fragrance and food industries. Although odors can be characterized by their odorant components, their chemical information cannot be directly related to the flavors we perceive. Recent research has revealed that neuronal activity related to glomeruli (which form part of the olfactory system) is closely connected to odor qualities. In this paper, we propose a neural network model of the olfactory system in mice to predict glomerular activity from odorant molecules. To adjust the parameters included in the model, a learning algorithm is also proposed. The results of simulation proved that the relationship between glomerular activity and odorant molecules could be approximated using the proposed model. In addition, the model could predict glomerular activity to a certain extent. These results suggest that the proposed model could be utilized to predict odor qualities for future application.

1 INTRODUCTION

As considerable evidence has been presented to show that odours have an effect on memory and emotions, the importance of smells has begun to be recognized beyond their role as components of flavor (Herz and Engen, 1996). Gas chromatography is a useful technique used to detect the odorant molecules (or simply *odorants*) contained in an odour (van Ruth, 2001), and the analyzed data are used to characterize the odour (Aznar et al., 2001; Semmelroch and Grosch, 1995). However, it is impossible to relate information about odorant molecules to odour qualities without the process of evaluation by human senses. One solution to this problem is to build a regression model to convert the data obtained from gas chromatography to the indices of sensory evaluation (Limpawattana et al., 2001). In this case, the regression model is specialized to the objective odorants, making it necessary to build different models for different kinds of odour.

Another solution is to build a model of the olfactory system based on biological insight. The relationship between odorants and odour qualities is mostly investigated from the field of biological research. The most widely supported stereochemical theory (Amoore, 1963) suggests that odour qualities largely depend on the shape of the odorant molecules involved. This theory is consistent with recent findings regarding the olfactory receptor gene family (Buck and Axel, 1991). The most important information directly related to odour qualities is considered to be that regarding activity on the glomeruli, which are distributed over the surface of the olfactory bulb (Mori and Yoshihara, 1995). Moreover, glomerular activity evoked by input from olfactory receptors is odour-specific, and odour qualities can be predicted from the activated region of the glomeruli (Youngentob et al., 2006).

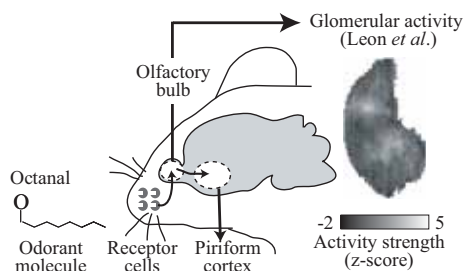Outside the field of biological research, there are few approaches that reveal the relationship between

Figure 1: Structure of the olfactory system of rats. Glomerular activity downloaded from the Glomerular Response Archive (Leon and Johnson, 2009).

Figure 2: Glomerular module arrangement adapted from the Glomerular Response Archive (Leon and Johnson, 2009).

odour qualities and odorants from the field of engineering. Most related engineering researches have focused on developing biomimetic algorithms to discriminate similar odours (Gutierrez-Osuna, 2002), but not to predict qualities for unknown odorants. This may be because a considerable data set is needed to approximate odorants to odour qualities, especially for the human senses. In regard to the olfactory system of rats, however, more than 300 types of glomerular activity evoked by different odorants are provided online (Leon and Johnson, 2009).

Against this background, we report on a neural network model of the olfactory system of rats to enable prediction of glomerular activity from odorant molecules, since the basic structure of the olfactory system in rats has a lot in common with that of human. We also propose a learning algorithm to adjust the parameters included in the model. This consists of a training algorithm for radial basis function (Chen et al., 1991) and the Nelder-Mead (simplex) method (Nelder and Mead, 1965).

This paper is organized as follows: In Section 2, biological knowledge regarding the olfactory system of rats is briefly explained. Section 3 proposes an olfactory model and a parameter-setting algorithm for parameter adjustment. Section 4 details simulations of parameter settings and prediction of glomerular activity in rats. Finally, Section 5 concludes the paper and outlines work planned for the future.

