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原　著

A Model for Odor Coding at the Receptors. Minoru YAMADA (Fisheries Laboratory, Faculty of Agriculture, Nagoya University, Nagoya, Japan) Shigeo YOMOSA (Department of Physics, Faculty of Science, Nagoya University, Nagoya, Japan) Masami HASEGAWA (Department of Biophysics and Biochemistry, Faculty of Science, University of Tokyo, Tokyo, Japan) Received July 3, 1970, *Botyu-kagaku* 35, 69, 1970.

8. 嗅覚受容器における匂い識別機構のモデル

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匂いの識別はいかにして行われているかという問題は，古来より論じられ，多くの学説を生んだが，今日なお明らかにされていない。ここでは昆虫嗅覚受容器が誘引物質，忌避物質をどう識別しているかを電気生理学的に調べ，この実験結果と従来明らかにされて来た知見に基づいて，脊椎，無脊椎動物共通にあてはまる匂い識別機構のモデルを仮説し，"匂い識別方程式" なるものをつくった。

Introduction

One of the most striking features of olfactory system is its power to discriminate among a large number of odors. Consequently, the manner by which odor quality is analyzed and encoded by olfactory system has long been a question of fundamental importance. However, it is painfully apparent that our understanding of this branch of physiology is little more advanced today than it was at its inception. This has been due in large part to a lamentable lack of understanding of the basic neurophysiological principles underlying this subject. This communication present a theoretical basis for olfactory discrimination based on the neurophysiological observation.

We had assumed at first that there might be a specific receptor or group of receptors for each subjectively distinguishable odor quality. Odor quality was thus coded in terms of activity or inactivity in particular receptors, and intensity in terms of the degree of that activity.

We become heartened in this notion of specific receptors by the existence of those congenital anosmias being collected by Amoore (1964). There are some people who cannot smell cyanides, others who cannot smell butyric acid or butyrates, others who cannot smell whatever the compound is that issues in the urine of one who has eaten asparagus. But these people seem to be able to distinguish other smells perfectly well. Their blindness is very similar to a notch defect in audition. It is this analogy with sound that underlies the quest for chemically specific receptors just as one searches for frequency specific elements in the ear[4]. Besides, in the electrophysiological study of the olfactory receptors of insects it was found that there does exist many odor-specific receptors (which we call "odor specialists") for the detection of food, or pheromones[2,7]. On the other hand, except for these "odor specialists" the bulk of the olfactory receptors in the antennae are not odor-specific. They respond differentially to the odorous compounds; that is, they respond more to some compounds than to others. Moreover, Gesteland *et al.* (1965) hypothesized, on the basis of their recordings from single olfactory receptors of the frog, that "……in the very limit we have utter chaos; that every fiber is sensitive, more or less, to every odor from being greatly inhibited to being highly excited, and the receptors are not like each other in their response to any group of odors." In such a situation it is evident that odor quality could not be coded in terms of activity or inactivity in particular receptors as we expected at first. Accordingly, the work to be reported here is an attempt to detect the behavior of single olfactory receptors of insects to their food attractant and repellent with a view toward understanding the mechanism of quality discrimination.

Materials and Methods

The antennal olfactory hair of the fruit-piercing

moth *Adris tyrannus amurensis* Staudinger, was used. The recording technique and the stimulating method were almost the same as that described by Yamada (1967). Single receptor recording is done extracellularly with a glass capillary electrode thrust into an antennal hair sensillum, while the indifferent electrode is placed in the hemolymph space of the antenna. This method permits simultaneous recordings of receptor potentials and nerve impulses.

Results and Discussion

Many receptors show a low rate of discharge at rest. This rate is almost rhythmic in some cases, and seems almost completely irregular in others. Olfactory stimuli either induce an impulse frequency increase, depress spontaneous discharges, or produce no response at all. Figure 1 shows responses of a receptor which has no spontaneous discharge to their food attractant (grape odor) and repellent (4-methyl-1-phenyl-hexen-3-one). When the receptor is stimulated, two components can be distinguished in the electrical response, a slow potential and spike potentials, as seen from Fig. 1 a and b. Since the main purpose of this paper is to explain the quality coding of odors, it is sufficient here to note that the slow potential (the generator potential) arises upon stimulation, accompanying the train of impulses and its polarity is negative at the recording point with reference to the hemolymph space of the body[8,12].