2 THE OLFACTORY SYSTEM OF RATS

Figure 1 shows the basic structure of the olfactory system in rats, 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 (Buck and Axel, 1991); these neurons are activated and send
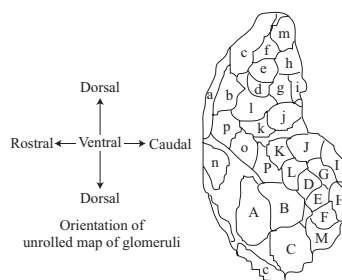
signals to the olfactory bulb. The axons from the receptors that express the same receptor terminate at the same point on the surface of the olfactory bulb (Mori and Yoshihara, 1995). The terminals of these axons form a small, round cluster called a glomerulus. A 2D map of glomerular distribution can be associated with receptor genes as well as with odorants, and is called an *odour map* (Mori and Yoshihara, 1995). The activity of the glomeruli is thus odour-specific. This activity is then communicated to the deeper layer of the olfactory bulb, which mainly consists of mitral and granule cells. The piriform cortex performs odour recognition based on the output of the mitral cells, whose information is modified according to glomerular activity. It has been reported that this activity represents important information that is closely related to the sense of smell in animals (Youngentob et al., 2006).

Glomerular activity for more than 300 kinds of odorant has been measured by Leon *et al* (Leon and Johnson, 2009), and is shown very clearly using color contour charts. From the results of this measurement, Johnson *et al*. (Johnson et al., 2005) defined assemblies of glomeruli as a *glomerular modules*, which respond to a specific molecular features such as the functional group. Figure 2 shows an unrolled map of glomeruli; the boundaries and unique letters denote the areas and symbols of the glomerular modules. More minor features, such as the length of the carbon chain, are coded within a module (Johnson and Leon, 2007). Accordingly, if these rules can be systematically approximated, glomerular activity evoked by untested odorants could be predicted.

3 MODEL

We assumed that glomerular activity can be expressed by a summation of Gaussian functions whose parameters are modulated by the activity of the receptors. Under this assumption, the radial basis function-like model shown in Figure 3 is proposed. The model con-
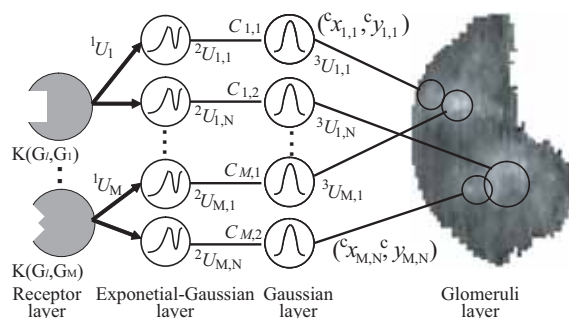
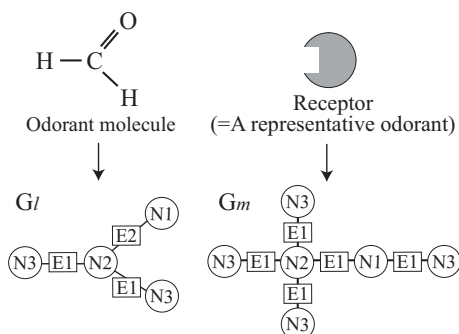Figure 3: The proposed model for the olfactory system of rats.

Figure 4: Labeled graphic expression of odorants for the graph kernel function.

sists of four layers: receptor, exponential-Gaussian, Gaussian, and glomeruli. This section describes the processes in each layer and the learning algorithm used.

3.1 Model Structure

The receptor layer consists of M units corresponding to the number of arbitrarily defined odorants (representative odorants), and each receptor unit is most strongly activated by a representative odorant. Since actual receptors are also activated by odorants with a structure similar to that of the representative odorant, the output of the receptor unit is defined as the similarity between the representative and input odorants. In this model, the graph kernel function $K(G_l, G_m)$ proposed by Kashima *et al* (Kashima et al., 2004) is introduced to calculate structural similarity between the molecules. In this function, the input odorant and representative odorant are expressed by the graphs G_l and G_m in Figure 4, where the atoms correspond to nodes and the bonds to edges. In addition, unique labels are allocated to the types of atoms and bonds. For example, hydrogen atoms (H) are labeled as N3 in Figure 4. The kernel function is then defined as:
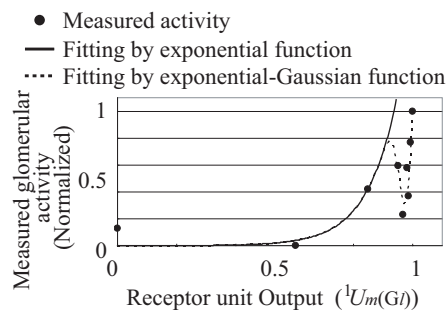

Figure 5: Example of exponential-Gaussian function fitting.

$$K(G_l, G_m) = \sum_{h_l} \sum_{h_m} p(h_l|G_l) p(h_m|G_m) K_L\left(b(h_l), b(h_m)\right), \quad (1)$$

where h_l and h_m are arbitrary paths in the graphs of G_l and G_m respectively, and $p(h_l|G_l)$ and $p(h_m|G_m)$ are the probabilities of the paths to be selected by the random walk algorithm. $K_L(b(h_l), b(h_m))$ is a function to compare the path selection as shown below:

$$K_L(b(h_l), b(h_m)) = \begin{cases} 1, & b(h_l) = b(h_m) \\ 0, & b(h_l) \neq b(h_m) \end{cases} \quad (2)$$

where $b(h_l)$ and $b(h_m)$ are the labels of path h_l and h_m, respectively. The output of the receptor layer $^1U_m(G_l)$ is defined as the generalized value calculated by Equation (3):

$$^1U_m(G_l) = \frac{K(G_m, G_l)}{\sqrt{(K(G_m, G_m) K(G_l, G_l))}}, \quad (3)$$

where $^1U_m(G_l)$ becomes 1 when the representative odorant is input ($G_l = G_m$).

The output of each Receptor unit is input into N exponential-Gaussian units so that the unit number in the exponential-Gaussian layer becomes MN. Exponential-Gaussian units play a role in controlling activity strength at the connected region on the Glomeruli layer. Figure 5 shows an example of the relationship between the output of a Receptor unit and the measured activity strength at the region of the glomeruli to which the Receptor unit is connected through the subsequent exponential-Gaussian and Gaussian units. As shown in Figure 5, the activity strength grows exponentially at first, then drops when the value of U_r approaches to 1. This trend may be caused by the structure of the glomeruli. Glomeruli that are topologically close to each other respond to similar odorants (Johnson and Leon, 2007), but also send inhibitory signals to each other (Aungst et al., 2003). As a result, when an odorant similar to the representative one is input, inhibitory signals from surrounding glomeruli suppress the excitatory input from

the receptors. Hence, the exponential-Gaussian unit is defined by the following equation to convert the receptor unit output into the activity of the glomeruli:

$$
\begin{aligned}
{}^2U_{m,n} &= a_1 \exp\left(a_2\,{}^1U_m(G_l)\right) \\
&- a_3 \exp\{-(10^{a_4})\left({}^1U_m(G_l)-a_5\right)^2\},
\end{aligned} \tag{4}
$$

where the first term on the right is an exponential function, the second term is the Gaussian function, and $a_1...a_5$ are the parameters defined by the learning algorithm described in Section 3.2.

The output of the exponential-Gaussian layer is input to the Gaussian layer through the connective weight $C_{m,n}$ as follows:

$$
{}^3u_{m,n} = C_{m,n}\,{}^2U_{m,n}, \tag{5}
$$

The Gaussian layer diffuses the activity to the neighboring region on the Glomeruli layer. The output of the Gaussian function is given by the following equation:

$$
\begin{aligned}
&{}^4U_{m,n}(x,y) \\
&= {}^3U_{m,n}\exp\left\{\frac{({}^cx_{m,n}-x)^2}{\alpha_{m,n}^2}+\frac{({}^cy_{m,n}-y)^2}{\beta_{m,n}^2}\right\},
\end{aligned} \tag{6}
$$

where the parameters $\alpha_{m,n}$ and $\beta_{m,n}$ control the width of the Gaussian curve.

The connections from the Gaussian layer to the glomeruli layer allocate the output of the Gaussian units to proper center coordinates $({}^cx_{m,n},\,{}^cy_{m,n})$ on the glomeruli layer. The inputs to each of the coordinates are added by

$$
V(x,y) = \sum_{m=1}^{M}\sum_{n=1}^{N}{}^4U_{m,n}(x,y), \tag{7}
$$

from which the estimated glomerular activity is obtained.

3.2 Learning Algorithm

To find proper parameters for the model, this section proposes a learning algorithm consisting of two steps. The adjustable parameters are the representative odorants G_m of the Receptor units, the parameters in the exponential-Gaussian units $a_i(i=1,2,...,5)$, the connective weights $C_{l,m}$ from the exponential-Gaussian layer to the Gaussian layer, and the center coordinates $({}^cx_{m,n},\,{}^cy_{m,n})$ to which the Gaussian units are connected. The first step determines the parameters Gm, $C_{l,m}$ and $({}^cx_{m,n},\,{}^cy_{m,n})$, and the second step adjusts $a_i(i=1,2,...,5)$. Note that, for simplification, the width of the Gaussian curves $\alpha_{m,n}$ and $\beta_{m,n}$ is fixed in this paper. To implement the algorithm, M

representative odorants $(G_{T,1}...G_{T,M})$ and the corresponding glomeruli activities $(V_{T,1}(x,y)... V_{T,M}(x,y))$ measured by Leon and Johnson (2009) are chosen in advance as a learning data set. Since the original activity patterns consist of graphical data in png format, they were converted to numerical data according to the color scale shown on the website (Leon and Johnson, 2009). The converted data were then normalized to a value range of [0,1].