At first we expected that food attractant and repellent would be very different in stimulative effects on each receptor, for behaviorally the insects respond in quite opposite manners to these two compounds[6]. Therefore it was rather astonishing that both food attractant and repellent induced a negative slow potential (depolarization of receptor membrane) accompanied by an increase in impulse frequency.

However, when we carefully compare the shapes of slow potentials and temporal patterns of impulse firing, there seems to exist some difference in the responses to food attractant and repellent. For example, food attractant induced the sustained negative monophasic potential accompanied by trains of impulses, while repellent evoked the irregular negative potential accompanied by the impulse frequency increased or decreased with a fall or a rise of the slow potential, respectively. Therefore, we might say that the temporal patterns of excitation provide the basis for odor discrimination. So far we have recorded the activities of more than 20 receptors in various regions of the antenna. Some of them responded to food attractant with a irregular negative potential, but with the sustained negative monophasic potential to repellent. However, in many receptors tested it is very hard to compare the differences of temporal pattern of excitation, for (1) the differences in response pattrns are very

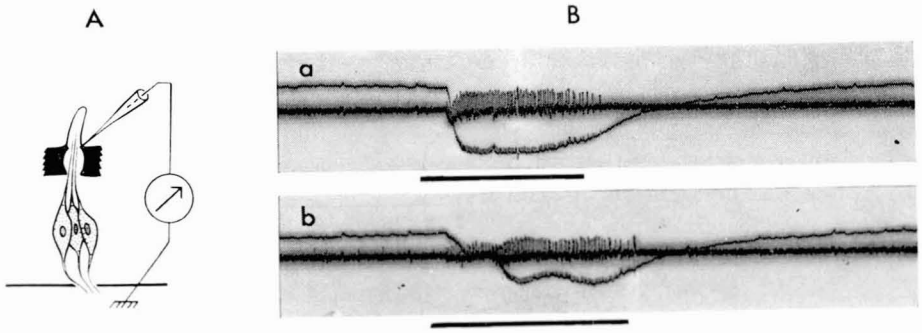

Fig. 1. A, Method of recording action potentials with glass capillary electrodes from a single olfactory sensillum. B, Responses of a receptor to food attractant (a), and repellent (b). Upper (D-C) tracings show receptor potential with nerve impulses; lower (R-C) tracings show only nerve impulses. The downward deflection represents negative potential at the recording electrode. The black bars below each tracing indicate the duration of the stimulation.

small; (2) the receptors do not always elicit a unique and stable response pattern to the repetitive stimulations of the same odor; (3) the stimuli to be tested are not quantitatively well controlled.

In the light of these observations it seems possible to assume that the receptors possess some degree of odor specificity. It is apparent, however, that the absolute amount of activity in any these receptors cannot by itself encode odor quality, because, as can be seen in Fig. 1 two chemicals can elicit impulse discharges in the same receptor. Furthermore, temporal patterns of excitation of a single receptor during stimulation seems impossible to provide the basis for quality discrimination, for the receptors could not have a unique and reproducible temporal patterns of excitation for each odorant under our experimental conditions.

How may olfactory receptors, with the properties outlined above, encode odor quality? It seems logical to assume that one mechanism basic to quality coding by this insect may involve the sort of combination of the activity of all individual olfactory receptors on the antenna.

From these reasonings we present the following equation as the model of quality coding (or "odor quality coding equation")

$$\vec{Y}_j=\sum_i C_{ji}\vec{X}_i \qquad (1)$$

where the direction of the vector $\vec{Y}_j$ represents the odor quality j; the length of the vector $\vec{Y}_j$ represents the intensity of odor quality j; the unit vector $\vec{X}_i$ denotes the unit activity of neurone i; and the coefficients C_{ji} is the sensitivity of neurone i to the compound j.

Implicit in this theory of coding is the assumption that (1) the relative amounts of activity elicited by different chemicals in each neurone will not be altered significantly by changes in stimulus concentration; (2) n vectors $\vec{X}_{i\,(i=1,2,\cdots\cdots,n)}$ are mutually orthogonal, for we would treat the characteristic of every neurone as independent; (3) temporal pattern of impulse firing in a single receptor during stimulation are ignored to simplify the coding problem.

According to the model, it would be possible, by simply having very many receptors possessing differential sensitivity, to distinguish very many compounds, for each odor quality could be expressed as a point in n coordinates system in space whose axes are mutually perpendicular straight lines. It could also be applicable to the coding of insect's sex attractants of the moths[7]. For example, insect sex attractants are very effective stimulant only to the sex attractant receptors, but not to the other olfactory receptors. Therefore, the equation (1) could be written in the form of Kronecker's delta function:

$$\vec{Y}_s=\sum_i A_i\delta_{si}\vec{X}_i,$$
$$\delta_{si}=\begin{cases}1 & (i=\text{sex attractant receptors})\\ 0 & (i\neq\text{sex attractant receptors})\end{cases} \qquad (2)$$

where $A_i\delta_{si}$ corresponds to C_{ji} of the equation (1). This equation implies that the absolute amount of activity in any one "odor specialist" could by itself encode quality.

The important features of these equation (1) and (2) are that 1) the transformation from chemical compound space to physiological smell space partakes the linear combinations of the activities in every olfactory receptor; 2) odor quality could be represented as the set of $\{C_{ji}\}_{i=1,2,\cdots\cdots,n}$; 3) because the direction of the vector $\vec{Y}_j$ represents the odor quality j, the following equation could be used as the criteria of odor similarity.

$$S_{jj'}=\cos\theta=\frac{\vec{Y}_j\cdot\vec{Y}_{j'}}{|\vec{Y}_j|\cdot|\vec{Y}_{j'}|},\quad -1\leqslant S_{jj'}\leqslant 1 \qquad (3)$$

We define S as the function to represent the degree of odor similarity, therefore, the large value means the high degree of odor similarity. It should be noted here that this equation makes it possble to measure quantitatively the degree of similarity between odorants in the numerical scales. Using the equation (3), we are going to classify the odor similarities of many compounds by the help of electric computer.

In conjunction with the above discussion, it is perhaps worth describing the classification of smells by man. Given sufficient training, some of us can become expert in picking out the parts of a complex odor, or small differences of the smell. But there is no way of telling these perceptions to others except by simile. Even when professional perfumers address each other, it is in a cant that evokes intuition rather than

understanding. In short there is no coherent account of how to tell one smell from another. In that sense, the equation (3) could be regarded as a new step to approach the mechanism of classification of odors.

Finally, in view of the fundamental likeness found in the response behavior of single olfactory receptors in insect antennae[2,7], and in the vertebrate olfactory mucosa[3,5], the equation (1) would appear to be the "quality coding equation" basic for the odor quality coding in the invertebrate as well as the vertebrate.

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Method for the Determination of Residues of Meobal® (3, 4-Dimethylphenyl *N*-Methyl Carbamate) in Rice Grains. Seizo Sumida, Masahiro Takaki, and Junshi Miyamoto (Research Department, Pesticides Division, Sumitomo Chemical Co., Ltd., Konohana-ku, Osaka, Japan) Received July 14, 1970, *Botyu-Kagaku* 35, 72, 1970.

9. 玄米中のメオバール® (3, 4-dimethylphenyl *N*-methyl carbamate) の残留分析

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玄米中のメオバールのガスクロマトグラフィーによる残留分析法を報告する．粉砕した玄米をジクロルメタン-アセトン-水の混合液で抽出し，抽出物をカラム及び薄層クロマトグラフィーでクリーンアップする．次に，得られた試料中のメオバールの加水分解及びジニトロフェニル化を同時的に行わせ DNP-メチルアミン (2, 4-dinitrophenyl methylamine) を得る．DNP-メチルアミンをエレクトロンキャプチャーガスクロマトグラフィーにより定量する．回収率は 0.5ppm レベルで 87% であった．本法によれば，0.01ppm 又はそれ以下までのメオバールの残留量を分析できる．

Meobal® (3, 4-dimethylphenyl *N*-methyl carbamate) is an insecticidal compound developed by Sumitomo Chemical Co., Ltd. for pest control mainly of rice plant. From the standpoint of public hygiene, it is quite important to have information on the residues of this compound left in the rice grains. Methods had been reported for the determination of *N*-methyl carbamates in a number of plants,[1,2] but they failed to give consistent results with rice grains, as tested in our laborotory. Under these circumstances, an attempt was made to develop a new method to serve our purposes.

We have reported elsewhere[3] that microquantities of *N*-methyl carbamates can be determined by converting them to 2, 4-dinitrophenyl methylamine (DNP-MA) in a novel fashion, *i.e.*, *N*-methyl carbamate is heated at 100°C and at pH 9 in the presence of 2,4-dinitro-1-fluorobenzene (DNFB). The carbamate breaks down under these