First Step. First, the receptor units responding to each representative odorant are defined, thus $G_m = G_{T,m}$.

Then, each instance of glomerular activity evoked by a representative odorant is approximated by the Gaussian functions using the learning algorithm for the radial basis function (RBF) (Chen et al., 1991). This approximation gives the center coordinates $({}^cx_{m,n},\,{}^cy_{m,n})$ and the peak value of the Gaussian unit. The peak obtained value is assigned to $C_{m,n}$. Note that the number of Gaussian function N is also an important parameter, and is analyzed in the next simulation section.

Second Step. The parameters included in each exponential-Gaussian unit are determined using the Nelder-Mead (simplex) method (Nelder and Mead, 1965); this algorithm minimizes the objective function defined below:

$$
E_{m,n} = \sum_{l=1}^{M}\left(V_{T,m}(x_{m,n},y_{m,n})-{}^1U_m(G_l)\right)^2. \tag{8}
$$

4 SIMULATION

This section reports on verification of the learning algorithm and the prediction ability of the model by comparing the output of the glomeruli layer with measured glomerular activity.

4.1 Learning

First, learning data as shown in Figure 6(a) were prepared to implement the learning algorithm. This data set consists of $M=8$ kinds of representative odorants $(G_m,\ m\in1,2,...,8)$ that share the functional group of alcohol with different carbon numbers and the corresponding measured glomerular activity $(V_{T,o}(x,y), o=m)$. This set was chosen because large shifts of the activation area in the glomeruli can be observed with increases in the carbon number. From Figure 6(a), it can be confirmed that the activation area shifts from the caudal to the rostral side (left to right) as the carbon number increases.
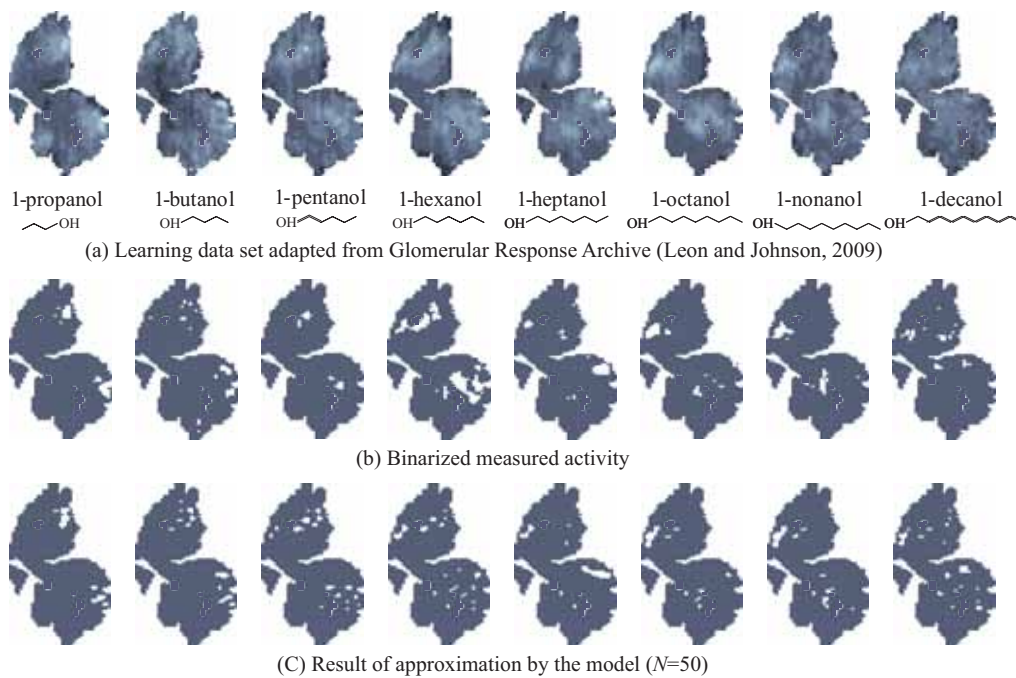
1-propanol   1-butanol   1-pentanol   1-hexanol   1-heptanol   1-octanol   1-nonanol   1-decanol

(a) Learning data set adapted from Glomerular Response Archive (Leon and Johnson, 2009)

(b) Binarized measured activity

(C) Result of approximation by the model (N=50)

Figure 6: Learning results.

To find the best Gaussian function number N, learning simulation was performed with $N = 1, 10, 20, ..., 70$. The other parameters were determined using the learning algorithm described in the previous section. To facilitate visual comparison of the outputs of the glomeruli layer $V_o(x,y)$ with the measured activities $V_{T,o}(x,y)$, both values are binarized; the top 5% of the values are converted to 1, and the others to 0. In addition, for quantitative comparison, the correlation of the glomeruli module activation rate is calculated between the binarized output of the glomeruli layer and the binarized measured activity. The activation rate $V'_{o,\mu}$ in the module μ is defined by the following equation:

$$V'_{o,\mu} = \frac{S^A_{o,\mu}}{S_{o,\mu}} \quad (\mu \in a, ..., p, A, ..., M, P) \quad (9)$$

where $S^A_{o,\mu}$ denotes the activated area, and $S_{o,\mu}$ is the whole area of the module μ.

After implementation of the learning algorithm, each representative odorant in the learning data set was input to the model, and the correlation outlined above was calculated. This procedure was repeated with different values of Gaussian function number N. Figure 7 shows the relationship between N and the average correlation over the learning data set. It can be seen that this correlation rises along with increases in N until $N = 50$, then gradually drops. From this result, $N = 50$ is determined as the best Gaussian function number for this learning data set. One of the rea-
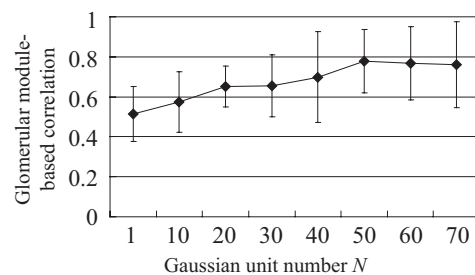

Figure 7: Relationship between glomerular module-based correlation and the Gaussian unit number.

sons for the decrease in correlation after $N = 50$ could be that the activity at the center of the extra Gaussian units does not obey the assumed relationship shown in Equation (4) and Figure 5.

Figure 6(b) and (c) show the measured activity and output of the glomeruli layer when $N = 50$, respectively. Comparing the figures shows that the model successfully reproduce the features seen in the measured activity. Specifically, the glomeruli layer output shows the same trend in the shift of activated area. These results suggest that the proposed learning algorithm can approximate the learning data set.

4.2 Prediction

Using the parameters determined in the learning simulation, odorants not included in the learning data set

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(a) Prediction data set adapted from Glomerular
Response Archive (Leon and Johnson, 2009)

(b) Binarized measured activity

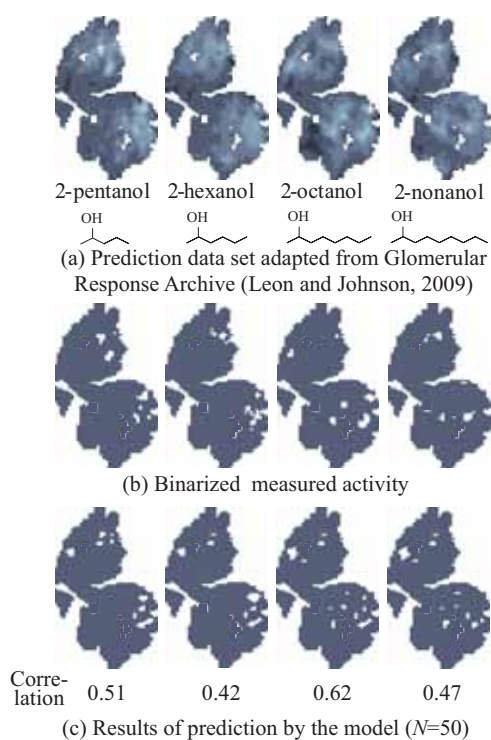| Corre-lation | 0.51 | 0.42 | 0.62 | 0.47 |

(c) Results of prediction by the model (N=50)

Figure 8: Prediction results.

were input to the model. The odorants for prediction are shown in Figure 8 (a). These data were chosen because they are structurally close to those of the learning data set. The binarized measured activitiy is shown in Figure 8 (b) and the binarized Glomeruli layer output is shown in Figure 8 (c). Although the predicted results are not as precise as the output for the odorants in the learning data set, this activity, especially on the lower side, captured the features of the measured activity. In addition, the shift of the activated area from the caudal to the rostral side (left to right) along with increases in the carbon number seems to be preserved. These results imply the feasibility of predicting glomerular activity using the proposed model.

5 CONCLUSIONS

In this paper, we proposed an olfactory model aimed at developing a novel algorithm to relate odorant molecules to odour qualities. The proposed model takes odorants as the input, from which glomerular activity is produced. In the model, odorants are expressed in graph form, and a graph kernel function is employed to estimate the response of of receptors to the odorants. A learning algorithm was also proposed to set the parameters included in the model. Using

the model and this learning algorithm, we performed simulation to learn a set of glomerular activities. The results indicated that the model could approximate the features of the learning data set. Further, we performed a prediction simulation using the parameters determined by the learning algorithm. Although the correlation between the output of the model and the measured activity was not as high as that of the learned data, it was observed that the features in the measured activity were captured. This indicates the feasibility of predicting glomerular activity.

In future work, we aim to improve the prediction ability of the model to enable the flavor of an odorant to be predicted. To achieve this, we plan to introduce other learning algorithms for feed-forward neural networks. In addition, the simulation needs to be performed using a larger data set.

ACKNOWLEDGEMENTS

REFERENCES

Amoore, J. (1963). Stereochemical theory of olfaction. *Nature*, 198:271–272.

Aungst, J. L., Heyward, P. M., Puche, A. C., Karnup, S. V., Hayar, A., Szabo, G., and Shipley, M. T. (2003). Centre-surround inhibition among olfactory bulb glomeruli. *Nature*, 426:623–329.

Aznar, M., Lopez, R., Cacho, J., and Ferreira, V. (2001). Identification and quantification of impact odorants of aged red wines from rioja. gc-olfactometry, quantitative gc-ms, and odor evaluation of hplc fractions. *Journal of Agricultural and Food Chemistry*, 49(6):2924–2929.

Buck, L. and Axel, R. (1991). A novel multigene family may encode odorant receptors: a molecular basis for odor recognition. *Cell*, 65:175–187.

Chen, S., Cowan, C., and Grant, P. (1991). Orthogonal least squares learning algorithm for radial basis function networks. *IEEE Transactions on Neural Networks*, 2(2):302–309.

Gutierrez-Osuna, R. (2002). Pattern analysis for machine olfaction: A review. *IEEE Sensors Journal*, 2(3):189–202.

Herz, R. and Engen, T. (1996). Odor memory review and analysis. *Psychonomic Bulletin and Review*, 3(3):300–313.

Johnson, B. A., Farahbod, H., and Leon, M. (2005). Interactions between odorant functional group and hydrocarbon structure influence activity in glomerular response modules in the rat olfactory bulb. *The Journal of Comparative Neurology*, 483(2):205–216.

Johnson, B. A. and Leon, M. (2007). Chemotopic odorant coding in a mammalian olfactory. *The Journal of Comparative Neurology*, 503(1):1–34.

Kashima, H., Tsuda, K., and Inokuschi, A. (2004). *Kernels for graphs*. MIT Press.

Leon, M. and Johnson, B. A. (2009). Glomerular response archive: http://leonserver.bio.uci.edu/.

Limpawattana, M., Yang, S., Yang, D., Kays, S., and Shewfelt, R. (2001). Relating sensory descriptors to volatile components in flavor of specialty rice types. *Journal of Food Science*, 73(9):S456–S460.

Mori, K. and Yoshihara, Y. (1995). Molecular recognition and olfactory processing in the mammalian olfactory system. *Progress in Neurobiology*, 45:585–619.

Nelder, J. and Mead, R. (1965). A simplex method for function minimization. *The Computer Journal*, 7(4):308–313.

Semmelroch, P. and Grosch, W. (1995). Analysis of roasted coffee powders and brews by gas chromatography-olfactometry of headspace samples. *Food Science and Technology*, 28(3):310 – 313.

van Ruth, S. (2001). Methods for gas chromatography-olfactometry: a review. *Biomolecular Engineering*, 17(4-5):121 – 128.

Youngentob, Johnson, B., Leon, M., Sheehe, P., and Kent, P. (2006). Predicting odorant quality perceptions from multidimensional scaling of olfactory bulb glomerular activity patterns. *Behavioral Neuroscience*, 120(6):1337–1345.